A232

TUFT CELLS COORDINATE RAPID EXPULSION OF THE TAPEWORM *H. DIMINUTA* BUT ARE NOT REQUIRED FOR ENHANCED IMMUNITY AGAINST THE NEMATODE, *H. POLYGYRUS*, IN MICE PREVIOUSLY INFECTED WITH *H. DIMINUTA*

S. Rajeev[2], A. Leon-Coria[1], A. Wang[2], C. Finney[1], D.M. Mckay[2]

1. University of Calgary Department of Biological Sciences, Calgary, AB, Canada; 2. University of Calgary Cumming School of Medicine, Calgary, AB, Canada

Background: The tuft cell is an important sentinel that monitors the gut lumen and coordinates immunity against parasitic nematodes. We showed small intestinal tuft cell hyperplasia 11 days post-infection (dpi.) with the tapeworm *Hymenolepis diminuta*: a time when the parasite is no longer present in murine hosts. This may be a way by which the host protects itself from subsequent helminth-infections, a common phenomenon in parasite-endemic world regions. We test this supposition using Pou2f3$^{-/-}$ mice that lack tuft cells.
Aims: To test the hypothesis that tuft cells are important in the anti-worm response in *H. diminuta* (*H.d.*)-infected mice subsequently infected with the nematode parasite *Heligosomoides polygyrus* (*H.p.*).
Methods: Male C57BL6 and Pou2f3$^{-/-}$ mice (8-12 weeks) were infected with 5 *H.d.* cysticercoids ± 200 *H.p.* larvae at 10 dpi with *H. diminuta* (non *H.p.* mice - control). Upon necropsy at 24 dpi *H. diminuta* (i.e. 14 dpi *H.p.* in co-infected mice), both worms were ennumerated in small intestinal washings, *H.p.* granulomas examined and fecal egg counts performed. Small intestinal segments were stained for tuft (DCLK1^{+}) and goblet cells (PAS^{+}). As a surrogate of successful infection, IL-4 and IL-10 were measured in supernatants from concanavalin-A treated splenocytes.
Results: Wild-type (WT) mice expel *H. diminuta* by 11 dpi and this was delayed in Pou2f3$^{-/-}$ mice, with worms readily detectable at 14 dpi and absent by 21 dpi. Despite the delayed expulsion, both WT and Pou2f3$^{-/-}$ mice showed increased splenic production of IL-4 and IL-10; however, unlike WT mice, *H. diminuta*-infected Pou2f3$^{-/-}$ mice show no increase in jejunal goblet cell numbers. Mice infected with *H. diminuta* displayed a degree of increased resistance to *H.p.*-infection defined by reduced worm and egg burdens, and increased granuloma formation in comparison to *H.p.*-only infected animals. In this sequential co-infection model, there were no significant differences between WT and Pou2f3$^{-/-}$ mice in the response to *H.p.*
Conclusions: The absence of tuft cells slows expulsion of *H. diminuta* from its non-permissive mouse host and correlates with diminished goblet cell hyperplasia. Hypothesizing that *H. diminuta*-evoked tuft cell hyperplasia would enhance the immune response to a subsequent infection with an unrelated nematode parasite proved incorrect. While *H. diminuta*-infected mice were partially protected from *H.p.*, response was similar in WT and Pou2f3$^{-/-}$ mice. Thus tuft cells are important in worm detection: yet, our co-infection data suggests that other events initiated by the primary worm infection impact the outcome of subsequent infection with a different helminth and tuft cells have a limited, if any, role to play in this helminth-host-helminth interaction.

Funding Agencies: CIHRNSERC, Eye's High International doctoral scholarship