**Advertisement for a PhD Public Defense**

**Date :** 2nd February, 2022

**Time :** 14:00 Hrs – 17:00 Hrs

**Venue :** Conference Room 1, Level 3, CoVAB, Makerere University

**Thesis Title :** UNDERSTANDING *TRYPANOSOMA BRUCEI BRUCEI* –

HOST INTERACTIONS ASSOCIATED WITH BIOLOGICAL BARRIER TRAVERSAL

**Course: :** PhD in Molecular Biology

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# ABSTRACT

*Trypanosoma brucei*, the causative agents of African Trypanosomiasis cross different biological barriers resulting in serious disorders. This study investigated *Trypanosome* parasite host interactions associated with biological barrier traversal and the mechanism used by *T .b. brucei* to traverse different biological barriers. A mouse model utilizing different *T. b. brucei* strains was employed to seek whether traversal of the blood-brain barrier (BBB) commences at the same time point for different strains of the same subspecies. Further, *in vitro* biological barrier models, the MDCKII and HDMEC models, together with confocal and scanning electron microscopy were used to determine the mechanism of traversal. Subsequently, a protein previously suspected to be involved in cell-cell adhesion, and a possible trypanosome ‘integrin’ was expressed both in the bacterial expression system and ectopically overexpressed in the trypanosome and later localized. Findings show that different strains of the same subspecies begin traversing the BBB at different time points and that both field isolates and laboratory strains as early as 3 days post infection, which is earlier than initially reported. Traversing of different biological barriers by *T. b. brucei* was found to differ, with the modification of the host plasma membrane in one of the barriers as it traverses through, by the formation of “possible cup-like structures independent of vascular adhesion molecule-1. Both paracellular and transcellular routes of traversal are utilized though with more preference to paracellular route. The expressed protein was found to localize in the mitochondria and not on the plasma membrane, ruling out the possibility of its involvement in cell-cell adhesion or BBB traversal. Taken together, the findings of this study suggest the possible involvement of different mechanisms and different virulence factors in BBB traversal. It also for the first time demonstrates the modification of the host plasma membrane as the *T. b. brucei* migrates across the microvasculature. Exploring the factors behind this modification may unveil trypanosome novel molecules that can be exploited in development of new interventions against African Trypanosomiasis.

**Key words:** *Trypanosoma brucei brucei*, traversal, biological barriers, mechanisms