

The pathogenesis of gastritis in the ileitis-prone samp1/yit mice

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The gastrointestinal tract faces the unique immunological challenge of coping with a dynamic and vast array of dietary and microbial antigens. Chronic inflammatory disease of the intestine as well as the stomach arises in genetically susceptible individuals that fail to properly regulate host responses to these luminal antigens. One example of chronic inflammatory diseases in the gut is inflammatory bowel disease which manifests as ulcerative colitis or Crohn's disease. Crohn's disease tends to affect the terminal ileum but in humans, disease can arise in virtually any site from the mouth to the anus. One of the most studied models of spontaneous Crohn's disease is the samp1/yit mouse model. These mice were shown to have many manifestations resembling human Crohn's disease including discontinuous and transmural chronic inflammation of the terminal ileum and in some cases, perianal fistulae. Other studies have shown that ileitis is associated with pro-inflammatory cytokine production. Although many immunological responses are perturbed, some evidence suggests that the primary defect lies in the epithelial cell barrier. In the process of studying epithelial permeability, we showed that the samp1/yit stomach also has increased permeability. Upon further examination, these mice were shown to have a marked, chronic gastritis with focal to diffuse aggregates of mononuclear cells of different lineages. These aggregates are located predominantly in the oxyntic mucosa with occasional lesions in the forestomach but relatively rare cellular infiltrates in the antral mucosa. Realtime RT PCR shows an increase in many of the pro-inflammatory Th cell-derived cytokines in the gastric mucosa of samp1/yit mice. The adoptive transfer of T cells into immunodeficient recipients induces ileitis, gastritis and duodenitis. However, many of the cells in the aggregates are B cells. samp1/yit B cells exacerbate ileitis when co-transferred into immunodeficient recipients, possibly by interfering with regulatory Th cell function. The gastritis is also enhanced by B cells. As samp1/yit mice are derived from AKR mice, we examined AKR mice and determined that they too, have an increase in gastritis. B cells also contribute to the inflammation. Thus, these data suggest samp1/yit mice display gastritis as well as ileitis and that B cells play a role in the pathogenesis of the inflammation of both sites.