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Abstract: Dysregulation of immune responses in inflammatory bowel diseases (IBD) results in intestinal inflammation and vascular injury while exacerbating systemic disease. CD39 is an ectonucleotidase, expressed by T regulatory cells and dendritic cells, that hydrolyzes extracellular nucleotides to modify those cellular immune responses implicated in IBD. Genetic polymorphisms of CD39 have been linked to Crohn’s disease while gene deletion in mice exacerbates dextran sodium sulphate-induced colitis. The aim of this study was to test how global deletion of CD39 in mice impacts other models of experimental colitis. Colitis was induced in CD39-null and -wt mice, using trinitrobenzene sulfonic acid (TNBS, 125 mg/kg) administered intrarectally. Oxazolone colitis (1.5% oxazolone in 50% alcohol) was induced in comparable groups. Morphology, clinical and molecular parameters, and FACS analyses of lamina propria mononuclear cells (LPMC) were examined in CD39-null mice. CD39 expression was analyzed in human IBD biopsies. Paradoxically, TNBS colitis in CD39-null mice was characterized by improved survival, favorable clinical scores, and decreased MPO activity, when compared to wt mice (P< 0.05). LPMC from TNBS colitis contained significantly increased amounts of T-cells (CD3(+) and CD4(+)) and TNF-α mRNA expression were increased over those in CD39 null
mice (P< 0.05). In contrast, oxazolone treated CD39-null and wt mice had comparable outcomes. In both ulcerative colitis and Crohn's disease, CD39 is present at high levels in intestinal tissue biopsies. TNBS colitis was attenuated in CD39-null mice whereas oxazolone-induced colitis was not impacted. Impaired adaptive cellular immune reactivity in the CD39-null environment appears protective in hapten-mediated Th1-type colitis. CD39 is expressed at high levels in clinical IBD tissues.