

Parabacteroides-derived acetate alleviates heparanase-exacerbated pancreatitis

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Abstract

Acute pancreatitis, which affects more than 34 out of every 100,000 people, is usually mild. However, some cases worsen rapidly, leading to hospitalization and even death. Acute pancreatitis is promoted by the enzyme heparanase and appears to be regulated by the gut microbiota, but the mechanisms and potential interplay of these factors are unknown. A recent study investigated these issues in mice with caerulein (Cn)-induced acute pancreatitis. Compared with wild-type (WT) mice, heparanase-overexpressing (Hpa-Tg) mice exhibited worse disease with neutrophil infiltration and had a different gut microbiota composition, but microbiota depletion and microbiota transfer between the groups attenuated heparanase's aggravating effect, indicating that the effect was gut microbiome-dependent. Statistical analysis revealed that *Parabacteroides* gut bacteria, which were less abundant in Hpa-Tg mice, were the major drivers of the group differences and reintroduction of *Parabacteroides* alleviated pancreatitis in the Hpa-Tg mice. The effects of *Parabacteroides* were related to acetate produced by the bacteria, and *Parabacteroides* administration and acetate administration both alleviated neutrophil infiltration in Hpa-Tg mice. Although the mechanisms linking heparanase, acetate and neutrophil infiltration need to be clarified, the results indicate the importance of the gut-pancreas axis in acute pancreatitis and suggest that acetate could be a useful treatment.