

### **What is the relevance to IBD research?**

IBD is thought to develop as a result of a complex interplay between inherited genetic factors and exposure to environmental/microbial factors likely found in the endogenous microflora. Substantive progress has been made in the past year in identifying the underlying genetic susceptibility variants that may be responsible for the onset of intestinal inflammation. It has been more difficult to elucidate the potential microbial or environmental influences that may trigger IBD in a susceptible host. The reasons for this difficulty in part relate to the inability to dissect the complex microbial environment that exists in humans who develop IBD.

In this Research Plan we propose to study a human model of development of ileal inflammation in individuals previously not affected by ileitis. We will study patients with confirmed ulcerative colitis with no previous involvement of their ileum who undergo colectomy and subsequent ileal pelvic pouch surgery as part of their treatment for IBD. These individuals commonly develop ileitis in the ileal reservoir despite the fact that they previously had disease limited to the colon. We believe this occurs as a result of genetic susceptibility to intestinal inflammation and recreation of a colonic-type environment in the ileal reservoir. By studying the genetic, serological and microbial profiles of individuals who develop ileitis compared to those that do not in this human model of IBD, we anticipate identifying the critical factors responsible for the *de novo* development of ileal inflammation. These factors are extremely likely to be broadly applicable to Crohn's disease and IBD in general and provide significant information to assist in understanding the early events that lead to IBD.