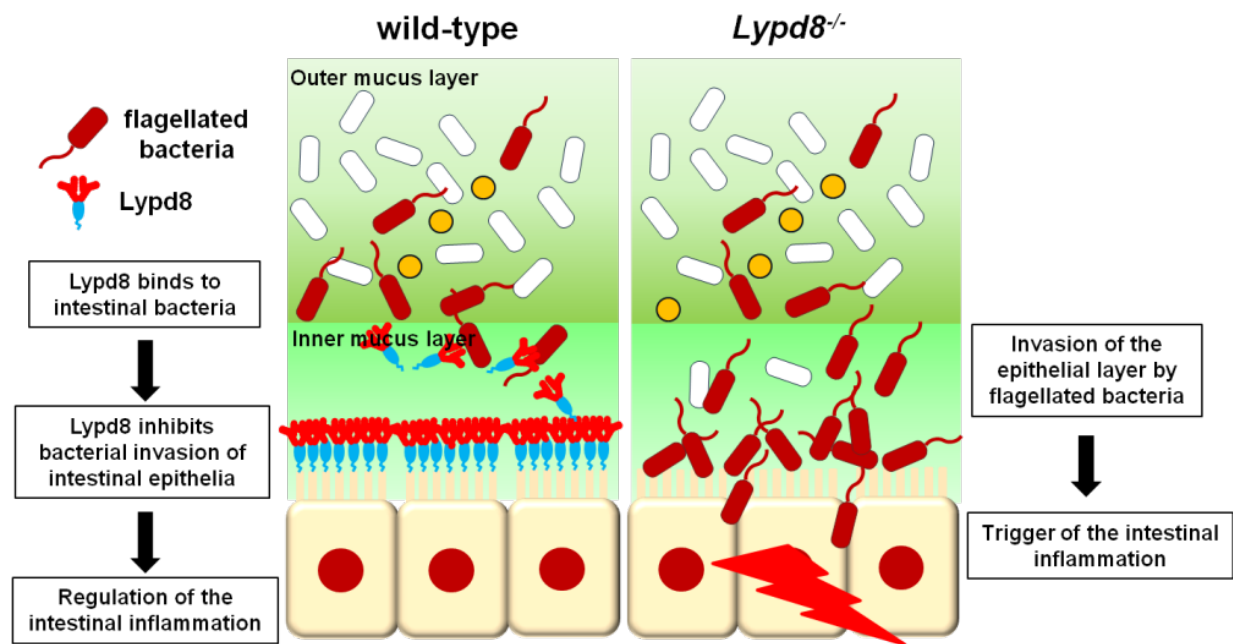


# Mechanism for inhibiting bacterial invasion of colonic epithelia elucidated

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Ly6/PLAUR domain containing 8 (Lypd8), which is a highly glycosylated GPI-anchored protein, is highly and selectively expressed in epithelial cells on the uppermost layer of the intestinal gland and shed into the intestinal lumen. Lypd8 inhibits intestinal bacterial invasion of the colonic mucosa by binding to the intestinal bacteria, and thereby regulates the intestinal inflammation. Credit: Osaka University

A group of researchers at Osaka University elucidated how a gene named Ly6/Plaur domain containing 8 (Lypd8) inhibits bacterial

invasion of colonic epithelia, regulating intestinal inflammation. This achievement may lead to the development of drugs for ulcerative colitis.

Inflammatory bowel diseases, or IBD, such as ulcerative colitis, are intractable diseases with unknown etiology. The number of patients with IBD in Japan has tremendously increased in recent years. However, there are no definitive treatments at present. Recently, the dysfunction of the intestinal mucosal barrier has been thought to be one of the causes for IBD. Indeed, in genetically-modified [mice](#) in which the mucosal barrier is defective, [intestinal bacteria](#) invade the colonic mucosa, and this causes high susceptibility to intestinal inflammation. Thus, it is important to understand how the mucosal barrier is formed for the elucidation of pathogenesis of IBD and development of effective therapy for IBD. In the colon, where a tremendous number of [bacteria](#) exist, colonic epithelial cells are surrounded by the thick mucus and are thereby protected from intestinal bacteria. However, the mechanism by which the [mucus layer](#) in the colon inhibits [bacterial invasion](#) had been unclear.

A research group led by Ryu Okumura, Specially Appointed Researcher, and Kiyoshi Takeda, Professor, at Department of Microbiology and Immunology, Graduate School of Medicine; Immunology Frontier Research Center, Osaka University focused on a gene named Ly6/Plaur domain containing 8 (Lypd8), which is highly and selectively expressed in colonic epithelial cells. This group found that Lypd8 is a highly glycosylated GPI-anchored protein, and is shed into the intestinal lumen. Human Lypd8 is also expressed in the colonic epithelia. This group found that Lypd 8 expression decreases in the colon of [ulcerative colitis](#) patients. In Lypd8-deficient mice, many intestinal bacteria invaded the inner mucus layer. Flagellated bacteria such as Proteus and Escherichia especially invaded the colonic mucosa in Lypd8-deficient mice. Many flagellated bacteria are known to be pathobionts implicated in intestinal inflammation. Therefore, this group analyzed the sensitivity to dextran

sulfate sodium (DSS)-induced [intestinal inflammation](#) in Lypd8-deficient mice. Lypd8-deficient mice showed severe DSS-induced colitis compared to wild-type mice. Lypd8 bound to flagella of bacteria. In addition, Lypd8 inhibited the motility of bacteria in semisolid agar plate.

This group's study demonstrates that Lypd8 highly expressed in the colonic epithelia is constitutively shed into the intestinal lumen and inhibits bacterial invasion of colonic epithelia by binding flagella and suppressing the motility of flagellated bacteria. Through this mechanism, Lypd8 regulates intestinal homeostasis.

**More information:** Ryu Okumura et al, Lypd8 promotes the segregation of flagellated microbiota and colonic epithelia, *Nature* (2016). [DOI: 10.1038/nature17406](https://doi.org/10.1038/nature17406)

Provided by Osaka University

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