MOLECULAR AND GENETIC BASIS OF DRUG RESISTANCE IN TRYPANOSOMA CONGOLENSE

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Isometamidium Chloride (ISM) is one of the principal drugs used to counteract *Trypanosoma congolense* infection in livestock, both as a prophylactic as well as a curative treatment. Numerous cases of ISM resistance have been reported in different African regions, representing a serious problem in the battle against animal African Trypanosomiasis (AAT). To identify genetic signatures associated with ISM resistance in *T. congolense*, the sensitive strain KTT/MSORO M7 has been selected to induce resistance in the murine host. The induction experiment started with the very low dose of 0.005 mg/kg of ISM. After an induction of 4 months, the strain became fully resistant to ISM 1mg/kg, the maximal dose used in livestock. 3 independent biological replicates of the ISM-resistant KTT/MSORO M7 strain have been generated. Differential ISM uptake has been observed by flow cytometry between the sensitive strain and the induced clones, and the drug compartmentalization and accumulation are currently being investigated by confocal microscopy. Full genomes of the sensitive strains and the induced drug resistance strains will be compared in order to identify the putative genomic changes associated with the acquisition of drug resistance. These will be validated using 54 ISM-resistant and -sensitive field-isolated strains that were recently sequenced for phylogenetic and population genetic analysis. The ultimate aim of this study is to characterize the main driving genetic variations responsible for the observed differential ISM uptake and the acquisition of drug resistance.