Biomarkers of triclabendazole efficacy against *Fasciola hepatica*

The liver fluke, *Fasciola hepatica*, is a zoonotic, food borne parasite and growing threat to global food security and public health. Current fasciolosis diagnosis is confined to complex laboratory methods, with no penside options for the farmer towards infection intensity or drug efficacy determination. In the absence of fluke vaccines, disease management relies on triclabendazole (TCBZ) despite widespread TCBZ resistance (TCBZ-R), as it is the only flukicidal compound active against pathogenic juveniles and long-lived adult flukes. There is mounting pressure to develop rapid diagnostics to measure fluke presence and drug efficacy. To this end, we have progressed with the discovery of a panel of TCBZ-associated secreted biomarker candidates. *In vitro* TBCZ response phenotypes and non-specific fitness-associated markers have been characterised and the recombinant expression in progress for eight diagnostic contenders for infection identification, post-TCBZ fluke survival (TCBZ-R) and successful TCBZ-specific treatment. Cathepsin L proteases are robust indicators of fluke presence, whereas inactive cathepsin L zymogens are conversely untapped biomarkers for fluke death and drug efficacy diagnoses, whereby they are non-specifically released by TCBZ-exposed susceptible adult flukes. Other candidates of the TCBZ-associated diagnostic phenotypes include survival proteins: calreticulin, enolase and glyceraldehyde-3-phosphate dehydrogenase; and susceptibility proteins: actin, deglycase DJ-1, gelsolin and triose phosphate isomerase. Recent developments in the biomarker validation pipeline shall be presented, reporting the progress of this broad panel of fluke and TCBZ efficacy diagnostic candidates.