Modelling host: parasitic nematode interactions with ovine 'mini-gut' organoids.

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Teladorsagia circumcincta is one of the most predominant gastrointestinal nematodes (GIN) of sheep in temperate regions. Reported resistance to anthelmintics is increasing and therefore research into new control strategies (e.g. vaccination) is vital. One area of interest for identification of potential vaccine candidates is extracellular vesicles (EVs). EVs are lipid membrane-enclosed packages which contain effector proteins and immune modulators and play important roles in establishing helminth infections. However, there are challenges in studying these interactions between the host and GIN due to the lack of accessibility of the infection site and the need to rely on *in vivo* infection models which may have ethical implications. Recently, ovine organoids have been developed which allow host-parasitic interactions to be studied in a physiologically-relevant and host-specific *in vitro* cell culture system. The overall aim of the project is to use ovine abomasum organoids to identify and characterise active components of *T. circumcincta* EVs at different infective life stages. The separation and characterisation of EVs from adult and fourth larval stage excretory/secretory products have been achieved. Protein characterisation of these EVs has revealed consistency with proteins found in EVs from other nematodes (e.g. CAP and ShKT domain-containing proteins and, tetraspanins). These EV proteins are bound by IgG in sera from sheep infected with, or vaccinated with excretory/secretory products (ESPs) from, *T. circumcincta*. To better characterise host-parasite interactions, “apical out” ovine abomasal organoids have been used to allow EVs to interact with the epithelial apical surface of the organoid. Further investigations are underway to look at the potential differences in using either apical-in or -out organoid models to look at interactions of ESPs and EVs at different cell interfaces.