African animal trypanosomosis (AAT) is an economically devastating and potentially fatal livestock disease caused by single or co-infection with *Trypanosoma* parasites *T. congolense, T. vivax,* and *T. brucei*. Chemotherapy and chemoprophylaxis are the core methods for AAT control. Concerningly, the two most widely used AAT trypanocides, diminazene aceturate and isometamidium chloride, are demonstrating increasing treatment failure. Drug resistance is widely suspected to be a major contributing factor; however, the transmission dynamics underlying the emergence and spread of resistant parasites remain poorly understood.

Substantial advances in functional genetic studies of trypanosomes have identified and validated specific genes associated with resistance to commonly used trypanocides. In *Trypanosoma congolense*, loss of the DMT gene confers resistance to isometamidium chloride, and in *Trypanosoma brucei*, loss of function of the TbAT1 gene results in diminazene aceturate resistance. These discoveries provide a solid foundation with which to investigate resistance in more complex systems using molecular methods.

A critical aspect of disease epidemiology for vector-borne pathogens is the ability to transmit efficiently through the arthropod vector. Given that drug selection pressure is imposed entirely in mammalian hosts (or *in vitro* during laboratory experiments), mutations that reduce parasite transmissibility via the vector would not be evident in those contexts. Critical knowledge gaps persist in our understanding of whether genetic mutations that confer drug resistance impose a fitness cost on the parasite during its development in the tsetse fly vector and subsequent transmission. Any such transmission fitness cost would have profound implications for the ability of drug resistance traits to transmit and persist in the field.

This PhD research determines whether parasite lines carrying defined drug resistance–associated mutations retain the capacity to successfully infect, develop within, and be transmitted by the tsetse fly, and assesses any potential fitness cost of resistance. Infection establishment in tsetse midguts and progression to transmissible forms in the salivary glands and mouthparts were compared between tsetse flies infected with resistant and drug-sensitive parasite lines of *T. congolense* and *T. brucei*. If resistance mutations reduce parasite transmissibility through the tsetse fly, their spread may be constrained in the absence of sustained drug pressure. Conversely, if resistant parasites maintain full transmission competence, current treatment practices may accelerate dissemination across endemic regions. Preliminary data indicate no significant differences in midgut infection or development of transmissible forms between resistant and drug-sensitive lines. These findings suggest that resistance-associated mutations do not impose detectable transmission fitness costs, with important implications for the spread and persistence of drug resistance in endemic regions.