“Nascent proteome dynamics in quiescent and proliferating *Leishmania mexicana* under purine starvation”

The Leishmaniases are a complex of diseases caused by protozoan parasites of the genus *Leishmania*. Disease control efforts are confounded by the increasing incidence of treatment failure (TF). Treatment failure is a multifactorial problem encompassing antileishmanial drug resistance, host-immunology factors, and parasite factors, such as the adoption of quiescent phenotypes. Quiescence is a reversible phenotype characterised by global downregulation in transcription, translation, and protein turnover rates, that facilitates parasite tolerance to many stressors and is implicated in persistence and relapse of symptomatic disease. Because *Leishmania spp* regulate gene expression at the post-transcriptional level, quiescence is likely initiated, maintained, and eventually exited through changes at the protein level. Our understanding of the dynamics of de novo protein synthesis during parasite stress responses remains poorly characterised. Furthermore, proteome remodelling during the early stages of reemergence could yield the key determinants involved in the revival of quiescent *Leishmania* and provide insight into novel mechanisms underlying persistence and relapse.

In this body of work, we present our findings looking at nascent proteome dynamics during purine starvation and early addback in *Leishmania mexicana*. Using Bioorthogonal non-canonical amino acid tagging (BONCAT) coupled to LFQ proteomics, we present a time lapse series of newly synthesised protein (NSP) changes reflective of the entry, maintenance, and recovery from a quiescent-like state. Here we identify over 500 purine-starved specific NSPs and over 300 NSPs from parasites in purine addback conditions which are absent from purine rich parasites. These unique signatures could generate new insights into the mechanisms and pathways necessary for parasite revival and recrudescence of the disease. Additionally, it provides a broad scope of potential novel drug targets to combat relapse associated TF.