REGIONAL CENTRE FOR BIOTECHNOLOGY
Journal Club

"The microbial metabolite butyrate regulates intestinal macrophage function via histone deacetylase inhibition"
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Abstract

Given the trillions of microbes that inhabit the mammalian intestines, the host immune system must constantly maintain a balance between tolerance to commensals and immunity against pathogens to avoid unnecessary immune responses against otherwise harmless bacteria. Mis-regulated responses can lead to inflammatory bowel diseases such as ulcerative colitis or Crohn's disease. The mechanisms by which the immune system maintains this critical balance remain largely undefined. Here, we demonstrate that the short-chain fatty acid n-butyrate, which is secreted in high amounts by commensal bacteria, can modulate the function of intestinal macrophages, the most abundant immune cell type in the lamina propria. Treatment of macrophages with n-butyrate led to the down-regulation of lipopolysaccharide-induced proinflammatory mediators, including nitric oxide, IL-6, and IL-12, but did not affect levels of TNF-α or MCP-1. These effects were independent of toll-like receptor signaling and activation of G-protein-coupled receptors, two pathways that could be affected by short-chain fatty acids. In this study, we provide several lines of evidence that suggest that these effects are due to the inhibition of histone deacetylases by n-butyrate. These findings elucidate a pathway in which the host may maintain tolerance to intestinal microbiota by rendering lamina propria macrophages hyporesponsive to commensal bacteria through the down-regulation of proinflammatory effectors.