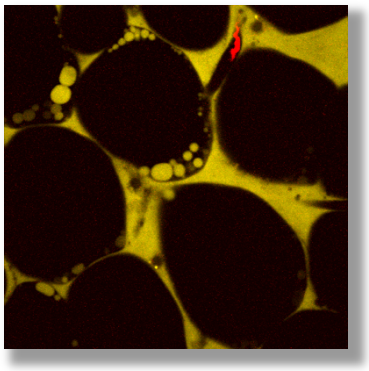
Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Imaging how Trypanosoma parasites interact with endothelial cells



Trypanosomiasis is a vector-borne parasitic disease largely restricted to Africa, which is lethal for humans, cattle, and wild animals if untreated. Trypanosoma brucei parasites live extracellularly in the blood, lymphatic system and interstitial spaces of organs. Our lab recently found that *T. brucei* parasites accumulate in adipose tissues (AT), as an important reservoir. This was not expected, and it is of key relevance for our understanding of parasite dynamics during infection in the mammalian host, and treatment efficiency.

How do trypanosomes extravasate to the adipose tissue? What is the role of the endothelial cells of the vasculature? **In this project, the student will use imaging tools to characterize how parasites interact with endothelial cells, and how parasites cross endothelial cell barriers.** The student will establish imaging-based methods to explore parasite interactions with endothelial cell receptors. These include the use of intravital microscopy to image parasite interactions with relevant transgenic mice; *in vitro* methods including the establishment of trans-well assays and co-cultures to explore host-parasite interactions using advanced fluorescence microscopy methods; and the use of optical clearance to make tissues transparent and generate an atlas of parasite interactions with specific endothelial cell receptors.

In this dissertation, the student will learn surgical procedures in mice to perform intravital microscopy; and various state-of-the-art methods for *in vitro* fluorescence microscopy and image analysis.

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Bibliography:

- Trindade, S. *et al. Trypanosoma brucei* Parasites Occupy and Functionally Adapt to the Adipose Tissue in Mice. *Cell Host Microbe* **19**, 837-848 (2016).
- De Niz, M. *et al.* Toolbox for in vivo imaging of host-parasite interactions at multiple scales. *Trends Parasitol* 35(3): 193-212 (2019).