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Review

Transcriptomics and proteomics in human African trypanosomiasis: Current status and perspectives

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ABSTRACT

Human African trypanosomiasis, or sleeping sickness, is a neglected vector-borne parasitic disease caused by protozoa of the species *Trypanosoma brucei* sensu lato. Within this complex species, *T. b. gambiense* is responsible for the chronic form of sleeping sickness in Western and Central Africa, whereas *T. b. rhodesiense* causes the acute form of the disease in East Africa. Presently, 1.5 million disability-adjusted life years (DALYs) per year are lost due to sleeping sickness. In addition, on the basis of the mortality, the disease is ranked ninth out of 25 human infectious and parasitic diseases in Africa. Diagnosis is complex and needs the intervention of a specialized skilled staff; treatment is difficult and expensive and has potentially life-threatening side effects. The use of transcriptomic and proteomic technologies, currently in rapid development and increasing in sensitivity and discriminating power, is already generating a large panel of promising results. The objective of these technologies is to significantly increase our knowledge of the molecular mechanisms governing the parasite establishment in its vector, the development cycle of the parasite during the parasite's intra-vector life, its interactions with the fly and the other microbial inhabitants of the gut, and finally human host-trypanosome interactions. Such fundamental investigations are expected to provide opportunities to identify key molecular events that would constitute accurate targets for further development of tools dedicated to field work for early, sensitive, and stage-discriminant diagnosis, epidemiology, new chemotherapy, and potentially vaccine development, all of which will contribute to fighting the disease. The present review highlights the contributions of the transcriptomic and proteomic analyses developed thus far in order to identify potential targets (genes or proteins) and biological pathways that may constitute a critical step in the identification of new targets for the development of new tools for diagnostic and therapeutic purposes.

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Contents

1. Epidemiology of human African trypanosomiasis

Human African trypanosomiasis (HAT) is caused by protozoan parasites of the species *Trypanosoma brucei* sensu lato, and belongs to the neglected tropical diseases, a group of chronic disabling infections affecting more than 1 billion people worldwide, mainly in Africa and mostly those living in rural areas, poor urban environments, or conflict zones. Two of the subspecies, *T. b. gambiense* and *T. b. rhodesiense*, are, respectively, responsible for the chronic form of HAT in Western and Central Africa, and the acute form of the disease in East Africa. The third subspecies, *T. b. brucei* does not infect humans but causes animal trypanosomiasis, also called Nagana, leading to economic losses estimated at US $4.5 billion/year to African agriculture [1]. HAT was first diagnosed more than 200 years ago [2], and the epidemics progressed during the first decades of the 20th century, then declined due to a) very active detection campaigns, b) attempts to establish a vector control, and finally c) extensive patient treatment. The epidemic decrease was such that, at the beginning of the 1960s, sleeping sickness was considered to be under control [3]. This led to decreased vigilance, inasmuch as the newly independent countries focused their efforts on other economic and social needs, with political problems in certain areas rendering sleeping sickness foci inaccessible. The disease became a re-emerging disease, such that in the past two decades the situation has become as bad as it was at the beginning of the 20th century. In 1998, 45,000 new cases were diagnosed [4], and a similar number of new cases were reported for 1999. In 2000, it was estimated 300,000 people were infected. However, as only 10–15% of the 60 million people living in risk areas are under control [5], one can consider that the number of infected people is probably highly underestimated.

2. Burden of sleeping sickness for populations

Sleeping sickness affects mostly geographically marginalized populations living in isolated rural areas. Consequently, the disease imposes a major burden upon rural poor populations that most often do not dispose of health facilities. Moreover, the disease is difficult to diagnose and some treatments are difficult to administer and/or tolerate [6]. Facing this frightening situation, the national control programs of most of the endemic countries, especially those in the central African region, with external financial support, have intensified medical surveys to diagnose and treat patients. The results seem promising, since WHO [7] has recently reported that the number of new diagnosed cases has considerably decreased, and the disease is considered again to be under control. Therefore, the time has come to instigate the elimination process by active epidemiologic surveys, diagnosis, and systematic treatment of all infected people.

Presently, 36 countries have been listed by WHO as being endemic for sleeping sickness. The chronic form of HAT is reported in 24 countries and accounts for more than 90% of reported cases of sleeping sickness. Among the 24 countries affected by *T. b. gambiense*, seven (Angola, Democratic Republic of Congo, Sudan, Chad, Central African Republic, Congo, and