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HOW CAN TSETSE POPULATION GENETICS CONTRIBUTE TO AFRICAN TRYPANOSOMIASIS CONTROL?

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In sub-Saharan Africa, tsetse transmitted Trypanosomiases have an enormous impact on both human health and economic development. Both the World Health Organisation and African countries through the Pan African Tsetse and Trypanosomiasis Eradication Campaign (PATTEC) have recently asserted their determination to rid the sub-continent of these diseases, and it is increasingly recognised that vector control should play an important role. This review mainly focuses on population genetics of tsetse of the palpalis group, the main vectors of sleeping sickness, and reports recent results on tsetse population structure and on measures of gene flow between populations in different countries (Burkina Faso, Senegal, Guinea, Ivory Coast). Implications of these studies for large-scale tsetse control programmes being undertaken in West Africa are important, particularly regarding the definition of control strategies (suppression or eradication).

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EVIDENCE THAT THE TYPE IIA STRAIN OF *TRYPANOSOMA CRUZI* IS ADAPTED TO CONGENITAL TRANSFER

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It is well known that *Trypanosoma cruzi* represents a genotypically diverse family of organisms. Although some studies have suggested that the pathological outcome to infection may be associated with specific isolates, no correlation between strain and modification in transmission strategy has been identified. We have previously demonstrated in mice that the Type IIa strain of *T. cruzi* found in the southeastern United States is transferred congenitally at a significantly higher rate than the Type I strain from the same region. Using an *in vitro* cell culture model for human placental syncytial trophoblasts, we have tested whether the Type IIa strain has an enhanced ability to invade and replicate in these cells. Cultures of BeWo cells were exposed to either a Type I or Type IIa isolate of *T. cruzi* and assessed microscopically at 48, 72, and 96 hours for the percentage of cells infected and the average number of intracellular amastigotes. Cultures exposed to Type IIa isolate had significantly higher percentages of infected cells, as well as increased average numbers of intracellular amastigotes. Control infections carried out in DH-82 canine macrophage cells found that the Type I isolate was at least equal to the Type IIa strain in the ability to invade and replicate under these non-placental cells. Our results confirm that significant differences exist in the ability of these two isolates to invade syncytial trophoblast cells, suggesting adaptations in the Type IIa strain toward congenital transmission. This study not only provides the first *in vitro* evidence of strain-associated tissue tropism for *T. cruzi*, but also supports previous hypotheses for the evolution of the Type II strain in placental animals.

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A NEW APPROACH TO IDENTIFYING DRUG LEADS FOR CHAGAS' DISEASE: HIGH THROUGHPUT SCREEN AGAINST AN INTRACELLULAR PATHOGEN

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Trypanosoma cruzi is the parasitic agent of American trypanosomiasis or Chagas' disease, a neglected infectious disease affecting around 10 million people and an overwhelming human and economic burden throughout Latin America. A surge of patients identified in developed countries in recent years has highlighted its importance in global health. Discovery of new chemotherapy without the severe side effects associated with nifurtimox or benznidazole is essential. It is becoming evident that multi-drug therapy can prevent or significantly delay the onset of Chagas' disease pathology. To facilitate the rapid screening of large drug-like libraries, we have recently developed and validated an image-based high throughput screening assay for the pathogenic amastigote stage of *T. cruzi*. Our assay can be used with a variety of *T. cruzi* isolates and host cells and simultaneously measure trypanocidal efficacy and drug cytotoxicity to mammalian host cells. We can use various parasites strains with different biological characteristics (*e.g. T. cruzi* resistant to nifurtimox and benznidazole, clinical strains) and a range of host cells from primary human cell cultures to established cell lines (e.g. muscle cells, macrophages, hepatocytes). Our high content assay can be easily adapted to screen drugs against other intracellular pathogens such as *Leishmania* and *Toxoplasma gondii*. We are currently exploring large libraries of compounds by high through put screening to identify hits with trypanocidal efficacy and drug-like properties.

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MOLECULAR GENETIC STUDIES OF *GLOSSINA FUSCIPES FUSCIPES* AND *TRYPANOSOMA BRUCEI RHODESIENSE* IN EASTERN UGANDA

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Tsetse flies (Diptera: Glossinidae) are vectors of several species of pathogenic trypanosomes in sub-Saharan Africa causing Human African Trypanosomiasis (HAT) and African Animal Trypanosomiasis. Uganda has two forms of parasites, *Trypanosoma brucei rhodesiense* and *T. b. gambiense* causing HAT. Tsetse flies infest two thirds of Uganda with *Glossina fuscipes fuscipes*, predominating followed by *G. pallidipes* and *G. morsitans*. Genetic studies indicate genetic differentiation of *G. f. fuscipes* into Southern and Northern as separated by Lake Kyoga with co-occurrence of the two populations in central Uganda. Studies have indicated high dispersal rates in *G. f. fuscipes*. Such dispersal rates need monitoring local patterns and stability of genetic homogeneity over time at spatial scales to provide useful information for designing effective control programs. Little is known about the genetic stability of *G. f. fuscipes* populations and the genetic changes associated with temporal changes. These regions also span the historical disease foci caused by *T. b. rhodesiense* parasites. No information is available on the fine scale differentiation of parasite populations resident in distinct flies, animal reservoirs and humans. This project is to analyze: (1) The spatial and temporal stability of the genetic structure of *G. f. fuscipes* spanning southern and northern tsetse populations and (2) Parasite genotypes in infected flies, animal reservoirs, and in humans along the same transect. We are using nuclear and mitochondrial DNA markers to assess *G. f.*