Inflamm Bowel Dis ● Volume 14, Number 12, December 2008

Abstracts from the 2008 Advances in Inflammatory Bowel Diseases, Crohn's & Colitis Foundation's National Clinical & Research Conference

Article first published online: 26 NOV 2008

P-0110.

Inflammatory Bowel Disease and Trichuris muris

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Inflammatory bowel disease (IBD) is a group of idiopathic chronic relapsing inflammatory conditions of the gastrointestinal tract. The precise etiology of IBD is unknown, although it is clearly multifactorial resulting from interplay of genetic, environmental and immunological factors. Epidemiological studies show that the incidence of IBD and other autoimmune disorders is low in the developing countries and more in the developed countries. Evidence suggests that therapeutic administration of helminth can reduce the symptoms of IBD in both animal models and man. However, one study show the rat tapeworm *Hymenolepis diminuta* infection results in significant exacerbation of oxazolone induced colitis in mice (Hunter et al., 2007). The mechanisms by which helminths interact with the gut immune system in IBD-susceptible hosts, particularly their effect on the onset and progression of colitis are poorly understood. To address this we have investigated the interaction between *Trichuris muris* and *the mdr1a (-/-)* mouse model, which lacks the epithelial barrier protein, p-glycoprotein and slowly develops a spontaneous colitis in the presence of a normal gut flora.

PURPOSE OF THE STUDY: Our aim was to investigate (i) whether *mdr1a* gene deletion, which makes the host susceptible to colitis, alters host susceptibility to *T.muris* infection and (ii) the effects of *T. muris* infection on the development of colitis in *mdr1a-/-* mice.

SUMMARIZED DESCRIPTION OF THE PROJECT: Pre-colitic *mdr1a-/-* or FVB congenic control mice were infected with approximately 175 embryonated *T. muris* ova at 5-9 weeks of age. Worm counts, immunological responses and gut histology were analyzed on day 19 post infection.

RESULTSANDCONCLUSIONS: The *mdr1a -/-* mice were unable to expel *T.muris* and had a higher worm burden at day 19 after infection compared to controls. This was associated with increased Th1 and Th2 cytokines, particularly IFN-gamma in the draining lymph nodes. Interestingly, there was also evidence that *T. muris* infection may accelerate the development of gut inflammation in the *mdr1a-/-* mice as judged by increased mucosal infiltration by CD4_,CD8_ and F4/80_ cells and other histological changes. However, the naıve *mdr1a-/-* mice and infected controls of the similar age failed to show any signs of gut inflammation. This study shows that infection with *Trichuris* may worsen colitis in the precolitic *mdr1a-/-* model. Thus, worsening of inflammation in infected knock out mice could be a complex interaction between the translocated bacterial products (due to absence of P-glycoprotein molecule) and immunomodulatory molecules of worm. Thus, this study highlights that a better understanding of the complex relationship between gut parasites and IBD-susceptible hosts is required.

Reference: HUNTER, M. M., WANG, A. & MCKAY, D. M. (2007) Helminth infection enhances disease in murine TH2 model of colitis Gastroenterology, 132, 1320-30.