

The local immune response to *Trypanosoma brucei* in the tissues of the abdomen

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Trypanosoma brucei is the causative agent of human and animal African trypanosomiasis, creating a significant burden on health care services and the local economy in sub-Saharan Africa. The parasite is able to survive and develop a chronic infection in the host, despite being highly immunogenic and eliciting a strong anti-trypanosome immune response. In early infection, parasites reside in the blood, lymph, and a variety of other tissues whilst in later infection, trypanosomes enter the brain causing severe neurological disturbances. This work aims to develop the understanding of immune cell activation in the presence of *Trypanosoma brucei* by exploring the links between immune response, parasite localisation and the associated clinical symptoms.

A bioluminescent *in vivo* model of African trypanosomiasis was used to observe tissue tropism and colonisation at early and late stages of infection, with parasites identified in all studied tissues including the colon, small intestine and omentum. Further analysis of the colon showed alterations to gut structure through histological staining of naïve and infected sections. We have observed significant enlargement of the omentum, a specialised immunological adipose tissue located in the peritoneal cavity shown to capture contaminants, such as translocating bacteria, which can enter the peritoneal space from the gut. Changes in immune cell populations of the colon lamina propria and mesenteric lymph nodes were also recorded. With an increasing understanding of the importance of the direct link between the brain and the gut, the presence of *Trypanosoma brucei* in the gut during infection provides a potential uncategorised link between perturbed brain function and immune response.

RNA sequencing analysis of tissues from naïve and infected mice revealed tissue specific differences in response to parasite presence, with many differentially regulated genes at both early and late stages of infection. There was a notable increase in macrophage related signatures in multiple tissues signifying a localised immune response to parasite presence. This was further studied *in vitro* comparing macrophage activation in the presence of trypanosomes and trypanosome secreted factors.