Lipid Lifelines: Mapping FAR gene profiles in Phylum Nematoda

Rose Taylor[1], Brian Smith[2], Angela Mousley[1], Louise Atkinson[1]

[1]School of Biological Sciences, Queens University Belfast

[2]School of Molecular Biosciences, University of Glasgow

Parasitic nematodes impose a significant global burden on human health and the agri-food sector, negatively impacting millions of people and resulting in substantial economic losses. While a select number of chemotherapeutics control infections, escalating resistance to anthelmintics emphasises the need for new strategies. Consequently, it is imperative to understand fundamental biology of parasitic nematodes to drive novel drug discovery.

Parasitic nematodes require lipids for reproduction, development, and cuticle maintenance, but are unable to synthesise these essential molecules *de novo*. To compensate, nematodes secrete soluble lipid binding proteins (LBPs) into the host environment to scavenge fatty acids and retinoids. Four LBP families are unique to nematodes: fatty acid and retinol binding proteins (FARs), nematode polyprotein allergens (NPAs), nematode-specific fatty acid binding proteins (nemFABPs) and dorylipophorins. Data on the structure and ligand-binding properties of some nematode LBPs are available; however, functional data remain sparse.

FARs have been implicated in parasitism, reproduction, and evasion of the host immune system, but their specific functions are uncharacterised. FAR gene orthology was previously reported for fifty-eight nematode species, however recent expansions in the number and quality of available nematode genomes necessitates an updated and more expansive analysis. This study employed an *in-silico* pipeline (HMM/BLASTp) to profile FAR conservation in 159 nematode species (206 nematode genomes), representing seven nematode clades and four distinct lifestyles (free-living, plant parasitic, animal parasitic and entomopathogenic nematodes). The analyses confirmed an absence of FARs in clades 1, 2 and 6 and corroborate an expansion of FAR genes in clades 9 and 10, where between 13 and 32 FAR genes appear to be encoded per species. This trend was observed at the genus level where the largest number of FARs was encoded by *Steinernema, Pristionchus,* and *Strongyloides* genera. No significant difference in FAR profiles was observed across nematode lifestyles. A subsequent analysis of publicly available parasitic nematode transcriptome datasets reveals life-stage-specific differences in FAR expression in key nematode species. For example, three FAR genes appear to be significantly downregulated in free-living adult females of *Strongyloides stercoralis* when compared to parasitic adult females. Finally, preliminary analyses of LC-MS/MS data from the body cavity fluid (pseudocoelomic fluid) of the gastrointestinal pig parasite, *Ascaris suum*, confirms the presence of several secreted FAR proteins. Ongoing analysis of excretory secretory products (ESPs) from *A. suum, Strongyloides ratti* and additional parasitic nematode species will provide further preliminary hypotheses on the function of specific FAR proteins and aid prioritisation of FAR candidates for functional characterisation in tractable nematode parasites.

Overall, these data will extend our understanding of FAR gene conservation in parasitic nematodes and seed downstream functional studies, which may have the potential to reveal novel anthelmintic targets for future parasitic nematode control.