A decrease in mitochondrial membrane potential may be associated with diminazene resistance in *Trypanosoma congolense.*

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Animal trypanosomiasis is a parasitic disease of livestock and *Trypanosoma congolense* is a major cause. It causes economic hardship in many developing regions due to illness and death of infected domestic animals. Although treatment is available, there are field reports of *Trypanosoma congolense* resistant to diminazene. This project therefore aimed to determine the mechanism by which *T. congolense* can develop resistance to diminazene to aid future drug administration, drug discovery and improve resistance reporting. Wild type *T. congolense* cell lines were exposed to increasing concentrations of diminazene in culture. Uptake of radiolabelled diminazene, fluorescence activated cell sorting (FACS), DAPI staining, DNA and RNA sequencing, and drug sensitivity assays were used to assess the mechanism/s of resistance. Previous studies on *Trypanosoma brucei* strains have shown loss of drug uptake to be the key drug resistance mechanism for many drugs, including diminazene; however, here we show that diminazene uptake in *T. congolense* did not differ between resistant and sensitive lines. A shift in mitochondrial membrane potential, however, was evident in resistant lines, indicating that this is linked to diminazene resistance in *T. congolense*. The implications of this mechanism with respect to limiting the development and/or spread of drug resistance will be discussed.