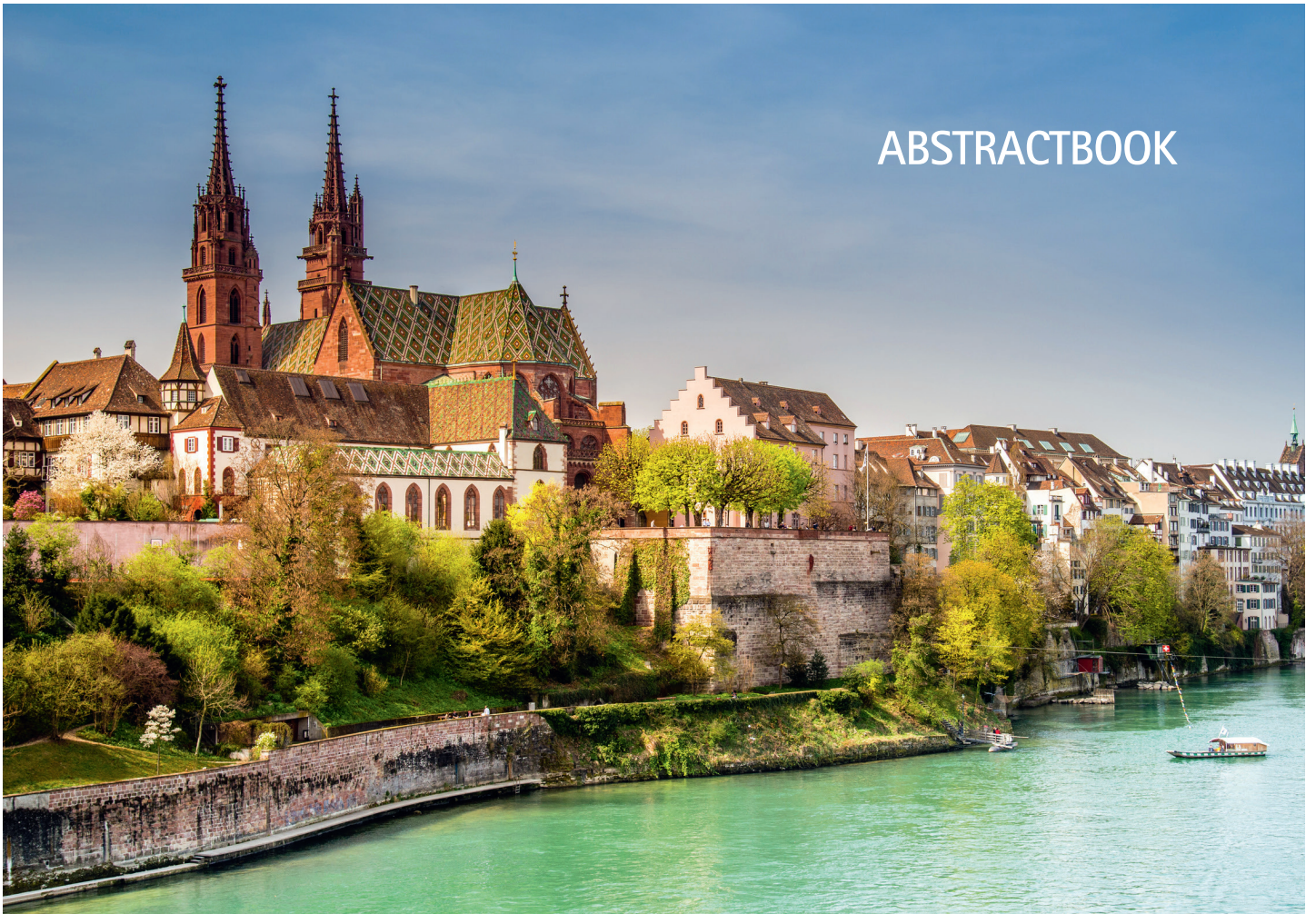


ABSTRACTBOOK



Joint annual meeting 2017

Swiss Society for Microbiology SSM

Swiss Society for Infectious Diseases SSI

Swiss Society for Hospital Hygiene SSHH

Swiss Society of Tropical Medicine and Parasitology SSTMP

Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel

sginf2017.congress-imk.ch



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Abstracts accepted as oral presentations

SSHH session Implementation/Innovation	HH1 – HH7
SSTMP OneHealth Symposium	O01 – O16
Cohort Session: SHCS and STCS	O17 – O20
Innovative diagnostic tests	O21 – O22
CM1 session Genomics/metagenomics	O23 – O26
Environmental Microbiology	O27 – O41; O86
Prokaryotic Biology	O42 – O55
Virology	O56 – O69
Biofilm	O70 – O73
Synthetic Biology	O74 – O75
Microbiome	O76 – O79
Migration	O80 – O81
Communicating Microbiology in the Digital Era	O82 – O83
Emerging pathogens	O84; O88
Zoonotic infection	O85; O87



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

SSHH Session - Implementation/Innovation

HH-1

Les 12 actions au bloc opératoire

P Deriaz; O Clerc; B Duvillard; P Vanderavero
Hôpital neuchâtelois

But

Dans le cadre de Swissnoso SSI Surveillance, nous avons constaté que l'HNE a des taux d'infections supérieurs à la moyenne pour la chirurgie colique. D'un commun accord avec les chirurgiens et avec le soutien des directions médicale et infirmière, nous avons mis sur pied "les 12 actions au BOP", dans le but de réduire ces infections, avec le leitmotiv "où il n'y a pas de standard, il ne peut pas y avoir d'amélioration".

Méthode

Chaque mois:

- Un nouveau thème est abordé avec l'appui d'ambassadeurs professionnels du terrain, dans le but de gagner en discipline et en standardisation des pratiques.
- Une procédure est établie.
- Un slogan court et percutant est mis en évidence.
- Si nécessaire, du matériel pédagogique est élaboré (ex: une vidéo de la désinfection chirurgicale des mains tournait en boucle près des lavabos).

Les thèmes abordés jusqu'ici sont:

- Désinfection chirurgicale des mains: et si vous... preniez 1 minute 30 pour réaliser une désinfection chirurgicale des mains dans les règles de l'art?
- Antibiotrophylaxie: et si vous... optimisiez l'antibiotrophylaxie?
- Protections faciale et oculaire: et si... les têtes intelligentes (se) protégeaient?
- Limitation des dérangements: s'il vous plaît, j'ai besoin de calme pour travailler!
- Le sondage vésical: et si le sondage vésical était... plus rare, plus court, plus sûr?
- Normothermie: et si vous... mainteniez le patient au chaud: objectif commun 36.5°!
- Préparation cutanée du patient: le patient / la patiente a fait sa part, à vous de faire la vôtre!

Résultats

Le succès des différentes actions est variable. La technique de désinfection chirurgicale des mains a été largement adoptée et des progrès ont été constatés dans l'administration de l'antibiotrophylaxie. Par contre, les lunettes de protection sont toujours peu portées et les bijoux sont réapparus presque aussi vite qu'ils avaient disparu. Les chirurgiens apprécient de pouvoir pointer le poster pour demander du silence, mais les va-et-vient n'ont pas diminué. Le choix de l'antiseptique avant pose d'une sonde vésicale n'est pas toujours le bon.

Conclusion

Le projet n'est pas terminé, mais son impact est mitigé. Certains nous reprochent que les actions visant à la discipline et la standardisation ne sont pas evidence based. Et les mêmes nous disent "oui, mais..." lorsque l'évidence est présente! L'impact sur les taux d'infection sera difficile à démontrer. Cependant, les professionnels renouent peu à peu le dialogue entre corporations, pour un but commun.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

HH-2

"Neues Hygienekonzept für das Universitätsspital Zürich" – Eindeutig, benutzerfreundlich, zugänglich

A Wolfensberger; M Meier; L Clack; H Sax
 Universitätsspital Zürich

Aims:

Schriftlich festgelegte Weisungen (Standard Operating Procedures) bilden die Basis einer zuverlässigen Organisation. Die unvollständige Umsetzung dieser Regeln in der Praxis scheitert u.a. häufig an einer geringen Zugänglichkeit und Benutzerfreundlichkeit. Durch ein grundlegendes Re-Design des Hygienekonzepts sollte die Umsetzung der Regeln erleichtert werden – mit dem Ziel, das infektiöse Risiko für Patienten, Besucher und Mitarbeitende im Universitätsspital Zürich zu reduzieren.

Methods:

Das Re-Design erfolgte mit einem Human Factors Engineering-Ansatz, d.h. einer Analyse der Arbeitsabläufe, einer interdisziplinären Erarbeitung der Regeln und einer iterativen Testung von Prototypen. Folgende Prinzipien wurden verfolgt: Hohe Zugänglichkeit der benötigten Information, Darstellung mit Abstufung des Detailgrades (das einfache, aktionsrelevante zuerst), hohe Konsistenz und Eindeutigkeit durch durchgehende Terminologie und Symbolik, Erleichterung der Merkbarkeit durch Symmetrien und Symbole, maximale Usability und zuletzt Implementierung durch eine multidimensionale Strategie bottom-up und top-down.

Results:

Das neue Hygienekonzept des USZ besteht aus folgenden Elementen. 1) Hygieneorder: wurde von mehr als 100 auf 35 meist zweiseitige, klar strukturierte Dokumente reduziert. 2) Intranetseite Spitalhygiene: grafisches Design, einheitlich strukturiert und schnell lesbar. 3) Signage: Türschilder für isolierte Patienten nach Prinzipien der Infografik. 4) Pocket-Card: Drehscheibe mit Information zu Isolationsmassnahmen und Infektionsprävention. 5) Minuten-Videos: Lehrvideos zu Isolationsmassnahmen. 6) Spitalhygiene-Film «Willkommen an Bord – Infektionsprävention am USZ»: fünfminütiger Film mit «Edutainment»-Charakter zum Thema Standardmassnahmen.

Conclusion: Das neue Hygienekonzept des USZ wurde im Juni 2016 im USZ implementiert und hat aufgrund des ansprechenden Designs, seiner Klarheit und Einfachheit und der teilweise verspielten und unterhaltenden Elemente viel Lob erhalten

Shared first Authorship: Aline Wolfensberger and Marie-Theres Meier.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

HH-3

Erfolgreiche Umsetzung eines neuen Hygiene-Schulungskonzeptes

I Schürmann; D Jegher; C Rohrer; E Sidler; E Rohrer; E Mossdorf; S Ambauen; J Weber; C Orasch
 Hirslanden Klinik St. Anna

Einleitung

Spitalhygiene dient der Prävention nosokomialer Infektionen und ist wichtig für die Patientensicherheit und Behandlungsqualität. Sie ist Aufgabe eines jeden Mitarbeiters (MA). Durch regelmässige Schulungen soll das notwendige Hygiene-Wissen vermittelt und aufgefrischt werden. Klassische Hygienefortbildungen wurden in unserer Klinik schlecht besucht.

Ziel

Umstrukturierung des Hygiene-Schulungskonzepts mit einem Angebot, welches das notwendige Wissen vermittelt, im Arbeitsalltag integriert ist und möglichst viele MA erreicht.

Methode

Nach der Analyse bisheriger Kommunikations-/Schulungsplattformen wurde das neue Hygiene-Schulungskonzept entwickelt. Die wichtigsten Hygienethemen wurden definiert und jeweils ein Schulungsthema pro Monat in 15 minütige, patientenzentrierte und praxisbezogene und kurzweilige Fortbildungen mit verschiedenen Präsentationsformen (Poster, Rollen- /Fragespiel etc.) gepackt. Die Fachexpertin Hygiene (FaH) schult auf jeder Abteilung das gleiche Thema, direkt auf Station/im Arbeitsbereich und während der Arbeitszeit. Für die Schulung der nicht-anwesenden MA sind die link nurses Hygiene (LNH) verantwortlich. Sie organisieren mit den von der FaH zur Verfügung gestellten Fortbildungs-Unterlagen die Nachschulungen. Es wurden 2 Punktprävalenzmessungen mit Fokus Venenkatheter sowie Händehygiene-Beobachtungen (vorher – nachher) durchgeführt. Nach 9 Monaten wurde mit einem strukturierten Fragebogen das Feedback der Geschulten eingeholt.

Resultate

Der Rücklauf der Fragebogen lag bei 75% (n=207).

Die Fragen „Sind die Hygiene-Schulungen für meine Arbeit wichtig“ wurden in 96.6% (n=200); „Kann das Gelernte in der täglichen Arbeit umgesetzt werden“ in 91%(n=188); „Wird mein Wissen aufgefrischt/lerne ich dazu“ in 89% (n=185) und „Ist das neue Schulungskonzept besser“ in 93% (n=160) positiv beantwortet.

60.3 % (n=1123) der 1863 angebotenen Schulungen wurden besucht, 79.8% davon von der FaH und 19.9% von den LNH durchgeführt.

An messbaren Parametern wurden ein nach den Schulungen verbesserter Umgang mit Venenkathetern mit einer Abnahme der Venenkatheter-Infektionen und eine Verbesserung der Händehygiene festgestellt.

Konklusion

Das neue Hygiene-Schulungskonzept mit kurzen, praxisbezogenen Fortbildungen direkt am Arbeitsplatz ist bei den MA sehr gut angekommen und hat zu messbar verbesserten Hygiene-Parametern geführt. Wir werden es weiterführen und die Nachschulungen optimieren, mit dem Ziel, möglichst alle MA den Schulungen zuzuführen.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

HH-4

Hand Hygiene campaign to improve compliance in nursing homes

L Qalla-Widmer; D Héquet; M Attinger; C Petignat
CHUV Unité HPCI

The Unit for Infection Control and Prevention of Canton Vaud (Switzerland) gives a high priority to preventing healthcare associated infections. Several studies have demonstrated that hand hygiene can significantly reduce the cross-transmission of pathogens. Unfortunately, health-care worker's observance to guidelines remains limited. In 2012-2014, a first successful hand hygiene campaign was conducted in nursing homes (NH) of the Canton Vaud. In order to sustain achievements, a second campaign was planned in 2016.

The purpose of this campaign was to assess hand hygiene compliance amongst the NH staff in 2016 and to determine the evolution over time, comparing the findings to previous campaign.

First, hand hygiene and gloves workshops were organized in NH. Then, direct observations were performed according to the WHO moments for hand hygiene. NH were very disparate in size and mission. In order to make the results comparable, we determined a percentage of observations by type of care (hygiene, technical, mobilization) according to the NH size. A percentage of observations needed was allocated to each type of care considering their frequency and the ability to observe nurses and nursing assistants.

We used an online data collection tool developed by Swissnoso (Cleanhands) that allows real-time performance feed-back to the observed caregivers.

In total, 115/160 (71%) NH took part in this campaign. A total of 15'226 hand hygiene opportunities was recorded over 8 months (1'425 hours of observations). Globally, hand hygiene compliance significantly improved from 75% to 80% ($p < 0.001$) compared to the 2012-2014 campaign. Compliance is lower for the indication "before contact" with the patient than for the indication "after contact", although compliance for both indications increased uniformly (+2% and +3% respectively). Compliance was identical for the two categories of observed healthcare workers. Nursing assistants showed the greatest improvement (+6%).

This campaign was successful in light of high participation rates and significant increase in global compliance rate reaching 80%. This accomplishment can be explained by the multimodal methodology of the awareness campaign, the repetition of the campaign over time. However, a global lower compliance rate "before patient" gives hints for developing future strategy to optimize hand hygiene compliance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

HH-5

Journée mondiale hygiène des mains: vers une communication événementielle participative

M Ku Moroni; M Attinger; C Petignat

CHUV Lausanne

Chaque année, l'Unité HPCI VAUD lance une campagne de sensibilisation pour la journée mondiale de l'hygiène des mains le 5 mai auprès du personnel soignant des structures sanitaires du canton. Etant une structure organisationnelle matricielle, nous laissons la responsabilité aux professionnels HPCI des établissements sanitaires vaudois de créer leur propre événement dans leur établissement en leur fournissant le matériel de la campagne et un site internet spécifique pour la journée du 5 mai.

Aims

Dynamiser l'image marketing de la campagne

Développer la synergie de groupe

Améliorer l'impact de la journée mondiale de l'hygiène des mains

Methods

En considérant les problématiques qui influent sur les résultats de l'événement, nous avons décidé de faire participer les professionnels HPCI des établissements à notre campagne :

- 1) En leur dédiant une place centrale : un blog d'actualités intégré au site internet de la journée mondiale. Il leur permet de communiquer auprès des soignants de leur établissement (programmes, lieux et ambiances des stands)
- 2) En utilisant une communication traditionnelle : création du matériel de campagne (affiches A2 avec les répondants HPCI à l'honneur, PLV, flyers), préparation des documentations papiers, goodies
- 3) En mettant à leur disposition du matériel didactique (quizz en ligne) au travers du site web. Création du site internet avec blog, commentaires, photos, vidéos,
- 4) En offrant une «surprise» comme produit d'appel : 9000 tablettes de chocolats à distribuer marqués aux couleurs et message de la journée mondiale. Création d'un buzz autour de la surprise, jeu de devinette à 5 indices

Results

- Le blog « Actu des stands » offre une meilleure visibilité des professionnels HPCI
- Il leur permet de promouvoir leur événement et de valoriser leur travail afin d'avoir plus de visites à leur stand
- Les photos/vidéos apportent de la convivialité
- La fréquence des publications montre une image plus dynamique
- L'interactivité des commentaires rassemble les professionnels de la santé de l'ensemble du canton
- Une plus grande implication des professionnels directement concernés par l'organisation de l'évènement

Conclusion

L'intégration des professionnels HPCI à une place centrale de l'évènement grâce à un blog dédié apporte un nouveau souffle. Cette nouvelle orientation stratégique a démontré un potentiel participatif et fédérateur très intéressant qui ouvre sur de nouvelles possibilités.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

HH-6

Peer monitoring und feedback: Verbesserung der Händehygiene-Adhärenz auf einer Intensivstation?

K Stiebeler; R Kuhn; R Fulchini; P Kohler; M Schlegel

Kantonsspital St. Gallen

Ausgangslage:

Die Beobachtung mit unmittelbarem Feedback gilt als anerkannte Methode zur Verbesserung der Händehygiene (HH)-Adhärenz. Am Kantonsspital St. Gallen (KSSG) erfolgt dies seit 2013 durch die Spitalhygiene (SH) mit der Applikation CleanHands. Bei stagnierenden Adhärenzraten um 70% soll eine Verbesserung erreicht werden, indem an Stelle der SH pflegerische Mitarbeiter (MA) gegenseitige Händehygiene-Beobachtungen durchführen und sich Feedbacks (Peer monitoring und feedback) geben.

Ziel:

Steigerung der HH-Adhärenz und Vertrautheit/Sicherheit mit den Indikationen der HH auf einer Intensivstation.

Methode:

Zur Überprüfung des Effekts der Intervention erfolgt zu Beginn und Ende des Projektes eine Messung der HH-Adhärenz durch die SH sowie die Evaluation der Selbsteinschätzung zum Wissen und Umsetzung der HH mittels eines Fragebogens. Nach Schulung über die vier Indikationen der HH (modifiziert nach WHO: Nach Patientenkontakt/-umgebung, Vor invasiver Tätigkeit, Nach Kontakt mit Körpersekret, Vor Patientenkontakt/-umgebung) und dem Umgang mit der Applikation CleanHands erfolgten die Beobachtungen durch die MA auf der Intensivstation.

Erste Resultate:

Die durch die SH zu Beginn des Projekts erfasste HH-Adhärenz im November 2016 betrug 68% (n=449), die von den MA während 5 Monaten durchgeführte Erfassung ergab eine signifikant höhere Adhärenz von 81% (n=2'704, P<0.001).

Der Fragebogen wurde an 52 MA abgegeben, wovon 47 zur Durchführung von HH-Beobachtungen geschult wurden. Bei einer Rücklaufquote von 100% bewerteten alle MA die HH wichtig in Bezug auf Patientensicherheit. 94% der Befragten gaben an, die Indikationen für die HH zu kennen, verpasste HH-Indikationen werden von 64% der MA bei ihren Kollegen bemerkt, jedoch nur 14% weisen die Kollegen darauf hin.

Die abschliessende HH-Beobachtung durch die SH und der Schlussfragebogen sind für Juni 2017 geplant.

Diskussion:

Die von den MA beobachtete HH-Adhärenz ist signifikant höher als der von der SH erhobene Ausgangswert. Inwieweit sich dieses verbesserte Ergebnis bestätigen lässt, wird mit der abschliessenden HH-Beobachtung durch die SH im Juni 2017 überprüft. Die Indikationen der HH scheinen bekannt zu sein, deren fehlende Umsetzung im Alltag wird von den MA zwar bemerkt, aber nicht angesprochen. Ob die Intervention diesbezüglich eine Verbesserung bewirkt, wird sich im abschliessenden Fragebogen zeigen.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

HH-7

Hygiene verstehen = Hygiene umsetzen

C Stutz; A Cathomas

Zuger Kantonsspital

Problemstellung:

Wie können in komplexen medizinischen Handlungen, Hygieneaspekte praktisch und einfach implementiert werden?

Hygiene muss im Arbeitsalltag umsetzbar sein, deshalb ist es notwendig praktische Abläufe und Prozesse zu kennen und zusammen mit den Fachpersonen (z.B. Anästhesie) zu definieren, wann welche Hygienemassnahmen (Momente der Händedesinfektion, der Gebrauch von Einweghandschuhen, Aufbereitung von Materialien und Flächen, etc.) nötig sind.

Die Praxis zeigt, dass diese Aspekte in komplexen medizinischen Handlungen schwierig umzusetzen sind und Unsicherheit herrscht, wann welche Massnahme angezeigt ist. Ungenügendes Fachwissen, fehlendes Bewusstsein, dass Hygienefehler eine nosokomiale Infektion bewirken können, wie auch die Einstellung, dass viele Massnahmen übertrieben oder unnötig sind, erschweren die Implementierung von Hygienemassnahmen. In unserem Projekt übertragen wir die Verantwortung für ihr Handeln den Fachpersonen, dabei unterstützen wir sie mit definierten Abläufen.

Ziel:

Medizinische Fachpersonen setzen Hygienemassnahmen korrekt im Arbeitsprozess um

Methoden:

Visualisierung von Prozessen und Darstellung der nötigen Hygienemassnahmen innerhalb der Prozesse

Vorgehen:

1. Prozesserhebung -> 2. Prozessdarstellung durch den Fachbereich, nach einem vorgegebenen Modell (Auly-Modell) -> 3. Ergänzen der erforderlichen Hygienemassnahmen in den einzelnen Prozessschritten durch die Experten der Spitalhygiene -> 4. Information und Schulung des Teams durch den Fachbereich (z.B. Anästhesie) -> 5. Umsetzung -> 6. Evaluation und Anpassung der Prozessschritte

Diskussion

Es gibt verschiedene Möglichkeiten, Wissen zu vermitteln. Optimal ist, wenn Massnahmen aus Überzeugung durchgeführt werden. Der Wissenstransfer scheitert aus verschiedenen Gründen z.B. spielen dabei „human factors“ eine grosse Rolle.

Tatsache ist, dass die Spitalhygiene seit langer Zeit erfolglos versucht, Hygiene-Basis-Wissen in die Praxis zu bringen.

Ob unsere neue Vorgehensweise den erwarteten Effekt bringt, wird sich bei der Evaluation zeigen.

Schlussfolgerung

Nicht alle Prozesse können abgebildet werden. Allerdings ist es häufiger möglich, als medizinische Fachpersonen jeweils zu Beginn der Diskussion und bei der Prozesserhebung denken. Erste Erkenntnisse zeigen, dass das neue und zeitgemässe Vorgehen Interesse weckt und sich die Mitarbeit der Fachbereiche sehr aktiv gestaltet. Der Start ist gelungen und die Rückmeldungen aus involvierten Bereichen sind positiv.

Workflow Map nach Markus Auly 2017 (Master Thesis)



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

SSTMP Symposium “OneHealth”

O01

An old drug reused: the activity of buparvaquone against the fox tapeworm *Echinococcus multilocularis*

R Rufener, L Dick, L Strübig, A Hemphill, B Lundström-Stadelmann

Institute of Parasitology, University of Berne, Vetsuisse Faculty, Berne, Switzerland

The metacestode-stage of the fox tapeworm *Echinococcus multilocularis* causes the lethal disease alveolar echinococcosis (AE) in humans, dogs and primates. Curative chemotherapeutical treatment cannot be achieved in patients to date, as the drugs in use do not act parasitocidal. Thus, new treatment options are urgently needed. AE is emerging and spreading in Europe, but the disease is still relatively rare, which does not attract big interest in pharmaceutical industry to further develop novel chemotherapeutics against the parasite. For this reason, we pursue a drug-repurposing approach, in which we focus on already marketed drugs or drug classes, or compounds from other areas of research, as they are more likely to be applied in patients suffering from AE. The public-private partnership organization medicines for malaria venture (MMV) is freely sharing their libraries of compounds and drugs, amongst them more recently the so-called “Pathogen box”, which includes 400 drug-like compounds against a range of neglected diseases.

The pathogen box was screened in vitro for its activity against *E. multilocularis* metacestodes, and eight compounds were active at a concentration of 10 μM already after 5 days of drug-incubation. These drugs were followed-up also at lower concentrations. In particular, one compound, buparvaquone, received further attention, as the drug is already marketed for the use against theileriosis in cattle. For this reason, the IC_{50} against metacestodes, as well as isolated parasite cells was determined (7.8 and 0.04 μM respectively). On intact metacestodes, the drug was acting parasitocidal in vitro down to 0.3 μM , which has never been observed with any other drug. On host cells, the drug did not act cytotoxic at all tested concentrations. On the ultrastructural level, buparvaquone applied at 0.3 μM for 5 days mostly affected undifferentiated cells and mitochondria, induced signs of apoptosis in germinal layer tissues at 1 μM , and microtriches degeneration and separation of germinal and laminated layer at 3 μM for 5 days. In an in vivo trial in intraperitoneally infected mice, animals were treated by peroral gavage of buparvaquone (100 mg/kg, 3 times per week, duration of 12 weeks), but no activity was observed. The differences between the in vitro and in vivo activity of buparvaquone could be due to its mode of action involving the oxidative phosphorylation. Therefore, the targets of buparvaquone in *E. multilocularis* are currently being further investigated.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O02

A systematic scoping review of west nile virus transmission models and interventions in the onehealth framework

M Zuske¹; M Runge¹; J Malinga¹; L Nzayisaba²; K Osman³; O Ikeh²; N Chitnis¹; J Zinsstag¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) University of Basel;

(3) University of Jigjiga

Aims:

West Nile Virus (WNV) affects humans, animals and their environments. Modelling of the transmission processes and potential preventive measures in the framework of OneHealth can provide deeper insights into the dynamics and economics of cross-species disease transmission and prevention. With the aim of developing a comprehensive understanding of the transmission processes and to identify the joint impact of interventions on the animal and human host populations and their ecosystem, we conducted a systematic scoping review on WNV transmission models.

Methods:

We used Cochrane methods for scoping reviews outlined by Anderson et al.[1]. The literature search was conducted using PubMed as database. We considered vectors as well as animal and human hosts equally and extracted data for all possible types of interventions which were further discussed on their impact on humans, animals and their environment. We included only modelling studies to identify transmission parameters as well as intervention effects.

Results:

The search yielded 288 initial references of which 273 were further scrutinized after removing duplicates. Abstract and full texts screening identified 68 modelling studies fitting our inclusion criteria. The majority (47) of the included studies were using data from North American countries. The vector alone (17) and the reservoir cycle (14) were the main targets in the included studies. The transmission from the vector or from the reservoir to human end hosts was the object of 16 studies. Only one study was found modelling a full transmission cycle consisting of the vector, the reservoir, equine and human hosts. Of the 68 included studies, 3 explicitly modelled effects of interventions on the WNV transmission for humans. These interventions were vector control interventions (larviciding and adulticiding), behavioural interventions (personal protection) and a blood screening intervention to reduce the risk of human to human transmission through blood transfusions.

Conclusion:

Despite the existence of many WNV transmission models, our scoping review identified a lack of models considering the OneHealth approach. Including humans, equines or other susceptible mammals in addition to the vector and the reservoir in simulations of the transmission of the disease would be a first step to implement economically reasonable and ecological compatible interventions.

[1] Armstrong A. et al. J Public Health (Oxf) 2011; 33 (1): 147



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O03

Come, sweet death, the trypanosome said

P Mäser

Swiss Tropical and Public Health Institute

Background.

Antigenic variation enables African trypanosomes to survive in the mammalian blood, where they find a rich supply of nutrients. They live on a diet of glucose, which they aerobically ferment in such a seemingly wasteful way that they only gain two molecules of ATP per molecule of glucose. Trypanosoma brucei bloodstream forms are estimated to consume their dry weight in glucose every hour. Unlike other eukaryotic cells, trypanosomatids possess dedicated organelles to digest glucose, the glycosomes. Glucose, as well as the glycolytic enzymes, needs to be imported into the glycosomes.

Results.

Kinetic modeling [2] has suggested that the compartmentalization of glycolysis protects the trypanosomes from biochemical burnout, which would happen if ATP consumption (during the initial steps of glycolysis) were faster than ATP production (further down the pathway). Thus the glycosomal membrane prevents hexokinase and phosphofructokinase from accessing the cytosolic ATP pool. In a collaboration led by the Institute of Structural Biology of the Helmholtz Zentrum Munich, we have recently shown [3] that small molecules designed to block the pockets of the glycosomal import receptor are highly toxic to trypanosomes. The compounds cause mislocalization of glycolytic enzymes to the cytosol, and their trypanocidal effect is exacerbated by glucose.

Conclusion.

After inhibition of glycosomal protein import, glucose turns from the trypanosome's favorite food to a deadly poison. This strategy works not only for African trypanosomes but also for *T. cruzi* and *Leishmania*, which will open new avenues for the specific chemotherapy of trypanosomatids.

- 1) Bach JS Music Gesang-Buch 1736: 868
- 2) Bakker BM et al. PNAS 2000: 97: 2087
- 3) Dawidowski M et al. Science 2017: 355: 1416



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O05

Switzerland's successful contribution to the global fight against malaria.

C Lengeler¹; C Küng²; S Hausmann³

(1) Swiss TPH;

(2) Medicus Mundi Switzerland;

(3) Swiss Agency for Development and Cooperation

Since the renewal of global malaria control efforts in 1998, Switzerland has made a substantial contribution to the global fight against malaria. Work on malaria is both wide ranging and deep, making significant contributions in a number of fields. In order to make these contributions more visible to a broader public, and also to strengthen financial resources in this area, all key actors in the country created the Swiss Malaria Group (SMG) in 2007. The main roles of the SMG are: (1) to network all malaria actors around a common long-term vision, (2) to give Swiss contributions a high degree of public visibility, and (3) to strengthen the Social Corporate Responsibility (SCR) case within the private sector. This presentation is giving a brief overview of major Swiss contributions in malaria research and control, and presents the work and achievements of the SMG and its members.

Few highlights about Swiss contributions will be presented in the following key areas: (1) basic discoveries on the biology of *Plasmodium* sp. (2) contributions to the drug, insecticide and vaccine discovery process, (3) the role of Swiss industry in product development, (4) the role of Non-Governmental Organizations in malaria control, and finally (5) bilateral and multi-lateral investments.

Hundreds of thousands of lives have been directly saved over the past 15 years thanks to Swiss research and implementation efforts. This is a major contribution made by a small but very innovative country. Efforts to bring these efforts to a broader political and general audience have had some successes. Among other, we estimate that “malaria” has become a household name in Switzerland, facilitating request for donor funding and boosting media interest.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O06

Impacts of land use changes on the ecology of arbovirus-Aedes mosquitoes in large industrial oil palm plantation areas in southeastern Côte d'Ivoire

BZJ Zahouli^{1,2,3,4}, GB Koudou^{3,5,6}, P Müller P^{1,2}, D Malone⁷, Y Tano^{4,6}, J Utzinger^{1,2}

(1) Swiss Tropical and Public Health Institute, Basel, Switzerland;

(2) University of Basel, Basel, Switzerland;

(3) Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Côte d'Ivoire;

(4) Unité de Formation et de Recherche Biosciences, Université Félix Houphouët-Boigny, Abidjan, Côte d'Ivoire;

(5) Centre for Neglected Tropical Diseases, Liverpool School of Tropical Medicine, Liverpool, United Kingdom;

(6) Université Nangui-Abrogoua, Abidjan, Côte d'Ivoire;

(7) Innovative Vector Control Consortium, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

Introduction:

Arbovirus-borne viruses (arboviruses) cause many diseases in Africa, and the ecology of mosquito vectors is likely to change with human-induced land use changes, including deforestation, agriculture, and urbanisation. This study explored the effects of land use changes on the ecology of Aedes mosquitoes along an anthropogenic disturbance of landscapes in oil palm plantation areas within yellow fever and dengue foci in southeastern Côte d'Ivoire.

Methods:

From January to October 2014, Aedes mosquitoes were sampled as eggs, larvae, pupae and adults among four macrohabitats: rainforest, polyculture, oil palm monoculture, and housing area. We used standardized sampling procedures such as bamboo-ovitraps, metallic-ovitraps, larval surveys, and human-baited double-net trap methods.

Results:

No Aedes-positive microhabitat, larvae and adults were found in oil palm monoculture. However, the highest abundance (n = 28,276; 60.9%) of Aedes mosquitoes was found in polyculture, while the highest species richness (11 species) was observed in rainforest. Aedes aegypti was the most abundant species. Aedes aegypti, Aedes dendrophilus and Aedes africanus were commonly encountered in all macrohabitats, except oil palm farm. Aedes females' egg-laying patterns and host-seeking behaviours varied significantly among macrohabitats. Significantly higher Aedes-positive microhabitats were artificial containers in villages (49.6%), followed by agriculturally-occurring containers in polyculture (38.9%), and naturally-occurring containers in rainforest (26.7%). Adult Aedes mosquito females presented higher biting rates in polyculture (21.48 specimens/human/day) and villages (4.48 specimens/human/day), and showed two peaks; the first peak at 7:00 a.m., and the second peak at 5:00 p.m. However, the nycthemeral biting cycles were interrupted from 10:00 a.m. to 2:00 p.m. in village, but exhibited continuous patterns in polyculture.

Conclusion:

In southeastern Côte d'Ivoire, the agricultural land use/land cover changes as result of rainforests into industrial oil palm plantations significantly influence the ecology (distribution and behaviour) of several anthropophilic and non-anthropophilic Aedes mosquito vectors leading to the increased risks of yellow and dengue transmission to workers in polyculture and people living in villages. Arbovirus-Aedes vector control strategy should encompass integrated approaches, including landscape epidemiology, ecotope-based vector control and oil palm cultivation practices.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O07

Impact of oxidative stress on resistance to parasites and life histories in *Anopheles gambiae*

A Rojas Mora; G Hauser; S Schjorring; J Koella

Université de Neuchâtel

When organisms face parasite infections, they can either invest resources into either reducing their parasite load - i.e. resistance – or minimize the deleterious effects of the parasite on health – i.e. tolerance -. Life history theory predicts that such an investment into either mechanism of defence against parasites would compromise investment into somatic or reproductive tissues, thus resulting in lower longevities and fecundity. While evidence for the former is largely found in the literature, the physiological proximate mechanisms regulating such trade-off are yet of interest. Reactive oxygen species (ROS) are by products of several physiological processes, which can result in cellular damage leading to illness, ageing, and cell death. However, the innate immune response relies largely on ROS, and it has been found that the activation of the immune response results in oxidative damage to host. Here, we hypothesize inter-individual differences in oxidative stress might explain variation in resistance to parasites and its consequences on longevity. To test this, we will experimentally infect *Anopheles gambiae* mosquitoes with either *Plasmodium berghei* or *Vavraia culicis*, and maintain them with either 10% sugar supplemented with an antioxidant (vitamin C, 1 mg/mL), a pro-oxidant (hydrogen peroxide, 4mM), or unsupplemented 10% sugar. We will follow all the individuals until their dead, and then measured the parasite loads that they bore. Further, a subset of individuals will be frozen alive at -80°C when the peak of parasite load is expected, and we will measure markers of oxidative damage (MDA, GSH:GSSG), antioxidant defences (total GSH, SOD, Cat, and GPx), total protein and lipid content, and parasite loads. Our results will provide insights on the proximate physiological mechanisms regulating resistance to parasites as well as the life history trajectories of individuals facing parasite infections.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O08

Surveillance of mosquito-borne viruses with honey-baited nucleic acid preservation cards

N Wipf^{1,2,3}, V Guidi V³, DRD Guedes⁵, RMR Barbosa⁵, M Tonolla³, O Engler⁴, P Müller^{1,2,3}

- (1) Vector Control Group, Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, Basel, Switzerland;
- (2) University of Basel, Basel, Switzerland;
- (3) Laboratory of Applied Microbiology, University of Applied Sciences and Arts of Southern Switzerland, Bellinzona, Switzerland;
- (4) Spiez Laboratory, Federal Office for Civil Protection, Spiez, Switzerland;
- (5) Department of Entomology, Centro de Pesquisas Aggeu Magalhães, Fundação Oswaldo Cruz, Recife, Brazil

Introduction:

The threat of arboviral infections is re-emerging in continental Europe as demonstrated by several locally transmitted chikungunya and dengue fever cases associated with the spread of the invasive Asian tiger mosquito, *Aedes albopictus*. The Asian tiger mosquito has also established stable populations in southern Switzerland with population levels sufficiently high that would theoretically allow for autochthonous disease transmissions. As part of the current surveillance efforts trapped mosquitoes are being analysed for the presence of arboviruses using RNA extractions and PCR diagnostics. However, the approach involves laborious identification of thousands of mosquitoes and requires a constant cold-chain to preserve the viral RNA. More recently, a new method using honey-soaked Flinders Technology Associates (FTA) filter papers has been proposed to collect saliva from mosquitoes that may be analysed for arboviruses.

Aim:

To evaluate whether FTA cards could be used to collect viruses from invasive mosquitoes in an area of low virus prevalence using different type of traps.

Methods:

Within a variety of traps, mosquitoes were allowed to feed on honey-baited, nucleic acid preserving FTA cards from which viral RNA can be directly purified and detected by RT-PCR.

Results:

In preliminary laboratory experiments, viable Zika and yellow fever virus was found to be promptly inactivated and stably preserved for more than one week on the FTA cards. In a field trial, honey-baited FTA cards were incorporated into CO₂ baited passive box traps as well as oviposition traps and set up in Recife, Brazil, where arboviruses are endemic. Several cards placed during the 2015 Zika outbreak in Recife were positive for dengue, chikungunya, western equine encephalitis and Zika virus. Based on these promising results, the approach of combining honey-baited FTA cards with mosquito traps was then implemented in the 2016 arbovirus surveillance in Ticino, Switzerland. In our presentation we will give the latest results on the recent survey and discuss how FTA cards could replace current practice of tedious processing of mosquito pools in an area of low virus prevalence.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O09

Etiology of Tropical Fever Syndrome: a Multiplex PCR approach

R Lienhard¹; AA Noda²; D Bandeira¹; I Rodriguez²; HH Siegrist¹; M Tritten¹

(1) ADMED Microbiologie;

(2) Institute of Tropical Medicine "Pedro Kouri"

Aims.

Patients presenting fever after a stay in a tropical country usually have malaria. However this non specific syndrome may be caused by many other pathogens. We tested a multiplex PCR assay (Fast-Track Diagnostic, Luxemburg) to assess the utility of such an approach.

Material and Method.

From 2015 to 2017, 234 samples including clinical blood, reference material and miscellaneous biological materials were examined. For every suspicion of malaria an aliquot of whole blood was kept frozen if not tested immediatly during the week. External Quality Assessment samples (QCMD) for Dengue (n=10) and Chikungunya (n=10) as well as strains of *Leptospira* spp (n=12) and *Rickettsia* spp (n=2) were extracted. DNA was obtained from extraction on an EasyMag instrument (bioMérieux). The Tropical Fever core PCR multiplex (fast-track Diagnostic, Luxemburg) run on Rotorgene (Qiagen) was used to assess the utility of such a syndromic approach.

Results and Discussion.

From 185 blood samples, 12 (6.5%) were inhibited as assessed by the absence of internal control amplification. We obtained 43 (23.3%) positive samples, 34 for *Plasmodium* sp. including 33 confirmed by blood smear or antigen and 1 patient with unexpected *P.vivax* identified by PCR only. Among 9 (4.9%) other unexpected results, three patients were positive for Dengue virus and 1 patient for *Rickettsia* sp in two samples. The last 5 results were positive for *Salmonella* spp. However, 2 samples from direct whole blood could not be confirmed by blood cultures. The remaining 3 were positive on blood culture, as required, with *Salmonella* Typhi, *Salmonella* Paratyphi A and *Salmonella* Typhimurium. None of the *Leptospira* interrogans, West Nile Virus or Chikungunya virus targets gave positive results. This does not prove the low incidence of such infections during the 2 year period, as serological investigations must be considered. Expected results for all reference materials confirmed sensitivity and specificity.

Conclusion.

This multiplex PCR showed enhanced sensitivity on tested pathogens. It is a helpful assay but serology will still be needed to complete the diagnosis. We would suggest replacing the target *Salmonella* for the more common Zika virus found directly in blood and urine samples.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O10

Burkholderia pseudomallei and environmental factors in Lao rivers

R Zimmermann¹; O Ribolzi²; A Pierret³; S Rattanavong⁴; J Zopfi⁵; D Dance⁶

- (1) University of Basel / Swiss Tropical and Public Health Institute / Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit;
- (2) Université de Toulouse / Institut de Recherche pour le Développement;
- (3) Institute of Ecology and Environmental Science Paris / Institut de Recherche pour le Développement;
- (4) Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit;
- (5) University of Basel;
- (6) Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit / University of Oxford

The environmental bacterium *Burkholderia pseudomallei*, the causative agent of melioidosis in humans, is endemic in tropical soils and has also been found in surface freshwaters. To investigate the distribution of this emerging pathogen in Lao PDR, its occurrence in rivers, and associated environmental factors, we studied 23 rivers (including the Mekong) in the South, Centre and North of the country, applying culture-based methods and a specific quantitative real-time PCR assay to water filters and streambed sediments. Geochemical measurements included turbidity, a proxy for suspended sediment load which was measured on-site using a turbidity meter and confirmed in the laboratory by dry weight measurements of water filters. *B. pseudomallei* was present in 9% of the rivers in the dry season. In contrast, we found the pathogen in the water of 57% of the rivers in the rainy season by at least one detection method. 35% of the *B. pseudomallei* positive river stations were associated with *B. pseudomallei* positive sediments. Turbidity correlated positively with the presence of *B. pseudomallei*. All *B. pseudomallei* positive rivers were situated in the South and Centre of the country. Our preliminary results provide evidence for a heterogeneous temporal and spatial distribution of *B. pseudomallei* in Lao PDR with a North-South contrast. The seasonal dynamics and predominant occurrence of *B. pseudomallei* in particle-rich water suggest that *B. pseudomallei* is washed out with eroded soil during periods of heavy rainfall and transported by rivers. In contrast to soil, river sediments do not seem to represent permanent natural habitats for *B. pseudomallei*. These findings will contribute to improved *B. pseudomallei* risk modelling and health management strategies.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTT

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O11

The Effect of Hand Gel Sanitizer on Travellers' Diarrhoea and Colonization with Multidrug Resistant Enterobacteriaceae in Travellers to South Asia – Preliminary Results of a Prospective Multicentre Randomized Trial

E Kuenzli¹; VK Jaeger²; V Sydow¹; S DeCrom³; K Kling¹; A Egli²; R Frei²; A Neumayr¹; C Hatz¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) University Hospital Basel;

(3) Epidemiology, Biostatistics and Prevention Institute, University of Zurich

Aim:

Travellers' diarrhoea (TD) and colonization with multidrug resistant Enterobacteriaceae are frequent health problems in travellers to South Asia with TD being a known risk factor for becoming colonised (1,2). In one retrospective study, the regular use of hand gel sanitizer was found to be associated with a decreased risk for TD (3). However, until now, there was no prospective study on the effect of the regular use of hand gel sanitizer on the occurrence of TD and on colonization rates with multidrug resistant Enterobacteriaceae. With this prospective multicentre randomized study, we evaluated the effect of the regular use of hand gel sanitizer while travelling on the occurrence of TD and on the colonization with multidrug resistant Enterobacteriaceae in travellers to South Asia.

Method:

A prospective multicentre randomized trial was carried out. Travellers staying in South Asia for up to 4 weeks were enrolled.

Results:

Of 161 travellers, 101 (62.7%) reported suffering from TD. Eighty percent (117/147) of travellers who screened negative for ESBL-prod. Enterobacteriaceae before travelling were colonized upon return. In the multivariate analysis, the regular use of hand gel sanitizer was associated with a reduced risk for TD (adjusted OR 0.43 (95% CI 0.19-0.98), $p=0.044$). With regard to colonization with ESBL-producing Enterobacteriaceae, a regular use of hand gel sanitizer was associated with a tendency towards an increased risk (OR 2.36 (95% CI 0.90-6.21), $p=0.082$). The only other factor associated with both outcomes was travelling to India as compared to other countries in South Asia.

Conclusion:

According to our preliminary results, the regular use of hand gel sanitizer while travelling in South Asia appears to reduce the risk for TD and shows a tendency towards increasing the risk for becoming colonized with ESBL-producing Enterobacteriaceae.

Acknowledgments:

We thank the travellers for participating in the study and Danica Nogarth for the laboratory work. The study was partially funded by IVF Hartmann AG.

References:

1. Steffen R. et al. JAMA 2015;313(1):71-80.
2. Arcilla MS. et al. Lancet Infect Dis 2017;17(1):78-85.
3. Henriey D. et al. Travel Med Infect Dis 2014;12(5):494-498.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O12

Appropriateness of malaria diagnosis and treatment of fever episode according to patient history and antimalarial blood measurement

J Gallay¹; E Pothin¹; D Mosha²; M Zuakulu²; E Lutahakana²; L Decosterd³; B Genton¹

(1) Swiss Tropical and Public Health Institute;

(2) Ifakara Health Institute;

(3) Lausanne University Hospital (CHUV)

Monitoring the impact of case management strategies in terms of use and compliance to RDT result as well as drug use is essential to evaluate the public health benefit they confer. Methodologies that rely on objective and standardized endpoints such as drug levels in the blood should be used. We evaluated diagnosis and treatment appropriateness in case of fever according to patient history and antimalarials blood concentration.

The survey took place in 2015 in three regions of Tanzania with different levels of malaria endemicity. Community surveys were conducted to collect information on demographics, health seeking behavior and case management in case of fever. Blood samples were collected as dried blood spots for further antimalarials measurements by LC-MS/MS. Health facility surveys collected information on diagnosis and treatment practices. Appropriate testing was defined as a patient with history of fever being tested for malaria and appropriate treatment as having antimalarial in the blood if the test result was positive or if the person was not tested.

In total, 6485 individuals were surveyed and 1344 (21%) had antimalarials detected in the blood. 1021 reported a febrile episode in the previous 2 weeks but only 664 (65%) of them sought care. 69% (172/248) of the individuals who sought care in health facilities were tested and 52% (130/248) appropriately treated. When other providers were sought, 6% (23/382) of persons were appropriately tested and 44% (169/382) appropriately treated. Results obtained through exit interviews in health facilities were close with 67% (151/226) of individuals tested and 66% (149/226) appropriately treated. Overall, the proportion of individuals treated was larger than that being tested (45% (301/664) treated, 30% (196/664) tested). Only about half of individuals with detectable levels of antimalarials in the blood were those having a test result positive or not being tested.

These results show that treatments are often not targeted to individuals that are sick with malaria. Efforts should be made to better follow WHO recommendations of systematic diagnostic testing and treatment upon result.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O13

Telemedicine for Patients with Travel-related Health Problems while Abroad: a Pilot Phase in a Swiss Travel Clinic

L. Rochat¹, V. D'Acremont^{1,3}, A. Rosat⁴, J. Thabard⁴, S. de Vallière^{1,2}, B. Genton^{1,2,3}

(1) Travel Clinic, Ambulatory Care and Community Medicine, University Hospital, Lausanne, Switzerland,

(2) Division of Infectious Diseases, University Hospital, Lausanne, Switzerland,

(3) Swiss Tropical and Public Health Institute, Basel, Switzerland,

(4) IT Department, Ambulatory Care and Community Medicine, University Hospital, Lausanne, Switzerland

Background:

Online telemedicine is potentially a useful tool to provide expert medical advice to individuals facing health issues while traveling in remote areas. A telemedicine service enabling contact through emails with the medical team at our travel clinic has been established. The 6-month pilot phase is ongoing.

Objectives:

- 1) to delineate the most common medical problems for which medical care is required while abroad
- 2) to describe the medical pathway followed by the clients and the clinical outcome of the problem they sought assistance for
- 3) to estimate the financial aspects of this service and adjust fees if necessary
- 4) to assess travelers' satisfaction

Method:

Travelers coming to our clinic for pre-travel advice are informed about the telemedicine service. In case of interest, she or he signs a contract and pays a fixed fee adjusted to the trip duration. In case of a medical problem while abroad, the traveler sends an email request on a standard semi-open format providing a description of the signs and symptoms of the disorder for which she or he seeks assistance. A senior travel medicine physician "on call" evaluates the situation and provides the appropriate preventive or curative measures within 24 hours and no later than 48 hours. An electronic application allows email exchanges, as well as collection of data on travelers' follow-up. The level of satisfaction of the subscribers is evaluated through an electronic evaluation survey 2 weeks after return.

Results:

The rate of travelers subscribing to the service, distribution of medical problems, number of emails and mean time spent by physicians to solve each medical problem, costs according to the number of hours worked by the physicians and the computer scientists, as well as the rate of satisfied travelers and reasons for non-satisfaction during the first 3 months of the pilot phase will be presented. The way forward for this telemedicine service will then be discussed.

Conclusions:

Due to the rapidly evolving technologies, telemedicine represents a promising tool to decrease distance barriers and provide remote medical assistance. A telemedicine service dedicated to travelers has been successfully established at a Swiss travel clinic. Based on the results of this pilot phase, a final web-based platform for telemedicine service will be developed.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O14

Exploring experimental cerebral malaria pathogenesis through the characterisation of host-derived plasma microparticle protein content

N Tiberti¹; SL Latham²; S Bush³; A Cohen²; RO Opoka⁴; CC John⁵; A Juillard²; GE Grau²; V Combes³

(1) University of Geneva / University of Technology Sydney;

(2) University of Sydney;

(3) University of Technology Sydney;

(4) Makerere University;

(5) Indiana University / University of Minnesota

Introduction

Cerebral malaria (CM) is a severe complication of a *Plasmodium falciparum* infection responsible for thousands of deaths in children under the age of 5 in sub-Saharan Africa. CM pathogenesis remains incompletely understood but a number of effectors have been proposed, including plasma microparticles (MPs). MP numbers are, indeed, increased in CM patients' circulation and, in the experimental cerebral malaria (ECM) mouse model, they can be localised within inflamed vessels, suggesting their involvement in vascular damage.

Aim

In the present work we define, for the first time, the protein cargo of host-derived MP during ECM with the overarching hypothesis that this characterisation could help understand CM pathogenesis.

Methods and Results

Using qualitative and quantitative high-throughput proteomics we compared MP proteins from non-infected and *P. berghei* ANKA-infected mice. More than 360 proteins were identified, 60 of which were differentially abundant, as determined by quantitative comparison using TMTM isobaric labelling. Network analyses showed that ECM MPs carry proteins implicated in molecular mechanisms relevant to CM pathogenesis, including endothelial activation. Among these proteins, the strict association of carbonic anhydrase I and S100A8 with ECM was verified by western blot on MP from DBA/1 and C57BL/6 mice and further confirmed, for S100A8, in MP from CM paediatric plasma samples.

Conclusion

These results demonstrate that MP protein cargo represents a novel ECM pathogenic trait to consider in the understanding of CM pathogenesis and show the potential of MPs as a source of CM candidate biomarkers.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O15

Safety of live vaccines under immunosuppressive or immunomodulatory therapy - a retrospective study in three Swiss Travel Clinics

F Huber¹; B Ehrensperger²; C Hatz¹; F Chappuis²; S Bühler¹; G Eperon²

(1) University of Zurich, Zurich, Switzerland;

(2) Hôpitaux Universitaires de Genève

Aims

Patients increasingly benefit from immunosuppressive/immunomodulatory medications for a range of conditions allowing them a lifestyle similar to healthy individuals, including travel.

However, the administration of live vaccines to immunodeficient patients bears the risk of replication of the attenuated vaccine microorganism. Therefore, live vaccines are generally contraindicated under immunosuppression.

Data on live vaccinations under immunosuppressive/immunomodulatory medication are scarce. We identified all travellers seeking pre-travel advice in three Swiss travel clinics with a live vaccine under immunosuppressive/immunomodulatory therapy to ascertain experienced side effects. A retrospective design was chosen, as it was unethical to perform a prospective study.

Methods

This study was conducted in the travel clinics of the University of Zurich, the Swiss TPH, Basel, and Geneva University Hospitals. Travellers under immunosuppressive/immunomodulatory therapy who received live vaccines (yellow fever vaccination (YFV), measles, mumps, rubella (MMR), varicella and oral typhoid vaccination (OTV)) between 2008 and 2015 were identified and interviewed with a pilot-tested questionnaire. Sixty age- and sex-matched controls (matched to Basel/Zurich travel clinics travellers) were included.

Results

197 patients were identified. 116 patients (59%) and 60 age- and sex-matched travellers were interviewed. The YFV was administered 92 times, MMR 21 times, varicella 4 times and OTV 6 times to patients under immunosuppressed/immunomodulatory therapy. In 74%, a primary YFV was given, and in 52% a primary MMR vaccination was administered. Most common medications were corticosteroids (n=45), mesalazine (n=28) and methotrexate (n=19). Live vaccines were also given under biological therapies, such as TNF-alpha inhibitors (n=6). Systemic reactions were observed in 12.1% of the immunosuppressed and in 14.3% of controls; local reactions in 7.8% of the immunosuppressed and in 12.7% of controls. In the control group, all reactions were classified as mild or moderate. In the immunosuppressed group 2/21 severe reactions were reported: severe local pain under interferon-beta and severe muscle/joint pain under sulfasalazine treatment.

Conclusion

Safety of live vaccines given to immunosuppressed patients cannot be concluded. However, it is re-assuring that in the examined patient groups no serious side effects or infections by the attenuated vaccine strain occurred.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O16

Bumped kinase inhibitors and their effects during experimental infection with the apicomplexan parasites *Neospora caninum* and *Toxoplasma gondii*. Proof of concept in pregnant mouse models

P Winzer¹, A Aguado-Martinez¹, J Müller¹, N Anghel¹, KK Ojo², WC Van Voorhis², A Hemphill¹

(1) Institute of Parasitology, Vetsuisse Faculty, University of Bern, Länggassstrasse 122, 3012 Bern, Switzerland ,

(2) Center for Emerging and Reemerging Infectious Diseases (CERID), Division of Allergy and Infectious Diseases, Department of Medicine, University of Washington, Seattle, Washington, USA

Neospora caninum and *Toxoplasma gondii* are closely related apicomplexan parasites, which can cause abortion and fetal defects in many animal species. While *N. caninum* is a veterinary problem and is most relevant in cattle, *T. gondii* causes abortion in sheep, and is also an important human pathogen, most notably when infection takes place during pregnancy, or in immune compromised patients. Bumped kinase inhibitors (BKIs), such as BKI-1294, target *T. gondii* and *N. caninum* calcium-dependent protein kinase 1 (TgCDPK1 and NcCDPK1, respectively), inhibit host cell invasion and interfere in tachyzoite proliferation in vitro by inducing the build-up of large schizont-like multinucleated complexes (MNCs), which are blocked at the final stages of cytokinesis. We now show that these MNCs remain viable for extended periods of time, and even at high concentrations, BKI-1294 does not exert parasitocidal effects in vitro. Thus, it is not fully understood whether the widely demonstrated in vivo efficacy of BKI-1294 therapy is associated with other undefined host factors. In pregnant inbred Balb/c mice infected with *N. caninum* tachyzoites, BKI-1294 treatments (50 mg/kg/day for 5 days), did not interfere in pregnancy outcome, protected dams from clinical signs of neosporosis and cerebral infection, and resulted in massively increased survival and excellent protection against transplacental transmission of offspring mice. In a recently established infection model consisting of outbred CD-1 mice orally infected with *T. gondii* oocysts, BKI-1294 treatments exhibited a similar efficacy readout. Several other BKIs are currently being studied, some with improved in vitro efficacy, pharmacokinetics and bioavailability. Thus, BKIs targeting CDPK1 are a potentially useful class of drugs for the treatment of toxoplasmosis and neosporosis during pregnancy, and possibly other diseases caused by apicomplexan parasites.

We acknowledge the financial support by the Swiss National Science Foundation [grant No. 310030_165782], the Public Health Service, National Institutes of Health, Bethesda, MD [grants R01 AI 111341 and R01 HD 080670], and the U.S. Department of Agriculture [grant 2014-67015-22106].



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Cohort Session: SHCS and STCS

O17

Clinical course, radiological manifestations, and outcome of *Pneumocystis pneumonia* in HIV patients and renal transplant recipients.

L Ebner^{1 #a ¶}, LN Walti^{2 ¶}, A Rauch², H Furrer², A Cusini², AMJ Meyer³, S Weiler^{3, #b}, U Huynh-Do³, J Heverhagen¹, S Arampatzis^{3 & *}, A Christe^{1 &}

(1) Department of Diagnostic, Interventional and Pediatric Radiology, Bern University Hospital and University of Bern, Bern, Switzerland

(2) Department of Infectious Diseases, Bern University Hospital and University of Bern, Bern, Switzerland

(3) Department of Hypertension, Nephrology and Clinical Pharmacology, Bern University Hospital and University of Bern, Bern, Switzerland

^{#a}Department of Radiology, Duke University Medical Center, Durham, NC.

^{#b}Department of Clinical Pharmacology and Toxicology, University Hospital Zurich, Zurich, Switzerland

Background:

Pneumocystis jirovecii pneumonia (PCP) is a frequent opportunistic infection in immunocompromised patients. In literature, presentation and outcome of PCP differs between patients with human immunodeficiency virus (HIV) infection and renal transplant recipients (RTRs).

Methods:

We conducted a cross-sectional study of patients with PCP based on the HIV and renal transplant registries at our institution. Radiological and clinical data from all confirmed PCP cases between 2005 and 2012 were compared.

Results:

Forty patients were included: 16 with HIV and 24 RTRs. Radiologically, HIV patients had significantly more areas of diffuse lung affection (81% HIV vs. 25% RTR; $p=0.02$), more ground glass nodules 5–10 mm (69% vs. 4 %; $p<0.001$) and enlarged hilar lymph nodes were found only in HIV patients (44%). Cough and dyspnea were the most common clinical signs (>80%) in both groups. Duration from illness onset to hospital presentation was longer in the HIV patients (median of 18 vs. 10 days ($p=0.02$)), implying a less fulminant clinical course. Sixty percent of PCP cases in RTRs occurred >12 months after transplantation. Lengths of hospitalization, admission rates to the intensive care unit, and requirements for mechanical ventilation were similar. Outcome in both groups was favourable.

Conclusions:

While important differences in radiological presentation of PCP between HIV patients and RTRs were found, clinical presentation was similar. PCP only rarely presented with fulminant respiratory symptoms requiring ICU admission, with similar results and outcomes for HIV patients and RTRs. Early diagnosis and treatment is mandatory for clinical success.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O19

High Incidence of Invasive Fungal Breakthrough Infections among Patients after Allogeneic Hematopoietic Stem Cell Transplantation

S Kuster^{1**}, S Stampf^{2**}, B Gerber³, V Bättig¹, M Weisser¹, S Gerull⁴, M Medinger⁴, J Passweg⁴, U Schanz⁵, C Garzoni⁶, C Berger⁷, Y Chalandon⁸, NJ Mueller⁹, C van Delden¹⁰, D Neofytos¹⁰, and N Khanna^{1***}, Swiss Transplant Cohort Study

(1) Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Basel

(2) Clinic for Transplantation Immunology and Nephrology (Swiss Transplant Cohort Study), University Hospital of Basel

(3) Division of Hematology, Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

(4) Division of Hematology, University Hospital of Basel

(5) Division of Hematology, University and University Hospital of Zurich

(6) Clinic of Internal Medicine and Infectious Diseases, Clinica Luganese, Lugano, Switzerland and Department of Infectious Diseases, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland.

(7) Division of Infectious Diseases and Hospital Epidemiology, University Children's Hospital Zurich

(8) Division of Hematology, University Hospital of Geneva

(9) Division of Infectious Diseases and Hospital Epidemiology, University Hospital of Zurich

(10) Transplant Infectious Diseases Unit, University Hospitals of Geneva

Aims:

To investigate the epidemiology and outcomes of invasive fungal infections (IFI) among allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients.

Methods:

Using the Swiss Transplant Cohort Study, we studied the epidemiology, risk factors, and outcomes of IFI on allo-HSCT recipients in Switzerland (01.2009-08.2013). Cumulative incidences were estimated and Cox-proportional hazard models were performed to analyse risk factors for IFI and mortality.

Results:

We included 479 allo-HSCT recipients with 90 IFIs: 49 possible, and 41 probable/proven (10 invasive candidiasis (IC), 31 invasive mold infections (IMI)) over 4.75 years. The one-year cumulative incidence for IC, probable/proven IMI, invasive aspergillosis (IA) and non-IA IMI was 2%, 5.7%, 3.5% and 2.1%, respectively. Breakthrough probable/proven IFI represented 58.5% of IFI with one-year cumulative incidence of 4.4%, more frequently caused by other-than-*Aspergillus fumigatus* molds and non-*albicans* *Candida* species than primary IFI (65% vs. 27.7%; $p=0.03$). Absence of myeloablative chemotherapy [hazard ratio (HR): 1.81, $p=0.04$], normal Karnofsky-Score [HR: 2.24, $p=0.02$] and IFI prior-to-allo-HSCT [HR: 0.06, $p<0.001$] were protective for all IFI post-transplant. One-year all-cause mortality was 24.7%. The presence of IA [HR: 12.18, $p<0.001$] and non-IA IMI [HR: 13.61, $p<0.001$] were strongest predictors of mortality. Six-week mortality among patients with IFI was 22.2%: 20%, 2%, 54.8%, 55% and 54.6% for IC, possible IMI, probable/proven IMI, IA and non-IA IMI, respectively.

Conclusions:

Possible and breakthrough IFI with rare and resistant fungal species represent the major burden of IFI post-allo-HSCT, underscoring the ongoing challenges to prevent IFI in these patients. Mortality remains high in patients with IMI after allo-HSCT.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O20

STCS-SHCS biobank: the value of stored samples

P Meylan and A Rauch

Institut de microbiologie, CHUV, Lausanne



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Innovative diagnostic tests

O21

Utility of direct pan-mycobacterial 16S rDNA PCR on clinical samples in the diagnostic of nontuberculous mycobacteria infections

S Andenmatten; O Opota; L Nicod; G Greub; K Jatton
 Lausanne University Hospital and University of Lausanne

Aims:

So far, culture remains the reference method for the microbiological diagnosis of mycobacterial infections. During the past 10 years, various molecular methods have been developed for the detection and identification of nontuberculous mycobacteria (NTM) directly from clinical samples to overcome the length of mycobacterial culture. We evaluated the added value of a 16s rDNA pan-mycobacterial PCR, developed and used in our tertiary care university hospital for genus detection and species identification after sequencing of nontuberculosis mycobacteria.

Methods:

We analyzed the comprehensive results of cultures, smear microscopy and pan-mycobacterial PCR directly on clinical samples during a 10 years period (2003-2013) representing 955 samples and 639 patients with clinical suspicion of pulmonary and extra-pulmonary infection with nontuberculosis mycobacteria.

Results:

Using mycobacterial culture as gold standard, the sensitivity of the pan-mycobacterial PCR was 61.7% [CI95% 53.4 -69.6%], the specificity was 99.1% [CI95% 98.2 -99.7%], the positive predictive value was 92.9 % [CI95 86% -97.1%] and the negative predictive value was 93.3% [CI95% 91.5 -94.9%]. The median time to identification for the pan-mycobacterial PCR was 6 days when positive compare to 35 days for the culture (p <0.0001).

Conclusion:

Despite a yet limited sensitivity, the pan-mycobacterial PCR displays an excellent specificity and significantly accelerate the time to diagnose NTM infections with a reduction of 29 days of the time to identification comparing to culture.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O22

Mobilome and Resistome Analysis of Canine multidrug resistant Methicillin-resistant *Staphylococcus sciuri* strain C2865 and Comparative Genomics of *S. sciuri* species group

E GOMEZ-SANZ¹; JM Haro-Moreno²; F Rodriguez-Valera³; C Torres⁴; M Loessner¹; T Smits⁵; M Lopez-Perez²

(1) ETH Zürich (ETHZ);

(2) Universidad Miguel Hernández;

(3) Universidad Miguel Hernández;;

(4) Universidad de La Rioja;

(5) ZHAW

Aims:

Methicillin-resistant *Staphylococcus sciuri* strain C2865 (canine nasal sample, Nigeria) showed thrimethoprim resistance for which all staphylococcal *df*r genes were negative. This strain was subjected to whole-genome-sequencing (WGS) to characterize its resistome and mobilome and to comparative genomics with all *S. sciuri* species group strains on the NCBI database for diversity analysis.

Methods:

Illumina Miseq was used for WGS of C2865. Trimmed reads were de-novo assembled using the SPAdes assembler. Protein-coding genes in the assembled contigs were predicted using Prodigal. Genes encoding tRNAs and rRNA operons were determined by tRNAscan-SE and RNAmmer. Additional annotation was done with NCBI NR, COG, and TIGRfam databases, and the RAST server.

The ANI between all 22 available *S. sciuri* group strains was calculated using JSpecies. WG alignments for all strains were constructed using the progressiveMauve algorithm, which were then used in ClonalFrame. Indels and SNPs between small genome regions such as genomic islands (GIs) were identified using nucmer from MUMmer3+ package.

Results:

The genome of *S. sciuri* C2865 revealed 2,937,715 bp in size and a GC content of 32.7%. Resulting contigs contain 2,927 CDSs, and 76 RNAs. In total, 1887 genes were categorized into COG functional groups.

A novel SCCmec cassette, lacking currently known *ccr* genes was identified in C2865. This cassette posed other antibiotic and metal resistance genes. Several resistance plasmids were detected. A novel plasmid containing a trimethoprim resistance gene, described for the first time in a marine *Exiguobacterium* strain, was identified. This plasmid carries additional resistance genes to aminoglycosides and erythromycin.

C2865 shared highest ID with *S. sciuri* Z8 and SNUD-18 belonging to a different group within the same species (95-96% ID; 83-85% ID with the other species of the group). WG alignment among all *S. sciuri* strains revealed 673 homologous regions >500 bp revealing a core genome of 1.7 Mb (60.7%) with 1,869 shared proteins. Genome alignment with the closely related strains reveal synteny was preserved and there were several GIs with differential gene content, some associated with novel integrated lysogenic or defective phages.

Conclusion

WGS is a powerful tool to characterize the resistome and mobilome of bacterial strains as well as to identify novel resistance platforms. Comparative genomics shows high *S. sciuri* intraspecies diversity and high genome plasticity.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

CM1 - Clinical Microbiology : Genomics-metagenomics

O23

Functional metagenomics: The nasal resistome in infants with cystic fibrosis

A Allemann¹; M Mika¹; I Korten²; P Latzin²; M Hilty¹

(1) Institute for Infectious Diseases, University of Bern, Switzerland;

(2) Division of Respiratory Medicine, Inselspital and University of Bern, Bern, Switzerland;

We previously described the microbiota profile of the upper respiratory tract in infants with cystic fibrosis (CF) within the first year of life¹. Using 16S RNA sequences, we received four distinct clusters for the dominant bacterial family: Moraxellaceae, Staphylococcaceae, Streptococcaceae and 'others'. However, the influence of antibiotic (AB) therapy on the upper respiratory tract microbiota composition and its resistance genes reservoir (the resistome) is poorly understood. In this study we aim to describe the resistome using a functional metagenomic method within infants with CF.

Samples were selected from a collection of nasal swabs taken bi-weekly from patients with CF during their first year of life. For the functional detection of AB resistance genes, DNA fragments were cloned and transformed into *E. coli*. Resistant clones were recovered by culturing against different classes of antibiotics and the genes conferring resistance were identified by nanopore sequencing (MinION).

We investigated the dynamics of the resistome by analysing 130 samples from 26 infants with CF over their first year of life. We detected resistance towards ampicillin (n=40, 30.8%), amoxicillin-clavulanic acid (n=16, 12.3%), cefuroxime (n=26, 20.0%), cotrimoxazole (n=45, 34.6%), chloramphenicol (n=16, 12.3%) and tetracycline (n=13, 10.0%). No significant difference was observed in resistant phenotypes in samples before or after an AB treatment for all antimicrobial tested. Nevertheless we noticed a trend for increased cefuroxime resistance in treated patients. Ampicillin resistance were significantly associated with the Staphylococcaceae cluster (P=0.02) whereas the samples of the Streptococcaceae cluster showed significantly less antibiotic resistance (P=0.04). As for the resistance mechanisms within a subset of samples, the gene *blaZ* was frequently identified (9.2% of 65 samples) in samples of the Staphylococcaceae cluster. Also, *bla_TEM* (4.6%) and *ampC* (3.0%) genes coding for β -lactamases were identified, mainly within clusters dominated by Moraxellaceae or 'other' bacteria.

Using functional metagenomics, we profiled the nasal bacterial microbiota and its resistome in infants with CF. We observed a significant association between cluster compositions with the resistome. Knowledge of the resistome has the potential to be a complimentary method as compared to traditional antibiotic testing and may lead to an improved personalised AB treatment regime in patients with CF.

Reference:

[1] Mika et al., *Lancet Resp Med*, 2016;4:627



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O24

Genomics of uncultured Chlamydiae

T Pillonel; G Greub

University Hospital Center and University of Lausanne

The phylum Chlamydiae forms a deep branching clade within bacteria. All known members of the phylum are obligate endosymbionts of eukaryotes. Metagenomic studies of environmental samples suggest a high diversity of chlamydial species, but only few representative strains were extensively described because of the difficulty to culture them. Genome sequencing provides an alternative approach to investigate the diversity, biology and evolution of the phylum. An increasing number of unclassified genomes exhibiting similarity to sequenced chlamydial genomes are submitted to public databases. Those sequences originate mostly from large scale metagenomic studies. The aim of this project is to perform whole genome comparative analysis of uncultured and cultured chlamydial strains in order to refine the taxonomy of the phylum and to investigate its metabolic diversity. Thirty-six genomes from 7 family-level lineages and 21 draft genomes derived from metagenomes were included in the analysis. Proteins were clustered into orthologous groups using Orthofinder. The genome quality was assessed using nearly universal proteins. Metabolic capacities were evaluated using the KEGG database, and proteins domains were identified using Interproscan. Metagenomics bins exhibited unequal quality, with 7 assemblies estimated to represent less than 90% of the complete genome. Phylogenetic reconstruction based on conserved single copy orthologs suggests the existence of 8 new clades, including 4 new family level lineages. Comparative analysis of predicted metabolic capacities indicated that chlamydial families does not reflect coherent groups with distinct metabolic profiles. With the identification of at least 4 yet undescribed family level lineages of the phylum Chlamydiae, this work highlights the promises of environmental metagenomics for the study of unculturable obligate symbionts of eukaryotes.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O25

IRIDA: Open, Integrated, Rapid Infectious Disease Analysis for Genomic Epidemiology

C Bertelli; FS Brinkman
 Simon Fraser University

Aims

Whole-genome sequencing (WGS) can provide researchers, epidemiologists, and other public health workers with the highest-resolution fingerprint of bacterial samples collected during an infectious disease outbreak, improving the ability to identify virulence/antimicrobial resistance determinants and show definitive, fine-grained relationships between isolates. Existing genomic data analysis tools and pipelines provide the means to infer these relationships, but remain complex and require considerable technical knowledge to execute, or else they are closed source and centralized, limiting public health agency use which must keep sensitive data within their jurisdiction.

Methods and Results

The Integrated Rapid Infectious Disease Analysis (IRIDA) web-based platform is designed to equip public health workers with the tools needed to analyze genomic data, without the complexity and technical barriers of existing tools, and it is open source and freely available for local use within a jurisdiction. IRIDA has been implemented in Canada's public health agency and utilizes secure storage of WGS data, epidemiological and application metadata, data analysis pipelines, visualization of results, and a federated data sharing model intended to facilitate communication between provincial and federal public health institutions in Canada. Metadata is encoded in an application ontology following community recognized standards and extending existing OBO domain ontologies (<http://www.obofoundry.org/>) to promote interoperability. Data analysis pipelines and execution provenance are transparently implemented using Galaxy, and federated data sharing and analysis is realized with a common REST API across platform instances.

Conclusion

IRIDA is free and open-source software suitable for an organization (from public health lab to hospital), which wishes to have integrated analysis capabilities within a jurisdiction, with the ability to link to external resources.

More information is available at <http://www.irida.ca>.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O26

Hepatic brucelloma assessed by next-generation sequencing (case report)

V Lazarevic¹, N Gaïa¹, St Emonet², M Girard¹, St Leo¹, A Cherkaoui², G Renzi², E Ruppé¹, L Rubbia-Brandt³, Ch Toso⁴, J Schrenzel^{1,2}

- (1) Genomic Research Laboratory, Department of Medical Specialties, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland
- (2) Bacteriology Laboratory, Department of Laboratories and Genetic Medicine, Geneva University Hospitals, Geneva, Switzerland
- (3) Visceral and Transplant Surgery, Department of Surgery, Geneva University Hospitals and Faculty of Medicine
- (4) Hepato-Pancreato-Biliary Centre, Department of Clinical Pathology, Geneva University Hospitals and Faculty of Medicine

Aims:

Human infections caused by *Brucella* (called brucellosis) are among the most common zoonoses with about 500,000 cases every year [1]. Isolation of *Brucella* is time- and resource-intensive and requires strict biosafety rules of level 3. *Brucella* sp. are often missed by the culture of clinical specimens but may be detected by serological tests. We aimed at identifying *Brucella* by whole metagenome shotgun sequencing (WMGS).

Methods:

We extracted DNA from the leftover of the necrotic hepatic lesion of a patient with a suspicion of chronic hepatic brucelloma. The extraction procedure included bacterial/fungal DNA enrichment procedure based on degradation of DNA released from host cells after their selective lysis. DNA was sequenced (2x250 bp) on an Illumina MiSeq instrument.

Results:

Nearly all (1,086,098/1,086,125) taxonomically classified (paired) reads corresponded to human genome sequence. Of 25 reads classified as bacterial, 23 were assigned to the genus *Brucella* and two corresponded to known reagent contaminants, *Beijerinckia* and *Propionibacterium*.

Conclusion:

To the best of our knowledge, this is the first report of the use of WMGS on a hepatic brucelloma sample. Since *Brucella* was dominant the sample dataset but absent in negative controls, the possibility that it originates from an exogenous source seems unlikely. Our data suggest that WMGS may be used together with other diagnostic procedures including radiological, serological and histological examinations to strengthen the diagnosis of hepatic brucelloma.

1. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The Lancet Infectious Diseases 2006;6:91-9.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Environmental Microbiology

O27

Aquatic microbial community growth on sub-milligram per L concentrations of fragrances

B Oezel Duygan; JR van der Meer
University of Lausanne

Assessment of the biodegradation potential of microbial communities is important to judge the environmental fate of polluting substances. Existing and Organisation for Economic Cooperation and Development (OECD) recommended biodegradation tests based on oxygen consumption or carbon dioxide (CO₂) evolution from added substrate are typically carried out at relatively high substrate concentrations (e.g. 100 mg C L⁻¹). However, pollutant concentrations at this level may cause toxicity to microbes and underestimate the potential for biodegradation. Also, since pollutant concentrations in the environment are often much lower, their biodegradation kinetics may be over-estimated from tests at higher concentrations. The aim of our work is to develop tests that enable to measure compound biodegradation at concentrations between 0.1 - 10 mg C L⁻¹.

The overall methodological concept of our biodegradation test is based on sensitive measurements of prokaryotic community size increase by flow cytometry at the expense of the added compound. We conducted our experiments with aquatic bacterial communities from Lake Geneva at initial cell densities of 1E4, 1E5 and 1E6 cells mL⁻¹ incubated for up to 7 days. As readily biodegradable substances we tested anthraquinone, phenol, sodium benzoate and 1-octanol compared to fragrances such as methyl jasmonate, precyclemone B and myrcene.

Community growth up to approximately 1E7 cells mL⁻¹ was observed at substrate concentrations of 1 - 10 mg C L⁻¹. The lowest measurable community size increase was observed for 0.1 mg C L⁻¹. Sodium benzoate, 1-octanol and phenol indeed supported rapid community growth, in contrast to anthraquinone and the fragrances. For sodium benzoate, we observed cell aggregation, which complicates bacterial community size measurements. One of the encountered difficulties is to relate community cell numbers with biomass quantity, in order to calculate growth yield and substrate utilization kinetics. Reported conversion coefficients range between 0.01 and 0.1 pg C per cell, with which we obtain up to 60% biomass yield from the added compounds. We have been analyzing the flow cytometric data of the complex natural bacterial communities to infer cell volume and cell mass for proper estimation of kinetic parameters.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O28

Characterization of a large 14-kb operon involved in conjugative transfer of ICElc in *Pseudomonas knackmussii* B13

A Vucicevic; J van der Meer

University of Lausanne, Department of Fundamental Microbiology, Lausanne, Switzerland

The Integrative and Conjugative Element ICElc of *Pseudomonas knackmussii* B13 is a mobile element carrying genes for chlorocatechol metabolism, enabling the host to completely degrade 3-chlorobenzoate (3-CBA). ICElc conjugation is initiated in 3-5% of individual cells in stationary phase, which will go through the development of a transfer competence state. Here we study regulation of expression of a 14-kb long gene cluster on ICElc (named the 81655 operon), which is implicated in the conjugative process.

Expression of the 81655 operon measured by microarray and RNAseq studies is the highest among all ICElc genes and is 60-fold upregulated in stationary phase. Expression of a single copy 81655 promoter-egfp gene insertion in *P. knackmussii* B13 is limited to 3% cells in stationary phase, indicating it belongs to the bistable transfer competence regulon. Interestingly and despite high transcript abundance, translation of the 81655 operon is rather poor. Here we test the hypothesis that 81655-mRNA forms a secondary structure that occludes the ribosome binding site, leading to the low translation rates. *P. knackmussii* B13 derivative strains were constructed carrying single copy 81655 promoter-egfp insertions with different mutations in the 5'UTR of the 81655 mRNA that might destabilize the secondary structure. Results show that not only some mutations increased EGFP fluorescence intensity, suggesting improved translation, but also larger subpopulation sizes of cells expressing mutated 5'UTR 81655 promoter. This indicates that the 5'UTR of 81655 contains sequence motifs important for relaying the bistable regulon.

References:

Stolz, A., Busse, H. J. & Kampfer, P. *Pseudomonas knackmussii* sp. nov. International journal of systematic and evolutionary microbiology 57, 572-576, doi:10.1099/ijs.0.64761-0 (2007).

Reinhard, F. & van der Meer, J. R. Life history analysis of integrative and conjugative element activation in growing microcolonies of *Pseudomonas*. Journal of bacteriology 196, 1425-1434, doi:10.1128/JB.01333-13 (2014).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O29

A small microbial community for the degradation of a pollutant

P Piccardi; S Mitri

UNIL-University of Lausanne

Manufacturing activity is unfortunately often associated with the production of toxic wastes, which are endangering both our health and the environment. Bioremediation, where microbes degrade polluted products, represents a great opportunity to solve this ecological problem in a low-cost and eco-friendly way. In our research, we are studying how microorganisms digest pollutants from metal-working fluids (MWF), a coolant and lubricant employed in the manufacturing industry. From previous research [1, 2], we obtained a synthetic bacterial community consisting of five strains capable of degrading MWF compounds. In this poster, I show the methods that we established to accurately and repeatedly determine the bacterial abundance in the MWF ecosystem and, in parallel, to evaluate the reduction of the pollution load. Our preliminary results show that the five-species community is more efficient at detoxifying MWF compared to when each species is cultivated alone. Interestingly, it seems that competition between the five species is significant. During our analysis, we also noticed the presence of biofilms. To have a better understanding of the spatial organization of the five strains within them, we are tagging them with fluorescent proteins. In this context, we already observed that the spatial structure can differ depending on which of the five species is present. Together, these observations suggest that bacterial interspecies interactions are important in determining the dynamics within this simple ecosystem. The next and exciting goal of this project is to elucidate why this system works and how we can deliberately interfere with it to make it more powerful and efficient. This research promises to offer new tools for designing microbial communities that could also serve in different domains, ranging from agriculture to medicine.

[1] van der Gast CJ, Thompson IP (2014) US Patent No. 8,703,475 B2

[2] van der Gast CJ, Knowles CJ, Starkey M, Thompson IP (2002) Selection of microbial consortia for treating metal-working fluids. J Industr Microbiol & Biotech 29:20-7



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O30

Microbial degradation pathways of sulfonamides and the presence of resistance genes in soil

B Kolvenbach¹; R Ji²; P Corvini¹

(1) Fachhochschule Nordwestschweiz, Hochschule für Life Sciences;

(2) Nanjing University, School of the Environment

Aims.

In Jiangsu province, intensive breeding of poultry makes large use of sulfonamides and traditionally farmers apply manure on agricultural fields as fertilizer. As the presence of even trace amounts of these antibiotics has been shown to foster the propagation of sulfonamide resistance genes (1), there is an interest in a better understanding of their fate and the propagation of sulfonamide resistance genes in soil. Previous studies have investigated the biodegradation of sulfonamides in the environment, finding that similar processes, driven by similar microorganisms, are occurring in various compartments, such as soil and activated sludge from wastewater treatment plants (2-5).

The aim of this project is to examine the fate of sulfonamides in manure-fertilized soils, the role of sulfonamide-degrading bacteria and possible implications on the abundance of genes known to confer sulfonamide resistance.

Methods.

Pristine soils and those heavily amended with poultry manure will be compared in a multi-disciplinary approach. Sulfonamide degradation and eventually mineralization will be assessed by means of radiolabelled sulfonamides in both batch tests and long-term lab-scale flow-through and lysimeter experiments. Metabolites will be identified in order to elucidate possible alternative sulfonamide degradation pathways. If present, novel sulfonamide degraders will be isolated and characterized. Additionally, the presence of both genes related to sulfonamide degradation and those related to resistance against sulfonamides will be assessed by quantitative PCR.

Conclusion.

Considering the current global initiative to target the spread of antibiotic resistance, knowledge on microbial pathways degrading sulfonamides in the environment is of great interest. It may even influence the design of future antimicrobial compounds, e.g. by including breaking points for facilitated degradation after their application.

References:

1. Heuer et al. Environ Microbiol 2007;9:657
2. Tappe et al. Appl Environ Microbiol 2013 :79 :2572
3. Topp et al. J Environ Qual 2013 :42 :173
4. Ricken et al. Appl Environ Microbiol 2013 :79 :5550
5. Herzog et al. BMC Microbiol 2013 :13 :276

Acknowledgements:

This project is funded in the frame of the SSSTC program.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O31

Comparison of bacterial communities from different stages of wastewater treatment

M Rosikiewicz¹; S Courtois²; S Aeby¹; G Medema³; L Hornstra³; B Galofre Porcar⁴; M Paraira Faus⁴; J Loret²; G Greub¹

(1) University Hospital Lausanne;

(2) SUEZ;

(3) KWR;

(4) Aigües de Barcelona

Aims:

The study was conducted in order to evaluate influence of wastewater treatment on microbial composition and presence of antibiotic resistance genes.

Methods:

The microbial profile of samples from different stages of wastewater treatment from 5 plants situated in France, Spain and Netherlands were investigated using 16S rRNA amplicon sequencing method and direct metagenomic approach.

Results:

The bacterial communities of raw wastewater samples were dominated in more than 90% by three major phyla: Proteobacteria, Bacteroides and Firmicutes. The water treatment procedure leads to substantial alteration of bacterial profiles with commonly observed reduction of bacteria belonging to Firmicutes phylum, changes in relative abundance of different classes of Proteobacteria and marked increase of abundance of less well studied phyla like Planctomycetes, Acidobacteria, Chloroflexi, Parcubacteria, Saccharibacteria, Gracilibacteria and Verrucomicrobia. On the level of genus we observed, among others, the decreased abundance of Faecalibacterium, Acinetobacter, Comamonas and Acidovorax and increased proportion of uncultured genera of family Neisseriaceae and Comamonadaceae, and Candidatus genera like Microtrix, Accumulibacter and Competibacter. The abundance of genus Arcobacter decreased after treatment in case of two Spanish plants where it was the most abundant genus present in raw wastewater, while in case of water treatment plants from France and Netherlands we observed substantially increased proportion of this genus after treatment. Our preliminary results of phylogenetic composition of bacteria inferred from direct metagenomic approach shows high consistency with profiles obtained with amplicon 16S rRNA study. We also observed decreased number of sequencing reads that match antibiotic resistance genes in libraries from treated water in comparison to raw wastewater samples.

Conclusions:

The analysis revealed that sewage treatment significantly modify bacterial profiles and successfully eliminate majority of antibiotic resistance genes present in raw wastewater.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O32

Bacterial communities and methanotrophy in anoxic lake waters

G Su

University of Basel, Biogeochemistry

The anaerobic oxidation of methane (AOM) with nitrate/nitrite as the terminal electron acceptor could play an important role in mitigating methane emissions from lacustrine environments to the atmosphere. We investigated AOM in the water column of the two hydrodynamically contrasting basins of Lake Lugano, Switzerland. The South Basin (Figino) undergoes seasonal stratification with the development of a benthic nepheloid layer and anoxia during summer, while the North Basin (Gandria) is permanently stratified. Both basins accumulate large amounts of CH₄ in the water column below the chemocline where maximum activities of methane oxidation were detected (0.18 μM/d in Figino and 0.08 μM/d in Gandria). We performed ¹⁴CH₄-label incubation experiments with concentrated biomass from anoxic layers of both basins, which were amended with nitrate/nitrite and we found 43-86% enhanced AOM rates after 32 days. In addition, depth-resolved analysis of the microbial communities in the water column of Gandria revealed the presence of Methyloirabaliaceae (a family known to perform nitrate/nitrite-dependent AOM), Methylococcaceae (type I methanotrophs) as well as Crenothrix (aerobic methanotrophs of the Methylococcales cluster); whereas in Figino only Methylococcaceae and Crenothrix were found. Interestingly, in situ methane oxidation rates in Figino were strongly correlated with the relative abundance of Methylococcaceae, while in Gandria Methyloirabaliaceae and Methylococcaceae represented the most abundant methanotrophs at depths where the maximum methane turnover was observed. We show that aerobic and anaerobic methanotrophs coexist below the permanent chemocline of the hydrodynamically stable North Basin where nitrate/nitrite-dependent AOM may contribute substantially to the overall CH₄ consumption. Our data from the South Basin, however, demonstrate that a dynamic mixing regime with seasonal anoxia does not support the development of stable populations of slow-growing Methyloirabaliaceae, even when the chemical conditions seem to be favorable for nitrate/nitrite-dependent AOM.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O33

Dynamics of Organotrophic and Chemolithotrophic Denitrification in the Water Column of the Meromictic North Basin of Lake Lugano

J Tischer; E Giglio; G Su; MF Lehmann; J Zopfi
 University of Basel

Lakes are important ecosystems where reactive nitrogen (N) species are removed from inland waters. Particularly, in redox transition zones of permanently stratified lakes, a variety of microbial processes occur in close vicinity, including nitrification, (nitrifier-) denitrification and anammox. Classical organotrophic denitrification and the potentially underestimated sulfur (S) dependent chemolithotrophic denitrification are important nitrate removal processes. The meromictic north basin of Lake Lugano represents an anthropogenically-influenced ecosystem, where a dominance of S-oxidizing denitrifiers over chemotrophic denitrifiers in the water column has been proposed, at least during some periods of the year. Within this context, nitrate isotopes can be used to characterize different denitrification pathways/metabolisms. Using a combination of biogeochemical and microbiological approaches, we aimed at studying (i) the seasonal dynamics of (and controls on) the different modes of denitrification, (ii) the identity of the responsible N-transforming microorganisms, and (iii) the isotopic fingerprints of organo- vs. lithotrophic nitrate reduction. Results from several incubation experiments show varying contributions of chemotrophic vs. S-driven denitrification, depending on water column depth, season, and availability of organic matter. The assessment of the general microbial diversity via high-throughput sequencing of 16S rRNA genes, as well as the analysis of N-transformation genes and nitrate isotopes will help to disentangle the different co-occurring and interdependent N-transformation metabolisms and to understand better the N-removal processes in Lake Lugano.

Wenk CB. et al. *Limnol Oceanogr* 2013;58:1



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O34

Assessment of Bacteria and Archaea in Metalworking Fluids Using Massive Parallel 16S rRNA Gene Tag Sequencing

P Küenzi¹; A Rüfenacht¹; N Di Maiuta²

(1) Blaser Swisslube AG;

(2) microSTECH AG

Aims

As water-miscible metalworking fluids (MWFs) provide a suitable basis of life for microorganisms, the majority are preserved by biocides. „Bio-concept” fluids on the other hand are bactericide-free, which intentionally leads to substantial bacterial populations. Earlier publications suggested that the diversity in MWFs is generally low, but these studies were largely based on heterotrophic plate counts. The aim was to explore bacterial and archaeal diversity in in-use metalworking fluids using high-throughput sequencing in absence and presence of PMA that allows differentiation between intact and physically damaged cells.

Methods

Mineral-oil based in-use “bio-concept” and preserved MWFs were collected world-wide from systems applying a wide range of metalworking operations. Genomic DNA was isolated using the PowerSoil® DNA Isolation Kit (MO BIO Labs). PMA treatment was performed [1] and amplicon libraries were generated as described elsewhere [2,3,4]. Fusion primers were generated from the bacterial universal primer pair EUB8m_f and EUB515_r to amplify 16S rRNA hypervariable regions V1, V2 and V3. Amplification of archaeal DNA was performed using primer pair oMT095/096, producing a 480 bps fragment [5,6].

Results

Samples from both fluid types were chosen: A median of 51 OTUs at genera level were detected per sample, but only 13 were present at or above 1.0% of the total population in any PMA-treated sample. *Acinetobacter* spp. and *Pseudomonas* spp. were the only OTUs detectable in every sample analyzed with a median abundance of 0.14% and 90.11% in “bio-concept” and 0.51% and 36.59% in preserved fluids, respectively. As *Pseudomonas* spp. was dominating in most samples, we resolved this genus on the species level and found the *P. oleovorans/pseudoalcaligenes* group to predominate. We also looked for archaea and detected *Methanobrevibacter* spp. in 2 of 78 samples analyzed.

Conclusion

We established that diversity is low and bacterial populations are mainly dominated by the *Pseudomonas* spp. We propose that they easily gain access through the water supply, and then propagate comfortably in the bactericide-free environment of “bio-concept” fluids whereas preservation generally represses growth, thus provoking a more limited, but unidirectional diversity. A role for the detected archaea has yet to be assigned but we suggest that they might survive in anaerobic and acidic zones of biofilms, but not in the MWF itself.

References

- [1] Nocker A et al. *Appl Environ Microbiol* (2007) 73: 5111.
- [2] Dethlefsen L et al. *PLOS Biol* (2008) 18: e280.
- [3] Lauber CL et al. *Appl Environ Microbiol* (2009) 75: 5111
- [4] Margulies M et al. *Nature* (2005) 437: 376
- [5] Klindworth A et al. *Nucleic Acids Res* (2013) 41: e1.
- [6] Takahashi S et al. *PLoS One* (2014) 9: e105592.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O35

Mycelia promote bacterial activity in dry and oligotrophic environments by hyphal transport and provision of water and nutrients

A Worrich; H Stryhanyuk; N Musat; S König; T Banitz; F Centler; K Frank; M Thullner; H Harms; H Richnow; A Miltner; M Kästner; LY Wick

Helmholtz Centre for Environmental Research UFZ

Fungal-bacterial interactions enable many ecosystem processes in natural and constructed environments. However, cooperative interactions of fungi and bacteria under shared environmental stress remain elusive. Here we used a spatially resolved synthetic microbial ecosystem to elucidate whether mycelia reduce bacterial water and nutrient stress in an else dry and oligotrophic microhabitat. We found that mycelia (*Fusarium oxysporum*, *Lyophyllum* sp. Karsten, *Pythium ultimum*) enabled the germination and subsequent growth of bacterial (*Bacillus subtilis*) spores in the vicinity of the hyphae. Using a unique combination of Time of Flight- and nanoscale Secondary Ion Mass Spectrometry (ToF- and nanoSIMS) coupled with stable isotope (¹³C,¹⁵N,¹⁸O) labeling, we interrelated spore germination to hyphal transfer of water, carbon and nitrogen. This work provides for the first time direct experimental evidence for the stimulation of bacterial activity by mycelial supply of scarce resources in dry and nutrient-free environments. We propose that mycelia may stimulate bacterial activity and thus contribute to sustain ecosystem functioning in dry and oligotrophic environments.

Worrich A. et al. Nat. Comm. (in press)



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O36

The plant-beneficial root-colonizer *Pseudomonas protegens* CHA0 persists in insects throughout different developmental stages and can be transmitted to new host plants

P Flury¹; P Vesga²; A Dominguez-Ferreras²; C Tinguely²; R Kleespies³; C Keel⁴; M Maurhofer²

(1) ETH Zürich (ETHZ)/ University of Lausanne;

(2) ETH Zürich (ETHZ);

(3) Julius Kühn-Institute, Federal Research Centre for Cultivated Plants;

(4) University of Lausanne

Aims

The discovery of insecticidal activity in root-colonizing pseudomonads, best-known for their plant-beneficial effects, raised not only questions about a possible application of this trait in pest control, but also about the ecological relevance of insects as alternative hosts for these bacteria. Since soil bacteria are limited in their inherent abilities of dispersal, insects as vectors might be welcome vehicles to overcome large distances. This study investigates whether *Pseudomonas protegens* CHA0 exhibits biocontrol activity against a root-feeding insect pest and whether insects could serve as a vector for dispersal of this plant-beneficial rhizobacterium.

Methods

In pot experiments larvae of the cabbage fly were feeding on roots colonized by *P. protegens* CHA0-gfp2. Emerging adult flies were exposed to new, bacteria free plants, imitating the natural situation in which flies search for new host plants to deposit eggs. Bacterial numbers (in roots and insects) and insect survival were monitored. Persistence of *P. protegens* CHA0 in insects throughout different life-stages was further assessed in additional insect species and investigated by microscopy methods.

Results

Our experiments demonstrate that the plant-beneficial and insecticidal bacterium *P. protegens* CHA0 can be transmitted from the roots of one plant to the roots of another plant by the cabbage root fly, *Delia radicum*. After ingestion by *D. radicum* larvae, CHA0 persisted inside the insect host until the pupal stage, a phenomenon, which was additionally observed in three other insect species belonging to different insect orders and exhibiting different degrees of susceptibility towards the bacteria. Next, CHA0 was successfully transmitted to a fresh plant host by emerging flies, as indicated by high levels of root colonization in the transmission microcosms. Because *D. radicum* is a major root pest on various cabbage crops, we further assessed the biocontrol potential of CHA0 against this insect species. No effect on insect survival could be detected, but morphological defects observed in parts of adult *D. radicum* indicate a negative impact of *P. protegens* CHA0 on insect development.

Conclusions

In summary, our results suggest that insects may play an important role as alternative habitats for certain plant-beneficial pseudomonads, not only by acting as hosts, but also as vectors for dispersal.

We thank Dylan Bär, Anja Taddei, Jana Schneider and Cornelia Ullrich for technical assistance and advice.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O37

Metabolic Regulation of Selenium and Sulfur Methylation by *Pseudomonas* sp.

Y LIU

FHNW

The trace element selenium (Se) which acts as a component of major metabolic pathways is essential for animals and humans health. However there are abundant Se deficiencies worldwide and millions of people may be affected by the accompanying endemic diseases (Fairweather-Tait et al. *Antioxid Redox Signal* 2011;14:1337). Methylation and subsequent volatilization is an important Se cycle process in natural environments which may lessen available Se in soils, ultimately limiting its entry into the food chain (Winkel et al. *Environ. Sci. Technol.* 2012;46:571). Se methylation is mostly regarded as a detoxification process for organisms since volatilization decreases the intracellular Se content. Hence most studies of Se volatilization were performed using Se concentrations 103 - 106 fold higher (mg / L) than those commonly found in the environment. A recent study revealed efficient volatilization from a natural wetland with very low Se concentrations (ng / L) (Vriens et al. *Nat. Commun.* 2014;5:3035). It seems implausible that these concentrations may induce any specific enzymes for Se detoxification. As a consequence, Se volatilization fluxes based on laboratory experiments using high Se concentrations may have limited relevance for cycling outside of Se contaminated environments. Here, we conducted a Se methylation study using a *Pseudomonas* strain at low $\mu\text{g} / \text{L}$ range of selenite. Methylated Se compounds were quantified by headspace SPME-GC-MS and the speciation and concentrations of Se oxyanions were measured by IC-ICP-MS. Transcriptional profiles of this strain responding to selenite exposure were analyzed by RNA-seq. During incubation the original selenite were depleted within log phase in all of the treatments. The bacteria culture produced both volatile organosulfides and organoselenides of which the predominant compounds were DMDS, DMDSe and their exchange product DMSeS. Although there is no significant difference of bacterial growth between all of the treatments, sulfur methylation was inhibited in higher selenite groups while promoted in lower selenite groups. In the higher selenite treatment, more than half of the original Se was methylated, whereas the methylation efficiency was less than one percent in lower selenite treatment.

References

- Fairweather-Tait, S. J., Bao, Y., Broadley, M. R., Collings, R., Ford, D., Hesketh, J. E. & Hurst, R. 2011: Selenium in Human Health and Disease. *Antioxidants & Redox Signaling*, 14, 1337-1383.
- Vriens, B., Lenz, M., Charlet, L., Berg, M. & Winkel, L. H. E. 2014: Natural wetland emissions of methylated trace elements. *Nature Communications*, 5, 3035.
- Winkel, L. H. E., Johnson, C. A., Lenz, M., Grundl, T., Leupin, O. X., Amini, M. & Charlet, L. 2012: Environmental Selenium Research: From Microscopic Processes to Global Understanding. *Environmental Science & Technology*, 46, 571-579



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O38

Microbial transformation pathways of sulfonamides in the aquatic environment

M Majewsky¹; BA Kolvenbach²; K Kroll²; A Timm³; HE Kohler⁴; PF Corvini²

(1) Heidelberg University Hospital;

(2) University of Applied Sciences Northwestern Switzerland;

(3) Karlsruhe Institute of Technology (KIT);

(4) Eawag, Swiss Federal Institute of Aquatic Science and Technology

Aims.

Sulfonamide antibiotics are widely used in human and veterinary medicine and consequently detected ubiquitously in the aquatic environment. Their mechanism of action and metabolism in humans has extensively been studied, however, many questions remain unanswered to date in view of their microbial degradation.

This study aimed to assess and elucidate the degradation pathways of sulfonamides. In this context, we hypothesized to use formed metabolites as indicators for the sulfonamide removal performance of wastewater treatment plants (WWTPs). Moreover, the abundance of sulfonamide degrading bacteria and their relationship to prevailing sulfonamide and other nutrient concentrations was investigated.

Methods.

Five WWTPs were comprehensively monitored two-weekly for 19 sulfonamides and metabolites for 18 months in influent and effluent along with sulfonamide mineralization batch tests (14C based), qPCR, metagenomics, and wastewater parameters. In parallel, spiked batch tests of sulfonamides and metabolites were carried out in order to identify the formed metabolites as well as their degradation and formation kinetics.

Results.

The 18 month time-series of influent concentrations shows that only three out of 19 sulfonamides are constantly entering the WWTPs, namely sulfamethoxazole, its acetylated metabolite, and sulfapyridine. Of the metabolites expected to be formed during sulfonamide degradation, only sulfanilamide was detected in the effluents. The metabolites indicated four possible pathways including two types of hydrolysis, ipso-substitution, and conjugation reactions. This was in detail elucidated in a series of batch tests.

Mineralization efficiencies of the sampled sludges were shown to be both dependent on the WWTP they had been taken from and the season they had been taken in. Interestingly, there were no correlations between mineralization performance of sludges in batch tests and the actual full-scale removal efficiencies of the WWTPs.

Conclusion.

It could be conferred that at least three microbial degradation pathways take place in parallel. The degradation kinetics differ greatly between the sulfonamides suggesting a dependency on their different molecular substitutions. It could be observed that the dominating sulfonamide, sulfamethoxazole, was transformed and back-transformed in and from at least four metabolites. The types of metabolites are particularly interesting due to their demonstrated antibacterial activity.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O39

Probing the evolutionary robustness of anti-virulence treatments

C Rezzoagli; D Wilson; M Weigert; S Wyder; R Kümmerli
University of Zurich

Aims:

Antivirulence treatments are therapeutic options that inhibit the expression or functioning of bacterial virulence factors. They are considered an efficient and evolutionarily robust way to manage infections because they exert weaker selection for resistance than conventional antibiotics. However, empirical evidence for the evolutionary robustness of anti-virulence treatments is still controversial. Here, we approach this issue by probing the evolutionary robustness of two anti-virulence treatments, gallium and flucytosine, which both target the iron-scavenging pyoverdine of *Pseudomonas aeruginosa*.

Methods:

We carried out an experimental evolution in human serum as an ex-vivo model and screened evolved lines for the evolution of resistance phenotypes both at the population and the individual clone level. Finally, to understand the genetic basis of potential resistance mechanisms, we sequenced the whole genome of evolved clones from the different treatment regimes.

Results:

We show that robustness of an anti-virulence treatment is dependent on its specific mode of action. When treating bacteria with flucytosine, a drug that requires enzymatic activation to inhibit siderophore synthesis within the cell, resistance can readily arise and spread. Genetic analysis confirmed that the inactivation of the gene *upp*, whose product converts flucytosine into its active form, is responsible for the evolution of resistance against the fluorinated pyrimidine. Conversely, there were fewer routes to resistance when treating bacteria with gallium (III), a metal ion that neutralizes secreted siderophores acting outside the cell, because standard resistance mechanisms, such as drug efflux and inactivation, cannot operate. Clones with partial gallium resistance had mutations in global transcriptional regulator, which lead to increased pyoverdine production or the upregulation of alternative iron-uptake systems.

Conclusion:

Our work highlights that anti-virulence approaches are not evolution proof per se, instead it is the mode of action, especially the extra-cellular inactivation of virulence factors and the fact that the drug cannot be easily degraded or modified, that confers evolutionary robustness.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O40

Metabolic cooperation in a sulfamethoxazole-degrading consortium composed by *Achromobacter denitrificans* PR1 and an unculturable bacterium from the Microbacteriaceae family

AC Reis¹; M Čvančarová²; K Kroll²; BA Kolvenbach³; PF Corvini²; OC Nunes¹

(1) Faculty of Engineering of University of Porto;

(2) Fachhochschule Nordwestschweiz, Hochschule für Life Sciences (FHNW, HLS);

(3) Fachhochschule Nordwestschweiz, Hochschule für Life (FHNW, HLS)

In this study, we aimed at characterizing the metabolic pathway for sulfamethoxazole (SMX) degradation by a microbial consortium composed by *Achromobacter denitrificans* PR1 and an unculturable member of Actinobacteria (strain GP). Furthermore, the role of each strain in the degradation of this micropollutant was also assessed.

LC-MS/MS was used to identify the metabolites produced by the consortium during the degradation of SMX in 16O₂ or 18O₂-containing atmosphere. The abundance of each strain during degradation of SMX was assessed by 16S rRNA gene clone library and by Fluorescence In Situ Hybridization (FISH). The metagenome of the microbial consortium was sequenced by Illumina Miseq and the genome of strain GP was obtained and functionally annotated.

Degradation of SMX by the consortium resulted in the accumulation of 3-amino-5-methylisoxazole and revealed new products resulting from the parallel mono-hydroxylation of the aniline moiety at two different positions: ipso (adjacent to the sulfonyl group) and ortho/meta. Additional side-reactions were also detected comprising a NIH shift and a possible Baeyer-Villiger rearrangement. Studies in 18O₂-containing atmosphere revealed that the degradation is initiated by introduction of a single hydroxyl group in the aniline moiety, suggesting that the responsible enzyme has monooxygenase activity. The unculturable bacterium was found to have highest 16S rRNA sequence similarity (96.75%) to *Leucobacter luti* RF6(T), indicating affiliation to the Microbacteriaceae family. Pure cultures of strain PR1 feed with SMX and spent-supernatant of the consortium were unable to degrade this antibiotic even after prolonged incubation time (2 weeks). Furthermore, strain GP was found to grow only in co-culture with strain PR1 and SMX degradation also only occurs in the same conditions, suggesting a possible metabolic cooperation between the strains. The metagenome data was mined for possible metabolic dependency of strain GP and the results will provide further insights into the relationship between these strains.

Our results suggests that degradation of SMX by this microbial consortium is initiated by an enzyme with monooxygenase activity. Furthermore, unspecific hydroxylation of the substrate suggests that SMX may not be this enzyme's primary substrate. Also, the metabolic cooperation within this consortium will provide valuable insights at different levels of microbial ecology of sulfonamide degrading strains.

Ana Reis is recipient of a PhD scholarship from the Portuguese Foundation for Science and Technology (FCT, grant reference: SFRH/BD/95814/2013). This work was financially supported by projects: (i) Beyond pollutant removal - understanding the biochemical mechanism of sulfonamide degradation in wastewater and the role of ipso-substitution (Swiss National Science Foundation grant No. 160332); (ii) POCI-01-0145-FEDER-006939 (LEPABE – UID/EQU/00511/2013) funded by the European Regional Development Fund (ERDF), through COMPETE2020 - Programa Operacional Competitividade e Internacionalização (POCI) and by national funds, through FCT; (iii) NORTE-01-0145-FEDER-000005 – LEPABE-2-ECO-INNOVATION, supported by North Portugal Regional Operational Program (NORTE 2020), under the Portugal 2020 Partnership Agreement, through ERDF.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O41

Spread of antibiotic resistance markers in Lake Ceresio and tributary rivers

F Mauri; A Demarta

University of applied sciences of Southern Switzerland

Antibiotic resistant bacteria and antibiotic resistance genes (ARGs) are considered important environmental contaminants but little is known yet about their fate in the environment or about how they affect the natural microbial populations. In the environment, especially in water affected by anthropic activities (discharge of hospital, urban and industrial waste water treatment plant and agricultural run-off), antibiotic determinants may become part of the environmental gene pool, may spread horizontally, and may move back to humans and animals via contaminated food and drinking water. However, there are scarce information about the presence and distribution of antibiotic resistance genes in aquatic ecosystems. The aim of this work was to observe if anthropic activities could influence the bacterial populations naturally present in water environments in terms of antibiotic resistance. To reach our objective we investigate the presence of antibiotic resistance genes and antibiotic resistance bacteria in water samples collected from Lake Ceresio and some tributary rivers.

We analyzed water samples by PCR to investigate the presence or absence of integrase gene and of 10 antibiotics resistance genes that confers resistance to the major classes of antibiotics used in clinical and veterinary (β -lactams, tetracycline, quinolones and sulphonamides). After the qualitative screening we quantified resistance genes using qPCR. Total count of viable cells in all water samples were evaluated by flow-cytometry and agar plate count. To investigate the prevalence of mesophilic resistant bacteria, selected colonies were identified by MALDI-TOF and plated on selective agar.

We found at least four quantifiable genes *sulII*, *qnrS*, *tetA*, *blaTEM* (104 – 101 copies/ml) especially in the rivers influenced by waste water treatment plants and in the lake near the potable water uptake plant. *Pseudomonas* spp., *Acinetobacter* spp., *Stenotrophomonas* spp., *Aeromonas* spp., *Enterobacteriaceae* and *Flavobacteriaceae* were the resistant bacterial population frequently found in water samples.

Our results indicate that rivers and lake are reservoir of ARGs and could be considered the ideal settings for the transmission of resistance from environmental non-pathogenic or potentially pathogenic bacteria to human pathogens. The presence of resistance genes near potable water uptake plant needs further investigations to evaluate the risk of their diffusion by drinking water.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Prokaryotic Biology

O42

Explosive cell lysis is involved in the biogenesis of staphylococcal “public goods” and membrane vesicles

D Losa¹; L Turnbull²; R Cavaliere²; B Raymond²; S Djordjevic²; C Whitchurch²

(1) University of Geneva / The itthree Institute, University of Technology Sydney;

(2) University of Technology Sydney

The Gram-positive *Staphylococcus aureus* is a major cause of nosocomial and community-acquired infections. Many of those develop into chronic infections and are difficult to eradicate due to the formation of biofilm - complex multi-cellular structures that enhance antibiotic resistance and evasion of human defences. Biofilms are characterized by cell attachment to a surface and encapsulation in self-produced extracellular polymeric substances, comprised of extracellular DNA (eDNA), membrane vesicles (MVs) and bacterial cytosolic proteins referred as “public goods”. These extracellular products enhance the structural integrity of biofilm matrix, protect the community from antimicrobial agents and contribute to virulence and chronic infection.

Since the mechanism of “public goods” production by *S. aureus* has not been fully elucidated yet, we monitored the expansion of Staphylococcal interstitial biofilms by time-lapse microscopy and the release of eDNA using a cell impermeant fluorescent dye specific for DNA. We found that occasionally individual cells within a cluster lysed and at the same time eDNA was produced. Two type of cell lysis were observed: slow lysis, in which DNA remained partially trapped inside dead cells and after several minutes it was released into the extracellular space; and explosive cell lysis, a rapid event occurring within seconds characterized by efficient eDNA released in bursts. Super-resolution microscopy (OMX 3D-SIM) also revealed the presence of MVs at the sites of eDNA smears. The main enzyme involved in cell lysis in *S. aureus* is the peptidoglycan hydrolase Atl. We found that mutants lacking atl showed significantly impaired explosive cell lysis, and were abrogated in the production of eDNA and MVs in interstitial biofilms. Finally, we also found that staphylococcal cell lysis accounts for MV production in response to antibiotic stress and is important for biofilm formation. This is the first time that the peptidoglycan hydrolase Atl has been shown to account for MV release and that Gram-positive cell lysis has been monitored live at the single cell level. Deciphering these mechanisms driving biofilm formation is essential to develop new approaches for treating bacterial infections and fighting antibiotic resistance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O43

Characterization of cell Division mechanisms in Chlamydia-related bacteria *Waddlia chondrophila*

F Bayramova; N Jacquier; G Greub

Lausanne University Hospital (CHUV)

Waddlia chondrophila is an intracellular obligate bacterium, member of the Chlamydiales order and known as a causative agent of abortion in ruminants and miscarriage in humans. The division of Chlamydiales is conserved among its members and differs from the classical division machinery by lacking the homologue of the bacteria division organizer FtsZ and certain division proteins homologues. Another specificity of the Chlamydiales order is an atypical peptidoglycan, which is required for chlamydial division. We recently described septal proteins, MreB, RodZ and NlpD, which play important roles in *W. chondrophila* cell division and in peptidoglycan remodeling.

The aim of this study is to characterize the composition of the chlamydial division machinery, describe the exact role of the septum proteins and their interactors involved in chlamydial division formation and peptidoglycan remodelling.

To get a complete picture of the chlamydial division assembly, interactors of the described septal protein RodZ were investigated by Yeast-two-hybrid assay. Several promising putative interactors of RodZ and peptidoglycan were selected. Gene expression and transcription pattern of the potential candidates were assessed by quantitative reverse transcription PCR (qRT-PCR). The recruitment and localization of the putative interactors during bacteria division was investigated using immunofluorescence imaging technique. Furthermore, the proteins were heterologously overexpressed in *E. coli* in stringent conditions and induced impaired bacterial growth and partial proliferation inhibition, along with morphology defects. Above mentioned results indicate that these proteins might be involved in bacterial proliferation. More work will help us to better characterize the exact role of these proteins in chlamydial division and in peptidoglycan remodelling.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O44

Metabolic regulation of the aspartate pathway in *M. tuberculosis* and its vulnerability during host infection.

E Hasenoehrl; DR Sajorda; L Berney-Meyer; M Berney
 Albert Einstein College of Medicine

Background:

A major constraint for developing new TB drugs is the limited number of validated targets for inhibitors. We are in the process of exploiting a largely untapped drug target space that is unique to *Mycobacterium tuberculosis*. Intracellular pathogens are faced with a variety of host-induced mechanisms that deplete essential nutrients from the pathogen-containing vacuole. Emerging evidence suggests that many intracellular pathogens manipulate the phagocytes to regain access to those nutrients. In contrast, *M. tuberculosis* is not able to scavenge essential amino acids in the host and relies on its own biosynthetic machinery. We are exploiting this metabolic vulnerability to identify new drug targets.

Methods & Results:

One of the most promising pathways is aspartate family amino acid biosynthesis. Using metabolomics, transcriptomics, animal experiments and conditional knockdowns we have identified several vulnerable enzymes that are involved in the biosynthesis of lysine, diaminopimelate, threonine, isoleucine, methionine and S-adenosylmethionine. Inactivation of these enzymes leads to rapid killing of *M. tuberculosis* in vitro and in mouse models during active and latent infection. Interestingly, the mechanisms of killing vary between different enzymes and are governed by interference with feedback control mechanisms leading to depletion or accumulation of key metabolites. Studying these regulatory mechanism at the cellular level unraveled an intricate web of allosteric and transcriptional control that is needed to maintain pathway homeostasis and guarantee balanced growth of *M. tuberculosis*.

Conclusions:

Our study provides new insights about *Mtb*'s intracellular lifestyle and metabolic regulation during unbalanced growth, and identifies several new promising drug targets.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O45

Population genomics of multidrug-resistant *Mycobacterium tuberculosis* strains from Georgia

S Gygli; L Jugheli; S Borrell; M Reinhard; S Gagneux

Swiss Tropical and Public Health Institute, University of Basel

Aims

The incidence of human tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), has decreased steadily over the past decades. However, the evolution of drug-resistant Mtb is threatening attempts to contain the epidemic. In 2015, 480000 cases caused by multidrug-resistant Mtb variants (resistant to rifampicin and isoniazid) were reported, mainly affecting the developing world and countries of the former Soviet Union.

The reproductive fitness of drug resistant Mtb variants is a key factor in determining if drug-resistant variants can be maintained (transmitted) in the population. It has long been assumed that drug resistance comes at a universal cost, reducing the pathogen's fitness –i.e. reducing the average number of secondary cases generated. However, some mutations appear to carry now or very low costs(1,2).

Understanding bacterial characteristics involved in the evolution and maintenance of drug resistance in the population is important for designing novel interventions. We are primarily interested in assessing whether drug-resistant Mtb variants are found in transmission clusters and identifying genetic determinants associated with such clusters. We are exploring these questions in a dataset from Georgia, a high-incidence country for multidrug-resistant Mtb.

Methods

The population-based collection of ~1000 Mtb whole genome sequences from Georgia consists of all phenotypically multidrug-resistant Mtb strains isolated during 2011 – 2013. We are assessing bacterial characteristics associated with transmission by comparing genome sequences of strains found in transmission clusters (defined by small genetic distance between strains) with unclustered strains. Furthermore, we are applying genome scan approaches to detect loci which are involved in local adaptation, whilst controlling for the strong population structure observed in Mtb(3).

Results/Conclusions

Preliminary analysis of the dataset revealed that a considerable proportion (80 %) of drug-resistant Mtb strains are clustered with at least one other strain, based on a clustering cut-off of ten single nucleotide polymorphisms. This indicates that in Georgia, the majority of multidrug-resistance in Mtb is not due to de novo evolution, but rather due to recent transmission. Furthermore, the presence of clustered strains in the dataset allows the possibility of studying genetic determinants involved in clustering and transmission. The final results of this ongoing study will be presented.

References

1. Gagneux S et al. Science 2006;312:1944
2. Borrell S et al. Evol Med Public Heal 2013;2013:65
3. Luu K. et al. Mol Ecol Resour 2017;17:67



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O46

In vivo envelope stress response of Salmonella

P Maturana, Dirk Bumann

Biozentrum of the University of Basel

The Salmonella envelope is involved in uptake of nutrients, excretion of waste products, sensing of external stimuli, and secretion of virulence factors. During infection, it is attacked by host effector mechanisms. Envelope stress is sensed by several different pathways, and among these the extracytoplasmic stress response sigma factor E (σ^E , encoded by *rpoE*) seems to be particularly relevant for systemic virulence in mice based on the strongly attenuated phenotype of an *rpoE* mutant (Humphreys et al, IAI 67, 1560). σ^E regulates expression of more than 300 genes including well-known virulence factors such as HtrA. However, it remains unclear which of these genes are particularly relevant for envelope maintenance and what kind of physiological problem they solve.

To address these questions, we generated a transposon library in a Salmonella Typhimurium *rpoE* strain. We used a transposon that carries 2 outward facing promoters with different strengths which could activate expression of genes around the transposon insertion site, in addition to disrupting genes hit by insertion. We infected BALB/c mice with this library and prepared spleen post infection. Whereas the parental *rpoE* strain was completely cleared from infected mice, several clones of the library could be isolated demonstrating partial rescue of virulence. Interestingly, one region carrying genes associated with outer membrane porins were hit in different dominating clones. Individual virulence tests revealed that these clones were able to survive for at least 5 days at high levels but did not show net in vivo growth. We used proteomics and clean mutations to demonstrate that the lack of one major porin enabled Salmonella *rpoE* to survive in mouse spleen.

We also performed another round of transposon mutagenesis on the rescued Salmonella strain to test if we can further rescue virulence. After 2 in vivo passages, we obtained 4 different clones that regained considerable in vivo growth capabilities. Intriguingly, some of the affected genes have also links to outer membrane porins. We are currently further analyzing these clones but the data already suggest that regulation and/or repair of outer membrane permeability determinants might be central to in vivo envelope stresses and associated virulence requirements. Together, our results indicate that surprisingly just a few genetic alterations can partially rescue the very strong attenuation caused by a defective major sigma factor with a large regulon.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O47

Treatment with various stress stimuli causes diverse persistent forms in *Waddlia chondrophila*

A Scherler; N Jacquier; C Kebbi-Beghdadi; G Greub

CHUV Lausanne, Université de Lausanne

Members of Chlamydiales order, such as *Chlamydia trachomatis* or *C. pneumoniae*, are human pathogens which can cause chronic infections. Apparition of chronic diseases might be due to the presence of enlarged and persistent forms named aberrant bodies (ABs). In vitro, presence of stimuli, such as β -lactam antibiotics or interferon-gamma, induces the formation of ABs. Clarke et al. have shown previously that each AB accumulates more than 16 chromosomal copies in *Chlamydia trachomatis* treated with penicillin, indicating that AB formation might be due to continuous DNA replication without division. However, mechanisms of ABs formation are poorly described.

In order to assess the impact of diverse stress stimuli on ABs morphology and DNA replication, we used *Waddlia chondrophila*, an obligate intracellular bacterium known to potentially cause miscarriage in humans, as model organism. ABs morphology and potential differences in DNA content were assessed by immunofluorescence and quantitative PCR.

According to their morphology and their number per host cell, two main subtypes of ABs could be defined: (i) small and multiples ABs versus (ii) large and rare ABs. DNA replication of *W. chondrophila* was generally not affected by the different stimuli, confirming the hypothesis that ABs are the consequence of continuous replication without division. Furthermore, the presence of distinct ABs subtypes seems to reflect different mechanisms of ABs formation. However, further studies are necessary to understand the molecular mechanisms involved in ABs formation. Indeed, the comprehension of biological mechanisms triggering the development of this persistent stage may reduce treatment failure against chronic chlamydial infections.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O48

Type VI Secretion System sheath subunits are added at the end distal to the basplate

A Vettiger; J Winter; L Lin; M Basler
 University of Basel

Aims:

The bacterial Type VI secretion system (T6SS) belongs to the family of contractile phage tails, including bacteriophages and R-type pyocins. These nanomachines translocate proteins into target cells by means of physical force generated during transition of the sheath from an extended high-energy state to a contracted low-energy conformation. This triggers the ejection of the inner Hcp tube associated with a sharp tip and effector proteins.

Currently, regulation of T6SS sheath length and assembly into extended state are unclear. Importantly, it is unknown how and where new subunits are incorporated into the growing sheath polymer.

Methods:

To determine the mechanism of sheath subunit incorporation, we photobleached an assembling polymer in ampicillin induced spheroplasts of *Vibrio cholerae* and monitored the localization and intensity of the bleached area over time.

Results:

Here, we show that the T6SS remains active in ampicillin induced *V. cholerae* spheroplasts lacking cell wall. Imaging of sheath dynamics showed that the sheath length correlates with increased cell diameter of spheroplasts and may reach up to several micrometers. This allowed us to analyze sheath assembly after partial photobleaching and show that subunits are exclusively added to the sheath at the end that is distal from the baseplate and cell envelope attachment.

Conclusions:

The observed mode of sheath assembly is likely common for all phage-like contractile nanomachines because structures and connectivity of sheath subunits are conserved. Overall, our study shows that large cells lacking cell wall may be used to study systems, which are intrinsically challenging to visualize by light microscopy in small bacterial cells.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O49

The Fitness and Mutation Rate Estimates of Fluoroquinolone-resistant *Mycobacterium tuberculosis*

R Castro; A Trauner; A Ross; J Feldmann; M Reinhard; S Borrell; S Gagneux

Swiss Tropical and Public Health Institute

Aims:

Fluoroquinolones (FQ) are being tested as a core drug in novel, first-line treatment regimens for tuberculosis (ref. 1,2,3). However, little is known on the evolution of FQ-resistant *Mycobacterium tuberculosis* (Mtb). FQ targets DNA gyrase, a conserved enzyme which modulates DNA topology. We hypothesize that FQ-resistance-conferring mutations in *gyrA*, which encodes a DNA gyrase subunit, will have fitness costs. Furthermore, the Mtb genetic background has been shown to have clinical implications, including differing associations with drug-resistance (ref. 4). Thus, we also hypothesize that the genetic background modulates phenotypes related to FQ-resistance, including FQ-susceptibility and in the rate of FQ-resistance acquisition.

Methods:

Cell growth assays were performed to estimate in vitro fitness costs. Optical density was measured every 24h, and growth rates were calculated during exponential phase.

Differences in FQ-susceptibility were determined by the colorimetric, microplate-based Alamar Blue assay (ref. 5).

Rates of FQ-resistance acquisition were determined using the Luria-Delbrück Fluctuation Analysis (ref. 6). Parallel cultures at mid-log phase were plated on specified drug. The mean number of mutations per culture was calculated using a MSS-Maximum Likelihood Estimate (MSS-MLE).

Results:

We demonstrate that the GyrAD94G mutation confers a low in vitro cost, regardless of genetic background, while GyrAG88C generally confers a high cost. No costs for FQ-resistance were observed for a Lineage 2 “Beijing” strain. We observe that strains from a Lineage 2 “Beijing” background were most susceptible (defined by having the lowest average minimum inhibitory concentration) to FQ, while strains from the Lineage 1 background were least susceptible.

Fluctuation analyses demonstrate that a Lineage 1 strain acquired FQ-resistance at a higher rate than a Lineage 2 strain. Furthermore, GyrAD94G mutants had a higher rate of streptomycin-resistance acquisition than wild-type strains, regardless of genetic background.

Conclusions:

FQ-resistance fitness costs are determined by the type of *gyrA* mutation and the Mtb genetic background. The genetic background also affects FQ-susceptibility levels, and FQ-resistance acquisition rates. Mutations in *gyrA* may also increase rates of further drug-resistance acquisition. Our findings have implications for future tuberculosis treatment regimens using FQ as a core drug.

References

- 1 Gillespie SH. et al. N Engl J Med 2014;371:1577
- 2 Jindani A. et al. N Engl J Med 2014;371:1599
- 3 Merle CS. et al. N Engl J Med 2014;371:1588
- 4 Coscolla M, Gagneux S. Semin Immunol 2014;26:431
- 5 Franzblau SG. et al. J Clin Microbiol 1998;36:362
- 6 Luria SE, Delbrück M. Genetics. 1943;28:491



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O51

The Yin and Yang of Type VI Secretion Regulation in Pandemic *Vibrio cholerae*

LC Metzger; M Blokesch

Global Health Institute, School of Life Sciences, Swiss Federal Institute of Technology Lausanne (EPFL)

Type VI secretion systems (T6SSs) are syringe-like nanomachines used for both interbacterial killing and intoxication of eukaryotic cells. T6SSs are widely distributed and some Gram-negative bacteria even contain multiple copies of the system. The pathogen *Vibrio cholerae* harbors only a single T6SS, which has been extensively studied for its structural aspects. In contrast, the underlying regulatory network is less well understood. A recent study showed that the T6SS is part of the natural competence regulon in pandemic *V. cholerae* strains and activated by the transformation regulator TfoX [1]. Here, we identified the TfoX homolog TfoY as a second regulator of T6SS, which itself is translationally controlled by the secondary messenger c-di-GMP. Importantly, despite activating the same T6SS, the co-regulated pathways and the associated phenotypes differ significantly for these two regulators. Hence, we suggest that *V. cholerae* uses its sole T6SS in response to diverse environmental cues and for distinctive outcomes: either to foster horizontal gene transfer through the forced release of prey-derived DNA or as part of a defensive reaction against predators [2].

References

- [1] Borgeaud S. et al., *Science* 2015; 347:63
- [2] Metzger L.C. et al., *Cell Rep* 2016;15:95



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O52

Identification of a unique cell cycle regulator in *Streptococcus pneumoniae* using CRISPRi, Tn-seq and en masse GFP-localization screening

J Veening

University of Lausanne

Several systems connecting chromosome segregation with division have been identified in model bacteria, but such a cell-cycle regulator has not been identified in *Streptococcus pneumoniae*. Based on results from transposon-sequencing (Tn-seq), we refined the list of essential genes in *S. pneumoniae* strain D39. Next, we created a knockdown library targeting 348 potentially essential genes by CRISPR interference (CRISPRi) and show a growth phenotype for 254 of them (73%). Since several general and conserved cell cycle proteins present in the pneumococcus (e.g. EzrA, FtsZ, FtsK) typically localize at mid-cell, we hypothesized that important cell-cycle regulators would have a similar localization pattern. To identify such proteins, we systematically tagged every essential protein of unknown function to a monomeric superfolder-GFP. By combining Tn-Seq, CRISPRi and GFP-localization data, we identified CcrZ (Cell Cycle Regulator protein Z), which co-localizes with FtsZ and is highly conserved in Streptococci. Marker frequency analysis, suppressor analysis and chromosome labeling experiments showed that, in absence of CcrZ, daughter chromosomes are not properly segregated prior to cell division. Together, these findings indicate that CcrZ acts as a link between DNA replication, chromosome segregation and cell division. Future work is aimed at revealing the mechanisms underlying cell-cycle control by CcrZ.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O53

Dissecting the bistable switch controlling mobility of an integrative and conjugative element in *Pseudomonas*

N Carraro¹; F Delavat²; X Richard³; S Sulser¹; JR van der Meer¹

(1) University of Lausanne;

(2) Institut Européen de la Mer;

(3) University of Fribourg

Mobile genetic elements play a pivotal role in the rapid evolution of bacterial genomes, favoring the fast acquisition of new functions, and the colonization of new niches. ICEclc is an integrative and conjugative element (ICE) of *Pseudomonas knackmussii* B13 that confers the ability to degrade and metabolize toxic chlorinated compounds. ICEs exhibit a curious lifestyle, remaining stably maintained as an integrated element in the bacterial chromosome, and occasionally excising as a circular molecule that can transfer to other cells by conjugation. The mechanisms controlling this intriguing bistable (ON/OFF) switch remain unclear. Previous work uncovered a three-gene operon coding for the repressor MfsR and the activator TciR that control early steps of the regulatory circuitry governing ICEclc activity. Further investigation using RNA-seq combined to single-cell fluorescent reporter assays revealed the presence of six bistable promoter regions controlling excision/integration as well as putative regulation and conjugative transfer functions of the ICEclc. Further experiments showed that induction of bistable expression in absence of the complete ICE can be achieved by a 6-kb ICEclc-borne fragment. The first trigger is TciR, which controls expression of an activator named BisR (bistability regulator), a new key regulator of ICEclc activation. BisR is essential to propagate the activation signal by stimulating transcription of downstream genes, which triggers a positive feedback loop leading to activation of the ICEclc mobility genes and subsequent conjugative transfer. Analytic and stochastic mathematical modeling predict that the positive feedback loop is decisive for bistable control of ICEclc behaviour. ICEclc bistability regulation network may have general significance for control of other related ICEs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O54

Use it or lose it: What do the genomes of *Kurthia* tell us about the evolution of sporulation in Firmicutes?

S Filippidou¹; T Junier²; D Poppleton³; T Wunderlin¹; N Jeanneret¹; I Palmieri¹; J Blom⁴; S Johnson⁵; P Chain⁵; S Gribaldo³; P Junier¹

- (1) University of Neuchâtel;
- (2) Swiss Institute of Bioinformatics, Lausanne;
- (3) Institut Pasteur, France;
- (4) Justus-Liebig-University Giessen;
- (5) Los Alamos National Laboratory

Firmicutes is one of the most abundant phyla and it is considered to have colonised every habitat on Earth. It consists of monoderm and diderm representatives, as well as of spore-forming and non-spore-forming (asporogenic species). On a phylogenetic level, endospore-formation and outer membrane are paraphyletic characteristics, making the understanding of the evolution of these traits in Firmicutes extremely challenging.

Here, we present the discovery of sporulation in a strain belonging to the genus *Kurthia* (*Kurthia* str. 11kri321), and we provide evidence for a sporulation in other four species of the same genus (*Kurthia huakii*, *K. massiliensis*, *K. senegalensis*). We also re-evaluate the phylogenetic affiliation of *Kurthia*. Finally, we provide insights on the evolution of sporulation and outer membrane in Firmicutes.

Induction of sporulation using various environmental and chemical parameters was tested in the four *Kurthia* species. The genome of *Kurthia* str. 11kri321 was sequenced and analysed for sporulation and outer membrane specific genes. A comparative analysis of the genomes of *Kurthia huakii*, *K. massiliensis*, and *K. senegalensis* was also performed. Finally, phylogenomic analysis was undertaken to verify the position of the genus *Kurthia* among Firmicutes.

Our results show that the genus *Kurthia* is a cryptosporulant lineage, rather than an asporogenic one. Genomic and phylogenetic analysis further supports a common origin for sporulation in Firmicutes, but show that derived models of sporulation exist. Furthermore, morphological data suggest that *Kurthia* might represent an intermediate state between an ancestral diderm and a derived monoderm, in which the outer membrane does not vary in composition. Our findings pave the path for further investigation of cryptosporulant or asporogenic species, the origin of sporulation and the evolution of the cell wall in Firmicutes.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O55

How a molecular killing device can drive bacterial evolution in *Vibrio cholerae*

N Matthey; M Blokesch

Swiss Federal Institute of Technology Lausanne (EPFL)

Natural competence for transformation is a mode of horizontal gene transfer (HGT), which involves the direct uptake and integration of exogenous DNA. Natural competence therefore represents an important driving force for bacterial adaptation and evolution. In the aquatic environment, the facultative human pathogen *Vibrio cholerae* resides either as a free-living bacterium or associated with zooplankton. The exoskeleton of the latter contains the polysaccharide chitin, which induces the natural competence program in *V. cholerae*.

We recently demonstrated that the type VI secretion system (T6SS) of pandemic *V. cholerae* strains is induced upon growth on chitinous surfaces [1]. The T6SS, which resembles an inverted contractile phage tail, is a killing device, as it delivers effector proteins into adjacent cells. A successful attack will provoke the lysis of the targeted prey and the release of the prey's genetic material. Such released DNA is subsequently available for absorption by the naturally competent predator. In this study, we tested the two hypotheses that 1) the T6SS can, by increasing the pool of DNA present in the environment, enhance evolution in *V. cholerae* and 2) that prey-released genetic material is superior to freely available DNA for the transfer of larger DNA fragments.

Reference

[1] Borgeaud S. et al. *Science*, 2015:347:63.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Virology

O56

Composition of the subcellular molecular environment of coronavirus replicase complexes identified by proximity labelling

P Vkovski¹; S Braga Lagache²; C Simillion³; M Heller²; V Thiel¹

(1) Institute of Virology and Immunology;

(2) Mass Spectrometry and Proteomics, University of Bern;

(3) Interfaculty Bioinformatics Unit and SIB Swiss Institute of Bioinformatics, University of Bern

The replication of coronaviruses and other positive-stranded RNA viruses is supported by a network of modified endomembranes. Coronaviruses have been shown to derive endoplasmic reticulum membranes into double-membrane vesicles and convoluted membranes to which RNA synthesis and replication are closely associated. However, the molecular mechanisms that entail the generation of coronaviral replicative organelles remain elusive.

We employed a biotin ligase-based proximity labelling approach to identify host factors and molecular pathways involved in the establishment and sustainment of coronavirus replicative structures. We generated a recombinant Murine Hepatitis Virus (MHV) expressing, from the ORF1a replicase gene, a promiscuous biotin ligase (BirA*) fused to non-structural protein 2. This method allows for identification of both viral and host factors found in the vicinity of the viral RTC during infection. Western blot and immunofluorescence analyses revealed that BirA* indeed becomes imbedded in the replication and transcription complex (RTC) of infected murine fibroblasts. Furthermore, biotinylated viral and host factors located in close proximity to the viral RTC could be efficiently affinity purified. Subsequent mass spectrometry identification revealed a set of host proteins significantly enriched over control infections. Importantly, all viral replicase gene products were biotinylated and efficiently detected after affinity purification, thereby confirming that the coronaviral RTC is indeed composed of the 16 non-structural proteins complexed together. Moreover, enriched factors comprise a catalogue of putative proviral factors that assist the establishment of viral replication, and antiviral proteins, such as cytosolic sensors and intrinsic restriction factors that target the coronavirus RTC and trigger the first steps of an antiviral innate immune response. Specifically, bioinformatic analysis pointed to the implication of factors mediating ER to Golgi-associated vesicle transport, which are currently under investigation as to their contribution during the viral replication cycle. Finally we demonstrated that this method is suitable for monitoring differential recruitment of cellular factors towards mutant virus replication complexes, thereby providing insights into the biology of coronavirus replication structures.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O57

MxB is an interferon-induced restriction factor of human herpesviruses

M Cramer; R Walker; FD Franzoso; N Caduff; C Gujer; M Bauer; K Boucke; F Steiner; T Kucera; A Zbinden; C Münz; C Fraefel; UF Greber; J Pavlovic
 University of Zurich

The human myxovirus resistance proteins MxA and MxB are expressed upon stimulation with type I and type III interferons (IFNs) in response to viral infection. While MxA is well-known to elicit potent antiviral activity against many viruses, MxB has long been unrecognized to serve any antiviral function. Recently, a potent antiviral effect of MxB against human immunodeficiency virus type 1 (HIV-1) and other primate lentiviruses has been discovered. Evolutionary analyses then indicated that MxB is likely to exert inhibitory activities against additional viruses. To test this hypothesis, we selected herpesviruses as representatives of nucleus-replicating large DNA viruses. Here, we demonstrate a specific role of MxB against different human herpesviruses.

To first assess the function of MxB against herpesviruses, we utilized T98G cells as a model due to their high endogenous MxB expression. Then, we tested MxB in absence of other IFN-induced genes by generating A549 cells stably overexpressing MxB (A549-MxB).

We observed that silencing of MxB expression in IFN-treated T98G cells partially rescued herpes simplex virus type I (HSV-1) replication. Moreover, HSV-1 replication was strongly inhibited in A549-MxB cells as compared to control cells. In line with this, HSV-1 replication in A549-MxB cells recovered to a large extent after siRNA-mediated knock-down of MxB. Similar results were obtained using HSV-2 and Kaposi's sarcoma-associated herpesvirus (KSHV). Immunofluorescence-, electron microscopy- and PCR-based experiments then revealed that MxB acts early upon infection, i.e. after tegument dissociation and cytoplasmic trafficking of capsids but prior to delivery of herpesviral DNA to the nucleus and subsequent viral immediate-early gene expression. Finally, mutational analyses showed that amino-terminal residues as well as the GTPase function of MxB are required to exert anti-herpesviral activity.

In conclusion, our data indicate that MxB interferes with nuclear entry of herpesviral DNA, suggesting a gatekeeper function of MxB at the nuclear pore.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O58

Homodimerisation-independent cleavage of dsRNA by a pestiviral endoribonuclease

C Lussi; M Schweizer

Institute of Virology and Immunology

Bovine virus diarrhea virus (BVDV), a pestivirus in the family Flaviviridae, causes persistent infection (PI) in cattle by entering the fetus early in gestation prior to development of adaptive immunity. In addition, the inhibition of interferon (IFN) type I synthesis plays an important role in escaping innate immunity and is a prerequisite for the birth of PI calves. Thus, pestiviruses express two IFN antagonists: the non-structural protein Npro that inhibits IFN induction in infected cells by degrading IRF-3, and the soluble glycoprotein Erns, which cleaves extracellularly added dsRNA prior to activation of non-infected cells.

Erns, which forms covalently-linked homodimers, belongs to the T2 family of ribonucleases that preferably degrade ssRNA. Accordingly, the crystallographic structure of the catalytic domain of Erns did not provide evidence for dsRNA to fit into the active site. Thus, it may well be envisaged that Erns independently cleaves both strands of dsRNA, which would be in accordance with the fact that ssRNA is degraded by this viral RNase more efficiently than dsRNA. Here we show that wild-type and a monomeric mutant, but not an RNase-inactive mutant form of Erns, were able to degrade RNA in a DNA/RNA hybrid as well as in a methylated RNA/RNA hybrid with the DNA and the methylated RNA strand being resistant to degradation. The fact that monomeric Erns is similarly able to cleave dsRNA and the RNA strand of the two different hybrids support our model that Erns might be a 'nicking endoribonuclease' degrading ssRNA within double-stranded substrates. This efficiently prevents the activation of pattern recognition receptors (PRRs) and helps to maintain a state of innate immunotolerance in PI animals.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O59

The small compound inhibitor K22 displays broad antiviral activity against different members of the Flaviviridae family and offers potential as pan-viral inhibitor

S Pfaender¹; R Züst²; H Stalder¹; J Portmann¹; O Engler²; M Alves¹; V Thiel¹

(1) Institute of Virology and Immunology;

(2) SPIEZ Laboratory

The family of Flaviviridae encompasses several highly relevant viruses, which cause widespread morbidity and mortality throughout the world. We have previously described the identification of a small compound inhibitor, K22, which exerts a potent antiviral activity against a broad range of coronaviruses upon targeting of the membrane-bound RNA replication step. To analyze the antiviral spectrum of this inhibitor we tested several members of the Flaviviridae family, which encode positive-strand RNA genomes and are assumed to replicate in tight association with reorganized host cell membranes. Virus-induced host cell membrane reorganization is believed to be an evolutionary conserved strategy which facilitates highly efficient viral genome replication and might at the same time contribute to evasion from host cell defense mechanisms. We could show that K22 is able to inhibit replication of several members of the Flaviviridae family, including emerging zika virus and yellow fever virus. It is tempting to speculate that K22 exerts its broad antiviral activity against several positive-strand RNA viruses via the same mechanism thereby presenting an attractive target for the development of a pan-viral inhibitor. Future studies analyzing the exact mode-of-action might present the first step towards generation of a new antiviral drug which could be used for broad therapeutic use in animals or humans.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O60

Characterization of HIV Latency and Reactivation by Single-Cell RNA-Seq

M Golumbeanu¹; S Cristinelli²; S Rato²; M Munoz²; N Beerenwinke¹; A Ciuffi²

(1) ETH Zurich;

(2) CHUV Lausanne, Université de Lausanne

Aims

Despite effective treatment, HIV can persist in part in latent reservoirs, considered today as a major obstacle towards HIV eradication. Understanding the switch between HIV latency and viral production from infected cells is essential for HIV cure strategies aiming at purging these reservoirs.

The high heterogeneity of HIV infected cells results in a further challenge to target and reactivate latent cells.

This work aims at (i) characterizing transcriptional heterogeneity during HIV latency and reactivation and (ii) identifying transcriptional programs leading to successful reactivation of HIV expression, thereby facilitating screening of future Latency Reactivating Agents (LRA) candidates.

Methods

Primary human CD4⁺ T cells were infected with an HIV-based vector encoding the gfp reporter gene. Successfully infected GFP⁺ cells were sorted by FACS, expanded in culture and allowed to return to a resting (latent) state. Latently infected cells were, either left untreated (control), or exposed to the histone deacetylase inhibitor SAHA (LRA), or to T-cell receptor (TCR)-mediated stimulation. Cells were monitored for GFP expression upon reactivation. RNA-Seq from bulk as well as Fluidigm-isolated single cells was performed for each condition. Transcriptional heterogeneity of HIV and host cell gene expression was explored using various statistical models.

Results

RNA-Seq data from 249 single cells was successfully obtained, correlating with each other ($r > 0.38$) as well as with bulk cells ($r > 0.63$). Principal component analysis identified two distinct clusters of cells, both within resting (control or SAHA-treated) and TCR-activated cells. Quantitative analysis of GFP expression of TCR-activated cells further defined two cell subsets, expressing low and high levels of GFP protein respectively. Differential expression analysis between the two clusters identified a set of 440 genes that were upregulated in the GFP^{high}-expressing subpopulation.

Conclusion

Single cell analysis of latently infected cells identified two distinct subpopulations in the resting, latent, state. Upon TCR-mediated stimulation, these two subpopulations behaved differently, expressing different levels of GFP and putatively differential susceptibility to reactivation. A better understanding of determinants leading to LRA-specific successful reactivation of HIV expression is essential for HIV eradication strategies.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O61

Dynamics of Proteo-Transcriptomic Response to HIV-1 Infection

M Golumbeanu¹; S Desfarges²; S Ferreira-Rato²; C Hernandez³; M Quadroni³; P Mohammadi¹; A Telenti⁴; N Beerenwinkel¹; A Ciuffi²

(1) ETH Zurich;

(2) Lausanne University Hospital and University of Lausanne;

(3) University of Lausanne;

(4) J. Craig Venter Institute

Aims

Upon cellular invasion of the host T-cell, the extent of HIV-1 infection success is elicited by a continuous interplay of host-virus interactions. During the 24-hour-long replication cycle, HIV-1 enters the host cell, integrates its genome, and utilizes the host cellular machinery in order to produce new virions. The continuous interaction between the virus and the host results in a complex palette of host transcriptional and proteomic changes. In this work, we present a comprehensive analysis aiming to define the dynamic proteo-transcriptomic response of the cell to infection and understand the key molecular players maintaining a balance between host support for viral replication and host defense response restricting infection.

Methods

A series of high-resolution, large-scale measurements have been conducted in uninfected and infected CD4+ T cells. Precisely, SupT1 cells were either mock-treated or infected with a VSV-G pseudotyped HIV-based vector (NL4-3ΔEnv/GFP) at a high multiplicity of infection to reach universal infection. Cells were collected at 6h intervals during 24h. Both mock and HIV-infected samples were subjected to transcriptome analysis with mRNA-Seq, and proteome and phosphoproteome analysis using SILAC.

We developed an elaborate bioinformatics analysis to process, model and extract valuable biological knowledge from the produced time-series omics data. Precisely, using a clustering method based on Gaussian mixed-effects models, implemented and available as an R Bioconductor software package, host genes were stratified based on their gene expression temporal patterns at RNA, protein and phospho-protein levels.

Results

This analysis allowed extracting multi-omics, dynamic expression signatures specific to HIV-1 infection, revealing a considerable amount of infection-specific post-transcriptional regulatory programs and indicating novel HIV dependency and restriction factors. Furthermore, our data analysis results are freely available through an interactive, stand-alone web application.

Conclusion

Integrated time-series proteo-transcriptomic analyses of HIV-1 and mock-infected T-cells define host response to HIV-1 infection. This study exposes novel regulation mechanisms of virus-host interaction through an integrated temporal investigation of different omics measurements. Our study constitutes a valuable resource since, to our knowledge, it is the first available time-series experiment conducted at the three omics levels.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O62

Spontaneous activation of latent HIV-1 promoters is linked to the cell cycle as revealed by a stable dual-fluorescence HIV-1-based vector

YL Kok¹; S Schmutz²; A Inderbitzin³; A Kelley³; M Shilaih³; V Vongrad³; R Kouyos³; C Berens⁴; H Günthard³; K Metzner³

(1) University Hospital Zürich;

(2) University of Zurich;

(3) University Hospital Zurich;

(4) Friedrich-Loeffler-Institut

Long-lived latently HIV-1-infected cells are rare in patients and they represent a major barrier to cure. We developed a dual-fluorescence HIV-1-based vector and verified its capacity to model HIV-1 infection and latency in SUP-T1 cells. This vector consists of Cerulean and mCherry cassettes to simultaneously report for the activity of the HIV-1 promoter (active vs latent) and to identify transduced cells, respectively. In addition to a constitutive promoter, the mCherry cassette is protected from position-effect variegation by a pair of flanking genetic insulators, thus ensuring its constitutive expression. The protective effects of these genetic insulators were demonstrated by long-term (up to 394 days post transduction) stable fluorescence profiles in all cell populations, i.e. those representing active and latent HIV-1 infections. In contrast, cells transduced with a vector variant without genetic insulators displayed a gradual decrease in fluorescence over time. Analysis of 1,948 unique vector integration sites confirmed its reproducibility of HIV-1 integration site patterns. Next, we sorted and analysed monoclonal cells representing latent infections and observed that the responsiveness of the HIV-1 promoter to TNF- α and SAHA activation differed among these monoclonal cells with different vector integration sites and integrity of the Cerulean cassettes. Interestingly, some latent monoclonal cells constantly exhibited a small population of cells with a spontaneously activated HIV-1 promoter among the majority that maintained a latent phenotype. Flow cytometric analysis showed that a higher fraction of cell populations with a spontaneously activated HIV-1 promoter was in the S and G2 phases of the cell cycle. We subsequently examined the transcriptomes of these two cell populations for differentially expressed genes from five latent monoclonal cells (two integration sites). Consistently, genes whose products are known to be required for cell cycle progression with some also involved in the HIV-1 replication cycle, e.g. NEAT1, EGR1, FOSB, and Y RNA, were upregulated in cell populations with a spontaneously activated HIV-1 promoter. On the other hand, cell populations that maintained a latent phenotype had more expression of RN7SK, the RNA product of which is known to sequester the transcription factor for HIV-1, P-TEFb. Taken together, our model revealed that the spontaneous reactivation of latent HIV-1 promoters is linked to the cell cycle.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O63

The impact of HIV-genetics on imprinting antibody responses: the Swiss 4.5K Screen

R Kouyos¹; P Rusert²; C Kadelka²; A Marzel¹; T Liechti³; M Schanz³; H Ebner³; H Günthard¹; A Trkola³

(1) Universitätsspital Zürich;

(2) University of Zurich;

(3) Institute of Medical Virology

Aims

A key question on the way towards an HIV-1 vaccine is the impact of viral genetics on the neutralization response: Will a given HIV-1 envelope immunogen induce the same antibody specificities across vaccinees? Here we addressed this by studying the influence of virus genetics in potential transmission pairs identified within a recently conducted systematic screen of HIV-1 neutralization in 4,484 individuals (Swiss 4.5K Screen; Rusert, Kouyos Nat Med 2016).

Methods

Potential transmission pairs were defined based on HIV-1 pol gene phylogenies and plasma neutralization activity against a 14 multi-clade pseudovirus panel and IgG1 binding activity to 13 HIV-1 Gag and Env antigens was determined. Neutralization and binding similarity within pairs was determined by Spearman correlation and a range of shuffling tests and similarity measures.

Results

We identified 303 potential transmission pairs within the Swiss 4.5K Screen. For 7/14 pseudoviruses, we observed a significant ($p < 0.05$) positive within-pair correlation of neutralization. The average Spearman correlation coefficient across all 14 viruses was weakly ($p = 0.11$) but significantly ($p_{\text{shuf}} < 0.001$) positive, even after controlling for viral subtype, infection-length and ethnicity ($p_{\text{shuf}} < 0.001$). Similarly, binding to different HIV-1 antigens was significantly correlated within pairs (average $p_{\text{spear}} = 0.12$, $p_{\text{shuf}} < 0.001$). Notably, we found that two elite neutralizers (top 1% of neutralizers) formed a transmission pair and exhibited highly similar neutralization ($p_{\text{spear}} = 0.73$) and binding ($p_{\text{spear}} = 0.29$) fingerprints. To generalize this finding, we developed a systematic approach to identify pairs with similar neutralization and binding responses. Over a broad range of thresholds, this method identified significantly more candidate pairs than expected by chance suggesting that the similarity of antibody responses in these transmission pairs is due to viral genetic factors.

Conclusion

Our results indicate that viral genetic factors significantly affect the breadth and specificity of the antibody responses to HIV-1. A large proportion of this effect is likely due to the env gene. Not all bnAb Envs may carry the capacity to imprint identical Ab specificity, thus utilizing Envs from bnAb inducers with proven transferability of antibody reactivities as identified here may be the ultimate immunogen candidates to base vaccine design on.

Reference

Rusert, P., Kouyos, R. D., Kadelka, C., Ebner, H., Schanz, M., Huber, M., et al. (2016). Determinants of HIV-1 broadly neutralizing antibody induction. *Nature Medicine*, 22(11), 1260–1267. <http://doi.org/10.1038/nm.4187>



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O64

THE HUMAN BLOOD VIROME AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION INVOLVES PERSISTENT INFECTION BY HUMAN PEGIVIRUS

D Vu¹; S Cordey²; F Simonetta³; F Brito⁴; M Docquier⁵; L Turin²; E Boely⁶; C Van Delden⁷; A Pradier⁸; Y Chalandon⁹; E Roosnek⁵; EM Zdobnov⁴; S Masouridi-Levrat⁹; L Kaiser¹⁰

- (1) University of Geneva Hospitals, Geneva, Switzerland / University of Barcelona, Barcelona, Spain;
- (2) University of Geneva Hospitals, Laboratory of virology, Geneva, Switzerland / Faculty of medicine, Geneva, Switzerland;
- (3) University of Geneva Hospitals, Geneva, Switzerland / Stanford University, USA;
- (4) Swiss Institute of Bioinformatics, Faculty of medicine, Geneva, Switzerland;
- (5) Faculty of medicine, Geneva, Switzerland;
- (6) University of Geneva Hospitals, Division of Infectious diseases, Geneva, Switzerland;
- (7) University of Geneva Hospitals, Division of Infectious diseases, Geneva, Switzerland / Faculty of medicine, Geneva, Switzerland;
- (8) University of Geneva Hospitals, Hematology, Geneva, Switzerland;
- (9) Faculty of medicine, Geneva, Switzerland / University of Geneva Hospitals, Hematology, Geneva, Switzerland;
- (10) Geneva University Hospitals (HUG)

As commensal viruses are defined by the immunological tolerance afforded to them, immunomodulatory therapy may shift the demarcation between innocuous viral resident and disease-causing pathogen. Thus, the role of these seemingly inert viruses should be re-evaluated in the context of immunotherapy such as is received during hematopoietic stem cell transplantation (HSCT).

Using next-generation sequencing, we screened the plasma virome of 40 allogeneic HSCT patients 34 days post-transplantation. Anellovirus, human pegivirus (HPgV), polyomavirus (PyV) and herpes virus were most frequently identified. Among the 15 patients with herpes viruses (38%), we identified cytomegalovirus (n=11), Epstein-Barr (n=3), herpes simplex-1 (n=2), herpes-6b (n=1) and herpes-7 (n=1). Polyomaviruses included Merkel cell (n=18), BK-PyV (n=4), PyV-6 (n=3) and JC-PyV (n=1). Papillomavirus and adenovirus were identified in 11 and 2 patients respectively. While little is known about HPgV, it was as prevalent as herpes virus (35%, n=14), leading us to expand HPgV screening in a second cohort of 122 HSCT recipients. Here, HPgV was detected at high viral load in 40% of samples and persisted for up to one year post-transplantation. Approximately 15% of infections appeared after transplantation, indicating transmission by blood products. While comparisons between patients with or without HPgV infection did not reveal a significant difference in engraftment, survival, graft-versus-host disease or relapse; HPgV-infected patients tended to perform better in each of these outcomes.

Our results show that HPgV is a prevalent component of the HSCT blood virome, persisting for several months after transplantation and deserving special attention in further research on immune reconstitution.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O65

BK polyomavirus microRNA expression: Impact of rearrangement and Sp1 site mutation in the non-coding control region

F Martelli¹; Z Wu²; S Delbue³; F Weissbach²; MC Giulioi¹; P Ferrante³; HH Hirsch²; S Giannecchini¹

(1) University of Florence;

(2) University of Basel;

(3) University of Milan

Aims

BK Polyomavirus (BKPv) infects >90% of the human population without ill effects, but causes nephropathy or hemorrhagic cystitis in immunosuppressed patients. In transplant patients, virulent BKPv variants emerge that carry rearrangements or point mutations of the non-coding control region (NCCR) that alter transcription factor binding sites and confer increased replicative fitness and cytopathology. BKPv also encodes microRNAs that modulate viral replication in infected cells and may affect non-infected cells by trafficking in exosomes. This study aimed to explore the relationship between BKPv NCCR and exosomal microRNA expression that affect virus infectivity.

Methods

Quantitative real-time PCR has been employed to analyze circulating exosomal BKPv microRNA expression of 12 BKPv-positive urine samples from multiple sclerosis patients under natalizumab therapy. To further study the roles of BKPv NCCR and microRNA, BKPv variants including NCCR archetype carrying point mutations inactivating one Sp1 binding site (sp1-4) were selected to infect COS-7 cells as well as a more natural host primary renal proximal tubule epithelial cells (RPTECs).

Results

In 7 patients with rearranged NCCR, high BKPv loads but reduced microRNA expression were found. Conversely, BKPv viral loads in presence of high viral miRNA expression were found in 5 patients shedding BKPv with archetype NCCR. To dissect the link of NCCR configuration and microRNA expression, BKPv variants were studied in Cos-7 cells and in RPTECs. Indeed, BKPv carrying rearranged NCCRs exhibited higher DNA replication, but reduced microRNA expression compared to archetype NCCR BKPv. Moreover, BKPv NCCR sp1-4 mutation was functionally equivalent to rearrangement and showed downregulated microRNA expression.

Conclusion

These results provide new insights how BKPv NCCR activity crosstalks host cell factors and with viral microRNA in regulating the switch from early to late viral gene expression that govern viral persistence and disease in immunocompromised subjects.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O66

Virus transmission during kidney transplantation assessed by viral metagenomics of living donors and recipients

P Schreiber¹; V Kufner²; K Hübel¹; O Zagordi²; S Schmutz²; C Bayard¹; M Greiner¹; A Zbinden²; R Capaul²; J Böni²; T Müller¹; N Mueller¹; A Trkola²; M Huber²

(1) University Hospital Zurich;

(2) University of Zurich

Aims

Before kidney transplantation, donors and recipients are routinely screened for a number of active or latent viral infections using specific tests. Little is known about other, untested, apathogenic viruses a donor might be infected with and likely will transmit. Here, we aimed to characterize the viral metagenome of both the donor and the recipient using metagenomic sequencing at time of transplantation as well as up to one year after.

Methods

Recipients of kidney grafts and the corresponding donors were enrolled at the time of transplantation. Follow-up study visits for recipients were scheduled 4-6 weeks and 1 year thereafter. At each visit, plasma, urine and stool samples were collected and patients were evaluated for signs of infection or transplant-related complications.

For metagenomic analysis, blood and urine samples were enriched for viruses, amplified using an anchored random PCR system and sequenced using high-throughput metagenomic sequencing. Viruses detected by sequencing were confirmed using real-time PCR.

Results

We analyzed a total of 14 living kidney donor/recipient pairs with a follow up of at least 1 year. Post transplant routine virus diagnostics revealed 5 cases of Cytomegalovirus (CMV) replication with 2 recipients suffering from CMV colitis and 3 recipients with asymptomatic viral replication and 5 cases of BK polyomavirus infection in blood. In 4 recipients, throat swabs tested positive for respiratory viruses (either Influenza-, Rhino- or Coronavirus) and a blood sample of one recipient was positive for Human herpesvirus 2.

In addition to routine diagnostics, metagenomic sequencing detected JC polyomavirus (JCPyV) in urine of 5 recipients. Moreover, Torque teno virus (TTV) was found frequently in time points after transplantation, as expected in patients under immunosuppressive therapy. JCPyV was detected in urine of all 5 donors with JCPyV-positive recipients. Phylogenetic analysis so far confirmed that donor and recipient were infected with the same strain in 2 cases, suggesting a transmission from the donor.

Conclusion

Using metagenomic sequencing, we detected transmission of JCPyV from infected kidney transplant donors to the recipients in several cases. Future studies within larger cohorts, enabling the analysis of possible associations with relevant transplant outcomes, such as rejection, graft loss or death of the recipient, may help to define the relevance of the donor's virome for the recipient.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O67

Ranid herpesvirus 3 (RHV3), a novel amphibian herpesvirus associated with proliferative dermatitis in free ranging common frogs (*Rana temporaria*)

F Origgi¹; B Schmidt²; P Lohmann³; P Otten⁴; L Aguilar Bultet¹; E Akdesir¹; T Wahli¹; V Gaschen¹; M Stoffel¹

(1) University of Bern;

(2) KARCH & University of Zurich, Zurich, Switzerland;

(3) Private Pract.;

(4) FASTER SA

Aims

The aim of this investigation was the characterization of a proliferative skin disease observed in free ranging common frogs (*Rana temporaria*) associated with the presence of intralesional herpesvirus-like particles.

Methods

Complete macroscopic, microscopic and ultrastructural investigation (electron microscopy-EM) was performed in order to characterize the pathology of the skin disease shown by the frogs and the intralesional viral particles. Next generation sequencing was carried out to sequence the whole genome of the associated herpesvirus. Phylogenetic analyses were also performed.

Results

The affected frogs showed a proliferative dermatitis. Histologic examination revealed the presence of intranuclear eosinophilic to amphophilic inclusions in the thickened skin. EM demonstrated the presence of herpesvirus-like particles in the affected skin. The whole genome of the associated herpesvirus was obtained by next generation sequencing. The sequence showed similarities with that of two previously characterized amphibian herpesviruses, named Ranid herpesvirus 1 (RHV1) and -2 (RHV2), however, significant differences were also observed between RHV1 and 2 and the novel virus that was tentatively named Ranid herpesvirus 3 (RHV3). RHV3 contains all the classic elements that characterize the herpesviruses of the family Alloherpesviridae and several putative immunomodulatory genes. Phylogenetic analyses cluster RHV3 unambiguously within the genus *Batrachovirus* in the family *Alloherpesviridae*.

Conclusions

Here we report the identification of a previously unknown amphibian herpesvirus. This agent is associated with proliferative skin disease in free ranging common frogs. The investigation of RHV3 and of its associated pathology will be important for a better understanding of amphibian disease ecology and conservation.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O68

Incorporation of IFITM3 into influenza A virus particles leads to increased sensitivity to antibody-mediated virus neutralization

C Lanz; EE Müller; BG Hale; S Stertz; S Stertz
 University of Zurich

Interferon-inducible transmembrane proteins (IFITMs) are potent antiviral factors active against various viruses, including influenza A virus (IAV). Localizing to either the plasma membrane or endosomes, IFITMs block the entry of incoming viral particles. Recently, it has been found that IFITMs also get incorporated into the membrane of HIV virions upon budding, thereby decreasing their infectivity. Here, we report our findings on IFITM incorporation into IAV particles. Making use of IAV VLPs having the M1 protein fused to beta lactamase we show that IAV VLPs incorporated IFITM3 and were reduced in their entry capacity when IFITM3 was present in the VLP producing cell. Interestingly, this effect was alleviated in a dose-dependent manner when increasing amounts of HA were co-transfected into the VLP producing cells. While we also observed incorporation of IFITM3 into wildtype IAV particles via Western Blotting and electron microscopy studies of purified virus, we did not detect a reduction in virus infectivity associated with incorporation of IFITM3. However, preliminary results suggest that IAV grown in the presence of IFITM3 shows increased sensitivity to neutralization by hemagglutinin-directed antibodies, potentially compromising the virus in an in vivo situation.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O69

Dissecting the molecular mechanisms of airborne transmission of hantaviruses

G Torriani¹; S Rothenberger¹; J Mayor¹; G Zimmer²; N Tischler³; S Kunz¹; O Engler⁴

(1) Lausanne University Hospital and University of Lausanne;

(2) University of Bern;

(3) Fundació Ciencia & Vida;

(4) Spiez Laboratory

Aims:

In this study we seek to investigate the largely unknown mechanisms underlying cell entry of hantaviruses into polarized human respiratory epithelial cells. The identification of the cellular factor hijacked by hantaviruses in order to enter host cells is essential for the development of novel strategies to combat pathogenic hantaviruses.

Methods:

Since hantavirus cell attachment and entry are mediated exclusively by the viral envelope, we have developed a pseudotype platform based on a recombinant vesicular stomatitis (VSV) reporter virus. Human alveolar type II epithelial cells (A549), a classical immortalized tissue culture model for human respiratory epithelia, were treated with a combination of specific inhibitors and siRNA silencing against components of clathrin-mediated endocytosis or macropinocytosis-related pathways. Cells were then infected and luciferase activity measured after 20 hours to assess productive infection.

Results:

We established an efficient production system for VSV pseudotypes bearing the glycoprotein of the Old World prototypic hantavirus Hantaan virus (HTNV) and the South American Andes virus (ANDV). Our studies reveal significant inhibition of VSV-HTNVGP and VSV-ANDVGP entry into A549 cells in presence of amiloride drugs that target sodium-proton exchanges, which are implicated in macropinocytosis. Inhibition of both pseudoviruses also occurs in presence of compounds that disturb actin fiber dynamics, another essential feature of macropinocytosis. However, only VSV-ANDVGP entry is dependent on GTPases Cdc42 and Rac1 and their downstream effectors, which are fundamental component of the RTK-activated macropinocytosis signaling cascade.

Conclusion:

Our results using pseudoviruses provide first evidence for a role of macropinocytosis-related pathways in hantavirus entry into human respiratory epithelial cells with important virus-specific differences. These observations are currently followed up and will be validated using pathogenic hantaviruses in Spiez Laboratory.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Biofilm

O70

Investigation of microorganisms in aerobic granular sludge actively involved in biological phosphorus removal

A Gelb; J Maillard; C Holliger

Swiss Federal Institute of Technology (EPFL)

One of the aims of the treatment of domestic and industrial wastewater is the removal of phosphorus prior to discharge into the environment. Since phosphorus concentrations in wastewater exceed the requirement of bacterial growth, biological phosphorus removal is based on the ability of a group of microorganisms, named “Polyphosphate Accumulating Organisms” (PAO), to form large quantities of polyphosphate in their cells.

In this work, we are focusing on bacteria actively involved in the phosphorus removal in a lab scale bioreactor operated with aerobic granular sludge technology. This cost-effective and land-saving alternative to conventional activated sludge processes is based on a complex microbial community intertwined in the biofilm structures of dense granules.

The aim of this study is to characterize the diversity of the different actors involved in the phosphorus removal and their implication in the carbon food web of the microbial community. This is of particular significance to define the microorganisms playing an important role in the phosphorus removal performance of aerobic granular sludge. Insights into the link between the metabolic functions of PAO and their structure in the granular biofilm will be revealed using Fluorescence in situ hybridization (FISH) based on taxa-specific fluorescent probes.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O71

Pseudomonads contact-dependent competition in mixed biofilms

G Purtschert^{1#}; G Cárcamo-Oyarce^{1,2#}; C Aguilar¹; L Eberl¹

(1) Department of Microbiology, Institute of Plant and Microbial Biology, University of Zurich

(2) Current address: Biological Engineering Department, Massachusetts Institute of Technology, Cambridge MA, US

#Both authors contributed equally

Bacterial biofilms represent the most relevant form of bacterial growth in natural and artificial environments. Since multiple bacterial species coexist within biofilm communities, the competition for resources and space has triggered the evolution competitive strategies to succeed and persist in these circumstances.

In this study, we evaluate competition ability of the plant-associated bacterium *Pseudomonas putida* strain IsoF in mixed species biofilms. Using different experimental approaches, we show how IsoF is able to outcompete various soil and plant associated *Pseudomonas* spp, in a contact-dependent manner. Moreover, IsoF antagonism is particularly effective in mixed-species biofilms. This was analyzed using a flow cell chamber where IsoF invaded and displaced pre-established biofilm of *P. putida* strain KT2240. We found by the screening of a transposon (mini-Tn5) mutant library that the mechanism responsible for IsoF contact-dependent-outcompetition is a putative type IV secretion system (T4SS). These mutant strains are not able to kill other bacteria nor displace biofilms, in contrast to the wild-type strain. Thus, we unravel the competition strategy of *P. putida* and we extend the understanding of bacterial interactions in multispecies biofilms and provide evidence of the involvement of a secretion system in biofilm defense and invasion.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O72

Promising attempts to 'biocontrol' the corn rootworm *Diabrotica virgifera virgifera* using *Pseudomonas* bacteria, entomopathogenic nematodes and arbuscular mycorrhizal fungi in field experiments in Missouri

N Imperiali¹; G Jaffuel²; R Campos-Herrera³; B Hibbard⁴; K Shelby⁴; T Ted²; C Keel¹

- (1) Université de Lausanne;
- (2) Université de Neuchâtel;
- (3) University of Algarve, Portugal;
- (4) University of Missouri;

The biological control of insect pests through the application of microbial inoculants is a very promising approach to sustain crop health and performance and to limit the use chemical pesticides. This may help counter problems related to the persistence of these chemicals in the environment, water and food, and to the development of resistance in target organisms. Of particular interest are root-colonizing *Pseudomonas* bacteria displaying insecticidal activity, entomopathogenic nematodes and arbuscular mycorrhizal fungi. In 2015 and 2016, two field experiments were performed at the Bradford Agricultural Research Station near Columbia, Missouri, USA. Corn was sown and seed furrows were inoculated with *Pseudomonas protegens* and *Pseudomonas chlororaphis*, alone or in combination with the entomopathogenic nematodes *Heterorhabditis bacteriophora* and *Steinernema feltiae* and the arbuscular mycorrhizal fungus *Rhizophagus irregularis*. After two weeks, half of the field (48 plots) was artificially infested with eggs of the Western corn rootworm (WCR) *Diabrotica virgifera virgifera*, a major insect pest of corn roots causing important economic problems and yield losses worldwide. At the end of the experiments (after two months), corn plants were assessed for growth and root damage and the survival and fitness of WCR larvae was recorded. In 2015, WCR infestation was ineffective due to extraordinarily heavy rainfalls; nevertheless, inoculants were found to promote the growth of corn. In 2016, WCR infestation was successful and an important effect on WCR larvae survival and fitness was observed in plots treated with *Pseudomonas* bacteria. In addition, corn roots were less damaged when treated with the nematodes. An additional experiment is currently prepared for 2017, in order to confirm these finding. Reduced *Diabrotica* incidence could also be observed in pot experiments in the greenhouse. The results obtained so far indicate a clear biocontrol potential of insecticidal pseudomonads and nematodes, which is a prerequisite for developing them as alternatives to currently used chemicals in agriculture.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O73

3D Printing of Anammox Biofilms

D Hausherr; BA Kolvenbach; P Corvini; P Shahgaldian
 FHNW

Aims

To alleviate the complications of an anammox reactor in wastewater treatment, such as growth of biofilm or retention of anammox bacteria, we propose encapsulating the involved bacteria and construct a 3D scaffold to precisely position the bacteria containing beads. As has been previously shown, encapsulation confers tolerance to pH and COD stress and impedes washout of anammox bacteria. But so far, no studies have encapsulated AOB and anammox together nor subsequently designed biofilm formation on a scaffold. This work will advance our understanding of the anammox process and its interactions with other bacteria and further its applicability to diverse types of wastewater. So far initial studies on the encapsulation process have been completed and viability assays performed.

Methodology

The bacteria are mixed with an alginate solution (2% w/v) to be added dropwise to a hardening solution (0.1 M CaCl₂), resulting alginate beads may be further coated with a chitosan layer before liquefying the alginate core to allow bacterial growth. Alternatively, alginate beads may also be applied directly to the bioprinting process. These beads are then placed in a solution suitable for bioprinting, which provides structural stability while only posing a minor obstacle to mass transfer. The resulting bacteria loaded scaffolds will be tested into 1L reactors, fed by synthetic wastewater and the growth and composition of the biofilms as well as nitrogen removal is monitored.

Results and conclusions

Initial results show good viability of encapsulated cells (*E. coli*) after performing liquification of the core. Additionally, incubating these cells in appropriate medium leads to growing cells to fill the cavity. And embedding the alginate-chitosan beads into a colloidal silicon dioxide (LUDOX) with activated TEOS showed promising results.

Building on these results we envision to further develop this new approach, promising a more stable and reproducible anammox process (as biofilms are produced as opposed to waiting for natural growth) and widening the scope of possible parameters for a streamlined WWTP process. This technique will allow us to control biofilm composition and structure to enhance the role of anammox process in nitrogen removal in wastewater. These artificial biofilms may also be applied to a plethora of other suitable tasks where precise architecture is needed.

References

1. Aslan, S. & Dahab, J. Hazard: Mater 2008:156:56
2. Dong, Y., Fan, S. Q., Shen, Y., Yang, J. X., Yan, P., Chen, Y. P., ... & Liu, S. Y. Sci.Rep. 2015:5
3. Jin, R. C., Yang, G. F., Yu, J. J. & Zheng, P. Chem. Eng. J. 2012:197:67
4. Kartal, B et al., FEMS Microbiol. Rev. 2013:37:428
5. Mutlu, B. R., Yeom, S., Tong, H.-W., Wackett, L. P. & Aksan, A., J. Mater. Chem. 2013:A1
6. Nassif, N et al., Nat. Mater. 2002:1:42
7. Sekaran, G., Karthikeyan, S., Gupta, V. K., Boopathy, R. & Maharaja, P., Mater. Sci. Eng. 2013:33:735
8. Stewart, P. S. & Franklin, M. J., Nat. Rev. Micro. 2008:6:199



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Synthetic Biology

O74

Computational DNA design algorithms to accelerate bio-systems engineering

Institute of Molecular Systems Biology, ETH Zürich

Recent advances in synthetic biology have resulted in an increasing demand for the de novo synthesis of large-scale DNA constructs. Still, efficient design and higher-order assembly of genome-scale DNA constructs remains a labor-intensive process. Given the complexity, computer assisted design tools that fragment large DNA sequences into fabricable DNA blocks are needed to pave the way towards streamlined assembly of biological systems. Here, we present the Genome Calligrapher and the Genome Partitioner, two computer-aided design web tools that enable fast and cost-effective streamlining of digitized genetic information into fabricable DNA sequences. By applying a neutral recoding algorithm, the Genome Calligrapher optimizes GC content and removes obstructive DNA features known to interfere with de novo DNA synthesis. The Genome Partitioner permits multi-level partitioning of genome-scale DNA designs. Both webtools are broadly applicable to translate in silico DNA designs into ready to order sequences that can be assembled with standardized protocols, thus offering new opportunities to harness the diversity of microbial genomes for synthetic biology applications.

The webtools can be accessed at

<https://christenlab.ethz.ch/GenomeCalligrapher> and

<https://christenlab.ethz.ch/GenomePartitioner>



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O75

Measuring microbial interactions in soil in high throughput

M Dubey; JR van der Meer

University of Lausanne

Microbial ecosystem engineering approaches often rely on the introduction of one or more specific species into an existing microbial community, but the survivability of an inoculant heavily relies on abiotic factors and highly dynamic biotic interactions. Deciphering the rules governing microbial species interactions in such a dynamic space is a strenuous task.

Our project is focused on better understanding the principles of success of establishing pure cultures in complex microbial ecosystems such as contained within soil. Here we develop a high-throughput co-cultivation approach that might enable us to study the "interactome", the identification of favourable and non-favourable species combinations that decide on the survival of the inoculant in the community. We use agarose micro-beads as growth chambers to randomly combine soil community members with or without pure culture inoculants. Growth of co-cultured species members is followed by microscopy and enables a global overview as well as individual assay of potentially positive effects of the inoculant on growth of the members in the soil as a function of different selective or non-selective carbon substrates. The resulting knowledge not only provides ample data in designing functional synthetic communities but also to construct new avenues for "synthetic ecology".



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Microbiome

O76

Whole-genome shotgun metagenomics reveal functionally distinct bacterial communities in individual honeybees

K Ellegaard; P Engel

UNIL-University of lausanne

Aims

The honeybee gut is colonized by a remarkably simple bacterial community, which is dominated by only 8-10 bacterial species. However, as for the vertebrate gut microbiota, these species are composed of a multitude of strains with highly variable gene content, thus providing a unique opportunity for studying strain-level dynamics and diversity in the setting of a natural community. In the current study, we address the following questions:

1. Are the bacterial species colonizing the honeybee composed of distinct evolutionary lineages ("sub-species"), with unique functional capacities? If so, do these sub-species co-exist within individual honeybees?
2. Do individual honeybees harbor distinct bacterial communities? If so, is the compositional profile related to honeybee life-stage or colony affiliation?

Methods

We have collected honeybees representing different colonies and life-stages, over a time-period of 2 years. A total of 54 gut bacterial communities were sampled individually and subjected to whole-genome shotgun sequencing, resulting in deep coverage sequence data for each bee.

To facilitate the analysis, we have established a database containing 50 genomes representing the core species known to colonize the honeybee gut. Using this database, we have predicted single-copy core genes and inferred robust phylogenies for each species. Based on the species phylogenies, strongly separated clusters were identified as candidate sub-species, and subsequently validated based on analysis of orthologous core genes extracted from de novo metagenome assemblies of the samples.

By mapping reads from all samples against our database, the coverage of all gene families within the database was quantified, and used to infer the distribution of species, sub-species and gene families across the experiment.

Results/Conclusion

Our study shows that, for some species, multiple sub-species co-exist in a remarkably stable manner within individual honeybees. Notably, in several cases, this co-existence results in a higher functional capacity than what is encoded in any individual genome of a species. Nevertheless, our analysis also reveals a large number of gene families which are variably present across samples, indicating that individual honeybees do harbor functionally distinct bacterial communities. Taken together, our results underscore the need to move beyond species-level metagenomics, in order to understand the function and evolution of microbial communities.

References

- Ellegaard KM and Engel P, *Frontiers in Microbiology*, 2016:7:1475
 Kwong WK and Moran NA, *Nature reviews Microbiology*, 2016:14:374
 Ellegaard KM et al., *BMC genomics*, 2015:16:284
 Engel et al., *PLoS Genetics*, 2014:10:e1004596
 Engel et al., *PNAS*, 2012:109:11002



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

077

The influence of working in close contact with pigs on the human nasal microbiota

J Kraemer¹; S Aebi²; A Oppliger³; M Hilty²

(1) Lausanne University Hospital (CHUV);

(2) University of Bern;

(3) CHUV-Lausanne University Hospital

Many zoonoses originate from swine and a colonization of humans with zoonotic strains might hold important implications for occupational and public health.

This study aimed to investigate the influences that daily contact to pigs has on the human nasal microbiota and this might ultimately give a deeper insight on how zoonotic microorganisms can successfully colonize humans.

We compared the nasal microbiota of pigs with the air microbiota from pig-farms and the nasal microbiota of individuals working in these pig farms in Switzerland. Pig farms (n=28) were visited in 2014 and 2015 and in total nasal swabs from 43 pig-farmers, 53 pigs and 26 air samples were collected. As controls, nasal swabs from 16 cow-farmers and 26 individuals with no contact to farm animals (non-exposed) were collected. Analysis of the microbiota was performed based on 16S rRNA high-throughput sequencing (Illumina MiSeq, 2x250 bp) and raw sequences were analyzed using dada2.

We found an overall higher bacterial-diversity (Shannon Diversity and Richness) in nasal samples from pig-farmers and cow-farmers compared to individuals with no contact to farm animals (p<0.001). Comparison of bacterial communities (beta-diversity) showed that the different sample groups formed distinct clusters (pigs, air, pig-farmers, cow-farmers and non-exposed) (p=0.001) and that the clusters from pigs, air and pig-farmers were mainly dependent on the relative abundance of their Sequence Variants (SVs, similar to Operational Taxonomic Units) rather than presence/absence of SVs. An unweighted screening method revealed 80 SVs with a significantly higher prevalence in pig-farm samples compared to control group samples. This suggests a transmission of SVs within pig-farms. Furthermore, we found that samples which originated from the same farm are more similar to each other than compared to samples from different farms, implying that the microbial composition is specific to each farm.

The results strongly indicate that the bacterial communities of farm's animals significantly alter the human nasal microbiota.

This work was supported by the Swiss National Foundation (SNF; grant 310030_152880 due to AO and MH).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

078

Cumulative effect of yeast extract and fructooligosaccharide supplementation on composition and metabolic activity of elderly gut microbiota in vitro

E Doo; C Schwab; C Chassard; C Lacroix
ETH Zurich

Concurrently with a decline in general health, the gut microbiota of the elderly is characterized by reduced stability compared to adults, and is impacted by living condition and diet. Dietary supplementation has been suggested to improve and stabilize elderly gut microbiota composition.

It was the aim of this study to investigate the impact of carbohydrate (fructo-oligosaccharides, FOS) and micronutrient (yeast extract with different nucleotide content, YE) supplementation on elderly gut microbiota using PolyFermS in vitro fermentation models with immobilized fecal microbiota (n=2). YEs (5 and 10 g L⁻¹), and FOS (10 g L⁻¹) were applied alone and in combination. Microbiota composition was investigated by 16S rRNA gene sequencing and by qPCR of selective bacterial groups. Short chain fatty acids (SCFAs) and metatranscriptomes were analysed as indicators of metabolic and transcriptional activity, respectively.

YE addition increased the abundance of the butyrate producing Roseburia/Eubacterium rectale group, Lactobacillus/Leuconostoc/Pediococcus spp. and bifidobacteria, and impacted SCFA formation with an increase of butyrate and a decrease of propionate levels in a nucleotide dose-dependent manner. FOS likewise enhanced the abundance of butyrate producers, Lactobacillus/Leuconostoc/Pediococcus spp. and Bifidobacterium spp., and significantly decreased Bacteroidetes. Supplementation of FOS stimulated butyrate formation (+120%), while propionate levels dropped to 60% compared to controls.

FOS and YE together cumulatively increased abundance of the Roseburia/E. rectale group, and butyrate formation, while abundance of Bacteroidetes and propionate levels were significantly reduced.

Gene expression analysis indicated that the addition of FOS caused major shifts in microbial transcription profiles with increases in relative abundance of the SEED category 'Carbohydrate Metabolism' mainly due to higher number of transcripts related to 'Di- and Oligosaccharide' utilization and 'Fermentation'. FOS and YE altered relative abundance of different categories related to 'Amino Acids and Derivatives'.

Our study highlights the suitability of the PolyFermS platform of continuous colonic fermentation to investigate the impact of nutritional components on gut microbiota. Our findings suggest that YEs rich in amino acids, vitamins and minerals, and FOS cumulatively enhanced formation of the beneficial SCFA butyrate by elderly gut microbiota.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O79

The skin and oral microbiome of West Highland White Terriers

S Rodriguez-Campos¹; A Rostaher²; L Zwickl²; N Fischer²; S Vidal¹; BW Brandt³; C Favrot²; V Perreten⁴

(1) Vetsuisse Faculty, University of Bern;

(2) Vetsuisse Faculty, University of Zurich;

(3) University of Amsterdam and Vrije Universiteit Amsterdam;

(4) University of Bern

Amplicon sequencing of hypervariable region(s) of 16S rDNA has revolutionized our approach to delineating microbial compositions. Next-generation sequencing previously revealed a highly diverse microbiota of the canine skin and oral mucosa and highlighted changes of the microbiota in inflammatory processes [1, 2]. In this study, we aimed at comparing oral and skin microbial profiles of cohabiting family members from different breeders (n = 17) of West Highland White Terriers. The study was carried out on puppies (n=107) during the first three weeks of life, and adults (bitches n=26 and stud dogs n=8). Samples were taken by rubbing dry swabs 40 times over the oral mucosa (n=135) and the skin (n=104). DNA extraction was performed from the tip of the swab (PowerSoil DNA Isolation Kit, MoBio). Libraries were prepared targeting hypervariable regions V3 and V4 of the 16S rDNA [3, 4]. The Illumina standard protocol was used with MiSeq Reagent Kit v3 for 2x300 bp sequencing. Processing of the amplicons was performed similarly to [5]. PAST software [6] was used for alpha diversity analysis and data ordination by principal component analysis. Significance between microbial profiles was determined using one-way PERMANOVA. The statistical difference in diversity was analyzed by two-sample t-test/Wilcoxon Mann–Whitney test (normally/non-normally distributed data). Statistically significant differences were considered for p values <0.05. The analyses showed a significant difference between the mouth (44.31% Proteobacteria, 25.25% Firmicutes, 16.78% Bacteroidetes, 7.44% Fusobacteria, 2.26% Actinobacteria, 3.85% others) and the skin (39.53% Firmicutes, 28.73% Proteobacteria, 10.99% Bacteroidetes, 8.43% Actinobacteria, 5.37% Fusobacteria, 6.71% others). Microbial profiles from the skin were statistically more diverse both by the number of observed operational taxonomic units as well as by the Shannon index. Moreover, we could find statistically significant differences in the microbial profile of dogs belonging to different breeders, while dogs from the same breeder showed a similar microbiota, even more similar in dogs from the same litter. However, the adults from the same breeder presented a higher microbial diversity and a different microbial profile than their own puppies. Our results suggest that not only the age, but also rearing and environmental factors, could influence the development of a specific skin and oral mucosa microbiota in cohabiting family members.

References

- [1] Rodriguez-Hoffmann A. et al. PLoS One 2014;9:e8319
- [2] Rodriguez Hoffmann A. Vet Dermatol 2017;28:60:e15
- [3] Klindworth et al. Nucleic Acids Res 2013;41:e1
- [4] Caporaso J.G. et al. Proc Natl Acad Sci USA 2011;108 Suppl 1:4516-4522
- [5] Kennedy R. et al. Vet Res 2016;47:49
- [6] Hammer Ø. et al. Palaeont Electronica 2001;4:9.

This study was financed by grant no 320030_152686 from the Swiss National Science Foundation.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Migration

O80

Shifts in methicillin-resistant *Staphylococcus aureus* clonality and antibiotic susceptibility at the University Hospital Zurich, Switzerland between 1995 and 2016

K Seidl¹; A Holzmann-Bürge¹; C Rachmühl¹; S Kuster¹; R Zbinden²; A Zinkernagel¹

(1) Universitätsspital Zürich;

(2) Universität Zürich

Aims.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a global epidemic threat. The aim of this study was to determine how MRSA clonality and resistance patterns changed over time at our tertiary care hospital in Switzerland, a hospital with low MRSA prevalence, during the last 21 years.

Methods.

The methicillin-resistant *Staphylococcus aureus* (MRSA) strains collected in 1995/1996 (n=34), and 2015/2016 (n=189) at the University Hospital Zurich, Switzerland, were analyzed by PFGE analysis of *Sma*I digests in combination with *spa*-typing. In addition, resistance levels to eight antibiotics (ciprofloxacin, clindamycin, erythromycin, tetracyclin, rifampicin, gentamicin, trimethoprim/sulfamethoxazole, and vancomycin) were compared for all isolates.

Results.

There were less than 20 new MRSA isolated per year in 1995/1996, 77 MRSA in 2015, and 112 in 2016. Of the 34 MRSA strains isolated in 1995/1996 five could not be recovered. Of the remaining isolates, 62.1% were of *spa*-type t051 and could be assigned to clonal complex (CC) 8. In 2015/2016 MRSA isolates were a lot more diverse in terms of the genetic background with four predominant *spa*-types accounting for 28.1% of the strains. These dominant clones included t002 (USA100, ST5, 10.6%), t032 (EMRSA15, ST22, 7.4%), t008 (CC8, 5.3%), and t019 (CC30, 4.8%). The increase in MRSA strains in 2016 vs. 2015 was mainly due to an increase of CC5 (additional 11) and CC22 isolates (additional 17 isolates). The Swiss drug clone, a community-acquired MRSA that was spread among injection drug users and was predominant at our hospital between 1998 and 2004 still occurred sporadically (in 2015 two (2.6%), and in 2016 three isolates (2.7%)). Although USA300 is the most prevalent MRSA clone in the United States of America the prevalence was low at our hospital (in 2015 one (1.3%) and in 2016 two isolates (1.8%)). While in 1995/1996 almost 80% of the strains were resistant to four or more antibiotics in addition to oxacillin, in 2015/2016 this was the case in only 11.6% of the strains.

Conclusion.

Our findings indicate that there was a major shift in clonality of MRSA during the last 21 years. More recent isolates (2015/2016) exhibit less multiresistance as compared to isolates from 1995/1996. Especially the recent increase in MRSA in 2016 vs. 2015 underlines the importance of infection control measures.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O81

Gut Microbiota Dynamics in Travelers Returning from India Colonized with Extended-Spectrum Cephalosporin-Resistant Enterobacteriaceae: a Longitudinal Study

J Pires¹; E Kuenzli²; J Kraemer³; S Kasraian¹; R Tinguely¹; C Hatz²; A Endimiani¹; M Hilty¹

(1) Institute for Infectious Diseases, University of Bern;

(2) Swiss Tropical and Public Health Institute, University of Basel;

(3) Institute for Work and Health, Universities of Lausanne and Geneva

Background:

Intestinal colonization by extended-spectrum cephalosporin-resistant Enterobacteriaceae (ESC-R-Ent) in healthy volunteers has been greatly attributed to travel to countries with high prevalence of these bacteria. However, the effects of ESC-R-Ent colonization on the travelers' gut microbiota are still unknown. In our study, we aim to characterize the microbiota of volunteers visiting India and correlate it with potential colonization status shifts.

Methods:

Forty volunteers living in Switzerland underwent stools screening before and after a trip to India, and 3, 6 and 12 months after traveling. ESC-R-Ent selective culture screening was performed as previously described (Pires J. et al, Front Microbiol 2016:7). Microbiota analysis was performed based on 16s rRNA high throughput sequencing using Illumina Miseq. OTUs were defined at 97% of sequence identity. Statistical analysis of microbial communities among colonized vs. non-colonized individuals were carried out in R.

Results:

Colonization before traveling was low (8%), rising to 76% after the trip. Colonization decreased over time, as rates of 33%, 26% and 18% were reported at 3, 6 and 12 months, respectively. A linear mixed model indicated that Shannon Diversity Index within an individual was slightly decreased in colonized subjects ($P=0.03$), but independent of travel ($P=0.12$). Beta-diversity also indicated that the microbial community in colonized individuals was minimally affected compared to non-colonized individuals (permutational MANOVA $P=0.007$, $R^2=0.008$). Hierarchical clustering of bacterial families grouped individuals into three different clusters. Based on relative abundance, cluster drivers were mainly Bacteroidaceae (clusters 1 and 3), Veillonellaceae (cluster 1), Acidamniococcaceae (cluster 3) and Prevotellaceae (cluster 2). Grouping into different clusters was not affected by travel ($P=0.85$) or colonization status ($P=0.13$). In general, individuals remained in their respective clusters over time.

Conclusion:

Our study revealed that despite the high rates of ESC-R-Ent carriage after traveling, discrete differences were identified between colonized and non-colonized individuals and a distinct microbiota was not associated with an increased risk for being colonized by these organisms. This stability of the microbiota indicates that other unknown factors may favor the colonization by ESC-R-Ent in healthy volunteers.

This work was supported by SNF grant No. 153377 due to AE. Pires J. et al, Front Microbiol 2016:7



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Communicating Microbiology in the Digital Era

O82

Monitoring outbreaks of science-communication in Switzerland: how sensitive are microbiologists to the outreach-bug *Loquentes physicus*?

M Creus

Laboratory of Molecular Evolution and “Habilitation” (Department of Chemistry, University of Basel), Computational Structural Biology Group, Biozentrum, University of Basel and Swiss Institute of Bioinformatics (SIB)

The Sandton Declaration on Sustainability (2012) stated that “Public engagement (by scientists) must be valued, and not seen as something best left to others.” Here, I present some initiatives of young scientists to engage in science communication and outreach activities in Switzerland, in particular Famelab and Science Slams. A personal perspective of both the pros and cons of participating in such activities will be presented, including a discussion on the motivation & goals of participants.

<http://globalyoungacademy.net/publications/the-gya-sandton-declaration-on-sustainability/>



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

O83

A computational model for influenza vaccine response of stem cell transplant patients

J Linnik

ETH Zurich - University Hospital Basel

Seasonal influenza results worldwide in millions of cases of severe illness and several hundred thousand deaths per year, and immunocompromised patients suffering chronic diseases or post-transplantation have a significantly increased mortality. While vaccination is the most effective therapy against influenza, its efficacy is limited in immunocompromised patients, especially early post-transplantation.

We develop a computational model of the vaccine response with the aim to predict the vaccine-induced antibody response in allogeneic hematopoietic stem cell transplant (HSCT) patients, using a minimal set of clinical, immunological and genetic markers. We identified markers that are associated with antibody levels before and after vaccination from two independent, multicenter HSCT patient cohorts. Clinical and genetic markers are mapped onto model parameters, while immunological markers define the initial conditions. Training and testing the vaccine response model on the two HSCT patient cohorts will allow for both an a priori classification of HSCT patients and an identification of novel personalized vaccination strategies.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Emerging pathogens

O84

Development of pseudovirion-based Ebola virus neutralization tests to detect antibodies elicited by vaccination

S Rothenberger¹; G Torriani¹; G Zimmer²; S Kunz¹; O Engler³

(1) University Hospital Center and University of Lausanne;

(2) Institute of Virology and Immunology;

(3) Spiez Laboratory

Aims:

Since the 2014 outbreak of Ebola virus disease (EVD), there has been a significant effort to develop a vaccine eliciting protective immunity for population at greater risk of disease during outbreaks. The objective of this study is to establish an optimized assay to measure neutralizing antibodies that are an important immunological correlate of vaccine-mediated protection against viral diseases.

Methods:

As with other enveloped viruses, EBOV entry into host cells requires virus-cell attachment, followed by the fusion of the viral and host cell membranes, a process that is mediated by the viral glycoprotein (GP). We have therefore produced a replication-deficient reporter virus bearing EBOV GP in its envelope that represents a powerful surrogate system for viral entry studies. By the process of pseudotyping, the viral GP, provided in trans, was incorporated into a replication-deficient vesicular stomatitis virus (VSV) recombinant in which the glycoprotein gene (G) was deleted and replaced with genes encoding fluorescent reporter protein (EGFP) and luciferase (Luc).

Results:

Pseudotypes were produced, carrying the GPs from EBOV variants Mayinga, Kikwit and Makona at a titer of 10⁶ to 10⁷ infectious units (IU) /mL. The specificity of the pseudoviruses was assessed using monoclonal antibody I1 directed against VSV G and monoclonal antibody KZ52, originally derived from an EVD survivor. The assay was further implemented using a set of International Reference Reagents established under the auspices of WHO. The results were compared to neutralization assays with authentic Ebola virus.

Conclusion:

A major obstacle for the assessment of the potency of EVD antibody therapies and vaccines is the absence of standardized methods to measure neutralizing antibody levels. We successfully established a pseudotype platform for EBOV which is suitable for the detection of neutralizing antibodies elicited by vaccination and that can be rapidly adapted to novel emerging viruses.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Zoonotic infection

O85

Discovery of new virulence factors secreted by Chlamydiales bacteria

L Pilloux; C Kebbi Beghdadi; G Greub

Lausanne University Hospital and University of Lausanne

Virulence factors are known to be secreted by intracellular bacteria to interact with their hosts. For classical Chlamydiaceae, several effector proteins were described to be able to modulate various host cell functions, leading to survival and replication of the bacteria. On the other hand, nothing is known about effector proteins secreted by Chlamydia-related bacteria, such as Waddlia chondrophila, an emerging pathogen for humans and animals.

We used a lysin to specifically permeabilize host cell membrane to identify effector proteins specifically secreted in the host cell cytoplasm. By mass spectrometry analysis, we could identify 31 bacterial proteins present in the host cell cytoplasm and released in the supernatant after permeabilization. We did not elucidate the mode of secretion of all of them but we could identify a Type III Secretion System (T3SS)-dependent secretion for at least two of these bacterial proteins.

The second approach was to identify, in silico, effector proteins secreted by T3SS. Four algorithms were used to predict a few proteins as secreted by T3SS with a good probability. Secretion was confirmed using an heterologous system.

Chaperone proteins are required by T3SS effectors for correct folding before secretion within host cell, and these chaperones exhibit high sequence homology. The last approach was to use these chaperones to bind effectors in a pull down assay analysed by mass spectrometry. We then increased the number of putative virulence identified.

This large screening led to the identification of new chlamydial secreted effector proteins, on which we are carrying out further investigations to increase our understanding of chlamydial evolution, biology and pathogenesis.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Environmental Microbiology

O86

Hybrid proteins for the screening of transcription regulators of reductive dehalogenase gene clusters

M Willemin; C Holliger; J Maillard

Ecole Polytechnique Fédérale de Lausanne (EPFL)

Organohalide respiring bacteria (OHRB) are able to couple energy conservation to reductive dehalogenation. Genes involved in OHR are organized in clusters. Research on the transcription regulation of the reductive dehalogenase (*rdh*) gene clusters (for a recent review, see [1]) revealed a new set of CRP/FNR-type transcription regulators, called *RdhK* [2,3]. Several members of this family have been characterized in *Desulfitobacterium hafniense*. *CprK1* (also known as *RdhK6* [3]) is responsible for the regulation of the chlorophenol *rdh* operon [4-5]. The binding of the *CprK1* N-terminal domain to 3-chloro-4-hydroxyphenylacetate (effector) promotes interaction of the C-terminal domain with a DNA target (dehalobox) in *rdh* promoters leading to transcription. Each of the 25 *rdh* gene clusters in *Dehalobacter restrictus* is associated with at least one copy of *rdhK*, suggesting an important regulation network of OHR. Moreover, the proximity of *rdhK* genes in *rdh* gene clusters [6] offers an indirect way to identify the substrate of yet uncharacterized *RdhA* enzymes, the key catalytic enzyme in OHR.

Overall this study aims to identify effectors and dehaloboxes recognized by *D. restrictus* *RdhK* regulators. Electrophoretic mobility shift assay (EMSA) has been used to characterize *CprK1* and other *RdhK* [5] and still represents a key methodology to detect tri-partite interactions. While *CprK1* serves as a model protein to optimise EMSA conditions, the challenge in testing each new *RdhK* protein resides in the high number of combinations of effectors and dehaloboxes. To circumvent this difficulty, we developed a strategy of hybrid proteins made by the N-domain from *CprK1*, fused to the C-domain from uncharacterised *RdhK*, or vice-versa. This strategy will be applied to screen either for the dehalobox or for the effector of the uncharacterised *RdhK* protein.

So far, as proof of concept, a protein hybrid, *RdhK-E61D*, was created by fusing *D. hafniense* *RdhK6* and *RdhK1* domains. Preliminary data show that this *RdhK* hybrid keeps specific binding activities for the effectors and dehaloboxes of their corresponding domains and share properties with both parental *RdhK*. Hybrids with *D. restrictus* *RdhK* were designed and their purification is ongoing. These data will be presented and discussed.

References:

- [1] Kruse T. et al. in *Organohalide-Respiring Bacteria* (Springer-Verlag, Adrian & Löffler, Eds) 2016:345
- [2] Villemur R. et al. *FEMS Microbiol Rev* 2006:30:706
- [3] Kim SH. et al. *BMC Microbiology* 2012:12:21
- [4] Gábor K. et al. *J Bacteriol* 2006:188:28318
- [5] Gábor K. et al. *Microbiology* 2008:154:36686
- [6] Rupakula A. et al. *Philos Trans R Soc Lond B Biol Sci* 2013:368:20120325



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Zoonotic infection

O87

Vancomycin Intermediate-Resistant *Staphylococcus aureus* (VISA) confers bacteriophage resistance

S McCallin; C Menzi; J Daraspe; F Oechslin; J Entenza; P Moreillon; G Resch

UNIL-University of lausanne

Antibiotic resistance in *Staphylococcus aureus* has expanded from methicillin resistance to mechanisms that confer decreased sensitivity to vancomycin, the end-line drug for treatment. Vancomycin Intermediate-resistant *S. aureus*, (VISA), is characterized by altered peptidoglycan metabolism that results in increased cell wall thickness and ultimately culminates in clinical failure. While bacteriophages have been proposed as an alternative treatment for many antibiotic-resistant infections, we have shown that the emergence of vancomycin resistance correlates with phage insensitivity.

The clinical isolate, PC3, was serially passed with or without subinhibitory concentrations of vancomycin for ≥ 10 days in order to induce or alleviate vancomycin-induced cell-wall alternations. Changes in the Minimum Inhibitory Concentration (MIC) and cell wall thickness were documented for vancomycin-free (MIC 2 $\mu\text{g}/\text{ml}$; 29.0 ± 4.8 nm) or -maintained (16 $\mu\text{g}/\text{ml}$; 50.3 ± 7.8 nm) strains. While the vancomycin-free strain was highly susceptible to phage infection, exposure to vancomycin resulted in a concomitant decrease in phage sensitivity, evident through phage titers, drop tests, and killing assays. Adsorption assays showed that phage was removed from surrounding media, and phage decreased by 3 log from initial titers after 24 hours, therefore indicating that phage receptors remain accessible on the cell surface of VISA. Transmission electron microscopy (TEM) on ultra-thin sections revealed that phage adsorption causes an invagination of the plasma membrane, which is also observed in the infection process of the vancomycin-free strain, but did not result in the intracellular production of new virions in the large majority of the population. Intracellular phage was detected through qPCR to support entry, but not replication, of phage DNA into vancomycin-maintained cells. The exact genetic mutation in VISA that responsible for phage resistance is currently being pinpointed.

Bacteriophage therapy has a lot to offer in wake of the ongoing antibiotic resistance crisis. However, it is important to understand the circumstances for which phage therapy is a viable option and how antibiotic resistance mechanisms alter phage efficacy. This is the first study investigating the influence of antibiotic-induced cell-wall changes on phage infectivity and holds clinical implications for the future of *S. aureus* phage therapy.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Emerging pathogens

O88

Ticks as new potential reservoir and vector for chlamydiae

L Pilloux¹; S Humbert¹; L Bell-Sakyi²; G Greub¹

(1) Lausanne University Hospital and University of Lausanne;

(2) The Tick Cell Biobank

Among members of the Chlamydiales order, several bacterial families are recognized as pathogenic for humans and animals. However, vectors and reservoirs of these chlamydiae are poorly described and remain to be better characterized. Arthropods, and particularly ticks, are known to be vectors of several intracellular bacteria, and Chlamydiales DNA was recovered from tick samples in several recent studies. To go further in the potential role of tick as vectors of chlamydiae, we have investigated the ability of chlamydiae to infect and grow within tick cell lines.

We have infected two tick cell lines, from hard ticks, with several species representative of a broad spectrum of families. Bacterial growth was assessed by qPCR and immunofluorescence microscopy. Recognized human pathogen *C. trachomatis* was able to enter cells, and despite its incapacity to replicate efficiently, the bacteria were able to persist within cells. It was also the case for *P. acanthamoebae*. However, despite the low temperature growth (28°C) of cells, *W. chondrophila* and *E. lausannensis* were able to enter and grow efficiently, inducing a lysis of tick cells 48 hours post-infection. Interestingly, in only one cell line, we could observe the presence of aberrant bodies, the persistent form of chlamydiae. These results suggest ticks as new hosts for chlamydiae, and highlight the need to further investigations on the role of ticks as reservoirs and vectors of these bacteria.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

Posters

Posters with Posterflash presentation	P01-P15
SSI	P04-P10; P35-P84
SSM	P85-P208; P222-P223
– Clinical Microbiology	P85-P153
– Environmental Microbiology	P154-P170
– Mycology	P171-P176
– Prokaryotic Biology	P177-P189
– Virology	P190-P208
SSTMP	P11-P15; P209-P221
SSHH	P01-P03; P16-P34



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P01

Welcome on Board! – An edutainment movie to promote basic infection prevention measures

A Wolfensberger; M Meier; L Clack; H Sax

Universitätsspital Zürich

Introduction:

Standard Precautions (SP) include a group of infection prevention and control (IPC) practices that apply to all patients (1) and are meant to ensure safety for patients, healthcare workers (HCW), and visitors. The HCW knowledge of SP, however, often proves to be scarce (2). We therefore produced an educational video about SP to improve HCW knowledge at the University Hospital Zurich, Switzerland, and potentially in healthcare institutions worldwide. Since it is well known that emotions help learners to focus and facilitate uptake of information into long-term memory, we chose to use humor as a central feature in this project, making it what is called 'edutainment'.

Methods:

As safety management in healthcare and aviation are often compared, we decided to produce a 'mash-up' between an in-flight safety video and infection prevention instructions. The audience witnesses a cabin crew/infection prevention team member giving instructions to a novice cabin crew member/healthcare worker. Six fundamental topics of SP are covered in the 5' movie: hand hygiene, use of personal protective equipment, professional appearance, respiratory hygiene, aseptic technique, environmental cleaning, and device disposal and reprocessing. The scenes were set inside an airplane (mock-up at a Swiss aviation crew training facility) with passengers appearing as patients. Fun and surprising moments chase each other throughout the script, including fast wordplay, exaggerations, and slapstick. The film was conceived and executed in a collaboration between ICP professionals and a professional film director and crew including a cast of two actors, 20 extras, a camera operator, a sound technician, a gaffer, a costume designer, a make-up artist, and two production assistants.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P02

Whole genome sequencing highlighted two small ST117 vancomycin-resistant *Enterococcus* outbreaks within a large ST80 outbreak

E Moulin; DS Blanc; MMH Abdelbary; N Demartines; G Greub; G Chaillou; L Senn
 CHUV-University Hospital

Despite low incidence of vancomycin-resistant *Enterococcus* (VRE) in Switzerland (0.3-2%), the Lausanne University Hospital experienced several VRE epidemic events in medical and surgical units since 2011. We used prospective whole genome sequencing (WGS) to investigate the last VRE outbreak (*E. faecium* vanA) that occurred in a 60-beds surgical ward.

Systematic screening for VRE (rectal swabs) was performed in all patients hospitalized in the epidemic ward on a weekly basis. Selective culture plates were used to isolate VRE. One isolate per patient was generally further analysed by whole genome sequencing (WGS) using MiSeq (Illumina). Isolates' sequence type (ST) was assigned from short reads data. Genome alignment of all isolates was acquired with Snippy by mapping against a reference. A maximum likelihood tree was constructed based on the number of "core genome single nucleotide polymorphisms" (SNPs). Contact precautions in isolation zones were applied in VRE cases and contacts, and environment disinfection was reinforced.

Following the identification of the first case, the weekly screening revealed 41 additional VRE positive patients between October 2016 and January 2017. Isolates from 35/42 (83%) patients harboured vanA gene cluster. Among the latter, 29 belonged to ST80 (26 highly related), five to ST117 (four with a low genetic diversity suggesting transmission), and one strain was not sequenced. All the seven van B isolates belonged to ST117 and WGS revealed that four were highly related. Thus, one major and two minor VRE lineages circulated in the same ward over the same period of time.

This study highlights the co-circulation of different VRE lineages inside the same ward. Combining epidemiological investigations with WGS analysis of the isolates enables to differentiate clusters of cases and allows better understanding and management of this kind of nosocomial outbreaks.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P03

Prävention von Zentralvenenkatheter-assoziiierter Bakteriämien – Verbesserungspotential bei den pflegerischen Massnahmen?

D Mesida; K Stefan; S Hugo

USZ

Background

Zentralvenenkatheter (ZVK)-assoziierte Bakteriämien (central line-associated bloodstream infections; CLABSI) gehören zu den häufigsten spitalerworbenen Infektionen und können für Patienten gefährlich werden mit einer Letalität von 4-25%. Sie sind mit längeren Spitalaufenthalten und hohen Kosten verbunden. Im Rahmen eines spitalweiten Projektes, die Infektionsrate auf 5% zu senken, werden die pflegerischen Präventionsmassnahmen von CLABSI evaluiert und optimiert.

Methoden

Erhebung und deskriptive Analyse des IST-Zustandes im Vergleich mit aktuellen Empfehlungen während 8 Wochen im 1. Quartal 2017 auf 4 Bettenstationen und je einer Intensiv- (IPS) und Überwachungsstation (IMC) im UniversitätsSpital Zürich (USZ). Patienten mit einem >2 Tage liegenden ZVK und alle involvierten Pflegefachpersonen wurden eingeschlossen. Erfassung der indizierten und nichtindizierten Kathetertage. Beobachtungen von 52 ZVK-Verbandswechseln (VW). Erfassung der Wechselintervalle bei 400 VW und 165 Infusionssystemen. Mittels eines Fragebogens wurden 124 Mitarbeiter über ZVK-Indikation und Umsetzung der Asepsis befragt.

Resultate

Die ZVK-Liegedauer betrug durchschnittlich 11 Tage. An 177 (15%) von 1183 Tagen lagen ZVK ohne valide Indikation. Der Ablauf und die Desinfektionsmittelwahl (Chlorhexidine-Alkohol 2%) wurde bei je 24 (46%), die Einwirkzeit bei 26 (50%) der 52 beobachteten korrekt umgesetzt; 37 (71%) wurden korrekt mit Tupfer durchgeführt. 15 VW (29%) wurden mit Wattestäbchen durchgeführt. Die Wechselintervalle waren bei 200 (50%) der VW und 97 (59%) der Infusionssysteme korrekt. Im Fragebogen gaben 36% resp. 9% der Mitarbeiter an, dass die tägliche Evaluation der ZVK-Indikation immer resp. selten stattfindet. Die Qualität der Umsetzung einzelner Präventionsmassnahmen war auf IPS, IMC und Abteilung unterschiedlich.

Conclusion

Im USZ besteht bezüglich Umsetzung von Präventionsmassnahmen bei der Katheterpflege Verbesserungspotenzial. Mittels der detaillierten Erhebung können nun die Prozesse und Strukturen gezielt optimiert und die Erkenntnisse besser in die Schulungen integriert werden.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P04

The within-host population dynamics of *Mycobacterium tuberculosis* vary with treatment efficacy.

A Trauner¹; Q Liu²; Q Gao²; S Gagneux¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) Institutes of Biomedical Sciences and Institute of Medical Microbiology, School of Basic Medical Sciences, Fudan University

Aims:

Combination therapy is one of the most effective tools for limiting the emergence of drug resistance. Despite the widespread adoption of combination therapy across diseases, drug resistance rates continue to rise, leading to failing treatment regimens. The mechanisms underlying treatment failure are well studied, but the processes governing the successful suppression of resistance by combination therapy are poorly understood. We address this question by studying the population dynamics of *Mycobacterium tuberculosis* within tuberculosis patients undergoing treatment with different combinations of antibiotics.

Methods:

We collected biweekly serial sputum samples from 12 tuberculosis patients undergoing treatment over a period of up to 24 weeks. We then generated very deep whole genome sequencing data (~1,000-fold genome-wide coverage) of the *M. tuberculosis* populations within each sample, using an Illumina HiSeq2000 instrument.

Results:

Our approach allowed us to detect transient genetic diversity driven by the apparently continuous turnover of minor alleles, which could serve as the source of drug-resistant bacteria. We observe that treatment efficacy has a clear impact on the population dynamics: sufficient drug pressure bears a clear signature of purifying selection leading to apparent genetic stability. In contrast, *M. tuberculosis* populations subject to less drug pressure show markedly different dynamics, including cases of acquisition of additional drug resistance.

Conclusion:

Our findings show that for a pathogen like *M. tuberculosis*, which is well adapted to the human host, purifying selection constrains the evolutionary trajectory to resistance in effectively treated individuals. Nonetheless, we also report a continuous turnover of minor variants, which could give rise to the emergence of drug resistance in cases of drug pressure weakening. Monitoring bacterial population dynamics could therefore provide an informative metric for assessing the efficacy of novel drug combinations.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P05

A systematic HCV-RNA screening in HIV-positive MSM reveals a high number of potential transmitters

DL Braun¹; R Kouyos²; B Hampel³; C Grube³; M Flepp⁴; C Béguelin⁵; M Stöckle⁶; P Schmid⁷; M Rougemont⁸; J Delaloye⁹; E Bernasconi¹⁰; H Günthard³; J Böni³; J Fehr³

(1) University Hospital Zurich and University of Zurich;

(2) University Hospital Zurich;

(3) Universitätsspital Zürich;

(4) Hirslanden Klinik Zürich;

(5) Inselspital Bern;

(6) Universitätsspital Basel;

(7) Kantonsspital St. Gallen;

(8) University Hospital Geneva;

(9) University Hospital Lausanne;

(10) Ospedale regionale di Lugano

The prevalence of sexually transmitted incident hepatitis C virus (HCV) infections among HIV-positive men who have sex with men (MSM) has increased worldwide. The Swiss HCVree Trial aims to implement a targeted HCV-RNA based assessment of the prevalence of replicating HCV infections in HIV-positive MSM participating in the Swiss HIV Cohort Study (SHCS), and thereafter to treat all HCV-RNA positive MSM with newest anti-HCV direct acting agents.

Between October 1st 2015 and May 31th 2016 we offered a systematic, intensified HCV-RNA polymerase chain reaction (PCR) based screening to all MSM participating in the SHCS. Participants were screened at least once at the occasion of the regular clinical HIV visit. Liver transaminases were measured simultaneously, considering >50 U/l as above the upper limit of normal. HCV-RNA testing was done centralized at a single lab using the Abbott RealTime HCV assay with a limit of detection of 12 IU/ml.

Overall, 4'257 individuals are recorded as MSM in the SHCS database, of them we screened 3'722 (87%) by HCV-RNA PCR. Hundred-seventy-eight out of the 3'722 MSM (4.8%) harbored a replicating HCV infection. Genotype (GT) 1 was the most prevalent GT (72%), followed by GT 4 (22%), GT 3 (5%), and GT 2 (1%). Of note, in 6 (5%) out of the 111 GT 1a infections resistance associated variants were detected. Of the 178 MSM with replicating HCV, 22 individuals (12%) had an incident HCV infection, without prior positive HCV test (e.g. HCV antibodies, HCV-RNA) recorded in the SHCS database. Six of the MSM with an incident HCV (27%) had a non-reactive anti-HCV test at the time-point of the positive HCV-RNA test. Following variables were significantly associated with a positive HCV-RNA screening test: younger age, elevated liver enzymes, condomless sex with occasional partners, intravenous drug use, non-injectable drug use, and previous syphilis.

We identified a high number of replicating HCV infections among HIV-positive MSM participating in the Swiss HIV Cohort Study, resulting in a 5% prevalence in this population. A substantial proportion of MSM with replicating HCV presented with a negative HCV-antibody-test. An intensified HCV-RNA based screening strategy among sexually active HIV-coinfected MSM should be considered to detect potential transmitters timely, to offer early universal treatment with DAAs in order to stop the chain of transmission, and hence to end the epidemic in this population.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P06

Community-acquired respiratory paramyxovirus infection after allogeneic hematopoietic stem cell transplantation: a single center experience

Y Spahr¹; S Tschudin-Sutter²; V Bättig²; F Compagno²; M Tamm²; J Halter²; S Gerull²; J Passweg²; HH Hirsch²; N Khanna²

(1) Kantonsspital St. Gallen;

(2) Universitätsspital Basel

Aims.

Respiratory tract infections (RTIs) with paramyxoviruses such as respiratory syncytial virus (RSV), parainfluenza virus (PIV) and human metapneumovirus (MPV) are associated with significant morbidity and mortality after allogeneic hematopoietic cell transplantation (alloHCT). While these viruses are closely related there are no comparisons regarding epidemiology, management and outcome of RTIs in alloHCT recipients.

Methods.

We retrospectively identified RSV, PIV or MPV RTIs in alloHCT recipients diagnosed by multiplex PCR from nasopharyngeal swabs or bronchoalveolar lavage samples from 06/2010 until 12/2014. Data on baseline characteristics, clinical presentation and course, treatment with systemic ribavirin (RBV) and/or intravenous immunoglobulin (IVIG), and outcome of RTI episodes were analysed. Severe immunodeficiency (SID) was defined as alloHCT ≤ 6 months, T or B cell depletion ≤ 3 months, graft-versus-host disease [grade ≥ 2], leukopenia, lymphopenia, or hypogammaglobulinemia < 4.5 g/L.

Results.

A total of 103 RTI episodes in 66 patients were identified, which occurred in 84.5% at > 100 days post-HCT. Lower RTIs existed only in one-third of the episodes. 63 episodes occurred in patients with SID and 19 fulfilled ≥ 2 SID criteria without differences between the 3 viruses.

A total of 39/103 episodes were treated with RBV $\pm$ IVIG and 24/103 with IVIG only. PIV RTIs received less often RBV $\pm$ IVIG than those with RSV or MPV ($p \leq 0.001$). There were 40 episodes, which did not receive any antiviral therapy. SID patients were more often treated with antiviral drugs ($p = 0.001$).

The median duration of viral shedding differed not between the 3 viruses. 6 episodes (5.8%) progressed from upper to lower RTI. 40/103 of RTI episodes required hospitalization. Patients with lower RTI were more often hospitalized than with upper RTI ($p < 0.001$). The overall mortality was 5.8% and did not differ between the 3 viruses. Patients fulfilling ≥ 2 SID criteria tended to have a higher progression rate ($p = 0.075$), needed more often hospitalization and transfer to the ICU ($p < 0.001$), and had a higher mortality ($p < 0.001$).

Conclusion.

Paramyxovirus RTIs are frequent > 100 days after alloHCT and clinically more severe in SID patients despite antiviral treatment. Although no definite conclusions about efficacy can be made, current mortality was lower as previously published. It seems that timely diagnosis and early treatment may have a major impact on morbidity and mortality of SID alloHCT patients.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P07

ESBL-colonization at ICU admission: Impact on subsequent infection, carbapenem-consumption and outcome

A Martinez¹; A Widmer²; R Frei³; H Pargger⁴; D Tuchscherer³; A Egli²; S Tschudin Sutter²

(1) Unveristy Hospital Basel;

(2) Universitätsspital Basel;

(3) University Hospital Basel;

(4) University Hospital Basel

Aims

We sought to determine if colonization with ESBL-PE predicts the risk for subsequent infection and impacts carbapenem-consumption and outcome in an ICU-cohort.

Methods

From 11/2014-08/2015, patients admitted to the medical or surgical ICU of the University Hospital Basel were routinely screened for ESBL-PE carriage on admission, providing requirement for mechanical ventilation and an expected ICU-stay of more than 48 hours. Odds ratios for colonization with ESBL-PE, infection with ESBL-PE and mortality were calculated. Length of hospital- and ICU-stay, and duration of carbapenem-exposure were compared using the Mann-Whitney U test.

Results

Among 302 patients, 24 (8.0%) were found to be colonized with ESBL-PE on ICU-admission. Known colonization with multidrug-resistant Gram-negative pathogens was associated with colonization with ESBL-PE.

During their ICU stay, patients with ESBL-PE colonization were not at increased risk for development of any infection (OR 1.14, 95%CI 0.49-2.66, $p=0.759$) or septic shock (0% vs. 3.6%, $p=1.000$). Infections with ESBL-PE occurred in four patients, of which three (75%) were identified as ESBL-PE-colonized on admission. ESBL-PE-colonization on admission was associated with subsequent ESBL-PE-infection (OR 39.57, 95%CI 3.94-397.17, $p=0.002$).

Colonization with ESBL-PE was not associated with an increased exposure to carbapenems (OR 1.89, 95%CI 0.66-5.39, $p=0.235$) or increased duration of carbapenem exposure (median 7 days, IQR 3-8 days vs. median 6 days, IQR 3-9 days, $p=0.983$). Duration of ICU- and hospital-stay did not differ between patients colonized and not colonized with ESBL-PE (median 8 days, interquartile range[IQR] 4-17 days vs. median 7 days, IQR 4-12, $p=0.885$ and median 16 days, IQR 10-30 days vs. median 19 days, IQR 11-34 days, $p=0.438$, respectively). Patients colonized with ESBL-PE were not at increased risk for death by any cause (OR 0.60, 95%CI 0.22-1.65, $p=0.321$) or death attributable to infection (OR 0.44, 95%CI 0.06-3.40, $p=0.431$).

Conclusion

Colonization with ESBL-PE was a reliable predictor for subsequent infection with ESBL-PE in this cohort of critically ill patients. Screening strategies for detection of ESBL-PE colonization on ICU admission may therefore allow to correctly allocate empiric carbapenem treatment. In contrast to prior studies, ESBL-PE colonization was not associated with increased use of carbapenems, increased length of hospital stay or mortality.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P08

Impact of introducing cerebrospinal fluid enterovirus polymerase chain reaction testing on duration of antimicrobial treatment and hospital stay in infants

F Barbey; P Paioni; C Berger

Universitäts- Kinderspital Zürich

Background and aim:

Enteroviruses are the main cause of aseptic meningitis in infants presenting with febrile illness at the emergency room. Infants <90 days of age presenting with fever undergo a septic workup including lumbar puncture and receive empirical antimicrobial treatment not to miss serious bacterial infection. Introducing enteroviral polymerase chain reaction testing in cerebrospinal fluid (CSF EV-PCR) may impact duration of antimicrobial treatment and hospital stay of these infants, if the test result is readily available. The aim of this study was to investigate this potential impact of introducing CSF EV-PCR in infants <90 days of age presenting with fever.

Methods:

Infants <90 days of age presenting with fever at the University Children's Hospital Zurich between June 2015 and October 2016 and for whom CSF EV-PCR testing was performed were investigated by chart review. Infants with bacterial meningitis were excluded. Duration of empirical antimicrobial treatment and hospital stay were compared between children with positive and negative CSF EV-PCR results as well as to a corresponding control group of infants before the introduction of CSF EV-PCR.

Results:

A total of 74 children were enrolled in the study, 47 in CSF EV-PCR group and 27 in the control group, respectively. The median age was 37 days in both groups (range 3 to 85 days). CSF EV-PCR tests were positive in 25 of 47 patients (53%). CSF EV-PCR positive patients showed a significant reduction in the mean duration of antimicrobial treatment compared to EV-PCR negative patients and to controls (23.1, 45.1 and 61.4 hours respectively, $p < 0.0001$), as well as a significant reduction in the mean duration of hospital stay (3.4, 5.0 and 4.0 days respectively, $p = 0.01$). Introduction of CSF EV-PCR significantly reduced the mean duration of antibiotic treatment, not only if positive but irrespectively of test results, compared to control group before test introduction (33.4 vs 61.4 hours respectively $p < 0.0001$), but had no impact on duration of hospital stay (4.1 vs 4.0 days, $p = 0.83$, respectively).

Conclusion:

The use of CSF EV-PCR test in septic workup of infants <90 days of age presenting with fever significantly reduced antibiotic use not only in those with enteroviral meningitis but overall. These findings advocate for systematic use of CSF EV-PCR test in infants presenting with fever in the first 90 days of life in order to shorten unnecessary antibiotic use and possibly hospital stay.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P09

Amoxicillin and levofloxacin differentially alter gut microbiota and innate immune response to acute lung infection with *P. aeruginosa*

E Ciarlo; D Le Roy; L Decosterd; C Pattaroni; G Greub; B Marsland; T Roger; B Guery
CHUV-Lausanne University Hospital

Background and aim.

The composition of the microbiota influences immune cell development and immune responses. Gut dysbiosis has been associated with altered lung immunity through the gut-lung axis. First line antibiotics widely prescribed in clinical practice may cause short and long term dysbiosis and alter host defenses. We aimed to define whether amoxicillin and levofloxacin alter gut microbiota and, if so, to analyze the impact of antibiotic treatment on *P. aeruginosa*-induced lung infection.

Methods.

Mice (n=15) were treated for 5 days with amoxicillin (100 mg/kg/day) and levofloxacin (50mg/kg/day) in the drinking water. Serum antibiotic levels were measured at day 2, 5 and 8. Composition of the gut microbiota was obtained following next-generation sequencing of hypervariable regions of 16S ribosomal DNA gene and analyses using the Shannon diversity index, PCoA plot based on the Bray-Curtis dissimilarity matrix and species hierarchical clustering. On day 8, animals (n=10) were challenged i.n. with 3×10^6 - 2×10^7 CFU *P. aeruginosa*. Severity scores were monitored every 8h. Lung permeability and bacterial burden were assessed 24h post infection.

Results.

Serum concentrations of amoxicillin and levofloxacin were 85.0 ± 24.4 and 17.4 ± 4.4 $\mu\text{g/L}$ and 1436 ± 550 and 1311 ± 139 $\mu\text{g/L}$ on day 2 and 5, respectively. Amoxicillin and levofloxacin concentrations dropped to 5.0 ± 1.5 and 51 ± 17 $\mu\text{g/L}$ 3 days after interruption of treatment. Both antibiotics decreased the Shannon diversity index. Amoxicillin increased the abundance of *Bacteroides* ssp. and *Lactobacillus* ssp., while levofloxacin treatment increased the abundance of *Lactobacillus* ssp. and segmented filamentous bacteria. *P. aeruginosa*-induced lung permeability was significantly increased in levofloxacin treated mice, with a lung injury index of 5.1 ± 4 vs 2.5 ± 2.2 and 1.5 ± 0.8 for water and amoxicillin treated groups respectively. As expected, in the non-infected control group lung injury index was very low (0.5 ± 0.3). Levofloxacin worsened severity score and bacterial burden of mice challenged with *P. aeruginosa* when compared to amoxicillin and water treated mice.

Conclusions.

Amoxicillin and levofloxacin differentially alter gut microbiota and host response to *P. aeruginosa* infection. We are further analyzing lung inflammatory response in terms of cell recruitment and cytokine production. Our data suggests that the choice of a first line antibiotic may have an important impact on susceptibility to infection.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P10

Assessment of therapeutic response in aortic graft infections with the use of

L Husmann¹; B Sah¹; B Ledergerber¹; A Anagnostopoulos¹; Z Rancic¹; D Mayer²; A Weber³; B Hasse¹

(1) University Hospital Zurich, University Zurich, Switzerland;

(2) Cantonal hospital Freiburg, Switzerland;

(3) Clinic for Cardiovascular surgery, University Hospital Zurich, University Zurich, Switzerland

Aims:

18F FDG PET/CT is a reliable tool for the diagnosis of aortic graft infection (AGI), and it may also be useful in the assessment of therapeutic response. We aimed to study the use of PET/CT in the long term monitoring of AGI and to assess the determinants of maximum standardized uptake value (SUVmax) course among patients.

Methods:

Participants of the prospective Vascular Graft Infection Cohort (VASGRA) from May 2013 to April 2017 were eligible for the study. Patients with microbiologically proven Samson III-V AGI underwent serial 18F-FDG PET/CT scannings at diagnosis and during follow up. Morphologic changes of PVGI were documented and the metabolic activity was assessed with the use of SUVmax. SUVmax values were calculated by two reviewers, blinded for clinical information. Multivariable logistic regression models were fit using generalized estimating equations (GEE) to investigate determinants of SUVmax.

Results:

A total of 58 participants with AGI and a median age of 66 (IQR 60-73) contributed to 221 18F FDG PET/CTs. The median SUVmax at baseline and at the end of follow up was 7.6 (IQR 6.1-9.7) and 4.4 (IQR 2.8-5.9), respectively. Square time, logCRP, focal uptake and graft material (PTFE, PET) were associated with SUVmax. 18F FDG PET/CTs results, laboratory parameters and clinical parameters contributed to the final decision of stopping the anti-infective therapy. The antimicrobial treatment was started, continued, escalated, de-escalated or stopped in 7.2%, 55%, 6.8%, 1.8% and 15% of patients, respectively. Thirty four out of 58 (60%) patients stopped antibiotic therapy and they are free of recurrence for a median 0.8 years (IQR 0.0-1.3). while 16 patients are still on antibiotics. In 121 patients (55%) additional incidental findings were detected on follow-up FDG-PET/CT, which had further impact on patient management.

Conclusions:

18F FDG PET/CT is useful for therapy control in AGI and should be included in the therapeutic algorithm. CRP, focal uptake and graft material influence SUVmax, which itself can be used for predictions of therapeutic response. As the antibiotic treatment duration of patients with AGI is not defined, predictions of response to therapy by the use of PET/CT may offer the potential for individualized treatment approaches.

We are grateful to our patients for their commitment and thank B. Ruehe, C. Rüegg, A. Wolfensberger., U. Matt, M. Greiner, A. Schmid and R. Pop for excellent patient care. We also thank C. Müller and S. Bürgin as our study nurses, and C. Laich and C. Vögtli for administrative assistance. The members of the VASGRA Cohort Study are: A. Anagnostopoulos, G. Bloemberg, B. Hasse (PI), L. Husmann, B. P. Keller, Ledergerber, M. Lachat, D. Mayer, Z. Rancic, A. Scherrer, A. Weber, R. Weber, R. Zbinden, A. Zinkernagel.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P11

Impact of the *M. tuberculosis* genetic background on the acquisition of DR-conferring mutations

S Borrell; R Castro; S Gagneux

Swiss Tropical and Public Health Institute, University of Basel

The extent of genetic diversity in *M. tuberculosis* (Mtb) is more pronounced than was traditionally believed, and can be classified into seven different geographically distributed lineages. The average inter lineage genetic distance is approximately 2000 single nucleotide polymorphisms (SNPs). The impact of this diversity on the baseline metabolism is still unknown. One of these lineages; the Beijing lineage has repeatedly been associated with drug resistant tuberculosis (DR-TB). The reason for this association is still not clear. To evaluate the influence of genetic background on the acquisition of specific Isoniazid (INH) resistance-conferring mutations, and to explore whether the Beijing lineage is better adapted to the potential physiological effects than other phylogenetical distant lineages, associations between lineage and INH-DR were sought.

We performed Luria-Delbruck fluctuation assay (LDFA), and found lineage-specific differences in the baseline INH-resistance acquisition rate, with Beijing showing a higher rate compared to the other lineages. Lineage specific INH-associated mutations were also explored. In addition, since Beijing intra lineage diversity shows a phylogeographical structure and epidemiological studies have evidenced differences on the Beijing-DR association depending on the strain geographical origin, we further explored the impact of intra lineage diversity on the basal INH-DR mutation rate performing LDFA of a collection of clinical Beijing strains globally distributed.

Overall, our findings support a role of Mtb lineage diversity in the emergence of global drug resistance and consequently on the specific evolution of drug-resistance within each lineage.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P12

Uncovering the extent of sub-microscopic malaria infections using ultra-sensitive diagnostics

N Hofmann¹; D Rodriguez-Rodriguez¹; E Nate²; I Mueller³; M Laman²; L Robinson³; I Felger¹

(1) Swiss Tropical and Public Health Institute;

(2) PNG Institute for Medical Research;

(3) The Walter and Eliza Hall Institute of Medical Research

Background and Aims

Sub-microscopic malaria infections are prevalent in asymptomatic carriers particularly in low-endemic settings and are considered an important reservoir for mosquito infection. Accurately defining the extent of sub-microscopic malaria infections is limited by the volume of blood analyzed and the sensitivity of the molecular diagnostic method used. We aimed to investigate i) the proportion of malaria infections missed using standard molecular diagnosis procedures, i.e. 18S rRNA qPCR on finger-prick blood volumes, and ii) the proportion of these ultra-low density infections that can be detected using ultra-sensitive qPCR on finger-prick blood volumes.

Methods

Venous blood samples were collected from 302 participants from Madang province, Papua New Guinea, (PNG) during the wet season of 2016/17. DNA was extracted from sample aliquots of 200 µL and 2 ml of blood, and used either directly or as concentrate for detection of *P. falciparum* and *P. vivax* infections using 18S rRNA and ultra-sensitive qPCR.

Results

Preliminary data suggests that in 2017 one third of *P. falciparum* and *P. vivax* infections are missed when using small volumes (200 µL) and standard 18S rRNA qPCR compared to high volumes (2 mL) combined with ultra-sensitive qPCR. Of the ultra-low density infections that were positive from high blood volumes only, 40% were also detected by a specific ultra-sensitive qPCR done in small-volume blood samples. The proportion of ultra-low density *P. falciparum* and *P. vivax* infections is comparable between villages, age groups, men and women, with the exception of children <10 years. In this young age group *P. falciparum* densities, but not *P. vivax* densities, are well detected by standard 18S rRNA qPCR.

Conclusion

Using finger-prick sampling in field studies for investigation of sub-microscopic malaria infections underestimates malaria prevalence in PNG by one third and equally for *P. falciparum* and *P. vivax*. Age patterns and village- or sex-specific differences in infection prevalence are accurately captured by standard molecular diagnosis.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P13

Clinical and laboratory predictors of death in African children with features of severe malaria: a systematic review and meta-analysis.

P Sypniewska¹; JF Duda²; I Locatelli¹; C Rambaud-Althaus³; F Althaus²; B Genton³

(1) University of Lausanne;

(2) International Committee of the Red Cross;

(3) Swiss Tropical and Public Health Institute

Aims

The criteria for defining severe malaria have evolved over the last 20 years. We aimed at assessing the strength of association of death with features currently characterizing severe malaria by using a systematic review and meta-analysis.

Methods

Electronic databases (Medline, Embase, Cochrane Database of Systematic Reviews, Thomson Reuters Web of Knowledge) were searched to identify publications including African children with severe malaria. PRISMA guidelines were followed. Selection was based on: design (epidemiological, clinical and treatment studies), setting (Africa), participants (children <15 years with severe malaria), outcome (survival/death rate), and prognostic indicators (clinical and laboratory features). Quality assessment was performed following the criteria of the 2011 Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2). Odds ratios (ORs) were calculated for each study and prognostic indicator, and, when a test was assessed in at least two studies, pooled estimates of ORs were computed using fixed- or random-effects meta-analysis.

Results

601 articles were identified and screened and 30 publications were retained. Features with the highest pooled ORs were: renal failure (5.96 [2.93-12.11]), coma score (4.83 [3.11-7.5]), hypoglycemia (4.59 [2.68-7.89]), shock (4.31 [2.15-8.64]), and deep breathing (3.8 [3.29-4.39]). Only half of the criteria had an OR > 2. Features with the lowest pooled ORs were: impaired consciousness (0.58 [0.25-1.37]), severe anemia (0.76 [0.5-1.13]), and prostration (1.12 [0.45-2.82]).

Conclusion

The findings of this meta-analysis show that the strength of association between the criteria defining severe malaria and death is quite variable from one to the other clinical and/or laboratory features (OR ranging from 0.58-5.96). This ranking allowed identifying features weakly associated with death, such as impaired consciousness and prostration, which could assist to refine case definition, and hence optimize antimalarial treatment.

References

Please contact the authors for a detailed list of references



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P14

Diarrhoea is expensive: healthcare costs of acute gastroenteritis and campylobacteriosis in Switzerland

C Schmutz^{1,2}, D Mäusezahl^{1,2}, PJ Bless^{1,2}, M Schwenkgenks^{3,4}, D Urbinello¹

(1) Swiss Tropical and Public Health Institute, Basel, Switzerland

(2) University of Basel, Basel, Switzerland

(3) Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland

(4) Institute of Pharmaceutical Medicine, University of Basel, Basel, Switzerland

Aims

The Swiss Federal Office of Public Health receives more than 7000 notifications of laboratory-confirmed campylobacter infections annually. Patients consulting at the primary care level due to acute gastroenteritis (AG) must be a multiple of this number considering that stool testing is not conducted routinely. This study aimed at estimating healthcare costs of AG and campylobacteriosis in Switzerland.

Methods

Publicly available data, results from previous studies and expert opinions were used to define patient management scenarios depending on the severity of AG (including campylobacteriosis), and to estimate individual costs for and the frequency of these patient management scenarios. Total healthcare costs due to AG and campylobacteriosis in Switzerland were calculated based on extrapolated individual costs.

Results

AG including campylobacteriosis led to healthcare costs of CHF 36-54 million in Switzerland in 2012. The “simplest” patient management scenario in our study – AG patients consulting a physician without stool testing – accounted for CHF 10.8-29.1 million. Healthcare costs of patients with a campylobacter-negative stool test were estimated at CHF 14.8 million. Laboratory-confirmed campylobacteriosis patients in the outpatient setting cost CHF 2.2 million. Finally, the most severe cases, hospitalised, laboratory-confirmed campylobacteriosis patients were estimated to account for CHF 7.8 million.

Conclusions

AG and campylobacteriosis do not only cause a considerable burden of disease but also lead to substantial healthcare costs in Switzerland. Non-healthcare costs, e.g. due to lost productivity, were not considered in our study but are likely a multiple of the estimated healthcare costs. The potential for cost savings, both in- and outside the healthcare sector, should be considered when planning and evaluating interventions targeting at a reduction of AG or campylobacteriosis in Switzerland.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P15

Metabolomic characterization of a nitro drug resistant *Giardia lamblia* strain

J. Müller¹, M. Vermathen², P. Vermathen³, N. Müller¹

(1) Institute of Parasitology, University of Bern, Länggassstrasse 122, CH-3012 Berne, Switzerland.

(2) Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH-3012 Bern, Switzerland.

(3) Departments of Radiology and Clinical Research, University & Inselspital, CH-3010 Bern, Switzerland.

Metronidazole and other nitro compounds have been used since five decades as a therapy of choice against giardiasis. As a consequence, resistance formation occurs more and more frequently. In order to elucidate the biochemical nature of resistance formation to nitro drugs, we have generated a metronidazole- and nitazoxanide-resistant *Giardia lamblia* WBC6 clone, the strain C4, and compared it to the wild-type with respect to their transcriptomics. In order to elucidate to which extent these strains differ in metabolomic patterns, we have compared the C4 to its corresponding wildtype using High-Resolution Magic Angle Spinning (HR-MAS) NMR. Moreover, we have compared NAD(P)(H) contents in both strains and performed oxygen consumption and resazurin reduction assays with both strains. The results of these ongoing experiments will be presented.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P16

Evaluation of antimicrobial activity of octenidine against multidrug-resistant Gram-negative pathogens

R Alvarez Marin¹; M Aires de Sousa²; N Kieffer¹; P Nordmann¹; L Poirel¹

(1) University Fribourg;

(2) Escola Superior de Saude da Cruz Vermelha Portuguesa

Aims.

Multi resistant Gram negative (MRGN) pathogens pose a major and growing threat for health care systems, as therapy of infections is often limited due to the lack of available systemic antibiotics. Well tolerated antiseptic molecules may be a very useful implementation in infection control, not only to reduce the dissemination of methicillin-resistant *Staphylococcus aureus* (MRSA), but also MRGN. As decolonization strategies with regard to MRSA are already implemented in high-risk areas (i.e. ICUs), this study aimed to investigate, if the same protocol might be concomitantly efficient against MRGN.

Methods.

A series of 5 different species (*Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*) was studied to prove efficacy under clinically relevant conditions according to an official test norm (EN13727). We used 5 clonally-unrelated isolates per species, including a single wild-type strain, and four MRGN isolates, corresponding either to the 3MGRN or 4MGRN definition of multidrug resistance. Octenidine (OCT, Schuelke & Mayr GmbH, Germany) susceptibility was evaluated with and without organic load.

Results.

A contact time of 30sec or 1min was fully effective for all isolates by using different OCT concentrations (0.01% and 0.05%), with a bacterial reduction factor of >5 log systematically observed. Growth kinetics were determined with two different wild-type strains (*A. baumannii* and *K. pneumoniae*), proving a time-dependent efficacy of OCT, mirroring what has been previously observed for MRSA.

Conclusion.

These results highlight that OCT, besides being a very effective agent against MRSA, may also be extremely useful to eradicate emerging highly resistant Gram-negative pathogens associated with nosocomial infections.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P17

Concomittant Outbreak of extended-spectrum beta-lactamase and carbapenemase-producing *Klebsiella pneumoniae* in a Swiss neonatal intensive care unit

E Moulin; MMH Abdelbary; DS Blanc; I Federli Hanachi; G Greub; M Roth-Kleiner; S Asner; C Petignat
CHUV-University Hospital

Extended-spectrum beta-lactamases (ESBL) and carbapenemase producing Enterobacteriaceae (CPE) outbreaks are associated with serious outcomes in neonatal intensive care units (NICU). Maternal colonisation was previously recognised as the most important factor associated with neonates colonisation. Suboptimal adherence to infection control procedures contributes to horizontal dissemination. In this study, we report concomitant outbreaks of ESBL and CPE *K.pneumoniae* among patients hospitalised in NICU of 40 beds at the Lausanne University Hospital in July 2016.

After initial detection from clinical samples of ESBL *K.pneumoniae* in 3 patients hospitalised in the neonatal intensive care unit, a weekly screening of the stools was conducted in all hospitalised infants. This measure was maintained until all positive patients left the unit. Relevant demographic and clinical data were extracted from hospital records. Samplings of the environment were performed and infection control practices were evaluated. Molecular analysis was executed by PCR in order to identify the enzyme responsible for carbapenemase resistance. The phylogenetic relationship between the isolates was determined by whole genome sequencing (WGS).

Screening of 108 neonate patients revealed that 3 additional infants were ESBL *K.pneumoniae* positive and 2 were CPE *K.pneumoniae* positive. PCR analysis documented the presence of OXA-48 in CPE isolates. WGS revealed that CPE isolates belonged to ST-968 and were highly related, suggesting transmission. Among the 6 patients with ESBL isolates, 4 had highly related isolated of ST-36. One patient had an isolate which did not grow and one had an isolate of ST-111. The latter case was previously thought to be the index case, which turn out not to be truth. Environmental samplings did not achieve to find an epidemic reservoir. Several breaches in prevention and control of infection practices were identified.

This report highlights the epidemic potential of resistant Enterobacteriaceae in hospital settings, even in countries reporting a low level of antimicrobial resistance, such as Switzerland. This underlines the need of strict adherence to infection control procedures, which should be reinforced after cluster identification. Combining early unit screenings together with WGS analysis of the isolates are recommended. WGS plays a major role in outbreak management by providing valuable data on potential epidemiological links between colonised patients.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P18

How effective is standard cleaning to remove dirt and microorganisms?

M Dangel¹; H Brunner²; M Matulin³; AF Widmer³

(1) Universitätsspital Basel;

(2) Bardusch AG;

(3) Universitätsspital Basel

Introduction

Environmental cleaning is a fundamental principle of infection prevention in hospitals, but its role in reducing transmission of healthcare-acquired pathogens has been difficult to prove experimentally.

Objectives

The aim of the present short study was to evaluate whether adenosine triphosphate (ATP) presence, measured by bioluminescence methods (surrogate marker for dirt), can predict microbiological contamination of hospital surfaces, measured by colony forming units (CFU)/100cm².

Methods

In four patient rooms we took Rodac plates from different places before and after cleaning. Simultaneously, we determined ATP testing (expressed as relative light units or RLU) from the same surfaces. The different places which we analysed were: floor under the patient's table, patient's table, armrest chair, bedside table, paper roll dispenser, flush tank button, toilet seat, floor at the entrance, door handle.

Results

A total 142 samples were taken, 72 Rodac plates and 70 ATP (2 missing data). All samples were positive for coagulase-negative Staphylococcus, Micococcus ssp, Bacillus and Corynebacterium species. Before cleaning, Staphylococcus aureus (MSSA) was found in 27.8% of the samples (10/36). After cleaning, MSSA was found in 22.2% (8/36) and in 2.7% (1/36) methicillin-resistant Staphylococcus aureus (MRSA) was found. Analysis of the MRSA strain by PFGE provides strong evidence that the strain originated from a patient of a room at the same ward, but 36.5 meters apart, who had been put on contact isolation.

Before and after cleaning, both dirt measured by ATP ($p < 0.04$) as well as microbiological contamination measured by (CFU)/100cm² ($p < 0.02$), resulted in a significant reduction. To our surprise, dirt removal and microbiological reduction were highly correlated ($p < 0.001$).

Conclusion

ATP reliably detects residual dirt and can be used for a surveillance of the quality of cleaning. However, detection of *S. aureus* and even MRSA requires microbiological analyses, as these microorganisms are not detectable by ATP. In conclusion, ATP and microbiological sampling provide supplementary information, although ATP predicts to some degree the level of microbiological contamination.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P19

Evaluation of a Methicillin-resistant *Staphylococcus aureus* Contact Screening Strategy in a Low Prevalence Setting

M Bächli¹; C Casanova²; M Küffer²; S Droz²; J Marschall³; R Sommerstein³

(1) Inselspital, Universitätsspital Bern;

(2) Institute for Infectious Diseases, University of Bern, Switzerland;

(3) Department of Infectious Diseases, Bern University Hospital, University of Bern

Background

The optimal screening strategy to identify secondary cases after contact with a methicillin-resistant *Staphylococcus aureus* (MRSA) index patient in a low prevalence setting is unknown. We evaluated the screening strategy at Bern University Hospital in Switzerland, from 2008-2014.

Methods

The spa type of all non-duplicate MRSA isolates at the institution during the study period was determined. The screening strategy consisted of screening contact patients who shared room or ward with a proven MRSA index patient by swab cultures. We traced back contacts one year without defining a minimal exposure time. Already discharged contact patients were screened upon readmission up to one year after exposure. Characteristics of index/contact (I/C) matched pairs were further described.

Results

From 2008-2014, we isolated 339 non-duplicate MRSA in our institution, with the predominant spa type being t002 (n=82; 24%). We identified 215 index patients that led to screening of 3013 contacts. Of these, 12 (0.4%) were MRSA positive and 6/12 (50%) had identical I/C spa type. The main I/C matches were spa type t002 (4/6; 67%). All six I/C matches occurred in “same-room” contacts. In the three I/C matches screened within eight days after last I/C contact the exposure time was ≥ 5 days. Three matches were identified upon readmission and demonstrated variable exposure times.

Conclusion

This extensive MRSA screening strategy revealed only few I/C matches based on spa-typing. Not all I/C pairs may represent transmissions given the limited resolution of spa-typing and/or very short exposure time. These data suggest that screening “same-room” contacts is sufficient in a low prevalence setting. Other elements of the strategy (such as readmission screening or “same ward” screening) yielded only very few matches and may be foregone.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P20

Control of a rotavirus gastroenteritis outbreak in three psychogeriatric units

M Gyger; C Petignat; I Nahimana Tessema

CHUV Lausanne

Introduction:

Rotavirus gastroenteritis, common in paediatric population is underestimated in adult. Even if the majority of non bacterial outbreak gastroenteritis is due to norovirus, the part of rotavirus is probably undervalued. Control of gastroenteritis is more complicated when the characteristics of patients make the implementation of recommendations in infection control difficult. We describe the rotavirus impact on the ward organization during an outbreak of gastroenteritis in the department of psychiatry of the Centre hospitalier universitaire vaudois of Lausanne.

Methods:

We collected data from patients and staff data members in epidemic period of gastroenteritis. Stools of symptomatic patients were sending to the laboratory for screening of norovirus and rotavirus. Additional measures to Standard Precautions and specials measures (eg: closing units to news admissions; postponing transfers of patients; management of staff members) were implemented.

Results:

From April 9th to 6th of May 2016, 17/31 patients and 10/78 staff members were affected with respectively an attack rate of 55% and 13%. Among patients, 88% (15/17) presented diarrhea first and that were associated with vomiting in 41% (7/17). The median duration of the disease in patients was 4 days (range; 1 to 12 days). 8/9 samples of stool screened were positives to rotavirus and negatives to norovirus. Three units were closed eleven days additionally to Measures of infection control.

Conclusion:

Control of rotavirus gastroenteritis remains a challenge in psychiatric facilities. The prevention involves routine and terminal cleaning of the patient environment and a particular attention in communication and coordination of different teams.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P21

Not all heater-cooler units are equal – different risk for environmental contamination with *Mycobacterium chimaera* during open heart surgery

RA Kühl¹; F Banderet¹; PM Keller²; D Meinel¹; A Egli¹; R Frei¹; T Döbele¹; F Eckstein¹; AF Widmer¹

(1) University Hospital Basel;

(2) University of Zurich

Aims:

M. chimaera infections have been linked to contaminated aerosols from heater-cooler units (HCUs) during open heart surgery, mainly associated with one type of HCU: the 3T HCU. In our institution, 4 patients were identified with *M. chimaera* infections, each operated before May 2014 using a 3T HCU. However, the contamination of and risk from HCUs of different manufacturers has not yet been systematically assessed.

Methods:

Since June 2014, all HCUs at the University Hospital Basel were continuously monitored for contamination with *M. chimaera*. Three types of HCUs (3T, HCU30 and HCU40) from two different manufacturers were in use during the surveillance. Monthly water samples from the patient- and cardioplegia-circuit as well as air samples next to the operation field before and while operating were obtained. Samples were processed according to the protocol of the National Reference Centre of Mycobacteria and incubated for >5 weeks on solid and liquid media. Air specimens were collected with a microbiological air sampler (MAS-100 NT®) using at least 160L/sample. Positive cultures for mycobacteria were identified by 16S rRNA gene sequencing.

Results:

In June/July 2014, contamination with *M. chimaera* was found in the water of all 3T units (in 8/47 samples, 17%) and HCU30 units (7/12 samples, 58%). During usage, aerosolisation of *M. chimaera* was detected with 3T (in 22/43 samples, 51%) but not HCU30 (0/4 samples, 0%). No aerosolisation occurred with any HCU switched off. By August 2014, all 3T HCUs were replaced by new 3T HCUs. Despite intensified disinfection procedures, *M. chimaera* grew in 2/42 (5%) water samples from 3T HCUs in 2015. In January 2016, all 3T units were replaced by the newest type HCU40. Afterwards, 0/100 (0%) samples obtained from this type of HCU were positive for *M. chimaera* over a surveillance period of 15 months. The integrated ventilator of 3T exhausted a much stronger air flow than HCU30/40 which reached the operation field. The sterile filtered tap water for the HCUs was always free of *M. chimaera*.

Conclusion:

Comparing three different HCUs, only HCU40 remained negative for *M. chimaera* in water and air sampling. In contrast to the 3T HCU, no aerosolisation of *M. chimaera* occurred with HCU30. The 3T type was linked to *M. chimaera* infections, the HCU30 to contamination of the device, but the HCU40 remained negative for *M. chimaera* during 15 months of intensified surveillance and appears to be different from other types of HCUs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P22

Hand hygiene adherence in relation to influenza season over six consecutive years

R Fulchini; P Kohler; C Kahlert; W Albrich; R Kuhn; M Schlegel
Kantonsspital St. Gallen

Background

Health care worker (HCW) adherence with hand hygiene (HH) is important to prevent healthcare-associated infections. We aimed to assess the impact of influenza season on HH adherence.

Methods

We performed a retrospective analysis comparing HH adherence at a Swiss tertiary care hospital during non-influenza periods with adherence during influenza seasons defined according to surveillance reports of the Federal Office of Public Health. HH adherence was monitored by direct observation according to “my five moments” (WHO) using the mobile application CleanHands. The data covered the period from December 20th 2010 until November 24th 2016. The X2-test was used to compare the differences in adherence between non-influenza and influenza seasons stratified for the respective years, professional groups, settings, departments and HH indications. Multivariable logistic regression was used to analyse the relationship between influenza season and HH adherence while controlling for the above mentioned covariates.

Results

A total of 12'740 HH opportunities were observed. Overall adherence was 77%. During influenza seasons HH adherence was higher compared to non-influenza periods with 80% vs. 76% ($p < 0.001$). The effect was most pronounced in the 2010/2011 season (87% vs. 80%, $p = 0.001$), among doctors (82% vs. 75%, $p < 0.001$) and in inpatient settings (81% vs. 78%, $p = 0.004$). In multivariable analysis influenza season was an independent predictor of increased HH adherence (OR=1.17, 95% CI 1.05-1.30). Independent factors associated with lower HH adherence were non-nurse/non-physician compared to nurses (OR=0.48, 95% CI 0.36-0.62), surgical theatre compared to medical wards (OR=0.53, 95% CI 0.44-0.64), and outpatient compared to inpatient setting (OR=0.43, 95% CI 0.35-0.53).

Conclusions

We identified influenza season as potential determinant that positively affects HH adherence of HCW, especially in physicians. Further systematic study is needed to verify this association and evaluate the clinical impact on transmission or nosocomial infection and implications for HCW education in a prospective setting.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P23

Evaluation eines einheitlichen Flächendesinfektionsmittels in einer Spitalgruppe

W Steiger¹; Y Fietze¹; W Girardi²; B Finke³; LM Ruga¹; J Marschall¹

(1) Inselspital, Universitätsspital Bern;

(2) Tiefenauspital Inselgruppe;

(3) Facility Services Inselgruppe, Inselspital Bern

Aims

Die existierenden Flächendesinfektionsmittel (FDM) in der Inselgruppe vereinheitlichen oder durch andere ersetzen.

Methode

1. Bildung einer interdisziplinären Arbeitsgruppe
2. Ist-Analyse (Bestandsaufnahme in 6 Spitälern)
3. Auswahlverfahren der FDM (objektiver Produktvergleich anhand einer Tabelle „ Vor- und Nachteile, vergl. Grafik)
4. Testung von 3 FDM (1 Aldehyd, 2 QAV) in verschiedenen Settings
5. Datenerhebung und Auswertung (Umfrageergebnisse anhand eines standardisierten Fragebogens, vergl. Grafik)
6. Entscheid

Resultate

Die Auswertung der Datenerhebungen:

Produkt 1: Kohrsolin®FF (Aldehyd)

Es zeigte sich, dass einzelne Mitarbeiter mit starken Vorbehalten auf das aldehydhaltige Produkt reagierten. Als Grund wurden Symptome wie Augenbrennen, Hustenreiz und Kopfschmerzen angegeben.

Produkt 2: terralin® protect.(QAV)

Das Produkt zeigte eine starke Streifenbildung und auf den Böden sowie einen Aufbau von klebrigen Belägen. Dies führte zu Mehraufwand durch zusätzliche Zwischenreinigungen.

Produkt 3: Incidin® Pro

Dieses Produkt wurde als das Beste beurteilt. Fast geruchlos, gute Reinigungsleistung und nur leichte Streifenbildung. Es zeigte sich aber, dass das Produkt einen starken Härtefehler aufwies, was zu Ausfällungen und Verkrustungen an den Arbeitsgeräten führte.

Schlussfolgerungen

Neben einem möglichst umfassenden Wirkungsspektrum ist eine interdisziplinäre Evaluation ein zentraler Gesichtspunkt bei der Auswahl eines neuen Flächendesinfektionsmittels.

Die Produkte 1 und 2 wiesen gemäss der Anwender deutliche Defizite auf, weshalb sie nicht in Betracht gezogen wurden. Ein QAV-basiertes Produkt wurde favorisiert.

Nachdem der Hersteller den Härtefehler durch eine Änderung der Formulierung behoben hatte, konnte das Produkt im Jahr 2016 erfolgreich in den sechs Spitälern der Inselgruppe implementiert werden.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P24

Can ICD-10 Coding Data Be Used for Surveillance of Hospital Acquired Pneumonia?

A Meier; M Meier; SP Kuster; H Sax; A Wolfensberger
 Universitätsspital Zürich

Background:

Surveillance of healthcare-associated infections (HAI), especially hospital-acquired pneumonia (HAP), is time- and resource-intensive and is performed according to established and validated definitions, e.g. by ECDC (European Centre for Disease Prevention and Control). Discharge diagnostic codes, according to International Classification of Diseases, tenth Revision (ICD-10), are primarily used for accountancy but constitute an attractive low-cost alternative for HAP surveillance.

Aim:

To evaluate if discharge diagnostic codes (ICD-10) can be of use for HAP surveillance.

Methods:

Comparison of ICD-coded HAP (ICD-HAP) with ECDC-defined HAP (ECDC-HAP; gold standard) through in-depth retrospective review of the electronic patient records. We reviewed all 164 medical histories of patients with an ICD-HAP among all 6,064 patients discharged during 2016 from four departments of the University Hospital Zurich. Additionally, we reviewed a random sample of 400 of the remaining 5900 patients without ICD-HAP for ECDC-HAP (100 patients per department).

Results:

The positive predictive value of ICD-HAP against ECDC-HAP was 55.5% (CI95%, 47.5-63.2%). Reasons for not fulfilling the ECDC-HAP definitions were the following: radiologic criteria (n=34, 46.6%), clinical symptoms absent or not documented (n=14, 19.2%), community-acquired pneumonia i.e. onset of symptoms less than 48 hours after admission (n=14, 19.2%), no fever, no leukocytosis, or no leucopenia (n=11, 15.1%).

Of the random sample with no ICD-HAP, seven of the 400 patients fulfilled ECDC-HAP criteria (1.8%; CI95% 0.7–3.8%). The percentage of missed HAP by ICD-HAP criteria was 0% (CI95% 0–3.6%) for two departments, 3% (CI95% 0.0-8.5%) and 4% (CI95% 1.1-9.9%) for one department each.

Conclusion:

ICD-10 coding data do not seem to be adequate for the detection of HAP according to ECDC definitions and therefore should not be used as an alternative method for HAP surveillance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P25

Analysis of two years sequential outbreaks of vancomycin-resistant *Enterococcus faecium* at a tertiary care hospital using whole-genome sequencing

MMH Abdelbary¹; E Moulin¹; A Kenfak Foguena¹; D Berthod¹; G Greub²; D Hequet¹; G Zanetti²; L Senn¹; DS Blanc²

(1) Lausanne University Hospital (CHUV);

(2) Lausanne University Hospital and University of Lausanne

Aim:

We used whole-genome sequencing (WGS) to investigate three sequential VREfm outbreaks, which occurred between November 2014 and October 2016 at the Lausanne University Hospital (CHUV). Methods: We analysed a total of 130 VREfm isolates that were retrieved from clinical samples and screening rectal swabs between November 2014 and October 2016 using WGS. All isolates were sequenced using the Illumina MiSeq platform. Multilocus sequence typing (MLST) and the identification of acquired antibiotic resistance genes were performed using the sequencing data. Comparative genome analysis of the assembled ordered draft genomes was performed using Mauve software. To infer the isolates' phylogeny, all paired-end reads were mapped to the publicly available VREfm reference genome Aus0004 (accession number: NC_017022). Subsequently, a maximum likelihood tree was constructed using single nucleotide polymorphisms (SNPs) from a core genome alignment.

Results:

The MLST analysis revealed that three different sequence types (ST), labelled ST17 (n = 54), ST80 (n = 51), and ST117 (n = 16), were the most predominant between the 130 VREfm genomes. WGS analysis showed that the first VREfm outbreak (January 2015 – March 2015) was caused by ST17, and revealed two undiscovered cases prior to the index case. The second (April 2016 – June 2016) and the third (October 2016) outbreaks were due to the introduction of two distinct phylogenetic lineages that belong to ST80, although they occurred in the same ward. Furthermore, we detected several transmission events of ST17, ST117 and ST18, which were not previously suspected from epidemiological data. On the basis of the core genome and epidemiological data, we were able to trace the majority of the transmission events between patients in each outbreak with a high degree of certainty. All sequenced isolates harboured vanA gene cluster with exception of three isolates that belong to ST18 carrying vanB gene cluster.

Conclusions:

The use of WGS allowed us to determine the dissemination of three distinct phylogenetic lineages of VREfm that caused sequential outbreaks over two years. In addition, our analysis revealed cases prior to the outbreaks, which highlighted unsuspected transmission events and allowed the adjustment of infection control measures. Combination of phylogenetic analysis and epidemiological data were able to detect patient-to-patient transmissions within the hospital and the index case of the first outbreak.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P26

Inferring the phylogenetic relatedness of understudied bacterial pathogen in the lack of closely related reference genome

MMH Abdelbary¹; L Senn¹; E Moulin¹; G Prod'homme²; A Croxatto²; G Greub²; DS Blanc²

(1) Lausanne University Hospital (CHUV);

(2) Lausanne University Hospital and University of Lausanne

Aim:

Whole-genome sequencing (WGS) has emerged as a powerful molecular typing method for outbreak analysis enabling the rapid discrimination between outbreak and non-outbreak isolates. However, such analysis can be challenging in the lack of closely related reference genome. In this study, we assessed the use of WGS in investigating an outbreak of relatively understudied bacterial pathogen such as *Burkholderia cepacia* with no publicly available closely related reference genome.

Methods:

Using Illumina MiSeq platform, we sequenced 11 *B. cepacia* isolates (seven from patients and four from disposable dermal gloves packages) that were collected during an outbreak between May and August 2016 at the university hospital of Lausanne. In addition, we included 11 *B. cepacia* genomes from the public database. WGS analysis was performed using a combination of both de novo assembly and mapping approaches.

Results:

Mapping the sequence reads from the 22 *B. cepacia* isolates to the five publicly available *B. cepacia* reference genomes revealed an average coverage between 51.7% and 68.4%. Therefore, we used the de novo assembled genome of the clinical isolate H32570 as a reference to maximise the accuracy of SNP calling (average reference genome coverage of 99.5 %). We were able to demonstrate that the 11 *B. cepacia* outbreak isolates were closely related and were phylogenetically distinct from the publicly available *B. cepacia* genomes. In addition, the pairwise SNPs distance analysis detected only 1-6 single-nucleotide polymorphisms (SNPs) differences among the outbreak isolates, which confirms that the contaminated disposable dermal gloves were the cause of the outbreak. Of note, no recombination events were detected among the outbreak isolates suggesting a clonal dissemination of the isolates core genomes and their divergence from a common ancestor, which probably happened very recently.

Conclusions:

The present study emphasizes the potential of WGS in outbreak investigations. We demonstrated the genetic relatedness between *B. cepacia* isolates that were isolated from the patients and the pre-moisturized disposable dermal gloves packages, which confirms the latter to be the cause of the outbreak. Furthermore, the WGS framework used in this study can be successfully applied for investigating outbreaks of understudied pathogens. However, further WGS-based studies are required to investigate the dissemination and the population structure of understudied pathogens.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P27

Influenza-Surveillance im Spital: Vielschichtig und komplex

D Flury¹; R Kuhn¹; B Pruzinova¹; G Rettenmund¹; K Stiebeler¹; D Nicca²; M Schlegel¹

(1) Kantonsspital St. Gallen;

(2) Universitätsspital Basel

Einleitung:

Mit dem Ziel, PatientInnen vor nosokomialer Influenza zu schützen, wurde 2014 das „Healthcare-associated Influenza Prevention“ Projekt (HaIP) gestartet. Dazu soll a) eine komplexe Intervention zur verbesserten Prävention in Spitälern entwickelt und b) eine Surveillance zur Monitorisierung von PatientInnen mit (nosokomialer) Influenza und des Präventionsverhaltens von medizinischem Personal zur Überprüfung der Wirksamkeit der Intervention aufgebaut werden. Hier werden die Resultate der Surveillance seit 2014 am Kantonsspital St. Gallen (KSSG), dargestellt.

Methodik:

Seit 2014 werden am KSSG, einem Tertiärspital mit 700 Betten, alle Kliniken mit Schulungen und Informationen aufgefordert, während der Grippezeit bei PatientInnen mit Symptomen einer Influenza eine Diagnostik durchzuführen und die PatientInnen entsprechend internen Richtlinien zu isolieren. Erfasst werden die Anzahl (nosokomialer) Influenza-Infektionen und die Adhärenz mit anerkannten Massnahmen zur Verhinderung nosokomialer Infektionen (Jährliche Impfung, Isolation bei (Vd auf) Influenza, Händedesinfektion, Tragen einer chirurgischen Maske, Hustenetikette).

Resultate:

Der Anteil nosokomialer Influenza (Anzahl PatientInnen mit nosokomialer Influenza zu Anzahl hospitalisierte PatientInnen mit Influenza) betrug in der Influenzasaison 2014/15 26%, für 2015/16 11% und 2016/17 8%. Unverändert blieben die Adhärenz mit der Händedesinfektion (ca.80%) und die Durchimpfungsraten (niedrig), während die Isolationen bei Influenza deutlich zunahmen: Influenzasaison 2014/15: Total 73%, davon 0 vorsorglichen Isolationen bei ausstehendem (positivem) Resultat des Influenzaabstrichs, 2015/16: 77%, davon 9% vorsorglich, Influenzasaison 2016/17: 84%, davon 31% vorsorglich.

Schlussfolgerungen:

Der Aufbau einer Surveillance von nosokomialer Influenza-Infektionen im Akutspital ist möglich, braucht jedoch Schulung und systematischen Aufbau. Obwohl noch keine spezifischen Interventionen durchgeführt wurden, ist die Zahl der Isolationen, insbesondere der vorsorglichen gestiegen. Die Implementierung einer systematischen Surveillance wirkt sich direkter auf die Präventionsmassnahme Isolation, als auf andere mit persönlichen Verhaltensweisen verbundenen Massnahmen wie Händehygiene und Impfung aus. Damit die Kombination aller Massnahmen als effektivste Prävention implementiert werden kann, sind spezifischere Interventionen notwendig.

Mit bestem Dank ans gesamte HaIP-Team (Laura Baldussi, Manuela Rasi, Adrian Egli, Anja Ulrich, Pietro Vernazza)



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P28

Comparison of risk factors for colonisation with multidrug-resistant Gram-negative bacteria and MRSA in repatriated patients

E Lemmenmeier¹; M Schlegel¹; B Mani²; WC Albrich¹

(1) Kantonsspital St. Gallen;

(2) Zentrum für Labormedizin

Aim:

To analyse risk factors for colonisation with multidrug-resistant Gram-negative bacteria (MRGN) and Methicillin-resistant *Staphylococcus aureus* (MRSA) on admission to our tertiary care hospital.

Methods:

All patients who had been hospitalised abroad within the last 6 months were screened for MRGN with rectal and for MRSA with nasal, throat and inguinal/axillar swabs. If open wounds or invasive devices were present, additional samples were obtained from wounds, urine or tracheal secretions. Samples for MRGN were incubated in an enrichment broth and subsequently inoculated on screening plates for ESBL and Oxa-48. Suspected ESBL and carbapenem resistance was investigated phenotypically and with PCR. Since our hospital does not require contact precautions for patients with ESBL-E.coli, these samples were not further investigated. Samples for MRSA were inoculated on screening plates and if growth was present agglutination for *pbp2a* was performed for MRSA confirmation. Pulse field gel electrophoresis was applied for typing.

Results:

217 patients underwent admission screening from June 2013 until April 2016. 46 (21%) were colonised with MRGN, but only 21 (9.7%) required contact precautions according to local guidelines. Most identified species were *E.coli* (n=28, 13%) and *K.pneumoniae* (n=14, 6.5%). Most resistance mechanisms were ESBL (n=42, 19.3%), 7 (3.7%) bacteria harboured carbapenemases. 8 (3.7%) patients showed colonisation with MRSA. 4 (1.8%) of them were also colonised with MRGN. 2/8 (25%) of the detected MRSA types are endemic in Eastern Switzerland. Risk factors for colonisation with MRGN differed from MRSA. In univariate analysis, we identified 6 risk factors for MRGN, 3 for MRSA colonisation. In logistic regression analysis diabetes remained an independent risk factor for MRSA colonisation, urinary catheter for MRGN. Colonisation with MRGN or MRSA resulted in longer hospital stay.

Conclusion:

In our admission screening we detected a higher colonisation rate for MRGN than for MRSA. A quarter of patients with MRSA colonisation might have acquired the MRSA in Switzerland with coincidental detection after repatriation. Acquisition abroad seems to play a more important role for MRGN than for MRSA. Colonisation with MRGN as well as MRSA resulted in longer hospital stay. As risk factors for colonisation differed between MRGN and MRSA, different screening strategies may be necessary for these pathogens.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P29

Performance of *Acinetobacter baumannii* screening among patients admitted in ICU at a Swiss tertiary care hospital

A Kenfak Foguena; D Blanc; A Croxatto; J Pagani; L Senn
Lausanne University Hospital (CHUV)

Aim:

Acinetobacter baumannii represents a major concern in intensive care units (ICU). Since the occurrence of a multidrug resistant *A. baumannii* outbreak in our burn unit in 2002-2004 (Zanetti et al. Infect Control Hosp Epidemiol. 2007), we implemented a systematic screening of high risk patients: sanitary repatriation from abroad, hospitalization abroad during the previous year or visit of the Indian subcontinent the previous year. However, we often face patients presenting with *A. baumannii* in clinical samples, despite negative screening on admission. The aim of this study was to evaluate the performance of our screening program.

Methods:

All high risk patients screened for *A. baumannii* on admission into the ICU of the Lausanne University Hospital were included. Screening consisted in rectal swab, throat swab, urine, bronchial sampling and wound swab if any. Cultures were performed using a selective broth containing sodium acetate as the only carbon source. To determine the performance of our screening strategy, we further classified patients according to the presence or absence of *A. baumannii* in clinical sample during their stay in ICU.

Results:

From 2010 to 2016, 76 patients were screened on admission, 13 (17.1%) of whom were colonized with *A. Baumannii*. Clinical samples during hospitalisation revealed *A. Baumannii* in three (4.8%) other patients 1, 6 and 20 days after admission. This interval may suggest the need of repeating screening in high risk patients. Despite local guidelines, the number of screened sites was inconstant. Overall, in the 16 infected or colonised patients the performance of the screening was different among sites: respiratory samples (60%, 3/5), throat (53%, 8/15), rectum (62%, 8/13) and urines (33%, 2/6).

Conclusion:

Our results showed that no clinical site is preferentially colonized with *A. Baumanii*, emphasizing the need to screen multiple sites (including respiratory tract). One may also consider repeating sampling in high risk patients.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P30

Evaluation eines Ausbruchs mit *Clostridium difficile* Ribotyp 027 in einer Spitalgruppe

A Künzli¹; S Bachmann¹; C Casanova²; J Marschall¹

(1) Inselspital, Universitätsspital Bern;

(2) Universität Bern

Hintergrund

Das klinische Bild von *Clostridium difficile*-Infekten variiert von Diarrhoe bis zur fulminanten Kolitis. Aerotolerante Sporen sichern dem Keim ein monatelanges Überleben in der Umwelt. Der hochvirulente Ribotyp 027 zeigt erhöhte Toxin- und Sporenbildung sowie eine entsprechend hohe Mortalitätsrate.

In unserem Spital geschah das erste Auftreten des Ribotyps 027 im Rahmen eines Ausbruchs: innert 22 Wochen wurde bei 18 Patienten ein *C. difficile* 027 nachgewiesen; hiervon sind vier Patienten an einer *C. difficile*-assoziierten Kolitis verstorben.

Methode

Zur Aufarbeitung des Ausbruchs wurde eine „Line List“ mit Patientencharakteristika, diagnostischen und klinischen Informationen sowie Aufenthaltsorten und -zeiten der Patienten erstellt. Bei allen Stuhlproben mit PCR-Verdacht auf *C. difficile* 027 wurde anschliessend eine Ribotypisierung der Isolate durchgeführt.

Resultate

Wir stellten fest, dass nicht in allen Labors der Spitalgruppe *C. difficile* auf den hypervirulenten Ribotyp getestet wurde. So wurde drei Wochen vor dem ersten Nachweis von 027 bei zwei der Patienten bloss das Vorkommen eines *C. difficile* bestätigt. In Folge wurden alle Stuhlproben mit positivem *C. difficile* Screeningtest der gesamten Spitalgruppe im zentralen Mikrobiologielabor analysiert. Die Phylogenieanalyse zeigte fehlende oder minimal divergente Nukleotidvarianten, was den starken epidemiologischen Zusammenhang zwischen den individuellen Fällen bestätigte.

Mit der „Line List“ wurden Zimmer mit einer Häufung betroffener Patienten identifiziert, welche sporizid gereinigt wurden. Trotz dieser Anpassung wurden erneut Patienten positiv getestet, bei welchen ein Zusammenhang mit bereits gereinigten Zimmern nicht ausgeschlossen werden konnte. Daher wurden die Isolations- und Reinigungsmaßnahmen verschärft und das Personal der gesamten Spitalgruppe auf den Ausbruch aufmerksam gemacht.

Schlussfolgerungen

Infektionen mit dem *C. difficile* Ribotyp 027 zeigen einen schweren Verlauf mit einer hohen Rezidivrate und Letalität. Die genaue Erfassung aller betroffenen Patienten und intensivierten Isolations- bzw. Reinigungsmaßnahmen werden als zentral für die Eindämmung eines Clusters von *C. difficile* 027 erachtet. Nicht jedes Labor untersucht derzeit Clostridienisolate auf hochvirulente Ribotypen, weswegen von verpassten Erkrankungen ausgegangen werden muss. Daher sollte die schweizweite Einführung einer Ribotypentestung und -erhebung diskutiert werden.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P31

Evaluation de la qualité de la surveillance de l'hygiène des mains dans un hôpital universitaire en Suisse

E Viaccoz; L Senn; A Kenfak Foguena
CHUV-Lausanne University Hospital;

But :

Le taux d'observance de l'hygiène des mains (HM) est significativement corrélé au taux d'infections associées aux soins. La mise en œuvre d'une surveillance de l'HM permet de suivre cet indicateur au cours du temps et d'évaluer l'impact d'interventions visant à améliorer l'observance. Les résultats doivent être fiables et reproductibles entre différents observateurs.

Le but de cet audit était d'évaluer la qualité de notre programme de surveillance de l'HM conduit par des spécialistes en prévention et contrôle de l'infection (PCI).

Méthode :

La concordance de la reconnaissance des 5 indications et de l'appréciation des pratiques de l'HM au sein d'une équipe de 7 spécialistes PCI (observateurs) a été évaluée. Pour cela, des soignants ont été observés simultanément par 2 observateurs (binôme). L'application CleanHands de Swissnoso qui permet la saisie en ligne des observations et l'analyse automatisée et comparative des résultats a été utilisée.

Les binômes avaient pour consigne d'observer chacun 20 opportunités à HM. Le choix des soignants observés était laissé libre aux binômes. Les observations étaient enregistrées au fur et à mesure dans CleanHands. Les données enregistrées ont ensuite été confrontées pour chaque binôme, pour en évaluer la concordance.

Résultats :

Quatre binômes d'observateurs ont observés au total 88 opportunités à l'HM, pour un taux d'observance global de 74%. L'appréciation globale du taux d'observance était concordante, avec une différence < 5% entre les observateurs de chaque binôme. Par contre, la reconnaissance du type d'indications à l'HM variait dans 17/88 (19%) des cas. Les divergences concernaient principalement les situations de concomitance d'indications et la reconnaissance de l'indication après environnement.

Conclusion :

L'évaluation globale du taux d'observance est concordante entre les différents observateurs. Par contre la variabilité dans la reconnaissance des indications à l'HM peut impacter significativement la reproductibilité des résultats par indications et la comparaison avec d'autres hôpitaux. Les observateurs doivent s'en tenir strictement aux descriptions des indications à HM selon les recommandations OMS et aux définitions de concomitance du manuel CleanHands. Une harmonisation de la reconnaissance des indications via la procédure Cleanhands et les définitions de l'OMS permettra de réduire cette disparité. Des évaluations internes de la qualité de la surveillance devraient être programmées régulièrement.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P32

Decolonization of Methicillin-resistant *Staphylococcus aureus*: risk factors for failure

B Müller-Steiert; S Burri; N Bartlomé; E Bucheli Laffer
Kantonsspital Aarau

Aim:

International guidelines promote decolonization of MRSA carriers to avoid transmission. However, various factors limit decolonization success in clinical practice. Using our MRSA-decolonization database and our daily experience, we aim to propose an algorithm to select patients with a reasonable chance of successful decolonization and discuss risk factors of failure.

Methods:

We perform routine decolonization for MRSA using a standardized protocol (Fig. 1) based on international recommendations. All patients are instructed individually by trained infection control staff (ICS). Success of decolonization is evaluated with 3 swab-sets (nose, throat and groin) every 4 weeks over a 12 week period and repeated decolonization is recommended in case of failure. Details on decolonization are prospectively collected in a database, which we used to identify major risk factors of decolonization failure.

Results:

In 2015 and 2016, 65 patients underwent decolonization, 15 of whom showed low compliance or were lost to contact. 18/50 (36%) patients with completed follow-up were successfully decolonized. 21 (42%) swab sets after decolonization are yet incomplete, but negative to date. Repeated decolonization was performed in 11 patients with a success rate of 60%. Success rates were very low (11%) in patients colonized in the vagina, trachea or bladder, despite use of systemic antibiotics in some cases. Another group with low success rate (21%) are asylum seekers living in collective households.

Conclusion:

Despite the use of a standardized protocol based upon current literature, our success rate in MRSA decolonization was low. This might be due lower false-negative testing due to longer follow-ups. As decolonization is time- and resource-consuming, a better patient selection using the above mentioned risk factors for failure is needed. An intensified procedure in subgroups with a high risk of failure could improve success rates. A prospective multi-center study evaluating additional interventions in difficult-to-decolonize groups could improve outcome.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P33

Korrelationen zwischen Feinstaubmenge, Pilzsporenkonzentration und invasiven Pilzinfekten im Zusammenhang mit intensiver Bautätigkeit an einem Universitätsspital: eine prospektive Studie über 15 Monate

E Rolli¹; A Künzli¹; E Lo Priore¹; W Steiger¹; B Jung¹; K Mühletahler²; A Atkinson¹; R Sommerstein¹; J Marschall¹

(1) Inselspital, Universitätsspital Bern;

(2) Universität Bern

Hintergrund

Das optimale Vorgehen zur Verhinderung von Pilzinfekten während Bauarbeiten an einem Spital ist unklar. Unser Ziel war es, Zusammenhänge zwischen Feinstaubkonzentration der Aussenluft, Sporen Mengen in Patientenzimmern und invasiven Pilzinfekten zu untersuchen mit der Hypothese, dass einfache Präventionsmassnahmen wie Fensterschliessung und Befeuchtung der Baustelle (insbesondere während des Abbruchs) ausreichen, um eine Erhöhung der Sporenkonzentration und der Schimmelpilzinfekte zu verhindern.

Methode

Von August 2015 bis Dezember 2016 wurden wöchentlich die Feinstaubkonzentration an drei Aussenstandorten, die Pilzsporenkonzentration auf sechs Abteilungen sowie meteorologische Daten und sichtbare Staubentwicklung dokumentiert. Die intensive Bautätigkeit (Abbruch) vom 30.05.2016 bis 16.08.2016 wurde den Phasen niedriger Aktivität (Rückbau) gegenübergestellt. Invasive Pilzinfekte wurden definiert als positive Galaktomannanwerte und/oder Lungenbiopsien mit Schimmelpilznachweis. Die Rate invasiver Pilzinfekte vor und während intensiver Bautätigkeit wurde verglichen. Wir benutzten Poisson mixed effect models, um Abbruchtätigkeit, Wetterdaten, Feinstaub- und Sporenkonzentration zu korrelieren.

Resultate

Die Feinstaubkonzentrationen variierten von 3-115µg/m³ (angegeben als Median der drei Messstandorte eines Messtages; IQR 16–53.6) und die Sporenkonzentrationen von 8-75CFU/m³ (Median jedes Messtages; IQR 8–40). Höhere Feinstaubkonzentrationen wurden durch das Wetter beeinflusst. Pilzsporenkonzentrationen auf den Abteilungen hingen vom Wetter und der Feinstaubkonzentration ab. Im Vergleich zum Rückbau fanden sich während des Abbruchs weder höhere Feinstaubmengen (OR 1.03, 95% CI 0.96-1.09) noch höhere Sporenkonzentrationen (OR 0.69; 95% CI 0.66-0.71, p<0.001). Während des einzigen Messtages mit sichtbarer Staubentwicklung zeigte sich eine erhöhte Feinstaubkonzentration (OR, 15.6, 95% CI 14.9-16.4; p<0.001) sowie eine erhöhte Sporenzahl (OR 6.8; 95% CI 4.76-9.72, p<0.001). Die jährliche Infektrate durch Schimmelpilze blieb während der Bauarbeiten unverändert (p=0.66).

Schlussfolgerungen

Gemäss diesen Daten wurde unter einfachen Präventionsmassnahmen bei intensiver Bautätigkeit keine Erhöhung der Sporenkonzentration in Innenräumen des Spitals festgestellt. Auch hatten die Abbrucharbeiten keinen Einfluss auf Infektionsraten durch Schimmelpilze. Sichtbarer Staub auf der Baustelle war ein Marker für erhöhte Sporenkonzentration in Innenräumen.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P34

Nosocomial influenza: Insights from the introduction of rapid in-house PCR-based detection of influenza viruses from nasopharyngeal swabs

M Egger; L Mathieu; R Boschung; S Duppenhaler; B Kessler
 Spital Emmental

Aims:

Isolation of patients with proven or suspected influenza is resource-consuming and neglects patients who are not screened for the disease. Therefore, we have not screened and isolated patients at our hospital so far but promote universal respiratory standard hygiene instead. As a basis for a future evaluation of this approach rapid in-house PCR-based detection (GeneXpert) of influenza viruses has been introduced during the 2016/2017 influenza season. We aimed to test the applicability of the method in daily practice and to get a crude measure of nosocomial influenza transmission at our hospital.

Methods:

Patient characteristics, data on the temporal relation between admission and influenza testing as well as on antibiotic use were retrospectively collected in all inpatients tested by GeneXpert between December 26th 2016 and March 4th 2017. Testing was recommended for patients with influenza-like illness (temperature $>37.8^{\circ}\text{C}$ and respiratory symptoms, arthralgia or headache), exacerbated COPD or pneumonia. In patients with multiple tests only the first positive test or, in case of consistently negative results, the first negative test was included. A first positive test later than 48h after admission was considered a possible, later than 96h a probable nosocomial case. Standard statistical methods were applied.

Results:

292 patients were included in the analysis, 138 (47%) were female, median age was 77 years (IQR 69-83). 100 (34%) were positive for influenza A and 3 (1%) for influenza B. 10 (9.7%) were possible, 8 (7.8%) probable nosocomial cases (all influenza A). 13 influenza cases (12.6%) were admitted from long term care, adding up to 21 health care-associated cases (20.4%). Nosocomial cases were no more likely to have been placed in 5-bed-rooms versus double or single rooms ($p=1.00$, Fisher's exact). Antibiotic days per 100 hospital days were significantly lower in patients with positive versus negative influenza virus detection (incidence rate ratio 0.85, 95%-CI 0.75 – 0.96).

Conclusion:

8 to 10% of influenza cases at our institution may be acquired in hospital. These rates appear at least not higher than those from institutions with an isolation strategy for influenza. Influenza detection may contribute to a reduction of antibiotic use.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P35

Are antibiotic resistant pathogens more common in subsequent episodes of diabetic foot infection?

I Uçkay; B Kressmann; D Pittet
Geneva University Hospitals

Aims:

After antibiotic therapy of an initial diabetic foot infection (DFI), pathogens isolated from subsequent episodes might become more resistant to commonly prescribed antibiotics. If so, this might require modifying current recommendations for selecting empiric antibiotic therapy. We investigated whether the Infectious Diseases Society of America (IDSA) DFI guideline recommendations should be modified based on the number of past DFI episodes.

Methods:

Single-center retrospective cohort survey of patients hospitalized for DFI.

Results:

We found 1018 DFI episodes in 482 adult patients, who were followed-up for a median of 3.3 years after the first DFI episode. The total number of episodes was 2257 and the median interval between recurrent episodes was 7.6 months. Among the recurrent DFIs, the causative pathogens were the same as in the previous episode in only 43% of cases (158/365).

Staphylococcus aureus was the predominant pathogen in all episodes (range, 1 to 13 episodes) and was not more prevalent with the increasing number of episodes. DFI were treated with systemic antibiotics for a median duration of 20 days (interquartile range, 11-35 days). Overall, there was no increase in the incidence of antibiotic resistances to methicillin, rifampicin, clindamycin or ciprofloxacin lacked significant increase over the episodes (Pearson- χ^2 -tests 0.76, 1.00, 0.06 and 0.46; corresponding p-for-trend values were 0.21, 0.27, 0.38, and 0.08, respectively).

Conclusion:

After a successful treatment of a DFI, recurrent episodes are frequent. A history of a previous DFI episode did not predict greater likelihood of an antibiotic resistant isolate in subsequent episodes. Thus, empirical broadening the spectrum of empiric antibiotic therapy for recurrent episodes of DFI does not appear necessary.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P36

Acute Transverse Myelitis as a complication of *Mycoplasma pneumoniae*. A case report

B Ferrario; T Salamone; T Fusi; E Bernasconi
Ospedale regionale di Lugano

Background:

Acute Transverse Myelitis (ATM) is a severe neurological complication of *Mycoplasma pneumoniae* (MP) infection, predominantly affecting young people. Diagnosis can be difficult, clinical evolution and prognosis may be severe. Central nervous system involvement is not completely understood, but autoimmune phenomena seem to have a major role in the development of myelitis.

Case report:

A 32-year-old patient presented to our emergency department for acute urinary retention. The patient reported fever associated with non-productive cough, lasting for 10 days. He has received a single dose of azithromycin. An accurate clinical examination showed weakness of the lower extremities and absence of abdominal reflexes. Laboratory findings were normal, the chest x-ray showed a right-sided pneumonia. In consideration of the clinical findings, we highly suspected a MP infection, which was later confirmed by a nasopharyngeal PCR assay. We completed the investigations with a cerebral and spine MRI, the latter showing diffuse signal enhancement and swelling. The cerebrospinal fluid (CSF) analysis showed pleocytosis, serology for MP in blood and CSF was negative. A MP pneumonia complicated by acute transverse myelitis was diagnosed.

The patient received corticosteroid treatment for 3 weeks and initial broad spectrum antibiotic and antiviral therapy was started (ceftriaxone 2 g/12h, amoxicillin 2 g/4h) associated with acyclovir (1 g/8h). The positivity for MP PCR assay led to an antibiotic switch to doxycycline for 14 days. The urinary retention resolved after catheter placement for three weeks. The patient showed a full recovery and was discharged after one week.

Conclusion:

MP diagnosis may be insidious, because pathognomonic signs are lacking. Therefore, the true incidence of respiratory infections caused by MP is probably underestimated. The nasopharyngeal PCR assay is the most sensitive and specific examination in the acute phase. Newer studies using molecular techniques have isolated MP in up to 35% of cases with lower respiratory tract infection.

ATM is a rare complication of MP infection with characteristic findings in the MRI. Further studies on a broader patients' population will be necessary to identify the adequate diagnostic and therapeutic approach for ATM and elucidate the role of antimicrobial and immunomodulating therapies. At the same time long-term prognosis needs to be further defined.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P37

PlyAZ3aT, the first phage lysin isolated from a *Streptococcus tigurinus* prophage

F Gauye; P Moreillon; G Resch

University of Lausanne

Aim.

Antibiotic resistance is increasing in Streptococci. The *Streptococcus mitis*-like *Streptococcus tigurinus* species is responsible for endocarditis, spondylodiscitis and meningitis. Bacteriophage lysins (lysins) were shown to be efficient antimicrobials when added externally to many Gram-positive. Our aim was to evaluate a newly purified *S. tigurinus* lysin PlyAZ3aT in the view of developing it as a new effective anti-pneumococcal agent.

Methods.

plyAZ3aT was cloned in pinIIIA vector and overexpressed in *E. coli*. Purified PlyAZ3aT was obtained through Fast Protein Liquid Chromatography (FPLC) on DEAE-sepharose. PlyAZ3aT was evaluated in vitro using classical assays. For in vivo evaluation, CD1 Swiss female mice were challenged i.p. with 10⁶ CFU of *Streptococcus pneumoniae* D39lux (D39lux) and treated i.p. with either PlyAZ3aT or the reference pneumococcal lysin Cpl-1. Mice were followed over 6 days and differences in survival were determined by Kaplan-Meier plots. Statistics were performed using the Gehan-Breslow-Wilcoxon test

Results.

plyAZ3aT was found on a prophage in the genome of *S. tigurinus* AZ3aT. It showed 80% identity with Cpl-1 at the N-terminal catalytic domain but not at the C-terminal cell wall binding domain (47% identity). PlyAZ3aT was found in vitro to be specific for streptococcal species known to harbour choline in their cell walls with an optimal activity at pH 4-7. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) for D39lux were significantly lower for PlyAZ3aT (<1 mg/L and 6 mg/L, respectively) than for Cpl-1 (8 mg/L and 32 mg/L, respectively). In vivo, repeated injections of PlyAZ3aT (3-time 600µg within 8h) were found to significantly improve the survival of mice challenged i.p. with D39lux (30% survival at day 6 versus 0% at day 2, p<0.0001). However, a similar regimen of Cpl-1 rescued 80% of mice at day 6 (p<0.0001).

Conclusion.

A new phage lysin showing promising anti-pneumococcal activity was purified. While more active than Cpl-1 in vitro on D39lux, PlyAZ3aT was found less active in a mouse model of D39lux-induced bacteremia. Additional experiments are necessary to elucidate the molecular mechanisms explaining the unexpected in vivo results obtained with two lysins harbouring very close lysozyme catalytic domains. Altogether, this work is contributing to the development of streptococcal and bacteriophage lysins in general as new antibacterial agents.

Acknowledgments.

We thank Léna Falconnet and Aurélie Marchet for excellent technical assistance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P38

Evaluation of new bacteriophages for the treatment of *Acinetobacter baumannii* associated experimental bacteremia

L Likhachvili¹; D Bolkvadze¹; N Balarjishvili¹; F Oechslin²; YA Que³; M Kutateladze¹; G Resch²

(1) Eliava Institute;

(2) University of Lausanne;

(3) Klinik für Intensivmedizin

Aim.

Acinetobacter baumannii bacteremia is an increasing concern and is associated with significant morbidity and mortality. Phage therapy, i.e. the therapeutic use of bacterio(phages), is currently considered a realistic alternative for patients in therapeutic dead-ends. Our aim was to evaluate newly isolated phages in a mouse model of bacteremia in the view of developing a new effective anti-*A. baumannii* phage cocktail.

Methods.

CD1 Swiss female mice were challenged i.p. with 10⁹ CFU of the MDRA clinical isolate Ab20 and treated i.p. 2h later with two lytic phages or imipenem (IM), alone or in combination. Mice were followed over 6 days and differences in survival were determined by Kaplan-Meier plots. Statistics were performed using the Gehan-Breslow-Wilcoxon test.

Results.

17 different phages were isolated from environmental samples. Phages from the Myoviridae, Podoviridae and Siphoviridae families harboured genomes between 41.2 to 193.3 kb in length. From genome sequencing, four phages were temperate and two harboured antibiotic resistance genes preventing them to be considered as potential therapeutic agents. A cocktail of vB_MAba18 and vB_SAbasLO was found to cover 65% of 170 clinical isolates. In vitro antibacterial activity and strong synergism against Ab20 was observed. However, while a single i.p. injection of vB_MAba18 alone (MOI=0.3) 2h post-infection significantly improved mouse survival (ca. 80% survival at day 6 versus ca. 20% at day 2 for non-treated animals, $p < 0.0001$, $n=6$), a similar protocol failed to show significant survival improvement with vB_SAbasLO alone (20% survival at day 6). Combination of both phages decreased significantly the efficacy of vB_MAba18 alone (ca. 50% survival at day 6, $n=6$). IM (60 mg/kg) did neither improve survival alone nor vB_MAbasLO efficacy.

Conclusions.

vB_MAbasLO monophage therapy was highly efficient in the treatment of an Ab20 induced bacteraemia. Surprisingly with respect to in vitro results, vB_SAbasLO alone showed no in vivo efficacy and a cocktail of both phages was less efficient compared to vB_MAbasLO alone. These unexpected observations are under investigation and efforts are performed to isolate new phages that could increase the coverage of the cocktail. Absence of effect with IM is likely related to the IM-resistance phenotype of Ab20. Altogether, this work is contributing to the development of *A. baumannii* phages in particular and phages in general as new antibacterial agents.

We thank Adrien Mamin, Léna Falconnet and Aurélie Marchet for excellent technical assistance. This work was supported by Swiss National Foundation for Scientific Research (SNF) grant N°IZ73Z0_152319 to G. Resch.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P39

Risk factors for colistin-resistant Enterobacteriaceae in a low endemicity setting for carbapenem-resistance – a matched case-control study

A Büchler¹; C Gehringer²; AF Widmer¹; A Egli¹; S Tschudin-Sutter¹

(1) Universitätsspital Basel;

(2) University of Basel Hospital

Aim

Emergence of colistin-resistance has been related to its increased use in clinical settings, following the global spread of carbapenem-resistant Gram-negative bacteria. The use of colistin in animal production may constitute a further source for spread of resistant strains. In Switzerland, carbapenem-resistance is still rare and consecutive use of colistin. However, colistin is commonly used in livestock animals. Given the importance of enhancing knowledge on the breach of this last resort antibiotic, we sought to determine risk factors for human colonization or infection with colistin-resistant *E. coli* and *K. pneumoniae* in a low-endemicity setting.

Methods

We performed a case control study at the University Hospital Basel, Switzerland. Patients with detection of colistin-resistant *E. coli* or *K. pneumoniae* isolated from any clinical sample submitted to the microbiology laboratory between 2011-2015 were included. For each case, three controls with detection of a colistin-susceptible strain of the identical genus were selected. Matching was performed according to the site and date of isolation and ward type. Pertinent clinical data was collected by medical chart review.

Conditional univariable logistic regression was used to calculate odds ratios for colistin resistance. All variables found to be significant in univariable analysis were included in the conditional multivariable regression model. P-values ≤ 0.05 were considered significant.

Results

Forty-two cases (33 with *E. coli* and 9 with *K. pneumoniae*) and 126 matched controls were identified. Baseline characteristics, comorbidities, prior exposure to different antibiotic classes and healthcare settings did not differ between cases and controls, except for prior exposure to carbapenems, hospitalization abroad and stay abroad during the prior three months. Only prior exposure to carbapenems remained associated in multivariable analyses (OR 5.00, 95%CI 1.19-20.92, $p=0.028$).

Conclusion

In a low-endemicity setting for carbapenem-resistance, exposure to carbapenems was the only risk factor for colonization or infection with colistin-resistant *E. coli* or *K. pneumoniae*, despite common use of colistin in animal production. Prior exposure to colistin was not related to detection of colistin-resistance, which mainly occurred in the absence of concurrent carbapenem-resistance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P40

Needle Aspiration as diagnostic procedure in chronic wounds

RJ Piso¹; S Jenni¹; U Schibli²

(1) Kantonsspital Olten;

(2) Bakteriologisches Labor Olten

Background:

More than 90% of chronic wound are colonized with bacteria, regardless if infection is present or not. So diagnosis of infected chronic wounds is based on clinical features. Choice of antibiotic treatment is normally done without knowledge of responsible bacterial strains, and a wound swap does rarely correlate with invasive bacteria. The aim of the study was to investigate if this technic could help detecting responsible bacteria and differentiate between infected and non-infected chronic wounds

Methods:

Infection of chronic wound was defined clinically, if perifocal redness, swelling and increased pain was present. Needle aspiration of the perifocal area after disinfection was done, with a 23 G needle and a BDPlastikpakTM Luer 1 ml syringe. In the subcutaneous space, the needle was moved fore- and backwards under aspiration, similar to a puncture for cytology. The needle was removed under aspiration and then directly injected in 0.2 ml NaCl 0.9% (microcuvette). This solution was microbiologically investigated according standard procedures.

Results:

Aspiration was performed in 35 patients. 22/35 had clinically signs of infections, while 13/35 were judged as without infection. Culture of aspiration was positive in 16/22 (73 %, CI95 51-87 %) patients with infection, and in 1/13 (8.3 % CI95 4-23%) patients without. The estimated sensitivity was 73 %, the specificity 92.3 %, the positive predictive value 94.1% and the negative predictive value 66.7 %.

Conclusion:

Culture of aspiration could help identifying infected chronic wounds and guide antibiotic treatment.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P41

Clostridium difficile point prevalence study, Switzerland

A Widmer; R Frei; R Schindler; V Spaniol; D Goldenberger; A Egli; S Tschudin Sutter
University Hospital Basel

Aim

We aimed to determine prevalence of CDI and ribotype-distribution in a variety of different Swiss hospitals.

Methods

On one day in winter and one day in summer 2015, all unformed stool specimens submitted as standard of care from 76 Swiss hospitals were collected. In addition, stool samples tested positive for toxigenic *C. difficile* within the prior week were collected from all participating institutions to obtain a more detailed estimate of ribotype distribution. A two-stage algorithm consisting in an enzyme immunoassay (EIA) for detection of glutamate dehydrogenase (GDH) and toxins A and B (C.DIFF QUIK CHEK COMPLETETM, Techlab/ALERE, USA), and PCR for detection of toxin B as stand-alone test were applied. Strain typing was performed using PCR ribotyping and prevalence was expressed by 10'000 patient bed-days.

Results

As determined by PCR, measured rates for detection of toxigenic *C. difficile* were 11.4/10'000 patient bed-days for the winter sampling date and 7.1/10'000 patient bed-days for the summer sampling date. As determined by EIA for GDH and toxins A and B, *C. difficile* detection rates were lower at 6.4/10'000 patient bed-days and 5.7/10'000 patient bed-days for both sampling periods, respectively. Measured rates were higher than the reported rate of 4.0/10'000 patient bed-days across all institutions. Testing rates were reported as 67.5/10'000 patient bed-days and measured as 55.4/10'000 patient bed-days and 68.0/10'000 patient bed-days for both sampling periods, respectively. *C. difficile* testing was not requested in 11.5% of positive samples as determined by PCR and 5.5% of positive samples as determined by EIA for GDH and toxins A and B.

A large diversity of *C. difficile* ribotypes was identified, the largest proportion not being referenced so far (31.5%), followed by PCR ribotypes 014 (16.4%), 001 (11.0%), 012 (8.2%), and 002 (6.8%). Among presumably hypervirulent strains, PCR ribotype 078 accounted for 5.5%, while PCR ribotype 027 was not identified during our study period.

Conclusion

C. difficile infection rates have increased over the last decade in Switzerland as reported for other European countries, despite the lacking predominance of hypervirulent ribotypes. Diagnosing *C. difficile* by PCR as a stand-alone test resulted in markedly increase prevalence rates as compared to EIA testing for GDH and toxins A and B, thus underscoring the need for consistent testing algorithms to compare rates between institutions and countries.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P42

Efficacy and safety of continuous infusions with elastomeric pumps for outpatient parenteral antibiotic therapy (OPAT)

R Voumard; T Buclin; L Decosterd; S de Vallière
 Policlinique Médicale Universitaire / CHUV

Background.

Continuous antimicrobial infusion using elastomeric pumps greatly simplifies the management of outpatients requiring antibiotics which are traditionally administered as multiple daily doses. This study aimed to evaluate the efficacy and safety of this mode of administration.

Methods.

Clinical outcomes and adverse events were recorded for all patients treated by continuous infusion with elastomeric pumps at the outpatient parenteral antimicrobial therapy (OPAT) unit of the University Hospital of Lausanne between December 2013 and January 2017. Clinical outcomes and adverse events were correlated with plasma drug levels, which were drawn in principle once a week.

Results.

During the study period 150 outpatients were treated by continuous intravenous infusions using flucloxacillin (70 patients), cefepime (36), vancomycin (32) and piperacillin/tazobactam (12). 143 patients (95%) were considered as cured 3 months after the end of treatment. 7 patients were considered treatment failures: 5 patients had a relapse, 2 patients needed readmission.

15 patients (10%) had an adverse event, which included neutropenia (4 cases), catheter-related thrombosis (3), rash (2), catheter-related infection, cholestasis, thrombocytosis, diarrhea, hypokalemia and renal failure (all 1). 2 patients needed readmission for their adverse events (febrile neutropenia, hypokalemia).

Plasma drug levels were available for 101 patients and the mean concentrations ($\pm$ standard deviation) for each antibiotic were as follows: flucloxacillin = 36 mg/L ($\pm$ 15.2), cefepime = 21.3 mg/L ($\pm$ 12.1), vancomycin = 17.2 mg/L ($\pm$ 5.3), piperacillin = 25.8 mg/L ($\pm$ 15.7). Based on these results we calculated that the free fractions of each antibiotic were 1-4 times higher than the epidemiological cut-off values (ECOFF) of the treated microorganisms. One patient with treatment failure had one of one plasma drug level of flucloxacillin which was considered as low.

Conclusion.

Continuous infusions of flucloxacillin, cefepime, vancomycin and piperacillin/tazobactam using elastomeric pumps seem to be an effective and safe approach to treat outpatients. Treatment failures and adverse events occurred at a similar rate as reported by other OPAT centers. The adequate plasma drug levels are an additional element indicating the efficacy of this approach.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P43

Comparing the cost-effectiveness of linezolid to trimethoprim/sulfamethoxazole plus rifampicin for the treatment of methicillin resistant *Staphylococcus aureus* (MRSA) infection: a healthcare system perspective

E Von Dach¹; C Morel¹; A Murthy²; L Pagani³; M Macedo-Vinas⁴; F Olearo¹; S Harbarth¹

(1) Geneva University Hospitals and Medical School;

(2) Incyte Corporation;

(3) Bolzano Central Hospital;

(4) Facultad de Medicina

Few independent studies have been conducted to compare the costs and benefits of drugs to treat MRSA infection. We conducted a cost-effectiveness analysis comparing two treatment strategies linezolid versus trimethoprim-sulfamethoxazole plus rifampicin to treat MRSA infection.

We collected costs from hospital expenditure data and effectiveness values from a clinical trial previously conducted in-house, complementing with additional estimates from the published literature to test for variation beyond the trial setting. In particular we tested potential differences between the drugs in terms of their toxicity and differential effects on different types of MRSA infection, those that were not captured in the clinical trial population. Effectiveness was expressed in terms of quality-adjusted life-years (QALYs). Sensitivity analyses were performed using Monte Carlo simulation to measure the effect of potential parameter changes on the base-case model results. Thresholds were explored to determine the price at which the generic form of the less cost-effective drug would have to be made available in order for the two regimes to equate on cost-effectiveness grounds.

Treatment of MRSA infection with trimethoprim-sulfamethoxazole plus rifampicin and linezolid were found to cost on average €146 and €2536 respectively, and lead to a gain of 0.916 and 0.881 QALY, respectively. Treatment with trimethoprim-sulfamethoxazole plus rifampicin was found to be more cost-effective than linezolid in the base case and remained dominant over linezolid in most alternative scenarios, including types of MRSA infection and potential disadvantages in terms of toxicity. With a willingness-to-pay threshold of €50 000 and €200 000 per QALY gained, trimethoprim-sulfamethoxazole plus rifampicin was dominant in 96% and 85% of model iterations. Recently, the price of generic linezolid was fixed in Switzerland with a 10% discount on the originator price. With this discount the combined treatment of trimethoprim-sulfamethoxazole plus rifampicin remains cost-effective compared to linezolid treatment. Indeed within the Swiss context studies a 95% discount on the current originator price of linezolid would be needed for it to represent better value for money compared to combined treatment.

Combined treatment of trimethoprim-sulfamethoxazole plus rifampicin is more cost-effective than the original and generic formulations of linezolid in the treatment of MRSA infection in the Swiss hospital context.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P44

Phenotypic differences in human macrophage responses to infection with *Mycobacterium tuberculosis*.

P Major; S Borrell; A Arbués; D Portevin; S Gagneux

Swiss Tropical and Public Health Institute, University of Basel

Mycobacterium tuberculosis is an obligate human pathogen that kills 1.8 million people annually, and latently infects one third of the global human population. Previous studies in our laboratory have shown differences in the phylogeographic distribution of the *Mycobacterium tuberculosis* complex (MTBC), demonstrating that some lineages are present throughout the world (generalists), whereas others are restricted to specific regions (specialists) (1). Consistent with this hypothesis, some specialist lineages have been associated with certain human ethnicities (2), suggesting regional long term host-pathogen coevolution. To explore the interactions between pathogen and host, we used an in vitro infection model of the macrophage cell line THP-1 and human blood derived macrophages with phylogenetically diverse strains of the MTBC (3), taking advantage of our in-house strain collection. These include strains from the globally spread Lineage 4, namely the generalist sublineage L4.3 (LAM) and the specialist L4.6.1 (Uganda) (4), as well as Lineage 5 strains (also known as *Mycobacterium africanum*) that are endemic West Africa. Our results indicate significant strain differences in infectivity of monocyte-derived macrophages from different donors, based on the obtained number of colony forming units over the course of infection, and the inflammatory responses based on cytokine measurements. We conclude that the phylogenetic MTBC strain background is associated with variable virulence in human macrophages. Our ongoing collaborations in West- and East Africa will allow us to assess macrophage responses to endemic and non-endemic MTB strains across these diverse human populations to test sympatric and allopatric host-pathogen associations, and better appreciate the global TB epidemiology integrating both host and pathogen diversity.

References

1. Coscolla M. and Gagneux S. *Semin Immunol* 2014;26:431.
2. Asante-Poku A. et al. *PLoS Negl Trop Dis* 2015;9:e3370.
3. Portevin D. et al. *PLoS Pathog* 2011;7:e1001307.
4. Stucki D. et al. *Nat Genet* 2016;48:1535.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P45

Bacteremias surveillance in hospitals of three Cantons of Switzerland: a fifteen year report (2001-2015)

D Héquet; C Petignat

Lausanne University Hospital

Bloodstream infections (BSI) are a leading cause of morbidity and mortality in hospitalized patients. Moreover, a significant concern is antibiotic resistance among causative agents.

We report a 15 year surveillance of community and nosocomial bacteremias in hospitals and clinics of three Cantons of Switzerland (VD, NE, JU). Data were collected by infection control nurses and centralized in a database. We analyzed the data according to 3 distinct periods: 2001-2005, 2006-2010 and 2011-2015.

From 2001-2015, we observed 11'788 BSI, 8858 community (75%) and 2930 nosocomial (25%). Community BSI proportion increased over the observation period (respectively 6.8, 8.39 and 10.11/1000 admissions). Mean age significantly increased over the years (from 64-69 years, $p<0.001$). The proportion of urinary related BSI increased over time from 15.1-25.9% ($p<0.001$). However, the proportion linked to a urinary catheter remained stable (from 44.1-47.4, $p=0.69$). E.coli is the most common microorganism (36.3% of community and 22.4% of nosocomial BSI). Proportion of Enterococci in nosocomial BSI significantly increased over time (from 6.1-10.4%, $p=0.03$). Moreover, the proportion of S.aureus with methicillin resistance (MRSA) significantly decreased over surveillance period from 5.7-2.9% ($p=0.05$) in community BSI and from 11.6-7.9% ($p=0.27$) in nosocomial BSI. Concomitantly, the proportion of E.coli with extended spectrum beta-lactamase (ESBL) significantly increased among community E.coli BSI, but not in nosocomial BSI (from 1.3-4.5% $p<0.001$ and 4.8-7.0% $p=0.32$, respectively).

Proportion of community BSI increased over time contributing to risk factors for developing nosocomial infections. Urinary related infections should be a priority target in order to prevent nosocomial BSI. Multidrug resistant bacteria distribution changed gradually, resulting in a significant MRSA decrease and an increase in ESBL E.coli in the community. This tendency, also not significant, is also true in nosocomial BSI and should be taken into account when treating the patient. Concomitantly, a special attention should be made to Enterococci seen the recent vancomycin-resistant Enterococci outbreaks in this part of Switzerland.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P46

Clostridium difficile infections in a swiss tertiary care hospital: Local epidemiology mirrors international data

S Haubitze; N Bartlomé; E Bucheli Laffer; C Spelters; H Fankhauser; C Fux
Kantonsspital Aarau

Aims:

Clostridium difficile infection (CDI) in hospitalized patients is associated with high recurrence rate and mortality. We sought to assess the local CDI epidemiology and treatment outcomes to guide management strategies.

Methods:

We conducted a retrospective quality control study collecting information on all adult cases with CDI at our hospital in the years 2014 to 2016. CDI was diagnosed in symptomatic patients with detection of specific glutamate dehydrogenase followed by positive PCR in stool samples (GeneXpert C. difficile, Cepheid CA/USA). Every case was followed for 60 days beyond treatment for CDI recurrence and death as endpoints. Relapse of diarrhea within 7 days after stopping treatment was defined as non-response and the subsequent treatment was therefore still counted as first treatment round. A new episode of CDI within 60 days after end of treatment was defined as recurrence. Details on therapy, preceding and concurrent risk factors were collected and analyzed by uni- and multivariate logistic regression providing odds ratios (OR) for CDI recurrence.

Results:

Between 2014 and 2016, 198 episodes of CDI in 191 patients were treated in our hospital. The median age was 71 (interquartile range (IQR) 59-79) years, 49% males; 54% had been hospitalized in the preceding 90 days, half of whom (24%) had been admitted to intensive care within 30 days before CDI diagnosis. 75% had undergone antibiotic treatment up to 30 days before CDI. 42% took proton pump inhibitors (PPI), 36% had solid or hematologic malignancy. In 16%, eGFR was <30 ml/min, with 3% being on hemodialysis. Ribotype 027/NAP1/BI was found in 4 cases (2%). Oral metronidazole was the primary treatment regimen in 94%. Recurrence rate was 20% and recurrence was independently associated with age above 70 years (adjusted OR 2.31, 95% confidence interval (CI) 1.06-4.99), presence of hematologic malignancy (adj. OR 7.57, 95%CI 1.79-31.95) and PPI use (adj. OR 2.48, 95%CI 1.01-6.08) (table 1). Overall mortality in the first 60 days since CDI diagnosis was 18% with _ being directly related to CDI.

Conclusions:

While recurrence rate was as expected from published literature we found an unexpectedly high mortality rate. CDI seems to be a strong indicator for terminal disease and frailty. Treatment regimens should be adapted for CDI patients with advanced age and hematologic malignancy. PPIs should be discontinued whenever possible.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P47

A Novel ex-vivo organ of Corti explant Culture Model to Investigate Inner Ear damage in Pneumococcal Meningitis

M Perny¹; M Solyga¹; D Grandgirard¹; M Roccio¹; P Senn²; S Leib¹

(1) University of Bern;

(2) University Hospital Geneva

Aims:

Hair cells (HCs) and spiral ganglion neurons, both responsible for hearing, are affected in experimental studies and clinical cases after pneumococcal meningitis. In the present study, we wanted to establish an ex vivo model allowing the detailed examination of hair cell loss using cultures of the organ of Corti (OC) exposed to different *S. pneumoniae* strains or to recombinant pneumolysin (PLY).

Methods:

Cochlear explants were isolated from 2-4 days old Wistar rats, the OCs were plated on the membrane of a Transwell® insert, pre-coated with Celltak® and cultured for 24 hours before challenge. OCs were exposed to different concentrations of *S.pneumoniae* (serotype 3, D39 wild type, D39ΔPLY) or to recombinant PLY. Different exposure times (1,2,4 or 24 hours) were evaluated, depending on the challenge. After challenge, cultures were washed with PBS and cultivated for additional 48 hours. Hair cells were labelled by immunostaining. The entire OC was imaged with confocal pictures and divided into 3 regions (base, middle and apex) (5-6 pictures each). The number of surviving outer (OHC) or inner (IHC) hair cells was assessed for each region of the explants.

Results:

In OC challenged with log₁₀ 8 colony forming unit / ml of *S.pneumoniae* serotype 3, a selective loss of OHCs was observed after 2, respectively 4 hours of incubation. At 4 hours, a significant decrease in OHC survival was observed in all regions (base: 46.1% survival ±13.9 of survival, p<0.01; middle turn: 49.9%±5.1 p<0.01; apex: 54.61%±17.7, p<0.01). A significant inverse correlation was found between the time of exposure and the number of surviving OHCs. In contrast, IHCs were not affected.. Using the wild type D39 strain, we observed a dose-dependent cell loss for both OHCs and IHCs. Dose dependency for D39ΔPLY was also observed for OHCs, while IHCs were only affected with the highest concentration. A significant lower cell survival was found in the basal and middle regions when comparing challenges with D39 and D39ΔPLY. Challenge with recombinant PLY resulted in a dose-dependent OHCs and IHCs loss. In all experiments, basal and middle regions were more affected than the apex region

Conclusions:

The present ex vivo system recapitulates important aspects of PM-associated hair cell loss, including the ototoxic effect of pneumolysin, and represents a new platform to investigate pathophysiologic mechanisms and to identify and develop otoprotective and/or otoregenerative therapeutic approaches.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P48

Reduced neuroinflammation and neurofunctional sequelae by combining adjuvant daptomycin with doxycycline in experimental pneumococcal meningitis

L Muri; D Grandgirard; M Perny; S Leib

Institute for Infectious Diseases, University of Bern, Switzerland

Aim

To improve the outcome of pneumococcal meningitis by combining adjuvant drug therapies – targeting different pathophysiological mechanisms during the acute phase of the disease – to synergistically reduce cortical and hippocampal brain damage as well as damage to the inner ear causing long-term neurologic sequelae.

Methods

Eleven day old Wistar rats were infected intracisternally with $7.6 \pm 3.3 \times 10^5$ cfu/ml *S.pneumoniae* and randomized for treatment with a combination adjuvant therapy (n=66) consisting of daptomycin (10mg/kg, s.c., single application) plus ceftriaxone (100mg/kg, i.p. every 12 hours) plus doxycycline (30mg/kg, i.p, once daily combined with ceftriaxone), or a monotherapy (n=66) with ceftriaxone (100mg, i.p., every 12 hours) plus saline (s.c., single application) in control animals.

Cortical damage and hippocampal apoptosis were assessed histomorphometrically 42 hours after infection. Cytokine expression levels were analysed using a magnetic multiplexing system. Three weeks after infection, evoked auditory potentials (ABR) were used to assess the hearing thresholds of the rats.

Results

At 42 hours after infection, combined adjuvant therapy with daptomycin plus doxycycline increased the survival rate from 62.7% in controls to 84.6% (log-rank $p=0.009$) and alleviated weight loss compared controls (+1.0% weight gain with combination therapy vs 3.3% weight loss in monotherapy, $p=0.002$). The cortex of infected rats showed significantly less damage in the animals with the combined treatment regimen (1.2% vs 5.0% damage of total cortex volume, $p=0.03$). In addition, expression of the inflammatory cytokines IL-1 β , IL-6 and IL-10 were significantly ($p<0.05$) reduced in the combined treatment group. Animals treated with combined adjunctive therapy showed a strong trend towards better hearing capacity three weeks after the infection (median hearing threshold of 65dB vs 80dB in controls, $p=0.077$). Mildly infected animals were protected from meningitis-induced hearing loss (median hearing threshold of 40dB vs 80dB in controls, $p=0.048$).

Conclusion

The combination therapy with the non-lytic antibiotic daptomycin and doxycycline with its inhibitory effect on microglia and matrix-metalloprotease (MMP) showed to be neuroprotective and otoprotective. These findings, together with the lower mortality identify the combination of adjuvant daptomycin with doxycycline as a promising therapeutic option to improve the outcome of pneumococcal meningitis.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P49

Microbiologically proven infections in the first year after adult allogeneic HSCT: the Swiss Transplant Cohort study

D Vu Cantero¹; J Dayer¹; S Masouridi-Levrat¹; C Combescure¹; E Boely¹; N Khanna Gremmelmaier²; N Mueller³; M Kleber²; M Medinger²; J Halter²; J Passweg²; AM Mueller³; U Schanz³; Y Chalandon¹; C van Delden¹; L Kaiser¹

(1) Geneva University Hospital;

(2) Universitätsspital Basel;

(3) University Hospital of Zurich

Aims:

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a major therapeutic option mainly for hematological diseases. Besides disease relapse, infections represent the main threat after HSCT, despite improvement in prophylaxis, methods of prevention, sensitive diagnostic tools, and attenuated protocols of immunosuppression. These all have changed the profile of infections in the last decades, reason why we intended to describe the recent epidemiology of infections occurring after allo-HSCT in Switzerland and to assess association with mortality.

Method:

Adult patients transplanted between 2010 and 2014 and infections occurring in the year following HSCT were eligible. Except for fungi, we only analyzed microbiologically proven infections. We used the Swiss transplant cohort study and the European Society for Blood and Marrow Transplantation databases to collect the data. We used Chi2 or Fisher exact and ANOVA or Kruskal-Wallis tests for categorical and continuous variables, respectively. We used quasi-Poisson regression model to determine the incidence rates (IR) of infection and Kaplan-Meier and log-rank tests for survival analyses and comparison between subgroups. We used multivariable Cox regression model to adjust for confounding factors.

Results:

We included 557 patients with a mean age of 50 years at HSCT. 96% of HSCT were first transplants. 92% of HSCT were complicated by ≥ 1 infection with a global IR of 3.86 infections per patient-year; the highest IR of 16.23 was identified in the pre-engraftment phase. Viruses were predominant, followed by bacteria, fungi and parasites (IR 2.57, 0.86, 0.40 and 0.02, respectively). Distinct patterns of infections were attributable to centers' management. At one year, relapse and mortality rates were 28% and 26%, respectively. The cause of death included relapse in 50% and infection in 34% of cases. After multivariable analyses, we identified the transplant center, a comorbidity score ≥ 2 , a high/very high disease risk index and infection with any pathogen in the last two months as risk factors for one-year mortality.

Conclusion:

Despite advances for limiting infections in HSCT patients, infections still occur in most of them and significantly affect their survival at one year, all pathogens included. The pre-engraftment phase is the most critical period and viruses are predominant among all pathogens. Specific management of infectious complications significantly affects their epidemiology.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P50

Case report: Fever after treatment with rituximab and bendamustin – don't forget the ticks!

J Nicoletti¹; V Bansal²; R Imoberdorf¹; J Gubler¹; U Karrer¹

(1) Kantonsspital Winterthur;

(2) Kantonsspital Winterthur

Case Report

A 79 year-old patient suffering from follicular lymphoma stage IV was referred to our clinic for evaluation of daily fever >39°C, fatigue, arthralgias, imbalance and weight loss. A recent relapse of lymphoma had been treated with rituximab and bendamustin. Clinical examination showed cachexia and slightly enlarged and indurated cervical, supraclavicular and axillary lymph nodes. Laboratory analyses demonstrated anemia (Hemoglobin 9.2g/dL; range: 14.4 - 17.5g/dL), elevated C-reactive protein (CRP 86mg/L; <5mg/L) and ferritin (1600mg/L; 22-275mg/L) but normal lactate dehydrogenase (LDH 165U/L; <220U/L). Blood cultures and serologies for infectious causes (Parvovirus B19, Brucella, Coxiella) were all negative. PET-CT showed increased Fluoro-deoxy-glucose (FDG)-uptake in bone marrow and lymph nodes (Figure 1) and needle biopsy of the latter demonstrated recurrent lymphoma. However, broad spectrum bacterial PCR (16s rRNA) from blood and lymph node was positive for *Candidatus Neoehrlichia mikurensis* establishing the diagnosis of neoehrlichiosis. Within a day after initiation of oral antibiotic therapy with doxycycline, fever ceased and the patient recovered swiftly (Figure 2). He did not recall a recent tick bite.

Discussion:

Candidatus Neoehrlichia mikurensis is a tick-transmitted, nonculturable intracellular bacterium recently identified to cause prolonged fever in immunocompromised patients particularly after rituximab¹. Additional symptoms include malaise, weight loss, myalgias, arthralgias and thromboembolic or vascular events. Up to 8% of Swiss Ixodes ticks are infested with *Ca. N. mikurensis*². Nevertheless, neoehrlichiosis remains a rarely identified disease suggesting only mild and transient symptoms in immunocompetent hosts. However, neoehrlichiosis should be actively searched for using molecular diagnostics in immunocompromised patients with fever and/or unexplained inflammation since exposure is easily possible in Switzerland and treatment with doxycycline is simple and highly effective.

References:

1) Grankvist et al., Clin Infect Dis. 2014;58(12):1716-22

2) Maurer et al., J Clin Microbiol. 2013;51(1):169-76



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P51

Case report: Adenovirus associated sepsis with pneumonia and enteritis in a heart transplant patient

U Karrer; J Nicoletti; R Werner; J Gubler
 Kantonsspital Winterthur

Introduction:

In solid organ transplant recipients, adenovirus (ADV) viremia is relatively common but often clinically silent. However, disseminated ADV-infection is associated with a high mortality. Since clinical symptoms of ADV infection are nonspecific, early and specific virological testing is essential to make a timely diagnosis.

Case:

In October 2015, a 43 year old male was admitted to our hospital with fever and watery diarrhea. The patient was under immunosuppressive therapy with sirolimus and mycophenolate after heart trans-plantation in 1987. Despite empiric antimicrobial therapy with azithromycin and ceftriaxone the patient's condition deteriorated and he developed a sepsis syndrome with severe cough, shortness of breath and acute-on-chronic renal failure leading to sirolimus accumulation. Computed tomography of the chest and bronchoscopy revealed a lobar pulmonary infiltrate with pleural effusion and purulent discharge. Bronchoalveolar lavage (BAL) was negative for bacterial, fungal and a variety of viral pathogens but strongly positive for ADV-DNA by polymerase chain reaction (PCR). Additionally, high copy numbers of ADV were found in plasma and stool. Thus, sirolimus was transiently interrupted, mycophenolate reduced and options for antiviral therapy were evaluated. Since treatment with cidofovir was likely to provoke additional nephrotoxicity, we applied for exceptional approval from Swissmedic and the manufacturer (Chimerix, Inc., NC, USA) to use the investigational drug brincidofovir (BCV). BCV is a lipid ester of cidofovir with documented anti-ADV activity but less nephro-toxicity. After alleviation of immunosuppression followed by BCV administration the viral load decreased rapidly, the serum level of sirolimus reached its target value and the patient recovered promptly.

Discussion / key messages:

Differential diagnosis of infections is very broad in immunodeficient patients and often mandates specific search for a variety of microorganisms by invasive procedures.

Reduction of immunosuppression to the lowest acceptable level is one cornerstone of successful management. Investigational drugs might be of use in situations with limited therapeutic options.

Applications for the use of investigational drugs may be granted within hours, if co-operations between drug manufacturers and regulatory agencies are already in place.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P52

Cytokine profiling in healthy children shows association of age with cytokine concentrations

M Decker; V Gotta; S Wellmann; N Ritz

Universitäts-Kinderspital beider Basel UKBB

Background:

Cytokine-based diagnostic assays are increasingly used in research and clinical practice. Assays developed for adults such as the interferon-gamma release assay for tuberculosis show inferior performance in children. Limited evidence suggests that release of cytokines is influenced by age but normal ranges of cytokines in children are lacking.

Methods:

Whole blood of healthy children (0-12 years) undergoing elective/diagnostic procedures was stimulated with SEB, PHA, *Candida albicans* or left unstimulated. Concentrations of eight cytokines measured by multiplex bead-based immunoassays and associations with age and other factors quantified by regression analysis.

Results:

271 children (median age 5.2 years) were included. In unstimulated samples IL-1ra, IP-10 and TNF- α concentrations decreased by up to -60% with age. Following antigen stimulation, an age-associated increase (ranging from +90% to +500%) was observed for all cytokines except IL-1ra (significant for IL-4, IFN- γ and TNF- α). Inter-individual variability in cytokine concentrations was large with a CV ranging from 42% to 1412%.

Conclusion:

Despite inter-individual variation age was identified as a strong influencing factor of cytokine concentrations. Age-specific normal values need to be considered for cytokine-based diagnostic purposes. These results are relevant for development of novel cytokine-based diagnostic assays and for optimal dosing of therapeutic agents targeting cytokines.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P53

The spectrum of care for paediatric refugees and asylum seekers in a European high income 2 country.

C Pohl; I Mack; T Schmitz; N Ritz

Universitäts-Kinderspital beider Basel UKBB

Background

Although there is increasing concern about the health of refugees and asylum seekers data on health issues and needs in this setting are particularly lacking for children. The aim of this retrospective study was to describe the epidemiology and spectrum of infections of admitted paediatric refugees and asylum seekers in a high income country.

Methods

We identified recent refugees and asylum seekers < 18 years of age admitted to our institution in 2015. A retrospective analysis was performed using electronic patient records.

Results

We identified 105 admissions in 93 patients with a mean age of 5.7 (IQR 2.6 - 14.5) years. Afghanistan, Syria and Eritrea were the most frequent countries of origin. The median duration of admission was 4 (IQR 2-6) days with infectious diseases and elective surgical interventions being the most common reason (54.8% and 16.1%, respectively).

Most infections were related to airway, skin and gastrointestinal tract in 46.4%, 20.2% and 11.9%, respectively. The prevalence of tropical infections was 11.9%. The main pathogens were Influenza-A-virus (13.8%), Staphylococcus aureus (10.3%) and Rhino/Enterovirus (10.3%). Previous medical non-infectious conditions were recorded in 13%.

Conclusion

The study revealed a high burden of infectious diseases mostly caused by well-known pathogens prevalent also in the local population. The incidence of tropical infectious diseases in contrast to other studies was relatively low. Further research is needed to optimize health care for this medically most vulnerable subpopulation of the refugee crisis.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P54

No association between fever and uninfected hematoma in postoperative orthopedic surgery and traumatology

I Uçkay

Aims:

According to widespread belief or clinical experience, uninfected hematoma can cause fever. However, epidemiological data regarding this assumption are lacking.

Methods:

Single-centre prospective observational study among adult orthopedic patients. Exclusion of surgical site and remote infections (including infected hematomas), skin rash, malignant hyperthermia, thrombosis, known atelectasis and incomplete data. All patients have anti-inflammatory medication and many have blood transfusions. The occurrence of hematoma and daily temperatures are notified for up to one week postoperatively. Fever is defined as any axillary temperature $\geq 38^{\circ}\text{C}$ (104°F), subfebrile temperatures as $\geq 37.2^{\circ}\text{C}$.

Results:

Among 405 patients in the study, 164 had (40%) fever, 221 (55%) subfebrile temperatures, and 166 (41%) yielded visible hematomas. Overall, fever was not associated with hematoma (67/164 vs. 99/241; Pearson- χ^2 , $p=0.96$). We equally found no association when setting the cut-off at subfebrile level (156/385 vs. 10/18; $p=0.21$) or when analyzing the temperatures only on Day 4 ($p=0.95$), Day 7, ($p=1.00$), or solely for cases requiring surgical re-intervention for hematoma (4/10 vs. 6/9; Fisher exact-test, $p=0.37$). As continuous variables, the maximum temperatures on each of the seven postoperative days were not higher for patients with hematoma (Wilcoxon-ranksum-tests; all $p>0.10$). In multivariate analysis, no parameter was associated with fever, including hematoma (odds ratio 0.9, 95%CI 0.3-2.3), emergency surgery (0.8, 0.3-2.3), or the Charlson co-morbidity index (0.7, 0.3-1.9).

Conclusions:

Within the time frame of one week postoperatively and real-life conditions, we failed to establish an epidemiological association between postoperative fever and the presence of hematoma in a large prospective observational study among adult orthopedic patients under anti-inflammatory drugs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P55

Prevalence of multidrug-resistant microorganisms in 699 asylum seekers at a tertiary care hospital in Switzerland

S Erb; A Egli; D Marc; W Andreas
 University Hospital Basel

Background

The increasing number of refugees seeking asylum in Europe in recent years poses new challenges for the European healthcare systems. Little is known about the carriage of multidrug resistant microorganisms (MDROs) in asylum seekers.

The goal of the study was to determine the prevalence of extended-spectrum beta-lactamase (ESBL) gram-negative microorganisms and methicillin-resistant *S. aureus* (MRSA) in asylum seekers presenting at a tertiary care hospital in Switzerland.

Methods

All asylum seekers aged >15 years referred from one of the national asylum centres to the University Hospital Basel from 9/2011 until 10/2016 were included. The hospital policy requires screening of all hospitalized asylum seekers for MRSA and gram-negative bacteria expressing extended spectrum betalactamases (ESBL). Positive cultures were further characterized by molecular typing with pulsed-field electrophoresis (PFGE).

Results

699 of total 38'901 (1.8%) asylum seekers registered at the asylum centre were referred to our hospital during the study period. 63.7% were male, median age was 27 years (IQR 21-35) and 47.8% were hospitalized. Most asylum seekers came from Eritrea (21.6%), Afghanistan (8.7%) and Syria (7.0%). In 119/699 (17.0%) patients, at least one screening sample for MDRO was processed. In 34/119 (28.6%) patients MRSA and/or ESBL-producing bacteria were detected, 2 patients being positive for both MRSA and ESBL. No Carbapenemase-producing gram-negative bacteria were found.

11 patients were colonized or infected with ESBL microorganisms. All were *E. coli* ESBL (1 patient in addition *P. mirabilis* ESBL). 4 of the patients originated from Syria, 3 from Somalia and 3 from other countries. In hospitalized patients 7/38 (18.4%) routine ESBL-screening at time of admission were positive.

MRSA was found in total 25 patients. The majority of the patients came from Eritrea (n=7). In hospitalized patients 14/58 (24.1%) routine MRSA-screening at time of admission were positive.

There were two clusters with 2 and 3 MRSA with highly correlated strains ($\geq 90\%$) by PFGE. In contrast, typing of 4 ESBL-strains did not show evidence for cross-transmission.

Conclusions

Around 20% of asylum seekers arriving in Europe are colonized with MRSA or ESBL pathogens. These data provide evidence for routine screening for MDRO on admission to guide antimicrobial treatment as well as to implement infection control procedures to limit spread in hospitals.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P56

Assessing the danger of self-sustained HIV epidemics in heterosexuals by population based phylogenetic cluster analysis

T Turk¹; N Bachmann¹; C Kadelka¹; J Böni²; S Yerly³; V Aubert⁴; T Klimkait⁵; M Battegay⁶; E Bernasconi⁷; A Calmy³; M Cavassini⁴; H Furrer⁸; M Hoffmann⁹; H Günthard¹; R Kouyos¹

(1) University Hospital Zurich; University of Zurich;

(2) University of Zurich;

(3) Geneva University Hospital;

(4) Lausanne University Hospital;

(5) University of Basel;

(6) Universitätsspital Basel;

(7) Regional Hospital Lugano;

(8) Bern University Hospital, University of Bern;

(9) Cantonal Hospital St. Gallen

Assessing the danger of transition of HIV transmission from a concentrated to a generalized epidemic is of major importance for public health. Although HIV transmission in Swiss heterosexuals has never led to a self-sustained epidemic, the unknown potential of imported infections either from abroad or from other transmission groups in Switzerland remains a large concern. We investigated how far from a self-sustained epidemic HIV transmission within Swiss heterosexuals is, and assessed its time trend and determinants.

From a phylogenetic tree containing Swiss and background HIV sequences, we identified 3100 Swiss heterosexual transmission clusters (estimated infection dates between September 1980 and July 2014). The demographic characteristics of the individuals forming these clusters were extracted from the highly- representative Swiss HIV Cohort Study. To capture the incomplete sampling of HIV sequences, the delayed introduction of the imported infections to the Swiss heterosexuals network, and potential factors associated with higher basic reproductive number R_0 , we extended the basic branching process model to infer transmission parameters.

Overall, the R_0 of HIV in Swiss heterosexuals was estimated to be 0.44 (95%-confidence interval 0.42-0.46). The model also showed that subtype B had lower R_0 (0.35) compared to non-B subtypes with the highest R_0 occurring for CRF02_AG (0.62), highlighting the heterogeneity between subtypes. When assessing the time trend, we found that R_0 was decreasing by 11% per 10 years (4%-17%). The multivariate model revealed that non-B subtype, reported sex with occasional partners and longer time to diagnosis were significantly associated with larger R_0 , while age and the earliest CD4 cell count did not exhibit significant effect.

These findings indicate that there is no imminent danger of a self-sustained epidemic among Swiss heterosexuals, but rather diminishing HIV transmission far below the epidemic threshold. Generally, our approach allows the assessment of the danger of a self-sustained epidemic from HIV sequence data.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-immk.ch

P57

Assessment of Humoral Immunity to Vaccine Preventable Diseases in Autologous Stem Cell Transplant Recipients

A Kritikos; A Cairolì; P Bochud; O Manuel; J Delaloye
CHUV-University Hospital

Background:

Hematopoietic stem cell transplant (HSCT) recipients are at risk for vaccine-preventable diseases. Recommendations for vaccination of HSCT recipients in existing guidelines do not differentiate between allogeneic and autologous cell transplantation. However, limited data are available on immunity to vaccine preventable diseases following autologous HSCT and on the immunogenicity of vaccines in this population. The aim of this study is to investigate the impact of autologous stem cell transplantation on humoral immunity to common vaccine preventable diseases.

Methods:

All patients (aged >18 years) receiving autologous HSCT at our institution between June 2014 and March 2016 were included. Antibody titers against vaccine preventable diseases were routinely measured before and 6 months after transplantation. Patients without protective titers were vaccinated at 6 months, according to existing guidelines. Antibody concentrations were measured again one month after vaccination.

Results:

During the study period, seventy-six patients received autologous HSCT at our institution. Data from 34/76 patients (45%) are currently available. 14/34 (41%) patients had protective titers for diphtheria prior to HSCT that persisted at 6 months post transplant in 9/14 patients (65%). All 24/34 (70%) patients who were seroprotected for tetanus before transplant had similar serum levels of antibodies 6 months after HSCT. With regard to H. influenzae antibodies, 28/34 (82%) patients were protected before HSCT and 4/15 patients (26%) lost their protective titers after transplant. Only 3/13 patients (23%) with protective titers prior to HSCT for hepatitis B and 3/22 (13.5%) for measles, respectively, showed a significant decline of antibody titers after transplant. At 6 months post transplant, 5 patients received the dT vaccine, 17 patients the PCV13 vaccine, and 4 patients the HBV vaccine. 5/5 showed protective immunity against diphtheria and tetanus 1 month after vaccination. We observed a response to PCV13 in 10/17 (59%) of patients and to HBV vaccine in 2/4 (50%) of patients.

Conclusions:

Our preliminary ongoing results suggest that humoral immunity to common vaccine-preventable diseases persists after autologous HSCT in a 65-100% of patients. The immunogenicity of these vaccines seems appropriate after transplantation. These data suggest that the current vaccination schedule aimed for allogeneic HSCT needs to be adapted for autologous HSCT patients.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P58

Less antibiotic use and remission in diabetic foot infections

I Uçkay; B Kressmann; D Lebowitz; E Von Dach; D Lew

(1)

Aims:

Diabetic foot infections (DFIs) are a source of systemic and local antibiotic misuse worldwide. DFI recur frequently. Only few studies aim to reduce their antibiotic prescription.

Methods:

In the frame of a clinical pathway for DFI, we conducted a multivariate, cluster-controlled (at patient's level) Cox regression model among adult patients hospitalized for DFI; defining treatment failure as a clinical recurrence ≥ 14 days after treatment end. Exclusion of total amputations.

Results:

Among 1018 DFI episodes in 482 patients, 392 were osteomyelitis cases, 626 soft tissue infections, 246 large abscesses, 322 cellulitis, 335 necrosis, and 313 cases with revascularization. We performed surgical debridement in 824 episodes (81%), of which 596 episodes (59%) involved partial amputation. The median total duration of antibiotic treatment was 20 days, 5 days of which was intravenous. After a median follow-up of three years, 251 episodes (251/1018; 25%) witnessed a second DFI episode or more at the same anatomical localization. In multivariate analysis, remission was inversely associated to diabetes mellitus type I (hazard ratio (HR) 0.3, 95%CI 0.2-0.6) and the number of surgical interventions (HR 0.8, 0.6-0.9). The total duration of antibiotic prescription or of its parenteral use had no influence (both HRs 1.0, 95%CI 0.99-1.01). More than 3 weeks of antibiotics had the same outcome than less than 3 weeks. More than 1 week of intravenous therapy had the same effect as less.

Conclusions:

We could not define the optimal duration of antibiotic therapy for DFI. In view of the known hazards of unnecessarily prolonged antibiotic therapy, these limited data might support shorter treatment duration; for which we started a prospective randomized trial.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P59

Validation of a point-of-care quantitative HCV-RNA test using capillary blood from the finger (Xpert® HCV Viral Load, Cepheid®)

A Bregenzer; N Warmann; C Ottiger; CA Fux
 Kantonsspital Aarau

Aims:

To compare point-of-care quantitative HCV-RNA measurement using 100µl capillary blood from the finger (Xpert® HCV Viral Load, Cepheid®) with the standard quantitative HCV-PCR test Cobas® performed in the laboratory with 1ml venous EDTA-plasma.

Methods:

Since 11/2016, patients of our Infectious Diseases Outpatient Clinic with an indication for HCV-RNA determination and written informed consent provided both venous and capillary blood for quantitative HCV-RNA measurement. Venous plasma was tested using Cobas® (quantification limit: 15 U/ml; result within 1 week). 100µl capillary blood collected from the finger with an EDTA-minivette was immediately transferred into an Xpert® HCV Viral Load cartridge (quantification limit: 10 U/ml; result within 105 minutes). The addition of 1ml Cepheid® blood sample diluent and the use of whole blood consisting of ~50% plasma resulted in a ~1:20 dilution compared to the Cobas® plasma sample.

Results:

Of 35 samples (from 30 patients), 20 (57.1%) tested positive with Cobas® (4 genotype (gt) 1; 8 gt 3; 8 gt 4). Sensitivity of the Xpert® assay using capillary blood was 90.0% (18/20) and specificity 100% (15/15) (PPV: 100% (18/18); NPV: 88.2% (15/17)). The 2 HCV-RNA-positive samples missed by Xpert® had low viral load (68 U/ml and <15 U/ml) and were both gt 4 one week after DAA (direct acting antiviral) start. In contrast, a gt 3 sample with 26 U/ml one week after DAA start also tested positive with Xpert® (<10 U/ml). Excluding two extreme outliers considered as technical failures, 15 samples (4 gt1; 6 gt 3; 5 gt 4) with quantitative results in both tests remained for the correlation analysis (HCV-RNA range with Cobas®: 3780-10.2 Mio. U/ml = 3.58-7.01 log U/ml). On average, Cobas® results were 18.6-times or 1.2 log higher, which corresponds to the dilution factor. Cobas® and Xpert® values were highly correlated, both before ($R^2=0.93$) and after log-transformation ($R^2=0.92$). The equation for the fitted regression line was "Cobas®(log U/ml)=1.022*Xpert®(log U/ml)+1.114".

Conclusions:

Point-of-care quantitative HCV-RNA measurement with capillary blood from the finger is a convenient, rapid and sufficiently reliable method to further evaluate HCV-antibody-positives, monitor HCV treatment response and detect HCV-re-infection. For patients with obliterated peripheral veins after long-term intravenous drug use, it removes a crucial barrier to HCV treatment and re-infection monitoring. Same-day results might improve linkage to care.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P60

Septic arthritis due to streptococci, pneumococci and enterococci in native and prosthetic joints – a 13 year retrospective study

H Lotz; W Albrich; C Strahm; B Jost; V Zdravkovic
 KSSG

Aims:

To describe clinical presentation, microbiology, treatment and outcome of native joint septic arthritis (SA) and prosthetic joint infection (PJI) due to streptococcal species and enterococci.

Methods:

Data were collected from medical records of all adults with SA and PJI caused by streptococci and enterococci at our tertiary care centre between 2003 and 2015.

Results:

We included 124 patients (36% female), with 144 affected joints (92 SA, 52 PJI). There were 72 patients with SA and 52 patients with PJI. Median ages were higher in PJI than SA (76 vs. 63 years, $p=0.01$). In 16 patients (13%) >1 joints were involved. 57 (62%) of native joints involved had underlying osteoarthritis, 9 (10%) previous surgery and 20 (22%) previous trauma. Among all 124 patients, 21 (16.9%) had a concomitant soft tissue infection overlying the affected joint, 12 (10%) endocarditis, 3 (2%) pneumonia and 5 (4%) osteomyelitis. Blood cultures were positive in 51 (41%). The knee was the mostly affected joint (46/144, 32%), followed by hip (37/144, 26%) and shoulder (23/144, 16%). β -haemolytic streptococci were the most commonly identified streptococcal species, followed by *Streptococcus pneumoniae* and viridans group streptococci; polymicrobial infections were identified in 23 patients (Figure). β -haemolytic streptococci and *S. pneumoniae* were more frequent in SA than PJI ($p=0.02$ for both), while viridans group streptococci were more frequent in PJI ($p=0.01$). The median durations of antimicrobial therapy were 40 days for SA and 100 days for PJI, respectively ($p<0.01$). Interventions in patients with SA included arthroscopic irrigation and debridement (30/72, 42%), arthrotomy (24/72, 33%) and amputation (5/72, 7%). Among 51 patients with PJI (excluding an early death before intervention), definitive treatment was DAIR ($n=19$), 2-stage exchange ($n=19$) and 1-stage exchange ($n=4$). The outcome was good in 56 (89%) and 44 (86%) of surviving patients with SA and PJI, respectively ($p=1.0$). 5 of 10 deaths were attributed to joint infection (4 patients with SA, 1 patient with both PJI and SA).

Conclusions:

Streptococcal arthritis affects mainly elderly patients with β -haemolytic streptococci being the most common in our cohort. SA concerned mostly previously manipulated or damaged joints. Most patients with SA underwent arthroscopic or open debridement while most patients with PJI underwent debridement and retention or two-stage exchange procedures



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P61

Low predictive value of the Pitt Bacteraemia Score in Staphylococcus aureus bloodstream infection: a validation study

JA Roth; S Tschudin-Sutter; M Dangel; R Frei; M Battegay; AF Widmer
 University Hospital Basel

Aims:

In Staphylococcus aureus bloodstream infections (BSIs), the Pitt Bacteraemia Score (PBS) has repeatedly been described as good estimate for short-term mortality, but little is known about its overall predictive performance. We therefore aimed to externally validate the PBS in a homogenous dataset of methicillin-susceptible *S. aureus* (MSSA) BSIs from the University Hospital Basel, an 800-bed tertiary care centre.

Methods:

All consecutive patients aged ≥ 18 years with a first MSSA BSI between January 2008 and December 2013 were eligible for the study. We excluded patients with a missing PBS at BSI onset. We extracted relevant data from our prospective in-house BSI database. BSI onset was defined as day of first positive blood culture. For prediction of 30-day all-cause mortality, we measured the overall discriminative power of the PBS at BSI onset by receiver-operating characteristics analysis; the calibration of the PBS was assessed using the Hosmer-Lemeshow goodness-of-fit statistic.

Results:

329 patients were included in the final analysis: 7 of 336 eligible patients were excluded because of a missing PBS at onset of MSSA BSI. The crude 30-day mortality was 13%. At BSI onset, 52% (170/329) and 19% of patients (63/329) had a PBS of 0 and 1 points, respectively; the concomitant specificity for 30-day all-cause mortality was 0% (PBS, 0 points) and 55% (PBS, 1 point). The overall performance of the PBS in predicting the 30-day all-cause mortality was lower than published with an area under the curve of 0.711 (95% confidence interval, 0.614–0.807; $P < 0.001$); Hosmer-Lemeshow statistics revealed a good calibration of the PBS with an insignificant P-value (chi-square goodness-of-fit test = 2.91, $P = 0.234$).

Conclusions:

In regard to short-term mortality, the PBS had a low predictive value in a homogenous patient population with MSSA BSI: There is a need for an improved clinical score to better predict mortality. We speculate that the performance of the PBS is even lower, if used in a heterogeneous population with all types of gram-positive and -negative BSIs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P62

Assessing the need for a PrEP-program by using the social media App Grindr®

B Hampel¹; K Kusejko²; D Braun³; J Harrison-Quintana⁴; R Kouyos²; J Fehr⁵

- (1) Universitätsspital Zürich;
- (2) University of Zurich, Zurich, Switzerland;
- (3) University Hospital Zurich, University of Zurich, Zurich;
- (4) Grindr;
- (5) University Hospital Zurich

Objectives

HIV preexposure prophylaxis (PrEP) is not approved in Switzerland and therefore must be paid for by the users themselves. We conducted a survey to find out whether men who have sex with men (MSM) in Switzerland are already taking PrEP, or are considering using it, and whether it is being taken under medical supervision or not.

Methods

Grindr® is a geosocial networking app for MSM. Between January 5 and January 24, 2017, users of the app who were located in Switzerland by global positioning system (GPS) were asked to participate in a ten-question survey on PrEP use.

Results

Of the 2455 people, who entered the survey, 1893 were included in the analysis. Eighty-two participants (4.3%) reported that they were currently taking PrEP, 64 of these (78%) said they were under medical supervision. Seven PrEP users (9%) declared they had not taken an HIV test within the previous 12 months. Nine-hundred-forty-four (49.9%) are considering taking PrEP in the next six months, and 1474 (77.9%) at some point in the future.

Conclusion

In an online-survey among sexually active MSM in Switzerland, only a minority of the approached individuals responded that they are currently using PrEP. However, the majority of the participants is considering taking PrEP in the future. We identified a substantial proportion of PrEP users taking PrEP outside of a medical setting. Hence, a national program facilitating access to medical care and providing PrEP is urgently needed.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P63

Sirtuin 3 deficiency does not alter host defenses against bacterial and fungal infections

E Ciarlo¹; T Heinonen¹; J Lugin¹; H Acha-Orbea²; D Le Roy¹; J Auwerx³; T Roger¹

(1) CHUV-Lausanne University Hospital;

(2) UNIL-University of lausanne;

(3) Ecole Polytechnique Fédérale de Lausanne (EPFL)

Background and aim.

Sirtuins 1-7 are NAD-dependent histone deacetylases. Besides histones, sirtuins target thousands of proteins, such as signal transduction regulators, metabolic enzymes and structural cell components. SIRT3 is the main mitochondrial deacetylase. SIRT3 regulates cell metabolism and redox homeostasis, and protects from aging and age-associated pathologies. SIRT3 drives both oncogenic and tumor-suppressive effects. SIRT3 deficiency promotes chronic inflammation-related disorders. These observations stimulated the development of activators and inhibitors of SIRT3 for clinical purposes. Within this context, our aim was to investigate whether SIRT3 targeting would impact on host resistance to infection.

Methods.

SIRT3 KO mice were housed in SPF conditions. Thymic and splenic subpopulations were analyzed by FACS. Bone marrow-derived macrophages and dendritic cells and splenocytes were stimulated with TLR ligands, bacteria, exotoxins and polyclonal activators and analyzed for intracellular signaling, cytokine production and proliferation. Mice (n=9-17/group) were challenged i.p. with LPS (20mg/kg) or 1-3x10⁴ CFU *E. coli*, i.n. with 30 CFU *K. pneumoniae* and i.v. with 10⁵ CFU *L. monocytogenes* or 10⁵, 3x10⁵ and 10⁶ CFU *C. albicans*. Blood, spleen and liver were collected 1-48 hours post-challenge to quantify cytokines and bacteria. Survival and severity scores were registered daily.

Results.

SIRT3 is expressed ubiquitously, including in immune organs. SIRT3^{-/-} mice develop normally and express normal absolute numbers of thymic and splenic immune subpopulations. SIRT3 deficiency does not affect microbial ligand-induced proliferation and cytokine production by splenocytes, macrophages and dendritic cells. Going well along with these observations, SIRT3 deficiency has no major impact on cytokine production, bacterial burden and survival in models of endotoxemia, *E. coli* peritonitis, *K. pneumoniae* pneumonia, listeriosis and candidiasis of diverse severity.

Conclusions.

Our data support the assumption that SIRT3 has no major impact on innate immune functions and host defenses against bacterial and fungal infections, at least in healthy immunocompetent hosts. The present data largely support the safety of SIRT3-oriented therapies, in terms of susceptibility to infections, for treating metabolic, oncologic and neurodegenerative diseases.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P64

Evaluation of quickSOFA to predict mortality in emergency departments of a low-income country

N Boillat-Blanco¹; Z Mbarack²; J Samaka²; T Mlaganile²; T Kazimoto²; A Mamin³; B Genton¹; L Kaiser³; V D'Acremont⁴

(1) University Hospital of Lausanne;

(2) Ifakara Health Institute;

(3) University Hospital of Geneva;

(4) Swiss Tropical and Public Health Institute

Aims

Fever is one of the most frequent reasons of attendance at health facilities. A bedside clinical score, quickSOFA (qSOFA), better identifies patients with suspected infection at high risk of mortality than systemic inflammatory response syndrome (SIRS). This score needs to be validated in outpatient clinics of low-income countries. We evaluated its performance in emergency departments of Dar es Salaam, Tanzania.

Methods

Consecutive patients ≥ 18 years with fever were recruited. Medical history, clinical examination and several rapid tests were performed (malaria, dengue, typhoid, HIV, Cryptococcus, tuberculosis, Streptococcus A, syphilis), as well as blood cultures and serological analyses. Multiplex PCR was done on nasal swabs and blood. Chest X-rays were performed according to WHO guidelines. Other investigations (urine, stool and CSF cultures, β -D-glucan, urine Histoplasma antigen) were done according to pre-defined algorithms. All final diagnoses and patient's management were based on pre-defined criteria. qSOFA was calculated (one point for each criteria: respiratory rate > 22 /min, Glasgow coma score < 14 , systolic blood pressure ≤ 100 mmHg) and 28-day outcome was assessed by a call. Sensitivity, specificity of qSOFA and SIRS with a cut-off > 2 and the area under the receiver operating characteristics curve (AUROC) were calculated using 28-day mortality as outcome.

Results

519 patients were included and had an HIV prevalence of 25%. Most common diagnoses were acute respiratory infections (36%) and dengue (21%). 15% had an unknown cause of fever.

32 (6%) patients died within 28 days. Patients who died were older (41 vs 29 years; $p < 0.001$), had a higher HIV prevalence (56 vs 23%; $p < 0.001$) and were less often infected by dengue (6 vs 27%; $p = 0.01$). qSOFA predicted subsequent death (AUROC = 0.80, 95%CI 0.73-0.87) better than SIRS (0.63, 0.54-0.73). 15% had a qSOFA > 2 and this cutoff had a sensitivity of 59% (95%CI 41-76) and a specificity of 88% (84-91) for predicting mortality. Relative to qSOFA lower than 2, patients with a score > 2 had a 10-fold odds increase in mortality.

Conclusion

qSOFA performs better than SIRS to predict mortality in the emergency departments of a low-income country. This tool can be easily implemented in low-resource countries as it relies on simple clinical measurements and it can help in identifying patients who need prompt management and higher surveillance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P65

Enhanced vincristine neurotoxicity in adult patients with haematological malignancies treated with fluconazole

F Tissot; O Spertini; O Marchetti; T Calandra; P Bochud

Centre Hospitalier Universitaire Vaudois and University of Lausanne

Aims.

Vincristine has been associated with clinically significant neurotoxicity in patients treated for acute lymphoblastic leukemia with concomitant use of lipophilic azoles (itraconazole, voriconazole, posaconazole). Few data exist regarding the interaction with fluconazole, which has weaker potential for drug interaction. The goal of this study was to assess the incidence of neurological adverse events in vincristine-treated patients with concomitant fluconazole exposure.

Methods.

Seven-year (2007-2014) retrospective study of all consecutive adult patients hospitalized in a 14-bed haemato-oncological unit and treated with vincristine. Demographic and clinical data were prospectively collected using an electronic database. Based on drugs half-lives, concomitant exposure was defined as fluconazole administered within 5 days of vincristine therapy. The incidence of neurological adverse events related to vincristine, defined and graded according to NCI classification, was measured in patients with (cases) and without (controls) exposure to fluconazole.

Results.

Among 56 vincristine-treated patients, 32 were exposed to fluconazole (median follow-up 152 days) and 24 were not (median follow-up 153 days). Neurological toxicity occurred in 22 patients, within a median of 13 days (IQR 9-25) after the first dose of vincristine. Among 28 reported adverse events (11 grade 3/4), constipation was the most frequent (n=15), followed by peripheral neuropathy (n=10), SIADH (n=2) and epilepsy (n=1). Vincristine was discontinued permanently in 10/22 patients (45%) and continued at a reduced dosage in 5/22 (23%). Although the overall incidence of neurological adverse events was similar between cases and controls (37% vs. 42%, p=0.8), definitive vincristine discontinuation was significantly more frequent in cases than in controls (67% vs. 20%, p=0.04). Neurotoxicity occurred earlier in cases than in controls (median 9 vs. 23 days after vincristine onset, p<0.01). Overall gastro-intestinal toxicity occurred in 34% vs. 17% (p=0.22) and peripheral neuropathy in 9% vs. 29% (p=0.08), respectively.

Conclusion.

Exposure to fluconazole resulted more frequently in permanent vincristine discontinuation due to early-onset grade 3 and 4 gastro-intestinal toxicity. These data suggest that fluconazole may enhance vincristine-related neurotoxicity despite its weaker potential for hepatic drug interactions compared to lipophilic azoles.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P66

Patient and health system delay among pulmonary tuberculosis patients of Switzerland: extent and determinants

C Auer¹; S Kiefer¹; M Zuske¹; C Schindler¹; K Wyss¹; J Blum¹; X Bosch-Capblanch¹; J Zellweger²; E Altpeter³; P Helbling³; M Maeusezahl-Feuz³

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) Swiss Lung Association;

(3) Federal Office of Public Health

Aims

TB is a rare disease in Switzerland (630 cases registered in 2016). General practitioners are, therefore, in general not fully familiar with symptoms and diagnostic approaches. Commissioned by the Federal Office of Public Health of Switzerland, the Swiss Tropical and Public Health Institute conducted a study with the aim to establish TB patient experiences, especially patient delay (time span from onset of symptoms to first consultation) and health system delay (time span from first consultation to start of TB treatment) and to identify determinants of these delays.

Methods

A prospective cross-sectional study was carried out in six cantons of Switzerland from November 2014 to June 2016 among notified adult TB patients. Patients were interviewed by medical staff of the cantonal lung associations. Face-to-face interviews with patients were carried out, with interpreters when needed. With 11 of these TB patients qualitative in-depth interviews were conducted. Eight healthcare providers were also interviewed.

Results

61.8% of the 252 cases registered by the participating lung associations were interviewed. 20.4% of them were born in Switzerland, 41.4% were foreign-born residents in Switzerland and 38.3% were or had been asylum seekers.

The most common symptoms were cough and tiredness.

Median patient delay was 5.2 weeks. Predictors of a long patient delay (> 5 weeks) were tiredness and presence of smoker's cough. Patients with Swiss citizenship were less likely to have a prolonged patient delay (> 5 weeks). Median health system delay was 2 weeks. For one quarter of the respondents, the health system delay was > 7 weeks. Patients with Swiss citizenship were more likely to have a prolonged health system delay (> 3 weeks). Protective factors against a long health system delay were being male and having undergone a chest X-ray at the first consultation.

The qualitative interviews showed that some doctors don't consider TB in their diagnostic procedures, indicated by repeated prescription of antibiotics good for 10 days. For some asylum seekers, the language barrier may contribute to a long health system delay. The healthcare providers emphasised the need for good communication between various actors.

Conclusion

Some TB patients – in particular Swiss women – have a comparatively long health system delay. General practitioners need to think of the possibility of TB disease, even among patients with atypical symptoms or patients born in a country with low TB incidence.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P67

Case report: A seizure can open another door – at the right time

M Büttcher¹; T Schmitt-Mechelke¹; C Relly²

(1) Children's Hospital Lucerne;

(2) University Children's Hospital Zurich, University of Zurich

Background

For the work up of a non-febrile generalised seizure in a child usually EEG and often cranial MRI are performed. Imaging can reveal an unexpected pathology that may not have been associated with the primary clinical presentation. These unexpected findings however, may have serious consequences.

Case Presentation Summary

A 3-year-old girl was referred to our neurology department for evaluation of 2 recent non-febrile generalised seizures. EEG detected a focal epileptogenic area with sharp-slow wave complexes suggesting structural epilepsy. Cranial MRI showed a focal subcortical heterotopia. On second look at the MRI we noticed bilateral cystic lesions of the parotid glands. The child was referred to our paediatric infectious disease specialist. An HIV screen was positive. From personal history she had been well and had a normal development, no recurrent or severe infections, mild flares of atopic eczema and self-limited papular skin lesions. On examination, parotid glands appeared normal. Her parents had adopted her at the age of 14 months from Kenia. Screening in Kenia allegedly had been "normal" and had not been repeated after arrival in Switzerland. Further HIV work-up showed a viral load of 53'000 copies/ml and a CD4 count of 730/μl (29%). No clinical, laboratory or radiological signs of opportunistic diseases were evident. Treatment with ABC, 3TC, LPV/r was started.

Learning Points/Discussion

When imaging is done, all organs should be judged and, if abnormal, evaluated. In children bilateral parotid enlargement as well as cystic lesions found by imaging should always prompt to search for HIV. Retrospectively she had no warning signs for this chronic viral infection. Every adopted child should have repeated screening, preferably by a paediatric infectious disease specialist lead adoption/immigration clinic.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P68

Propionibacterium avidum – a virulent pathogen causing hip periprosthetic joint infection

Y Achermann¹; J Liu²; R Zbinden³; P Zingg⁴; A Anagnostoopoulos¹; E Barnard²; R Sutter⁴; H Li⁵; A McDowell⁶; A Zinkernagel¹

- (1) University Hospital Zurich and University of Zurich;
- (2) David Geffen School of Medicine;
- (3) University of Zurich;
- (4) University Hospital Balgrist;
- (5) Department of Molecular and Medical Pharmacology;
- (6) University of Ulster

Background.

Propionibacteria are important members of the human skin microbiota, but are also opportunistic pathogens associated with periprosthetic joint infections (PJI). While the role of *Propionibacterium acnes* in PJI has been widely described, knowledge regarding the capacity of *Propionibacterium avidum* to cause PJI is limited.

Methods.

An unusual cluster of four hip PJIs caused by *P. avidum* in one orthopedic center in 2015 prompted us to retrospectively identify and analyze clinical data related to previous *P. avidum* PJI cases (1997-2015). We also characterized the hemolytic and biofilm-producing capacity of our four clinical *P. avidum* strains isolated in 2015 and investigated their phylogenetic relationships by whole genome sequencing.

Results.

We retrospectively identified 12 *P. avidum* PJIs, with the majority being hip-related infections (n=10). Preoperative synovial fluid cultures were *P. avidum* positive in 63.6% of cases. Six out of 12 patients (50%) were treated with an exchange of the prosthesis. In all but one of the six patients treated with debridement-retention of the prosthesis, treatment failed thus requiring a two-stage revision. The isolated *P. avidum* strains showed a more pronounced hemolytic activity (p= 0.01), but a similar biofilm-forming ability when compared to *P. acnes*. Whole genome sequencing identified two phylogenetic clusters highly related to recently published *P. avidum* PJI strains.

Conclusions.

We describe the largest series of *P. avidum* PJI predominantly located in the hip. Phylogenetic similarity of our *P. avidum* strains to PJI strains isolated in Sweden suggests these invasive lineages may be common.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P69

HLA-E genotype seems to impact on the immune control of Epstein-Barr virus in infectious mononucleosis

T Azzi; M Hug; C Berger; D Nadal

University Children's Hospital of Zurich

Aims

The Epstein-Barr virus (EBV) is the causative agent of the infectious mononucleosis (IM) syndrome and is associated with B cell cancers. Individuals suffering from IM are at increased risk of developing EBV+ Hodgkin lymphoma. Most EBV-associated diseases are linked to deficiency in the immune control of this oncogenic virus. We previously described the proliferation of natural killer (NK) cells bearing the NKG2A inhibitory receptor in IM patients, suggesting a protective role of this NK cell subset. The ligand of NKG2A is HLA-E, which is encoded by two main alleles (*101 and *103). Both alleles are found worldwide and are associated with 3 different genotypes (two homozygous and one heterozygous). Therefore, we assessed the influence of the HLA-E genotype on the immune response to EBV in IM patients.

Methods

We genotyped the HLA-E gene of 48 pediatric IM patients who were prospectively enrolled at the University Children's Hospital of Zurich between 2007 and 2016. We compared quantitative virological (EBV DNA copy numbers in plasma and peripheral blood mononuclear cells) and immunological (lymphocyte counts) parameters of IM patients at diagnosis according to their HLA-E genotype.

Results

Nine IM patients were classified as HLA-E*101/*101, 23 as heterozygous (*101/*103) and 15 as *103/*103. The ages of the patients were comparable between the three groups (median: 9 vs. 10 vs. 9 years) as was duration of symptoms at diagnosis (median: 10 vs. 8 vs. 7 days). Heterozygous individuals exhibited 6-fold lower numbers of EBV DNA copies in plasma compared to HLA-E*101 homozygous (median 371 vs. 2264 copies/ml, $P = 0.01$). No significant differences were found in the levels of EBV DNA copies in peripheral blood mononuclear cells. IM patients homozygous for HLA-E*101 exhibited lower counts of reactive lymphocytes compared the heterozygous and HLA-E*103 homozygous individuals (median 0.61 vs. 0.97 vs. 1.67 G/l, $P = 0.02$ and 0.01).

Conclusion

IM patients heterozygous for HLA-E*101 and *103 exhibited lower levels of EBV DNA in plasma, suggesting a better immune control of EBV in the presence of both alleles. However, the allele HLA-E*103 was associated with higher numbers of reactive lymphocytes and might be linked to an increased T cell-mediated immunopathology in IM. Thus, the HLA-E genotype seems to influence the course of the acute symptomatic EBV infection and might therefore impact on the outcome of EBV-associated diseases.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P70

The role of the adaptive immune system in clearing *Bartonella* infection

LK Siewert

University of Basel

Bartonellae are fastidious gram-negative bacteria causing long-lasting intra-erythrocytic bacteremia in their reservoir hosts. Several species, adapted to the human host or zoonotic pathogens, can cause a diverse array of disease symptoms in humans. However, not much is known about the immune mechanisms controlling *Bartonella* infection. The aim of this project is to understand the immunobiology of *Bartonella* spp. in mice.

Intra dermal infection of several murine knock-out strains revealed important roles for both, antibodies and T-cells, in clearing the infection. Interestingly, the prolonged bacteremia observed with mice lacking all types of T-cells could not be observed using mice lacking either classical T-help or T-killing alone.

Further investigation of the antibody response showed that opsonization (Fcγ-receptor binding), complement activation and class-switch - although happening in the WT mouse - are neglectable for clearance from the blood. These findings strongly suggest neutralization of the bacteria by antibodies as a key step in clearance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P71

Effect of older age as independent risk factor for hospitalisation for pneumonia and associated detrimental outcome in adults in Switzerland

W Albrich¹; F Rassouli²; F Baty²

(1) KSSG;

(2) Kantonsspital St. Gallen

Aims:

To quantify the effect of age as independent risk factor for hospitalisation for pneumonia, increased length of stay (LOS) and mortality in patients with pneumonia

Methods:

We used a national database of all hospitalisations in Switzerland which includes diagnoses (ICD10-coded) to obtain the number of hospitalisations for pneumonia as primary or non-primary diagnosis among adults ≥ 18 y from 2002 to 2015. We calculated the effects of older age and of those comorbidities, which are official Swiss 13-valent pneumococcal conjugate vaccine (PCV13) indications, on hospitalisation for pneumonia, LOS and all-cause in-hospital mortality.

Results:

Among patients ≥ 50 y pneumonia was diagnosed in 3.4% of hospitalisations, which was higher than among patients < 50 y (0.7%, $p < 0.001$). The effect was similar for age ≥ 65 y (4.3% vs. 1.1%, $p < 0.001$). Similarly, the proportion of hospitalisations with a diagnosis of pneumonia was higher in patients with than without each of the PCV13 indications (except for cerebrospinal fluid leak). Patients with any of the PCV13 indications had a pneumonia diagnosis in 7.2% of hospitalisations compared to 1.4% if no PCV13 indication was present ($p < 0.001$). Age ≥ 50 y (OR 3.5, $p < 0.001$), age ≥ 65 y (OR 3.0, $p < 0.001$) and presence of any PCV13 indication were independent risk factors for pneumonia hospitalisation with a negative interaction between age and PCV13 indications ($p < 0.001$). Median LOS and all-cause in-hospital mortality were greater in patients ≥ 65 y (vs. < 65 y) and in patients ≥ 50 y (vs. < 50 y) independent of the presence of PCV13 indications both in patients with and in patients without a pneumonia diagnosis. Among patients ≥ 50 y with a pneumonia diagnosis, median LOS was 10 [IQR: 6-18] days for patients without a PCV13 indication vs. 11 [IQR: 7-19] days in patients with any PCV13 indication ($p < 0.001$); in patients < 50 y, the respective median LOS were 5 [IQR: 3-10] and 9 [IQR: 5-17] days ($p < 0.001$). Similarly, all-cause in-hospital mortalities among patients ≥ 50 y with a pneumonia diagnosis were 11.5% vs. 12.9% for patients without PCV13 indications vs. patients with any PCV13 indications ($p < 0.001$), but only 2.7% vs. 6.0% for patients < 50 y without a PCV13 indication vs. patients with any PCV13 indications ($p < 0.001$).

Conclusion:

Older age is a risk factor for hospitalisation with pneumonia, longer LOS and higher mortality similarly to and independent of PCV13 indications. Our data suggest that these increased risks already occur in patients ≥ 50 y.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P72

Diagnostic yield of bacterial stool cultures in a tertiary care hospital according to the timepoint of sampling

D Widmer; N Bartlomé; H Fankhauser; A Sigel; CA Fux
 Kantonsspital Aarau

Background:

Infectious diarrhea is frequent and causes substantial morbidity and mortality. Therefore, stool cultures (SC) are frequently ordered. However, they only rarely turn out positive. Several studies have documented that the positivity rate of SC taken beyond hospitalization day 3 is <1%. We wanted to evaluate the diagnostic yield of SC according to the timepoint of sampling in our tertiary care hospital, define risk factors for SC positivity and estimate associated costs.

Methods:

Retrospective analysis of all SC collected in adult patients between 2010 and 2016 comparing outpatients with hospitalized patients and stratified for the day of testing. We performed chart reviews to characterize all patients with positive SC >2 days after admission or with repetitive positive testing. In a case control study including SC collected within the first 3 days, we compared all 42 cases with *Salmonella* spp., all 137 patients with *Campylobacter* spp. enterocolitis occurring between 2014 and 2016 and 200 negative controls in order to identify risk factors for SC positivity.

Results:

Of 7'632 SC, 1'892 (24.8%) were performed on day 1, 1'197 (15.7%) on day 2, 698 (9.1%) on day 3 and 3'854 (50.4%) beyond day 3. Overall, 407 SC (5.3%) turned out positive including 356 *campylobacter* spp., 42 *salmonella* spp, 4 *shigella* spp. and 4 *yersinia* spp. Positivity rates were 13.1% for day 1 (NNT=8), 8.4% for day 2 (NNT=12), 4.6% for day 3 (NNT=22) and 0.7% later on (NNT=142). In 21/27 patients with a positive SC later than day 3, diarrhea had already started before, resulting in only 6 patients with a later onset of symptoms and a positive SC after 7-19 days (positivity rate 0.2%, NNT=642). SC revealed *Campylobacter* spp. in 4 and *Salmonella* spp. in 2 cases. Two patients each had hematological neoplasias and chronic infections and had been repetitively exposed to antibiotics. We identified 6 patients with repetitive positive cultures between day 8 and 42, including 2 treatment failures, one clinical cure and 3 oligosymptomatic, untreated cases. In 6 patients, the same species was cultured >180 days later.

Conclusion:

Despite strong evidence in the literature, the majority of SC are performed >3days after hospitalisation, resulting in high costs but little clinical impact. Diagnostic yield can be improved by restricting testing to patients with defined risk factors and clinical indication for antibiotic treatment, in particular dysentery and immunosuppression.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P73

The Bartonella effector protein Bep10 inhibits NF- κ B activation in Macrophages by manipulating the phosphatidylinositol 4-Phosphate-5 kinase 1 (PIP5K1)

S Siemer

Biozentrum of the University of Basel

The facultative intracellular bacteria *Bartonella* spp. share a common infection strategy to invade and colonize mammals in a host-specific manner. The VirB/VirD4 type IV secretion system (VirB/D4 T4SS) is essential for the pathogenicity of most *Bartonella* species by injecting an arsenal of effector proteins into host cells. Thus, defining the role of these Type IV effector proteins is a key to understand pathogenesis.

We found that one effector protein of *Bartonella rochalimae* called Bep10 inhibits NF- κ B and p38 MAPK activation in Raw 264.7 macrophages upon LPS stimulation. This inhibition is associated with a decreased production of pro-inflammatory cytokines like TNF α and IL-6. These results were also confirmed using mouse peritoneal macrophages.

A two-hybrid screen leads to the identification of the PIP5K1 kinase as a potential target of Bep10. Altogether, these data are consistent with the role of the PIP5K1 kinase in NF- κ B activation. Now we are trying to understand the molecular mechanism of Bep10 on the PIP5K1.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P74

Feasibility and impact of HIV screening among asylum seekers.

L Cochand¹; E Masserey²; P Bodenmann³; N Troillet⁴

- (1) Central Institute, Valais Hospital, Sion;
- (2) Canton of Vaud;
- (3) Centre Hospitalier Universitaire Vaudois and University of Lausanne;
- (4) Central Institute, Valais Hospital and University of Lausanne

Aims.

Asylum seekers face an increased risk of infection, delayed diagnosis and transmission for HIV. (1) In Switzerland, this vulnerable population faces several barriers to access HIV screening facilities. This study aims at evaluating the feasibility and the impact of a voluntary HIV screening for newly arrived asylum seekers in the 2 Swiss cantons of Vaud (VD) and Valais (VS). More generally, this study seeks to meet the national and international standards for early detection and effective treatment of HIV infections in order to reduce the morbidity, mortality, and transmission of the virus. (2,3)

Methods.

A voluntary and free of charge HIV screening test was offered during their first routine medical check-up to newly arrived asylum seekers in VS (November 2015 - June 2016) and VD (June – October 2016). A written consent was asked in VS before vaccines' status check and catch-up by using standard forms translated in different languages. After a protocol amendment by the ethical committee, an oral consent was asked in VD during a personal nursing visit with an interpreter. Pregnant women and children <16 were excluded.

Results.

807 asylum seekers were offered the HIV test (VS 451, VD 356). Their mean age was 27.6 years, 61.2% were males, 67.4% were single, 60.5% arrived from Sub-Saharan Africa. The overall acceptance rate was 72.2% (VS 63.2%, VD 83.7%). Two persons were newly diagnosed with HIV, 5 were already known as HIV positive (overall HIV prevalence rate: 0.87%). All were rapidly referred to infectious diseases specialists. Factors associated with the non-acceptance in multivariate analysis were a female sex (OR: 0.70; 95%CI: 0.50-0.97) and having been registered in VS (0.34; 0.23-0.48), whereas a Sub-Saharan origin was associated with acceptance as compared to other origins (2.16; 1.50-2.96).

Conclusion.

The acceptance rate of the HIV test was high among asylum seekers in VS and VD. This offer appeared to respond to a real demand among this population, particularly among persons from regions where HIV is highly endemic. It seems essential to guarantee an equitable access to the Swiss health care system. A simplified oral consent may enhance the acceptance rate, but requires the availability of interpreters.

References

- 1) Wolbers M. et al. HIV Med. 2008;9:397.
- 2) Office fédérale de la santé publique. Programme national Migration et santé. 2013.
- 3) European Centre for Disease Prevention and Control (ECDC). ECDC Guidance. 2010.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P75

Randomized Trial of Bictegravir or Dolutegravir with Emtricitabine and Tenofovir Alafenamide for Initial HIV Therapy

P Sax¹; E DeJesus²; DW Douglas Ward³; P Benson⁴; K White⁵; H Martin⁵; H Rovini⁶; E Quirk⁵

(1) Division of Infectious Diseases;

(2) Orlando Immunology Center;

(3) Dupont Circle Physicians;

(4) Be Well Medical;

(5) Gilead Sciences;

(6) Gilead Sciences Switzerland

Background

Bictegravir (BIC, GS-9883) is a novel, unboosted, once-daily INSTI that demonstrated potent activity in a 10-day monotherapy study and has in vitro activity against most INSTI-resistant viruses.

Methods

Treatment naïve, HIV-infected adults were randomized 2:1 to receive blinded treatment once daily with BIC 75 mg or dolutegravir (DTG) 50 mg; both were given with open label emtricitabine 200 mg/tenofovir alafenamide 25 mg (FTC/TAF). Treatments were administered without regard for food for 48 weeks. The primary endpoint was the proportion with HIV RNA <50 copies/mL (c/mL) at Week (W) 24 using snapshot analysis. Noninferiority was assessed through 95% confidence intervals (CI) at W24 and W48. Safety (adverse events and laboratory results through W48) was a secondary endpoint.

Results

Of 98 patients enrolled, 65 were randomized to BIC+FTC/TAF and 33 to DTG+FTC/TAF. Most subjects were male, had asymptomatic HIV infection, with median HIV-1 RNA 4.4-4.5 log₁₀; baseline characteristics were balanced between arms. Virologic success (HIV-1 RNA <50 c/mL) at W24 was 97% for the BIC arm and 94% for the DTG arm, and at W48 was 97% and 91%, respectively. One subject in the DTG arm had HIV-1 RNA >50 c/mL at W48. No viral resistance was detected in the BIC+FTC/TAF arm. Mean CD4 count increases at W48 were 258 cells/μL in the BIC arm and 192 cells/μL in the DTG arm. There were no treatment-related serious adverse events and no deaths. The most commonly reported adverse events were diarrhea (12% each) and nausea (8% BIC, 12% DTG). One subject in the BIC arm discontinued due to an adverse event of urticaria following the W24 visit. Median changes in estimated glomerular filtration by Cockcroft-Gault (GFR_{CG}) at W48 were -7.0 mL/min for BIC and -11.3 mL/min for DTG, with no discontinuations due to renal adverse events.

Conclusions

BIC+FTC/TAF and DTG+FTC/TAF both demonstrated high virologic response rates at W24 that were maintained at W48. No treatment-emergent resistance was detected in the BIC+FTC/TAF arm through W48. Both treatments were well tolerated, and no significant safety signal was detected in either arm. Estimated GFR_{CG} changes were consistent with known inhibition of tubular creatinine transport by BIC and DTG. Further evaluation of BIC for the treatment of HIV infection is warranted.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P76

Tularaemia in Switzerland, 2004 to 2016

E Altpeter¹; N Schürch²; M Wittwer²

(1) Federal Office of Public Health;

(2) Federal Office of civil Protection

Aim:

To describe the epidemiology of tularaemia in Switzerland since introduction of mandatory reporting in 2003.

Methods:

Mandatory reporting in Switzerland

Results:

Tularaemia is an emerging infection in Switzerland – in most cases reported to be transmitted by ticks. In accordance with arthropods as predominant vector, the glandular / ulceroglandular manifestation of the disease is most common (44% of the reported cases). We received only few case reports in 2004. We observe a steady increase up to 50 cases in 2016 corresponding to an incidence of 0.6 per 100'000 inhabitants. A part of this increase is due to an improved case definition in 2012. Men (N=183) are more likely to be affected than women (N=85). The median age fluctuated between 40 to 60 years. Cases cluster in space in three regions of Switzerland: northeast, middle and Middle West below 1500 meters altitude. The spatial data is in agreement with field studies assessing the prevalence of *F.tularensis holarctica* in ticks and wild animals, which indicate a higher prevalence of the pathogen in the northeast and middle part of Switzerland.

Conclusion:

Tularaemia is rare, but on the rise within the last 10 years. Considering blood sucking arthropods (e.g. ticks) as most important vectors, climatic changes may have an influence on the elevated prevalence of the disease. Due to the incline of reported cases and the endemic establishment of the pathogen in the environment, physicians diagnosing infectious diseases should consider tularaemia.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P77

Microparticles loaded with daptomycin are successful in the treatment of experimental methicillin-resistant staphylococcus aureus implant-associated infections

A Woischnig¹; L Gonçalves²; I Ribeiro²; A Bettencourt²; N Khanna³

- (1) Department of Biomedicine and Division of Infectious Diseases and Hospital Epidemiology, University and University Hospital; Basel, Switzerland,;
- (2) Research Institute for Medicines (iMed.Ulisboa), Faculty of Pharmacy, Universidade de Lisboa;
- (3) Department of Biomedicine and Division of Infectious Diseases and Hospital Epidemiology, University and University Hospital; Basel, Switzerland

Background/Aim:

Daptomycin (DAP) alone was highly efficient against stationary methicillin-resistant *Staphylococcus aureus* (MRSA) in vitro, but failed to eradicate MRSA in an experimental model of implant-associated infection¹. We therefore investigated the effect of a better local drug delivery using DAP-loaded acrylic microparticles (MP)² to treat implant-associated MRSA infection in the mouse foreign-body infection model.

Methods:

Teflon cages were infected with 5×10^2 CFU of MRSA 43300. The infection was confirmed at day 1 (directly before treatment start) and treated for 2 days directly into the cage. Mice (n=5) were randomized into 4 treatment groups: (i) saline, (ii) empty MP, (iii) 50 mg/kg DAP, or (iv) MP loaded with 50 mg/kg DAP (DAP-MP). Empty and loaded MPs (1.2 μ m, average size) were obtained by double emulsion-solvent evaporation methodology². The efficacy of each treatment against planktonic bacteria was expressed as bacterial counts (log₁₀ CFU/mL) at day 3 (end of treatment) and at day 5 (day of explantation). Furthermore, the DAP levels in tissue cage fluid (TCF) were measured using HPLC. The effect against adherent bacteria was assessed on day 5 by cage sonication and plating of adherent bacteria. To examine the cure rate (number of cages without growth divided by number of cages per treatment group) sonicated cages were transferred into fresh medium at 37°C and plated after 48 h.

Results:

Before treatment all cages were infected with 4.8×10^5 planktonic CFU/mL. DAP alone showed a >3 log decrease in planktonic bacteria. DAP-MP showed a clearance in planktonic MRSA. DAP levels at day 3 were 41.9 μ g/mL and 68.9 μ g/mL and at day 5 0 μ g/mL and 13.0 μ g/mL for DAP alone and DAP-MP, respectively. DAP alone showed a >3 log decrease in adherent bacteria, but failed to cure the infection due to undetectable DAP levels after day 3. DAP-MP decreased the adherent bacteria by more than 3 log and cured in 60%.

Conclusions:

Local DAP-microparticles are more efficacious in clearing biofilm-associated infection than parenteral DAP, which is linked to the prolonged higher DAP concentration at the site of infection. DAP-microparticles are therefore a promising future application mode for the treatment of implant-associated MRSA infections.

References

- 1) John AK. et al, Antimicrob Agents Chemother. 2009 Jul;53(7):2719-24
- 2) Ferreira IS. et al, Int J Nanomedicine. 2015 Jul 7;10:4351-66



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P78

Dual disseminated infection with *Rhizopus pusillus* and azole-resistant *Aspergillus fumigatus*: a case report

F Franzeck; V Bättig; S Dräger; G Stehle; M Medinger; J Passweg; N Khanna

Universitätsklinik Basel

A 60-year old male patient was diagnosed with therapy-related myelodysplastic syndrome in March 2016. Consecutive treatment consisted of 2 induction chemotherapy cycles followed by allogeneic HSCT from a haploidentical son in July 2016. The protocol at our institution does not include mold-active antifungal prophylaxis.

Three weeks after HSCT, he developed severe cutaneous and gastrointestinal graft-versus-host disease, which was steroid-refractory. Therefore second-line treatment with alemtuzumab and vedolizumab was administered between day 60 and 80 post-HSCT.

Probable pulmonary aspergillosis (positive galactomannan in serum) was diagnosed on day 13. Pulmonary lesions responded well to the treatment with voriconazole. On day 84, new pulmonary lesions were noted. Repeat bronchoscopy returned a positive PCR for *Rhizomucor pusillus*, which led to a switch to liposomal amphotericin B. On day 98 the patient developed neurological deterioration and brain MRI revealed multiple acute lesions with a high suspicion of CNS dissemination. The following weeks showed radiological progress of all manifestations with no evidence of further organ dissemination on PET/CT. On day 101 a sputum sample showed growth of *Aspergillus fumigatus* resistant to all azoles. The TR34/L98H mutation was confirmed. The uncontrolled situation led to dual therapy with the addition of isavuconazole. The patient improved clinically and radiologically and was managed as an outpatient from 6 months post-transplant with continued dual therapy. Therapeutic drug monitoring (TDM) of isavuconazole from serum was in the previously published range. The TDM from cerebrospinal fluid showed 1% of the serum level. Steroid and calcineurin treatment was tapered to 10mg daily and 25mg daily, respectively.

However, 2 months later (8 months after HSCT) the patient presented with pulmonary hemorrhage and new back pain under ongoing treatment with liposomal amphotericin B and isavuconazole. A lobectomy was performed and fittingly, *Rhizomucor pusillus* was detected in PCR of the pulmonary tissue. Simultaneously, vertebral osteomyelitis with culture positive azole-resistant *Aspergillus fumigatus* was diagnosed. Treatment was switched from isavuconazole to caspofungin and liposomal amphotericin B was retained.

This case highlights challenges in management of disseminated invasive mold infection with multiple pathogens including azole-resistant *A. fumigatus* and treatment experience with the new compound isavuconazole.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P79

When your dog suddenly barks silently

V Bansal Zweifel¹; I Marcaccini¹; S Hasler²; A Miller²; U Karrer²; P Ballmer²; J Gubler²

(1) Kantonsspital Winterthur;

(2) Kantonsspital Winterthur

Case Description

A 59-year-old patient was admitted due to acute onset of dizziness, vomiting and bilateral hearing loss. A week earlier, his illness started with influenza-like symptoms, followed by severe nausea, protracted emesis, progressive dizziness, vertigo and unstable gait. Almost complete bilateral hearing loss occurred the day before admission. The patient lived alone with numerous small animals (goats, cats, dogs), he consumed alcohol excessively. On examination, he had a temperature of 38.2°C, looked ill with signs of severe vestibulo-cochlear failure (unsteady gait with drift to left, Weber and Rinne-testing was not heard, bilateral positive head impulse test and spontaneous left-beating nystagmus) but no neck stiffness. Blood tests showed leucocytosis of 20.7 G/l with marked left shift, thrombocytopenia of 43 G/l, and C-reactive protein of 85 mg/l. Cerebrospinal fluid (CSF) analysis revealed a polynuclear pleocytosis of 493/μl, with a lactate of 3.3 mmol/l (N<2.0). Treatment with ceftriaxone, amoxicillin and aciclovir was started. A cerebral MRI disclosed multiple small subacute supratentorial ischemic lesions. The echocardiography demonstrated an apical akinesia as sequela of a myocardial infarction and a thrombus within the apex. Coronary angiography was normal without coronary stenosis.

Cultures of blood and CSF were negative. However, broad-spectrum PCR of the CSF was positive for *Capnocytophaga canimorsus*. The patient was treated with i.v. Ceftriaxone for 10 d, recovered slowly of his neurologic deficits over 6 months but at the end needed a cochlear implant for persisting deafness.

Discussion

Capnocytophaga canimorsus, a slow growing gram negative rod, is part of the commensal oral flora of dogs and cats. It can cause severe septic infection, especially in immunocompromised patients (i.e. asplenia, liver cirrhosis, excessive alcohol consumption). *C. canimorsus* infection activates the blood coagulation cascade; thromboembolic myocardial infarction has been described in patients with *C. canimorsus* sepsis and normal coronary arteries. Meningitis due to *C. canimorsus* goes along with a high rate of sensorineuronal hearing loss. Our patient with typical risk factors of dog and cat exposure, combined with excessive alcohol consumption, suffered from two classical complications of systemic *C. canimorsus* infection, notably meningitis with bilateral hearing loss and thromboembolic cardiac involvement despite normal coronary arteries.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P80

Treatment of *Helicobacter pylori* unmasking Whipple's Disease

C Hochuli; G Bösch-Schätti; S Hasler; J Gubler
Kantonsspital Winterthur

Introduction

Whipple's Disease is a rare, systemic infection caused by the intracellular bacterium *Tropheryma whippelii*. In classic gastrointestinal Whipple's disease, typical PAS-positive foamy macrophages in the lamina propria of duodenal mucosa lead to the diagnosis.

We present a case of a 54-year old man with a 10 years long history of multiple inflammatory symptoms of unknown cause, diagnosed as Whipple's disease suspected by the effect of treatment for *Helicobacter pylori* gastritis.

Case presentation

54-year old man presenting over 10 years the following symptoms and signs: Intermittent fevers, arthralgias, recurrent soft tissue swelling and systemic inflammation (C-reactive protein up to 200mg/l). Extensive testing and imaging including PET/CT scans, bone marrow biopsy, and more, revealed no malignancy, nor infectious or autoimmune diseases. Gastroduodenoscopy (2009), found no histological signs for *T. whippelii* in a duodenal biopsy.

History clue and tests leading to the diagnosis

The retrospective history of intermittent relief of symptoms following eradication treatment for *H. pylori* gastritis with amoxicillin, metronidazole and pantoprazole in 2010 led to a suspicion of the infectious origin and directed diagnostic procedures:

- Positive results for *T. whippelii* by PCR testing of duodenal mucosa and stool.
- Repetition of duodenal biopsy showing no histological evidence of *T. whippelii*.

Outcome

Treatment with Ceftriaxone iv for 14 days followed by doxycycline and hydroxychloroquine for 12 months (ongoing) led to rapid disappearance of previous symptoms and normalization of inflammatory parameters. The patient has been free of symptoms since August 2016.

Key messages:

- Whipple's Disease can mimic multiple conditions. Typical histological findings prove the diagnosis, absence of these does not rule it out.
- *T. whippelii* is highly sensitive to multiple antimicrobials, clinical response is often very rapid.
- Detection of *T. whippelii* DNA by PCR in gastrointestinal samples supports but does not prove the diagnosis of Whipple's disease, due to a significant rate of commensal gastrointestinal carriage of the bacterium.
- Probable diagnosis in our patient has been strongly supported by the clinical response to treatment.

References

- [1] Marth T. et al. Lancet Infect Dis. 2016;3:e13-22.
- [2] Lagier JC, et al. J Antimicrob Chemother 2014;69:219-27.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P81

Asymptomatic congenital tuberculosis

PM Meyer Sauter¹; E Marques-Maggio²; C Relly¹; PM Keller³; CF Clarenbach²; C Berger¹

(1) University Children's Hospital Zurich;

(2) University Hospital Zurich;

(3) University of Zurich

Aims:

Congenital tuberculosis (TB) is described as a rare, but severe disease. In contrast to the cases with severe symptoms reported so far, we describe a first child with asymptomatic congenital TB.

Results:

An 8-week-old girl was investigated because of newly diagnosed TB in her mother, which presented the first time 4 weeks after birth with a cough that emerged at 21 weeks gestation, during treatment of indeterminate colitis with the anti-TNF- α antibody adalimumab. She was HIV negative. No radiographic studies were conducted so far. The interferon-gamma release assay, performed before pregnancy under treatment with prednisolone because of colitis, was negative. Her CT scan 4 weeks after delivery showed numerous nodules and tree-in-bud opacities, a pattern characteristic for miliary TB. Lung biopsy tissue specimens revealed necrotizing granuloma with a single acid-fast bacillus, and *Mycobacterium tuberculosis* (MTB) was detected by polymerase chain reaction. Bronchoalveolar lavage was negative for MTB, arguing against postnatal transmission of MTB. TB contact investigations led to the investigation of this child and were otherwise negative.

The child, at the age of 8 weeks at first assessment, was in an excellent general condition. Pregnancy induced by in vitro fertilization, birth, and neonatal period were unremarkable. Physical examination, laboratory evaluation, abdominal ultrasound, and chest X-ray were normal. Surprisingly, the tuberculin skin test was positive with an induration of 9x6 mm at 8 weeks of age, and 20x10 mm at 10 weeks of age. Three gastric aspirates did not show AFB by microscopy, but one grew MTB in culture after 3 weeks. Ambulatory anti-tuberculosis treatment was initiated for 6 months. The 18 months follow-up was uneventful.

Conclusion:

This case illustrates the challenges in diagnosing congenital TB and raises the question whether congenital TB can present as asymptomatic infection.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P82

Temporomandibular joint involvement in Lyme borreliosis – a reported case

T Badel¹; D Rosić²; L Krapac³; N Lukić⁴; D Zadravec⁵

- (1) School of Dental Medicine;
- (2) Outpatient Center for Rheumatic Diseases, Physiotherapy and Rehabilitation, “dr. Drago Čop”;
- (3) Academy of Medical Sciences of Croatia;
- (4) Center of Dental Medicine;
- (5) Clinical Hospital “Sestre milosrdnice”, University of Zagreb

Aims:

The aim of this paper is to analyze the involvement of the temporomandibular joint (TMJ) in seronegative reactive spondyloarthropathy caused by Lyme disease or borreliosis.

Methods:

In a prospective study of TMJ disorders, the data were collected from 25 patients with systemic inflammatory rheumatic disease (mean age 53.2 years) between 2001 and 2015. Each patient experienced TMJ pain measured on a visual analogue scale (VAS; ranging from 0 to 10). The diagnosis of TMJ was confirmed by magnetic resonance imaging (MRI).

Results:

TMJ disorders were attributed to the following diagnoses of rheumatic inflammatory diseases (number; % of patients): rheumatoid arthritis (8; 32%), psoriatic arthritis (5; 20%), seronegative spondyloarthropathies (7; 28%), Sjögren's syndrome (3; 12%) and mixed connective tissue diseases and Crohn's disease to one patient (4%). We report a case of a 48-year-old female patient with seronegative reactive spondyloarthropathy. Lyme borreliosis occurred as a subfebrile condition (up to 37.7°C) about twelve days after tick bite at her right upper leg. She had pain in the lumbar region palpatory pain in the presacral region at S-2 vertebral level with mild edema and without clearly expressed erythema migrans. The patient's laboratory test showed a border sedimentation rate of 28 mm/h. Also migrating mialgias have developed towards the pubic region of the buttocks and the lower back, the pain in the lower back followed by a subfebrile condition. Computerized tomography showed left-sided sacroilitis. The serological examinations for *Borrelia burgdorferi* showed IgM antibody borderline results and IgM antibody positive results. The first orofacial complaints which occurred a month after symptoms of Lyme disease included a reduced mobility of the mandible, pain of right TMJ when chewing. Pain in the TMJ was moderately strong (VAS = 6.5). MRI of the right TMJ showed arthritic changes and nonreduced anteriorly displaced disc with the presence of inflammatory synovial fluid. Doxycycline for 30 day has been used to treat certain joint manifestations of Lyme disease. The McKenzie method of physical therapy for TMJ pain was applied. The exercise helped relieve pain in TMJ during a 12-month-follow-up.

Conclusion:

Although the large joints are most typically affected in Lyme borreliosis, there are also periods of disease activity involving smaller joints, including the TMJ.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P83

No sexual transmission of Hepatitis B in a serodiscordant couple with high HbsAG titer, but low viral load

RJ Piso; B Erhart

Kantonsspital Olten

Background:

Hepatitis B is defined by positive surface antigen (HBsAG), and transmissibility is traditionally linked to surface antigen too. Patients with chronic inactive carrier state may have high HbsAG levels but low viral DNA titer. It is not clear if these patients may transmit Hepatitis B.

Case report:

A patient was documented with chronic Non-Active Hepatitis B. HBsAG was 24000 IU/ml, ALAT 30 U/l, HBV-DNA 302 IU/ml, and HBeAG negative. His pregnant spouse (third trimester) had no protective antibodies but was HBsAG and Anti-HBc negative.

Discussion:

Despite having sexual relationship for more than two years and living together, no transmission of Hepatitis B had occurred. It is known that inactive carriers can have high HBsAG levels but low viral loads. Even if traditionally HBsAg has been linked to transmissibility of Hepatitis B, this factor does not seem to have importance for infectiousness.

There might be a threshold of viral load (HBV-DNA), which is necessary for transmitting Hepatitis B through sexual contact. Patients under nucleosid therapy might be also non-infectious despite persistent high HBsAg titers.

Conclusion:

Viral load, measured by HBV-DNA, and not Hepatitis B surface antigen is responsible for transmissibility of Hepatitis



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P84

Case report: Chemical coxarthrititis after ventrogluteal testosterone injection

J Waldvogel; T Bühler; A Mendez; P Neyer; K Baertschi; M Bargetzi; R Fiumefreddo; A Conen; C Fux
 Kantonsspital Aarau

We report an acute right-sided coxarthrititis occurring within hours after an ipsilateral ventrogluteal intramuscular injection of testosterone undecanoate (Nebido®). The clinical suspicion of a septic monoarthritis was supported by the sonographic detection of an intraarticular effusion and the aspiration of pus-like synovial fluid. Microscopy revealed a neutrophil-rich fluid with fat bubbles, yet no microorganisms or crystals. Hip arthroscopy showed extensive fibrin deposits with pronounced synovialitis (Gächter stage II), but normal cartilage. Bacterial cultures from blood, synovial fluid and a synovial biopsy, all of which were taken without antimicrobial pretreatment, revealed no pathogen, reason for which a bacterial infection could be excluded. Liquid chromatography-mass spectrometry of the synovial fluid and a vial of Nebido® showed an identical pattern, suggesting a chemical arthritis caused by accidental intraarticular injection of the depot testosterone. After arthroscopic joint lavage, all symptoms cleared within a few days. As for bacterial arthritis, fast diagnosis and rigorous treatment were key for an optimal functional outcome.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P85

Molecular investigation of a multistate polymicrobial outbreak associated with contaminated total parenteral nutrition in Brazil and identification of clinically relevant *Phytobacter* species as cause for past and present epidemics

M Pillonetto¹; L Arend²; SMT Gomes³; MAA Oliveira⁴; LN Timm⁵; AF Martins⁶; AL Barth⁶; TH Smits⁷; MT Mira¹; F Rezzonico⁷

- (1) Pontifícia Universidade Católica do Paraná;
- (2) Central Public Health Laboratory – State of Paraná;
- (3) Brazilian Health Surveillance Agency;
- (4) Ezequiel Dias Foundation;
- (5) Central Public Health Laboratory – State of Rio Grande do Sul;
- (6) Federal University of Rio Grande do Sul, Hospital de Clínicas;
- (7) Zurich University of Applied Sciences

Aims

Between November 2013 and June 2014, 56 cases of bacteremia (15 deaths) associated with the use of Total Parenteral Nutrition (TPN) and/or calcium gluconate (CG) were reported in four Brazilian states. While two bacterial species involved in the outbreak could readily be identified as *Acinetobacter baumannii* and *Rhizobium radiobacter*, for a third species standard clinical identification protocols such as biochemical panels or 16S rRNA gene sequencing pointed to the former *Erwinia herbicola*-*Enterobacter agglomerans* complex (EEC), but yielded contradictory results. The aim of this work was a detailed description of the outbreak using molecular tools and the identification of the enterobacterial species involved.

Methods

Multi-locus sequence analysis (MLSA) and rep-PCR were implemented for identification of the bacterial species involved and to assess clonality of the outbreak isolates, respectively. Biochemical panels were used to obtain a phenotypic profile of the unidentified EEC isolates.

Results

Within each species, TPN and blood isolates proved to be largely clonal, whereas the *R. radiobacter* isolates retrieved from CG were found to be unrelated. MLSA of EEC representative isolate 5110RM suggested the latter to be closely related to *Phytobacter diazotrophicus* DSM 17806T, the type strain of a recently described species isolated from wild rice in China, as well as to a number of clinical strains isolated in the United States in the 1970's that were previously assigned to Brenner's Biotype XII of the EEC based on DNA-DNA similarity. Both MLSA and whole-genome sequence data analysis supported the existence of two separate species within the genus *Phytobacter* as well as the distinctiveness of the latter from nearby genera such as *Kosakonia* or *Citrobacter*. The name *Phytobacter ursingii* sp. nov. was proposed for the second species.

Conclusions

While both *Phytobacter* species contain plasmid-based multidrug resistant isolates, their relevance for clinical surveillance is given, as bacteria from this genus were repeatedly isolated in clinical settings in the past, but were often misidentified as *Pantoea agglomerans*. We are currently designing assays to detect *Phytobacter* in clinical samples. These will enable to study their diversity, spread and will help to prevent further septicemia outbreaks by their implementation in surveillance programs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P86

Intra- and interspecies genomic diversity of clinical isolates of *Phytobacter* species from different geographical and temporal origin

F Rezzonico¹; L Arend²; H Faoro³; HR D'Espindula⁴; MT Mira⁴; J Blom⁵; JF Pothier¹; M Pillonetto⁴; TH Smits¹

(1) Zurich University of Applied Sciences;

(2) Central Public Health Laboratory – State of Paraná;

(3) Carlos Chagas Institute;

(4) Pontifícia Universidade Católica do Paraná;

(5) Justus-Liebig-University Giessen

Aim

The recently described genus *Phytobacter* has been found to harbour clinical isolates from a septicemia outbreak occurring in Brazilian hospitals between 2013 and 2014. Furthermore, strains previously included in Biotype XII (Brenner, 1984) of the former *Erwinia herbicola*-*Enterobacter agglomerans* complex (EEC) and isolated in United States in the 1970's during similar outbreaks could now also be assigned to this genus. The aim of this work was to study the intra- and interspecies genomic diversity of the isolates belonging to the genus *Phytobacter*, with particular focus on those of clinical origin.

Methods

The genomes of multiple isolates of different geographical and temporal origin belonging to *P. diazotrophicus* and *P. ursingii*, the two species currently assigned to the genus, were sequenced on the Illumina MiSeq platform, assembled and compared in silico using EDGAR 2.0. Genome sequences of two *Enterobacteriaceae* isolates retrieved from the NCBI database under erroneous species designation were also included in this genus and in the comparison.

Results

Genome data revealed that the genus is clearly distinct from other *Enterobacteriaceae*, with *Kosakonia* being the nearest neighbour. Comparative genomics identified several genus-specific features like the ability of nitrogen fixation from N₂, while at the species level the genetic differences underlying the differential substrate utilization between *P. diazotrophicus* and *P. ursingii* could be confirmed. Analysis of CRISPR arrays showed that *cas* genes, only found in one isolate, must have been present in other isolates as well, as remnants of CRISPR arrays were found in their genomes. Presence of phages and plasmids, including some conferring multidrug resistances, indicate that the diversity may largely be influenced by horizontal gene transfer.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P87

Identification and characterization of Wace1, *W. chondrophila* effector protein secreted by Type III secretion system within host cell cytoplasm

C Kebbi Beghdadi; L Pilloux; G Greub

Lausanne University Hospital and University of Lausanne

Waddlia chondrophila belongs to the Chlamydiales order and is considered as an emerging pathogen causing adverse pregnancy outcomes in humans and abortion in ruminants. Like all chlamydiae, *W. chondrophila* genome encodes a complete Type 3 Secretion System (T3SS) known to secrete effector proteins. These effector proteins exhibit poor sequence homologies and they are key player in the interactions between these strict intracellular bacteria and their host cells. Several effectors have been described for classical chlamydiae, but nothing is known about effectors of Chlamydia-related bacteria. In a previous study, we have identified Wace1 as an immunogenic protein of *W. chondrophila*. We observed that Wace1 is secreted in the host cytoplasm. With an in silico prediction based on algorithms, we could predict that Wace1 might be secreted through T3SS with a high probability. To assess secretion by the T3SS, we succeeded in expressing Wace1 in a heterologous system, and we could observe secretion of the protein in this system. Moreover inhibition of the secretion by specific T3SS inhibitors confirmed Wace1 as the first effector protein secreted through *W. chondrophila* T3SS. RNA and protein expression profiles were analyzed and in accordance with a secretion of Wace1 during the early/mid phase of the infection. This timing suggests a role for this protein in establishing optimal conditions to sustain the bacteria exponential growth. Determining the interacting host cell components will provide valuable insights into the function of this putative T3SS effector and open perspectives for the development of new drugs against chlamydia



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P89

Chlamydia-related bacteria induce inflammasome activation

L Pilloux; D Le Roy; T Roger; G Greub

Lausanne University Hospital and University of Lausanne

Inflammasomes are key multiproteic complexes assembled in response to several stimuli such as pathogenic microorganisms. Once activated, inflammasomes induce a cascade of signalisation leading to the secretion of the pro-inflammatory cytokines interleukin-1 β (IL-1 β) and IL-18, and a rapid pro-inflammatory cell death named pyroptosis. *C. trachomatis* and *C. pneumoniae* are known to induce NLRP3/ASC inflammasome, but virtually nothing is known about relationship between Chlamydia-related bacteria and this signalling pathway.

Parachlamydia acanthamoebae, *Waddlia chondrophila*, and *Estrella lausannensis* have the ability to enter and grow more or less efficiently within macrophages. In our model of mouse bone marrow-derived macrophages (BMDM), the 3 bacteria are able to enter cells, but only *W. chondrophila* is able to replicate efficiently. Despite its inability to grow within these cells, *P. acanthamoebae* is able to induce cell mortality by apoptosis, in less than 36 hours. *E. lausannensis* induces a dramatic cell death up 80 % in only 4 hours. This cell death is associated to cleavage of Caspase-1, IL1- β , and IL18, and secretion of IL1- β , and IL18. Cell death present pyroptotic features. We are still trying to identify which inflammasome is involved, but it is not the same than those activated by classical chlamydiae. Further investigations are needed to understand the differences between bacteria of the Chlamydiales order leading to inflammasome activation or inhibition, and then to understand their pathogenicity towards humans and animals.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P90

Serological Diagnosis of Syphilis Reinfection

K Mischler; M Glatz; J Fehr; P Bosshard
 University Hospital of Zurich

Aims:

Syphilis is one of the most common sexually transmitted infections (STI) and the incidence has increased in the last few years world-wide, including many European countries and the US. Up to 60% of cases occur in men who have sex with men (MSM), many of whom are HIV-coinfected and many of whom experience more than one syphilis episode. However, only a limited number of studies has investigated syphilis reinfections. In the presented study, we focus on syphilis reinfection and its serologic diagnosis.

Methods:

All patients at the University Hospital Zurich with syphilis diagnosis from 1999-2015 were included. A reinfection was defined as ≥ 4 -fold increase of VDRL/RPR serum titre. Data were extracted from patient charts. Individuals lacking proof of syphilis, both clinically and by laboratory methods, and those under a therapy > 2 weeks before the visit date were excluded from the analysis.

Results:

Of 495 patients with syphilis, 185 patients (37,4%) had a syphilis reinfection. Of these, 135 (72.9%) had one, 38 (20.5%) had two, and 12 (12.9%) had three or more reinfections. Compared to patients with one syphilis episode, patients with reinfections were more often male (98.9% vs. 92.4%, $p=.004$), MSM (87% vs. 70%, $p<.0001$) or bisexual (7.6% vs. 2.9%, $p=.03$), and had a co-infection with HIV (92.9% vs. 55.5%, $p<.0001$) or another STI (58.4% vs. 34.6%, $p<.0001$), particularly a chlamydia infection. Syphilis reinfections were more frequently diagnosed during latent stage than patients with one syphilis episode (40.9% vs. 0.9%, $p<.0001$), but less often during primary stage (20.7% vs. 28.7%, $p=.043$) or secondary stage (37.9% vs. 60.6%, $p<.0001$) syphilis. Independent from the syphilis stage, patients with syphilis reinfection had higher VDRL/RPR and TPPA serum titres but lower IgM serum titres than patients with one syphilis episode.

Conclusion:

Syphilis reinfection affects one third of all syphilis patients in Switzerland, in particular MSM. Reinfections predominantly occur in HIV-infected individuals and are frequently accompanied by additional STIs. Most reinfected patients are diagnosed during the latent stage, when they are free of clinical symptoms. This often occurs during yearly screening investigations in HIV patients. For diagnosis, it is important to notice that reinfected patients often present with high VDRL/RPR and TPPA titres and low IgM titres.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P91

New insights into *Mycobacterium kansasii* virulence

F Tagini; T Pillonel; G Prod'homme; K Jaton; G Greub

Lausanne University Hospital and University of Lausanne

Aim:

Mycobacterium kansasii, a member of non-tuberculous mycobacteria, is an opportunistic pathogen known to infect immunosuppressed patients or patients with underlying lung diseases. *M. kansasii* is a closely related species of *Mycobacterium tuberculosis* and shares a high number of virulence factors with *M. tuberculosis*, such as the ESX-1 locus, encoding for a type VII secretion system. Seven *M. kansasii* subtypes are known so far and subtype I is the most common and pathogenic subtype compared to other subtypes. Thus, comparative genomics between subtype I and other subtypes is of high interest to better understand *M. kansasii* virulence.

Methods:

The analysis was performed in two steps, (i) a preliminary analysis where we sequenced 11 *M. kansasii* strains and (ii) an extended analysis including 40 *M. kansasii* strains, isolated from patients between 2007 and 2016. All genomes available on NCBI were also included in our analysis. Average nucleotide identities (ANI) between subtypes were determined. Identification of orthologous groups was done using Orthofinder. Concatenated amino acid sequences of single copy orthologous groups shared between all organisms were aligned to reconstruct the species phylogeny. Comparison of orthologous groups was performed with homemade scripts.

Results:

In the preliminary analysis, ANI and core-genome alignment revealed that each subtype cluster with itself in single clades. However, subtype III strains are split into two different clades, sharing only 90.0% mean ANI between clades, compared to >99% within clades. By comparing orthologous groups between subtype I and other subtypes in the preliminary analysis, several orthogroups could be related to virulence such as 10 groups with genes encoding for PE/PPE family proteins and 8 for ESX-1 secretion associated proteins (EspA/B/D/E/F/H). By contrast, only 4 orthologous groups with homologs of PPE family proteins and 1 EspF homolog are specific to subtype III, a less pathogenic and frequently isolated subtype. Results of the extended analysis will be provided during the congress.

Conclusion:

Our preliminary analysis revealed (i) the limitations of the current subtype classification which does not reflect the gene content (ii) that subtype I strains exhibit a higher number of putative virulence factors than less pathogenic subtypes. Overall, our study gives new insights into *M. kansasii* genomics.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P92

Screening culture medium for multiple aminoglycoside-resistant Gram negatives

P Nordmann; A Mazé; J Dobias; A Jayol; L Poirel

University of Fribourg

Introduction.

The worldwide spread of ESBLs and carbapenemases in Enterobacteriaceae worldwide makes therapeutic options more and more limited. Aminoglycosides (AG) may still be considered as valuable treatment options. However, plasmid-mediated 16S rRNA methylases (RMTA) conferring a high level of resistance to multiple AG is increasingly reported. Those 16S RMTA are ArmA, RmtB to RmtF, and NpmA, with ArmA being the most frequently identified.

Aims.

The SuperAminoglycoside medium (containing amikacin [AK] plus gentamicin [GM]) was developed for screening multiple AG resistance in Gram-negative bacteria (Enterobacteriaceae, *P. aeruginosa*, *A. baumannii*).

Methods.

The screening medium was based on the Eosine-Methylene-Blue (EMB) medium being selective for Gram negatives, differentiating lactose fermenters (black colonies) from non-fermenters (colorless or light lavender). The optimal final concentration of AK and GM were 30 mg/L each. Daptomycin was added as anti-Gram positive molecule at a final concentration of 10 mg/L, and amphotericin B was added as anti-fungi molecule at a final concentration of 5 mg/L.

The SuperAminoglycoside medium was evaluated by using AG-susceptible (n=13) and AG-resistant (n=47) Gram-negatives isolates, including 16S RMTA producers (n=20). Using an inoculum of ~10⁸ CFU/ml, serial 10-fold dilutions of the isolates were made and 100 µl plated onto the medium. Spiked fecal samples were also tested using pooled feces from healthy volunteers.

Results.

The lowest limit of detection was above the cut-off value of 10³ CFU/ml, being $\geq 1 \times 10^6$ CFU/ml for all the AG susceptible isolates and for the isolates expressing AG-modifying enzymes. On the contrary, the 16S RMTA producers grew on the SuperAminoglycoside medium in 24 h and the lowest limit of detection was below the cut-off value. Sensitivity and specificity of the medium for selecting AK- and GM resistant isolates producing 16S RMTA were of 96% (26/27) and 100%, respectively. The spiked 16S RMTA producers (except the NpmA producer) in stools grew with a lowest detection limit ranging from 10¹ to 10² CFU/ml

Conclusions.

Overall, this medium offers the possibility to select for multiple AG-resistant Enterobacteriaceae, *P. aeruginosa* and *A. baumannii*. The use of this selective medium may contribute to rapidly identify carriers of multidrug-resistant isolates producing plasmid-mediated 16S RMTA, and consequently to rapidly implement infection control measures in order to limit their spread.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P93

Evaluation of the Phoenix automated microbiology system to detect plasmid-mediated and chromosomally-encoded colistin resistance in Enterobacteriaceae

A Jayol¹; L Poiriel¹; V Dubois²; P Nordmann¹

(1) University of Fribourg;

(2) University of Bordeaux

Introduction

Increasing antibiotic resistance in gram-negative bacteria has recently lead to an increasing use of colistin. Therapeutic usage of polymyxins necessitates the availability of rapid and reliable technique for colistin susceptibility testing. However, methods routinely used to determine colistin susceptibility (disk diffusion method, Etest strips) are not reliable (high rate of false-susceptibility), while the dilution methods considered as the reference technique are tedious and time-consuming. No study has evaluated the performance of the Phoenix automated system to detect colistin resistance among gram negatives rods.

Aims

The objective of this study was to evaluate the respective performances of the BD Phoenix automated system, the newly-developed Rapid Polymyxin NP test and the broth microdilution (BMD) reference method to detect colistin resistance in Enterobacteriaceae, and particularly those producing MCR-1 and MCR-2.

Material

Colistin susceptibility of 123 enterobacterial clinical isolates (40 colistin-susceptible and 83 colistin-resistant isolates) was tested with the Phoenix automated system, the Rapid Polymyxin NP test and the BMD method. Molecular mechanisms responsible for plasmid-mediated and chromosomally-encoded colistin resistance mechanisms were investigated by PCR and sequencing.

Results

Considering BMD as a reference method, the Phoenix system failed to detect ten colistin-resistant isolates (one *Escherichia coli*, one *Klebsiella pneumoniae*, seven *Enterobacter* spp., and one *Salmonella enterica*). The Rapid Polymyxin NP test failed to detect the same single *E. coli* isolate. Those two latter methods detected the sixteen *E. coli*, *K. pneumoniae* and *S. enterica* isolates producing the plasmid-encoded MCR-1 and MCR-2.

Conclusion

The Phoenix system and the Rapid Polymyxin NP test are reliable techniques for detecting plasmid-mediated MCR-1 and MCR-2-related colistin resistance. However, a high rate of false susceptibility was observed with the Phoenix system, indicating that susceptibility results obtained with that system should be confirmed by BMD method. By contrast, the Rapid Polymyxin NP test showed a good agreement with the BMD method and results were obtained rapidly (within two hours). The BMD method should be performed if MIC values are needed.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P94

A novel specific real time PCR reveals that *Simkania negevensis* is not an important pathogen in Western Europe

M Vouga; D Baud; C Kebbi-Beghdadi; L Julia; G Greub
Lausanne University Hospital and University of Lausanne

Aims

Several Chlamydia-related bacteria have been recently discovered, including *Simkania negevensis* that was discovered in Israel in 1992 as a cell culture contaminant. Previous reports have reported a high seroprevalence of *S. negevensis* worldwide and an association with respiratory diseases, such as pneumonia and bronchiolitis, is suspected. On the other hand, recent studies have failed to show a significant association. The lack of specific diagnostic tools has hammered out definite conclusions regarding the clinical relevance of this emerging bacterium.

Methods

We developed a specific quantitative real-time TaqMan polymerase chain reaction (PCR), which was subsequently applied to 477 clinical samples (respiratory, urogenital, cardiac and hepatic samples) taken from patients hospitalized in Lausanne (Switzerland). In parallel, a seroprevalence survey, based on a micro-immunofluorescence assay, was performed among 683 European pregnant women and 105 asymptomatic Swiss young men; recommended positivity cut-offs were used (titer $\geq 1:64$ for IgG ; $\geq 1:32$ for IgM).

Results

All the 477 samples tested negative for *S. negevensis* by PCR. These results were confirmed by a pan-Chlamydiales PCR used as gold standard. Congruently, a 0.5% (4/788) seroprevalence was observed suggesting a low exposition to *S. negevensis* among the tested population. This contrasted with previous reports. Though geographical characteristics and specific exposure in some populations may explain these variations, the higher specificity of the diagnostic tools and cut-offs used could alternatively explain these discrepancies.

We conclude that *S. negevensis* is not clinically relevant in Western Europe.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P95

Comparison of EUCAST and CLSI Breakpoints for Interpretation of Echinocandins MICs Tested by Sensititre YeastOne among *Candida* spp. Isolates of the FUNGINOS Candidemia Study.

A Kritikos¹; D Sanglard²; R Frei²; K Muehlethaler³; J Schrenzel⁴; R Zbinden⁵; N Khanna Gremmelmaier⁶; J Garbino⁴; C Van Delden⁴; S Zimmerli⁷; A Imhof⁸; C Ruef⁹; J Fehr¹⁰; K Boggian¹¹; UM Flückiger¹²; A Conen¹³; P Bochud¹; T Calandra¹; O Marchetti¹; F Lamoth¹

- (1) CHUV-University Hospital;
- (2) Institute of Microbiology;
- (3) Institute for Infectious Diseases, University of Bern, Switzerland;
- (4) Geneva University Hospitals (HUG);
- (5) University Hospital of Zurich;
- (6) University of Basel Hospital;
- (7) Bern University Hospital;
- (8) SRO Spital Langenthal;
- (9) Klinik Hirslanden Zürich;
- (10) Universitätsspital Zürich;
- (11) Kantonsspital St. Gallen;
- (12) Hirslanden Klinik Aarau;
- (13) Kantonsspital Aarau

Background/Aim :

Candida spp. are the most frequent cause of fungemia. Echinocandins are the first-choice treatment of candidemia. Emerging resistance to echinocandins associated with mutations in hot spot regions of the beta-glucan synthase gene (FKS) is a concern. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the Clinical and Laboratory Standards Institute (CLSI) have established different clinical breakpoints for antifungal susceptibility tested by broth dilution method. Applicability of these cut-offs for testing by the Sensititre Yeast One (SYO) commercial kit is unclear.

The aim of this study was to assess the appropriateness of EUCAST and CLSI breakpoints in interpreting minimal inhibitory concentrations (MICs) of echinocandins tested by SYO in a 10-year national collection of *Candida* spp. bloodstream isolates.

Methods :

All *Candida* spp. bloodstream isolates were prospectively collected between 2004 and 2013 in 26 Swiss hospitals participating in the FUNGINOS Candidemia Study. MICs for caspofungin were measured by SYO in 1784 isolates (2004-2013). MICs for micafungin and anidulafungin, included later in the SYO panel, were measured in 434 isolates (2011-2013). Mutations associated with echinocandin resistance were screened by sequencing of the FKS1 and FKS2 hot spot region for all isolates with echinocandin MICs above the EUCAST/CLSI breakpoints and/or above the epidemiological cut-off value (ECV 97.5%).

Results :

Sequencing of FKS1 hotspot 1 was performed in 81 isolates with the highest MICs according to the above mentioned criteria. No mutation was recovered. Sequencing of FKS2 hotspot 1 (*C. glabrata* only) was performed for 27 *C. glabrata* isolates. One mutation (S663P) was recovered in one isolate. Despite increasing echinocandin consumption, the rate of echinocandin resistance remained very low in this 10-year prospective survey in Switzerland. Only one FKS mutation was detected. Consistent with this finding, only 0.5% strains were considered as non-susceptible to echinocandins applying CLSI breakpoints. In contrast, a resistance rate as high as 11% was reported when applying EUCAST breakpoints.

Conclusion :

Our data indicate that EUCAST criteria overestimate echinocandin resistance for *Candida* isolates tested by Sensititre Yeast One. CLSI criteria seem more appropriate, but the intermediate « I » category is questionable (no mutation in this setting).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P96

Evaluation of three commercialized broth microdilution systems to determine colistin susceptibility in gram negative rods

A Jayol¹; L Poiriel¹; C André²; V Dubois²; P Nordmann¹

(1) University of Fribourg;

(2) University of Bordeaux

Introduction

Colistin is considered as a last resort antibiotic for treating infections with multidrug-resistant Gram-negative rods. However, colistin susceptibility testing is currently challenging. Disk diffusion method and E-test systems give high rates of false susceptibility. Since 2016, the EUCAST recommend the broth microdilution method (BMD) to determine colistin susceptibility, but this method is difficult to implement in routine labs for practical reasons.

Aims

The objective of this study was consequently to compare three commercialized BMD panels (the Microscan system (Beckman Coulter), the Sensititre system (ThermoFisher Scientific) and the UMIC system (Biocentric) to determine colistin susceptibility of Gram negatives.

Methods

A collection of 200 isolates was tested, including 50 colistin-susceptible isolates and 150 colistin-resistant isolates of various Gram-negative species possessing various polymyxin resistance mechanisms (intrinsic, acquired and chromosomally-encode

d, acquired and plasmid-mediated, and unknown).

The BMD manual reference method was performed and interpreted according to the EUCAST guidelines and the BMD commercialized panels were prepared as recommended by the manufacturers.

Results

Both Sensititre and UMIC systems failed to detect two colistin *Salmonella enterica* (MIC = 4 mg/L). Those isolates were identified as heteroresistant using population analysis profile.

The Sensititre system gave also false susceptibility results for two colistin-heteroresistant *E. cloacae* (MIC = 4 mg/L) and one *S. maltophilia* isolate (MIC of 32 mg/L).

The UMIC system failed to detect several colistin-resistant isolates exhibiting a low level resistance level (MIC ranging from 4 to 8 mg/L), including *mcr-1* and *mcr-2* positive isolates.

The Microscan system showed an excellent sensitivity for the detection of colistin resistance. However, it gave a high rate of false-resistant results for *P. aeruginosa* and *S. maltophilia* (50 %) due to an overestimation of the MIC for those species.

Conclusion

The Sensititre system exhibited excellent performances for the detection of colistin resistance in Gram negative rods, except for some colistin-heteroresistant isolates. The Microscan system showed overall good sensitivity for the detection of colistin-resistant isolates. The poorest performances were obtained with the UMIC system that failed to detect many isolates with a low level of colistin resistance (MIC = 4-8 mg/L), including MCR-producing isolates.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P97

Moraxella as sources of MCR-like polymyxin resistance determinants

L Poirel; N Kieffer; Y Larpin; P Nordmann
 University Fribourg

Aim

The *mcr-1/2* acquired genes are plasmid-mediated phosphoethanolamine transferase genes conferring resistance to colistin in enterobacterial isolates. Their dissemination represents a great concern since colistin is one of the last resort antibiotic to treat infections caused by carbapenemase-producing Enterobacteriaceae. Although those genes have been reported in numerous countries in clinical, food and environmental samples, the origin of *mcr*-like genes remains unknown. Our study aimed to identify putative *mcr-1/2* progenitors in a collection of *Moraxella* isolates.

Methods

A collection of eleven different *Moraxella* species was screened by PCR using degenerated primers for amplifying the *mcr-1* gene. The genetic environment of the different *mcr*-like genes identified was determined by digestion and ligation of genomic DNAs of putative MCR-like producers in order to create DNA-loops, followed by inverse PCR performed on those circularized DNA fragments. The *mcr*-like genes were cloned into an arabinose inducible pBAD vector (Invitrogen) using *SacI* and *XbaI* restriction sites. Induction of the *mcr*-like genes was performed in Muller Hinton broth supplemented with 1% L-arabinose for 1 hour.

Results:

MCR-like genes were identified into *Moraxella porci*, *Moraxella osloensis*, *Moraxella lincolnii* and *Moraxella pluranimalium*. The mobile element IS_{Apl1} which is widely associated with the *mcr-1* gene was found non-associated in *M. porci* and *M. pluranimalium*. The IS1595 previously described in association with the acquired *mcr-2* gene was identified in *M. pluranimalium*. Amino acids sequences analysis showed that the MCR determinants from *M. porci*, *M. lincolnii* and *M. osloensis* have between 59% and 70% of identity with MCR-1 or MCR-2. Noticeably, the MCR determinant from *M. pluranimalium* (MCR-PLU) showed 82% identity with MCR-1, and 98.5% with MCR-2. Once produced in *E. coli*, MCR-PLU conferred a 130-fold increased MIC value of colistin reaching 4 µg/ml.

Conclusion:

This study indicates that *Moraxella* species constitute a reservoir of *mcr*-like genes and that *M. pluranimalium* may be considered as the progenitor of the *mcr-2* gene, harboring this gene on its chromosome. Noteworthy, *M. pluranimalium* showed full susceptibility to colistin (MIC of 0.06 µg/ml) suggesting a lack of expression of the intrinsic *mcr-2*-like gene.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P98

In vitro Analysis of ISApI1-Mediated Mobilization of the Colistin Resistance Gene *mcr-1*

N Kieffer; L Poirel; P Nordmann

University of Fribourg

Aim

The plasmid-mediated *mcr-1* gene encodes a phosphoethanolamine transferase conferring resistance to polymyxins. Spread of this gene has been reported worldwide in *E. coli* and *K. pneumoniae*, either from human or animal isolates. The *mcr-1* gene is often described in association with one or two copies of the ISApI1 insertion sequence (IS30 family). It has been speculated that ISApI1 might play an important role in the mobilization of *mcr-1*. Our aim was to demonstrate the mobilization of *mcr-1* by ISApI1 mobile elements.

Methods

A truncated version of *mcr-1* by the *bla*TEM-1 gene was generated by PCR. Two different genetic structures were constructed: (i) a single copy of ISApI1 associated with the truncated *mcr-1* gene and (ii) two copies of ISApI1 bracketing the truncated *mcr-1* gene. The two constructs were cloned into plasmid pNK1 (p15A-pTOPO-ΔlacP). Recombinant plasmids were then transferred by electroporation into RZ211 *E. coli* strain that carries the conjugative IS-free pOX38 plasmid conferring resistance to gentamicin (GMN). Clones AMPR-KANR-GMNR were selected for conjugation experiment.

Conjugation experiments were performed using the azide-resistant J53 strain as recipient. Selection of the isolates was performed using plates containing azide (100μg/ml), GMN (10μg/ml) and AMP (100μg/ml). AMPR-GMNR-AzideR and KANS colonies were retained for further investigations.

Location of the transposition events was identified by inverse PCR using the PstI restriction enzyme. Digested products were self-circularized using the T4 ligase.

Results

Transposants showing an AMPR-GMNR-AzideR-KANS phenotype were recovered from the conjugation assay. Inverse PCR and sequencing identified seven different insertion sites of the mobilized structure in plasmid pOX38. Duplication of the target sites made of 2-bp direct repeats were identified at both extremities of the constructs each time. AT-rich regions were identified at the 5'- and 3'-surrounding regions of the mobilized structures, which is in accordance with previous observations showing AT-rich regions being hotspots for the insertion of IS30 elements. No transposant was detected using the construction encompassing only one copy of ISApI1 element.

Conclusion

This study is the first evidencing the mobilization of the *mcr-1* gene and confirming the involvement of ISApI1 in the transposition of *mcr-1*.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P99

Exposure to molds in the indoor environment and respiratory health in older residents living in Lausanne

H Niculita-Hirzel¹; P Wild²; D Savova-Bianchi³; A Hirzel⁴; B Santos-Eggimann⁵

(1) Institute for Work and Health, Universities of Lausanne and Geneva;

(2) INRS;

(3) Institut for Work and Health;

(4) Computer Science Center, University of Lausanne;

(5) Institute of Social and Preventive Medicine, University of Lausanne

Aims.

Indoor air pollution has been associated to adverse respiratory health effects in children, in adults and in older persons. However, although a large number of studies explored the impact of airborne fungal particle content on the respiratory health of children or adults, only scarce information exists on older persons' exposure to airborne fungal particles in the indoor environment and on the consequences of such an exposure on their respiratory health. The specific objective of the present study was to contribute to filling the gaps in the knowledge on the airborne mold profiles that affect the respiratory health in the older population.

Methods.

The mold species profile was determined in the indoor air of 270 residences of 289 Lausanne inhabitants older than 65 years that are a part of the Lc65+ cohort. Electrostatic dust collector (EDC) sampling devices have been used to sample the microbiome during summer, autumn and winter periods between June 2014 and February 2015. The diversity of viable fungal species have been determined from samples cultured on DG18 media, although that of fungal species represented by the overall fungal particles - viable and dead – have been characterized directly from the EDC samples by high throughput sequencing of the ITS1 region. The respiratory health data as well as characteristics of the buildings were extracted from Lc65+ database database linked to the federal buildings register. The season effect on fungal species diversity has been tested. Association of viable and overall mold community profiles with the respiratory symptoms of the inhabitants was determined by unconditional logistic regressions.

Results and conclusion.

The season has been found to play a strong effect on the fungal community composition, the building specific genera being detectable only during the cold season. *Penicillium* and *Aspergillus* have been found as dominant fungal contaminants of living space by both methods - culture and high throughput sequencing. However, additional building specific fungal genera have been identified thanks to the high throughput sequencing. Occupants exposed mostly to cultivable *Aspergillus* have been found to present a higher prevalence of cough, although those exposed to any *Aureobasidium* particles had a higher prevalence of self-reported asthma medication. This finding points out the importance to adapt the sampling method to the respiratory pathology studied.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P100

Application of Next Generation Sequencing on blood culture bacterial pellet for genomics studies of fastidious agents of bloodstream infections: a septic abortion due to *Sneathia sanguinegens*

O Opota¹; S Laurent¹; M Barchi²; S Trachsel²; A Cometa²; G Greub¹

(1) Lausanne University Hospital and University of Lausanne;

(2) Établissements Hospitaliers du Nord Vaudois

Aims:

Next generation sequencing (NGS) technologies give to clinical microbiology laboratories rapid and cost-effective access to bacterial genome allowing the prediction of antibiotic susceptibility (resistome), the identification of virulence associated genes (virulome) and precise strain identification (typing and taxogenomics). We recently experienced a septic abortion that occurred at 15 weeks of pregnancy in a patient for which the blood cultures returned positive for a Gram negative bacterium, unculturable on agar plate, impairing precise phenotypic strain identification. The aim of this work was to establish the feasibility of NGS on a bacterial pellet obtained with our subculture-independent ammonium-chloride-based method of bacterial concentration/purification from positive blood culture.

Methods:

A bacterial pellet was performed using the ammonium-chloride concentration/ purification method directly from the positive blood culture bottle and used for genomic DNA extraction and purification with the Wizard Genomic DNA purification kit (Promega) followed by enrichment with the NEBNext Microbiome DNA Enrichment kit (New England Biolabs). The purified genomic DNA was subjected to whole-genome shotgun sequencing with a MiSeq sequencer (Illumina). After in silico filtering of the sequences from human origin, the genome assembly was performed using software Spades v3.10.1 (Bankevitch et al., 2012).

Results:

This method resulted in the successful assembly of a genome with coverage of 100x, corresponding to the anaerobic bacterium *Sneathia sanguinegens* already associated with postpartum bacteremia. The genome of *Sneathia sanguinegens* was made with 57 contigs and a N50 of 115'155 which corresponded to an estimated genome size of 1'415'471bp with an average GC content of 27.06 % with the presence of 2 rRNA operon, 36 tRNA encoding genes, and 1355 proteins.

Conclusion:

This method allowed strain identification and gave us access to the genome of *Sneathia sanguinegens* for ongoing virulome analysis of a potentially under-diagnosed fastidious etiologic agent of gyneco-obstetrical infections. This work demonstrates the feasibility of combining ammonium-chloride bacterial pellet preparation method from positive blood culture with NGS analysis and its integration into current microbiology laboratory workflow.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P101

CXCL13 as a diagnostic marker of neuroborreliosis in children, a retrospective case-control study

M Remy¹; N Schöbi²; L Kottanattu²; S Pfister¹; A Duppenhaler²; F Suter¹

(1) Institute for Infectious Diseases, University of Bern, Switzerland;

(2) Bern University Hospital, University of Bern

Aim:

Lyme neuroborreliosis (LNB) is a frequent manifestation of Lyme disease in children and its current diagnosis which requires a proof of intrathecal antibody production has limitations. The elevation of the chemokine CXCL13 in the cerebrospinal fluid (CSF) of adult patients with LNB has been demonstrated and suggested as a new diagnostic marker. Our aim is to evaluate the diagnostic value of CSF CXCL13 in children with suspected Lyme neuroborreliosis (LNB) and to determine a cut-off concentration of CSF CXCL13 that should discriminate between LNB and other central nervous system (CNS) infections in pediatric patients.

Methods:

We measured CXCL13 by ELISA in the CSF of 185 children with CNS symptoms referring to LNB and diagnosed with definite LNB (n=53), possible LNB (n=41) or other CNS affections (viral meningitis, inflammatory diseases, idiopathic facial palsy or headache, n=91).

Results:

CXCL13 was significantly elevated in the CSF of children with definite LNB (median 774.7 pg/ml) compared to non-LNB patients which exhibited low concentrations of CXCL13 (median 4.5 pg/ml). A cut-off of 55 pg/ml resulted in a sensitivity of 96.7% and a specificity of 98.1% for the diagnosis of definite early LNB using antibody index as a gold standard. The positive and negative predictive values of the test were respectively 94.6% and 98.9%. Elevated CSF CXCL13 levels were also detected in 3 cases of viral meningitis (1 enterovirus, 2 varicella-zoster-virus) while other CNS affections such as idiopathic facial palsies did not lead to any CXCL13 elevation. In patients with possible LNB where a definitive diagnosis could not be obtained, CXCL13 ranged from 4.5 to 1'418.6 pg/ml (median 16.7 pg/ml) and 27% of these patients had elevated CXCL13 values.

Conclusion:

We confirm that also in children CSF CXCL13 is highly elevated during early LNB. This marker is highly sensitive and specific and should help to differentiate LNB from other CNS affections in pediatric patients.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P102

Complete nucleotide sequence of *Staphylococcus xylosus* plasmid pJW2311 harboring the novel macrolide, lincosamide, and streptogramin B resistance gene *erm*(48)

JR Wipf¹; MC Riley²; SA Kania²; DA Bemis²; S Andreis³; S Schwendener³; V Perreten³

(1) Rockefeller University;

(2) College of Veterinary Medicine, University of Tennessee;

(3) University of Bern

Aims

Staphylococcus xylosus is an important cause of subclinical bovine mastitis. *S. xylosus* strain JW2311 was isolated from bovine mastitis milk in Switzerland and exhibited high resistance to erythromycin and inducible resistance to clindamycin. Aim of the study was to identify the mechanism of clindamycin resistance in *S. xylosus* JW2311 and to determine if it is located on a mobile genetic element.

Methods

Whole genome sequencing (Illumina®) of strain JW2311; Comparative BlastN analysis with known macrolide, lincosamide and streptogramin B (MLSB) resistance genes; Cloning and expression of a putative resistance gene candidate in *Staphylococcus aureus* RN4220 to demonstrate functionality and inducible expression; Transformation assays by conjugation and electroporation; Confirmation of plasmid structure by whole-genome sequencing (Roche 454®); Plasmid annotation using Prodigal, Prokka, and RAST predictions; function prediction using pBLAST and ExPASy PROSITE.

Results

Whole-genome sequencing of strain JW2311 identified a novel MLSB resistance gene *erm*(48) located on a new staphylococcal plasmid designated pJW2311 (ENA acc.no. LT223129). The 49, 273 bp plasmid contained 49 open reading frames (orfs), including the macrolide resistance genes *erm*(48), *mph*(C), and *msr*(A). Remaining orfs encoded for membrane transport proteins and metabolic enzymes such as oxidoreductases, transferases or hydrolases. Furthermore, integrated IS431 and transposases were identified. The RepA protein of the plasmid exhibited an internal *oriV* and showed highest nucleotide similarity (70 %) to the rep family 20 of Gram-positive bacterial plasmids, suggesting replication to occur via the theta-mode. The overall plasmid G + C content was similar to *S. xylosus*, while the region surrounding *erm*(48) exhibited a lower content which indicated the acquisition of this region from a different source. pJW2311 was transformed into *Staphylococcus aureus* by electroporation. The plasmid did not contain a transfer (*tra*) complex and conjugation experiments were unsuccessful.

Conclusions

Recently, multiple MLSB resistance elements were identified by whole-genome sequencing in staphylococci from bovine milk (1, 2). The discovery of plasmid pJW2311 in *S. xylosus* highlights the role of dairy cows as a reservoir for new mobile genetic elements and resistance genes.

References

1. Wipf JRK. et al. Antimicrob Agents Chemother. 2014;58(10):6133.
2. Wipf JRK. et al. Antimicrob Agents Chemother. 2015;59(6):3578.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P103

Temporal trends and regional distribution of carbapenemase-producing Enterobacteriaceae in Switzerland from 2013 to 2016

A Ramette¹; R Zbinden²; J Schrenzel³; P Nordmann⁴; D Perisa⁵; A Kronenberg¹

(1) University of Bern;

(2) University of Zurich;

(3) Geneva University Hospitals (HUG);

(4) University Fribourg;

(5) Federal Office of Public Health

Aims:

Carbapenemase-producing Enterobacteriaceae (CPE) are becoming more prevalent globally, which reduces considerably therapeutic options for such infections. This study aims to provide the first temporal and regional trends of CPE numbers in Switzerland, as no data was so far available.

Methods:

From 2013 to 2015, the Swiss Society for Microbiology defined a network of 8 Swiss expert laboratories to which all Swiss microbiology laboratories were asked to send all suspected human CPE isolates for characterization according to EUCAST guidelines. From 2016 onwards, CPE was defined as notifiable disease, and all Swiss laboratories are to declare their CPE findings to the Federal Office of Public Health directly. Data from 2016 thus originates from 27 Laboratories. All data were collated by the Swiss Antibiotic Resistance Centre ANRESIS for epidemiological analysis.

Results:

After exclusion of duplicate entries, a total of 416 isolates originating from 361 patients were identified, with 69, 89, 121 and 142 isolates reported from 2013, 2014, 2015 and 2016, respectively. The species most frequently isolated were *Klebsiella pneumoniae* (n=240, 60%), *Escherichia coli* (n=95, 24%), and *Enterobacter* spp. n=25, 6%). Out of 418 carbapenemase genotypes, the most frequently found were OXA (n=193, 46%, mostly OXA-48 with n=181, 43%), KPC (n=105, 25%) and NDM (n=71, 17%). From 2013 to 2016, the number of KPC-harboring isolates was relatively stable (about 25 per year in total), whereas in this time period both numbers of NDM and OXA harboring isolates increased, from 9 to 25, and from 30 to 60 cases, respectively. At the regional level, highest numbers of CRE isolates were identified in the Geneva and North East regions. Further analyses on the impact of travel-related cases, autochthonous cases, possible outbreaks, and on the effect of the type of reporting (expert laboratories vs. mandatory) will be presented.

Conclusion:

OXA-48, KPC- and NDM-type carbapenemases are the most prevalent in Switzerland, and molecular data indicate a variety of different carbapenemase resistance alleles present in Switzerland. Overall the numbers of OXA-48 and NDM producers are increasing as observed in other European countries such as in France. The distinct temporal trends and regional distribution that were identified in the surveillance data collected by the FOPH and ANRESIS underline the necessity of sustaining surveillance and epidemiological analyses of CRE isolates in Switzerland.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P104

A variant surface glycoprotein is associated with suramin resistance in *Trypanosoma brucei*

N Wiedemar¹; FE Graf²; E Ndomba³; C Kunz Renggli¹; M Cal¹; RS Schmidt¹; T Wenzler⁴; P Mäser¹

- (1) Swiss Tropical and Public Health Institute;
- (2) University of Gothenburg;
- (3) Ifakara Health Institute;
- (4) University of Bern

Investigation of drug resistance mechanisms is a possible approach to gain new insights on drug target, transport, and mode of action. Suramin, first synthesized around a hundred years ago, is still in use against first stage acute sleeping sickness caused by *T. brucei* rhodesiense. Despite its use for such a long time, the drug target and mode of action are still poorly understood. In our lab we observed a very quickly emerging in vitro resistance to suramin in *T. brucei*. When exposed to high suramin concentrations, the parasites were able to recover within days. These recovered parasites showed a massively lower suramin susceptibility and the experiment was highly reproducible. The aim of the present project is to investigate the mechanisms behind this phenomenon.

For that purpose a *T. b. rhodesiense* strain was cloned and selected with suramin. Subsequently the drug susceptibility of the clone and its selected derivatives was determined and RNA was isolated to measure their gene expression. Next-generation mRNA sequencing was carried out and the gene expression was analysed and compared between suramin sensitive and resistant parasites. The differentially expressed genes were investigated by reverse-transcriptase qPCR in order to verify their different expression patterns in sensitive and resistant parasites. Reverse genetic manipulation of the candidate genes was performed to confirm their effect on drug susceptibility.

Resistant parasites were obtained after only 6 days of selection and showed a resistance factor around 90-fold when compared to the susceptible parent clone. Gene expression analysis revealed very few differences between resistant and sensitive parasites. In fact the only difference was found in their variant surface glycoprotein genes (VSG): The resistant parasites had all switched to the same VSG. In an additionally investigated clone and strain a switch to a highly similar VSG was observed in the resistant derivatives. Finally, the VSG which was expressed in the suramin sensitive clone, was re-introduced into the active expression site of one of the resistant derivatives; this manipulation led to a complete loss of the resistance.

These experiments clearly show an involvement of VSGs in drug susceptibility. The switch to one particular VSG generated highly suramin-resistant parasites in vitro.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P106

Evaluation of the MBT Sepsityper IVD Kit® for direct identification of microorganisms from positive blood culture bottles on IVD MALDI Biotyper

R Anic; D Dimitrijevic; A Stroehle

MCL Laboratories

Objective :

The MBT Sepsityper® is an in-vitro diagnostic tool to identify microorganisms from positive blood culture bottles using the IVD MALDI Biotyper. Combined with different clinical and diagnostic methods it is in use for early identification of bloodstream infections.

Materials and Methods:

From 50 randomly collected patients 110 blood culture bottles (100 positive and 10 negative) were tested including two different products from two manufacturers, Becton-Dickinson and BioMérieux. The original manufacturer protocol was used for blood culture bottles from Becton-Dickinson. The protocol has to be adapted for blood culture bottles from BioMérieux with charcoal particles by an additional filtration step. Identification by MBT Sepsityper was compared to identification from cultivated colonies. Correct identification by MBT Sepsityper® was limited to scores of ≥ 2.0 on IVD MALDI Biotyper (Bruker).

Results:

39 enterobacteriaceae, 15 *Staphylococcus aureus*, 6 *Enterococcus faecalis* as well as 16 additional different organisms were correctly identified at scores of ≥ 2.0 . In mixed infections including a gram negative and a gram positive organism the gram negative was correctly identified. Direct identification of *Streptococcus pneumoniae* (7 cases) failed. For 6 different isolates as *Bacteroides fragilis* (2) *Streptococcus gallolyticus*, *Bifidobacterium longum*, *Parabacteroides jonsonii*, a *Propionimicrobium lymphophilum* and 1 of 2 isolates of *Bacteroides vulgatus*, *Staphylococcus hominis*, *Streptococcus sinensis* and *Candida albicans* MBT Sepsityper® results showed scores < 2.0 or not reliable results. In 7 mixed cultures 6 times *Enterococcus faecalis* was missed, once *Citrobacter freundii*.

Conclusion:

For organisms as enterobacteriaceae or *Staphylococcus aureus* reliable results can be expected. Other microorganisms, mostly gram positive or anaerobe isolates, may show scores < 2.0 or non reliable results by direct MBT Sepsityper® method. Direct identification of *Streptococcus pneumoniae* failed probably due to autolysis during the isolation process.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P107

A novel species of *Corynebacterium* isolated from feline otitis

S Kittl¹; I Brodard¹; P Roosje²; S Gobeli Brawand¹

(1) Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern;

(2) Division of Clinical Dermatology, Vetsuisse Faculty, University of Bern

The role and appropriate therapy of corynebacteria in canine and feline otitis remains unclear, however, some cases with corynebacteria as the likely cause have been described [1]. In human medicine the problem of otitis due to these frequently resistant bacteria has also only recently received more attention [2]. We present here a presumptively new species of *Corynebacterium* isolated from a case of feline otitis.

A 7-month- old Maine Coon cat was presented to the Small Animal Teaching Hospital at the University of Bern with acute neurological signs consistent with unilateral otitis media / interna. Six weeks earlier an inflammatory aural polyp had been removed followed initially by a full recovery. Otoscopic and cytologic examination revealed brown-coloured fluid in the external canal with numerous extra –and intracellular rod-shaped bacteria and neutrophils. A deep ear swab was submitted for culture to the Institute of Veterinary Bacteriology for analysis.

Coryneform bacteria could be isolated in pure culture, however, species identification was not possible with VITEK® 2 Compact (Biomérieux) or Maldi-ToF MS (Bruker). 16S rRNA gene sequencing revealed 98.6% identity with *Corynebacterium variabile* (NR_025314.1), 98.0% with *Corynebacterium terpenotabidum* (NR_121699.1) and 97.8% with *Corynebacterium glycinophilum* (NR_121782.1), thus the strain could not be assigned to a described species. However the 16S rRNA sequence showed a 100% identity with the whole genome shotgun sequence of designated (but not validly named) *Corynebacterium provencense* (NZ_LT160593.1) isolated from human stools.

Furthermore, a partial *rpoB* sequence was generated according to Khamis et al [3] which showed 89% identity with *Corynebacterium terpenotabidum* (CP003696.1) and 88% with *Corynebacterium variabile* (AY492272.1). Again, 99.8% identity was observed with designated *Corynebacterium provencense* (NZ_LT160592.1) indicating that our strain is likely to belong to the same species.

According to EUCAST breakpoints for *Corynebacterium* spp. our strain tested resistant to clindamycin, penicillin and ciprofloxacin but susceptible to tetracycline, gentamicin and vancomycin.

The isolation of our strain from a clinical sample in pure culture highlights its potential pathogenicity. Furthermore, isolation of the same species from a human sample and the resistance to several antibiotics indicate that our results could be of value not only for veterinary, but also for human medicine.

References

1. Hennevelde K. et al. J Am Anim Hosp Assoc 2012;48(5):320
2. Crowson M.G. et al. Otol Neurotol 2015;36(2):244
3. Khamis A. et al. J Clin Microbiol 2004;42(9):3925



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P108

Single center validation of the Seegene Allplex™ GI Bacteria and STI Bacteria multiplex real-time PCR panels

D Goldenberger; S Paladin; K Feuz; B Derengowski; V Courtet; A Egli
 University Hospital Basel

Aims

Gastrointestinal and sexually transmitted infections (STI) can be caused by a broad variety of pathogens. Traditional culture-based microbiological diagnostics often lack specificity, sensitivity, and speed. Novel syndromic multiplex PCR systems may have the potential to improve the diagnostic performance, broaden the spectra of potential pathogens, and reduce the time to specific treatments. We compared the novel Seegene Allplex PCR gastrointestinal and STI batch-based panels with routine laboratory methods and evaluated the potential use for routine application in our laboratory.

Methods

The analytical sensitivity of the Seegene Allplex Bacteria Panel I for *Salmonella*, *Shigella*, and *Campylobacter* was determined using a ten-fold serial dilution and comparison to culture-based methods. Multiple reference strains from our strain collection were included to evaluate the specificity of this panel. In addition, routine stool samples were analyzed and compared with findings from standard culture diagnostics. The Seegene Allplex STI essential assay detecting 7 pathogens was also validated using routine urogenital samples in comparison to the Abbott RealTime CT/NG test and the MYCOPLASMA DUO (BIO-RAD) test.

Results

The analytical sensitivity for *Salmonella*, *Shigella*, and *Campylobacter* was 1800 CFU/ml, 10 CFU/ml, and 720 CFU/ml, respectively. The stool matrix had no influence on the PCR efficiency indicating a thorough DNA purification process. A total of 33 reference strains were tested showing correct results in all isolates. We analyzed 121 stool samples from the routine and found a high conformity of both methods (92%). 6/40 *Campylobacter* spp. and 2/12 *Salmonella* spp. could not be detected with Seegene. In two cases additional pathogens could be found by the Seegene panel. In addition, urogenital samples (n=55) showed a high accordance with the routine methods. In 7/12 *C. trachomatis* positive samples, the Seegene STI panel detected additional pathogens. The Seegene STI panel could discriminate between *Ureaplasma parvum* and *U. urealyticum*.

Conclusion

Overall, the new Seegene Allplex™ detection system is relatively easy to handle. The user friendly IVD software provides Ct values for positive results. The system allows a rapid and reliable detection of a broad-range of gastrointestinal and STI pathogens. In addition, the use of additional panels could further extend the spectrum of micro-organisms.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P109

Evaluation of VITEK MS® for identification of non tuberculosis Mycobacteria from solid and liquid cultures.

D Constantin; L Tissières Lovey; G Praz

ICHV

Aim

The aim of this study is to evaluate the performance of matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) for a rapid and correct identification of non tuberculosis Mycobacteria (NTM) in clinical samples.

Material and methods

The detection of Mycobacteria is performed on BacT/Alert® and samples are also subcultured on solid media (Löwenstein-Jensen, Coletsos).

42 positives cultures (solid and liquid), identified with polymerase chain reaction (PCR) were tested according to the manufacturer's instructions as follows.

For inactivation, 3 mL of the liquid medium was transferred in a 5 mL conical tube and centrifuged at 3'000 g. After decantation, the pellet was resuspended with 500 uL Ethanol 70% and the suspension was transferred in a 1.5 mL microtube containing 0.5 mm glass beads.

Inactivation for solid medium: 1 uL full loop of colonies was transferred in a 1.5 mL microtube containing 0.5 mm glass beads with 500 uL Ethanol 70 %.

The glass beads microtubes were placed in a bead beater for 5 minutes and incubated at room temperature for 10 minutes (inactivation time).

For the extraction, the samples were vortexed and transferred in a 2 mL microtube. After 2 min. centrifugation at 14'000 g, the supernatant was discarded and the pellet was completely resuspended with 10 ul formic acid 70%. 10 ul acetonitrile was added and after homogenization, the suspension was centrifuged 2 min. at 14'000 g. 1 uL of supernatant was immediately deposited on spot(s). After complete drying, 1 uL of CHCA matrix was added. The sample was ready for MS.

Results

34/42 (80%) isolates were correctly identified to the species level with a score higher than 99 %.

3/10 isolates belonging to the Mycobacterium avium-intracellulare complex had no Vitek MS identification (not in the data base?).

For 5 strains, we had either discrepancies or no results. Further investigations were processed.

Conclusion

MALDI-TOF MS is a promising tool for the identification of NTM. Furthermore, the procedure is fast, inexpensive, easy to perform and achieves a faster identification of non tuberculosis Mycobacteria in comparison with traditional methods.

Rapid identification of NTM has an important clinical impact for patient care. The data base needs to be completed for species of clinical significance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P110

Human infections with Shiga toxin-producing *Escherichia coli*, Switzerland, 2010–2014

H Hächler¹; L Fierz¹; N Cernela¹; E Hauser²; M Nüesch-Inderbinnen¹; R Stephan¹

(1) Universität Zürich;

(2) Bundesinstitut für Risikoforschung

A total of 95 Shiga toxin producing *E. coli* (STEC) isolated from human patients in Switzerland during 2010–2014 were characterized by O serotyping and molecular subtyping. The five most common serotypes were O157, O145, O26, O103, and O146. Of the 95 strains, 35 (36.8%) carried *stx1* genes only, 42 strains (44.2%) carried *stx2* only and 18 (18.9%) harbored combinations of *stx1* and *stx2* genes. *Stx1a* (43strains) and *stx2a* (32strains) were the most frequently detected *stx* subtypes. Genes for intimin (*eae*), hemolysin (*hly*), iron-regulated adhesion (*iha*) and the subtilase cytotoxin subtypes *subAB1*, *subAB2-1*, *subAB2-2* or *subAB2-3* were detected in 70.5%, 83.2%, 74.7% and 20% of the strains, respectively. Multilocus sequence typing assigned the majority (58.9%) of the isolates to five different clonal complexes (CC), 11, 32, 29, 20, and 165, respectively. CC11 included all O157 and O55 isolates. CC32 comprised seven (58.3%) of the O145 isolates, the remaining belonged to sequence type (ST) 342. CC29 contained isolates of the O26, O111 and O118 serogroups, and CC20 encompassed isolates of O103. CC165 included six (66.7%) of the isolates showing nontypable (ONT) O antigens and ST301, all harbored *stx2d*, *eae* and *hly*, and four additionally harbored *iha*. Compared to data from Switzerland from the years 2000–2009, an increase of the proportion of non-O157 STEC infections was observed as well as an increase of infections due to STEC O146. Furthermore, a decline of the highly virulent German clone STEC O26 ST29 from 40.74% for the time span of 2000–2009, to 1.1% for 2010–2014 was observed. The detection of STEC ONT ST301 harboring *stx2d*, *eae*, *hly*, and *iha* suggests an ongoing emergence of a clonal group of highly pathogenic STEC. Serotyping and molecular subtyping of clinical STEC isolates provides useful information for food safety efforts and effective public health protection.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P111

Salmonella enterica serovar Infantis from food and human infections, Switzerland, 2010-2015

M Nüesch-Inderbinen¹; DH Hindermann¹; G Gopinathrao²; H Chase²; F Negrete²; D Althaus¹; K Zurfluh¹; BD Tall²; R Stephan¹

(1) Universität Zürich;

(2) Food and Drug Administration

We characterized 520 *Salmonella enterica* serovar Infantis isolates recovered from food (poultry meat), human infections, and environmental sources from the years 2010, 2013 and 2015 in Switzerland by antimicrobial susceptibility testing, pulsed-field gel electrophoresis (PFGE) analysis, and whole genome sequencing (WGS) performed on 32 isolates. The majority (74.8%) was multidrug resistant (MDR). PFGE analysis revealed that 270 (51.9%) isolates shared an identity of 90%. All isolates subjected to WGS belonged to sequence type (ST) 32 or a double-locus variant thereof (one isolate). Seven (21.9%) of the sequenced isolates were phylogenetically related to the prevalent broiler-associated Hungarian clone B. Three isolates harboring blaCTX-M-65 on a predicted large (~320 kb) plasmid grouped in a distinct cluster. This study documents the persistence of the Hungarian clone B and related clones in food and human isolates between 2010 and 2015, and the emergence of a blaCTX-M-65 harboring MDR *S. serovar Infantis* lineage.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P112

Characteristics of *Escherichia coli* causing community acquired urinary tract infection

M Nüesch-Inderbinen¹; M Baschera¹; H Hächler¹; H Nüesch²; R Stephan¹

(1) Universität Zürich;

(2) Practice for General Medicine

Urinary tract infections (UTIs) are among the most common bacterial infections acquired in the community and in hospitals. The majority of infections are caused by uropathogenic *E. coli* (UPEC). The first choice agents for treatment of uncomplicated UTI include fluoroquinolones (ciprofloxacin or norfloxacin), fosfomycin, trimethoprim/sulfamethoxazole and nitrofurantoin.

Forty-seven urine samples positive for *Escherichia coli* from 44 patients (81% female, aged 16–87 years old) reporting to their general practitioner with clinical symptoms of urinary tract infection were collected between February and October 2016.

Isolates were subjected to antimicrobial susceptibility profiling, PCR-based phylotyping, multilocus sequence typing, and PCR-based detection of the virulence-associated genes *papA*, *papEF*, *fyuA*, *traT*, *hlyA*, *yfcv* and the pathogenicity island marker PAI. Isolates displaying resistance to third generation cephalosporins were tested by PCR for the presence of extended-spectrum β -lactamase genes (*blaESBL*), and isolates displaying resistance to nalidixic acid were analysed for the presence of point mutations within the *gyrA* and *parC* genes and for the presence of plasmid-mediated fluoroquinolone resistance genes *aac(6')-Ib-cr*, *qnrA*, *qnrB*, *qnrC*, *qnrD*, *qnrS*, and *qepA*. All 47 isolates were screened for the presence of the plasmid-mediated azithromycin resistance gene *mphA* and the colistin resistance genes *mcr-1* and *mcr-2*.

Resistance to ciprofloxacin and trimethoprim/sulfamethoxazole was detected in 17% and 31.9% of the isolates, respectively. All isolates remained susceptible to fosfomycin and nitrofurantoin. The most common lineages were *E. coli* B2 ST131 and D ST69 (both 14.9%), followed by B2 ST141 (10.6%) and B2 ST73 (6.4%). The highest number of virulence genes was found among B2 ST12 and B2 ST141 isolates. Two B2 ST131 isolates carried *blaCTX-M-14*, and two B2 ST131 and one D ST69 harboured *blaCTX-M-15*. Six (12.8) of the isolates harboured *mphA*. None of the isolates tested positive for *mcr-1* or *mcr-2*.

This study describes the clonal structure, virulence potential and antibiotic susceptibility of UPEC causing community acquired UTI in a population of a suburban community in the area of Zürich, Switzerland.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P113

Serological diagnosis of EBV infection: Comparison of two serological tests

L Clerc¹; N Degonda¹; F Descloux Palard¹; A Dupas¹; V Evanno¹; A Monney¹; R Lienhard²; C Marti¹

(1) Laboratoire Promed SA;

(2) Fondation ADMED

Aims:

Diagnosis of infectious mononucleosis is based on clinical, hematological and serological data. Standard serological approach is based mainly on the determination of IgM and IgG VCA and IgG EBNA.

The aim of this study was to evaluate and compare two commercially available serological tests used to diagnose EBV infection.

Methods:

In our lab, the determination of EBV serology is performed routinely using the tests VCA IgM, VCA IgG and EBNA IgG (GenBio, USA) running on a DS2 Elisa processing system (Dynex Technologies, USA). Frozen sera of 58 patients (35 females, 23 males, from 1 y.o. to 70 y. o.) and 15 External Quality Controls (NEQAS) were assayed in parallel with the new Virclia® tests (Vircell, Spain)

Results:

Patient serums: The results of 42 serums are identical with both methods (72.4%). The discordant results were tested with additional tests on Liaison XL (Diasorin) and correlation was evaluated with clinical aspect and heterophile antibodies. External quality controls: 13 out of 15 results are corrected according to the NEQAS. Two results are equivocal but are highly method dependent. The data and results will be presented in more detail on the poster.

Conclusion:

In this comparison, different results were observed according to the method, leading sometimes to different serological diagnosis. Thus, it is essential to test and compare new serological method before to introduce them in the routine. Furthermore, serological tests has always to be interpreted in the appropriate clinical content and if not clear, has to be repeated again after 2-3 weeks (seroconversion).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P114

Local outbreak of *Listeria monocytogenes* serotype 4b sequence type 6 due to contaminated meat pâté

D Althaus¹; M Jermini²; P Giannini²; G Martinetti³; D Reinholz⁴; M Nüesch-Inderbinen¹; A Lehner¹; R Stephan¹

(1) Universität Zürich;

(2) Cantonal Laboratory Ticino;

(3) Ente Ospedaliero Cantonale, Bellinzona;

(4) Office of the Chief Medical Officer of Canton Ticino

Listeria monocytogenes is a foodborne pathogen with the ability to multiply at refrigeration temperatures, and to persist in food-processing environments and equipment. Listeriosis, although rare, is a potentially fatal infection, with the growing number of the elderly in the population, pregnant women and immunocompromised persons at particular risk. In 2014, the EU notification rate was 0.52 cases per 100,000 population, representing a 30% increase compared with 2013 and reflecting a statistically significant increasing trend of listeriosis between 2008-2014. Although most cases of listeriosis are sporadic, small and large outbreaks occur regularly. So far, four outbreaks of listeriosis have been reported in Switzerland involving soft cheese in two outbreaks, cooked ham and ready-to-eat salad in one outbreak each, respectively (Büla, Bille, & Glauser, 1995; Bille et al., 2005; Hächler et al., 2013; Stephan et al., 2015).

We describe a local outbreak of listeriosis that occurred in the canton of Ticino, located in southern Switzerland, during the Christmas holiday season of 2015/2016 due to contaminated meat pâté. Five cases of confirmed and two cases of probable infection due to *Listeria monocytogenes* serotype 4b, sequence type 6 belonging to a single PFGE pulsotype pattern were registered. *L. monocytogenes* was detected in blood samples (four cases), and pleural fluid (one case). Furthermore, *L. monocytogenes* 4bST6 was detected in a stool sample of an asymptomatic person exposed to a common food. Forthwith, the food safety authority and a local gourmet meat producer reported *L. monocytogenes* contamination of meat pâté. Analysis of further food and environmental samples from the premises of the producer yielded isolates matching the clinical strains and confirmed the presence of *L. monocytogenes* 4bST6 in the mincing machine as the cause of the food contamination.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P115

Key characteristics of mcr-1 harbouring plasmids from strains of different origins isolated in Switzerland

K Zurfluh¹; J Klumpp²; P Nordmann³; L Poirel³; R Stephan¹

- (1) Universität Zürich;
- (2) ETH Zurich;
- (3) University of Fribourg

Plasmid-encoded MCR-1 has been identified now mainly from *E. coli* but more rarely from a few other enterobacterial isolates (i.e. *K. pneumoniae*, *Citrobacter freundii*, and *Salmonella* spp. *enterica*). MCR-1 is a phosphoethanolamine transferase that adds phosphoethanolamine to the lipid A. This resistance trait is transferable by conjugation and has been reported so far in Enterobacteriaceae mostly from animal isolates, but also from human isolates and from food products. Despite the fact that still limited data are available, it is of note that the mcr-1 gene has been identified already all over the world, in both animal and human samples. It seems that the animal reservoir of *E. coli* is currently the main reservoir of mcr-1 so far identified. The studies that focused on the genetics of acquisition of the mcr-1 gene show that a diversity of plasmids bearing this gene, with many of them corresponding to previously described plasmid backbones.

The mcr-1-harboring plasmids of 9 *E. coli* strains (5 food isolates, 1 environmental isolate, 3 human isolates) were transferred to *E. coli* DH5 α by transformation. After plasmid extraction, full plasmid sequences from 10 mcr-1 harbouring plasmids were obtained by PacBio sequencing. From *E. coli* ColR598 (ST47/CC10), an isolate from a 1.5 year old boy with diarrhea and with a travelling history to Vietnam, two mcr-1 harboring plasmids pColR598_1 and pColR598_2 were extracted.

The plasmid sizes of the 10 plasmids ranged between 33.252bp and 247.885bp. They belonged to four different Inc types (IncX4, IncI2, IncHI1, IncHI2). Three different organization structures of the mcr-1 gene cassette were found (ISAp1-mcr1-orf; Tn6330; mcr1-orf). Only one of the 10 plasmids harboured additional resistance genes (estX-3, aadA2, aadA1a, aadA1b, cmlA1, sul3, dfrA1b, mefB, tetA, blaCTX-M-1).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P116

Monitoring of time to positivity of plastic blood culture vials from Becton Dickinson

G Prod'homme; A Croxatto; C Durussel; G Greub
 CHUV-University Hospital

Aims:

Becton Dickinson has recently introduced plastic vials to replace glass vials with the BACTEC blood culture system. When introducing these new plastic vials, we monitored the time to positivity (TTP) of the plastic vials and compared it with the TTP of glass.

Methods:

TTP from positive monobacterial blood culture from adults (age >18 years) obtained during the 16 first weeks following introduction of plastic vials were compared to the TTP obtained with glass vials during a three months period preceding the introduction of the plastic vials. The TTP of pediatric vials were excluded due to insufficient cases number. During the study, the transport of blood culture vials remained unchanged. Non parametric Mann-Whitney test was used to compare TTP obtained with the two different vials types. Results: A total of 799 positive blood cultures were analyzed from 260 patients, 55% being aerobic vials. For anaerobic vials, the median TTP was 10 hours (interquartile range (IQR): 7 to 17) with plastic vials compared to 11 hours (IQR: 8 to 17) with glass vials ($p=0.1$). For aerobic vials, the median TTP was 13 hours (IQR: 8 to 22) with plastic vials compared to 13 hours (IQR: 9 to 22.5) with glass vials ($P=0.3$). Comparison of the TTP from the first patients' positive blood culture of the twelve more prevalent bacteria covering 80% of bacteremia (*Escherichia coli*, *Staphylococcus aureus*, coagulase negative staphylococci, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides fragilis*, *Enterococcus faecalis*, *Enterococcus faecium*, *Enterobacter cloacae*, *Candida albicans*, *Streptococcus pneumoniae*, *Proteus mirabilis*) gave the following results:

(1) for anaerobic vials, the median TTP was 10 hours (IQR: 7.3 to 18.8) with plastic vials compared to 10 hours (IQR: 7 to 16) with glass vials ($p=0.5$), (2) for aerobic vials the median TTP was 14 hours (IQR: 8 to 21.8) with plastic vials compared to 14 hours (IQR: 9 to 23) with glass vials ($p=0.1$). No statistical difference was observed for slow growing bacteria such as *Candida* spp., *Propionibacterium* spp., *Lactobacillus* spp., *Micrococcus* spp., HACEK group, *Corynebacterium* spp., *Actinomyces* spp., and *Prevotella* spp. However the denominator was insufficient for definite conclusion.

Conclusion:

This study shows that no statistically significant difference of TTP between plastic and glass blood culture vials was observed during the 16 weeks following introduction of aerobic and anaerobic plastic vials from Becton Dickinson.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P117

Development of a new molecular typing system for *Treponema pallidum* subsp. *pallidum*

L Grillová¹; A Gayet-Ageron²; H Bagheri³; K Nieselt⁴; F Gonzalez⁵; D Šmajš¹; N Arora⁶; P Bosshard⁷

- (1) Masaryk University;
- (2) University Hospital of Geneva;
- (3) Repsol Technology Center;
- (4) University of Tübingen;
- (5) Unidad Mixta Infección y Salud Pública FISABIO/Universidad de Valencia;
- (6) University of Zurich;
- (7) University Hospital of Zurich

Background

Treponema pallidum subsp. *pallidum* (TPA) is the causative agent of syphilis, a sexually transmitted infection with increasing incidence worldwide. Typing is important to i) map the geographical distribution of strains, ii) investigate the association of specific strains with specific groups of patients, iii) gain insights on macrolide resistance, which is critical for treatment. However, our genetic understanding of syphilis is limited by the difficulty in cultivating the pathogen, and the low amount of DNA present in clinical specimens. Whole genome data from clinical specimens can be exploited to select marker loci for a high resolution typing scheme.

Methods

The loci for TPA typing were designed based on whole genome sequencing data from 30 samples obtained from patients between 1912-2013; 12 were from strains passed through rabbits and 18 were obtained from patients by hybridization capture method (Arora N. et al., Nature Microbiology). The set contained TPA strains from the two genetically distinct groups; SS14-like and Nichols-like strains. The new molecular typing scheme was applied to 139 positive clinical samples collected from 2011-2015 in five cities in Switzerland and France; Zurich, Lausanne, Geneva, Lyon, Paris.

Results

The concatenated sequences of the five candidate loci TP0548, TP0136, TP0705, TP0462 and TP0865 were able to distinguish 11 different haplotypes. This represents 42% of the 26 haplotypes distinguished when using genome-wide data. Given the time and money constraints of laboratories, we determined the smallest set of markers that provided similar resolution. When using only three genes (TP0136, TP0548 and TP0705), we obtained the same resolution as when using all candidate loci. By applying this scheme to 90 typeable Swiss and French samples, we found 21 different haplotypes (17 SS14-like and 4 Nichols-like). In Zurich, we found 14% Nichols-like strains, whereas in all other cities only SS14-like strains were found. A total of 68 samples (79%) harboured mutations associated with macrolide resistance.

Conclusion

We present a new molecular typing scheme of TPA based on the sequencing of the three genes. This scheme is able to clearly identify the two genetically distinct groups of TPA (SS14 and Nichols), and to further distinguish the strains within these groups. The additional analysis of the 23S rDNA gene allows evaluation of macrolide resistance/sensitivity.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P118

Engineering biomolecules for advanced nanocellulose based antimicrobial coatings

R Weishaupt¹; L Heuberger¹; G Faccop¹; G Siqueira²; T Zimmermann²; K Maniura¹

(1) Empa, St.Gallen;

(2) Empa, Dübendorf

Introduction

Nosocomial infections are today by far the most common complication affecting hospitalized patients. In this regard, the development of coatings that prevent pathogen associated surface colonization at an early stage is of utmost interest. Nanocelluloses (NC) from both, plant- and microbial origin are highly durable materials, which cause low inflammatory response and can, promote tissue regeneration if deployed as wound dressing or body implant. Their high specific surface area and concurrent hydrophilic properties allocate nanocelluloses as excellent carrier material for various biomolecules.

The development of nanocellulose-based implant coatings that preclude inflammation and elicit broad-spectrum antimicrobial activity would be highly advantageous. Cationic antimicrobial peptides (AMPs) are among the most prominent candidates for such applications. The therapeutic potential of AMP's are currently explored extensively in research and development. However, the majority of these studies have focused on free peptides and only few addressed the development of molecular tools for efficient surface immobilization or cytotoxicity aspects.

Methods

A synthetic AMP sequence was either recombined with a peptide (CBP) or protein based carbohydrate-binding motif (CBM). Solid phase synthesis and recombinant expression in combination with column chromatography was applied to produce the engineered ligands. The antimicrobial potential against clinical isolates of *P. aeruginosa* sp. and *S. aureus* sp was measured using a modified killing assay. The minimal inhibitory concentration (MIC) was taken as the concentration at which no growth was observed.

Results

The peptide-based ligands were found to be highly antimicrobial in solution with MIC values as low as 1.6 µg/mL for the unmodified AMP and 8 µg/mL for the CBP tagged AMP. Co-incubation of cell free extract revealed selective and stable binding of the protein-based ligands to the nanocellulose substrate via their concomitant CBM. The addition of a site-specific protease successfully exposed the antimicrobial moiety by cleaving off the fluorescent protection tag.

Conclusions

Current results confirm the potential of the developed strategy for efficient functionalization of NC substrates with active biomolecules. Currently the antimicrobial potential of the protein-based constructs in solution and immobilized to NC substrates are being addressed.

Acknowledgements

The authors thank Matthias Buhmann, Beatrice Gutt & Qun Ren-Zulian

References

- Burke JP. N. Engl. J. Med. 2003; 348(7):651–656.
- Bottan, S., et al. ACS Nano. 2014; 9(1): 206-219.
- Weishaupt, R., et al. Biomacromolecules. 2015; 16(11): 3640–3650.
- Hilpert, K., et al. Chem. Biol. 2009; 16(1): 58-69.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P119

The National Pneumococcal Center of Switzerland: Hunting new emerging pneumococcal serotypes by using nuclear magnetic resonance (NMR)

L Troxler; J Furrer; M Hilty
Universität Bern

The National Pneumococcal Center of Switzerland analyzes about 1000 pneumococcal isolates from cases of invasive pneumococcal disease (IPD) each year. Conventional serotyping methods like the Quellung reaction can identify known serotypes, but cannot reveal potentially new serotypes. After the introduction of the 13-valent pneumococcal conjugate vaccine (PCV13) in Switzerland, the prevalence of new non-PCV13 serotypes is rising. Therefore we aim to use nuclear magnetic resonance (NMR) methods to analyze the capsular composition of *S. pneumoniae* in strains with inconclusive serotyping results and to investigate the serotype identity in strains displaying a different genetic subtype.

To this end, the pneumococcal polysaccharide capsules of genetic subtypes of serotype 19A, an emerging genetic subtype of serotype 23B and strains which displayed uncertain results in Quellung reactions were analyzed by NMR measurement using a method developed at the Pneumococcal Center for comparison to reference strains. In the NMR spectra, the anomeric region between 6 and 4 parts per million served as a “Fingerprint” region where differences in capsule composition are most readily apparent.

We showed that there was no phenotypical difference among the genetic subtypes within serotype 19A[1], as well as between types 23B and 23B-1. Furthermore, two strains in our study were found to express a capsule composed of a mixture of both serotypes 6A and 6C although there were only minimal genomic differences in the capsule region. This is the first time this hybrid was detected in Swiss pneumococcal samples.

In conclusion, we showed that our NMR method can be used to distinguish new serotypes from mere genetic subtypes and provide more insight in cases where conventional serotyping methods do not suffice. It remains to be seen whether the found 6AC hybrid serotype strains is a true non-PCV13 serotype and therefore will become more prevalent in the years to come. In the future the National Pneumococcal Center of Switzerland will continue to analyze unconventional strains in the search for new emerging serotypes of *S. pneumoniae* using this newly established NMR methodology.

Reference

[1] Brugger SD, Troxler LJ, Rüfenacht S, Frey PM, Morand B, Geyer R, Mühlemann K, Höck S, Thormann W, Furrer J, Christen S, Hilty M. Infect Immun (2016) 84:3152–3160.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P120

The gut mucus and its protective role in *Salmonella Typhimurium* infection

M Furter¹; ME Sellin¹; GC Hansson²; W Hardt¹

(1) ETH Zurich;

(2) University of Gothenburg

Aims

A layer of viscous mucus lines the gut tissue and protects it from the resident microbiota, but also from incoming pathogens. It is unclear, how pathogens overcome this protective layer and reach their host tissues. Here, we address the question how *Salmonella Typhimurium* (*S. Tm*) interacts with the gut mucus and infects its host tissue.

Methods

We used live-microscopy to track single *S. Tm* swimming on explanted gut tissue. The mucus covering these explants was either visualized by adding fluorescent beads or by using *Muc2-mCherry* mice. These mice produce fluorescently tagged gut mucins, which we imaged in their nascent state, without prior fixation. For analysis of the mucus organization along the entire gut, we also imaged Methacarn-fixed tissue samples stained for *Muc2*.

Results

S. Tm accumulated at the mucus surface between 20 and 60 μm above colon tissue explants. Single-cell analysis revealed that the mucus protects the epithelium from direct access by *S. Tm*. Furthermore, incoming *S. Tm* are forced onto circular near-surface swimming along the mucus surface. A fraction of *S. Tm* was immobilized at the mucus surface. Immobilization depended on motility and was absent in *S. Tm* with paralyzed flagella. Near-surface swimming might allow *S. Tm* to scan for permissive sites in the mucus layer that allow tissue invasion. Therefore, we analyzed the mucus organization and appearance along the gut. We found that the cecal tissue, in contrast to the colon and the small intestine, was not only sparsely covered with mucus. Consistently, *S. Tm* invaded cecum tissue tenfold more efficiently than colon tissue, despite equal gut luminal loads.

Conclusions

We conclude that the mucus acts as physical barrier that either binds or enforces near-surface swimming of *S. Tm* and thus impedes tissue invasion. An intact mucus layer is crucial for gut homeostasis and controlling pathogen infections. This is reflected in an increased tissue invasion rate in the murine cecum, where the mucus is not completely covering the host tissue.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P121

Identification of mixed bloodstream infections directly from positive blood cultures by MALDI-TOF mass-spectrometry with observation of fundamental differences between Biotyper® Sepsityper module versions.

C Gehringer; D Hohler; M Osthoff; S Bassetti; A Egli
 University Hospital Basel

Background:

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) enables fast and reliable identification of bacteria directly from positive blood cultures. This diagnostic analysis, however, only provides singular results, i.e. identifies only one species. Thereby this incompletely reflects the complexity of polymicrobial bloodstream infections (BSI) that are adequately captured by conventional culture-based microbiological identification. Recent advancements in software analysis promises to allow the simultaneous identification of up to two species from the same mass spectra thereby addressing this diagnostic gap.

Methods:

This study compares the standard identification Biotyper® Compass software (Version 4.1, 6903 MSP library) on a Bruker Microflex LT, designed to identify only one species at a time, with two versions of the Sepsityper module, designed to identify up to two organisms from the same sample simultaneously (all Bruker Daltonics, Bremen, Germany). Mass spectra were obtained following manufacturer's recommendation (Sepsityper preparation protocol) on 233 routine clinical samples of BSIs. Overnight cultures on agar plates with subsequent MALDI-TOF MS and 16s rDNA sequence identification (if required) served as gold standard.

Results:

Identification (including incomplete identification of mixed infections) directly from positive blood cultures was successful in 213/233 (91.4%) and 217/233 (93.1%) samples using the standard and the Sepsityper software, respectively. 21 of 233 cultures were mixed infections. The sensitivity to detect the presence of a mixed infection after software update to version 1.1 decreased from 71.4% to 14.3% with an increase in specificity from 78.3% to 99.5%. Software version 1.0 showed an additional error rate of 19.8% (42/212) in the monomicrobial samples with mainly false positive reporting of mixed infection.

Conclusions:

The ability to identify monomicrobial cultures was almost identical between the standard and the Sepsityper version 1.1. The most recent version 1.1 of the mixed infection algorithm supplemented only 2 correct identifications of mixed infections and 1 partial identification in a case of >2 polymicrobial infection. This updated algorithm seems to conserve the specificity of the standard identification method but shows only a very small, but potential clinically relevant benefit in case of mixed infections.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P122

Screening for bacteriuria: evaluation of more than 47,000 urine samples analysed by test strip, flow cytometry and microbiological culture

C Gehringer; A Regeniter; K Rentsch; S Tschudin-Sutter; S Bassetti; A Egli
 University Hospital Basel

Background:

Diagnosis of urinary tract infections (UTI) usually requires the presence of symptoms and bacteriuria defined by conventional microbiological culture. Bacterial and leucocyte counts in the urine determined by flow cytometry promise to be a time and resource saving screening method for relevant bacteriuria, but cut-off values are a matter of debate. This study addresses those uncertainties by an analysis of a combined microbiological culture and urine flow cytometry dataset.

Material/methods:

Species identification and colony-forming unit (CFU/ml) quantification from microbiological cultures of blood-agar and non-selective CHROMagar were matched to corresponding cellular (leucocytes/erythrocytes/epithelial cells) and bacterial counts per μ l urine obtained from an UX-2000 flow cytometer (Sysmex, Kobe, Japan). Results comprise all samples that were sent to the diagnostic laboratories of the University Hospital of Basel between 2013 and 2015 and for which bacterial culture and flow cytometry data were available (local standard of practice). A positive microbiological culture was defined with more than 100,000 CFU/ml on any positive culture plate.

Results:

Matching the microbiological reference standard with flow cytometry data resulted in a set of 47,572 urine samples (34.4% of which had relevant bacteriuria) of 26,256 patients. Prediction of a positive microbiological culture by bacterial counts measured by flow cytometry was most accurate and was a better predictor than leucocyte counts independent of the source of the urine (area under the receiver operator curve (AUC) of 93% and 79%, respectively). All available surrogate markers (nitrite, leukocyte esterase, leukocyte count, in combination or alone) were inferior to direct bacterial concentration measured by flow cytometry in estimating bacteriuria defined by microbiological culture.

Conclusions:

The results emphasize the possibility of using bacterial counts from flow cytometry to predict relevant bacteriuria, yielding clinically relevant information that is usually available within a few hours after sampling. The data was obtained from routine laboratory results from a diverse set of patients over three years and underlines the robustness of these findings. 20 bacteria/ μ l as lower “rule out” and 200 bacteria/ μ l as upper “rule in” cut-off concentration appear to be pragmatic values for bacteriuria with sufficient sensitivity and specificity of > 95% and ~ 90%, respectively.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P123

Evaluation of the ELiTe InGenius sample-to-result PCR system with focus on the quantification of Cytomegalovirus and Epstein-Barr virus and the detection of Varicella-Zoster virus

R Vonlanthen; A Bonnet Pierroz; A Dumoulin
Hôpital du Valais - Institut Central

Aims

The ELiTe InGenius (ELITechGroup) is an all-in-one, sample-to-result PCR system integrating nucleic acid extraction, amplification and results analysis of up to 12 clinical samples. The aim of the present project was to evaluate the performance of the quantitative Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) PCR assay and of the qualitative Varicella-Zoster virus (VZV) PCR assay on this system, as well as its integration into our laboratory.

Methods

For the CMV and EBV PCR, the Elitech PCR reagents and operating procedures were used to test patient samples (CMV: 17 plasma, 5 urine samples; EBV: 40 plasma samples), reference quantification standards (Qnostics) and external quality control panels (CMV only, QCMD). The comparator assays were the quantitative CMV assay for CAP/CTM (Roche Diagnostics) and results from a reference laboratory for EBV. For the qualitative VZV PCR, serial dilutions of a positive skin lesion were analysed on the InGenius, using in-house or Elitech PCR reagents, in order to evaluate the limit of detection for this method. The comparator assay consisted of extraction on the NucliSENSE EasyMag system (bioMérieux), followed by amplification using the same in-house PCR on a Rotorgene Q system (Qiagen).

Results

The Bland-Altman bias in quantification was 0.085 log IU/ml for CMV (26 data points, QCMD and Qnostics panels), and -0.389 log IU/ml for EBV (12 data points, Qnostics panel). The results of the QCMD quality control panel for CMV were good, with only one educational low-positive sample (2.207 log IU/ml) not detected by the InGenius system. Good qualitative and quantitative agreements were also observed with patient samples for the CMV PCR (quantitative bias 0.289 log IU/ml). For the EBV PCR, the difference in sample matrix between the comparator assay (whole blood) and the InGenius system (plasma) did not allow definitive conclusions especially for low-positive samples. In high-positive samples, the qualitative agreement was good. The in-house PCR and the Elitech VZV assay performed equally well on the InGenius system as with our standard procedure.

Conclusion

The ELiTe InGenius is a very versatile open platform that allows the use of in-house PCR reagents, as well as robust proprietary assays. Its format and its ease of use make it a good option for low- to medium-throughput parameters or smaller laboratories.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P124

Increased detection and isolation of Campylobacteraceae using a novel chromogenic medium

G Jost; F de Marval; N Liassine

Dianalabs

Aims

Multiplex PCR assays have proved to be more accurate than conventional methods in detecting *Campylobacter jejuni/coli* in stool specimens. However, culture remains necessary for the detection of other species, such as the emergent enteropathogen, *Arcobacter* spp., and for the antimicrobial susceptibility testing (AST). In order to increase the culture sensitivity for such bacteria, a novel chromogenic medium, the CASA medium, was evaluated in comparison to the Campylosel medium and to the PCR assay.

Methods

Between August 2016 and March 2017, over two separate periods of two months each, in summer and in winter, a total of 1665 clinical stool specimens were tested for the detection of Campylobacteraceae on the CASA medium (bioMérieux). Simultaneously, the routine protocol was applied: culture using Campylosel medium (bioMérieux) and PCR assay that detects *C.jejuni/coli* using BD MAXTM EBP (BD). The media were incubated at 37°C for 48h in a microaerophilic atmosphere. AST was assessed by E-test and interpreted according to the current EUCAST recommendations.

Results

Of the 1665 stools, 124 (7.4%) were positive by PCR assay, 112 by CASA medium and 105 by Campylosel medium. One case of *C.jejuni* was detected by culture by both media but missed by PCR.

The sensitivity of the CASA medium was higher (79%) than the Campylosel medium (76.6%).

Moreover, *Arcobacter butzleri* was detected more frequently through CASA (n=13) than through Campylosel (n=10) medium. All cases of *A.butzleri* were related to enteric disease.

C.jejuni was the dominant species detected by culture, both in summer (n=56) and winter (n= 29). In summer, it was followed by *C. coli* (n= 10) and *A.butzleri* (n= 8), whereas in winter-period, *A.butzleri* represented the second most frequent species (n=5), followed by *C. coli* (n=2) and *C.curvus* (n=1).

The fluoroquinolone resistance was 55.9% for *C.jejuni*, 75% for *C.coli* and 6.7% for *Arcobacter* spp. A low-level macrolide resistance (MIC: 6-8 mg/L) was frequently observed in *A.butzleri* (R: 46.2%).

Conclusions

The current work highlights the increased sensitivity of the CASA medium compared to the Campylosel medium in the detection of *Campylobacter* spp. and *Arcobacter* spp. As *Arcobacter* spp. are not detected by PCR, we introduced the CASA medium instead of the Campylosel medium for the detection of Campylobacteraceae in combination with the PCR assay.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P125

Clinical impact of the Type VI secretion system on virulence of *Campylobacter* spp. during infection

J Agnetti¹; M Schneider¹; S Ursich²; M Basler²; S Tschudin-Sutter¹; A Egli¹

(1) Universitätsspital Basel;

(2) University of Basel

Aims:

The clinical course of *Campylobacter* infection varies in symptoms and severity depending on host factors, virulence of the pathogen and initiated therapy. Type VI secretion system (T6SS) has been identified as a novel virulence factor, which mediates contact-dependent injection of enzymes and toxins into a competing bacterium or host cell and facilitates the colonisation of a host organism. We aimed to compare the clinical course of *Campylobacter* infection caused by strains with and without T6SS and identify possible associations between this virulence factor and the clinical manifestations of disease.

Methods:

From April 2015 to January 2017, 161 cases with detection of *Campylobacter* spp. in any clinical isolate were identified at the University Hospital of Basel for this observational case-control study. T6SS PCR targeted the Hcp gene. The medical charts were reviewed. Characteristics of disease and of the host were compared in a uni- and multivariate analysis between T6SS-positive (case) and negative strains (controls). The following factors were defined as clinical endpoints: Hospitalisation, antibiotic therapy, ICU stay, development of bacteremia and in-hospital mortality. Other co-variables like epidemiologic, demographic and clinical factors were recorded for the statistical model.

Results:

In a preliminary data analysis, 15.7% of all tested *Campylobacter* spp. were T6SS positive. 7.1% belonged to *C. coli* and 18.2% to *C. jejuni*. T6SS-positive strains showed a strong trend for being more resistant against Ciprofloxacin ($p=0.06$). Both T6SS- positive and -negative strains showed a similar distribution across all age groups and both genders. Patients infected with T6SS-positive strains showed, in comparison to T6SS-negative strains, a higher score in the Charlson Comorbidity Index ($p<0.001$), were more likely to have a solid organ transplant ($p=0.004$), and were more likely to be under immunosuppressant therapy ($p=0.005$). A higher comorbidity score proved as an independent risk factor in a multivariate analysis. Additionally, patients with a T6SS-positive strain were less likely to report fever history ($p=0.023$).

Conclusion:

A higher burden of underlying diseases and an immunocompromised state were associated with infection with T6SS-positive *Campylobacter*. These preliminary results call for further investigation and validation on a larger cohort.

References:

1 Hachani A, Wood TE, Filloux A. Current Opinion in Microbiology 2016;29:81.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P126

Validity and applicability of direct susceptibility testing from urine specimens

I Voellmy; S Pranghofer; L Berlinger; M Altwegg

Bioanalytica AG

Growing numbers of antibiotic resistances increase the importance of rapid and reliable susceptibility testing to tailor antibiotic therapy. This is vital for systemic life-threatening infections, including urinary tract infections as they can lead to bacteraemia. Direct susceptibility testing from urine specimens can reduce analysis time by up to 24 h. Despite several supportive studies conducted since the 1970s, this procedure has not been widely adopted. We compared disk diffusion tests on Mueller–Hinton agar performed directly from urine specimens with standardised procedures defined by EUCAST. We included 137 urine specimens containing $\geq 10^5$ CFU/ml Enterobacteriaceae. An overall agreement of 97.6 % was observed for seven frequently used antibiotics in 920 tests: Ampicilline (100%; 120/120), Amoxicilline/Clavulanic acid (97.1%; 133/137), Cefuroxime (98.5%; 135/137), Fosfomycine (96.4%; 132/137), Nitrofurantoin (96.5%; 111/115), Norfloxacin (97.8%; 134/137), Trimethoprim/Sulfamethoxazole (97.1%; 133/137). Very major errors (i.e. inhibition zones classified resistant in standardised, but sensitive in direct testing) were observed in seven cases only. Thus, our data confirm reliability of direct test procedures in our laboratory setup.

However, assessment of test efficiency may also be crucial prior to integration in diagnostic procedures. In a second study, we investigated two aspects: 1) proportion of urine specimens which will benefit from accelerated procedures and 2) evaluation of workload for technicians: EUCAST procedures are more time-consuming, whereas direct susceptibility procedures require verification in some cases. To our knowledge, these issues have not been addressed in previous studies. A total of 798 urine specimens were screened for presence of leucocytes and nitrite using Multistix® 10 SG (Siemens) and, if positive for either or both parameters, underwent direct susceptibility testing (59.0%; 471/798). Of these 39.5% (186/471) were used in reports, 22.5% (106/471) required verification using standardised procedures and 38.0% (179/471) were discarded. Only 18 screening-negative specimens showed sufficient growth of Enterobacteriaceae to possibly benefit from direct susceptibility testing. Our data indicate potential benefits from accelerated susceptibility testing for more than one third of screening-positive specimens. However, additional strategies to improve cost-effectiveness would be helpful.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P127

Burkholderia stabilis outbreak associated with contaminated wash gloves: description and whole genome sequence of an opportunistic pathogen

H Seth-Smith¹; D Meinel¹; DS Blanc²; MM Abdelbary²; S Droz³; U Führer⁴; C Casanova³; C Lang⁵; O Dubuis⁵; M Schlegel⁶; R Sommerstein⁷; AF Widmer¹; PM Keller⁸; J Marschall⁷; A Egli¹

- (1) Universitätsspital Basel;
- (2) CHUV Lausanne;
- (3) Universität Bern;
- (4) Spital Biel;
- (5) Viollier;
- (6) Kantonsspital St. Gallen;
- (7) Inselspital, Universitätsspital Bern;
- (8) Universität Zürich

Aims:

Burkholderia cepacia complex (BCC) can cause sporadic outbreaks through contamination of medical devices and solutions. In 2016, a nosocomial outbreak of *Burkholderia* sp. occurred in Switzerland. BCC have large, genomes of approximately 8Mb, organized in three chromosomes and a plasmid, providing them with the genetic flexibility to survive in diverse environments. We aimed to describe the genomic features of these bacteria.

Methods:

Isolates were obtained from patients (n=23) and from the contaminated source (n=9). Whole genome sequencing (Illumina Miseq) was performed on all isolates, and on one strain by Pacific Biosciences, with subsequent analyses in CLC genomics workbench and Artemis.

Results:

MALDI-TOF identification indicated that the outbreak strains were BCC, possibly *B. stabilis*, whereas VITEK2 was unable to resolve further than *B. cepacia* group or *Acinetobacter lwoffii*. PFGE typing suggested that a single strain caused the outbreak, with 76% relatedness between isolates. Extraction of MLST locus information from whole genome sequences resulted in the assignment of a novel MLST type, 1095, most closely related to *B. stabilis* (sharing 4/7 alleles). Additional fine resolution comparisons of genomes indicated that the genomes of all strains differ by a maximum of 2 single nucleotide polymorphisms (SNPs), which therefore constitutes a highly clonal outbreak. A full genome assembly combined PacBio and Illumina data, resulting in a genome draft comprising 8 scaffolds. Digital DNA:DNA hybridization against *B. stabilis*, ATCC BAA-67 (isolated from a cystic fibrosis patient) gave a score of 84.2%, confirming the outbreak strain to be *B. stabilis*. Gene-by-gene analysis of the genome draft indicated that >900 of the 7531 coding sequences annotated are unique to the outbreak strain, including the presence of a novel plasmid and several prophages not previously identified in *Burkholderia*.

Conclusions:

A strain of *B. stabilis* contaminating patient wash gloves was responsible for a Switzerland-wide outbreak, showing that *B. stabilis* contamination can cause major nosocomial outbreaks associated with detergent-containing medical products. In our opinion, clusters of BCC cases call for thorough review of the material used for patient care. Detailed identification of the outbreak strain was performed, including a full genome sequence. This is the first genomic description of an outbreak-related strain of *B. stabilis*.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P128

Evaluation of a New Commercial Microarray for the Detection of the Mcr-1 Gene

OJ Bernasconi¹; L Principe²; R Tinguely¹; V Perreten³; F Luzzaro²; A Endimiani¹

(1) Institute for Infectious Diseases, University of Bern, Switzerland;

(2) A. Manzoni Hospital;

(3) Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern

Aims:

The recent emergence of the plasmid-mediated *mcr*-1/-2 genes conferring polymyxin resistance in Enterobacteriaceae represents a serious public-health concern. A rapid and reliable method is needed to perform a quick detection of such genes, especially for isolates resistant to last-generation cephalosporins and carbapenems. In this work, we evaluated the ability of a new commercial microarray system to detect simultaneously clinically important β -lactamases genes (*bla*) and *mcr*-1.

Methods:

The former CT103XL microarray platform (Check-Points, The Netherlands) was able to detect numerous class A, B, C, and D *bla*. In the new version (new-CT103XL), three spots to detect *mcr*-1 and *mcr*-2 have been added. To evaluate its performance, we have so far tested 68 *E. coli*, 15 *K. pneumoniae* and 1 *Salmonella* spp. Isolates were phenotypically (e.g., MIC for colistin) and molecularly (e.g., PCR/sequencing for *mcr*-1/-2) characterized in previous studies. The collection included: 38 colistin-resistant (of which 19 *mcr*-1-positive), 32 carbapenemase- (including KPC, NDM, VIM, OXA-48), and 29 ESBL- and/or pAmpC-producing strains.

Results:

The new-CT103XL system correctly identified the 19 *mcr*-1-positive Enterobacteriaceae with no false-positive strains (both sensitivity and specificity of 100%). The *bla* content of these 19 strains (including 13 TEM-1-like, one CMY-2, and 3 CTX-M-15-like producers) was also correctly reported by the microarray. For the overall detection of *bla*, the agreement between new-CT103XL and molecular characterization in detecting carbapenemases, ESBLs, and/or pAmpCs was >90%.

Conclusion:

The new-CT103XL is an accurate tool to detect simultaneously *mcr*-1 and clinically important *bla*. This platform could be used in epidemiological or infection control studies where large collections of isolates need to be characterized. Furthermore, its use in clinical practice may lead to more appropriate use of antimicrobial agents, reducing costs and improving patient outcomes.

This work was supported by SNF grant 153377 due to AE.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P129

Rapid Polymyxin NP test for the detection of mcr-1/mcr-2 mediated polymyxin resistance

Y Larpin¹; J Dobias¹; L Poiriel²; R Stephan³; J Decousser⁴; J Madec⁵; P Nordmann¹

- (1) University of Fribourg;
- (2) University Fribourg;
- (3) Vetsuisse University;
- (4) Hopital Henri Mondor;
- (5) ANSES

Aims

Polymyxins are becoming the last-resort antibiotics against multi-drug resistant Enterobacteriaceae. However current antibiotic susceptibility techniques to determine polymyxin resistance are not reliable. The broth microdilution method (BMD) is the reference technique recommended by the CLSI and the EUCAST. However that broth dilution technique is time consuming (24h). The Rapid Polymyxin NP test has been developed to detect polymyxin resistance in Enterobacteriaceae. It is based on detection of glucose metabolism associated with bacterial growth in the presence of a given concentration of polymyxin B or colistin. When growth occurs (resistant strain), formation of acid metabolism in less than 2 hours is evidenced by a color change of a pH indicator. Here, our aim was to evaluate this Rapid Polymyxin NP test for detecting enterobacterial isolates producing MCR-1/MCR-2-mediated polymyxin resistance with strains belonging to a variety of enterobacterial species of environmental, animals and human origins.

Methods

A total of seventy non-duplicate mcr-1 and mcr-2 positive Enterobacteriaceae from different origins, isolated between 2011 and 2016, has been tested. The phylogenetic groups of MCR-producing *E. coli* have been determined to confirm their ecological niche, using the Clermont quadruplex PCR. The MCR producers included 5 in-vitro obtained MCR-1 transconjugants obtained in a previous study. Those transconjugants permitted to test additional enterobacterial species that produce MCR-1. BMD in cation-adjusted Mueller-Hinton broth (Bio-Rad) was performed to determine the MIC.

Results

The MIC of colistin for MCR-1/MCR-2 producers were variable (4-64 µg/ml) but overall low. All resistant strains were detected as being resistant by using the Rapid Polymyxin NP test with a sensitivity of 100% whatever the species or the origin of the strain were. Whatever the phylogenetic group of *E. coli* strains was, all resistant strains were detected by using the Rapid Polymyxin NP test.

Conclusion

The Rapid Polymyxin NP test showed excellent sensibility and specificity toward all kind of Enterobacteriaceae harboring mcr-1 and mcr-2 transferable genes, despite the fact that many of them exhibited quite low MIC values. This test will therefore be very useful to rapidly identify (2h) MCR-producing isolates from humans, animal husbandry, and the environment.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P130

PCR or Maldi-TOF for Rapid Identification of Bacteria from Positive Blood Cultures?

I Amrein; S Pranghofer; M Altwegg
Bioanalytica AG

Aim:

Studies have demonstrated that rapid organism identification (ID) results in improved outcomes in bloodstream infections. Maldi-TOF and multiplex PCR have the potential to provide useful ID results from positive blood cultures (BCs) significantly faster than conventional culture. Our goal was to determine which method would be most adequate to be used in our routine diagnostic laboratory with regular opening hours from 7.30am to 6pm during the week, from 7.30am to 1pm on Saturdays and from 9am to 11am on Sundays.

Methods:

In a prospective study we compared Maldi-TOF (Bruker, Microflex) and the FilmArray® Blood Culture Identification Panel (BCID; bioMérieux) with conventional culture (with Maldi-TOF from colonies for ID) for direct ID from 100 positive blood cultures (BACTECTM FX). Culture, Maldi and PCR were done within 1 hour for BCs that turned positive during opening hours and the other day for all others. Hands-on time and the time needed from starting the workup of a positive bottle until the availability of the corresponding result were recorded.

Results:

ID results were available within approx. 30min for Maldi, 70min for PCR and an average of 14h 14min (median: 14h 18min; max. 43h) for culture. Hands-on time was about 8min (discontinuous) for Maldi and 6min (continuous) for PCR.

BCID correctly identified bacteria from 81 BCs. No result was obtained by BCID for 17 BCs of which 16 contained bacteria not covered by the panel, and two organisms, also not covered by the panel, were misidentified (*Aerococcus* sp. as *Staphylococcus* sp. and *Citrobacter* sp. as *Proteus* sp.). Correct identification by Maldi was obtained for 21 or 28 BCs depending on the minimum score (>2.0 or >1.8, respectively) defined as acceptable ID. No result was obtained for 72. Most likely this is due to insufficient numbers of bacteria on the target as indicated by the absence of visible peaks and the fact that the same bacteria were easily identified from culture plates. There was no obvious correlation between the fraction of correct IDs by Maldi and the time point when BCs turned positive (during or after opening hours).

Conclusions:

Multiplex PCR with the BCID panel is user-friendly and, despite significantly higher reagent costs, more suitable for rapid ID from positive blood cultures than Maldi-TOF (which returns a low identification rate) or conventional culture (which provides results with an average delay of more than 14 hours).

We thank Géraldine Jost, Dianalabs, Geneva, for providing the alternative protocol for sample preparation and bioMérieux Switzerland for discounted FilmArray(TM) reagents.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P131

Sensitive detection and differentiation of *Bordetella* sp. in clinical specimens by automated real-time PCR on BD MAX

K Egli; L Risch; M Risch; T Bodmer
 LMZ Dr Risch

Aims:

Bordetella pertussis and *B. parapertussis* are the main cause of whooping cough or pertussis. Infections by *B. parapertussis* tend to take a milder clinical course. The BD *Bordetella* multiplex real-time PCR assay (BioGX, USA) simultaneously detects and differentiates *B. pertussis*, *B. parapertussis* and *B. holmesii*. Its targets are the toxin gene (*ptxS1*), IS481 and IS1001 element. Here we evaluated the feasibility and performance of the automated multiplex real-time PCR assay running on the BD MAX (Becton Dickinson, Switzerland) in comparison to either FilmArray assay (Biofire, bioMérieux S.A.) or Seegene Allplex Respiratory Panel (BÜHLMANN Laboratories AG) as the reference.

Material/methods:

LOD studies using two-fold dilutions of quantified DNA of each pathogen preceded the evaluation of blinded EQA specimens (QCMD). Finally, clinical specimens, such as nasopharyngeal swabs/washes were tested. DNA was extracted using the BD MAX ExK DNA-1 kit. Amplification and detection was done using *B. pertussis*, *B. parapertussis*, *B. holmesii*, Pertussis Toxin Open System Reagents for BD MAX.

Results:

LOD of the bacterial targets ranged from 4 (IS481) to 13 (*ptxS1*) genome equivalents. Ten specimens of the EQA panel containing different *Bordetella* sp. at various concentrations were correctly identified. The percentage of datasets reporting the correct result for each panel sample was between 46.2% and 98.5% (197 participating laboratories) and pointed to the challenging nature of this panel. The main cause of the low percentage of correct results was the misidentification of *B. holmesii* as *B. pertussis*. A total of 34 clinical specimens were studied. Inhibition was found in one (2.8%) of them. *B. pertussis* was detected in 17 out of 18 positive specimen (94%) in one of the reference tests. Two specimens revealed a dual infection with *B. pertussis* and *B. parapertussis*. The presence of various respiratory pathogens did not interfere with the assay's specificity.

Conclusions:

Analytical as well as clinical sensitivities of the BD MAX Pertussis assay were excellent for all targets. The BD MAX Open Mode platform resulted in an easy-to-use, automated test with minimal hands-on time. Our data show that it allows for the sensitive and specific detection of all three *Bordetella* sp.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P132

A PCR-based Approach for Diagnosis of Vaginitis

N Wohlwend; R Ilijazi; S Thiermann; M Risch; M Ritzler

LMZ Dr Risch

Aims:

Vaginitis is characterized by three main categories, i.e. bacterial vaginosis (BV), yeast infection and Trichomoniasis. BV is the most common cause of vaginitis in women of reproductive age. In an epidemiological point of view BV remains a challenge due to the imprecise way in which the diagnosis is made. All methods such as clinical criteria, microscopy, culture and molecular diagnostic methods have all failed to date. Here, we tested a new syndrome, PCR-based approach for clarification of vaginitis.

Methods:

The BD™ MAX Vaginal Panel (VP) is a multiplex real-time PCR assay for the detection of *Candida* spp., *T. vaginalis* and BV (*Lactobacillus* spp., *G. vaginalis*, *A. vaginae*, BVAB-2 and *Megasphaera*-1). The detection of BV is based on combining the detection level of *Lactobacillus* spp. with the detection level of the bacteria associated with BV. In this study, we tested the performance of the VP by comparing the sensitivity of 4 different transport media, i.e. UVE (Becton Dickinson), ESwab™ (Copan), SwabAX (Axonlab), and our in-house PCR media by serial 10-fold dilutions of *G. vaginalis*, *C. albicans* and *C. glabrata*. Afterwards 98 randomly selected urogenital swabs (SwabAX) from our patient collective in March 2017 were analysed. Specimens were simultaneously tested by microscopy, culture methods and by PCR. *T. vaginalis* was excluded from the study.

Results:

No significant difference between the four transport media could be observed. The media performed equivalent in sensitivity. The clinical samples (SwabAX) were tested for BV and *Candida* vaginitis. The reference method yielded in 17 (17%) BV and 17 (17%) *Candida*, respectively; the respective results obtained by multiplex PCR were 14 (14%) BV and 25 (26%) *Candida*. Sensitivity and specificity for BV were 65% and 96%, respectively. The PCR detection rate for *Candida* was higher than by culture with a sensitivity and specificity 100% and 90%, respectively.

Conclusion:

Here, we present a syndromic based approach for timely and specific diagnosis of vaginitis. Usually, conventional culture methods take 48 hours; in contrast, using the VP reporting may take less than 4 hours. In addition, the panel allows for semi-quantitative interpretation of the results and the clarification of BV is no longer based on clue cells and *G. vaginalis* only. The lack of sensitivity in BV is rather due to the test specific algorithm, than not detecting the targets, e.g. *G. vaginalis*. However, further investigations are needed.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P133

First Evaluation of the Mueller-Hinton Rapid Medium for an Enterobacteriaceae Antibiotic Susceptibility Testing directly from positive Blood Culture.

D Bandeira; M Tritten; A Jacquet; HH Siegrist; R Lienhard
ADMEDMicrobiologie

Aim.

To set up a protocol to assess the validity of Mueller-Hinton Rapid, MHR® Medium for Kirby Bauer antibiotic susceptibility testing (AST) in 6 hours on enterobacteriaceae from positive blood culture.

Material and Method.

Mueller-Hinton agar (MH) (Axonlab, Baden, Suisse) and MHR® (i2a, Montpellier, France), media were tested on square plates for routine AST using SirScan (Axonlab, Baden, Suisse). Positive Blood culture isolates identified as enterobacteriaceae by Maldi-TOF were processed. A bacterial pellet was obtained by centrifugation in a gel tube of the positive blood culture, and enterobacteriaceae identified by Maldi-TOF were included. The pellet was then used to prepare a 0.5 McFarland inoculum. Two media were inoculated following the EUCAST procedure. Disk diffusion AST was incubated in the SirScan auto for 18 ± 2 hours on MH and MHR®. However, after 6 hours, the first automatic reading was recorded for MHR®. Antibigram pictures were analysed and interpreted according to EUCAST and disk diffusion diameter values were compared.

Results and Discussion.

From October 2016 to December 2016, we tested 47 strains *Escherichia coli* (N= 37), *Salmonella enterica*. (n= 5), *Klebsiella pneumoniae* (n= 4) and *Citrobacter freundii* (n= 1). Interpreted SIR concordance is the final aim of this study, however, as samples were mainly susceptible *E.coli* strains, we looked here at diameter variations. Results between MH, MHR at 6h and MH of routine Lab globally showed similar disk diffusion diameter values. Values on MHR showed substantially smaller diameters for Ticarcillin and co-amoxyclav disks at 6h compared to 16h. SIR interpretation was concordant for the majority of antibiotics. First there was no significant difference between MH and MHR after 16hours incubation with 99.3% concordance on 1235 values. Out of 1237 measurements on MHR 6h and 16h, 1181 (95.3%) were concordant and 58 (4.7%) appeared resistant at 6h and sensitive at 16h.

Conclusion.

It seems possible to give reliable information after 6h AST for the majority of tested antibiotics. However, extending species and AST resistance profiles are needed to assess its reliability.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P134

In Vitro Activity of Three Commercial Bacteriophage Cocktails against *Salmonella* spp. and *Shigella* spp. Isolates of Human Origin

OJ Bernasconi; V Donà; R Tinguely; A Endimiani

Institute for Infectious Diseases, University of Bern, Switzerland

Aims:

In developing countries, *Salmonella* and *Shigella* infections are responsible for million deaths annually and these mortality rates are prone to increase due to the emergence of resistance to usually implemented antibiotics. In this overall scenario, new alternative and cost-effective therapeutic approaches are needed. To our knowledge, data regarding the in vitro activity of commercial bacteriophage cocktails against large collections of *Salmonella* and *Shigella* spp. strains are still lacking.

Methods:

We investigated the activity of three commercial bacteriophage cocktails (INTESTI, Septaphage, PYO) against a collection of contemporary *Salmonella* (n=30) and *Shigella* spp. (n=20) isolated in Switzerland. Phage susceptibility was determined by implementing the spot test with the double agar overlay method. For all strains (n=50) susceptibility tests were performed in duplicate and at distinct days. Strains showing confluent lysis (+++), semi-confluent lysis (++), opaque lysis (+), and “taches vierges” (+) were defined as susceptible, whereas those showing no activity were defined as resistant.

Results:

The overall susceptibility of *Salmonella* spp. to INTESTI and Septaphage was 86.7% (of which 23/30 with “+++” or “++++”) and 76.7% (none of which with “+++” nor “++++”), respectively. With regard to *Shigella* spp., the overall susceptibility to INTESTI and Septaphage was 95% (of which 9/20 with “+++” or “++++”) and 55% (of which 3/20 with “+++” or “++++”), respectively. PYO showed to be active against only 10% (of which 2/30 with “+++” or “++++”) of *Salmonella* spp. but to 95% (of which 7/20 with “+++” or “++++”) of *Shigella* spp.

Conclusion:

We showed the distinct spectrum and lytic activity of commercial bacteriophage cocktails targeting *Salmonella* and *Shigella* species. In particular, Septaphage proved to be active against 68% of the tested strains, whereas INTESTI exhibited a strong response versus 90% of them. Therefore, our results seem promising, especially for the latter biopreparation against *Salmonella enterica* infections. Nevertheless, such speculation should be supported by further animal studies couplet with human clinical trials in order to confirm its efficacy and to prove its safety. The sum of these steps, if successful, could lead to the maturation - also in Western countries - of an alternative approach for the treatment of bacillary dysenteries and salmonellosis.

This work was supported by SNF grant No. 153377 due to AE.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P135

Honig: Bestimmung der antibiotischen Wirksamkeit

R Küttel¹; W Regli¹; S Gobeli²

(1) labor-zentral.ch;

(2) Institut für Veterinärbakteriologie

Honig ist ein altbekanntes Naturheilmittel, das in den letzten Jahren neu entdeckt worden ist. Seine schonende Wirkung bei Wunden und vor allem sein antibiotischer Effekt spielen in Anbetracht zunehmende Resistenzen gegen viele bakterielle Krankheitserreger eine wichtige Rolle.

In dieser Arbeit haben wir verschiedene Honigsorten auf antibiotische Wirkung gegen bakterielle Krankheitserreger untersucht. Es konnte gezeigt werden, dass insbesondere Manukahonig, und in geringerem Masse auch Wald- und Berghonig antibiotische Wirkung entfalten.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P136

Molecular confirmation of early syphilis: is *polA*, *tp47* or 16S rDNA the most feasible PCR target?

AA Noda¹; I Rodriguez¹; R Lienhard²

(1) Institute of Tropical Medicine "Pedro Kouri";

(2) ADMEDMicrobiologie

Aims.

In the last years, it has been a global re-emergence of this disease (Hook EW, 2016) with a strong impact in Public Health. Serological diagnostic often fails at very early stages of infection and sometimes becomes difficult for atypically located syphilitic ulcers. Consistent with the need of a rapid and early confirmatory syphilis diagnosis PCR-based methods are evaluated.

Material and Method.

During 5 years-period (2012-2016), 288 samples (264 genital swabs and 24 serums) from Cuban patients suffering genital ulcer diseases (GUD) were collected. Additionally 11 genital swabs and 21 sera from Swiss patients with suspicion of syphilis were tested. Finally throat samples (n=51) and genital samples (n=23) from Swiss patients known positive by PCR for any pathogen and negative for syphilis by serology were considered to challenge specificity. DNA eluate from clinical sample was obtained using the Qiamp Minikit (QIAGEN). Standard protocols based on TaqMan probes were optimized in order to improve the analytical sensitivity using DNA from Nichols reference strain. PCR protocols for *polA*, *tp47* and 16S rDNA were tested under the same reaction mix and run program conditions.

Results and Discussion.

Specificity reached 100% as none of the samples reacted in either one of the 3 PCR. In genital lesions, targeting *polA* was significantly more sensitive with 52% (137/264) positive rate than *tp47* or 16S showing respectively 44% (116/264) and 43% (114/264) positive rates. Hundred and three Cuban samples (39%) were positive for the 3 targets. *Treponema pallidum* DNA was detected exclusively on 25 samples (9.5%) targeting *polA* but only on 4 (1.5%) and 3 (1.1%) samples when using respectively *tp47* or 16S. Detection in sera was less sensitive and not significantly different targeting *polA*, *tp47* or 16S; we obtained positivity rate of 33% (8/24), 25% (6/24) and 17% (4/24) respectively. Only 1 sample was detected by the three PCR. On Swiss samples PCR confirmed 1 (4.8%) serum and 2 (18.2%) genital swabs positive for syphilis serology.

Conclusion.

None of the primers showed 100% concordance but *polA* showed the best results. PCR on ulcers give a rapid and specific answer in early and atypical sites of infection. Moreover it enables strains typing and *Treponema* epidemiology.

References

Hook EW. Lancet 2016; DOI: [http://dx.doi.org/10.1016/S0140-6736\(16\)32411-4](http://dx.doi.org/10.1016/S0140-6736(16)32411-4). Gayet-Ageron A, Combescure C, Lautenschlager S, Ninet B, Pernegera TV. J Clin Microbiol 2015;53:3522-9.

Natasha Arora, Verena J. Schuenemann, Günter Jäger et al. Nature Microbiology, Article number: 16245 (2016) doi:10.1038/nmicrobiol.2016.245



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P137

Emergence of clinical *Klebsiella pneumoniae* co-producing OXA-232 carbapenemase and RmtF 16S ribosomal methylase in Switzerland

S Mancini¹; M Tritten Arber²; R Lienhard²; L Poirel¹; P Nordmann¹

(1) University of Fribourg;

(2) ADMED Microbiologie

Aims:

Due to the emergence and dissemination of pan-drug resistant bacteria and the scarcity of novel molecules with antimicrobial activity, rapid and accurate detection of antibiotic resistance is of paramount importance for the timely choice of the appropriate therapy and for the implementation of measures to prevent outbreaks. The scope of the National Reference Laboratory for the Rapid Detection of Antibiotic Resistance and Resistance Mechanisms, also known as NARA (Nationale Referenz-Laboratorium zur Früherkennung neuer Antibiotikaresistenzen und Resistenz-Mechanismen), is to provide support for the rapid identification of emerging antibiotic resistances and related outbreaks at the national level.

Methods:

Using molecular techniques, clinical isolates have been used to investigate clonal relatedness and to identify antibiotic resistance determinants, such as extended-spectrum β -lactamases (ESBL), carbapenemases, 16S ribosomal methylase that confer broad-spectrum resistance towards aminoglycosides, fosfomycin and colistin resistance genes.

Results:

We report here an outbreak (February-May 2017) of *Klebsiella pneumoniae* ST231 recovered from five different local patients, two hospitalized in the medicine ward of a private hospital in Western Switzerland and two non-hospitalized at the private ENT physician facility. Molecular profiling showed that six clinical isolates were clonally-related. All isolates produced the ESBL CTX-M-15 and the 16S ribosomal methylase RmtF, both located on the same plasmid of ca. 145 kb in-size. Moreover, four isolates showed resistance to carbapenems and produced an OXA-48-like carbapenemase variant, namely OXA-232, whose gene was located into a 6,141-bp plasmid. Noteworthy, two out of the six clonally-related isolates were negative for OXA-232, and showed susceptibility to carbapenems. Strikingly, an outbreak of a *K. pneumoniae* clone with identical features was reported in Singapore in 2013.

Conclusion:

Here we report the first outbreak of a *K. pneumoniae* fully resistant to β -lactamases and aminoglycosides in Switzerland. Rapid detection by NARA led to the timely implementation of measures that may have contributed to prevent further spread of this multidrug resistant strain.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P138

Staphylococcus aureus cell-to-cell variation in growth-resumption after stress

C Vulin¹; N Leimer²; M Huemer²; M Ackermann¹; A Zinkernagel²

(1) ETH Zurich;

(2) Universitätsspital Zürich/ Universität Zürich

Staphylococcus aureus small colony variant (SCV) is a colony phenotype associated with chronic infections. Aiming to study the link between the observed phenotype and the relation to persisters or other growth-arrested bacteria we focused on the bacteria-to-bacteria variability in a recovered population, and survival after antibiotic challenge.

We recently showed that SCVs are selected by varying environmental factors including acidity. Thus, we assessed single cell fate at the microscopic and macroscopic level after low pH challenge including low pH media, intracellular localization and abscess material from both mice and patient. We followed bacterial growth over time using single-cell microscopy and automated agar plate imaging. We quantitatively compared the lag time and antibiotic challenge survival of previously stressed bacteria as compared to unstressed bacteria.

We found that previously stressed bacteria formed colonies with a wide range of colony radius, whereas the colony radius of previously unstressed bacteria had a smaller variability. By comparison of the lag time and growth rate distributions, we conclude that the small colony radius of bacteria surviving acidic stress resulted from delayed growth and not from slow growth or colony size limitation, a clear distinction from stable SCVs that are slow-growing due to auxotrophic defects. The proportion of bacteria with a long lag time correlated with the proportion of bacteria surviving an antibiotic challenge. Antibiotics further delayed first division time in stressed bacteria but not in control bacteria.

Macroscopically observed heterogeneous *Staphylococcus aureus* populations as well as cell-to-cell variation observed after stress are due to delayed growth. This growth delay then leads to increased antibiotic tolerance and survival.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P139

Transposition of Tn1213 Encoding the blaPER-1 Extended Spectrum β -lactamase

S Mancini; L Poiriel; P Nordmann

University of Fribourg

Aims:

PER-1 is an extended spectrum β -lactamase commonly identified in *P. aeruginosa* and *Acinetobacter* spp and Enterobacteriaceae. The blaPER-1 gene is widespread in particular in Turkey and Korea and has been also reported in other countries such as in France, Belgium, Japan, Russia, and Romania. Genetic analysis of several blaPER-1 genes reveals that the β -lactamase gene is part of a composite transposon named Tn1213 made by two distinct insertion sequences, namely ISPa12 and ISPa13. In-silico analysis reveals an 8 bp-long duplication site at the extremities of the two insertion elements, suggesting that the whole ISPa12-blaPER-1-ISPa13 structure (named Tn1213) might be able to move by transposition. The aim of this study was to analyze the functionality of the putative Tn1213 composite transposon.

Methods:

The ISPa12-blaPER-1-ISPa13 structure was cloned in a low-copy plasmid and transformed in *E. coli* strain RZ201 containing a conjugative pOX38 F plasmid. To select transposition events from the recombinant to the transfer proficient plasmid pOX38 conjugational mating-out assays were performed using the *E. coli* strain RZ201 as a donor and the azide-resistant *E. coli* strain JE53 as a recipient. The insertion sites of the ISPa12-blaPER-1-ISPa13 structure in the transposants was determined by using an inverse PCR-strategy. The transposition frequency was determined by dividing the number of the transposants by the number of the donor strains.

Results:

The mobility of the ISPa12-blaPER-1-ISPa13 structure was experimentally demonstrated in *E. coli*. A 9-bp instead of the predicted 8-bp duplication at the target site, representing the signature of transposition, was systematically generated. Transposition frequency was low and estimated to be around 1×10^{-8} .

Conclusion:

The results provide evidence of the functionality of the Tn1213 composite transposon and insights in the possible mechanisms responsible for the dissemination of the blaPER-1 gene in Enterobacteriaceae.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P140

Deciphering the Complete Deletion of the mgrB Locus in a Colistin-Resistant *Klebsiella pneumoniae*

OJ Bernasconi¹; V Donà¹; J Pires¹; E Kuenzli²; C Hatz³; V Perreten⁴; A Endimiani¹

(1) Institute for Infectious Diseases, University of Bern, Switzerland;

(2) Swiss Tropical and Public Health Institute;

(3) University of Zurich - Institute for Social and Preventive Medicine;

(4) Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern

Aims:

Most of the colistin-resistant (Col-R) *K. pneumoniae* isolates possess alterations of the two-component systems PhoP/Q and PmrA/B. These systems respond to environmental stimuli increasing the expression of the operon pmrHFIJKLM whose products are responsible for lipid A modifications leading to decreased affinity for polymyxins. This process is regulated by a negative feedback of mgrB. Thus, its inactivation leads to polymyxin resistance. The most common mgrB alteration is the insertional inactivation, but premature stop codons, missense or nonsense point mutations, as well as partial or complete deletion (Δ) of the mgrB locus are also described. In the latter case, no PCR amplification of the locus is obtained making the chromosomal Δ site unknown.

Methods:

During an ongoing survey, a Col-R *K. pneumoniae* strain (96R-Kp) was found in the stools of a woman collected after a trip to India. Colonies were identified using MALDI-TOF MS, while MICs were obtained using microdilution GNX2F panels (Trek Diagnostics). PCRs for detecting the mcr-1/-2 genes and to map the mgrB locus were performed. The strain underwent whole genome sequencing (WGS) with Illumina MiSeq.

Results:

96R-Kp showed to be resistant to both colistin and polymyxin B (MICs $>4 \mu\text{g/ml}$; Etest MIC for colistin of $32 \mu\text{g/ml}$), but not to other antibiotics. The mcr-1/-2 were not detected by PCRs. PCR mapping of the mgrB locus was also attempted with previously described primers, but no amplification was obtained. Based on the WGS results, 96R-Kp carried only the intrinsic blaSHV-1 and was of ST2261. The strain lacked a large region of 5.4-kb containing 10 genes including mgrB. According to a BLAST search, the mgrB locus of *K. pneumoniae* is included in a highly conserved $\sim 15\text{-kb}$ region. However, it is not clear why and what was the advantage for 96R-Kp to lose this essential locus.

Conclusion:

This is the first study reporting the whole genome sequence of a *K. pneumoniae* Col-R lacking a large region containing the mgrB gene, thus providing detailed knowledge on the chromosomal location and genetic environment of the excised site. We speculate that most of the strains previously described as PCR-negative for the mgrB locus have an identical or similar large deletion. Therefore, larger collection of Col-R *K. pneumoniae* strains should be analyzed to decipher both mechanisms and reasons of this complete deletion of the mgrB locus.

This work was supported by SNF grant No. 153377 due to AE.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P141

Complete nucleotide sequence of a multidrug resistance plasmid from an enterotoxigenic *Escherichia coli* K88 from pig

V Dona¹; PA Brand¹; S Gobeli¹; A Endimiani²; V Perreten¹

(1) Vetsuisse Faculty, University of Bern;

(2) University of Bern

Aims:

Pathogenic *Escherichia coli* is a predominant causative agent of diarrhea in pigs. The wide use of antibiotics in pigs has selected for multidrug-resistant (MDR) strains. The aim of our study was to determine the genetic location of the antibiotic resistance genes in a MDR enterotoxigenic *E. coli* (ETEC), revealing a MDR plasmid.

Methods:

The presence of toxin encoding genes and serotyping were performed on the *E. coli* strain 14/OD0056 isolated from pig with diarrhea in 2014 using PCR and agglutination test, respectively. Total DNA was extracted and whole genome (WGS) and plasmid sequencing (WPS) were performed with the Pacbio platform. After assembly, the scaffolds were corrected with read-mapped Illumina reads and further characterized implementing online platforms (i.e., Plasmid-, resistance-, and virulence gene-typing were performed with PlasmidFinder, ResFinder, and VirulenceFinder, respectively). MICs of 14 antibiotics were obtained by EUVSEC Sensitre plates and interpreted based on the EUCAST.

Results:

The *E. coli* isolate belonged to serotype K88ac and harbored genes encoding toxins EAST-1, STb, LT-I and adhesin F4, which are typically found in ETEC strains. WGS and WPS revealed also the presence of a 207 kb MDR IncHI1 plasmid. This plasmid harbored genes associated with resistance to aminoglycosides [*aac*(3)-IIa, *aph*(3')-Ic, *aadA*1, *strA/B*], beta-lactams (*bla*TEM-1), sulphonamides (*sul*1, *sul*2), trimethoprim (*dfrA*1) and tetracycline (*tetB*), reflecting the resistance phenotype. Additionally, genes encoding a quaternary ammonium compound efflux transporter (*emrE*) and tunicamycin resistance (*tmrB*) were found.

Conclusions:

This ETEC isolate harbored a plasmid conferring resistance to antibiotics that are used to treat *E. coli* diarrhea in pigs, including sulphonamides, trimethoprim, and tetracycline, but also aminoglycosides and quaternary ammonium compounds. The presence of genes conferring resistance to several classes of antibiotics and disinfectants on the same plasmid shows that the use of either one of these antimicrobials can contribute to the selection of such MDR elements in pathogenic *E. coli* from pigs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P142

Prevalence of *Bordetella pertussis*, *Bordetella parapertussis* and *Bordetella holmesii* in western Switzerland

R Lienhard¹; D Bandeira¹; M Tritten¹; K JATON²

(1) ADMED Microbiologie;

(2) CHUV-University Hospital

Background

The detection of *Bordetella* spp. in respiratory specimens is preferentially performed by PCR. The main targets are insertion sequences (IS) as IS481 for *B. pertussis*, IS 1001 for *B. parapertussis* and hIS1001 for *B. holmesii*. However, it has been demonstrated that the IS481 insertion sequence is not specific to *B. pertussis* and that it may also be found in *B. holmesii* strains giving false positive PCR results for *B. pertussis*. This is pointed out in the molecular external quality controls of Glasgow. Moreover this poor specificity may be quite misleading with regards to the epidemiology of whooping cough and the efficacy of the vaccine.

Objective

To estimate the prevalence of the different species of *Bordetella* spp. in the respiratory specimens in western Switzerland in order to determine whether there is a need to implement PCRs differentiating the species of *Bordetella* spp.

Methods

From 2010 to 2015, 1392 respiratory specimens were tested in parallel by real-time PCR targeting the IS481 and IS1001 insertion sequences for the detection of *B. pertussis* and *B. parapertussis* respectively. A third PCR, multiplex RIDA GENE of rbiopharm, targeting 3 genes, IS481, IS1001 and hIS1001, was used retrospectively on the DNA found positive for *B. pertussis* in order to differentiate *B. pertussis* from *B. holmesii*. Moreover, prospectively, during the period 2015 to August 2016, we analyze the results obtained on 216 other samples that were tested for by RIDA GENE only.

Results

A total of 1608 samples were tested and 214 were found positive for *B. pertussis* (13.3%) and 7 for *B. parapertussis* (0.43%). Of the 172 DNA that were found positive for *B. pertussis*, 165 were positive by RIDA GENE, giving a sensitivity of 95.8% (Kappa test = 0.81 (0.67-0.94).) Interestingly, no sample was positive for *B. holmesii*.

Conclusions

These results confirm that *B. holmesii* is not an epidemiological problem in western Switzerland. On the other hand, in rare cases, *B. parapertussis* could be detected. But at this stage, in first intention, a PCR targeting only one gene (IS 481+) is sufficient for *Bordetella* spp.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P143

Comparison of four different phenotypic assays for colistin susceptibility testing in Enterobacteriaceae and non-fermenting bacteria

N Joosse-Konrad¹; V Hinic¹; C Lang²; D Burki³; A Egli¹

(1) Universitätsspital Basel;

(2) Viollier;

(3) Kantonsspital Luzern

Aims:

The global spread of multi-drug resistant gram-negative bacteria increased the usage of second-line treatments including colistin. Therefore, reliable susceptibility testing for colistin is important in routine diagnostics. However, EUCAST issued a warning regarding disk diffusion and Etest for colistin antibiotic susceptibility testing (AST), since these test methods seem to underestimate resistance. We aimed to validate and compare the performance of four different diagnostic assays for colistin AST.

Methods:

In this interim analysis, 64 isolates were tested, including *Klebsiella* spp. (n=19), *E. coli* (n=17), *Hafnia alvei* (n=10), and *Acinetobacter* spp. (n=7). Four different phenotypic assays for colistin AST were compared: VITEK 2 (bioMérieux), MIC Test Strip (Liofilchem Diagnostici), UMIC (Biocentric), and Rapid Polymyxin NP Test (ELITechGroup). Minimal inhibitory concentrations (MIC) were interpreted according to EUCAST. Reading of the assays was performed according to manufacturer's instructions by two independent persons in a blinded fashion. Eazyplex® SuperBug mcr (Amplex) was used to determine the presence of the mcr-1/mcr-2 gene.

Results:

Out of 64 strains included in the interim analysis, 32 were colistin susceptible and 32 colistin resistant according to VITEK 2. Two isolates were mcr-1 positive, all were mcr-2 negative. In comparison to VITEK 2, MIC Test Strip showed the most discrepant results (n=4), whereas 3 of 4 strains showed a susceptible result in the MIC Test Strip. These 3 Enterobacteriaceae strains showed a MIC of 2mg/L close to the breakpoint (>2mg/L, R). In contrast, UMIC showed 2 discrepant and Rapid Polymyxin NP (excluding *Acinetobacter* spp. and *Pseudomonas* spp.) no discrepant result in comparison to VITEK 2.

In resistant strains, MIC Test Strip showed lower MIC values in comparison to VITEK 2 or UMIC (median 4mg/L, 12mg/L, and 24mg/L, respectively). The MICs were in 19/32 (60%) and 22/32 (69%) lower in MIC Test Strip compared to VITEK 2 and UMIC, respectively.

Conclusion:

All four diagnostic assays showed a minimal concordance of 94% for colistin susceptibility category. The highest rate of discrepant results was observed with the MIC Test Strip. In particular, determination of MIC values showed large differences between all test systems. These findings need to be compared with gold standard methods for MIC determination and within a larger cohort.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P144

Evaluation of rapid biochemical test β -Carba for detection of carbapenemase-producing Gram-negative bacteria

V Hinic; J Reist; A Egli
 Universitätsspital Basel

Background:

β -Carba test (Bio-Rad) is a commercially available phenotypic rapid test for the detection of carbapenemase-producing Enterobacteriaceae. The principle of this test is based on the change of color of a chromogenic substrate in the presence of carbapenemase enzyme activity. In this study, we assessed its performance on carbapenemase-producing Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.

Material/methods:

Fifty five well-characterized carbapenemase-producing clinical isolates were included in this study: 35 Enterobacteriaceae (8 KPC, 8 NDM, 7 VIM, 10 OXA-48-like and 2 NDM/OXA-48-like), 10 *Pseudomonas* spp. (6 VIM, 3 IMP and 1 SPM) and 10 *A. baumannii* (5 OXA-23, 3 OXA-40, 1 OXA-58 and 1 NDM/OXA-23). Additionally, 63 carbapenemase-negative strains were analyzed including 10 ESBL- and 12 AmpC-producing isolates. To ensure objective reading and interpretation, all strains were coded and tested blinded. β -Carba test was performed according to the instructions of the manufacturer. Apart from interpretation after 30 minutes, we evaluated the test at two additional timepoints: 1 hour and 1,5 hours.

Results:

The overall sensitivity and specificity of β -Carba test read after 30 min was 98.2% (54/55) and 92.1% (58/63), respectively. The calculated sensitivity in the 1h reading increased to 100% (55/55) and specificity decreased to 88.9% (56/63). After 1.5 hours the sensitivity was 100% (55/55), while the specificity further dropped to 85.7% (54/63). Interestingly, the carbapenemase-negative strains showing false positive results were almost exclusively *P. aeruginosa* (8 *P. aeruginosa* and 1 *Proteus mirabilis* ESBL-producer). The calculated sensitivity and specificity of the assay without *P. aeruginosa* were following: 30 min 97.8% (44/45) and 97.8% (44/45); 1h 100% (45/45), 97.8% (44/45); and 1.5h 100 % (45/45), 97.8% (44/45).

Conclusions:

The sensitivity of the β -Carba test estimated after 30 min of incubation (as recommended by the manufacturer) was 98.2%, but when evaluated after 1 hour, the sensitivity increased to 100%. Low specificity of the test (false positive readings) is found almost exclusively in *P. aeruginosa*, which can probably be explained by strong pigment production of these strains. In conclusion, β -Carba is a rapid and reliable test for detection of carbapenemases in Enterobacteriaceae, *A. baumannii* and *P. aeruginosa*.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P145

Nontuberculous Mycobacteria identification by MALDI Biotyper Mycobacteria Library 4.0 Bruker

C Maffiol¹; A Champion¹; A Ströhle¹; C Casanova²

(1) MCL Laboratories;

(2) Institute for Infectious Diseases, University of Bern, Switzerland

Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) has already demonstrated its ability to correctly identify nontuberculous mycobacteria (NTM). In 2016 the new version 4.0 of the Mycobacteria library of Bruker was released. The update covers now 159 of the currently known 169 Mycobacteria species with a higher sensitivity for mycobacteria identifications.

This study evaluates the efficacy of the new Mycobacteria library v. 4.0 and the utility of using MALDI-TOF MS for the identification of NTM in our clinical microbiology laboratory.

34 Mycobacterium spp. isolates from various clinical specimens previously identified by molecular techniques (16S rRNA or hsp65 sequencing) were tested. Identification was performed by MALDI-TOF following the recommended protocol for mycobacteria « MycoEX ».

The v.4.0 allowed the identification of all Mycobacteria species from 12 different species including rarely isolated species such as *M. asiaticum* and *M. bohemicum*, all with a high identification score >1.9.

Based on these results we would consider introducing the identification of NTM by MALDI-TOF in the routine clinical diagnostics of our laboratory.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P146

In vivo evolution of *Staphylococcus epidermidis* in a patient with pacemaker-associated endocarditis

V Dengler Haunreiter*, N Leimer*, D Wipfli*, C Rachmühl*, Y Achermann*, S Benussi, R Zbinden and Annelies S. Zinkernagel*

Universitätsspital Zürich

Staphylococcus epidermidis is a frequent cause of foreign body associated biofilm infections. *S. epidermidis* adhere to implanted biomedical devices such as prosthetic joints or pacemakers and form a biofilm. The bacteria embedded in the extracellular biofilm matrix are protected from antibiotics to a certain extent making treatment inefficient. Thus, these infections usually require surgical removal of the implant in order to cure the infection. We describe the case of a patient diagnosed with a *S. epidermidis* pacemaker-associated endocarditis. The patient had an infected pacemaker pocket and developed a bacteremia despite being under antibiotic therapy with rifampicin and ciprofloxacin. The pacemaker was removed after the bacteremia had developed. We phenotypically analyzed the *S. epidermidis* isolates recovered during the course of the persisting infection aiming to identify reasons for the treatment failure. The isolates differed in their morphological phenotypes but all belonged to the same multi-locus sequence type confirming an in vivo evolution and ruling out a reinfection with another strain. Later isolates from the pacemaker exposed to rifampicin had developed rifampicin resistance but were still susceptible to other antibiotics used. The bacterial isolates recovered from the electrode, the pacemaker pocket and the blood showed decreased biofilm forming capacity compared to isolates from the pacemaker at time of removal as quantified in in vitro assays. Bacteremia isolates clearly differed from all other isolates, in particular in formation of bacterial clumps. Altogether, the case highlights the ability of *S. epidermidis* to adapt and persist under antibiotic treatment without removal of the implant.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P147

Using MALDI-TOF MS typing for an outbreak investigation of *K. pneumoniae* in a neonatal intensive care unit

M Oberle¹; G Konetzny¹; C Mohr¹; P Meyer¹; C Ottiger¹; H Fankhauser¹; A Egli²; CA Fux¹; E Bucheli Laffer¹

(1) Kantonsspital Aarau;

(2) Universitätsspital Basel

Background:

MALDI-TOF MS typing is a cheap and fast method with potential to identify types within one species. An accumulation of *Klebsiella pneumoniae* infections in preterm infants (PI) with fatal necrotizing enterocolitis (NEC) in December 2015 and between February and May 2016 stimulated a prospective analysis in the neonatal intensive care unit (NICU). We investigated *K. pneumoniae* grown from clinical and surveillance samples (intestinal colonisation) in an attempt to identify potential nosocomial strains circulating in the NICU at the Cantonal Hospital of Aarau, Switzerland.

Material/methods:

164 stool samples from 56 PI born between February and October 2016 were collected and cultured on MacConkey agar. Peak lists with isolate-specific peaks were established by visually analysing the spectra to identify MALDI TOF MS types. These types were compared with pulsed field gel electrophoresis (PFGE). Hospital infection control specialists assessed the risk of transmission among positive cases by identifying potential within-hospital contacts based on a review of all available documents.

Results:

A total of 18/56 (32%) *K. pneumoniae* isolates were collected from PI. Five isolates from blood culture and one from a bronchial secretion were collected from six PI with fatal outcomes (4 cases with NEC). The remaining 12 isolates (one survivor with NEC) were collected from stool samples. One additional isolate was collected from the urine of a mother of one of the fatal NEC case. Overall 19 *K. pneumoniae* isolates could be allocated to 8 MALDI-TOF MS types (=type 1 - 8). Types 2, 3, 5, and 8 were nosocomially transmitted within the NICU but occurred only sequentially and became undetectable after 2 - 4 documented transmissions. The plausibility for nosocomial transmission was supported by the simultaneous hospital stays and/ or close vicinity. Type 4 was found in a mother and her child and type 7 was isolated in twins suggesting intra partum or familial transmission. The remaining two types were isolated from one individual each; an environmental or a familial source must be postulated.

Conclusions:

MALDI-TOF MS types with discriminating peaks showed excellent correlation with PFGE. Its use for a prompt and cost-effective outbreak investigation seems reasonable. But the impact and the specificity of this technique will be investigated further by comparing MALDI-TOF MS typing with whole genome sequencing analysis.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P148

PCR is significantly more sensitive than microscopy for the detection of protozoa in stool specimens

C Omlin¹; S Steiner¹; EC Claas²; M Altwegg¹; L Berlinger¹

(1) Bioanalytica AG;

(2) Leiden University Medical Centre

Aim:

In Switzerland microscopy is still the standard procedure for diagnosing gastrointestinal parasitic infections. However, microscopy has a limited sensitivity (50-95%), is laborious and requires skilled personnel. Pathogenic *Entamoeba histolytica* cannot be distinguished morphologically from apathogenic *E. dispar*, and cryptosporidia need to be ordered separately due to the different staining method. In contrast, molecular methods have proven to be highly sensitive and specific in the detection of selected protozoa. We were interested in the performance of the BD Max Enteric Parasite Panel (BD Max EPP) compared to routine microscopy for the detection of *Giardia lamblia*, *Cryptosporidium hominis/parvum* and *E. histolytica*.

Methods:

25 stool specimens tested positive by Biofire FilmArray Gastro Panel (FilmArray GP) were analysed by microscopy and BD Max EPP (*Giardia lamblia* n=10, *Cryptosporidium hominis/parvum* n=16, *E. histolytica* n=0). Selected samples from molecular external quality control (QCMD) and Swiss TPH together with some specimens being positive by microscopy were also analysed by BD Max EPP. 78 consecutive stool samples with request for protozoa microscopy were analysed to determine the specificity of BD Max EPP. Discrepancy analysis was performed with a molecular, laboratory-developed test by an external laboratory.

Results:

Comparison of BD Max EPP and microscopy to FilmArray GP showed a sensitivity of BD Max EPP of 100% for *G. lamblia* and 75% for *C. hominis/parvum*. Microscopy had a sensitivity of 66.7% and 62.5%, respectively. In the additional samples BD Max EPP detected 4/4 *Cryptosporidium* spp., 5/5 *G. lamblia* and 4/5 *E. histolytica* correctly. Only one of the 78 consecutive specimens was positive (*G. lamblia*, EPP positive, microscopy negative), illustrating the low prevalence of protozoa infections. The specificity of BD Max EPP was 98.7%.

Conclusion:

PCR is significantly more sensitive than microscopy in the detection of protozoa from stool specimens. The FilmArray GP has a high diagnostic specificity in the detection of *G. lamblia* and cryptosporidia as 8/10 *G. lamblia* and 16/16 cryptosporidia positive specimens could be confirmed by at least one of the methods.

Acknowledgement:

We thank Dr. H. Marti from the Swiss TPH for the *E. histolytica/dispar* samples



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P149

Computational models able to predict phage-bacteria relationships through genomics data analysis

D Leite¹; X Brochet¹; G Resch²; Y Que³; A Neves¹; C Peña-Reyes¹

(1) School of Business and Engineering Vaud (HEIG-VD), University of Applied Sciences of Western Switzerland (HES-SO) - SIB Swiss Institute of Bioinformatics;

(2) University of Lausanne;

(3) Bern University Hospital, University of Bern

The emergence and rapid dissemination of antibiotic resistance, worldwide, threatens medical progress and calls for innovative approaches for the management of multidrug resistant infections. Phage-therapy, i.e., the use of viruses (phages) that specifically infect and kill bacteria during their life cycle, is a re-emerging and promising alternative to solve this problem. The success of phage therapy mainly relies on the exact matching between the target pathogenic bacteria and the therapeutic phage. Currently, there are only a few tools or methodologies that efficiently predict phage-bacteria interactions suitable for the phage therapy, and the pairs phage-bacterium are thus empirically tested in laboratory. In this paper we present an original methodology, based on an ensemble-learning approach, to predict whether or not a given pair of phage-bacteria would interact. Using publicly available information from Genbank and phagesdb.org, we assembled a dataset containing more than two thousand phage-bacterium interactions with their corresponding genomes. A set of informative features, extracted from these genomes, form the base of the quantitative datasets used to train our predictive models. These features include the distribution of predicted protein-protein interaction scores, as well as the amino acid frequency, the chemical composition, and the molecular weight of such proteins. Using an independent test dataset to evaluate the performance of our methodology, our approach gets encouraging performance with more than 90% of accuracy, specificity, and sensitivity.

Carvalho Leite D.M et al. Lecture Notes in Computer Science, vol 10209. Springer, Cham:pp360-371



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P150

Enabling phyletic-based comparison and visualization of genomic islands for tens to hundreds of microbial genomes.

C Bertelli; AC Lim; A Spencer; JA Peltier; FS Brinkman
 Simon Fraser University

Aims

Genomic islands (GIs), commonly defined as clusters of genes of probable horizontal origin, are of interest since they disproportionately encode environmental and medically important adaptations, including novel metabolic abilities, virulence factors (VFs), and certain antimicrobial resistance (AMR) genes. While microbial genome sequencing has become rapid and inexpensive, current computational methods for GI analysis are not amenable for rapid, user-friendly, and scalable analysis of the thousands of genomes being sequenced. To fill this gap, we are developing IslandCompare, an open-source computational pipeline and web-based visualization resource to compare GIs across several to hundreds of bacterial genomes.

Methods

In IslandCompare, GI predictions are performed using two of the most accurate GI prediction tools based on nucleotide composition biases: SIGI-HMM(1) and the newly released IslandPath-DIMOB v1.0.0(2) that features a 11.7% increase in recall and a 5.3% increase in precision compared to the previous version. A bacterial core-genome phylogeny is computed using Parsnp(3) and pairwise regions of similarity between isolates are calculated with Mauve(4). Genomic islands are clustered in groups by sequence similarity using MASH(5) and a python implementation of Markov Clustering Algorithm.

Results

The IslandCompare web interface displays the core-genome phylogenetic tree in an interactive, user-friendly display that allows selection of monophyletic groups of bacteria. At each tree leaf, genomes are displayed linearly with groups of GIs highlighted in different colors. A zoom-in functionality permits further visualization of genes and their annotation. Finally, individual comparative views are available for each group of GIs for finer analyses.

Conclusion

IslandCompare will facilitate more robust, flexible analysis and comparison of GIs, complementing existing tools like IslandViewer(6), and enabling more efficient larger-scale analysis of infectious disease outbreaks and microbial evolution. The genome visualization developed may be adapted to visualize any genome feature for hundreds of phyletically-organized linear genomes, with broad applications.

References:

1. Waack, S. et al. BMC Bioinformatics 7, 142 (2006).
2. Bertelli, C et al. submitted.
3. Treangen, T. J., et al. Genome Biol. 15, 524 (2014).
4. Darling, A. C. E., et al. Genome Res. 14, 1394–1403 (2004).
5. Ondov, B. D. et al. Genome Biol. 17, 132 (2016).
6. Bertelli, C. et al. Nucleic Acids Res. 17, 132 (2017).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P151

A phenotypic algorithm for screening and confirmation of Beta-Lactam resistance in Enterobacteriaceae

R Höhener; J Gubler; U Karrer
 Kantonsspital Winterthur

Background:

Due to the worldwide dissemination of extended spectrum beta-lactamase (ESBL) and carbapenemase (CP) producing enterobacteriaceae it is of paramount importance in medical microbiology to detect resistant clinical isolates rapidly and with high sensitivity.

Methods:

We used a collection of 230 isolates of Enterobacteriaceae with known expression of different beta-lactamases to develop a diagnostic algorithm for the screening and confirmation of AmpC, ESBL and CP by Kirby-Bauer disc diffusion. For screening, we used inhibition zone diameters (IZD) of cefoxitin (FOX<18mm) for AmpC, ceftriaxon (CRO<23mm) and/or ceftazidime (CAZ<22mm) for ESBL and meropenem (MEM<25mm) for CP. For confirmation, inhibition zone diameter were compared between discs of antibiotics alone (cefotaxim, CTX; CAZ; FOX; MEM) and combidiscs containing the same antibiotic and a specific beta-lactamase inhibitor: cloxacillin for AmpC, clavulanic acid for ESBL and EDTA or boronic acid for CP. Temocillin (TMO<11mm) was used as an additional indicator for OXA-48 type CP. The performance of the Rapidec CarbaNP® was tested in CP-suspicious isolates.

Results:

According to our goldstandard, 133 isolates expressed ESBL, 92 AmpC (26 double-positive) and 42 were CP-positive. Of the latter, most isolates additionally expressed ESBL and/or AmpC. Overall, our algorithm identified 93.9% of all isolates correctly. ESBL- and AmpC-expression was identified with a sensitivity of 98.2% and 100% and with a specificity of 94.8% and 99.1%, respectively, if correctly identified CP-producers were excluded. Phenotypic CP-screening and confirmation demonstrated a sensitivity of 100% and specificity 96.3%, which was somewhat reduced by the lack of OXA-48 specific CP-inhibitors. Phenotypic CP-screening followed by confirmation with the Rapidec CarbaNP® test exhibited a sensitivity 95.2% and a specificity of 99.5%.

Discussion:

This phenotypic algorithm performed with a high sensitivity of 99.1% and an acceptable specificity 94.8% for the detection of ESBL, AmpC and CP. With this and its simple integration in the daily workflow, it seems very well suited for the purpose of beta-lactamase detection. The need for additional PCR-based CP-confirmation was limited to 20 isolates with possible OXA-48 expression (14 positive, 6 negative). Although the Rapidec CarbaNP® test could be used for CP-confirmation as well we experienced some problems in the detection of OXA-48 like CP.

References

- 1) Polsfuss et al., Clin Microbiol Infect. 2012;18:1194-204
- 2) Polsfuss et al., J Clin Microbiol. 2011;49:2798-803
- 3) Maurer et al., J Clin Microbiol. 2015;53:95-104
- 4) Nordmann et al., Emerg Infect Dis. 2012;18:1503-1507



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P152

***Pseudomonas aeruginosa* PAO1 gene expression profile in human burn wound exudate**

MR Gonzalez¹; B Fleuchot¹; P Jafari²; LA Applegate²; W Raffoul²; Y Que³; K Perron¹

(1) University of Geneva;

(2) CHUV Lausanne;

(3) Inselspital, Universitätsspital Bern

Background

Burn wound sepsis are currently the main cause of morbidity and mortality after severe burn injury. Bacterial pathogens such as *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Acinetobacter baumannii* impair patient recovery and lead to fatal issue. The specialized medical care required after burn injury faces major challenges to prevent bacterial development on the burn wounds. The Biological Biodegradable and anti-Bacterial Burn-wound Bandages (B5) platform, granted by Swiss TransMed, was created in order to improve the current biological dressing used to treat burn wound and to better understand the bacterial pathogenesis in a wound environment.

Aims

Our specific research topics are i) the pathogenicity characterization of the major burn wound pathogen *P. aeruginosa* while growing in burn wound exudate and ii) the analysis of burn wound exudate composition in order to establish of an artificial burn wound medium.

Results

We investigated the effect of human burn wound exudates (BWE) on the virulence of those pathogens. BWE were collected within 7 days after burn trauma from 5 burn patients. Growth assay in BWE showed that *P. aeruginosa* species were the only pathogens able to proliferate as opposed to *A. baumannii* or *S. aureus*. Synthesis of typical *P. aeruginosa* virulence factors such as pyocyanin and pyoverdine were even enhanced compared to standard laboratory medium. A whole genome expression analysis of *P. aeruginosa* PAO1 was performed using RNA-Seq approach, which allowed us to gain insight into various bacteria pathways expression profiles. A detailed chemical composition analysis of BWE was done, which enabled us to determine the major components of BWE and underline the metabolic modifications induced by burn trauma. These data are essential for the development of an artificial medium mimicking the burn wound environment and the establishment of an in vitro system to analyze the initial steps of burn wound infections.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P153

Native lipoproteins as subunit vaccines against *Mycobacterium tuberculosis*

K Becker¹, C Lin², M Aebi², P Sander¹

(1) Institute of Medical Microbiology, University Zürich, Zürich, Switzerland;

(2) Institute of Microbiology, ETH Zürich, Zürich, Switzerland

Mycobacterium tuberculosis possesses a unique and almost impermeable cell envelope in which lipoproteins are abundant. These proteins fulfil crucial functions in cell homeostasis and virulence and are immunodominant antigens. In mice, specific lipoproteins have generated a protective immune response against tuberculosis when administered as DNA-vaccine or as protein-vaccine produced in recombinant *E. coli*. However, both approaches ignore the native posttranslational modifications of these proteins. Di- or triacylation with partly species specific fatty acids at the N-terminus of lipoproteins forms a lipid anchor which acts as strong TLR-2 agonist thereby conferring adjuvant potential to posttranslationally modified lipoproteins. Next to their lipidation, mycobacterial lipoproteins have also been reported to be glycosylated. The mode and function of glycosylation on lipoprotein localization, stability and immunogenicity is poorly understood. By mass-spectrometry, we performed a detailed analysis of the glycosylation pattern and identified glycosylation sites of the *M. tuberculosis* model proteins LppX and Mpt83 heterologously expressed in slow- and fast-growing mycobacteria. Glycosylation deficient lipoproteins were generated by site-directed mutagenesis in order to assess the function of this second posttranslational modification. While LppX possesses minor glycan moieties with up to three hexoses, Mpt83 is more extensively modified. Immunization with both proteins containing their full set of native mycobacteria-specific posttranslational modifications is performed to investigate a putative role of lipoprotein lipidation and glycosylation in immunogenicity and protection.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P154

Organic Acid Production by Fungi: Comparison on Various Media and Effect of the Interaction with Bacteria

F Palmieri; S Bindschedler; P Junier

University of Neuchâtel

In fungi, low molecular weight organic acids (LMWOA) production can have important roles in processes as diverse as pathogenesis, competition, mineral weathering or lignocellulose degradation. More recently, LMWOA have been identified as being involved in the interaction between fungi and bacteria. This is particularly true in the case of oxalic acid, especially in soils. Several factors can influence LMWOA production. One of those is the availability of divalent cations. They trigger LMWOA production either as enzymatic co-factors or as a detoxification mechanism.

The aim of this study is to evaluate the production of LMWOA in fungi on different media, in the presence of divalent cations (i.e. Mn^{2+} or Ca^{2+}), as well as bacteria. In this way the effect of cations and interactive bacteria in LMWOA production can be assessed.

LMWOA production in selected fungi will be confirmed by using various culture media and subsequent acid detection and quantification. Co-cultures of fungi and soil bacteria that interact with fungi will then be performed. LMWOA production will also be assessed chemically and the production of mineral complexes in the presence of divalent cations will be measured with optical microscopy or SEM.

Half of the fungal strains initially screened produced large amounts of organic acids in all media tested. With this study, we can gain new insights concerning the factors influencing LMWOA metabolism in fungi and the effect of those metabolites in the interaction with bacteria.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P155

Discover the mechanism of sulfonamide biodegradation in wastewater treatment plants, in situ and on a molecular level

K Kroll¹; A Timm²; R Peschke²; M Roos-Majewsky³; H Kohler⁴; B Kolvenbach¹; P Corvini¹

(1) Fachhochschule Nordwestschweiz, Hochschule für Life Sciences (FHNW, HLS);

(2) Karlsruhe Institute of Technology (KIT);

(3) Universitätsklinikum Heidelberg;

(4) Eawag, Swiss Federal Institute of Aquatic Science and Technology

In *Microbacterium* sp. strain BR1, which had been isolated from activated sludge, the ability to biodegrade sulfonamides and use them sources of carbon and energy was discovered. This strain was further investigated to understand the biochemical and molecular biological mechanisms of this process. The degradation of sulfonamides was found to occur via a typical ipso-substitution degradation pathway. Several genes were found to be involved in the biodegradation homologues of which could also be identified by DNA sequence analyses in other degrading strains.

The main focus of our research is the investigation of sulfonamide degradation in five different WWTP, two in Germany and three in Switzerland. These WWTP were sampled over the course of one year on a biweekly time interval. In the influent and effluent samples, we quantified 21 compounds, both sulfonamide antibiotic and potential metabolites by HPLC-MS to assess removal performances. We also looked into the ability of the different activated sludges to degrade sulfonamides by an assay in lab scale format using radiolabelled sulfamethoxazole. In addition, the abundance of the known resistance genes *sul1* and *sul2* were determined by real-time PCR.

Analysis of the parent compounds and respective metabolites indicates that the sulfonamide degradation pathway elucidated for *Microbacterium* sp. BR1 is contributing to sulfonamide degradation in the WWTP. Throughout the campaign, the sulfonamide removal efficiencies of the WWTPs showed a characteristic pattern for each WWTP. This pattern deviates from the generally accepted conception that the removal of micropollutants correlates with nitrogen removal processes implemented in WWTP. Interestingly, the removal performances in the WWTP deviated from results obtained for samples of the respective sludges in benchmark degradation assays. The apparent significance of the ipso-pathway could be deduced from detecting the specific metabolite 3-amino-5-methylisoxazole. Applying a multifactorial approach consisting of chemical analyses, biochemical assays with radiolabeled substrates, quantitative PCR and Next Generation Sequencing, we could contribute to a better understanding of the removal of sulfonamide traces during the wastewater treatment process.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P156

Functionality of fusion sites in chimeric methyl-accepting chemotaxis proteins is dependent on position, length and composition

V Maffenbeier; M Brunner; JR Van Der Meer
 Université de Lausanne

Classical bioreporter construction for ecotoxicology depends much on existing specific transcription factors and internalization of the ligand 1 (Robbens J. et al. Appl Microbiol Biotechnol 2010, 88:1007–1025). Chimeric methyl-accepting chemotaxis proteins (MCPs) offer an alternative approach for detecting ligands outside the cell. Hybrid MCP chimera can be produced that exploit the sensory capabilities of bacteria and link ligand-binding to de novo reporter gene expression. A large natural variety of MCPs exist, but the rules for functional chimera construction are not well known.

In order to determine the possibilities and constraints to create functional chimera we fused the ligand binding region of the Escherichia coli Trg galactose/ribose receptor at different positions with the signal transducer region of EnvZ in a conserved so-called HAMP domain. Functional signaling of the Trg-EnvZ hybrids is tested by expression of the *gfpmut2* gene under control of the *PompC* regulated EnvZ-OmpR phosphorylation cascade. E. coli carrying the different chimeric MCPs were exposed to varying ribose levels and fluorescence was measured as a direct proxy for functionality by flow cytometry.

Our results show that only some HAMP fusion positions produce functional signaling hybrids. Functionalities can be influenced by inserting one or two amino acids at the HAMP fusion position, and can be further improved by random mutagenesis of the fusion site. Fusion sites with hydrophobic amino acids were on average more likely to result in functional HAMP fusions. In order to show the generality of our approach we are expanding the construction of hybrid chemoreceptors to a fusion protein between the organic-acid ligand binding region of McpS from *P. putida* and EnvZ of *E. coli*.

Robbens J. et al. Appl Microbiol Biotechnol 2010, 88:1007–1025



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P157

Changing the ligand-binding specificity of *Escherichia coli* periplasmic binding protein RbsB by rational design and screening

D Tavares; JR Van der Meer
 University of Lausanne

Biosensors have proven to be a powerful and cheap tool for analytics of specific target molecules or conditions (e.g., toxicity). Bioreporter bacteria are genetically engineered to produce a measurable signal in form of a reporter protein in response to a specific target present in their environment. The design of bioreporter bacteria typically starts with known sensory/regulatory proteins, but it has been proposed that computational prediction of ligand-binding interactions in a well-known receptor protein could lead to design of mutant proteins with novel target recognition specificities. Here a mutant library based on the ribose binding protein of *Escherichia coli* (RbsB) was produced with the goal to obtain mutations which would permit binding of ribose-similar molecules such as 1,3-cyclohexanediol (13CHD). Rosetta simulation was used to predict critical amino acid residues and potential mutations in the RbsB binding pocket which might permit binding of the two new ligands. The result was a set of 2 million mutants containing one of 5 possible substitutions at each of 9 amino acid positions. The library was introduced into an *E. coli* expression strain, which carries a hybrid signaling pathway through which GFP is produced upon binding of the ligand by the (mutant) RbsB. For better reproducibility, clones were grown as individual microcolonies in alginate beads which were screened by fluorescence activated cell sorting (FACS) for gain-of-function GFP expression in presence of 13CHD. Alternate rounds of screening and separation were performed to enrich potential responsive mutants but to eliminate constitutive GFP producers. So far, six mutants have been isolated that result in up to 1.5x induction of GFP with 13CHD. These mutants completely lost the capacity to react to ribose. The RbsB mutants are currently being characterized in terms of periplasmic space expression by using direct peptide mass identification. Isothermal microcalorimetry on purified mutant protein confirmed the gain of binding to 13CHD and absence of binding to ribose.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P158

Disentangling metabolic functions of honey bee gut bacteria

L Kesnerova¹; P Engel¹; R Mars²

(1) Université de Lausanne;

(2) ETH Zurich

Gut microbiota carry out diverse metabolic activities, which are critical for establishing mutualistic interactions with the host and among community members. However, due to the complexity of the gut microbiota, it is highly challenging to identify the contribution of individual members to the overall metabolic activity of the community. Thus, it is currently unexplored how much of the metabolic output of the complete microbial ecosystem can be explained by the functions of its constituent species. To address this question, we focused on the honey bee gut microbiota, a relatively simple community having a long evolutionary association with its host. Using untargeted metabolomics, we first characterized overall metabolic changes between microbiota-free bees and bees colonized with a reconstituted community resembling the native honey bee gut microbiota. We then carried out mono colonizations to determine the contribution of individual community members to the overall metabolic changes in the gut. We identified 372 metabolic changes between microbiota-free and colonized bees, 299 of which could be explained by mono-colonizations. Most of the identified bacterial substrates originated from the pollen-diet of bees, including flavonoids, phenolamides, and omega hydroxy acids which are all major constituents of the recalcitrant outer pollen wall. Strikingly, distinct community members contributed to the conversion of these plant-derived compounds indicating substrate specificity and possible cross-feeding interactions. Fermentation seemed to be the major bacterial metabolism in the honey bee gut, as several organic acids accumulated in the presence of the gut microbiota. Moreover, we discovered that a specific symbiont of the community stimulates the production of host hormones and signaling molecules suggesting a direct impact on bee physiology and development. Overall, our study provides new insights into the metabolic functions of the bee gut microbiota and highlights the usefulness of high throughput untargeted metabolomics to study symbiotic interactions within microbial communities and with their host.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-immk.ch

P159

Immune stimulation by the gut symbiont *Frischella perrara* in its host the honey bee (*Apis mellifera*) (1)

O Emery; K Schmidt; P Engel

University of Lausanne

Honey bees possess a simple yet specific gut microbiota in which most of the bacterial community is composed of only nine species (2–4). Among these, *Frischella perrara* specifically causes the so-called scab phenotype which corresponds to a dark colored band that develops on the epithelial side of the pylorus, which coincides with the main ecological niche of *F. perrara* (5). In insects, the production of dark substances typically corresponds to melanization, a reaction which can be triggered in response to wounding or to pathogenic infections (6–9), raising the question whether the gut symbiont *F. perrara* induces an immune response from its host.

Our aim was to investigate the impact of *F. perrara* on honey bee gene expression in the gut of 10 days old worker bees. In order to do so, we conducted experimental bacterial mono-colonizations with either *F. perrara* or *Snodgrassella alvi* (i.e. another honey bee gut symbiont that does not cause the scab phenotype) and compared host gene expression in these conditions and in non-colonized bees using RNAseq. In order to determine if the same gene expression changes would also occur under hive conditions, we compared gene expression in the gut of bees taken from the hive which displayed the scab phenotype versus those which did not.

We show that colonization with *F. perrara* leads to a higher number of differentially expressed host genes relative to non-colonized bees in comparison to colonization with *S. alvi*. Interestingly, the most highly upregulated genes by *F. perrara* colonization correspond to immune responsive genes and we also observed upregulation of genes of the melanization cascade. In fact, GO categories related to the immune response were significantly enriched among upregulated genes in *F. perrara* colonized bees compared to *S. alvi* colonized bees, as well as GO categories related to transport mechanisms. Strikingly, many of the gene expression changes observed between mono-colonizations also occurred between hive bees with the phenotype versus without.

Our transcriptome analysis gives first insights of this particular host-symbiont interaction, providing evidence that the scab phenotype indeed corresponds to melanization and that *F. perrara* leads to a potent host immune response as well as possible changes in gut homeostasis. We hypothesize that this response may keep the number of *F. perrara* bacteria in check and that it may prevent subsequent gut colonization by pathogens.

References

1. Emery O et al. Mol. Ecol. 2017;26:2576–2590
2. Kwong et al. Nat. Rev. Microbiol. 2016;14:374–384
3. Engel P et al. Proc. Natl. Acad. Sci. 2012;109:11002–11007
4. Martinson VG et al. Mol. Ecol. 2011;20:619–628
5. Engel P et al. mBio 2015;6:e00193-15
6. Binggeli O et al. PLoS Pathog. 2014;10:e1004067
7. Cerenius L et al. Trends Immunol. 2008;29:263–271
8. Cerenius L et al. Immunol. Rev. 2004;198:116–126
9. Gallo MJ et al. PLoS Biol. 2004;2:e239



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P160

Phenotypic variation of a gut symbiont in honey bees impacts host colonisation and interbacterial interactions.

K Schmidt; P Engel

University of Lausanne

Most animals are associated with complex gut microbial communities influencing host metabolism, development and health. The gut microbiota of honey bees consists of a simple, but highly specialised bacterial community of 8 species. The longstanding evolutionary association between these bacteria and the host has resulted in a spatially structured community in which microbe-microbe and microbe-host interactions are likely of great importance to maintain homeostasis. One member of the honey bee gut microbiota, *Frischella perrara*, induces a characteristic immune response in the gut resulting in localised melanisation of host tissue (scab phenotype) and the production of antimicrobial peptides(1). We aim to unravel the molecular mechanism lying behind this specific host-microbe interaction and to understand how *F. perrara* impacts other gut bacteria. We found that *F. perrara* exhibits two colony morphologies during in vitro cultivation: yellow and white. These morphologies have been observed in divergent *F. perrara* strains isolated from bees. Thus, we started to characterise phenotypic differences between these two colony types that may be relevant for the ecology and function in the bee gut. Monocolonisation of microbiota-free bees with *F. perrara* revealed striking differences between the yellow and white morphology. *Fp* yellow colonised the bee gut at high levels (comparable to *F. perrara* levels in hive bees) and also induced the characteristic melanisation response in the gut. In contrast, the white morphology revealed lower colonisation levels and did not induce a melanisation response. In addition, we found that *F. perrara* yellow is killing *E. coli* in vitro while the white morphology does not. We are currently investigating whether *F. perrara* might also interact with bee gut bacteria in the same way as with *E. coli*. We will carry out RNAseq analysis between the white and yellow morphology to identify genes that are differentially regulated and may explain the observed phenotypic differences in vitro and vivo. It will help to understand the genetic basis of how this gut symbiont interacts with the host, how it induces the scab phenotype, and competes with other bacteria for colonising the same niche. Phenotypic variation is likely a critical property of many gut bacteria to colonise and persist in multispecies communities. Our future experiments will focus on identifying possible advantages of *F. perrara* to exhibit phenotypic variation in the gut ecosystem.

1. Emery O. et al Mol Ecol. 2017;9:2576



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P161

Detection, Growth, and Survival of Enteropathogenic Escherichia coli (EPEC) in Soils

MC Montealegre¹; F Böni¹; S Roy²; MI Hossain²; L Caduff¹; T Navab-Danashmend¹; A Faruque²; M Aminul Islam²; T Julian¹

(1) Eawag, Swiss Federal Institute of Aquatic Science and Technology;

(2) International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)

Enteropathogenic *E. coli* (EPEC) is one of the main causes of diarrheal diseases in low- and middle- income countries. Understanding the factors that influence the fate of EPEC outside its host is crucial, as environmental persistence increases exposure, transmission, and infection risks. The objectives of this work are to: a) determine the prevalence of *E. coli* in natural soil samples collected in households (HH) in Bangladesh, b) investigate EPEC growth/persistence potential in soil and, c) identify main factors driving its survival. *E. coli* concentrations from soil and fecal samples from human (H), cattle (C) and chicken (CH) collected in 52 HH in Mirzapur, Bangladesh were estimated via pour plate method. *E. coli* and EPEC isolates were identified using the API-20E system and detection of the *eae* gene, respectively. The potential for growth/survival in soil microcosms of 4 EPEC (2H & 2C) isolates were studied in a standard soil and in 10 soils collected in the HH. To understand the impact of the indigenous soil microbiota on the dynamics of EPEC survival, autoclaved (A) or non-autoclaved (NA) soil were seeded with each strain at 10³ CFU/g of dry soil. With the aim of letting EPEC to adapt to soil before facing competition, A soil was first seeded and incubated for 7 days followed by mixing with NA soil (A:NA). The microcosms were maintained at 30°C and the fate of EPEC was followed for up to 84 days. *E. coli* was detected in 23/52 of the soil samples and in all the fecal samples, while EPEC was detected in 7 fecal samples (4CH, 2H & 1C). EPEC isolates survived for up to 84 days in the standard A soil, while in NA soil, EPEC were not detected at day 14. Adapting EPEC in A soil before facing competition in NA soil (A:NA) extended survival to 28 days. We did not observe statistically significant differences in the concentration of each strain at any time point. When we evaluated survival of 1 EPEC isolate in 10 Bangladeshi soils under the A:NA condition, the survival dynamics were dependent on the soil. In 4/5 soils where *E. coli* have been previously detected, EPEC was able to persist for 14 days after NA soil was spiked, while in 4/5 soils with no previous *E. coli* detection, EPEC was not detected as early as the time of NA spiking. Overall, these findings indicate that EPEC survival is highly dependent on the intrinsic soil characteristics. Further studies are warranted to elucidate the permissive/limiting factors that play a role EPEC persistence in soils.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P162

Tetrasphaera japonica, a model to study the metabolism of polyphosphate-accumulating organisms in real wastewater treatment plants?

M Cerruti, Holliger; J Maillard

Ecole Polytechnique Fédérale de Lausanne (EPFL)

Polyphosphate-accumulating organisms (PAOs) are responsible for phosphorus (P) removal in biological wastewater treatment (WWT). The metabolic model for PAOs in anaerobic-aerobic sequential batch reactors involves carbon uptake during the anaerobic phase, using the hydrolysis of polyphosphate (polyP) as energy source, followed by phosphate removal (and build-up of polyP) during the aerobic phase. A net phosphate removal balance from the water is achieved as PAOs are only able to grow during the aerobic phase. While *Candidatus Accumulibacter phosphatis* has been extensively studied [1] and is recognized as the major PAO in lab-scale WWT systems, *Tetrasphaera* spp. emerges as key player in P removal in real WWT plants [2-3]. However, the PAO metabolism of *Tetrasphaera* spp. remains unexplored. Therefore, the aim of this study is to shed light on this, both at the physiological and molecular levels.

Tetrasphaera japonica (Tja) was cultivated in various media, its growth was monitored at the level of protein content and its PAO metabolism was challenged in anaerobic-aerobic batch cycles by following phosphate and carbon in the culture supernatant. A method for quantifying polyP in Tja biomass is developed, as well as molecular methods to investigate the transcription of three key genes involved in P metabolism, *ppk1* (polyphosphate kinase), *pit* and *cysP/pit* (phosphate transporters).

Highest biomass production was achieved in modified R2A medium after three days of cultivation. Despite some difficulty in Tja behaviour during anaerobic-aerobic cycle experiments, when P release and carbon uptake were shown in the anaerobic phase, P uptake could clearly be observed in the following aerobic phase, confirming the PAO metabolism of Tja. Currently, the transcription of *ppk1*, *pit* and *cysP/pit* genes is under investigation during the anaerobic-aerobic cycles in order to understand the molecular background of PAO metabolism.

References:

- [1] He et al, 2011, *Microb Biotechnol* 4:603
- [2] Nguyen et al, 2011, *FEMS Microbiol Ecol* 76:256
- [3] Stokholm-Bjerregaard et al, 2017, *Front Microbiol* 8:718



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P163

The multi-dimensionality of social interactions in *Pseudomonas* communities

J Kramer; E Butaite; R Kümmerli

University of Zürich

Microorganisms frequently cooperate by secreting enzymes, biosurfactants, metal-chelating agents, and a variety of other costly metabolites. These extracellular products typically constitute public goods that can also benefit individuals other than the producer. Cooperation in the production of public goods can substantially increase community productivity. However, it is also vulnerable to ‘cheating’, since public goods can be exploited by individuals that do not contribute to the common pool of resources. Numerous studies have revealed mechanisms that constrain the fitness of cheats and thus promote cooperation despite this ‘social dilemma’. However, these studies typically consider just one model trait and a limited number of bacterial strains at a time. By contrast, natural bacterial communities usually feature interactions among multiple strains that simultaneously invest into multiple public goods. Intriguingly, the expression of public goods is often linked at the regulatory level, suggesting that changes in the expression of one public good could also affect the expression of other public goods. Thus far, however, it remains unclear whether and how such regulatory linkage affects interaction networks in natural bacterial communities.

Here, we shed light on this issue by investigating the public goods repertoire of 320 strains from 16 natural *Pseudomonas* communities. In particular, we screened each community member for the production of three public goods: pyoverdine, a siderophore used to scavenge iron; proteases used to digest proteins outside the cell; and biosurfactants used to move on surfaces. The production of pyoverdine was quantified based on its natural fluorescence. Conversely, proteolytic activity and biosurfactant production were quantified using a protease assay on milk-agar plates and a modified drop-collapse assay, respectively. Our preliminary results show that strains producing low levels of pyoverdine also invest little in the production of proteases. This positive regulatory linkage indicates that communities could consist of ‘super-cooperators’ (that produce multiple public goods) and ‘super-cheats’ (that are deficient for the production of multiple public goods). This combination would suggest that interaction networks in natural bacterial communities are predominantly shaped by competitive interactions. We will further explore this notion by investigating to what extent public goods are cross-used at the community level.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P164

Investigating the role of the microbial secondary metabolite streptol glucoside in the *Psychotria kirkii*-*Candidatus Burkholderia kirkii* interaction.

A Georgiou; A Bailly; L Eberl
 University of Zürich

An obligate plant-bacterium symbiosis was described between *Psychotria kirkii* and its bacterial symbiont *Candidatus Burkholderia kirkii*. Nodulated *P. kirkii* leaves produce significant amounts of the microbial secondary metabolite streptol glucoside (SG), a potent sugar-like allelochemical that suppresses the germination of other plant species but not of the host plant. *Arabidopsis thaliana* seedlings treated with sub-lethal SG doses display malformed, short roots with radially swollen tissues in the elongation zone. This phenotype is reminiscent of cell-wall remodelling defective mutants, such as *rsw3*, impaired in a glucosidase II α -subunit. To identify the potential target of this secondary compound, we characterized the wild type *A. thaliana* response to *P. kirkii* crude leaf extracts and pure chemically synthesized SG and streptol. We demonstrated that both streptol and SG have a strong inhibitory effect on *Arabidopsis* germination and root growth. In addition, microscope observations in the meristematic and elongation zone of the primary root of treated plants revealed a shorter meristematic zone with normal division rates but with an early increase in cell size, suggesting an effect on cell wall remodelling. Competition assays with exogenous sugar sources against SG treatments shown a significant restoration of the phenotype to near-control levels in the presence of monosaccharides, specifically glucose and fructose. In order to evaluate the SG inhibition potential against α - and β -glucosidases, enzymatic assays using *Arabidopsis* roots crude extracts and purified enzymes demonstrated that glucosidases are likely not the targets for this compound. Additional studies will be conducted with a range of halogenic-derivatives in order to assess potential cell-wall remodelling protein targets such as β -expansins, xyloglucan modifying enzymes and other endoglucanases.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P165

Immobilization of laccase on Relizyme supports and its application for removal of pharmaceuticals from municipal wastewater

M Cvancarova; F Bonacci; L Girardin; P Corvini
 FHNW

The aim of this study is to investigate biodegradation of various pharmaceuticals by laccase. Laccase is an extracellular enzyme which can be produced by white rot fungi and have already been applied in the successful removal of various persistent organic micropollutants [1-3]. Laccase from *Pycnoporus sanguineus* was immobilized onto HFA Relizyme resin beads. The resin has two functional groups. First group (ethylendiamino) is able to promote the physical adsorption of proteins and the second group (epoxy) is responsible for covalent binding of the enzyme [4]. Immobilization has been previously shown to significantly stabilize enzymatic activity [5-6]. In this study the municipal wastewater was spiked with 9 common pharmaceuticals (500 ng/L of each compound) and the efficiency of the immobilized laccase to remove these micropollutants was tested in a batch reactor. To determine residual concentrations of the micropollutants the samples were preconcentrated using SPE HLB Oasis car-tridges and analyzed by LC-MS. The first results indicate that celiprolol and atenolol acid were significantly degraded by laccase in 24h of incubation. Diazepam and niflumic acid were removed by adsorption onto the resin support which reached 70 and 97%, respectively. Elimination of amisulpride was not achieved by the laccase. Continuous packed bed reactor (PBR) with the solid biocatalyst is currently tested. PBR is simple to operate in comparison with e.g. membrane bioreactor [7] and hence it could be a promising tool to increase the applicability of laccase in bioremediation processes.

References:

- [1] Fernando T. et al. *Appl Environ Microbiol* 1990;56:1666.
- [2] Cajthaml T. et al. *Folia Microbiol (Praha)* 2008;53:289.
- [3] Čvančarová M. et al. *Chemosphere* 2012;88:1317.
- [4] Mateo C. et al. *Nat Protoc* 2007;2:1022.
- [5] Mateo C. et al. *Biochem Soc T* 2007;35:1593.
- [6] Zimmermann YS. et al. *Appl Microbiol Biotechnol* 2011;92:169.
- [7] Gasser CA et al. *Appl Microbiol Biotechnol* 2014;98:3305.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P166

Carriage of Extended-Spectrum β -Lactamase-Producing Enterobacteriaceae and Methicillin-Resistant *Staphylococcus aureus* in Pig Farms in Switzerland

J Kraemer¹; J Pires²; A Endimiani²; M Hilty²; A Oppliger³

(1) Lausanne University Hospital (CHUV);

(2) University of Bern;

(3) CHUV-Lausanne University Hospital

The aims of this study were to assess the change in prevalence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Swiss pig farms in 2015 compared to 2008 (Oppliger et al) and to estimate the presence of extended-spectrum β -lactamase-producing Enterobacteriaceae (ESBL-E) in pigs and pig farmers.

Twenty-nine pig farms in Switzerland were visited in 2015 and nasal swabs were taken from 77 piglets and 47 pig farmers. One air sample and one pig fecal sample were collected per farm and 25 farmers agreed to donate a fecal sample. ESBL-E were identified and assessed as described in Pires et al. and MRSA were identified according to Oppliger et al.

The prevalence of MRSA in nasal swabs from pigs and workers was 7.7% and 12%, respectively. MRSA was also found in air samples of 20% of investigated farms. Within each farm one individual spa type was found across all positive MRSA samples (found spa types: t034, t1594, t011 and t899). In the ESBL-E screening, 12% (3/25) of the farmers were carriers of ESBL-E and two piglet fecal samples were positive (6.9%). Nasal carriage of ESBL-E was detected in two pigs (2.6%). All ESBL-positive bacteria were identified as *E. coli* and nearly all β -lactamase genes belonged to CTX-M group 1. Isolates belonged mostly to ST10 (n=3), and the remaining isolates to ST131, ST58, ST59 and ST205. In four farms, there was a co-occurrence of MRSA and ESBL-E. No carbapenemase producers were found.

Our study demonstrates that the prevalence in pig farms has increased four-fold in 7 years (from 7% to 31%) for MRSA and that the ESBL-E prevalence was 24%. Additionally, the fact that MRSA spa-types are shared within the same farms indicates a possible transmission of these bacteria within this environment.

This work was supported by the Swiss National Foundation (SNF; grant 310030_152880 due to AO and MH). It was also partially supported by SNF grant 153377 (due to AE).

References:

Oppliger A. et al. Appl Environ Microbiol 2012 :78 :8010

Pires J. et al. Front Microbiol 2016 :7 :1069



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P167

Production and reconstitution of the flavin-binding domain of PceC, a membrane-bound flavoprotein possibly involved in organohalide respiration

G Buttet; M Willemin; M Schreier; C Holliger; J Maillard
 Swiss Federal Institute of Technology (EPFL)

Organohalide respiration (OHR) is a bacterial energy metabolism taking advantage of halogenated compounds – such as tetrachloroethene (PCE), a major groundwater pollutant – as terminal electron acceptors. Three major models of the electron-transport chain involved in OHR exist [1], however many redox components are not yet identified or remain unexplored. The PceC protein is encoded in the pceABCT gene cluster of *Dehalobacter restrictus* and *Desulfitobacterium hafniense* and was initially predicted to be a membrane-bound regulatory protein [2]. However, detailed sequence analysis revealed that it may harbour a covalently attached flavin mononucleotide (FMN) cofactor and resembles some redox enzymes involved in electron transport chain of other respiratory pathways. The overall aim of this study is to characterize PceC and obtain first insight in its involvement as redox partner in OHR metabolism.

After several unsuccessful trials, the FMN-binding domain of PceC (PceC-FBD) was produced as inclusion bodies in *E. coli*, denatured in urea and successfully reconstituted in vitro with the use of Ftp1, a flavin-transferase of *D. hafniense*. Dialysis reconstitution baths with decreasing concentration of urea revealed to be the most effective way to bring FMN into PceC-FBD, and thus make it soluble. Mass spectrometry analyses unambiguously confirmed the presence of FMN attached to the predicted threonine residue (Thr168) of PceC. Initial characterization of the redox properties of reconstituted PceC-FBD by cyclic voltammetry suggests that it could participate in transferring electrons to PceA, the key catalytic subunit in PCE reductive dehalogenation.

Additional evidence in electron transfer is needed and will be addressed in the next future. Also the native membrane topology of the FMN-binding domain of PceC protein is currently under investigation.

References

- [1] Mayer-Blackwell K. et al. In Organohalide-respiring bacteria, Springer 2016.
- [2] Maillard J. et al. Environ Microbiol 2005;7:107.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P168

Biotechnology for the preservation of archaeological waterlogged wood

M Albelda Berenguer¹; M Monachon¹; C Jacquet¹; P Junier¹; C Rémazeilles²; EJ Schofield³; E Joseph⁴

(1) University of Neuchâtel;

(2) University of La Rochelle;

(3) The Mary Rose Trust;

(4) University of Neuchâtel/HES-SO

Aims

Archaeological waterlogged wood encounters serious problems after excavation due to the accumulation of sulfur and iron compounds [1,2]. Exposure of these compounds to oxygen results in salts precipitation and acidification, causing structural damage [3]. In order to overcome this phenomenon, the aim of this study is to develop an extraction protocol of sulfur and iron compounds using a biological approach. Two different strategies are proposed: the oxidation of iron and sulfur species by selected bacteria and, the removal of ferric iron using microbial siderophores.

Methods

Thiobacillus denitrificans was used to oxidize sulfur compounds commonly found in waterlogged wood. Oak wood samples impregnated with a solution containing iron and sulfur were used to assess the efficiency of the bacterial treatment. The model wood samples were characterized before and after treatment with environmental scanning electron microscope coupled with X-ray energy dispersive spectroscopy (ESEM-EDS) and μ -Raman spectroscopy. Additionally, synchrotron-X-ray fluorescence (Sy-XRF) allowed the distinction of the oxidation state of sulfur present in the wood. The formation of sulfate ions by bacteria was also measured by ion chromatography. Finally, Fourier transform infrared (FTIR) spectroscopy was carried out to assess the possible consequences of the biological treatment on the wood structure. In addition, the siderophore production of selected bacterial strains was evaluated for iron extraction.

Results

Before treatment, mackinawite (FeS) and mineral sulfur (α -S₈) were detected in the impregnated wood. Sy-XRF maps showed mostly reduced sulfur. After treatment with *T. denitrificans*, mineral sulfur was observed but not mackinawite. Also, the presence of oxidized sulfur was predominant in Sy-XRF maps. The formation of sulfates was then confirmed by ion chromatography. Furthermore, the lignin/carbohydrates ratio obtained from FTIR spectra was not significantly different between untreated and treated samples, indicating that the bacteria induced no degradation of wood cells. Additionally, some strains showed high ability to complex ferric ions and further experiments are ongoing to isolate these compounds.

Conclusion

These results showed that *T. denitrificans* is able to metabolize sulfur compounds present in wood. This suggests the feasibility of an alternative biotechnological procedure for the preventive extraction of sulfur species from archaeological waterlogged wood.

Acknowledgements

The authors would like to acknowledge the University of Neuchâtel for overheads funding 8.2, and the Swiss National Science Foundation for the founding of MICMAC (MICRobes for the Archaeological wood Conservation, PP00P2_163653 / 1, 2016-2020) project.

References

- [1] Sandström M. et al. Nature 2002;415:893.
- [2] Fors Y. et al. Chem Soc Rev 2006;35:399.
- [3] Schofield EJ. et al. J Cult Herit 2016;18:306.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P169

Evolution of microbial communities and nutrient removal performances in aerobic granular sludge sequencing batch reactor during change of substrate

A Adler

Ecole Polytechnique Fédérale de Lausanne (EPFL)

Aerobic granular sludge (AGS) is a promising alternative wastewater treatment to the conventional activated sludge system. As AGS has enhanced settling abilities and provides different redox conditions across the granules at the same time, the processes based on AGS allow substantial space, energy and chemical products savings. Basic understanding of this processes has mainly been obtained in laboratory-scale studies with soluble synthetic wastewaters. Yet, the microbial communities obtained with this simple substrates appears to be significantly different from those growing in reactors treating real wastewater. The aim of this study is to increase our understanding on the influence of hydrolysable organic matter on these microbial communities and their metabolism. The wastewater composition of an AGS sequencing batch reactor was progressively changed, from volatile fatty acids (VFA) to a mixture of VFA, glucose and amino acids. In a second step, monomeric compounds (glucose and amino acids) will be replaced with their polymeric form (starch and oligo-peptides). After the first transition, the AGS had kept its high settling ability and an efficient phosphorus- and nitrogen-removal was recovered. Molecular analyses showed a clear shift of the microbial community from Betaproteobacteria to Actinobacteria. Further analysis will reveal how the metabolism of the AGS was impacted by these changes in the influent composition.

A. Adler, E. Reynaert, M. Layer, N. Derlon, E. Morgenroth and C. Holliger, Influence of wastewater composition on aerobic granular sludge microbial communities and their nutrient removal performances, IWA Biofim Reactor Conference 2017, Dublin, Ireland



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P170

Metabolite toxicity promotes the evolution of substrate cross-feeding, but depends on initial frequencies

J Dolinšek; DR Johnson

Eawag, Swiss Federal Institute of Aquatic Science and Technology, ETH Zürich

Aims

A typical feature of metabolic pathways is that they produce and potentially accumulate toxic intermediate metabolites. One plausible solution to this problem is substrate cross-feeding, whereby a second genotype specializes at consuming the toxic metabolite, thus reducing its concentration and deleterious effects. Our goal here was to test whether a second genotype that consumes a toxic metabolite (specialist genotype) can invade into and coexist with a genotype that completely performs the metabolic pathway but transiently accumulates the toxic metabolite (completely consuming genotype). If the specialist genotype can invade, we determined the evolutionary consequences of such an invasion.

Methods

Our model system is based on the denitrifying bacterium *Pseudomonas stutzeri*, which can completely consume nitrate to nitrogen gas but transiently accumulates the toxic intermediate nitrite (completely consuming genotype). We constructed an isogenic mutant from this strain that cannot consume nitrate but can consume the toxic metabolite nitrite (specialist genotype). We then constructed assemblages of the two genotypes and asked whether they could coexist with each other.

Results

We found that the completely consuming and specialist genotypes could invade into populations of the other, and thus co-exist with each other via nitrite cross-feeding. Over the evolutionary timescales, however, the completely consuming genotype outcompeted the specialist genotype if (and only if) specialist genotype was initially rare. The underlying cause of this is that the completely consuming genotype rapidly evolved streamlined a metabolism where nitrite no longer accumulated, thus preventing nitrite toxicity and eliminating the necessary niche space for the specialist to invade into.

Conclusion

Our results demonstrate that metabolite toxicity promotes the evolution of cross-feeding, but this outcome depends on the initial frequencies of the two genotypes. Thus, the frequency of one genotype can have profound effects on the evolutionary trajectories of other genotypes.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P171

Antifungal drug susceptibility testing in *Malassezia* spp.

CKM Leong; A Buttafuoco; B Schmid; M Glatz; PP Bosshard

Universitätsspital Zürich

Aims:

Malassezia spp. are lipid dependent yeasts frequently isolated from mammalian skin. It is attributed a pathogenic role in common skin diseases such as atopic dermatitis and may occasionally cause severe systemic infections in infants or immunocompromised individuals. Severe skin diseases or systemic infections require topical or systemic antifungal treatment. No standardized guidelines for resistance testing in *Malassezia* spp. are currently available because they are slow growing and require specialized testing conditions.

We aimed to:

- (1) To optimize culture conditions of *Malassezia* species in broth media in conditions which are stable for colorimetric readouts
- (2) To determine the most effective antifungals for the treatment of *Malassezia* spp. infection
- (3) To investigate if some species of *Malassezia* are more susceptible to certain antifungals as compared to others

Methods:

An optimized broth dilution method together with the colorimetric indicator resazurin was adapted from NCCLS/EUCAST guidelines and used for the drug susceptibility testing of 11 commonly used antifungals. MICs were determined based on visual colour change and fluorescence readings. 13 reference and 40 clinical *Malassezia* strains were tested.

Results:

All strains showed intrinsic resistance to the echinocandin drug class as well as to griseofulvin. The azoles itraconazole, posaconazole and voriconazole were the most effective antifungals. Fluconazole had the widest MIC ranges and was the least effective drug for many strains, especially for strains of animal-host associated species. *M. furfur* had the widest range of MIC values for most drugs.

Conclusion:

We have developed an optimized broth microdilution assay compatible with the colorimetric indicator resazurin for the fast and efficient profiling of drug susceptibility in *Malassezia* spp. Drug resistance profiling of 53 strains of *Malassezia* spp. has shown that some species are intrinsically more resistant to some drugs than others. Voriconazole, itraconazole and posaconazole were found to be the most effective in inhibiting *Malassezia* growth. These results were consistent with known findings on *Malassezia* drug susceptibility and most strains tested were within published MIC ranges of the tested drugs.

Reference:

Leong C. et al. J. Clin. Microbiol. 2017. Apr 5. epub:JCM.00338-17



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P172

Dermatophyte drug susceptibility testing using optimized growth conditions and broth microdilution methods

R Curatolo; CKM Leong; B Schmid; M Glatz; PP Bosshard

Universitätsspital Zürich

Aims:

Dermatophyte infections are the most common fungal infection worldwide and affect up to 25% of the global population. For other clinically relevant fungi such as *Candida* spp., extensive studies on the profiles and mechanisms of antifungal drugs resistance have been carried out. However, information on the susceptibility of dermatophytes against antifungals and its influence on clinical outcomes of dermatophyte infection is limited and confounded by inconsistencies between test assay performance and interpretation. In this study, we aim to identify key parameters which hamper the correct execution according to the CLSI guideline and propose further methods for standardization and refinement.

Methods:

13 common antifungals were tested over a range of different growth conditions with strains of *Trichophyton rubrum* and *T. interdigitale* with a broth microdilution assay. For amphotericin B, MICs were read as the lowest concentration that prevented growth. For the echinocandins, the minimal effective concentration (MEC) was read as the lowest concentration that altered hyphal growth considerably. For all other antifungals, MICs were read as the lowest concentration that resulted in 80% reduction of growth as compared to the control. Inoculum quantitation was performed by plating 0.01 ml on Potato dextrose agar and counting 50-500 colonies.

Results:

Based on our comparisons, we identified inoculum density, ambient temperature during growth and incubation time as key parameters influencing the performance of dermatophyte MIC testing. Growth did not differ between inocula of 104 or 105 CFU/ml. However, an inoculum with 103 CFU/ml, as recommended by CLSI, resulted in lower MICs and insufficient growth as compared to the higher densities. Growth was slower at 25°C than at 29°C or 35°C. At 35°C reading was hampered by condensed water on the plate lid. An incubation time of 4 or 7 days was sufficient. It turned out that reading the MEC under a microscope as described by EUCAST was more reliable than by eye as mentioned by CLSI.

Conclusion:

Current guidelines are not optimized for dermatophyte drug susceptibility testing. We propose to use an inoculum density of 104 CFU/ml and incubating at 29°C. MICs and MECs (examined microscopically) can be read after 4 or 7 days.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P173

Evaluation of VITEK MS® for the identification of clinical molds and dermatophytes from solid cultures.

D Constantin; L Tissières Lovey; G Praz

ICHV

Aim

The aim of this study is to evaluate the performance of matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) for a rapid and correct identification of molds and dermatophytes from cultures of clinical samples.

Material and methods

59 positives cultures from reference strains (30 molds/29 dermatophytes) were tested according to the manufacturer's instructions as follows.

For inactivation, a circle of 1 to 2 cm diameter of culture was collected from a Sabouraud medium using a wet swab and transferred in a 2 mL conical tube containing 900 uL Ethanol 70%. After vortexing it was centrifuged at 10'000 - 14'000 g for 2 minutes. After decantation, the pellet was resuspended with 40 uL formic acid 70% and 40 uL acetonitrile. After another centrifugation at 10'000 - 14'000 g for 2 minutes, 1 uL of supernatant was deposited on spot(s). After complete drying, 1 uL of CHCA matrix was added. The sample was ready for MS.

Results

49/59 strains were correctly identified to the species level (83%) with a score higher than 99%.

5 strains (4 dermatophytes and 1 mold) were not identified.

5 strains were correctly identified to the genus level. Two species were not in the data base.

4 Trichophyton mentagrophytes were identified as T. interdigitale. Both belong to T. mentagrophytes group.

If the strain is not in the data base, no result is obtained avoiding misidentification. Some species as Fusarium are not in the data base.

Conclusion

For a first screening, this method is a promising routine tool. Compared with conventional morphology-based techniques, MALDI-TOF is relatively inexpensive, involves a rapid result turnaround time and yields more accurate results without the need for highly qualified staff.

The data base needs continuous improvements for better identifications of molds and dermatophytes.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P174

The *Pneumocystis jirovecii* Gsc1 catalytic subunit of the 1,3- β glucan synthase is sensitive to caspofungin

A Luraschi; P Hauser

Centre Hospitalier Universitaire Vaudois and University of Lausanne

Aim:

Pneumocystis jirovecii is an extracellular fungal parasite of clinical importance. The pneumonia it causes is the second most frequent life-threatening invasive fungal infection worldwide. The most efficient drug against this pathogen is cotrimoxazole. However, because the emergence of resistance toward this drug and the side effects it may cause in patients, the development of new drugs is crucial. Echinocandins are a promising class of antifungals that inhibit the catalytic subunit Gsc1 of the enzymatic complex involved in the synthesis of 1,3- β glucan, an essential constituent of cell wall in most fungi. Studies in rodent models suggested the efficacy of the echinocandin caspofungin to treat *Pneumocystis pneumonia*. Nevertheless, its efficacy against *P. jirovecii* in humans remains presently a controversial issue. The aim of this study was to assess the sensitivity of the *P. jirovecii* Gsc1 catalytic subunit to caspofungin.

Methods:

In absence of an established in vitro culture method for *P. jirovecii*, we used functional complementation of the *S. cerevisiae* GSC1 deletant. In order to ascertain the function and sensitivity of the *P. jirovecii* Gsc1, spot test on medium supplemented or not with caspofungin was used. In the fungal pathogen *Candida albicans*, resistance to echinocandins has been reported to be conferred by point mutations leading to amino acid substitutions. We used site-directed mutagenesis to introduce the corresponding mutations in the *P. jirovecii* gsc1 gene leading to F714S and S718P substitutions. Complementation with the *S. cerevisiae* GSC1 gene was used as control.

Results:

The *S. cerevisiae* GSC1 deletant showed an increased sensitivity to caspofungin compared to the wild type. In presence of the *S. cerevisiae* GSC1 gene, a total restoration of the wild type growth was observed. In presence of the *P. jirovecii* gsc1 gene, a partial restoration of the wild type growth was observed. The latter restoration increased in presence of one substitution (S718P), and increased more in the presence of the two substitutions (F714S + S718P).

Conclusion:

The decrease of sensitivity conferred by the substitutions shows that the *P. jirovecii* Gsc1 catalytic subunit is sensitive to caspofungin. This sensitivity should be quantified to evaluate if it is sufficient to be used in the clinical practice. Caspofungin would have to be used in combination with cotrimoxazole because it targets only the forms of *P. jirovecii* with a wall, i.e. the asci.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P175

Identification of mediators of antifungal tolerance in *Candida albicans*

E Delarze

CHUV-University Hospital

Antifungal tolerance can be defined as the ability of *C. albicans* cells to survive at high drug concentrations but without acquiring mutations associated with resistance. The mechanisms mediating drug tolerance are still not well understood. In this study we aimed to identify mediators of tolerance to fluconazole (FLC) using two different approaches. First, the tolerance profile of 26 clinical *C. albicans* isolates against FLC using the EUCAST drug susceptibility assay was assessed. Tolerant strains were identified by their ability to sustain residual growth after 24h at a drug concentration above the FLC resistance breakpoint ($> 4\mu\text{g/ml}$). This screening revealed different profiles grouped from low to high tolerance. These FLC-tolerant strains are candidates for further characterization by genetic and transcriptomic approaches and will be used to test the importance of drug tolerance in animal models. In a second approach, in order to identify genetic mediators of tolerance, we used a collection of 582 tetracycline-inducible overexpression barcoded strains, which were pooled and maintained under FLC pressure for five days of repeated subcultures. This strategy was used to enrich the pool in FLC-resistant and/or FLC-tolerant strains. After amplification and sequencing of all barcodes from the cultures, the fractional index of each strain in the population was calculated. The FLC susceptibility profile of enriched strains yielded the identification of two potential tolerance mediators (GZF3 and CRZ1). When overexpressed, these genes contributed to increase tolerance to FLC as compared to controls. The potential role of these two genes upon tolerance is now under investigation.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P176

DEMONSTRATING THE PRESENCE OF CLONAL INTERFERENCE IN CANDIDA ALBICANS

M Paxtot Bertran¹; S Matuszewski²; S Vuilleumier²; E Beaudoin³; AT Coste¹

(1) CHUV-University Hospital;

(2) École Polytechnique Fédérale de Lausanne (EPFL);

(3) University of Lausanne

Background:

Candida albicans is an opportunistic commensal fungus that can cause benign to severe systemic infection also called candidaemia. Despite the use of current antifungal drugs, candidaemia, continues to be fatal in up to 50% of cases worldwide, partially due to antifungal resistance. If mechanisms of resistance are well described (1), a better study of population dynamics and fundamental biology of *C. albicans* is still needed to understand the emergence and fixation of mutations responsible for antifungal resistance. Recent studies using mice infected with pool of *C. albicans* strains suggested the presence of a “pool” effect which may be assimilated to clonal interference in *C. albicans* population (2,3). This last phenomenon is known to participate in the fate of beneficial mutations such as point mutations with a selective resistance advantage in asexual populations.

Aim:

The aim of the present study was to identify clonal interference in pools of *C. albicans* strains in vitro and in vivo using *Galleria mellonella* as infection model.

Methods: A deep mutational scanning approach was used to highlight clonal interference using two *C. albicans* transcription factor mutants. These mutants were previously identified as behaving differently in pool and in single strain infections. They will be tested here in (i) two different pools of strains, (ii) in presence of the wild-type reference only and (iii) alone.

Results/Conclusion:

The relative proportion of each strain in pool was quantified using high-throughput sequencing and a FASTQ file processing pipeline developed during this study. No conclusive results were obtained with the two selected mutants. However, the experimental and analytical approaches used in this study represent a preliminary approach for future development on clonal interference in *C. albicans*.

References

- (1) Sanglard D. et al. FEMS Yeast Res. 2009 Oct;9(7):1029-50.
- (2) Vandeputte P. et al. PLoS One. 2011;6(10):e26962.
- (3) Amorim-Vaz S. et al. Front Microbiol. 2015 May 5;6:367.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P177

The effect of restriction-modification (RM) systems on the phenotype of *Burkholderia cenocepacia* H111

O Mannweiler; K Agnoli; L Eberl

University of Zurich

DNA methylation is known to be the major epigenetic modification mechanism in bacteria, protecting the genome and maintaining its integrity. It is carried out by RM systems that consist of methylases (M) and restriction endonucleases (R) responsible for methylation of 'self' DNA, and restriction of 'foreign' DNA (bearing different methylation patterns). Bacteria can also possess so called 'orphan' methylases that can influence important cellular processes like DNA replication, DNA repair and regulation of gene expression. So far little is known about the influence of RM systems on bacterial phenotypes.

We first carried out in silico comparisons of the RM systems present within the sequenced strains of the *Burkholderia cepacia* complex, a group of 18 closely related but metabolically versatile bacterial species, which are able to occupy a variety of environmental niches. This revealed the presence of two core RM systems within the Bcc. Using PacBio SMRT technology, we sequenced the methylomes of certain Bcc members, and also RM system mutants of *Burkholderia cenocepacia* H111. This allowed us to verify and assign the predicted motifs to their corresponding core methylases, and also identified a further palindromic motif, which could be the recognition site of a type I RM system.

We have investigated the impact of the H111 RM systems by comparing the phenotypes exhibited by H111 with defined single and multiple RM system mutants. Our preliminary results show that mutants lacking certain of the RM systems have a higher transfer efficiency rate compared to H111 wildtype, confirming that these systems contribute to protecting the genome against incoming DNA. We are currently constructing a RM system null-mutant in *B. cenocepacia* H111 to investigate the importance of methylation on phenotypes such as osmotic and oxidative stress, antifungal activity and pathogenicity.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P178

Maintenance of *Salmonella Typhimurium* cooperative virulence by horizontal gene transfer: a model for the evolution of social traits in bacterial pathogens

E Bakkeren; W Hardt; M Diard
 ETH Zurich

Aims:

Virulence in bacterial pathogens can be costly. In *Salmonella enterica* Serovar Typhimurium (*S. Tm*) there is a fitness cost associated with the expression of the Type Three Secretion System-1 (TTSS-1) [1]. *S. Tm* triggers inflammation via TTSS-1, creating a favourable niche in the murine gut. Since TTSS-1 expression is associated with a fitness cost, genetic variants (cheaters) can arise that profit from inflammation without paying the cost of virulence expression. Mutations in *hild*, the gene encoding for the central regulator of TTSS-1 expression, were found to arise within-host [2]. Horizontal gene transfer (HGT) of mobile elements encoding a functional cooperative allele may restore, or even lead to the emergence of cooperative virulence [3]. We aim to demonstrate this concept using *S. Tm* cooperative virulence as a model.

Methods:

We have cloned *hild* into P2, a conjugative plasmid in *S. Tm* SL1344 that is highly transferred in vivo. Using SL1344 carrying P2*hild* (pVir) as a donor and a genetically avirulent recipient strain (*S. Tm* 14028S Δ *hild*) that does not carry P2, we perform experimental HGT in the murine model for non-typhoidal Salmonellosis. To evaluate virulence at the clonal level, we perform a colony Western blot on clones from feces probing for SipC [2], a virulence factor regulated by *HilD*. An ELISA for lipocalin-2, a marker of inflammation, allows for a quantitative readout for the inflammatory state of the gut.

Results:

We show that HGT can restore expression of TTSS-1 in genetically avirulent recipient strains. Transfer of pVir in vivo is efficient, leading to 100% of recipients acquiring pVir by day 2 post infection. Clones of this transconjugant population are phenotypically virulent in vivo, triggering inflammation.

Conclusion:

HGT may be a mechanism by which cooperative virulence could emerge and be maintained when mutations causing cheating behavior occur.

References

1. Sturm A. et al. PLoS Pathog 2011;7:7.
2. Diard M. et al. Nature 2013;494:7437.
3. Smith J. Proc Biol Sci 2001;268:1462.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P179

Transfer of an integrative and conjugative element in *Pseudomonas* may be triggered by oxidative stress

R Moritz¹; F Delavat²; JR van der Meer¹

(1) University of Lausanne;

(2) Institut Européen de la Mer

Horizontal gene transfer is a common process among bacteria allowing them to acquire new capacities, including antibiotic resistance and specific catabolic abilities. The integrative and conjugative element (ICE) ICE_{clc} from *Pseudomonas knackmussii* B13 confers its host the ability to degrade 3-chlorobenzoate (CBA). The ICE_{clc} element has a particular lifecycle, consisting of a stable integrated form in the genome, occasionally excising, circularising and transferring by conjugation to a recipient cell in which it integrates the genome. Cells which can transfer the ICE have to go through a development phase which has been named transfer competence development and is initiated in a small proportion of cells under stationary phase after growth with CBA.

Here we are interested in studying the possible trigger(s) that favor development of the transfer competence state. One of the hypotheses is that the ICE tries to escape cells that are in bad shape in order to survive in a hopefully healthier cell. We thus tested whether oxidative stress is an indicator of cell health and correlates to activity of the ICE. An oxidative stress bioreporter was constructed placing the *gfp* gene under the control of the promoter PAHPC in *Pseudomonas putida* with or without ICE_{clc}. The functionality of the reporter was successfully calibrated using UV-A, paraquat and hydrogen peroxide. Next we tested whether growth on CBA is more stressful for cells than succinate. Indeed, exponentially growing cells on CBA display more fluorescence from PAHPC than succinate-growing cells. CBA thus seems to be stressful for the cells and may be the trigger for transfer competent cells in the following stationary phase. In future we will use time-lapse microscopy in order to deduce the life history of cells initiating transfer competence, which may correlate with them having undergone a higher oxidative stress in exponential phase.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P180

Characterization of the general stress response of the Alphaproteobacterium *Sphingomonas melonis* Fr1

L Gottschlich; M Bortfeld-Miller; JA Vorholt
 ETH Zürich (ETHZ)

The phyllosphere represents a harsh environment characterized by constantly changing conditions. Colonizing bacteria are able to counteract different stress stimuli with a specific as well as the general stress response (GSR). The latter leads to cross-protection against a variety of stresses. In Alphaproteobacteria, the Pak-PhyR-NepR-EcfG cascade is the core pathway regulating the GSR. Stress stimuli are sensed by PhyR activating histidine kinases (Paks). Subsequent phosphorylation of the response regulator PhyR leads to complex formation with the anti-sigma factor NepR and results in release of the alternative extracytoplasmic function sigma factor EcfG, which in turn leads to differential gene expression. In *Sphingomonas melonis* Fr1, several single domain response regulators, as well as the putative phosphatase PhyP have been identified as additional regulators. The single domain response regulator SdrG is especially important for a positive regulation of GSR.

Here, we used RNA sequencing experiments to gain further insights into GSR related transcriptional changes in *S. melonis* Fr1 and the regulatory cascade triggering the environmental response. The transcriptome of knockout strains lacking different regulatory core elements were compared to wildtype under GSR inducing conditions. In addition, transcriptional changes of wildtype and the EcfG knockout strain were correlated to each other under different stress conditions.

Analysis of the EcfG regulon revealed that many of the regulated genes relate to stress response. Genes regulated by the Paks, PhyR and SdrG are congruent with the EcfG regulon, thus demonstrating that the crucial elements of the regulatory network upstream of EcfG have been identified. In contrast to salt and oxidative stress, the exposure to ethanol stress was sufficient to induce differential expression of EcfG regulated genes. Notably, a combination of all three stresses had a synergistic effect, which suggests that exposure to multiple stresses is needed for full induction of GSR. Surprisingly, only the combination of the three stresses could reveal an unexpected regulatory link between GSR and motility/biofilm formation at the transcriptional and phenotypic level.

Identification of the EcfG regulon represents another step towards a complete understanding of GSR in *S. melonis* Fr1. This analysis also confirmed SdrG as a core regulator of GSR and therefore demonstrates the need for further characterization of its mode of action.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P181

Beyond blood cells: Bovine in vitro models for *Mycoplasma bovis* infection

C Josi¹; S Bürki¹; O Wellnitz²; P Pilo¹

(1) Institute of Veterinary Bacteriology, Vetsuisse Faculty, University of Bern;

(2) Institute of Veterinary Physiology, Vetsuisse Faculty, University of Bern

Mycoplasma bovis causes bovine mycoplasmosis. The major clinical manifestations range from pneumonia to mastitis, arthritis and otitis. *M. bovis* affects cattle worldwide leading to enormous economic losses in the dairy and beef industries. In Western Central Europe, an increase in the number of severe mastitis cases was reported in the mid-2000s. Subsequent studies demonstrated a parallel switch in the genotype of circulating strains that might be associated with the current mammary gland pathology. At the molecular level, there is limited understanding of the mechanisms of pathogenicity of *M. bovis* and host-pathogen interactions were primarily studied using primary bovine blood cells. Additionally, research mainly focused on the invasion of white and red blood cells, the modulation of the host immune response, cytotoxicity and the proliferation of bovine cells. To date little is known about the impact of *M. bovis* on other cell types present in infected tissues. For this reason, we are developing bovine in vitro systems to investigate host-*M. bovis* interaction using cell lines (MDBK: bovine epithelial kidney cells and Bomac: bovine macrophages) and primary cells (PECT: bovine embryonic turbinate cells and bMEC: bovine epithelial mammary gland cells). Two strains representative of the circulating genotypes were selected to perform the experiments.

Adhesion of *M. bovis* strains was assessed for all cell types tested. Cell invasion and persistence of *M. bovis* was observed in the four tested bovine cell types using the gentamicin-protection assay. Additionally, these infection models were used to assess the host response after *M. bovis* infection.

Adhesion capacity to the different bovine cell types was similar for both *M. bovis* strains. Nevertheless, differences in permissivity of bovine cells upon infection with the two *M. bovis* strains were detected more particularly concerning bMEC cells. Infection with *M. bovis* resulted in variable induction of apoptosis and cytotoxic effects depending on the cell type and *M. bovis* strain.

In summary, the findings concerning bMEC cells might be linked to the increased severity of mastitis cases of the newly circulating *M. bovis* genotype. In conclusion, thorough analysis of the host cell response after *M. bovis* infection in appropriate cell models could be an important step in understanding the mechanisms of pathogenicity of different *M. bovis* strains in different bovine tissues.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P182

Impact of HIV co-infection on human T-Cell epitope evolution of *Mycobacterium tuberculosis*

C Loiseau¹; D Brites¹; L Fenner²; S Gagneux¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) Institute of Social and Preventive Medicine

Human Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), is a leading cause of death worldwide, killing more people than any other infectious disease (1). Furthermore, with 25% of the TB burden caused by HIV/Mtb co-infection, HIV is an important driver of TB incidence.

Mtb transmission requires lung tissue destruction mediated by the host immune system. In HIV-negative patients, most human T-Cell epitopes are highly conserved, suggesting that immune recognition is required for successful Mtb transmission (2,3).

By depleting the CD4+ T-cells of its host, HIV changes the immunological environment in which Mtb evolves, therefore imposing a new selective pressure on the bacterium. In this study we explore how HIV co-infection affects the evolution of human T-Cell epitope regions in Mtb. We hypothesize that in an immunosuppressed environment, relaxed selection will drive the accumulation of mutations in human T-Cell epitopes of Mtb.

We are currently analysing a phylogenetically diverse collection of a few hundred Mtb whole genome sequences. We are focusing on the human T-Cell epitope regions from HIV-positive and HIV-negative patients. Using comparative genomics and sequence diversity metrics such as nucleotide diversity and dN/dS ratio, we are assessing whether epitope regions of Mtb evolving in HIV-positive TB patients are more diverse compared to HIV-negative TB patients. Furthermore, the diversity of the human T-Cell epitopes in Mtb isolates from HIV-positive patients is evaluated as a function of the degree of immunosuppression as measured by the number of CD4+ T-cell counts in a subset of samples.

We expect human T-Cell epitope regions to be enriched for non-synonymous mutations in HIV-co-infected individuals compared to HIV-negative individuals and that these differences will be more pronounced in isolates evolving in lower CD4+ T-cell counts.

The findings from this study will reinforce our current understanding of epitope conservation in Mtb and shed light on the mechanisms of host-pathogen interaction. If the epitope regions of Mtb from immuno-compromised patients are significantly more diverse than those from immuno-competent patients, this might indicate that the host immune system, through CD4+ T-cells, imposes purifying selection on Mtb which in turn profits from the recognition by human T cells. Furthermore, it would bring new insights which could be used in the design of TB vaccines in HIV co-infected population.

References

1. World Health Organization. Global tuberculosis report. 2016
2. Comas I. et al. Nature Genetics 2010 :42 :498
3. Coscolla M. et al. Cell Host & Microbes 2015:18:538



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P183

Characterisation of a novel membrane-targeting toxin delivered by the bacterial Type VI secretion system

G Mariano; K Trunk; S Coulthurst

College of Life Sciences, University of Dundee

The Type VI secretion system (T6SS) belongs to the category of one-step bacterial protein secretion systems and is widely distributed amongst Gram-negative species. T6SSs are encoded by large and variable gene clusters, however within these loci is possible to recognize fourteen genes that are strongly conserved. These genes encode fourteen highly conserved “core” components, named TssA-M and PAAR, which form a large, envelope spanning machinery, enabling delivery of toxins directly into eukaryotic or prokaryotic target cells¹⁻³.

To date, it has been shown that many anti-bacterial T6SS-dependent toxins can be categorized into different families: peptidoglycan amidase and glycosidase enzymes, phospholipases, probable membrane pore forming proteins and nucleases⁴⁻⁶ while other candidate toxins still have an unknown function. Moreover, these anti-bacterial toxins are encoded adjacent to specific cognate immunity proteins, which specifically binds the toxin to inhibit its activity. Previous work has identified one T6SS in *S. marcescens* Db10, which targets and efficiently kills other bacterial cells and plays a role in anti-bacterial competition^{5,7}. Many putative anti-bacterial toxins secreted by this T6SS have been identified. While some of these toxins have been characterized and their function has been determined, little is known about the others⁸. The aim of this project is to characterize one of these newly identified toxins, Ssp6, including validation of its role as an antibacterial toxin and its association with a cognate immunity protein together with initial investigation into its molecular function. By using co-culture assays, co-IP, fluorescence microscopy and FACS we confirmed that the toxin is indeed a T6SS effector and that inhibition of its activity in sister cells depends on direct interaction with a cognate immunity protein. Additionally, we have generated new insight into its mode of action against target cells, causing inhibition of growth in target cells. Furthermore, we were able to prove that Ssp6 is a membrane-targeting toxin, being able to alter permeability of target cell's membrane and to dissipate their membrane potential.

References

1. Durand E et al., Trends Microbiol., 22 (2014), pp. 498–507
2. Cianfanelli F.R. et al., Trends in microbiology, 2016. 24(1): p. 51-62.
3. Brunet Y.R., et al., PLoS Genet, 2015. 11(10): p. e1005545.
4. Alcoforado Diniz J et al., . Journal of Bacteriology. 2015;197(14):2350-2360.
5. English G et al.,Molecular Microbiology. 2012;86(4):921-936.
6. Russell AB et al., Nature. 2013;496(7446):508-512
7. Murdoch S.L., et al., Journal of bacteriology, 2011. 193(21): p. 6057-6069.
8. Fritsch, M.J., et al., Molecular & Cellular Proteomics, 2013. 12(10): p. 2735-2749.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P184

An interplay of two global second messengers regulates *Caulobacter crescentus* growth and behavior

V Shyp; BN Dubey; J Nesper; T Schirmer; U Jenal

University of Basel

Introduction/Aims.

Caulobacter crescentus is an oligotrophic bacterium with an asymmetric division cycle, which periodically shuttles cells between a motile swarmer (SW) and a sessile, surface attached stalked cell (ST) to optimize growth and survival in dilute nutrients environments. Second messengers play a pivotal role in *Caulobacter* cell differentiation and in the adaptation to external conditions. The accumulation of (p)ppGpp in response to nutrient deprivation extends the motile SW phase of the cell cycle thereby promoting bacterial spreading in the environment. In contrast, c-di-GMP promotes the SW-to-ST cell differentiation and growth on surfaces. How these two global signaling molecules interfere and how their antagonistic response is coordinated to integrate environmental and developmental control, has remained unclear.

Methods.

We used structural (X-ray crystallography, NMR) and biochemical analyses (Capture compound mass spectrometry, ITC, UV-crosslink assay) to study novel *C. crescentus* effector proteins binding to nucleotide second messengers. Using a molecular genetics approach, we investigated the function and role of one candidate protein in *C. crescentus* growth and behavior.

Results.

We identified and characterized a novel protein from *C. crescentus*, PcpA, which binds both (p)ppGpp and c-di-GMP. Structural analysis of PcpA showed that a (p)ppGpp monomer and a c-di-GMP dimer bind to the same ligand binding pocket with the guanine moiety of (p)ppGpp overlapping with one of the four guanine moieties of the c-di-GMP dimer. Together with biochemical binding studies, this indicated that the two ligands compete for binding of PcpA. Functional analysis demonstrated that PcpA blocks *C. crescentus* surface colonization in dilute environments by inhibiting the production of the primary *Caulobacter* surface adhesin. Moreover, PcpA promotes the adaptation of *Caulobacter* cells to nutrients downshift. Its function is stimulated by (p)ppGpp and is antagonized by c-di-GMP under conditions where (p)ppGpp levels remain low.

Conclusion.

We propose that in *C. crescentus* PcpA integrates nutritional signals via (p)ppGpp binding with developmental transitions via c-di-GMP binding. The identification of the first common target protein for c-di-GMP and (p)ppGpp opens up studies to uncover the molecular and cellular basis for this important second messenger interference in bacteria.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P185

The temperature-dependent essential genome of a bacterium across its entire growth temperature range

L Del Medico; M Christen; B Christen

ETH Zürich "Institute of Molecular Systems Biology"

Aims

We aim at identifying the complete set of genetic features a bacterial cell needs for sustaining growth across its entire growth temperature range. We study the cell cycle model organism *Caulobacter crescentus*, a mesophilic α -proteobacterium thriving at moderate temperatures from 5 to 40°C. We seek to find all genes that are essential for viability and growth of *Caulobacter* under any growth temperature and, in turn, to find genes whose encoded functions become conditionally essential, reflecting the bacterial response to temperature-induced challenges.

Methods

We use an unbiased transposon sequencing approach to probe genome-wide gene essentiality across the entire *Caulobacter* growth temperature range. We generated eight Tn5 transposon mutant libraries, each consisting of millions of *Caulobacter* cells harbouring a genomic transposon insertion. We subjected each mutant library to a different temperature selection in the range of 5 to 40°C. Mutants with transposon insertions in genes related to growth and survival are lost from the mutant pool. Retrieving the survivors and mapping all genomic transposon insertion sites via high-throughput sequencing, allows for an insertion pattern based classification of genes into essential and non-essential.

Results

From any temperature selection, we retrieved an average of 380'000 unique transposon insertions across the 4 Mb *Caulobacter* genome. Based on insertions patterns, we identified a set of 345 core genes being essential under any growth temperature. In contrast, 530 genes become conditionally essential, encoding temperature-dependent cellular functions. Of these conditionally essential genes, 138 genes are specifically required for survival under a low temperature regime. On the other hand, high temperatures require the specific functionality of 259 genes. Together, the core and conditionally essential genes encompass 25% of the entire *Caulobacter* genome. Using hierarchical clustering, we are able to group conditionally essential genes into functional modules required by the cell for adaption to different growth temperatures.

Conclusion

The herein generated transposon insertion data set allows us to draw the genetic essentiality landscape of *Caulobacter* with base-pair accuracy across its entire temperature growth range. Our findings highlight the dynamic nature of the essential genome of a bacterial cell and provide new insights into the cellular responses required to cope with temperature-induced challenges.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P186

Hfq RNA chaperone as a new anti-bacterial target to fight *Pseudomonas aeruginosa*

S Leoni; V Ducret; K Perron

University of Geneva

Antimicrobial resistance (AMR) represents a major threat that urgently requires the development of new antimicrobial drugs. One of the emerging strategies to efficiently tackle this issue is to target bacterial virulence, rather than aiming at the viability of the cell. To fight *Pseudomonas aeruginosa* infections, we investigated a new virulence target which may represent a resource against AMR.

Hfq is a RNA chaperone required for *P. aeruginosa* virulence which acts as an essential component for its environmental-sensing ability.

In order to find molecules capable to interact with the functionality of Hfq we used the 5'UTR of *phzM* mRNA, known to be a direct target of Hfq. This region was fused to the gene encoding an unstable *gfp* version and transformed into *P. aeruginosa*. In the presence of Hfq, no fluorescence was observed due to the translational repression mediated by Hfq. As control, when this fusion is transformed in an *hfq* mutant strain we observed an intense fluorescence. The screening procedure has been optimized for 96 wells plates and fungal extracts are currently under investigation.

This system has also been adapted to work in an *E. coli* nonpathogenic strain allowing the all scientific community to performed Hfq inhibitors screening.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P187

The Zur protein is involved in Zinc export in *Pseudomonas aeruginosa*

V Ducret; M Auberson; K Perron

University of Geneva

Zinc (Zn) is one of the most important metal for all living organisms. It plays a role either as structural or as catalytic component for several enzymes. For bacterial pathogens, Zn acquisition and Zn efflux are key processes controlling their survival, development, virulence and, most importantly, their antimicrobial resistance (AMR)

We have previously observed in *Pseudomonas aeruginosa*, an important opportunistic pathogen, that an excess of Zn induces the expression of the metal-inducible CzcRS two-component system (TCS). This, in turn, activates the expression of a metal efflux pump, induces carbapenem resistance and stimulates its virulence.

In order to understand how Zn homeostasis could modulate the pathogenicity of *P. aeruginosa* we recently investigated the Zn import system. The major uptake system for this metal is the ABC transporter called ZnuABC. It is composed of the periplasmic Zn binding protein ZnuA, the transmembrane channel ZnuB and the cytoplasmic ATPase ZnuC. The expression of znuABC is tightly regulated by the transcriptional regulator Zur that repress this import machinery in presence of Zn. Surprisingly we found that a zur mutant is strongly affected in the czcCBA export machinery expression. Using a panel of znuA, znuB and znuC mutants we found that the positive effect of Zur on Zn export is not due to a consequence of metal mislocalization. Moreover, qRT-PCR and western-blot experiments suggest that Zur is necessary for controlling the basal level of czcRS TCS expression.

Altogether these results suggest a new role for the Zn uptake-regulator, Zur protein. As a matter of fact, it appears to be involved not only within the Zn starvation response, but also during excess of this metal. Zur is therefore a putative global regulator of Zn homeostasis in *P. aeruginosa*. Hence, its role within the virulence and AMR ought to be investigated further.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P188

Deciphering the mechanisms of persister formation in *Brucella abortus*

S Mode; M Québatte; C Dehio

Biozentrum of the University of Basel

Despite antibiotic treatment, persistent and chronic infections have been observed during decades for many bacterial pathogens, independently from the development of antibiotic resistance. Accumulating evidence point towards the importance of transiently drug-tolerant persister bacteria for this manifestation. Persisters are cells that survive prolonged exposure to a bactericidal antibiotic despite being genetically susceptible. The gram negative bacteria of the genus *Brucella* are responsible for brucellosis (malta fever), a worldwide occurring zoonosis. In cattle, brucellosis can cause abortion, reduced fertility and reduced milk production leading to economic problems in endemic regions. Moreover, humans can also be contaminated by *Brucella* through contact with infected animals or by consuming raw dairy products. Human brucellosis causes intermittent bouts of fever, pain, headaches and/or weakness and can evolve into a chronic form causing serious complications. The current World Health Organization recommendations for human brucellosis treatment is a combination of streptomycin 1 g daily for 3 weeks and doxycycline 100 mg twice daily for 6 weeks. Despite this harsh therapy a high rate of relapse is observed, ranging from 5% to 15%, representing a significant morbidity factor. Importantly, the underlying reasons of this high relapse rate are currently unknown. Here we address the possible importance of transiently drug-tolerant *Brucella* in this context.

Although circumstantial evidences suggest that bacterial persistence plays a central role in *Brucella* pathogenesis, the presence of bone fide persisters in *Brucella* has not yet been reported in literature. The classical approach to assess and quantify the presence of bacterial persisters is to follow the killing kinetics upon addition of a bactericidal antibiotic to a growing culture. A resulting biphasic killing curve constitute the characteristic signature of persisters-containing culture, with a sensitive, rapidly killed population and persistent population, with much slower killing kinetics. Here we present the results from in-vitro killing of *Brucella abortus* by different antibiotics and present evidence for biphasic killing for at least two antibiotics, demonstrating for the first time presence of persisters in *Brucella* cultures. Further, we present our approaches to decipher the underlying mechanisms resulting in persister formation as well as their implication in *Brucella* pathogenicity.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P189

Determinants of *Caulobacter crescentus* flagellin glycosylation and flagellar assembly

S Ardisson

Department of Microbiology and Molecular Medicine, University of Geneva, Switzerland

Sialic acid and the closely related pseudaminic acid (Pse) are known essential components of capsular polysaccharides that can influence the virulence or symbiotic capacity of bacteria. While sialic acid produced by *Neisseria* species is involved in the evasion of the host immune system, Pse is required for an efficient symbiotic interaction of the α -proteobacterium *Sinorhizobium fredii* NGR234 with its host. However these sugars are also involved in protein glycosylation, particularly in the case of flagellin, the structural subunit of the flagellar filament, in several bacterial pathogens. We explored the function and cell cycle-regulation of flagellin glycosylation in the aquatic synchronizable α -proteobacterium *Caulobacter crescentus*, whose motility is under control of the cell cycle regulatory circuit and is conferred by a single polar flagellum in the non-replicative swarmer cell. The flagellum is shed when the swarmer cell progresses through the cell cycle and differentiates into a replicative non-motile stalked cell that will express and assemble flagellar proteins by the end of the cell cycle. Based on homology to components of the Pse biosynthetic pathway in *S. fredii*, we identified a Pse biosynthetic pathway in *Caulobacter*. Interestingly, our results show that Pse is not required for capsulation in *Caulobacter*, whereas flagellin post-translational modification by Pse is essential for export and assembly into a functional filament. The expression of the genes responsible for the Pse biosynthesis is under control of the cell cycle regulatory circuit. We identified a novel glycosyl-transferase required for flagellin glycosylation, which we are currently characterizing in term of function and regulation, and we succeeded in reconstituting *Caulobacter* flagellin glycosylation in a heterologous host. Finally, we are exploring whether Pse is used to glycosylate proteins other than flagellins and are deciphering how specificity is achieved.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P190

Evaluation of RIDAGENE Sapovirus and Astrovirus real-time PCR assays in Norovirus-negative clinical fecal samples.

A Wanzenried; J Huder; R Capaul; P Redli; J Böni; A Zbinden
Institute of Medical Virology

Aims

Norovirus (NoV) is the leading viral agent of acute gastroenteritis (AGE) across all age groups. With the availability and application of molecular assays capable of detecting a broad range of viruses, other enteric viruses such as sapovirus (SaV) and astrovirus (AstV) were increasingly identified as infectious agent of AGE. SaV and AstV were reported to affect children under the age of 5 years. In adults, there is limited data of SaV and AstV as most stool samples are investigated only for NoV. Thus, these pathogens might be underestimated as causative agents of AGE in adults. We sought to analyse stool samples for the presence of AstV and SaV, which were previously suspected for AGE caused by NoV but tested negative by specific real-time RT-PCR.

Methods

During January to February 2015 and September 2015 to January 2016, 152 clinical stool samples of the Institute of Medical Virology, University of Zurich, were retrospectively analyzed. All specimens had been previously tested negative for NoV group I and II by an in-house real-time TaqMan RT-PCR. The fecal samples were derived from patients with a mean age of 56.9 years and an SD of 19 years. The samples were evaluated by the commercial real-time RT-PCR kits RIDAGENE Sapovirus and RIDAGENE viral stool panel II (R-Biopharm, Darmstadt, Germany) including AstV, adenovirus and rotavirus.

Results

In total, 135 (88.8%) specimens were tested negative for SaV, AstV, rotavirus and adenovirus. In twelve specimens (7.9%), enteric viruses were detected either by the RIDAGENE Sapovirus kit or the viral stool panel II kit or both. Rotavirus was detected in four specimens (2.6%), AstV in three specimens (2.0%), adenovirus in three specimens (2.0%), respectively, and two specimens showed a co-infection of adenovirus and SaV (1.3%). In five (3.3%) specimens, the RT-PCR was inhibited.

Conclusion

The RIDAGENE Sapovirus and viral stool panel II kits are useful tools for the detection of enteric viruses other than NoV in fecal samples, i.e., SaV, AstV, rotavirus and adenovirus. Although the prevalence of SaV and AstV seems low in adults (3.3%), accurate identification of these pathogens is important since severe cases and outbreaks were reported.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P191

Real-time sequencing of clinically relevant RNA viruses

A Ramette; M Gorgievski-Hrisoho; M Terrazos; J Steinlin-Schopfer; P Bittel; F Suter; S Leib
University of Bern

Aims:

Although next-generation sequencing (NGS) technologies have revolutionized our understanding of microbiology, short-read technologies often cannot assemble complex genomes satisfactorily due to the presence of repetitive elements or of genomic rearrangements. In the case of Enteroviruses, which are RNA viruses that affect millions of people worldwide each year, PCR detection of enterovirus in the clinical microbiology laboratory is the most sensitive method for diagnosis, and is often complemented by Sanger sequencing of protein coding genes. Yet, point mutations and recombination events are frequent and can potentially lead to negative PCR results when new viral variants appear. In this study, we developed a wet lab solution and assessed bioinformatic pipelines to obtain whole genomes of viruses from various clinical samples within a minimum amount of time.

Methods:

We used the long-read single-molecule Oxford Nanopore MinION sequencing technology to provide genome-wide information on RNA viruses, and assessed the feasibility of direct RNA sequencing. The MinION apparatus is a pocket-size instrument that sequences strands of nucleic acids by monitoring changes in ionic current generated by single-stranded molecules threading through pores embedded into an electrically insulated membrane. MinION also offers the unique feature of being able to sequence RNA directly, rather than sequencing the products of reverse transcribed and PCR-amplified sequences.

Results:

We sequenced cDNA from various species of Enterovirus using the MinION platform and assessed its ability to sequence cDNA molecules directly or via additional amplification steps, with good accuracy in terms of abundance and distribution of sequence lengths. Long cDNA reads covering nearly the complete genomes (7-8 kbases) of the tested strains were obtained routinely within minutes to few hours, and further sample multiplexing enabled several genomes to be sequenced in parallel in a cost-effective way.

Conclusion:

Over 95% of the genomes of enterovirus were recovered with 97–99 % accuracy and the quick sample-to-answer turnaround time represents a timeframe amenable to actionable clinical and public health diagnostics.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P192

Enteroviruses in acute gastroenteritis patients in Switzerland

R Gosert¹; U Heininger²; HH Hirsch³

(1) University of Basel;

(2) University of Basel Children's Hospital;

(3) Universität Basel

Gastrointestinal infections have a major impact on morbidity and mortality worldwide, but the contribution of enteroviruses is unclear. To determine the magnitude of enterovirus infections in Switzerland, we investigated 677 stool samples from 504 patients submitted for gastroenteritis panel testing. Median age of the patients was 6.6 years (IQR 1.1-50.6; pediatric <18 years). By multiplex nucleic acid testing (NAT) using the Luminex xTAG gastrointestinal pathogen panel (GPP) and by quantitative NAT for entero-/poliovirus, we detected 334 pathogens including 42 co-infections in 291 samples resulting in a positive rate of 43% (291/677). The 291 positive samples originated from 250 individuals (157 male) at an average of 1.34 pathogen per positive patient. Pediatric patients contributed 69% (172/249) of the single infections and 81% (34/42) of the co-infections. Enterovirus was detected in 5.3% (36/677) of the samples, more abundant were only rotavirus with 18.6% (126/677) and norovirus with 12.1% (82/677), respectively. Enterovirus was mainly identified in children, with viral loads up to 1.4e8 Geq/mL (gram) feces. Clostridium difficile was detected in 5.5% (37/677) and Campylobacter jejuni in 2.2% (15/677) of the samples, respectively. Adenovirus, E. coli O157, Salmonella, Shiga toxin-producing E. coli (STEC), Shigella, Giardia lamblia, Cryptosporidium, and Entamoeba histolytica were found at a frequency of ≤6, while poliovirus, Vibrio cholerae, Yersinia enterocolitica, and Enterotoxigenic E. coli (ETEC) was not identified. In conclusion, enterovirus was detected in 5.3% of stool samples and in 24 infections identified as the only pathogen suggesting that enterovirus was the causative agent of acute infectious diarrhea.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P193

Organic carbon and nitrogen at the crossroads of fungi and bacteria mutualism

A Lohberger¹; A Lohberger²; J Spangenberg²; Y Ventura³; N Jeanneret³; S Bindschedler³; E Verrecchia²; R Bshary³; P Junier³

(1) Université de Neuchâtel;

(2) University of Lausanne;

(3) University of Neuchâtel

Roles of organic carbon (Corg) and nitrogen (Norg) as stabilising factors of the interaction between the ectomycorrhizal and saprophytic fungal genus *Morchella* spp. and the soil model bacterium *Pseudomonas putida* were investigated. In *Morchella crassipes*, a complex mutualistic interaction coined bacterial farming, has been previously described. During this interaction three phases were identified: dispersal of bacteria on the fungal mycelium, rearing by the fungus, and harvesting of bacteria. So far, it has been shown that the bacterium benefits during dispersal and rearing, whereas the fungus benefits during harvesting. However, a direct benefit for the fungus during the first two phases remains unidentified.

In this study, we further investigated a possible direct benefit for the fungus as a result of bacterial dispersal. We tested bacteria moving on the fungal mycelium in a medium containing Corg and Norg, which led to an increase in proteolytic activity by the fungal partner. This increase in proteolytic activity was a general feature of several *Morchella* spp., but required the presence of living bacteria. Comparing the biomasses of both partners as a proxy to fitness, we showed that a truly mutualistic interaction only appears when Corg and Norg are provided in excess. When changing conditions to Corg excess, the fungus took advantage, whereas with Norg without excess Corg, the bacterial partner is favoured. We conclude that the Corg/Norg ratio is one of the key nutritional factors to determine the outcome of interactions between soil fungi and bacteria.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P194

Phylogenetic analysis of PEDV as a requirement for the establishment of a diagnostic pan-strain PEDV real-time RT-PCR

P Rogger¹; H Stalder¹; C Kristen-Burmann²; G Tekes²; V Thiel¹

(1) Institute of Virology and Immunology;

(2) Institute of Virology

Porcine epidemic diarrhea (PED) is a devastating enteric disease especially of young piglets that poses severe economical and animal health threats. An increase of outbreaks since 2010 in Asia, especially in China and since 2013 in the USA and the emergence of highly pathogenic PEDV strains exemplified that PEDV may also become problematic in Europe. PED outbreaks were not observed in Switzerland since more than 20 years, however, infection with a highly pathogenic PEDV strain had been reported in the Ukraine. In order to raise the preparedness for future PEDV outbreaks in a most probably naive population like in Switzerland we focus on the establishment of a real-time RT-PCR method based on the newest sequence data currently available on public databases.

For this purpose we downloaded all available full length genomes and selected genes of PEDV. Referring to this data we performed genome wide alignments to detect conserved regions for the selection of appropriate primers and probes. Notably, on the basis of a comprehensive phylogenetic analysis we could gain insight into the worldwide distribution of several genetic PEDV variants, providing an estimate of strains that might reach Europe within a possible future outbreak. Surprisingly, this analysis also revealed a likely origin of highly pathogenic US-PEDV strains in Asia, but not China.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P195

Intramolecular regulation of bacteriophage lysins explain complex multi-domain architecture and prevents untoward lysis of neighboring bacterial cells

F Oechslin¹; C Menzi¹; P Majcherczyk¹; P Moreillon²; G Resch²

(1) UNIL-University of lausanne;

(2) University of Lausanne

Bacteriophage (phage) lysins represent a fascinating family of peptidoglycan hydrolases that are indispensable for bacterial lysis and release of the phage progeny at the end of its replicating cycle. Lysins can come in a variety of multi-modular forms that may have evolved in order to adapt to their bacterial hosts. However, several questions remain open regarding their function in the phage biology. For instance, what is the purpose of multi-modularity in terms of bacterial lysis knowing that most of them carry one silent domain? Is this an evolutionary byproduct on the way to be lost? Moreover, how are these lysins regulated in order to prevent untoward lysis of neighboring bacteria that might carry sibling prophages or represent potential new preys?

Here we used the multi-domain PlySK1249 lysin [1] as a model. PlySK1249 reunifies one bacteriolytic amidase (Ami) and one non-bacteriolytic endopeptidase (CHAP) peptidoglycan-hydrolase, and one cell-wall binding domain (CWBD). Unlike others, we could observe by overexpressing each separate domains that both Ami and CHAP strongly synergized for lysing whole bacteria, although CHAP alone did not lyse cells on its own. However, optical and electron microscopy observations disclosed unexpected non-lytic effects of CHAP, including bacterial cell dechainig and bacterial surface alteration, without genuine lysis. Moreover, analysis of peptidoglycan degradation products by HPLC and LC-MS confirmed that both Ami and CHAP synergized for full bacterial wall digestion, even though CHAP did not lyse whole bacteria *sensu stricto*. In the present case, CHAP resolves the stem peptides network to mostly dimers, which were enough to maintain a loose glycan-peptide meshwork and prevent lysis. CWBD affinity was also studied by ELISA and diffusion assays. CWBD did not confer bacterial species specificity, but rather retained the lysin to the wall and wall debris, simultaneously promoting lysis and preventing lysin diffusion and untoward lysis of neighboring bacteria. Finally, while PlySK1249 was stable in buffer solution, it underwent progressive inactivation by autocatalytic cleavage in the presence of peptidoglycan as confirmed by western blotting.

In summary, the present observations provide logical explanations for the multi-modular architecture of phage lysins. Domains were observed to act coordinately in order to optimize bacterial lysis while curbing lysin diffusion and inactivating it after lysis completion.

Reference

1. Oechslin F, Daraspe J, Giddey M, Moreillon P, Resch G. Antimicrobial agents and chemotherapy 2013; 57:6276-83.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P196

BK Polyomavirus-Specific 9mer CD8 T Cell Responses Correlate with Clearance of BK Viremia in Kidney Transplant Recipients: First Report from the Swiss Transplant Cohort Study

S Wilk¹; C Leboeuf¹; R Achermann²; I Binet³; D Golshayan⁴; K Hadaya⁵; C Hirzel⁶; M Hoffmann³; U Huynh-do⁷; M Koller²; O Manuel⁸; T Müller⁹; N Mueller⁹; S Schaub²; C Vandelden⁵; F Weissbach¹; H Hirsch¹

- (1) University of Basel;
- (2) University Hospital Basel;
- (3) Cantonal Hospital St. Gallen;
- (4) Centre Hospitalier Universitaire Vaudois and University of Lausanne;
- (5) University Hospitals Geneva;
- (6) Bern University Hospital;
- (7) Inselspital Bern;
- (8) University Hospital of Lausanne;
- (9) University Hospital Zurich

Aims:

Although persisting asymptomatically in immunocompetent individuals, BK polyomavirus (BKPyV) causes premature kidney transplant (KT) failure in 1–15% of patients. Since preventive and therapeutic antivirals are lacking, most programs screen for BKPyV-viremia and, if positive, reduce immunosuppression. However, efficient strategies and markers based on viremia dynamics and patients' immune responses, which could guide the reduction of immunosuppression, are missing. Hence, the aim of the study was to gain more insights into BKPyV viremia and related patients' humoral and cellular immunity.

Methods:

To evaluate the relationship of viremia and BKPyV-specific immunity, we examined prospectively cryopreserved plasma and peripheral blood mononuclear cells at the time of transplantation (T0) and at 6 mo (T6) and 12 mo (T12) after transplant from 28 viremic KT patients and 68 nonviremic controls matched for the transplantation period.

Results:

BKPyV IgG seroprevalence was comparable between cases (89.3%) and controls (91.2%; $p = 0.8635$), but cases had lower antibody levels ($p = 0.022$) at T0. Antibody levels increased at T6 and T12 but were not correlated with viremia clearance. BKPyV-specific T cell responses to pools of overlapping 15mers (15mer peptide pool [15mP]) or immunodominant CD8 9mers (9mer peptide pool [9mP]) from the early viral gene region were not different between cases and controls at T0; however, clearance of viremia was associated with stronger 9mP responses at T6 ($p = 0.042$) and T12 ($p = 0.048$), whereas 15mP responses were not informative (T6 $p = 0.359$; T12 $p = 0.856$). BKPyV-specific T cells could be expanded in vitro from all patients after transplant, permitting identification of 78 immunodominant 9mer epitopes including 50 new ones across different HLA class I.

Conclusion:

9mP-responses may be a novel marker of reconstituting CD8 T cell function that warrants further study as a complement of plasma BKPyV loads for guiding immunosuppression reduction.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P197

HIV genotype and drug resistance profile in vertically infected children

F Compagno¹; K Nägele²; C Kahlert³; I Hoesli⁴; K Aebi-Popp⁵; B Martinez de Tejada Weber⁶; P Paioni⁷; S Yerly-Ferrillo⁶; J Böni⁸; M Battegay⁴; C Rudin⁹; HH Hirsch²

(1) University of Basel;

(2) Universität Basel;

(3) Cantonal Hospital St.Gallen and Children Hospital of Eastern Switzerland;

(4) Universitätsspital Basel;

(5) Bern University Hospital;

(6) University Hospital Geneva;

(7) University Children's Hospital Zurich;

(8) University of Zurich;

(9) University Children's Hospital, University of Basel

Background:

The availability and timely administration of effective combined anti-retroviral therapy (cART) not only reduced the rate of mother-to-child transmission (MTCT), but also improved the prognosis of HIV-infected newborns. With respect to cART efficacy, one of the main concerns in HIV-infected children is drug resistance (DR). While DR-HIV strains may result from suboptimal adherence and dosing in the HIV-infected child, defined as selected DR (sDR), they may also originate from MTCT, defined as transmitted DR (tDR). The aim of this study is to evaluate the frequency of tDR in HIV infected children.

Methods:

We performed a retrospective analysis of prospectively entered data of HIV transmission in mother-child (MC) pairs of the MoCHiV cohort. Genotype and DR profile of each MC-pair were determined around birth time to identify tDR. Children were tested at all available follow-up time points to define the genetic evolution of HIV and to investigate the emergence of new sDR. Sanger sequencing was performed from plasma and PBMC samples. Data regarding viral load, CD4+ T-cell count, cART, adherence and clinical information completed our results.

Results:

The study population comprised 22 MC pairs. Almost all mothers (95,5%) were treatment-naïve before pregnancy and only 50% received antiretroviral therapy (intrapartum zidovudine or cART). Children were followed for approximately 15 years. The most prevalent subtype was B, found in 59% of MC pairs. Considering only major DR, sDR emerged in 16 children (72%), while we identified one case of tDR (4,5%). CD4+ T-cell counts were significantly lower in the sDR group. The number of ART changes during pediatric lifetime was greater in those with sDR (6.4 vs. 4 times), but early cART (<10 months of age) seemed to be protective (sDR 68% vs. 100%).

Conclusion:

The rate of tDR was lower than in other studies, but within the previously described range. Children who were managed by early ART were more prone to develop sDR and therefore underwent more ART changes. Since some children presented sDR without being exposed to any previous treatment, adherence and the possibility of tDR mutations that may have escaped detection by standard diagnostic tools could play a role in the development of MC DR. These findings strengthen the notion that sensitive baseline resistance profile testing with specific attention to minority variants determined by next-generation sequencing (NGS) may be important for successful HIV management in MC pairs.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P198

Quantification and Commutability of CMV DNA in Human Plasma Samples depends on Target Sequence and Amplicon Length

K Nägele¹; I Lautenschlager²; K Bir¹; I Helanterä²; R Loginov²; HH Hirsch³

(1) Universität Basel;

(2) Helsinki University Hospital and University of Helsinki;

(3) Universität Basel & Universitätsspital Basel

Background:

The optimal management of human cytomegalovirus in transplant patients is based on the sensitive and specific quantification of viral DNA as recommended by current guidelines for recipients of solid organ transplantation (SOT) and hematopoietic cell transplantation (HCT). Recently, a CMV variant was used in the external quality assurance program UKNEQAS, which resulted in under-quantification or false-negative results with the Roche CAP/CTM-CMV assay. However, the exact mutation and the impact on CMV load quantification was not defined.

Methods:

The UKNEQAS sample was sequenced in the presumed CAP/CTM target sequence and compared with the CMV AD169 strain (acc.no.X17403). Three new quantitative TaqMan PCR assays were designed targeting the same CMV UL54 region. They differed only in the position of the reverse primers generating amplicon lengths of 361bp, 254bp and 95bp. CMV loads were determined using plasmid, UKNEQAS samples and prospectively collected patient samples sent for CMV viral load testing. CMV loads were compared with or without DNase digestion prior to nucleic acid extraction and quantification.

Results:

Using CMV AD169 as reference, 8 mutations were identified, of which one was likely to affect quantification, since it was critically located in the reverse primer target. The new assays allowed reproducible quantification of plasmid target, but differed in Ct values and derived loads up to 1log₁₀ copies/mL that inversely correlated with amplicon size. All novel real-time CMV UL54 targeted in-house assays were able to detect the UKNEQAS samples. Quantification of patient samples confirmed this inverse correlation of amplicon size with viral loads, but varying up to 2.5log₁₀ copies/mL suggesting additional factors. Pre-treatment of patient plasma with DNase prior to extraction and quantification resulted in more than 95% reductions, indicating that large parts of the CMV loads were not protected, and hence not encapsidated in virions.

Conclusions:

The difference in quantification between qPCRs with different target lengths and the pronounced sensitivity to DNase digestion indicates that short, fragmented CMV DNA in plasma of transplant patients significantly contributes to patient viral loads, presumably from ruptured host cells replicating CMV. Thus, besides extraction and sample matrix, CMV amplicon size and naked CMV fragmentation are obstacles to commutability of CMV load assays for standardized clinical use in therapy start and stop.

References

- Kotton CN, et al. Transplantation. 2013;96(4):p.333-60.
- Ljungman P, Hakki M, Boeckh M. Hematol Oncol Clin North Am. 2011;25(1):p.151-69.
- Hirsch HH, Lautenschlager I, Pinsky BA, Cardenoso L, Aslam S, Cobb B, Vilchez RA, Valsamakis A. Clin Infect Dis. 2013;56(3):p.367-73.
- Preiksaitis, JK, et al. Clin Infect Dis. 2016;63(5):p.583-9.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P199

Quantifying the Fitness Cost of HIV-1 Drug Resistance Mutations through Phylodynamics

D Kühnert¹; R Kouyos¹; G Shirreff²; J Pecerska²; A Scherrer¹; J Böni³; S Yerly⁴; T Klimkait⁵; V Aubert⁶; H Günthard¹; T Stadler²; S Bonhoeffer²

- (1) USZ;
- (2) ETH Zurich;
- (3) University of Zurich;
- (4) Geneva University Hospital;
- (5) University of Basel;
- (6) University Hospital Lausanne

Drug resistant HIV is a major threat to the long-term efficacy of antiretroviral treatment. Around 10% of ART-naïve patients in Europe are infected with drug-resistant HIV type 1. Hence it is important to understand the dynamics of transmitted drug resistance evolution. Thanks to routinely performed drug resistance tests, HIV sequence data is increasingly available and can be used to reconstruct the phylogenetic relationship among viral lineages.

In this study we employ a phylodynamic approach to quantify the fitness costs of major resistance mutations in the Swiss HIV cohort. The viral phylogeny reflects the transmission tree, which we model using stochastic birth-death-sampling processes with two types: hosts infected by a sensitive or resistant strain. This allows quantification of fitness cost as the ratio between transmission rates of hosts infected by drug resistant strains and transmission rates of hosts infected by drug sensitive strains. The resistance mutations 41L, 67N, 70R, 184V, 210W, 215D, 215S and 219Q (nRTI-related) and 103N, 138A (NNRTI-related) in the reverse transcriptase and the 90M mutation in the protease gene are included in this study. Among the considered resistance mutations, only the 90M mutation in the protease gene was found to have significantly higher fitness than the drug sensitive strains. The following mutations associated with resistance to reverse transcriptase inhibitors were found to be less fit than the sensitive strains: 67N, 70R, 184V, 219Q. The highest posterior density intervals of the transmission ratios for the remaining resistance mutations included in this study all included 1, suggesting that these mutations do not have a significant effect on viral transmissibility within the Swiss HIV cohort. These patterns are consistent with alternative measures of the fitness cost of resistance mutations. Overall, we have developed and validated a novel phylodynamic approach to estimate the transmission fitness cost of drug resistance mutations.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P200

Bictegravir has Potent Activity against Wild-Type and INSTI-Resistant HIV-1 and has a Longer Dissociation Half-Life than Dolutegravir, Elvitegravir and Raltegravir

K White¹; A Niedziela-Majka¹; N Novikov¹; M Miller¹; H Jin¹; S Lazerwith¹; T Edinger²; M Tsiang¹

(1) Gilead Sciences;

(2) Gilead Sciences Switzerland

Background

Bictegravir (BIC) is a novel HIV-1 integrase strand transfer inhibitor (INSTI) with potent activity against HIV-1 in vitro and in vivo. For INSTIs, the high barrier to drug resistance is correlated with a long dissociation half-life ($t_{1/2}$) from HIV-1 integrase (IN)/DNA complexes. The antiviral activity and dissociation $t_{1/2}$ of BIC are compared to dolutegravir (DTG), elvitegravir (EVG), and raltegravir (RAL).

Methods

47 patient-derived HIV-1 isolates with INSTI resistance mutations were phenotyped. The apparent dissociation $t_{1/2}$ of 3H-labelled INSTIs were measured using WT and the clinically relevant G140S/Q148H mutant IN/DNA complexes with a scintillation proximity assay and analyzed using single exponential decay and equilibrium binding models.

Results

Patient-derived HIV-1 isolates ($n=47$) with high-level INSTI resistance had a significantly lower mean fold-change for BIC (2.8-fold) vs DTG (5.8), RAL (>100), and EVG (>106) ($p<0.04$ for BIC versus DTG); of those, 13 isolates exhibited ≥ 2 -fold lower resistance to BIC than DTG and 34 isolates had similar BIC and DTG activity. 23 HIV isolates with G140S+Q148H $\pm$ other mutations in IN had mean phenotypic fold-change values of 3.6 for BIC, 8.1 for DTG, and >100 for EVG and RAL ($p<0.01$ for DTG vs BIC). The dissociation $t_{1/2}$ of INSTIs from WT IN/DNA complexes using the single exponential decay model was longer for BIC compared to DTG, EVG, and RAL (BIC 134 h; DTG 79 h; RAL 14 h; EVG 3.6 h; $p<0.001$). The equilibrium binding model resulted in overall shorter dissociation $t_{1/2}$ values that may be more physiologically relevant, but the BIC dissociation $t_{1/2}$ remained significantly longer than the other INSTIs (BIC 38 h; DTG 16 h; RAL 5.2 h; EVG 1.5 h; $p\leq 0.017$). Dissociation $t_{1/2}$ values from G140S/Q148H mutant HIV IN/DNA complexes were shorter than wild-type but longer for BIC compared to DTG by both models (single exponential BIC 5.5 h; DTG 2 h; equilibrium binding model: BIC 2.5 h; DTG 0.45 h; both $p<0.01$). EVG and RAL had no measurable association, consistent with high-level resistance.

Conclusion

BIC displayed significantly higher antiviral activity in vitro relative to DTG, EVG, and RAL. BIC also has a longer dissociation $t_{1/2}$ than DTG, EVG, and RAL from wild-type and mutant IN/DNA complexes. These results support the study of BIC in a treatment-experienced, INSTI-resistant population.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P201

No impact of RASs on the high efficacy of SOF/VEL/VOX for 12 weeks in DAA-experienced patients: an integrated resistance analysis of the POLARIS-1 and POLARIS-4 studies

C Sarrazin¹; CL Cooper²; MP Manns³; R Reddy⁴; K Kowdley⁵; C Oberle⁶; H Dvory-Sobol⁷; E Svarovskia⁷; R Martin⁷; G Camus⁷; BP Doehle⁷; L Stamm⁷; RH Hyland⁷; DM Brainard⁷; H Mo⁷; SC Gordon⁸; M Bourliere⁹; S Zeuzem¹⁰; SL Flamm¹¹

- (1) Medizinische Klinik 1;
- (2) University of Ottawa;
- (3) Hannover Medical School;
- (4) University of Pennsylvania;
- (5) Swedish Medical Center;
- (6) Gilead Sciences Switzerland;
- (7) Gilead Sciences;
- (8) Henry Ford Health System;
- (9) Hôpital Saint Joseph;
- (10) Johann Wolfgang Goethe University Medical Center;
- (11) Northwestern University

Background:

The pangenotypic combination of sofosbuvir (SOF), velpatasvir (VEL), and voxilaprevir (VOX), inhibit distinct HCV targets, the NS5B polymerase, the NS5A protein, and NS3/4A protease, respectively. In Phase 3 studies, SOF/VEL/VOX administered for 12 weeks demonstrated a 96% SVR12 rate in NS5A inhibitor-experienced patients in POLARIS-1, and a 97% SVR12 rate in DAA-experienced patient who had not previously received an NS5A inhibitor in POLARIS-4. Here, we evaluate the effect of baseline resistance associated substitutions (RASs) on treatment outcome and the emergence of RASs in patients who experienced virologic failure.

Methods:

NS3, NS5A, and NS5B deep sequencing was performed at baseline for all patients and at the time of virologic failure. NS3 and NS5A class RASs as well as VOX or VEL-specific RASs that confer >2.5-fold changes in EC50 were evaluated. Results are reported using a 15% cutoff.

Results:

In POLARIS-1, 79% of NS5A inhibitor-experienced patients (205/260) had baseline NS3 and/or NS5A class RASs. Of these, 75% (196/260) had baseline NS5A RASs, the most common RASs. The SVR12 rates were similar in subjects with or without NS3 and/or NS5A class RASs, and with or without VOX or VEL-specific RASs. RASs at NS5A position Y93 were present in 25% of patients, of whom 63 (95%) achieved SVR12; all patients with ≥2 NS5A RASs achieved SVR12 (n=77). 95% (18/19) of patients with NS5B nucleoside inhibitor (NI) RASs achieved SVR12; 2 patients had S282T at baseline and achieved SVR12. In POLARIS-4, the overall prevalence of baseline NS3 and/or NS5A class RASs was 47% (83/178) and all achieved SVR12. All patients with NS5B NI RASs (n=14) achieved SVR12. No NS3, NS5A, or NS5B NI RASs emerged in any patients who relapsed following treatment with SOF/VEL/VOX for 12 weeks (POLARIS-1, n=6, POLARIS-4, n=1).

Conclusions:

Baseline RASs had no impact on the virologic response in DAA-experienced patients following treatment with SOF/VEL/VOX for 12 weeks. Viral relapse was not associated with emergence of viral resistance.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P202

Improved Bone and Renal Safety of Switching from Tenofovir Disoproxil Fumarate (TDF) to Tenofovir Alafenamide (TAF): Preliminary Results From 2 Phase 3 Studies in HBeAg-positive and HBeAg-negative Patients with Chronic Hepatitis B (CHB)

HL Chan¹; S Fung²; WK Seto³; E Gane⁴; C Oberle⁵; JF Flaherty⁶; V Suri⁶; L Lin⁶; A Gaggar⁶; M Subramian⁶; WL Chuang⁷; K Agarwal⁸; HL Janssen⁹; M Buti¹⁰

(1) The Chinese University of Hong Kong;

(2) Toronto General Hospital;

(3) Queen Mary Hospital;

(4) Auckland Clinical Studies;

(5) Gilead Sciences Switzerland;

(6) Gilead Sciences;

(7) Kaohsiung Medical University Hospital;

(8) Kings College Hospital;

(9) Toronto Western Hospital;

(10) Hospital General Universitari Vall d'Hebron

Background and Aims:

Treatment with TAF has shown less bone and renal effects with similar efficacy rates compared to TDF in two large multinational Phase 3 studies after 48 weeks of therapy. Here, we evaluate patients who have completed 96 weeks of double blind treatment with TAF or TDF and have switched to open label treatment with TAF to determine changes in bone mineral density, creatinine clearance, and the maintenance of viral suppression.

Methods:

In two identically-designed Phase 3 studies, immune active CHB patients who were HBeAg negative (GS-US-320-0108; N=425) or HBeAg positive (GS-US-320-0110; N=873) were randomized to and treated with TAF 25 mg QD or TDF 300 mg QD. A subset of patients (N=200 in Study 0108 and N=340 in Study 0110) in these ongoing 8 year studies had completed 96 weeks of double-blind (DB) treatment with TAF or TDF and switched to open-label (OL) TAF 25 mg QD at the time of the Week 96 analysis. Dual energy X-ray absorptiometry (DXA) scans were evaluated every 24 weeks as were serial assessments of creatinine clearance and viral suppression. Analyses included subjects with values at Week 96 and Week 120 for creatinine clearance (n=362), spine BMD (n=228) or hip BMD (n=222).

Results:

A total of 540 subjects had entered the OL TAF phase after 96 weeks of blinded therapy across both studies. Creatinine clearance improved significantly in patients switched from DB TDF to OL TAF at Week 120 compared to Week 96 (N=117, mean (SD) change=+2.43 (12.81) ml/min, p=0.04); and remained stable in those previously receiving TAF. BMD also showed improvement at Week 120 from Week 96 among patients switched from DB TDF to OL TAF (hip: N=58, mean (SD) % change=+0.71% (1.43), p=0.0004; spine: N=60, mean (SD) % change=+1.41% (2.30), p<.0001). BMD changes in hip and spine for DB TAF patients entering the OL TAF period were relatively stable. Compared to results at Week 96, high rates of virologic control were maintained across subjects in both studies during the OL period (97-99% and 80-83% in Studies 0108 and 0110, respectively).

Conclusions:

Patients who switched from TDF to TAF treatment demonstrated rapid improvements in BMD and creatinine clearance within the first 24 weeks of treatment, and virologic control was maintained. Longer term data is required to establish the benefits of switching to TAF for treatment of CHB.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P203

Drug-Drug Interaction Profile of Sofosbuvir/Velpatasvir/Voxilaprevir Fixed-Dose Combination

KL Garrison¹; B Kirby¹; C Oberle²; L Stamm¹; G Ma¹; A Vu¹; J Ling¹; A Mathias¹

(1) Gilead Sciences;

(2) Gilead Sciences Switzerland

Introduction:

A fixed-dose combo of HCV NS5B inhibitor sofosbuvir (SOF), NS5A inhibitor velpatasvir (VEL) and NS3/4A inhibitor voxilaprevir (VOX) is being developed for treatment of HCV infection. The drug-drug interaction (DDI) profile of SOF/VEL/VOX (S/V/V) was characterized using in vitro and Phase 1 clinical data.

Methods:

The Phase 1 program evaluated DDIs between S/V/V and drug transporter and CYP probes, immunosuppressants, HIV antiretrovirals (ARV), and oral contraceptives (OC). S/V/V 400/100/100 mg ± VOX 100 mg was administered to healthy volunteers.

Results:

No clinically relevant interactions were observed upon administration of S/V/V or its components with CYP or UGT1A1 substrates. Pravastatin (OATP substrate) and rosuvastatin (ROSU; BCRP/OATP substrate) AUC were ↑116% and ↑639% respectively when administered with S/V/V; co-use of ROSU with S/V/V is not recommended. Total dabigatran AUC was ↑161% following administration of S/V/V with dabigatran etexilate (P-gp substrate). S/V/V did not alter the PK of bicitgravir, cobicistat, darunavir, elvitegravir, emtricitabine, rilpivirine, tenofovir alafenamide (TAF) or tenofovir (from TAF or tenofovir disoproxil fumarate). No changes in ethinyl estradiol (EE) or norgestrel PK were seen when S/V/V was administered with EE/norgestimate; use of OCs with S/V/V is allowed.

VOX AUC was ↑84% when administered with voriconazole; use of CYP3A inhibitors was permitted in Phase 3 trials. SOF, VEL and VOX AUC were ↓72%, ↓82% and ↓73% respectively when administered with multiple-dose RIF; use of potent P-gp/CYP inducers with S/V/V is not recommended. VOX exposure was ↑691% and ↑839% following coadministration with single dose rifampin (RIF) and cyclosporine A respectively; co-use of potent OATP inhibitors with S/V/V is not recommended. There was no change in VOX PK when administered with the intestinal OATP inhibitor grapefruit juice. Unboosted ARV regimens generally did not alter SOF, GS-331007, VEL or VOX PK except VEL AUC was ↓53% when administered with efavirenz (EFV); co-use of EFV with S/V/V is not recommended. Boosted ARV regimens containing mixed transport and CYP inhibitors did not impact SOF, GS-331007 or VEL PK, while VOX AUC was ↑143-171%. VOX AUC was ↑331% following a single dose of ATV/r with S/V/V; co-use of ATV/r with S/V/V is not recommended.

Conclusion:

S/V/V exhibits a favorable DDI profile allowing use with many drugs commonly used by HCV-infected patients.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P204

The 13 Human Polyomavirus differ in Early Viral Gene Region Expression Depending on the Host Cell and Large T-antigen

E Tasih Ajuh¹; R Gosert¹; T Bethge²; H Hirsch¹

(1) University of Basel;

(2) Kantonsspital Aarau

There are at least 76 polyomaviruses (PyVs) infecting vertebrates, including 13 human polyomaviruses (HPyVs). The HPyV genome is circular-double stranded DNA containing, the early viral region (EVGR), late viral region (LVGR) and a non-coding control region (NCCR), acting as the viral bi-directional promoter. The NCCR coordinate the timing, course, and level of EVGR and LVGR expression. BKPyV and JCPyV point mutants and rearranged NCCRs have been identified in disease, and shown to increase EVGR expression and viral replication. Comparative studies on the NCCR activity of the other HPyVs are scarce. Gaining insights into HPyVs NCCR activity in cell cultures would anticipate cell culture for propagating HPyVs. We compared NCCR-driven EVGR and LVGR expression of the novel HPyVs in different cell culture systems

NCCRs of all 13 HPyVs cloned into a bidirectional reporter vector (pRG13D12) with DsRed2 and EGFP as markers of EVGR and LVGR, respectively. Expression monitored in HEK293, HEK293T, and HEK293TT to estimate the potential effect of SV40 large T-antigen (LTag) and selected cell lines reflecting different human organs using fluorescence microscopy and flow cytometry analysis.

Using archetype and rearranged NCCR of BKPyV as a reference, we found that MCPyV and HPyV12 NCCR were the strongest in most cell lines. JCPyV and KIPyV were stronger in some other cells, while HPyV 6 and TSPyV displayed the lowest EVGR expression. “Rearranged” variants from patients, HPyV7-PITT1 and HPyV-PITT2 displayed higher EVGR and LVGR activity than the corresponding “archetype” suggesting that the NCCR are important pathogenicity determinants. EVGR and LVGR expression of most HPyVs were increased in HEK293T and HEK293TT, suggesting that the reporter results were modulated by LTag expression as expected in the viral life cycle. This response was also seen for HPyV6, HPyV7 suggesting the importance of HPyVs co-infection in viral replication and pathology. The numbers of early or total number of LTag-binding sites on NCCRs do not correlate to the fold–EVGR expression increase, since SV40-LTag is not the cognate LTag of the individual HPyV. Mutagenesis of LTag-binding sites, 1,2 or 3,4 of BKPyV_{ww} abolished viral genome replication in RPTEC cells, implying 1,2 or 3,4 LTag-binding sites are important for viral genome replication.

The data are important for understanding HPyV replication and host factors, could permit identifying suitable cell culture conditions for the novel HPyV.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P205

The effect of the 2013 national HIV testing recommendations on HIV testing practices in a Swiss university hospital

T Lazzarino¹; R Mamin²; S Martenet²; O Hugli²; M Cavassini²; K Darling³

(1) University of Lausanne;

(2) Lausanne University Hospital (CHUV);

(3) CHUV

Aims

Despite HIV testing recommendations published by the Federal Office of Public Health (FOPH) since 2007, almost half of patients in Switzerland newly presenting for HIV care are diagnosed late (with CD4 counts <350 cells/mm³ and/or AIDS-defining illness at diagnosis). We reported that the 2010 FOPH HIV testing recommendations had no effect on HIV testing practice in clinical services at our 1500-bed teaching hospital (1). The aim of the current study was to examine the effect on testing practice of the 2013 FOPH testing recommendations.

Methods

Retrospective study performed at Lausanne University Hospital (LUH), Lausanne, Switzerland. Clinical services managing medical conditions listed in the 2013 FOPH testing recommendations as HIV-testing indications were examined. Two hospital databases were used: the Immunology Service database (for number of HIV tests requested by each service) and the central hospital database (for number of patients seen at each service during the same period). HIV testing rates were expressed as percentage of tests performed per number of patients seen. Rates were examined during the two years before and the two years after the 2013 FOPH testing recommendations: 1st January 2012 and 31st December 2015.

Results

During the four-year study period, 163,288 patients were seen at the ten clinical services. Of these, 10,045 (6.1%) were tested for HIV, resulting in 36 new HIV diagnoses. The mean testing rate increased significantly from 7.4% before to 10.5% after the recommendations ($P=0.01$). Testing rate increases were most marked in the emergency department (from 3.9% to 5.9%) and the oncology service (from 3% to 5.3%) ($P<0.001$ in each case). Both these services had been the target of local clinical trials on HIV testing.

Conclusion

In this single-centre study, we have observed that, overall, HIV testing rates increased significantly after the 2013 FOPH recommendations. The increase was particularly pronounced in the clinical services which had educational interventions in the context of clinical trials on HIV testing. As these services had among the lowest testing rates prior to 2012, our observed improvement in testing rates suggests that local engagement with HIV testing measures complements the effect of national testing guidelines. This simple two-database method of measuring testing rates enables health care centres to concentrate efforts on clinical services in which testing rates can be optimised.

References:

1. Darling KEA. et al. PLoS ONE 2012; 7: e39299



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P206

Assessment of the Antiviral Activity of MxA against Influenza A Virus

F Steiner¹; S Spirig²; M Crameri²; E Moritz²; J Pavlovic²

(1) University of Zurich, Zurich, Switzerland;

(2) University of Zurich

Human MxA protein belongs to the family of dynamin-like large GTPases and exerts antiviral activity primarily against negative-stranded RNA viruses, including influenza A (IAV). MxA is able to form higher order oligomeric structures. However, the mode of action of MxA remains unknown. There is increasing evidence that MxA targets the IAV nucleoprotein (NP) in conjunction with UAP56, a cellular DEAD-box RNA helicase, which is required for efficient IAV replication due to its chaperone activity for viral NP. In order to better understand the molecular mechanism of action of MxA we analyzed in detail the interplay between MxA, UAP56 and the viral target NP.

By performing co-immunoprecipitation (co-IP) as well as split-GFP experiments we were able to show that NP binds (the dimeric form of) MxA as well as UAP56. In order to narrow down the interaction domains of MxA and UAP56 with NP, we introduced N- and/or C- terminal deletions and point mutations to identify the binding regions of the trimeric complex. Furthermore, we were able to identify the residues in NP important for binding the MxA-UAP56 complex.

From a mechanistic point of view, we are investigating the importance of the oligomeric state of MxA as well as its GTPase function. We have evidence that a functional G-domain is important for proper localization of MxA but is dispensable for its binding to UAP56. The oligomeric state on the other hand is crucial for the binding of MxA to NP since this binding is increased if MxA is rendered dimeric.

We are currently testing whether binding of MxA to UAP-NP dimers leads to the sequestration of UAP56 and hence inhibition of IAV replication.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P207

Effects of PEG-IFN α on the HIV-1 DNA levels in HIV-1/HCV co-infected individuals

V Strouvelle; D Braun; V Vongrad; YL Kok; R Kouyos; K Metzner; H Günthard

Universitätsspital Zürich

Studies exploring effects of PEG-IFN α (pIFN α) on total HIV-1 DNA levels in HIV-suppressed patients have varied; therefore in a retrospective longitudinal study we assessed the effects of pIFN α on HIV-1 DNA levels in PBMC from Swiss HIV Cohort Study patients.

Patients inclusion criteria were: 1. HIV-1/HCV co-infected, 2. on ART, 3. virally suppressed (< 50 HIV-1 RNA copies/ml of plasma) for >6 months, and 4. treated with pIFN α for ≥ 24 weeks. Samples were collected before, during, and post pIFN α treatment (all follow-up time points available). Patients were categorised into three groups: Chronic HIV infection ($n=22$), Acute HIV infection ($n=8$), and a control group of no ART during pIFN α treatment ($n=10$). Patients with >1 pIFN α treatment were also included in the chronic group ($n=4$). HIV-1 DNA from HIV-1/HCV co-infected patients was quantified by an in-house qPCR assay measuring the U3-R region of the HIV-1 LTR. Clinical data were assessed for the effects of IFN α on the HIV-1 viral load (VL), lymphocyte and CD4 cell populations. Wilcoxon matched-pairs signed rank test was applied to all data sets to investigate significance.

A total of 247 samples were quantified for HIV-1 DNA with a mean number of time points (range) of 6.6 (2-12) in chronic, 5.6 (2-10) in acute and 5.7 (3-9) in the no ART groups. Maximum follow-up time was 112 months post-pIFN α . Patients were all Caucasian, mainly male (90%) with a mean age of 42 yrs. (27-55) and infected with HIV-1 subtype B (92.5%). pIFN α treatment caused general and CD4-lymphopenia in all patients as previously described. All ART treated patients maintained an undetectable VL. In non-ART-treated patients, pIFN α treatment decreased the HIV viral load by 0.89 log on average. Pre-pIFN α HIV-1 DNA levels were on average 0.3 log higher in the chronic vs. the acute group. Total HIV-1 DNA levels remained stable before, during, and after pIFN α treatment with no clear trend found to suggest an effect of pIFN α on HIV-1 DNA levels in PBMCs. Repeated IFN α administration did not have an additional effect on HIV-1 DNA levels in the four patients studied.

In contrast to other studies, our large longitudinal study in a well characterized patient group did not reveal any effect of pIFN α on the latent reservoir as measured by a HIV-1 DNA qPCR assay in PBMCs. Notably, repeated pIFN α treatment did not affect HIV-1 DNA levels. Cumulatively, no discernible effect of pIFN α on HIV-1 DNA in HIV-1/HCV co-infected individuals was detected.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P208

Prevalence of Transmitted HIV-1 Drug Resistance in Cameroon in the Years 2015/16

H Mbunkah¹; S Schmutz²; A Marzel¹; NN Nsanwe³; E Mbu³; LM Besong⁴; BA Sama⁵; E Oroch⁶; R Kouyos¹; K Metzner¹

- (1) Universitätsspital Zürich;
- (2) University of Zurich;
- (3) Bamenda Regional Hospital, Cameroon;
- (4) District Hospital Kumba, Cameroon;
- (5) District Hospital Ndop, Cameroon;
- (6) Regional Hospital Ngaoundere, Cameroon

Aims:

The benefits of combination antiretroviral therapy can be compromised by the development of drug resistance. In resource-limited settings like Cameroon, many patients receiving first-line drugs develop virological failure and may transmit drug resistant viruses to newly infected persons. In order to determine the most recent prevalence, types and transmission patterns of resistance-associated mutations, we monitored HIV-1 drug resistance using next-generation sequencing.

Methods:

We developed an HIV-1 protease and reverse transcriptase drug resistance genotyping assay applicable to dried blood spot samples (DBS) and also universal - genotyping all heterogeneous HIV-1 subtypes of at least group M. DBS samples and questionnaires were collected from 360 newly diagnosed and drug-naïve HIV-1 patients in four hospitals in semi-urban to urban areas with some of the highest HIV-1 prevalence rates in Cameroon. RNA was extracted and a 1.4kb fragment of the pol gene was amplified using two overlapping nested RT-PCRs. Successful amplicons were sequenced with next-generation sequencing and the Stanford HIV Sequence Database was used to interpret resistance mutations.

Results:

All major group M HIV-1 subtypes were detected using the assay developed with an overall analytical sensitivity of 103 RNA copies/mL. The overlapping split strategy used in the PCRs showed a high sensitivity for the DBS: An 82.8% (298/360) amplification success rate was obtained with the DBS. All patients had no viral load records but a mean CD4 count of 300.2 ± 198.9 cells/ μ L (Table 1). Subtype diversity was quite high with the commonest subtypes being: CRF02_AG (63.4%), CRF22_01A1 (9.7%), and F2 (5%), as well as other circulating and unique recombinant forms. Major resistance-associated mutations to Nucleotide Reverse Transcriptase Inhibitors was 3%, resistance to Non-Nucleoside Reverse Transcriptase Inhibitors was 10.4% and 0.3% for resistance mutations to Protease Inhibitors. The major mutations M184V, E138A/G, K103N and M46I were most common. Having unprotected sex with an HIV positive person was the only significant risky sexual behavior attributed with drug resistance.

Conclusion:

Transmitted HIV-1 drug resistance in Cameroon is low to moderate but has increased compared to previous reports in 2011. This evidence depicts a public health problem with possible implications on prevention, treatment and monitoring of HIV-1 infections in the country.

Acknowledgements:

We heartily thank the patients and staff of the HIV treatment centres in Cameroon. We also thank the Swiss Federal Commission for Scholarships, the Hartmann Müller Foundation for Medical Research and ESTHER Switzerland for funding contributions to this project.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P209

Predictors of detecting antimalarials drugs in the blood in community surveys in Tanzania

J Gallay¹; E Pothin¹; D Mosha²; M Zuakulu²; E Lutahakana²; L Decosterd³; B Genton¹

(1) Swiss Tropical and Public Health Institute;

(2) Ifakara Health Institute;

(3) Lausanne University Hospital (CHUV)

Measuring antimalarials in the blood can provide accurate estimate of overall levels of circulating drugs, an important driver of emergence of parasite resistance. The aim of the study was to estimate the prevalence of individuals with antimalarials in their blood and to determine the predictors of detecting antimalarials in the blood.

Community-based x-sectional surveys were conducted in 2015 in three regions of Tanzania with different levels of malaria endemicity. Information on demographics, history of fever and drug use were collected as well as dried blood spot samples for further antimalarial analysis by LC-MS/MS. In addition, RDT and treatment availability were investigated through health facility and drug stores surveys. Multilevel mixed effects logistic regression models were used to estimate odds ratios for having lumefantrine (LF), sulfadoxine-pyrimethamine (SP) or any antimalarial in the blood.

The survey included 6485 individuals. Prevalence of antimalarials in the blood was 21% (1344/6485). By multivariate analysis, amongst the significant associations, a febrile episode in the previous two weeks had higher odds ratios of detecting antimalarials (OR=2.1), LF (OR=2.6) and SP (OR=1.6) in the blood, followed by the region, living close to a health facility and the proportion of drug stores having RDTs in stock. Higher proportion of drug stores that had antimalarials in stock was significantly associated with higher odds of detecting any antimalarial (OR=2.8) and LF (OR=2.0) in the blood, followed by malaria prevalence, young age and sleeping under a bed net. Being pregnant was associated with having SP (OR=3.9) and any antimalarials (OR=1.9) in the blood. Old age was associated with higher odds of having SP in the blood and living in a rural district with higher odds of having LF in the blood.

These data show that the amount of antimalarial drug pressure is high in the population. The main predictors of antimalarial detection in the blood were expected. Measuring drug concentrations in the blood could provide a new tool to monitor drug use, which should help better targeting specific interventions, and hence decrease drug pressure.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P210

Effects of malaria infection on different mosquito's behavioral responses against insecticides

K Thiévent¹; S Moore²; J Koella¹

(1) Université de Neuchâtel;

(2) Swiss Tropical and Public Health Institute

Residual indoor spraying (IRS) and insecticide treated bed nets (ITNs) are two major ways to control malaria vectors. Insecticides spatially repel, irritate and/or kill mosquitoes. Understanding how these properties of insecticides vary under different conditions is necessary to understand the epidemiological impact of using IRS and/or ITNs for the control of malaria. In particular, we should know how malaria influences insecticides spatial repellency and contact irritancy as personal protection is most important when mosquitoes are infectious, whereas community protection is most effective during the developmental stage of malaria. As it is known that malaria parasites alter the behaviour of mosquitoes, we expected a difference in mosquito repellence between infected and uninfected mosquitoes. In a first step, we measured in the lab the repellency and contact irritancy induced by permethrin for uninfected *Anopheles gambiae* mosquitoes, *A. gambiae* infected with the non-transmissible stage (oocyst) and with the infectious stage (sporozoites) of the rodent malaria *Plasmodium berghei*. In a second step, we compared in the Bagamoyo Research and Training Unit laboratory the repellency of permethrin treated nets between *Anopheles arabiensis* mosquitoes infected or not with sporozoites of the human malaria *Plasmodium falciparum*. In both studies, we found that mosquitoes harbouring sporozoites in their salivary glands were less repelled by permethrin treated nets compared to control mosquitoes. These results suggest that malaria infection may have an impact on mosquito control with IRS or ITNs through a reduction of their repellency on infected mosquitoes.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P211

Use of C-reactive protein and procalcitonin to target antibiotic prescriptions for undifferentiated fever in children under-five: results from a randomized clinical trial in Tanzania.

K Keitel¹; J Samaka²; J Masimba²; T Mlaganile²; F Kagoro²; B Genton³; V D'Acremont⁴

- (1) Swiss Tropical and Public Health Institute;
- (2) Ifakara Health Institute;
- (3) Lausanne University Hospital;
- (4) Lausanne University Hospital and University of Lausanne

At the outpatient level about 1/4 of febrile children have no localizing symptoms, and test negative for malaria. Given the lack of diagnostic tools, antibiotic overuse is a major challenge. We assessed the use of point-of-care inflammatory marker results (C-reactive protein [CRP] and procalcitonin [PCT]; intervention arm) versus disease-specific criteria (urine dipstick, typhoid rapid test, or ear discharge; control arm) in deciding on antibiotic prescription for undifferentiated fever among pediatric outpatients (sub-cohort of a larger trial, e-POCT, that included consecutive febrile patients). Antibiotics were prescribed only to children with CRP $\geq 80\text{mg/L}$ or PCT $\geq 4\mu\text{g/L}$ (intervention), and to patients with positive urine dipstick, typhoid test or acute ear discharge (control). 13% (52/401) met criteria for antibiotic prescription in the intervention, versus 16% (67/413) in the control arm ($p=0.19$). 12% (47/402) had PCT $\geq 4\mu\text{g/L}$, 2% (8/402) CRP $\geq 80\text{mg/L}$ and 1% (3/402) both. There were 3 clinical failures (1 death) and 6 clinical failures (3 deaths) by day 7 in the intervention and control arms ($p=0.33$). 1.2% (10/814) and 2.7% (22/814) had a positive blood or urine culture, respectively (result available late in the episode, not used for clinical management). In the intervention arm, 3/4 and 9/13 of children with positive blood /urine culture, respectively, had been identified by CRP/PCT and thus treated with antibiotics. In the control arm, 2/6 of those with positive blood culture (1 positive urine dipstick, 1 ear discharge) were treated. All patients with positive blood/urine culture but not treated with antibiotics were cured at day 7. In the Dar es Salaam outpatient population, using a simplified approach of combined CRP and PCT cutoffs to decide on antibiotic prescription among children with undifferentiated fever was comparable in terms of antibiotic prescription and clinical outcome to a disease-specific diagnostic strategy. The limited relationship between the presence of bacterial disease and clinical outcome speaks in favor of using host biomarkers to identify serious infection; whatever type of pathogen is causing it.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P212

Varying impact of malaria interventions at district level – implications of a mathematical model for strategic planning

M Runge¹; E Pothin¹; R Mandike²; A Mohamed²; S Rumisha³; F Molteni¹; T Smith¹; C Lengeler¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) Ministry of Health;

(3) National Institute for Medical Research

National Malaria Control Programs (NMCPs) are tasked with identifying the most efficient intervention packages and their optimal deployment strategies. Mathematical models can provide guidance in this process by predicting the impact of potential intervention packages in different settings. Tanzania is currently re-defining the national malaria strategic plan and goals for 2020 which should be tailored to local variations in the impacts of different interventions.

We calibrated a population-based dynamic differential model at sub-regional level to provide support for the update of the 2017-2020 national strategic plan for Tanzania. Estimates of prevalence and intervention coverage were obtained from various country-wide datasets including malaria indicator surveys, Insecticidal Treated Nets (ITN) distribution data and predictions from the Malaria Atlas Project (MAP). Models were fitted to prevalence data while estimating the baseline level of transmission as well as the relative ratio between indoors and outdoors biting mosquitoes. The impacts of a selection of potential interventions were simulated per district, projecting the prevalence in 2020 and the average number of cases averted between 2017 and 2020.

In low transmission and urban areas, ITNs are expected to have limited impact on the transmission intensity compared to Indoor Residual Spraying (IRS). Irrespective of other interventions, in high transmission settings, ITNs are indispensable and ITN coverage must be at least maintained to avoid rebound of both transmission and burden. At moderate transmission intensity both IRS with a high coverage and the maintenance of the current ITN coverage are expected to lower the transmission. The greatest impact was predicted when these were combined with increasing case management coverage.

The modelling results suggest that depending on the local setting, the most appropriate interventions will vary, and the most effective strategy therefore involves sub-national stratification. The integration of this modelling framework into the NMCP strategic planning should ensure that an appropriate strategy will be implemented.

The malERA Consultative Group on Modeling, PLoS Med. 2011 Jan; 8(1): e1000403.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P213

Larval *Echinococcus multilocularis* infection reduces Dextran Sulfate Sodium (DSS)-induced colitis in mice by attenuating Th1/Th17 mediated immune reactions

J Wang

Universität Bern

Aim:

Previous studies documented parasite-mediated immune suppression to be a hallmark triggering infection outcome in both chronic human and murine alveolar echinococcosis (AE). So far, little is known about the putative immune-mediated secondary systemic effect of this helminthic infection on other concomitant diseases, e.g. endogenous gut inflammation. In this study, we examined the effects of *E. multilocularis* infection on murine Dextran sodium sulfate (DSS)-induced colitis.

Methods:

At 3 months post *E. multilocularis* infection (chronic stage), the mice were challenged with 3% DSS in the drinking water for 5 days plus subsequently with tap water (alone) for another 4 days. At necropsy, target tissues/organs were collected, fixed in 10% buffered-formalin and routinely processed for paraffin embedding. Four μ m sections were stained with Hematoxylin and Eosin (H&E) for assessing inflammatory reaction. Cytokine levels were measured by flow cytometry and quantitative RT-PCR. Colitis severity was assessed by colon length, weight loss and by a semiquantitative score of morphologic changes by board-certified veterinary pathologists (CG, AP).

Results:

The histopathological analysis of the colon showed a significant reduction and inhibition of DSS-induced gut inflammation by concomitant *E. multilocularis* infection, which occurred through down-regulation of Th1/Th17 T cell responses in the colon tissue.

Conclusions:

E. multilocularis infection markedly reduced severity of DSS-induced gut inflammation upon down-regulation of Th1/Th17 cytokine expression, and attenuated CD11b⁺ DC maturation. Prospectively, targeting bioactive metabolites of *E. multilocularis* could be an option to develop an immunotherapy tool against colitis, and putatively also against other immune disorders that exhibit a similar pathogenesis.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P214

Comparison of two commercial Concentration Devices for the Recovery of intestinal Parasites in Stools with the Reference Method.

M Tritten; J Stauffer; HH Siegrist; R Lienhard
 ADMEDMicrobiologie

Aims:

To compare the efficacy of three systems for fixation and concentration of parasites in stools.

Methods:

One hundred and twenty-one fresh stool samples were examined for parasites with three fixation-concentration devices: (a) our reference in-house SAF concentration method, (b) StorAX SAF (Axonlab AG, Baden), both based on the Formalin-Ethyl Acetate sedimentation procedure and (c) Mini-System Paragreen (Biolife Italiana Srl, Milano) whose fixative solution contains citric acid and an unspecified heterocyclic compound, based on a filtration sedimentation principle. Thirty-eight stools were examined prospectively and 83 were prepared by spiking negative fresh stools with well defined positive samples before processing. Each stool was homogenised and distributed into the three fixation containers, processed according to our laboratory or manufacturers' instructions and examined according to our routine procedure.

Results:

Ninety-seven stools yielded one or more parasites by one or more methods and 24 stools remained negative with all 3 methods. Seventy-nine stools harboured only one species, 16 yielded 2 species and 2 specimens contained 3 or more parasites. Among the 121 stools, the routine SAF correctly scored 92 samples (76 %) (true negatives + true concordant positives), StorAX 89 samples (74%) and Mini-System Paragreen 113 samples (93%). Eighty-one stools gave concordant results with all 3 methods (67%) and 40 (33%) were discordant. According to the parasites themselves, more helminths, especially *Enterobius* sp. eggs and more protozoa, especially *Giardia lamblia*, were recovered by the Mini-system Paragreen. *Strongyloides* sp. larvae were also easily recovered by this system.

Regarding practical aspects, the in-house SAF and StorAX containers can easily be given to the patients with simple instructions. The mini-system Paragreen is a small device and the amount of stool added to the fixative solution in the container is critical due to a fast saturation of the filters.

Conclusion:

None of the three systems allowed recovering all parasites, confirming the need to examine 2 or 3 stools. The commercial devices offer a good alternative to in-house SAF, among those the mini-system Paragreen proved a better efficacy in recovering light ova and protozoa.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P215

Evaluation of Loop-mediated isothermal amplification (LAMP) for malaria diagnosis at the Point-of-Care

CA Antunes Moniz; I Felger

Swiss Tropical and Public Health Institute, University of Basel

The widely used Rapid Diagnostic Tests (RDTs) and light microscopy have lower sensitivity when compared with molecular methods, making more difficult to detect asymptomatic carriers. PCR is very sensitive and specific but it is more expensive and needs proper infrastructures, which is a disadvantage for field studies in limited resources areas. Isothermal methods like loop-mediated isothermal amplification (LAMP) present an alternative.

Aims:

The study aimed to validate and optimize protocols for the detection of malaria using LAMP and to compare the results to the performance of real-time PCR assays. A comparison of extraction methods was made to optimise a suitable protocol to be applied in the field in combination with LAMP.

Methods:

Two generic LAMP assays that detect all species of the genus *Plasmodium* were tested. Molecular markers targeted the 18S rRNA genes and mitochondrial DNA (mtDNA). Several detection dyes were evaluated: SYBR Green I, Hydroxynaphtol Blue and Calcein. In addition we designed a fluorescently labelled primer (Q-FIP:Fd). Amplification from dried blood spots (DBS) on filter paper was tested using a boil and spin protocol in combination with Q-FIP:Fd detection. In parallel a commercial LAMP kit was tested.

Results:

The sensitivity of LAMP was good and could be even improved by the use of calcein, which has the advantage of real-time detection in contrast to other dyes. However, amplification in the negative control (NTC) was often observed. This was also found when a commercial kit was used. For the 18S rRNA target, amplification in the negative control was observed with all detection methods. For the mtDNA target with Q-FIP:Fd detection, no amplification in the negative control was observed. Q-FIP:Fd detection was also successful on DBS on filter paper.

Conclusion:

The isothermal method LAMP in combination with DBS sampling with simple boil and spin DNA extraction has potential for use in POC setting with limited resources. The major concern is unspecific amplification. Introduction of a fluorescently labelled primer (Q-FIP:Fd) helps to avoid detection of unspecific products.

References

- Han, E. et al. J. Clin. Microbiol. 2007;45:2521
- Liu W. et al. Sci. Rep. 2017;7:40125.
- Notomi T. et al. Nucleic Acids Res. 2000;28:E63.
- Polley S.D. et al. J. Clin. Microbiol. 2010;48:2866
- Poon, L.L.M. et al. Clin. Chem. 2006;52:303
- Tanner N.A. et al. BioTechniques 2012;53:81



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P216

A green fluorescent *Trypanosoma cruzi* line to increase sensitivity of an in vitro drug screening assay

AF Fesser¹; RS Schmidt¹; F Olmo²; JM Kelly²; P Mäser¹; M Cal¹; C Kunz¹; M Kaiser¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) London School of Hygiene and Tropical Health

Both drugs used for the etiological treatment of Chagas' disease have issues with drug safety and efficacy. Unfortunately, the current drug discovery pipeline for Chagas' disease is not very well equipped as only a very small number of compounds passes the hit-to-lead phase. One of the reasons might be the limited number of suitable in vitro assays. This showcases the need for more sensitive and more predictable in vitro assays. The emergence of high-content imaging based assays has increased sensitivity, read-out quality, read-out quantity and the through-put of compounds. We hereby propose to employ a fluorescent transgenic parasite line which facilitates assays with continuous time course and assays with a high sensitivity and specificity for low parasite numbers. Additionally, this parasite line should be employed more easily for target identification procedures.

At this stage, we have obtained a parasite line expressing the enhanced green fluorescent protein stably throughout all major life-cycle stages. We have characterized the parental line concerning their epimastigote sensitivity against benchmark drugs. Additionally, we have sequenced the whole genome on an Illumina platform in order to facilitate target identification procedures.

In the future, we plan to compare the sensitivity of the mammalian stages of the transgenic parasite line against benchmark drugs to the sensitivity of its parental line in order to confirm the validity of its use. The transgenic parasite line will be employed in the development of new high-content assays. These assays will enlarge the portfolio of our drug screening facility.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
Swiss Society for Infectious Diseases SSI
Swiss Society for Hospital Hygiene SSHH
Swiss Society of Tropical Medicine and Parasitology SSTMP
Swiss Society of Tropical and Travel Medicine SSTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P217

Serodiagnosis of *Angiostrongylus cantonensis* infection by Western Blot

B Nickel¹; Y Nguyen²; B Rossi²; H Marti¹

(1) Swiss Tropical and Public Health Institute, University of Basel;

(2) Hôpital Beaujon

Introduction

Angiostrongylus cantonensis is a parasitic nematode endemic in Southeast Asia, the Pacific islands and the Caribbean, causing eosinophilic meningitis in humans. Humans become infected by consumption of raw food containing third stage larvae, e.g. infected snails, contaminated vegetables or freshwater shrimps. The larvae do not survive in humans longer than a few weeks to months, but the infection can lead to severe neurological symptoms which need treatment.

We show the development and validation of a specific Western Blot for serodiagnosis of angiostrongyliasis and report the case of a patient diagnosed with *A. cantonensis* infection without recent travel history to endemic regions.

Methods

A Western Blot was developed based on soluble antigens prepared from adult *A. cantonensis* worms isolated from infected rats. The immunoblot was validated with a panel of positive sera, negative sera from healthy blood donors, and with sera of other parasitic infections. Diagnosis of the patient was based on clinical symptoms, and *Angiostrongylus* infection was confirmed by Western Blot with both, serum and CSF samples.

Results

The Western Blot with soluble antigen of *A. cantonensis* exhibits a good sensitivity and specificity, but can be negative in the acute phase of the infection. Positive sera or CSF samples show specific reactivity at 31 kDa.

A patient with eosinophilic meningitis without travel history to *Angiostrongylus*-endemic regions was examined. CT and MRI of the brain were normal, and there was no sign of malignancy in thoracic and abdominal CT. All diagnostic tests for relevant viral, bacterial or fungal infections were negative. Serology for several other tissue helminth infections was negative as well. Finally, the diagnostic *Angiostrongylus* Western Blot revealed reactivity of serum and CSF samples towards the specific 31 kDa-antigen. The patient received anthelmintic treatment leading to complete regression of symptoms.

Conclusions

The *Angiostrongylus* Western Blot is a suitable serodiagnostic test for identification of *A. cantonensis* infections. In cases of eosinophilic meningitis an *Angiostrongylus* infection should be considered, even without travel history to endemic regions.

The presented case shows that consumption of contaminated vegetables or other food imported from endemic areas might lead to an infection with *A. cantonensis* in a non-endemic region.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P218

Antibiotic-resistant *E. coli* in drinking water samples from rural Andean households in Cajamarca, Peru

SM Hartinger^{1,2,3}, M Riveros¹, G Salmon-Mulanovich^{1,2,3}, H Verastegui^{1,2,3}, N.Nuño^{2,3}, G Bendezu¹, TJ Ochoa^{1,4}, D Mäusezahl²

(1) Universidad Peruana Cayetano Heredia, Lima, Peru

(2) Swiss Tropical and Public Health Institute, Basel, Switzerland

(3) University of Basel, Basel, Switzerland

(4) University of Texas School of Public Health, Houston, United States

Antibiotic resistance in pathogenic bacteria is a serious public health issue. The growing threat is a cause for concern and action to prevent the emergence of new resistant strains and the spread of existing ones to humans via the environment. This study was aimed at identifying faecal pathogens in drinking water obtained from rural Andean households from Cajamarca, Peru and measuring the antibiotic resistance profile of *Escherichia coli*. The study was embedded within a community-randomised controlled trial among 102 communities in the northern highlands of the Cajamarca Region, Peru. Generic *Escherichia coli* was isolated from drinking water of 320 households at baseline measurements. The antibiotic resistance pattern was determined against twelve commonly used antibiotics, using the Kirby bauer method. Out of 314 samples collected, 55.4% (n=174) were positive for thermotolerant coliforms. *E. coli* was isolated in 74% of these (n=117), *Klebsiella* spp. in 15.8% (n=25), *Enterobacter* spp. 10.1% (n=16) and *Citrobacter* spp. in 5% (n=8). We isolated multiple thermotolerant bacteria in 14% of the samples. The *E. coli* antibiotic resistance profile showed highest resistance against tetracycline (37.6%), followed by ampicillin (34.2%), sulfatrimethoprim (21.4%), and naladixic acid (13%). The high prevalence of faecal contamination in drinking water highlights the importance of household water treatment methods. Likewise, the high levels of antibiotic resistance found, urges to identify the origins of potential environmental contamination or misuse of antibiotics. Elucidating means for the safe disposal of antibiotic containing waste in this context and promoting such practices is essential.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P219

Drugs against alveolar echinococcosis: New faces and old friends

R Rufener, S Kunz, D Ritler, A Hemphill, B Lundström-Stadelmann
 University of Berne

Alveolar Echinococcosis (AE) is a zoonotic disease caused by the fox tapeworm *Echinococcus multilocularis*. Humans and other mammals get infected by ingesting infectious *E. multilocularis* eggs, which contain an oncosphere that will migrate predominantly to the liver and differentiate into a metacestode, thus causing AE. Treating AE is a challenging task, because the disease is usually detected at a late stage when curative surgery is not possible anymore. Current chemotherapeutic treatment is only palliative, thus necessitating the development of alternative and improved treatment options.

Our aim is to find and describe new compounds against AE. To do so, we screened drug libraries for molecules active against *E. multilocularis* metacestodes by applying a range of different in vitro tests (such as the PGI assay or the Alamar Blue assay). By screening the open access Medicines for Malaria Venture (MMV) Malaria Box, we identified one compound (MMV665807) with exceptional activities against metacestodes and isolated germinal layer cells. Additionally, the compound had low cytotoxicity against human and mammalian cells, hence indicating selective toxicity and a potential therapeutic window.

MMV665807 is a structural analogue of niclosamide, which is a well-known anthelmintic drug from the 1960ies with activity against intestinal infections of various adult-stage cestodes. More recently, niclosamide was also found to be active against a wide range of different cancers and other diseases. When tested in vitro against *E. multilocularis* metacestodes, niclosamide displayed a similar toxicity as MMV665807.

In a subsequent in vivo experiment, MMV665807 failed to be active in mice with secondary echinococcosis, and a respective trial using niclosamide is currently in progress. Transmission electron microscopy of metacestodes treated with MMV665807 revealed drug-induced alteration in the parasite ultrastructure, most notably in the mitochondria of the germinal layer cells. Additional affinity chromatography showed that MMV665807 binds to the calmodulin orthologue EM-cmd1. EM-cmd1 was expressed as a recombinant protein, and current experiments focus on the question whether MMV665807 and niclosamide can inhibit the functional activity of EM-cmd1. To do so, we developed an assay based on calmodulin-dependant phosphodiesterase to indirectly measure the activity of EM-cmd1.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P220

Land Use Regression modelling of outdoor NO₂ and PM_{2.5} concentrations in the urban Western Cape, South Africa

A Saucy^{1, 2}, M Rössli^{1, 2}, N Künzli^{1, 2}, M-Y Tsai¹, C Sieber^{1, 2}, T Olaniyan³, R Baatjes³, M Jeebhay³, M Davey¹, R Naidoo⁴, M Aqiel Dalvie³, K de Hoogh¹

(1) Swiss Tropical and Public Health Institute, Switzerland, Department of Epidemiology and Public Health EPH, Basel, Switzerland

(2) University of Basel, Faculty of Science, Basel, Switzerland

(3) University of Cape Town, School of Public Health and Family Medicine, South Africa

(4) University of Kwazulu-Natal, Department of Community Health, Durban, South Africa

The aim of the study is to characterize and model spatial distribution of air pollutants in three neighbourhoods in the Western Cape, South Africa. Intra-urban air pollution, especially traffic-related air pollution, has been associated with many adverse health effects, such as cardiovascular or respiratory disorders. Accurate and regular air quality monitoring is necessary to evaluate the air quality situation and advise policy makers. Land Use Regression (LUR) models are often used, as they can describe small-scale spatial variation in air pollution levels based on several monitoring sites and geographical predictor variables. They are also particularly suitable for resource limited settings where many informal sources contribute to exposure and where emission inventories are rarely available.

Methods

For this purpose, weekly measurements of NO₂ and PM_{2.5} were performed in the three areas (Khayelitsha, Milnerton and Noordhoek) during summer 2015-2016. They were temporally adjusted to obtain seasonal means using routinely monitored pollution data in Cape Town region. We developed two overall LUR models using a supervised stepwise land use regression method based on 94 and 87 sites for NO₂ and PM_{2.5} respectively. The tested predictor variables were already available at the province level or collected on site. The models were validated using leave-one-out-cross-validation and were tested for spatial autocorrelation (Moran's I statistics) and Cook's Distance.

Results

Measured air pollution levels were generally low. Mean NO₂ was 14.6 µg/m³ and mean PM_{2.5} was 7.2 µg/m³. The NO₂ model explained 64% of the variance (R²) in the study areas and was found to have a correct internal validity (LOOCV R² = 61%). The PM_{2.5} model presented lower explanatory power (R² = 32%, LOOCV R² = 27%). The best predictor variables for NO₂ modelling were mainly traffic related variables (major roads and bus routes) but also proximity to land use elements such as commercial area or informal settlements. Smaller local sources such as open grills and waste burning sites seemed to be good predictors for PM_{2.5} spatial variability, together with other traffic related variables. NO₂ and PM_{2.5} mean summer exposure was predicted for home and school locations of about 400 pupils at primary schools in the study areas involved in an epidemiological health study. Mean predicted concentration was 16 µg/m³ [10.0-20.5 µg/m³] and 10.7 µg/m³ [4.9-15.1 µg/m³] for PM_{2.5}.

Conclusion

This research shows that land use regression modelling can be successfully applied to informal urban settings in South Africa using similar predictor variables than in similar studies performed in Europe and North America. We could also provide NO₂ and PM_{2.5} seasonal exposure estimates and maps for the selected study areas.

This research is part of the Joint South Africa-Swiss bilateral Research Chair in global environmental health (SARChI) and was additionally funded by the Swiss-South African Joint Research Programme (SSAJRP).



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P221

Motility-based in vitro screening for the identification of new anti-cestodal compounds

D Ritler¹, R Rufener¹, J Bouvier², H Sager², A Hemphill¹, B Stadelmann¹

(1) Institute of Parasitology, University of Berne, Vetsuisse Faculty, Berne, Switzerland

(2) Elanco; Animal Health Research Center, St-Aubin, Switzerland

To date, the only drug used for the treatment of intestinal cestode infections is praziquantel. This has important implications, especially with regard to the potential risk of drug resistance formation. Thus, novel drugs to treat intestinal cestode infections must be identified, and these will also help to prevent diseases caused by the larval stages of cestodes. In the nematode world, novel compounds with activity against adult stages have been identified using movement-based high throughput in vitro drug screens, which can be carried out in microwell format and at high throughput. In contrast, establishing an in vitro-screening assay against adult cestodes is more complex, since adult cestodes cannot be cultured in microwell format due to their size and the unavailability of suitable culture methods. We here present a screening assay that employs *Echinococcus multilocularis* protoscoleces, which represent the precursors of the adult tapeworm scolex ("head"), and are thus regarded as pre-adult stage, serving as a model for adult cestodes. Protoscoleces are small-sized organisms and fit into microwell plates, they are produced in large numbers as a by-product of strain-maintenance, and are easy to handle regarding safety regulations.

The presented in vitro drug screening assay is carried out in 384 well format, and measures protoscolex movement by digital image analysis. Active compounds can be directly assessed microscopically in terms of morphological effects. The use of 384 well microwell plates minimizes the parasite and compound consumption and allows for rapid screening of large numbers of chemicals. A new DMSO-based protoscolex activation protocol was established to increase the movement output during screening, and the read-out for drug efficacy is loss of movement. Standard drugs such as praziquantel and nitazoxanide served as positive-controls, and monepantel and albendazole as negative-controls. The expected dose-dependent effects on protoscolex movement and morphology was demonstrated, and individual praziquantel enantiomers differed with regard to their minimal inhibitory concentrations. A new compound derived from the open access MMV (Medicines for Malaria Venture) Malaria Box exhibited excellent in vitro activity. Corresponding morphological alterations were visualized by scanning electron microscopy, which showed that this compound exhibits a mode of action clearly distinct from praziquantel. Currently, the assay is applied for the screening of the MMV Pathogen Box. Several promising compounds were identified, which are currently being further evaluated.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P222

Antibody-mediated virus control in “tolerant” congenitally infected virus carriers

Peter Reuther¹, Katrin Martin¹, Yusuf Ertuna¹, Doron Merkler², Daniel Pinschewer¹

(1) Department of Biomedicine, Experimental Virology, University of Basel, 4009 Basel, Switzerland

(2) Departement de Pathologie et Immunologie, University of Geneva, 1211 Geneva, Switzerland

Neonatal exposure of mice to Lymphocytic choriomeningitis virus (LCMV) results in antiviral tolerance and life-long co-existence of virus and host. Despite the thymic deletion of antiviral T cell precursors, such LCMV carriers mount anti-LCMV antibody responses. The role of these antibodies in the control of the congenital infection remains poorly defined. Furthermore, it has not been possible to physically identify the cells, which provided help to the antibody producing B cells.

We infected newborn wt mice or B cell receptor repertoire-restricted (BCRres) mice with a recombinant, trisegmented reporter virus encoding a Cre-recombinase (r3LCMV). While viral titers dropped dramatically in wt mice after a phase of high-level viremia by week eight accompanied by production of GP-1-binding IgG antibodies, viremia remained at high levels in BCRres mice. Moreover, histological analysis revealed that the virus had formed foci of infected hepatocytes in the liver of BCRres mice, whereas individual infected cells were scattered randomly throughout the liver of wt animals. In order to further characterize the antibody response required for control of the congenital infection, we infected newborn MHCII-deficient and AID-deficient mice. Both strains were not able to control the viral infection indicating that both conventional T cell help as well as class switch and/or somatic hypermutation are a prerequisite. Importantly, the fact that MHCII-deficient animals failed to control the viral infection points to the conclusion that tolerance of CD4 positive T cells was incomplete.

To gain insight into the mechanism by which antibodies control the congenital infection, we employed a reporter mouse strain expressing eYFP upon Cre/lox-recombination. Neonatal infection with the Cre-recombinase encoding r3LCMV revealed that the majority of hepatocytes had recombined but was not acutely infected anymore at week 12 post infection suggesting a noncytolytic clearance mechanism.

Altogether, these observations supported the interpretation that neonatally infected carrier mice mounted T cell help-dependent antiviral antibody responses, which partially controlled viremia probably by facilitating noncytolytic clearance of infected cells.



Joint annual meeting 2017

Swiss Society for Microbiology SSM
 Swiss Society for Infectious Diseases SSI
 Swiss Society for Hospital Hygiene SSHH
 Swiss Society of Tropical Medicine and Parasitology SSTMP
 Swiss Society of Tropical and Travel Medicine SSTTM

August 30 – September 01, 2017

Congress Center Basel | sginf2017.congress-imk.ch

P223

Identification of *Waddlia chondrophila* proteins involved in transcriptional regulation

M de Barsy¹; L Hergot¹; PH Viollier²; G Greub¹

(1) Lausanne University Hospital and University of Lausanne;

(2) University of Geneva

Waddlia chondrophila is an emerging pathogen belonging to the Chlamydiales order responsible for abortion in bovine and miscarriage in human. Chlamydiales order includes nine different families; the most studied one being the Chlamydiaceae since it includes important human pathogens such as *Chlamydia trachomatis* and *Chlamydia pneumoniae*.

Transcriptional regulation is an essential process for all living organisms. In bacteria, it is achieved at three different levels, (i) the RNA polymerase level (sigma factors...), (ii) the promoter level (transcription factors) and (iii) the DNA structure level (nucleoid-associated protein, histone-like proteins...). Sigma factors and DNA supercoiling are well studied in Chlamydiaceae while conserved transcription factors and their regulatory networks have recently been studied among Chlamydiae phylum.

Here, we propose to identify new factors involved in transcriptional regulation using heparin chromatography followed by mass spectrometry. With this original approach, we could identify nine proteins from the soluble fraction of purified *W. chondrophila*. Among them, eight were confirmed individually by heparin chromatography. We raised antibodies against three of them and performed ChIPseq analysis. Two of them showed a similar pattern, with 617 shared peaks, suggesting that these two proteins may form a complex. The third one, harbour a typical pattern of a chromatin associated protein, i.e. a binding along all the genome. Currently, we are investigating their specific role in the transcriptional regulation of *W. chondrophila*.

The identification of new transcription factors and their regulon will improve our understanding of the global transcriptional regulation of chlamydiae and could be used as new drug targets.