ABSTRACT

Intestine is a unique tissue where a variety of environmental factors including commensal microbiota and dietary components exist. In a healthy condition, activity of intestinal immunity is finely regulated to prevent inflammatory responses to these environmental factors. Dysregulated interaction of intestinal environmental factors and intestinal immunity causes development of inflammatory bowel disease (IBD) represented by Crohn’s disease and ulcerative colitis.

We are analyzing the mechanisms by which gut homeostasis is regulated by focusing on intestinal innate immunity. There are several unique subsets of innate immune cells in the murine intestinal lamina propria, which regulate immune responses positively and negatively. We then identified human counterparts of these cell subsets in the human colon, and activity of these subsets were altered in IBD patients. Thus, intestinal innate immune cells are critically involved in the pathogenesis of intestinal inflammation.

We also analyze barrier function of colonic epithelial cells that are responsible for segregation of intestinal environmental factors and immunity, contributing to prevention of intestinal inflammation. Indeed, the presence of bacteria on the epithelial surface of the large intestine was reported in several mouse models of intestinal inflammation. We identified a molecule that is produced from the epithelial cells and is responsible for the segregation of microbiota and the host immunity. This molecule is thus essential for the maintenance of gut homeostasis.