SLEEPING SICKNESS: THE WAKE-UP OF TRANSLATIONAL BIOMARKER RESEARCH

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Human African trypanosomiasis (HAT), or sleeping sickness, is a parasitic tropical disease. It progresses from a haemolymphatic first stage (S1) to a neurological second stage (S2) due to invasion of parasites into the central nervous system (CNS). As treatment depends on the stage of the disease, there is a critical need for tools that efficiently discriminate the two stages of HAT. We hypothesized that markers of brain damage discovered by proteomic strategies and inflammation-related proteins could be used individually or in combination to discriminate between the two stages of disease.

The combined discovery strategies more than 100 proteins significantly differentially expressed between the two stages of the disease. Thirty-six of these potential markers were verified on 100 patients and the best 8 were further validated on a large multi-centric cohort (n=600). This final study showed that MMP-9, IgM, CXCL13 and neopterin most accurately distinguished S1 and S2 patients, with AUCs above 95%. Their further evaluation on Melarsoprol stage 2 treated patients for 12 months demonstrated the ability of neopterin and CXCL13 to detect relapsed patients. These markers were also clearly associated with the presence of neurological signs.

In conclusion, this study highlighted the value of CXCL13 and neopterin as markers of staging and test of cure of sleeping sickness patients. The health care impact of this potential discovery on HAT, a neglected African disease affecting the rural poor, is critical to allow appropriate therapeutic interventions.