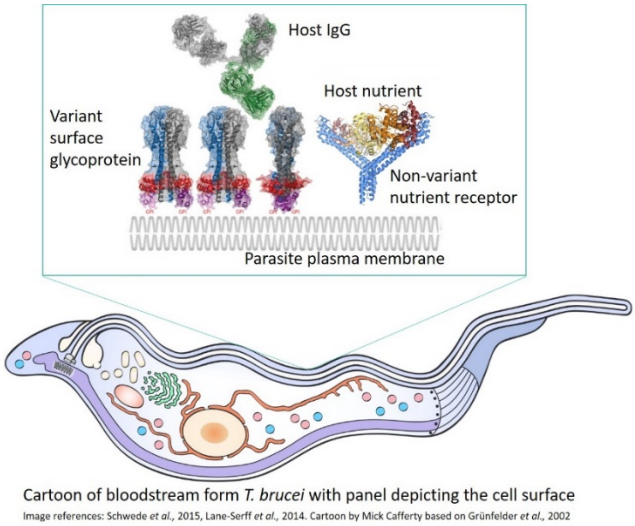
# The landscape of a parasite surface: Characterisation of the exposed invariant epitopes on the surface of African trypanosomes as putative targets of novel immunotherapeutics



Cartoon of bloodstream form *T. brucei* with panel depicting the cell surface

Image references: Schwede *et al.*, 2015, Lane-Serff *et al.*, 2014. Cartoon by Mick Cafferty based on Grünfelder *et al.*, 2002

**Supervisory team:**
**Main supervisor:** Dr Paula MacGregor (University of Bristol)
**Second supervisor:** Dr Fabio Parmeggiani (University of Bristol)
Prof Imre Berger (University of Bristol)
**Non-academic (CASE) supervisor:** Dr Andrea Gonzalez-Munoz (AstraZeneca)

**Host institution**: University of Bristol

**CASE partner:** AstraZeneca

**Project description:**

In-silico target identification of the exposed invariant epitopes on the surface of African trypanosomes for the design and development of novel immunotherapeutics.

Several trypanosome species are pathogens of humans and livestock in sub-Saharan Africa. Successful infection and transmission rely on the ability of the trypanosome to detect, interact with, and adapt to its environment. As extracellular parasites, the trypanosome cell surface acts as the molecular interface between the parasite and its external environment and functions in nutrient acquisition, signalling, and countering host innate and adaptive immune attack.

The major surface protein, the Variant Surface Glycoprotein (VSG), has been well characterised and plays important roles in host immune evasion. The non-variant surface proteins are largely protected from detection by the host immune system through shielding by the VSG. However, the functions of some of these proteins necessitate that they protrude out of the VSG layer. This requirement provides a potential weakness in the parasite's armoury.

Antibody-drug conjugates are an increasing class of oncological immunotherapeutics. We have recently shown that antibody-drug conjugates can be targeted to the trypanosome cell surface through a non-variant surface protein and lead to efficient killing of the parasite in vitro and in vivo.

This PhD project will use in silico structural modelling methods to predict exposed epitopes at the parasite cell surface and determine to what degree these should be accessible to immunotherapeutics. We will then assess those predictions experimentally. This will serve as a model system for in silico target identification methods for the rational design and development of novel immunotherapeutics for in general and provide a comprehensive analysis of the parasite cell surface landscape.

This studentship will be primarily based in the School of Biological Sciences at the University of Bristol under the supervision of Dr Paula MacGregor and Dr Fabio Parmeggiani, but will include placements at AstraZeneca, Grant Park, Cambridge under the supervision of Dr Andrea Gonzalez-Munoz. Please contact Paula MacGregor for informal enquiries (paula.macgregor@bristol.ac.uk).

An interest in computational biology would be advantageous.

Key references: Macleod, O.J.S., *et al.,* 2020. An African trypanosome receptor exploits host factor H for transmission to the tsetse vector. *Nature Communications,* 11(1): 1326. MacGregor, P., *et al.,* 2019. A single dose of antibody-drug conjugate cures a stage 1 model of African trypanosomiasis. PLOS Neglected Tropical Diseases, 13(5): e0007373. Schwede, A., *et al.,* 2015. How does the VSG coat of bloodstream form African trypanosomes interact with external proteins? *PLOS Pathogens,* 11(12): e1005259.