

## **Developmental Regulation and Functional Prediction of microRNAs in an Expanded *Fasciola hepatica* miRNome**

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*Fasciola hepatica* is a parasite of human and veterinary importance. In humans, fascioliasis case estimates range from 1.6 to 2 million people infected with a further 90 million at risk. Closer to home *F. hepatica* costs the UK ruminant industry over £20 million annually through yield losses and liver condemnation. Triclabendazole is the only drug effective against both the juvenile and the adult stage of the parasite; resistance to this and the few other available drugs is a major issue for fluke control. Micro (mi)RNA were first discovered in the early 90s as non-coding RNAs responsible for post transcriptional regulation of gene expression. Recent years have seen reports that miRNAs are secreted by parasites into their host environment and can manipulate expression of host genes. Our goal is to better understand the intracellular and host interacting functions of *F. hepatica* miRNAs. To this end, we have used small RNA sequencing to expand the *F. hepatica* miRNome to 150 mature miRNAs, many of which appear unique to *Fasciola*. Our study is the first to measure transcriptional changes in these miRNAs through fluke development. We show, for the first time that certain miRNAs are life stage dependent suggesting a function specific to that stage with the highest number of miRNAs found in metacercariae. To examine host-interacting functions of secreted miRNAs, we examined interactions between extracellular vesicle (EV) miRNAs and cow/sheep transcripts through *in silico* analysis. Reactome pathway analysis of these mRNA targets revealed that the majority of those secreted miRNA were involved in general gene expression pathways and signal transduction and as such suggests the involvement of these within fluke induced immunosuppression or cellular pathology.

This work will form the basis of future functional genomic work to confirm these *in silico* predictions. Research carried out here has vastly expanded on the knowledge base of host parasite interactions within *Fasciola hepatica* and will go a long way to potentially discovering novel control and drug targets that are desperately needed.