

Schistosomes are long lived parasitic blood flukes that have developed mechanisms of immunomodulation to achieve survival of their infected human host. In addition to suppressing host responses to the parasite itself, these immunomodulatory effects dampen responses to co-infections and vaccines, while also reducing incidence of autoimmunity and allergy. However the molecular basis by which schistosomes turn-off immune responses is unclear.

Chronic schistosomiasis pathology is driven by host responses to parasite eggs trapped in tissue, and eggs are known to be key drivers of type 2 immunity and regulatory responses. As such, egg-secreted proteins likely include immune modulators. Using published proteomic and transcriptomic datasets from the *Schistosoma mansoni* parasite, we have identified a total of 130 candidates that are either actively transcribed or secreted by parasite eggs. We have focused our study on extracellular proteins, which are most likely to directly interact with host cells.

Bioinformatic analysis was performed to identify egg proteins that either contain a signal peptide or are predicted to be extracellular. Because these proteins often contain post-translational modifications such as disulfide bonds, to confer biochemically active conformation, we used Human Embryonic Kidney (HEK) 293-6E cells as a heterologous expression system.

The extracellular domain of each candidate was identified and codon-optimised for recombinant expression in mammalian cells. Recombinant parasite proteins were also designed to contain a C-terminal sequence for enzymatic biotinylation to allow immobilisation on streptavidin-coated solid phases. Out of 36 proteins, so far 23 have been successfully expressed and validated by SDS-PAGE and western blot.

This new protein resource will be used in SAVEXIS, an ELISA-based protein interaction assay, against an array of 1500 human cell receptors, to identify new host: parasite interactions. The results of this screen will be used to inform which egg proteins interact with host receptors and will be further validated in cellular and *in vivo* assays with the aim of understanding how *S. mansoni* modulates the human immune system. This work could also lead to the identification of novel candidates for the treatment of autoimmune and allergic diseases.