

 Immune Disease Institute	Office of Technology Development 800 Huntington Avenue Boston, Massachusetts 02115 www.idi.harvard.edu
IDI 03-008	TREATMENT AND PREVENTION OF INFLAMMATORY BOWEL DISEASE

Application: Inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis

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Invention Summary:

Inflammatory bowel disease (IBD) is caused by chronic immune activation and inflammation within the gastrointestinal tract. Over one million Americans suffer from IBD. Although the intestinal immune response is known to differ from that in other organs in the body, the basis for its distinctiveness is not known. One reason for the different activation pathways of gut mucosal T-cells compared with peripheral T-cells is that distinct antigen presenting cells may stimulate T-cells in the mucosa. Dr. Narasimhaswamy and his colleagues have identified a novel type of antigen presenting cell in the gut mucosa (APC^{IEL}) that critically regulates the expansion and differentiation of intestinal T-cells. Further experiments show that the T-cell activation via APC^{IEL} is dependent on costimulation by an activation molecule constitutively expressed by APC^{IEL} and could be abrogated by treatment with a blocking antibody or small molecule. When the costimulatory molecule/ligand of the activation molecule is blocked by antibody treatment, both CD8 and CD4 T-cell responses in the gut mucosa are effectively abrogated after an oral infection. Murine model studies are underway to determine if administration of a blocking antibody or a soluble ligand-Ig chimera can prevent the development of IBD. Preliminary studies indicate that similar APC may exist in the human intestine. Further studies are planned to determine whether their number and/or function is altered in patients with Crohn's disease and ulcerative colitis.

Supporting Publications: *J Immunol.* 2007 Jan 15;178(2):652-6.
Nature Immunology 2005;6, 698-706.
N Engl J Med 347, 417-29 (2002)
Nat Rev Immunol 3, 331-41 (2003)
Nat Immunol 4, 49-54 (2003)

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