Elucidating host and parasite factors involved in ***Leishmania*** quiescence and reactivation

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Macrophages play significant roles in immune responses including pathogen clearance and killing, and presentation of antigen to T cells. Despite their antimicrobial properties, macrophages serve as niches for long-term survival of diverse pathogens, including *Leishmania spp.* The outcome of macrophage infection by Leishmania is influenced by both host and parasite factors that are incompletely understood. We wish to understand the dynamics of the interaction between host and parasite and to investigate the contribution of immune response and parasite phenotype. Specifically, we wish to explore a role for quiescent or persistent parasites in subversion of a protective immune response.

We have established a long-term macrophage infection model in which quiescent parasites can be observed up to 2 weeks after infection using CFSE Cell tracer dye and Bromodeoxyuridine labelling.

In order to elucidate the host factors involved in Leishmania quiescence we have manipulated the activation state of infected macrophages to observe changes in the emergence of *L.mexicana* quiescence. Through this we aim to identify immunological determinants involved in parasite quiescence and persistence

Moreover to separate quiescent from actively proliferating parasites, we have performed metabolomic and proteomic analysis of purine-stared *L. mexicana,* a model of induced quiescence. We have identified pathways and hypothesise a role for these in quiescence of intracellular, persistent *L. mexicana*. We have knocked out some genes involved in these pathways using CRISPR Cas9 technology and aim to determine their importance in the establishment of quiescence of *Leishmania* in our macrophage model of persistence.

Our ongoing study will help to elucidate the dynamics between host immune status and quiescence that will help to increase understanding of parasite persistence and treatment failure in a clinical setting.