

Title: Is it a Fluke or is it Reproducible? Isolate Variation in the Liver Fluke *Fasciola hepatica*

Babatunde, O. S¹., Leonard, J¹., Steele¹, C., Cramer, R²., Brophy, P. M¹. and Morpew, R. M¹.

¹Department of Life Sciences, Aberystwyth University, Aberystwyth, UK.

² Department of Biomedical, Molecular and Analytical Chemistry, University of Reading, Reading, UK.

Abstract

Fascioliasis is a disease caused by *Fasciola hepatica*, which infects livestock and humans and thus poses a substantial threat to food security and human health. The control and management of *F. hepatica* depend solely on triclabendazole (TCBZ) in the absence of vaccines. The over-dependence on TCBZ for the control and management of fascioliasis has led to the establishment of TCBZ-resistant *F. hepatica*. Further complications arise in tracking resistance through limited diagnostics to differentiate between resistant and susceptible liver fluke. Recent work has identified a major locus and the gene content likely conferring TCBZ resistance. Hence, there is a need to further confirm potential TCBZ resistance targets, particularly at the protein level. Therefore, the current study aims to utilize an in-depth proteomic approach to confirm the protein profiles from isolates of *F. hepatica* varying in their TCBZ susceptibility. Specifically, proteomic profiles are generated from somatic cells, extracellular vesicles (EVs), and EV-depleted excretory-secretory products. Four different isolates of *F. hepatica* have been utilized, two TCBZ susceptible (Aberystwyth and Italian) and two TCBZ resistant (Penrith and Kilmarnock). Initially, somatic proteins have been extracted from the four *F. hepatica* isolates and fractionated via 1-D SDS PAGE prior to mass spectrometry (GeLC) or a combination of size exclusion chromatography (SEC) prior to 1-D SDS PAGE and mass spectrometry (SEC-GeLC) to provide in-depth somatic proteome profile to date. Results from this work aim to support the future confirmation of TCBZ targets confirming resistance. In addition, it will provide further insights into diagnostics for improved control and management of fascioliasis.