ABSTRACT

Human African Trypanosomiasis (HAT) is a disease of major economic importance in Sub-Saharan Africa. The HAT is caused by Trypanosoma brucei *rhodesiense* (*Tbr*) parasite in eastern and southern Africa, with suramin as drug of choice for treatment of early stage of the disease. Suramin treatment failures has been observed among HAT patients in *Tbr* foci in Uganda. In this study, we assessed *Tbr* parasite strains isolated from HAT patients responsive (*Tbr* EATRO-232) and non-responsive (*Tbr* EATRO-734) to suramin treatment in Busoga, Uganda for 1) putative role of suramin resistance in the treatment failure 2) correlation of suramin resistance with *Tbr* pathogenicity and 3) proteomic pathways underpinning the potential suramin resistance phenotype *in vivo*. We first assessed suramin response in each isolate by infecting male Swiss white mice followed by treatment using a series of suramin doses. We then assessed relative pathogenicity of the two *Tbr* isolates by assessing changes pathogenicity indices (prepatent period, survival and mortality). We finally isolated proteins from mice infected by the isolates, and assessed their proteomic profiles using mass spectrometry. We established putative resistance to 2.5 mg/kg suramin in the parasite *Tbr* EATRO-734. We established that *Tbr* EATRO-734 proliferated slower and has significantly enriched pathways associated with detoxification and metabolism of energy and drugs relative to *Tbr* EATRO-232. The *Tbr* EATRO-734 also has more abundantly expressed mitochondrion proteins and enzymes than *Tbr* EATRO-232. The suramin treatment failure may be linked to the relatively higher resistance to suramin in *Tbr* EATRO-734 than *Tbr* EATRO-232, among other host and parasite specific factors. However, the *Tbr* EATRO-734 appears to be less pathogenic than *Tbr* EATRO-232, as evidenced by its lower rate of parasitaemia. The *Tbr* EATRO-734 putatively surmount suramin challenges through induction of energy metabolism pathways. These cellular and molecular processes may be involved in suramin resistance in *Tbr*.