## Alkaline phosphatase relieves colitis in obese mice subjected to forced exercise via its antiinflammatory and intestinal microbiota-shaping properties

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December 28, 2022

## Abstract

Background and Purpose Intestinal alkaline phosphatase (IAP) is an important apical brush border enzyme that dephosphorylates lipopolysaccharide released from bacteria. Considering its protective effect, we determined the effect of intragastric administration of IAP on the course of experimental colitis in mice exercising on a forced treadmill with diet-induced obesity. Experimental approach C57BL/6 mice with TNBS colitis fed a high-fat diet (HFD) were subjected to forced treadmill exercise with or without intragastric treatment with IAP. Grip muscle strength and disease activity index (DAI) were monitored, pro-and anti-inflammatory cytokines and markers of oxidative stress were measured by Luminex and ELISA, respectively. The mRNA expression of the barrier proteins ZO-1, MUC2 and claudins was assessed by RT-PCR, and the fecal composition of the intestinal microbiota was assessed by the NGS. Key results Significant increases in DAI, MDA+4-HNE in the colonic mucosa, and plasma leptin, MCP, TNF- $\alpha$ , IL-6, and IL-17a were observed in obese mice with colitis on a treadmill, and these effects have been significantly reduced by IAP treatment. IAP increased ZO-1, claudins and Muc2 mRNAs expression in the colonic mucosa. NGS revealed the relative proportion of Firmicutes in favor of higher Verrucomicbiota content and reducing the incidence of pathogenic Clostridia and Odoribacter. Conclusions and Implications IAP treatment ameliorates the worsening effect of forced exercise on murine colitis due to attenuation of oxidative stress, downregulation of pro-inflammatory biomarkers in the colonic mucosa, and beneficial changes in the gut microbiota. IAP deserves attention as promising candidate in future clinical trials of ulcerative colitis.

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