Abstract submission for BSP 2021

Title: Identification and RNA profiling of ovine tuft cells in response to gastro-intestinal nematode infections

K A Hildersley[4]; T N McNeilly[1]; V Gillan[3]; T D Otto2; R M Maizels[2]; E Devaney[3]; C Britton[3];
[1] Moredun Research institute, UK;
[2] Institute of Infection, Immunity & Inflammation, University of Glasgow, UK;
[3] Institute of Biodiversity, Animal Health, & Comparative Medicine, University of Glasgow, UK;
[4] Moredun Research Institute and Institute of Biodiversity, Animal Health & Comparative Medicine, University of Glasgow, UK

Abstract

Gastrointestinal (GI) nematodes are a major health and economic concern in production animals such as sheep. As anthelmintic resistance is becoming an increasing challenge for controlling livestock parasites, it is important to improve our understanding of host immune mechanisms to aid development of new control methods. Tuft cells (TCs) are of interest in mucosal immunology due to their proposed function in sensing changes in the environment of the gut lumen. Tuft cells are the sole source of IL-25 in the intestine and are key in initiating the type 2 immune response to GI nematodes. Tuft cells have been characterised from the murine small intestine (SI) by immunohistochemistry (IHC) and their frequency was shown to increase significantly during infection with *Nippostrongylus brasiliensis* and *Heligmosomoides polygyrus.* Single cell RNA-sequencing (scRNA-seq) of murine SI epithelial cells has provided additional insight into murine TC function and how they interact with the lumen of the GI tract. However, little is known about TCs in other species and in other regions of the GI tract. In this project, we demonstrated the presence of TCs in the ovine abomasum (true stomach) by IHC using antibodies to murine TC markers POU2F3 and GFI1B. We confirmed that ovine POU2F3+ cells also significantly increased in number over the course of infection with the important livestock GI nematodes *Teladorsagia circumcincta* and *Haemonchus contortus.* Next, we characterised ovine abomasal tuft cells following *T. circumcincta* infection by scRNA-seq. Gene expression profiling demonstrated that many murine TC genes are conserved in ovine abomasal TCs e.g., *il17rb, avil* and *alox5*, but that the surface receptor repertoire differed from those of murine SI TCs e.g., succinate receptor *sucnr1* was not expressed in ovine TC. We also identified distinct sub-populations of ovine tuft cells at different stages of maturation. The scRNA-seq experiment was validated using RNAscope *in situ* hybridisation, which confirmed co-expression of tuft cell genes identified by scRNA-seq. For the first time, TCs have been identified in the ovine abomasum and shown to increase in number over the course of GI nematode infections with a distinctive gene expression profile marking their differentiation and maturation.