Inflammatory bowel disease (IBD) is one of the most common immune-mediated diseases in the United States costing the average patient tens of thousands of dollars annually, and greatly diminishing quality-of-life. While there is no universal cure for IBD, recently developed treatments targeting the immunological basis of disease have proven successful in managing clinical symptoms. However, these pharmaceutical therapies such as infliximab carry several side effects and are not efficacious in all patients. Thus, more selective treatments are needed. One necessary step in the development of such agents is a more precise understanding of which cells in the gastrointestinal tract are primary contributors to the pathogenesis of IBD.

We demonstrate that a rare subset of cells in the gastrointestinal tract expressing CD8-alpha is present in significantly different numbers in mouse strains considered susceptible or resistant to a microbially induced model of IBD. Additionally, we show that cells derived from the target organ of susceptible mice prior to and shortly after induction of the disease process are prone to production of greater levels of certain inflammatory mediators. Lastly, we describe the generation of a mouse strain susceptible to the disease model but selectively lacking the subset of dendritic cells expressing CD8-alpha, to be used in future studies.

One of the most serious sequela to IBD is colitis-associated colorectal cancer (CAC). Diagnosis of colorectal cancer in general is reliant on tests that suffer from either poor sensitivity or specificity (such as fecal occult blood tests), or invasiveness (such as colonoscopy). Newer genetic tests have been developed for the identification of hereditary risk factors, however CAC follows a molecular pathway distinct from that of familial forms of colorectal cancer. Thus, the development of noninvasive screening assays for CAC with high sensitivity and specificity would increase compliance with screening recommendations and enhance detection and survival of patients with CAC.

We report here the development of a novel screening technique capable of detecting the earliest stages of CAC in a microbially induced mouse model. Using fecal gene expression-based biomarkers, rRNA derived from colonocytes sloughed in the feces, we were able to accurately predict which mice would develop CAC several weeks later, as well as predict the severity of disease. While the optimal markers of disease identified in the present studies are likely specific to this model of CAC, the proof-of-concept portends a powerful new method of diagnostics for CAC in humans.