From the Cover: CD39 deletion exacerbates experimental murine colitis and human polymorphisms increase susceptibility to inflammatory bowel disease.

Abstract:
CD39/ENTPD1 hydrolyzes proinflammatory nucleotides to generate adenosine. As purinergic mediators have been implicated in intestinal inflammation, we hypothesized that CD39 might protect against inflammatory bowel disease. We studied these possibilities in a mouse model of colitis using mice with global CD39 deletion. We then tested whether human genetic polymorphisms in the CD39 gene might influence susceptibility to Crohn's disease. We induced colitis in mice using Dextran Sodium Sulfate (DSS). Readouts included disease activity scores, histological evidence of injury, and markers of inflammatory activity. We used HapMap cell lines to find SNPs that tag for CD39 expression, and then compared the frequency of subjects with high vs. low CD39-expression genotypes in a case-control cohort for Crohn's disease. Mice null for CD39 were highly susceptible to DSS injury, with heterozygote mice showing an intermediate phenotype compared to wild type (WT). We identified a common SNP that tags CD39 mRNA expression levels in man. The SNP tagging low levels of CD39 expression was associated with increased susceptibility to Crohn's disease in a case-control cohort comprised of 1,748 Crohn's patients and 2,936 controls (P = 0.005-0.0006). Our data
indicate that CD39 deficiency exacerbates murine colitis and suggest that CD39 polymorphisms are associated with inflammatory bowel disease in humans.