Characterising the ovine small intestinal tuft cell response following parasitic nematode infection.

KA Hildersley[1]; V Gillan[2]; TD Otto[3]; D Smith[1]; RM Maizels[3]; E Devaney[2]; C Britton[2]; TN McNeilly[1];
[1] Moredun Research institute, UK; [2] Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, UK, UK; [3] School of Infection and Immunity, University of Glasgow, UK

Tuft cells are of major interest in mucosal immunology due to their proposed function in sensing changes in the gut lumen environment and their role in initiating the Type-2 T-helper immune response to gastro-intestinal (GI) nematodes. Characterisation of murine tuft cells has built a profile of intestinal tuft cell specific markers, and differentiation of tuft cells following type-2 cytokine stimulation has been demonstrated in murine small intestinal (SI) organoids. 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 immune based control methods. We have previously demonstrated that tuft cell numbers in the ovine abomasum (equivalent of the gastric stomach) increase following infection with the economically important gastric nematode, *Teladorsagia circumcincta.* Characterisation of the gene expression profile of ovine gastric tuft cells by single cell RNA-sequencing (scRNA-seq) demonstrated that genes involved in tuft cell functions such as taste receptor signalling and eicosanoid biosynthesis are conserved between mice, humans and sheep; however, the cell surface receptor repertoire was different between gastric sheep and intestinal mouse and human tuft cells, suggesting either organ- or species-specific differences in receptor expression. The aim of this study was to characterise ovine intestinal tuft cell responses following intestinal GIN infection and compare ovine gastric and intestinal tuft cell at the transcriptomic level. Using antibodies to conserved tuft cell markers, we demonstrate that tuft cell numbers increase following infection with the ovine intestinal nematode, *Trichostrongylus colubriformis*. Transcriptomic analysis by scRNA-seq analysis identified an ovine SI tuft cell cluster which shares marker genes in common with the murine SI tuft cells, but more genes were conserved between the ovine SI and gastric stomach than the ovine and murine SI. Furthermore, using recently established ovine duodenum organoid cultures, we demonstrate for the first time that stimulation with type-2 cytokines IL-4 and IL-13 is sufficient to induce ovine tuft cell differentiation. These results indicate that despite organ-specific differences in surface receptor expression, ovine tuft cells expand following both gastric and intestinal GIN infection. Furthermore, differentiation of tuft cells by type-2 cytokines appears to be conserved between different mammalian species.