Instituto de Medicina Molecular João Lobo Antunes

MSc Project Proposal

Title: Identification of parasite proteins that mediate binding to blood vessels

Synopsis:

Trypanosoma congolense is an extracellular parasite and the main cause of animal trypanosomiasis or nagana in African cattle. Nagana is a life-threatening disease and a major constraint for African socio-economic development. It has an estimated annual economic impact of USD $4.5 billion [1], it puts 46 million cattle at risk [2], and is a potential zoonotic source of Human sleeping sickness [3,4].

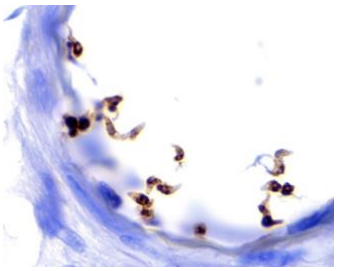

Figure 1 *Trypanosoma congolense* sequestered to a mouse arteriole in the adipose tissue.

T. congolense is vector-borne, alternating between the tsetse fly and a mammalian host. In the mammal, the parasite replicates in the blood, where it can bind to the endothelial cell lining of the vasculature. Previously, we showed that this process, known as sequestration (Fig.1), is a virulence factor that affects disease progression and outcome [5]. Specifically, increased parasite sequestration in the brain results in cerebral trypanosomiasis, characterized by brain pathology, immune cell recruitment, and ultimately early death due to $CD4^+$ T cell accumulation in the brain parenchyma [5]. Further work on *T. congolense* sequestration is limited because we do not know which parasite proteins mediate sequestration to the endothelium.

We compared the gene expression profiles of sequestered and non-sequestered parasites and identified a set of genes that are candidates for sequestration mediators. In this project, the student will validate up to 5 gene candidates by developing and characterising gene knock-out (KO) *T. congolense* mutants. Furthermore, the student will characterise the role of those genes in sequestration by assessing the sequestration capacity of the mutant parasite lines *in vitro* and *in vivo.*

The knowledge originating from this project is essential for the successful development of therapeutic strategies that interfere with parasite survival in the mammalian host and reduce host pathology.

To conduct this project, the student will acquire skills in molecular, cell, and infection biology. Key techniques to be learnt include cloning, transfection, cell culture, light and fluorescence microscopy, flow cytometry, and laboratory animal handling. The student will work in close collaboration with the supervisor, who investigates parasite sequestration using 'omics technologies and tissue bioengineering approaches. At IMM, the student will have the opportunity to interact with an international research community, meet students from the LisbonBioMed PhD program, attend weekly seminars and present and discuss their work.

This project is expected to start in February 2023.

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Co-Supervisor (if applicable): Luisa Figueiredo, lmf@medicina.ulisboa.pt

Bibliography:

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4 Truc, P. *et al.* (2013) Atypical Human Infections by Animal Trypanosomes. *PLoS Negl. Trop. Dis.* 7,
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