

Abstract Title: **Small Intestinal Responses to *Giardia muris* Infection in Tuft Cell-Deficient Mice**

Introduction: Enteric tuft cells (ETCs) possess the ability to modulate host immune responses to enteric parasitic infections and aid in parasite clearance. They sense luminal signals via various cell surface receptors and secrete the cytokine IL-25, which engages type 2 innate lymphoid cells and other cytokines in the lamina propria for further host responses, such as tuft and goblet cell hyperplasia (Schneider et al., 2019). Infection with the intestinal protozoan *Giardia* causes intestinal barrier dysfunction (Allain et al., 2017) and we have previously shown that infection results in altered goblet cell numbers (Amat et al., 2017), however the ETC response is unknown during the acute and clearance phases of infection. *Giardia* infection can impact the host in regions of the intestine beyond where active *Giardia* reside in the jejunum (Barash et al., 2017; Halliez et al., 2016). We aim to investigate the role of tuft cells upon *Giardia* infection by assessing both tuft and goblet cell quantities in the small intestine at the site of active colonization and further downstream. **Methods:** A time-series infection study was conducted on 5–7-week-old C57Bl/6 or tuft cell-deficient (*Pou2f3*^{-/-}) mice. Mice were orally infected with *Giardia muris* trophozoites (5×10^4). At days 4, 11 and 21 following infection, parasite burden was measured in the duodenum, and the proximal jejunum and distal ileum were collected for further analysis. Paraffin embedded jejunum and ileum tissue underwent immunofluorescence (IF) staining and periodic acid-Schiff (PAS)/Alcian blue (AB) staining for visualization and quantification of tuft and goblet cells, respectively. Double-cortin like kinase 1 (DCLK1) antibodies (Gerbe et al., 2009) were used for IF staining. Quantitative PCR (qPCR) was performed on *Dclk1* (tuft cell marker) and *Atoh1* (transcription factor defining secretory cell types in the intestinal epithelium). **Results:** Tuft cell numbers were elevated in C57Bl/6 *G. muris* infected mice at day 21 post-infection in the jejunum and ileum, while at day 11, tuft cell numbers were decreased in the ileum of infected mice. Goblet cell numbers increased in *Giardia* infected C57Bl/6 mice in the jejunum at days 4 and 21 post-infection and in the ileum at day 21. Goblet cell numbers in *Pou2f3*^{-/-} mice did not differ between *Giardia* infected and uninfected mice in both the jejunum and ileum. *Dclk1* and *Atoh1* gene expression was elevated in *Giardia* infected C57Bl/6 mice at day 4 in the jejunum and day 11 in the ileum. **Conclusions:** *Giardia* infection is associated with tuft and goblet cell hyperplasia in the jejunum and the ileum, demonstrating that *Giardia* can illicit cell hyperplasia downstream of its site of colonization. Elevated gene expression of *Dclk1* and *Atoh1* was present earlier (day 4) in the jejunum and later (day 11) in the ileum, suggesting that signals for gene expression start proximally in the intestine and move distally over time during *Giardia* infection.