

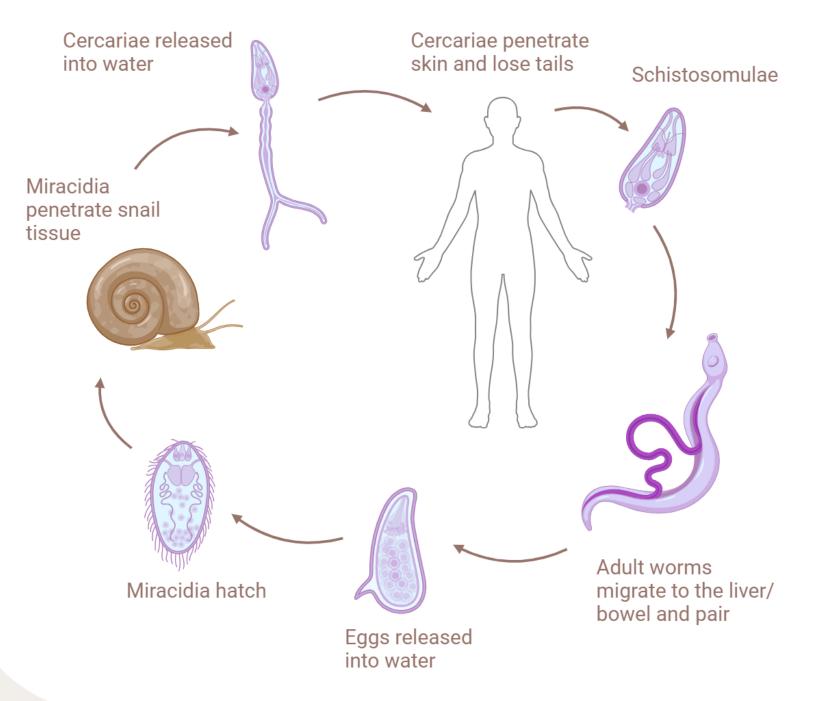
Schistosoma mansoni Micro-Exon Genes (MEGs)



Zaina Ibnahaten¹ Nicole Muller-Sienerth² Gavin Wright^{1,3} Cecile Crosnier^{1,3}

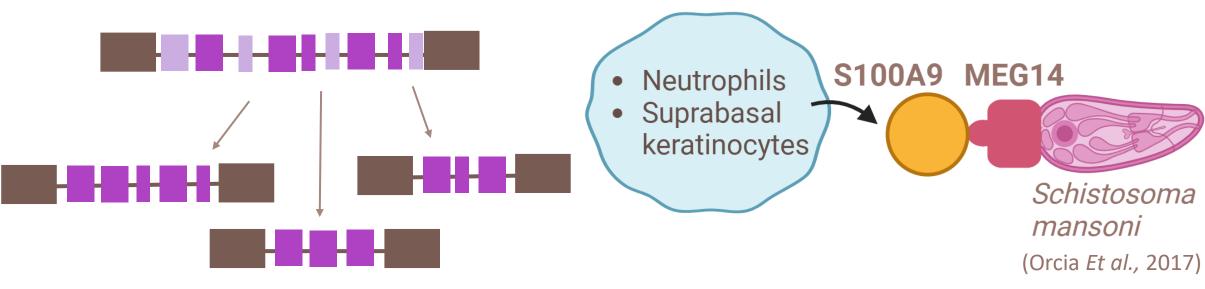
¹ Department of Biology, University of York, United Kingdom. ² Wellcome Sanger Institute, Cambridge, United Kingdom . ³ York Biomedical Research Institute, University of York, United Kingdom

Schistosoma mansoni Lifecycle



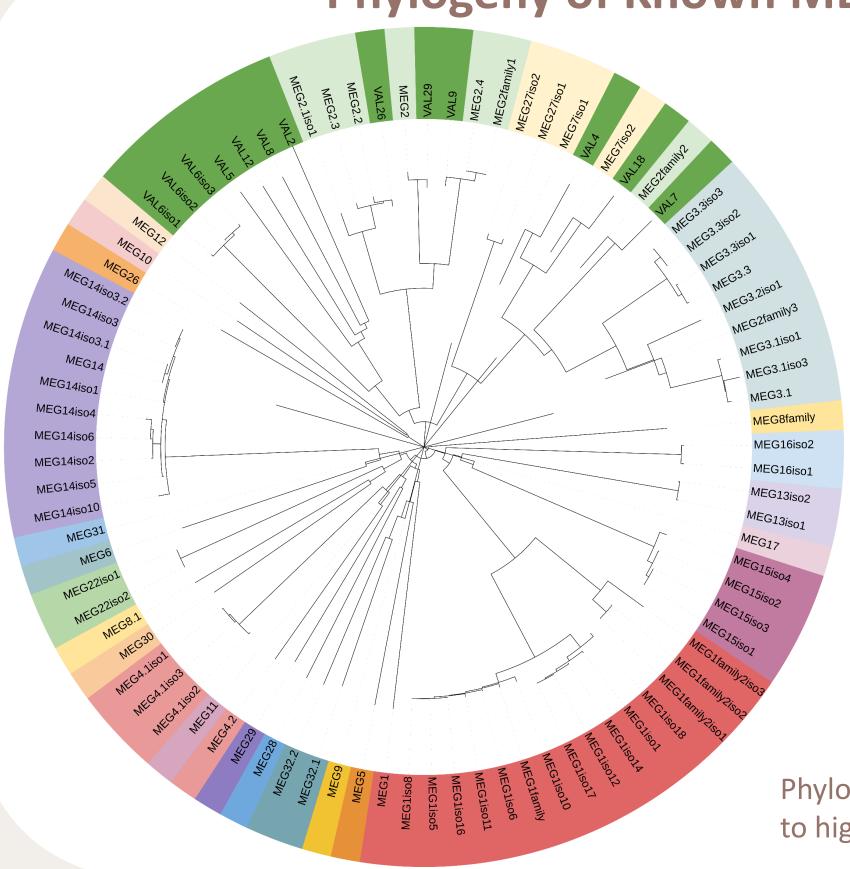
- Can survive in the host for up to 30 years
- How the parasite succeeds in avoiding immune attack is not fully understood

Alternative Splicing and Immune Evasion



- Protein variation through alternative splicing of micro-exons
- The near endless combinations of MEGs secreted or expressed on tegument surface is believed to protect against the adaptive immune response (DeMarco Et al., 2010)
- Also hypothesised that MEG interactions with human immune receptors could dampen the immune response (Orcia Et al., 2017)

Phylogeny of Known MEG Variants



- 35 individual MEGs identified through shotgun RNA sequencing
- 87 isoforms identified
 (so far!) (Nedvědová Et al., 2023)
- Long read RNA sequencing may reveal more variants

Phylogenetic tree colour coded to highlight MEG families

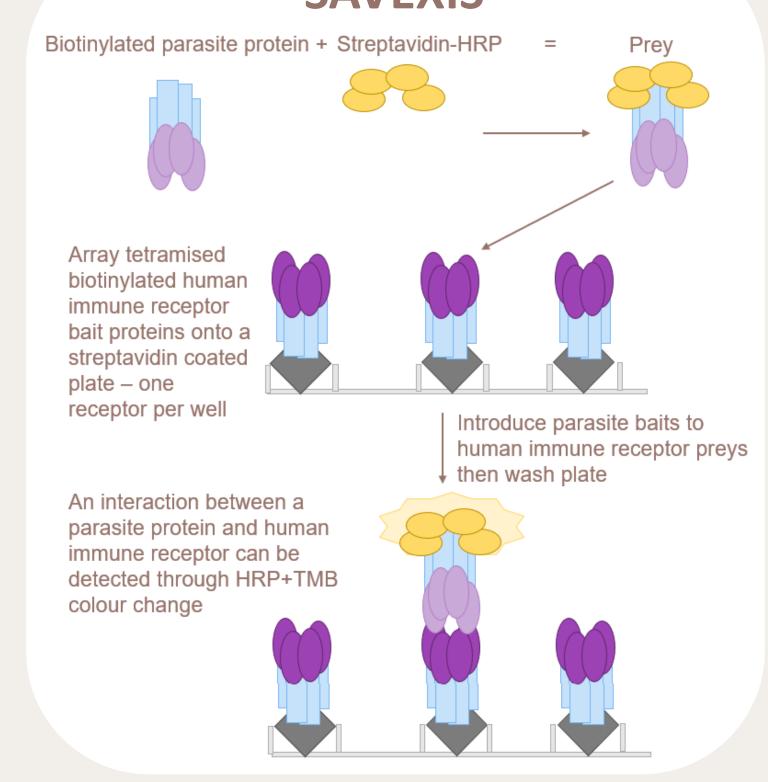
Micro-Exon Genes

- Protein coding sequence comprised primarily of micro-exons
- Micro-exons have lengths that are palindromic and multiples of 3 (from 6 to 81bp) (DeMarco Et al., 2010, Berriman Et al., 2009)
- Very high non-synonymous/synonymous
 substitution rates (Philippsen Et al., 2015)
- MEGs are primarily transcribed in the intramammalian stages
- Oesophageal gland is a hotspot for MEG
 transcription (Wilson Et al., 2015, Diaz Soria Et al., 2020)
- Sm-foxA knockdown blocks oesophageal gland development, knockdowns cannot establish infection in immunocompetent mice (Lee Et al., 2020)

My Project

- To identify new MEG alternative transcripts to create a transcriptomic dataset
- To test the binding and interaction of these MEGs to host proteins through SAVEXIS





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References

Berriman, M., Haas, B.J., LoVerde, P.T., Wilson, R.A., Dillon, G.P., Cerqueira, G.C., Mashiyama, S.T., Al-Lazikani, B., Andrade, L.F., Ashton, P.D. and Aslett, M.A., 2009. The genome of the blood fluke Schistosoma mansoni. Nature.

DeMarco, R., Mathieson, W., Manuel, S.J., Dillon, G.P., Curwen, R.S., Ashton, P.D., Ivens, A.C., Berriman, M., Verjovski-Almeida, S. and Wilson, R.A., 2010. Protein variation in blood-dwelling schistosome worms generated by differential splicing of micro-exon gene transcripts. Genome research.

Lee, J., Chong, T. and Newmark, P.A., 2020. The esophageal gland mediates host immune evasion by the human parasite Schistosoma mansoni. Proceedings of the National Academy of Sciences.

Diaz Soria, C.L., Lee, J., Chong, T.,
Coghlan, A., Tracey, A., Young, M.D., Andrews, T., Hall, C., Ng, B.L., Rawlinson, K. and Doyle, S.R., 2020. Single-cell atlas of the first intra-mammalian developmental stage of the human parasite Schistosoma mansoni. Nature communications.

Nedvědová, Š., De Stefano, D.,
Walker, O., Hologne, M. and Miele, A.E., 2023. Revisiting Schistosoma mansoni Micro-Exon Gene (MEG) Protein Family: A Tour into Conserved Motifs and Annotation. Biomolecules.

Orcia, D., Zeraik, A.E., Lopes, J.L., Macedo, J.N., Dos Santos, C.R., Oliveira, K.C., Anderson, L., Wallace, B.A., Verjovski-Almeida, S., Araujo, A.P. and DeMarco, R., 2017. Interaction of an esophageal MEG protein from schistosomes with a human S100 protein involved in inflammatory response. Biochimica et Biophysica Acta (BBA)-General Subjects.

Philippsen, G.S., Wilson, R.A. and DeMarco, R., 2015. Accelerated evolution of schistosome genes coding for proteins located at the host–parasite interface. Genome Biology and Evolution. Wilson, R.A., Li, X.H., MacDonald, S., Neves, L.X., Vitoriano-Souza, J., Leite, L.C., Farias, L.P., James, S., Ashton, P.D., DeMarco, R. and Castro Borges, W., 2015. The schistosome esophagus is a 'hotspot'for microexon and lysosomal hydrolase gene expression: implications for blood processing.