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Microbiota-derived metabolites shape mucosal barrier and immunity

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Human intestinal microbiota is a complex community composed of more than 500 species. The total genes of gut microbiota outnumber our genes by more than 100-fold. Many of these microbial genes are involved in main metabolic pathways such as carbon metabolism and amino acid synthesis. Using the abundant genes, commensal microbiota actively perform microbial fermentation and produce a diversity of metabolites. We demonstrated that certain microbial metabolites regulate barrier functions as well as mucosal immunity. For instance, butyrate mainly produced by bacterial species belonging to Clostridiales cluster IV and XIVa plays a critical role in development of intestinal regulatory T (Treg) cells in response to bacterial colonization early in life. Butyrate facilitates induction of Foxp3, the master transcription factor of Treg cells, by enhancing histone acetylation of regulatory regions of the gene though inhibition of histone deacetylase (HDAC). Butyrate also enhances IgA responses in the gut through a T cell-independent IgA class switch pathway. Collectively, microbial butyrate maintains unique phenotypes of gut microenvironment to maintain gut immune homeostasis.