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IBD

ELAFIN—A POTENTIAL IBD THERAPY

Patients with IBD have decreased mucosal expression of the protease inhibitor elafin, which results in increased elastolytic activity in the colon. Researchers have now engineered two food-grade strains of lactic acid bacteria (*Lactococcus lactis* and *L. casei*) that successfully deliver elafin to the intestinal mucosa in a mouse model of colitis. These treated mice had reduced inflammation and their intestinal homeostasis was restored.

Elafin is known to have anti-inflammatory properties at mucosal surfaces. "We thus reasoned that the oral delivery of elafin might be of value for the treatment of IBD," write the researchers. However, delivering protease inhibitors to the gut can be problematic, as they can interfere with digestive functions. The protease inhibitors must also be delivered in small quantities to the site of injury, where they would be released steadily. The researchers, therefore, engineered lactic acid bacteria to deliver recombinant human elafin directly to the intestinal mucosa.

The research team used a mouse model of colitis (induced by dextran sodium sulphate) to test the efficacy of their elafin-expressing bacteria. For 7 days, the mice received an oral dose of *L. lactis* or *L. casei* that either did or did not express elafin. The elastolytic activity in inflammed colon tissue was considerably reduced in the mice that received elafin, returning to patterns seen in noninflammed tissue of treatment-naive mice. By contrast, the mice that received wild-type bacteria showed no change in their elastolytic activity.

The effect of elafin on markers of inflammation (colon thickness and granulocyte infiltration) was also examined in the mouse model of colitis. Both these markers were reduced in mice that received either *L. lactis* or *L. casei* that expressed elafin compared with mice that received the wild-type bacteria. Levels of inflammatory cytokines were also reduced following administration of elafin.

The authors conclude that elafin-expressing probiotics can effectively reduce the symptoms of colitis in a mouse model, and protect against mucosal erosion and T-cell-mediated damage. However, they caution that further work is needed before elafin-expressing probiotics can be used in humans with IBD.

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Original article Motta, J.-P. *et al.* Food-grade bacteria expressing elafin protect against inflammation and restore colon homeostasis. *Sci. Transl. Med.* **4**, 158ra144