PARASITIC INFECTIONS
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W.45. Evaluation of Immune Events Occurring in the Intestinal Mucosae During *Trichinella Spiralis* Infection

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The protective role of the intestinal immune response remains unclear. The kinetics of cell phenotype, immunoglobulins, cytokines and eotaxin were determined analyzing their correlation with worm expulsion. Wistar rats duodeni were obtained on 1–13 days post-infection (dpi), subjected to the Perfext method to be used in ELISAs or to determine the intestinal adult worm (AW) burdens. Histochemical and indirect immunofluorescence techniques were employed to determine anti-newborn larvae (NBL) immunoglobulins and cell phenotype. a) IgA,IgE,IgG1 and IgG2a anti-muscle larvae excretory-secretory products (ESP) were positive from 1–2dpi. By 6dpi IgG2a negativized, when IgG1 started to increase. b) IgA and IgE anti-AW-ESP were detected on 1dpi and 3 dpi respectively, with a marked peak of IgA on 13dpi. c) Anti-NBL IgE was detected by 6dpi and IgA by 13dpi. d) INFγ,TNFα,IL-4,IL-10 and eotaxin were found on 1-6dpi. e) Histopathological changes with a significant early increase of CD4+,CD8αα+,TCRγδ+,IgE+,IgA+, eosinophils and mast cells were found. 1-There is an early mixed innate-Th1-Th2 type response with important immunohistopathological change finally polarizing to Th2, priming the intestine for AW expulsion. 2-Parasite stage specific IgE suggest a protective role of this immunoglobulin. 3-The increase in the levels of IgA-anti-AW during the late phase of the infection suggests its mucosal homeostatic role.

W.46. Parasite Products Bypass the Need for Thymic Stromal Lymphopoietin in Th2 Immune Responses by Directly Modulating Dendritic Cell Function

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The involvement of thymic stromal lymphopoietin (TSLP) in allergy has lead to the conviction that TSLP functions to promote inflammatory Th2 cell responses. In contrast to this view we now report that TSLP-TSLP receptor complex (TSLPR) interactions have no functional impact on the development of protective Th2 immune responses following infection with two enteric helminth pathogens, *Heligmosomoides polygyrus* (*H. polygyrus*) and *Nippostrongylus brasiliensis* (*N. brasiliensis*). Mice deficient in the TSLP binding chain of the TSLPR complex exhibited normal Th2 cell differentiation, protective immunity and memory responses following infection with these two parasites. In contrast, protective Th2-mediated immunity against the helminth *Trichuris muris* (*T. muris*) did require TSLP-TSLPR interactions. TSLP has been previously reported to inhibit IL-12 production by dendritic cells (DC). We therefore examined the ability of excretory-secretory (ES) products from all three helminthes to modulate DC IL-12 production. ES products from *H. polygyrus* and *N. brasiliensis*, but not *T. muris*, were found to suppress LPS-induced IL-12 production by DC. Taken together, our data indicated that TSLP is not an absolute requirement for Th2 immune responses. However, in cases where the pathogen does not directly modulate host responsiveness, TSLP can act to promote Th2 differentiation by suppressing IL-12 production.

W.47. Early Response of Mucosal Epithelial Cells During *Toxoplasma Gondii* Infection

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The primary roles of intestinal epithelial cells are to participate in nutrient uptake and provide a physical barrier against infection. However, recent studies have suggested that epithelial cells play a more central role in the development of inflammation during infection and pathology. *Toxoplasma gondii* (*T. gondii*) is an orally acquired protozoan intracellular parasite that induces intestinal pathology (ileitis) in C57BL/6 mice. We have hypothesized a role for epithelial cells in the initial response to *T. gondii* infection, which may contribute to development of ileitis. Using an *in vitro* system, we were able to study the outcome of early contact between *T. gondii* and epithelial cells is isolation. Here we show that human intestinal epithelial cells infected with *T. gondii* elicited rapid MAPK phosphorylation, NF-κB nuclear translocation, and secretion of interleukin (IL)-8. Both ERK1/2 activation and IL-8 secretion responses were MyD88 dependent and partially dependent on TLR2. Type I, II and III parasites were all recognized by this pathway. Furthermore, we identified additional *T. gondii*-regulated cytokine and chemokine genes using a pathway-focused array. Together, our data support a model where the intestinal epithelial cells directly respond to *T. gondii* early during infection and likely contribute to the development of inflammatory pathology. Further study of these pathways will define the role of epithelial cells in the generation of this pathology.

W.48. T Follicular Helper Cells are IL-4-producing Th2 Cells During Helminth Infection

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Interleukin (IL)-4 is the quintessential type 2 cytokine produced by CD4+ T helper 2 cells in response to infection with helminth parasites. IL-4 not only promotes the differentiation of Th2 cells, it is also critical to stimulate antibody isotype switching by B cells to IgG1 and IgE. However, the location of IL-4 producing T cells in the lymph nodes is currently unclear. Using IL-4 dual reporter mice we examined the Th2 response and IL-4 production during infection with the enteric nematode Heligmosomoides polygyrus. We found that while IL-4 competent Th2

cells are localized throughout the B and T cell areas of the draining mesenteric lymph nodes of infected animals, IL-4 producing Th2 cells are restricted to the B cell follicles and associate with germinal centers. Consistent with their follicular localization, IL-4 producers express CXCR5, PD-1, ICOS and IL-21, a phenotype characteristic of T follicular helper (Tfh) cells. Furthermore, while IL-4 was dispensable for the generation of Th2 and Tfh cells, deletion of IL-4 or its receptor severely compromised B cell expansion and maturation. Our study is the first to identify the location of IL-4 production in the lymph nodes during helminth infection and recognizes Tfh cells as the dominant source of this effector cytokine.