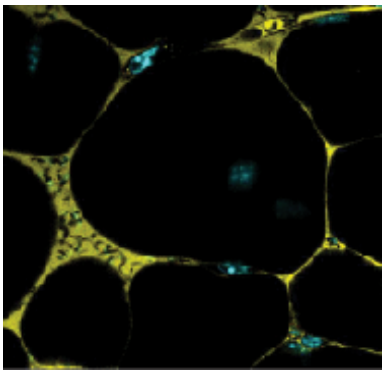
Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Are There Persisters in Adipose Tissue Populations?

Synopsis:



The sleeping sickness parasite (*Trypanosoma brucei*) senses and adapts to its different surrounding environments. In our lab at iMM, we have shown that when this parasite colonizes the adipose tissue, it metabolically adapts to catabolize lipids (Trindade *et al*, 2016). **Does tissue adaptation result in the emergence of persisters?** This will be the topic of this project.

In a mouse infected with a monomorphic *T. brucei* laboratory strain, within the first week of infection, we found in the adipose tissue parasites that show characteristics of persistence. These parasites divide twice as slow as its blood counterparts do. In this project, the student will study the occurrence of persister parasites in a more natural parasite strain and determine whether such persisters exist in multiple organs and throughout infection.

The student will infect mice with a pleomorphic parasite strain, that more closely resembles the natural strains and 1 and 2 weeks later, characterize the proliferative state of the parasites by assessing parasite load in different tissues of the animal, the protein synthesis activity of the parasites, its cell cycle profile and its capacity to divide. By infecting different KO mice (e.g. Rag KO); the student will also determine which host component(s) might be promoting the persister phenotype.

With this work, we will understand how widespread persistence is in *T. brucei* infection. Given that bacterial persistence is a natural cause of antibiotic resistance, our study may shed light on drug resistance in sleeping sickness.

METHODOLOGY: This work will involve mice infections, organs collection, DNA extraction, quantitative PCR, and the use of different biochemical assays together with flow cytometry and microscopy analysis of isolated cells.

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Webpage of the group

Bibliography:

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