How do Lactobacilli treat Helicobacter pylori-related diseases?

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Helicobacter pylori lipopolysaccharide, the major virulent factor of H. pylori, triggers interleukin-8 production in gastric epithelia through activating Toll-like receptor 4 pathways, leading to gastric mucosal inflammation. A research team in China demonstrated that Lactobacillus bulgaricus decreased H. pylori Sydney strain 1 lipopolysaccharide-induced interleukin-8 production through inhibiting the activation of Toll-like receptor 4.

Some studies have demonstrated *H. pylori* stimulates the release of interleukin-8 (IL-8) from gastric epithelia, which initiates inflammatory damage to gastric mucosa and plays a crucial role in the pathogenesis of *H. pylori* infections. *H. pylori* lipopolysaccharide (*H. pylori*-LPS) is the major initiator in *H. pylori*-induced IL-8 production via activation of Toll-like receptor 4 (TLR4) pathway in gastric epithelia.

Considering the novel finding that *H. pylori* is an indigenous biota in gastric microflora including *Lactobacilli* and hypothesis that the disturbance of gastric microecosystem plays a more important role in pathogenetic mechanisms of *H. pylori*, the eradiation of *H. pylori* doesn't seem justified to everyone.

The speculation on validity of restoration of the gastric microecosystem has been demonstrated by therapeutic effects of *Lactobacilli* administration on *H. pylori*-associated diseases. But whether *Lactobacilli* inhibit *H. pylori*-LPS-induced IL-8 production through blocking *H. pylori*-LPS-activated TLR4 pathway hasn't been well researched.

A research article to be published on August 28, 2008 in the *World Journal of Gastroenterology* addresses this question. The research team led by Prof. Hong-Sheng Ma from West China Hospital of Sichuan University treated SGC-7901 cells with *H. pylori* Sydney strain 1 lipopolysaccharide (*H. pylori*SS1-LPS) in the absence or presence of a pretreatment with viable Lactobacillus bulgaricus (LBG). The results indicated that viable LBG prevented *H. pylori*SS1-LPS-activated TLR4 pathway in SGC-7901 cells, leading to its inhibitory effect on IL-8 production stimulated by *H. pylori*SS1-LPS.

Considering some evidence implied that supernatant recovered from *Lactobacilli* culture MRS broth contained some latent soluble proteins secreted by *Lactobacilli*, SGC-7901 cells were treated with *H. pylori*SS1-LPS in the absence or presence of a pretreatment with supernatant recovered from LBG culture MRS broth (LBG-S). It was demonstrated that LBG-S had the same inhibitory effect on *H. pylori*SS1-LPS-activated TLR4 signaling transduction as viable LBG. In a recent novel study, two soluble proteins with molecular sizes of 75 and 40 kDa were purified from supernatant recovered from Lactobacillus rhamnosus GG culture MRS broth and named p75 and p40 respectively, which ameliorated apoptosis of intestinal epithelia treated with tumor necrosis factor α, interferon-γ or IL-1α and promoted cell growth through activating Akt and blocking p38 mitogen-activated protein kinase and stress-activated protein kinase/c-Jun amino-terminal kinase signaling. So LBG-S in this experiment probably contained the similar or even same proteins, which could intervene in *H. pylori*SS1-LPS-activated TLR4 signaling through modulating other pathways in SGC-7901 cells.

This evaluation of LBG as a probiotic model revealed an important and novel relationship between *H. pylori*-LPS-activated TLR4 signaling and selective microflora. This report adds to our understanding of the signal pathways in the gastric epithelia involved in inflammatory responses that

are regulated by probiotics and pathogenic bacteria composing the gastric microecosystem. Further studies of the soluble components secreted by *Lactobacilli* may benefit to the exploration of new drugs against *H. pylori*-associated diseases in the future.

Reference: Zhou C, Ma FZ, Deng XJ, Yuan H, Ma HS. Lactobacilli inhibit interleukin-8 production induced by Helicobacter pylori lipopolysaccharide-activated Toll-like receptor 4. World J Gastroenterol 2008; 14(32): 5090-5095 www.wjgnet.com/1007-9327/14/5090.asp

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