

Exploiting Omics Approaches to Unravel Endocannabinoid Biology in *Strongyloides* Parasites

Luke Cadd, Bethany Crooks, Nikki Marks, Aaron Maule, Angela Mousley, Louise Atkinson

Microbes & Pathogen Biology, The Institute for Global Food Security, School of Biological Sciences, Queen's University Belfast, Northern Ireland

Parasitic nematodes infect >1.5 billion of the world's population, significantly affecting LMIC populations, where many of the most problematic pathogens are the soil-transmitted helminths. Overreliance on a limited number of anthelmintics exacerbates drug resistance pressures, thus there is a pressing need to identify novel therapies for parasite control ahead of a resistance crisis. The optimisation of appropriate end-to-end strategies, in relevant and tractable parasitic nematodes, is required for the identification and validation of novel anthelmintic targets from therapeutically unexploited facets of nematode biology. The nematode endocannabinoid (EC) system remains a relatively uncharacterised aspect of nematode neurosignalling. EC-signalling has been linked to key roles including cholesterol mobilisation, ageing, axon regeneration, locomotion, feeding and nociception in the free-living nematode *Caenorhabditis elegans* however, its role and importance in parasites is unclear. Key facets of the EC-system are broadly conserved across the nematode phylum including in key parasite species (unpublished), and that EC-signalling may play a putative role in parasitic nematode host immune modulation. This project will develop a drug target prioritisation pipeline in the tractable parasite *Strongyloides ratti* by interfacing *in silico* bioinformatics, optimised *in vitro* bioassays, and functional genomics approaches and, in tandem, exploit this to explore the drug target potential of parasitic nematode EC-signalling. Our data: (i) reveal an extensive EC-signalling network in 30 lifestyle-diverse nematodes representing 7 clades; (ii) provide an optimised bioassay toolkit for the elucidation of pre- and post- functional genomics phenotypes in *Strongyloides* spp. and, (iii) begin to probe NPR-19 (EC-receptor) function using functional genomics (RNAi) in *S. ratti*. Characterisation of the EC-system using the *Strongyloides* functional genomics pipeline will enhance our understanding of parasitic nematode biology, and may reveal novel anthelmintic targets for the control of medically and agriculturally importance parasites.