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IBD

Probiotics for IBD: a need for histamine?

> …histamine generation is important for mediating the anti-inflammatory effects of *L. reuteri* 6475

Treatment with *Lactobacillus reuteri* reduces intestinal inflammation in a mouse model of colitis via a mechanism dependent on intestinal histamine signalling, according to new research published in *mBio*.

Current pharmacological treatments for IBD typically target inflammatory signalling pathways in host cells. The intestinal microbiota composition is altered in patients with IBD, meaning modulation of the patients gut microbiota might be a therapeutic option. In previous work, the researchers showed that the commensal bacteria *Lactobacillus reuteri* inhibited TNF synthesis by human monocytes *in vitro*. However, these anti-inflammatory effects are lost if *L. reuteri* strains are used that lack genes encoding enzymes to convert histidine into histamine.

In the new study, Gao and colleagues investigated whether treatment with *L. reuteri* could suppress inflammation in a mouse model of colitis, and if these effects were dependent on genes encoding enzymes for histamine generation. Adult female mice were given a *L. reuteri* strain capable of generating histamine (*L. reuteri* 6475) or inert media by once daily orogastric gavage for 7 days. The mice then received intrarectal 2,4,6-trinitrobenzenesulfonic acid (TNBS) to induce colitis, or a control compound. TNBS-exposed mice receiving *L. reuteri* 6475 had less severe colitis, as assessed by the Wallace (macroscopic colitis) and Ameho (microscopic colitis) scoring systems, compared with TNBS-exposed mice not receiving *L. reuteri* 6475.

A mutant *L. reuteri* 6475 strain lacking histamine conversion genes did not suppress TNBS-induced colitis in mice, suggesting histamine generation is necessary for *L. reuteri* 6475 to suppress inflammation. Lastly, the researchers showed that the anti-inflammatory effects of *L. reuteri* 6475 in TNBS-exposed mice were dependent on the histamine H_2 receptor. Inhibiting signalling via this receptor suppressed the anti-inflammatory effects of *L. reuteri* 6475, whereas blocking the histamine H_1 receptor had no effect.

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ORIGINAL ARTICLE Gao, C. *et al.* Histamine H2 receptor-mediated suppression of intestinal inflammation by probiotic *Lactobacillus reuteri*. *mBio* http://dx.doi.org/10.1128/mBio.01358-15