The molecular basis of heat shock signalling in African trypanosomes

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The heat shock (HS) response represents a significant virulence factor for African trypanosomes, with disease manifesting in the mammalian host as periodic fever which is sensed by the parasites, requiring adaptation to this stress. Eukaryotic cells typically trigger general protein translation arrest to prevent accumulation of misfolded proteins, whilst increasing the expression of proteins which aid protein folding and degradation.

While a HS response does occur in *Trypanosoma brucei*, the molecular mechanisms mediating this response are not understood. Transcription factors are not present to mediate a global response to the stimulus, and translational arrest is independent of the mechanism found in mammals. Preliminary evidence suggests regulation occurs through a novel post-transcriptional mechanism involving dynamic phosphorylation of unique regulatory RNA binding complexes (Ooi et al., 2020). We aim to combine global quantitative proteomics with phosphoproteomics to kinetically profile trypanosome HS signalling, and examine the role of specific phosphorylation events on post-transcriptional regulators.

We are examining the HS response in both *T. brucei* and the less well characterised *T. congolense*, the leading cause of AAT (Animal African Trypanosomiasis), utilising novel genetic manipulation techniques now possible in this organism. These parasites co-infect the same hosts with exposure to similar evolutionary selective pressures, and it is expected they will show some similarities in their host interactions. We will show data examining the impact of key early phosphorylation events on HS response components TbDHH1, TbPABP2 and TbZC3H11 in survival and progression through the parasite HS response.