Establishing an *in vitro* culture method and genetic approaches to investigate the infection biology of the parasitic nematode *Teladorsagia circumcincta*

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The Trichostrongylid scour worms *Trichostrongylus* and *Teladorsagia* infect the gastrointestinal tract of their ruminant hosts, causing tissue damage and significant weight loss. Some livestock acquire protective immunity to scour worms, indicating that vaccination is a promising therapeutic approach. The precise mechanisms of immunity are poorly understood and development of an effective vaccine to protect livestock is needed. Effective vaccine design requires knowledge of how scour worms establish infection and mediate host-parasite interactions during infection. Ability to culture larval stages as they develop, together with the application of reverse genetics approaches such as RNA interference (RNAi) or CRISPR-Cas9 should aid vaccine design. We aim to better understand the biology of scour worms by modulating expression of genes encoding putative virulence factors and genes essential for worm development.

We have developed a culture system to grow parasitic stages of *Teladorsagia circumcincta in vitro.* Infective L3 larvae were ex-sheathed and grown in medium formulated from egg yolk (Rose, 1973), resulting in ~30% of xL3 molting and developing to L4 stage. L4 larvae that have undergone ecdysis are viable *in vitro* for over 4 weeks, and display a significant increase in worm length. We observed sexual dimorphism of L4 stages, with the development of male or female tail morphology indicative of differentiation to late-stage L4. Initial studies using ovine abomasal organoids to co-culture *T. circumcincta* larvae will also be discussed.

Using our *in vitro* larval culture system, we aim to modulate the expression of putative parasite virulence factors and determine any phenotypic effects. These initial advances in our ability to culture *T. circumcincta in vitro* hold promise for application of genetic manipulation and ultimately to elucidate the role of parasitic virulence factors in establishing infection. This knowledge will contribute to our understanding of disease progression and antigen discovery for the development of a scour worm vaccine.