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Human African trypanosomiasis biomarkers: from discovery to translation towards field applications

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Introduction Human African trypanosomiasis (HAT) is a neglected parasitic disease affecting rural communities in sub-Saharan Africa. The disease progresses from a first heamolymphatic stage (S1) to a second meningo-encephalitic stage (S2), when trypanosome parasites penetrate into the central nervous system. Determination of the stage of disease and early detection of relapses during the post-therapeutic follow-up represent key issues to properly and safely treat patients. Current methods, based on counting of the white blood cells (WBC) and the detection of parasites in the cerebrospinal fluid (CSF) are, in fact, either not specific or not sensitive enough.
Methods and key results In this project we investigated CSF from HAT patients using different approaches, including proteomics and hypothesis driven discovery to highlight new promising markers. Eight candidates were identified to be able to stratify patients according to the stage of disease progression. Following their evaluation on a multicentre cohort, neopterin was validated as a powerful CSF staging marker for *T. b. gambiense* HAT. This metabolite, at a concentration of 14 nmol/L, was able to accurately discriminate between S1 and S2 patients before treatment (SP 88%, SE 88%). Interestingly, neopterin resulted also to be the best test-of-cure marker being able to discriminate between cured and relapsed S2 patients as soon as 6 months after treatment with 87% specificity and 92% sensitivity and showing higher accuracy than WBC.
Conclusions In order to translate this marker into a field test, a first prototype of point-of-care testing (POCT) has been produced. Its first evaluation on stored samples has shown the feasibility of the assay for rapid neopterin detection in the CSF and promising results for both staging and test of cure applications. Further optimization will be crucial to translate this POCT into the field to ameliorate patients' management and to contribute to HAT control.