

Genetically engineered bacteria could help in Crohn's and colitis

November 2 2012, by Lin Edwards

(Medical Xpress)—A new study in mice has shown that genetically engineered bacteria can protect against inflammatory bowel disease (IBD), which includes a host of conditions including ulcerative colitis and Crohn's disease.

IBD conditions are serious ailments in which the gut becomes inflamed and damaged, sometimes so severely that surgery to remove the inflamed sections is the only treatment currently available. The conditions arise when the immune system attacks the gut, for reasons that are poorly understood. Symptoms include cramps, ulcers, weight loss, diarrhea, and the inflammation can result in intestinal scarring and a greater risk of developing [bowel cancer](#).

The study, led by Jean-Paul Motta of the Centre de Physiopathologie de Toulouse Purpan (CPTP) in Toulouse, France, genetically modified two strains of Lactobacillus bacteria by splicing a gene into their DNA that instructs cells to manufacture the naturally-occurring protein, elafin, which the team had noted was deficient in patients with IBD. The bacteria are probiotic and do not cause harm in humans.

Elafin blocks the actions of members of the [protease](#) group of enzymes, which are known to play a role in inflammation. It is expressed in the skin and lungs during healing of trauma. As reported in [Phys.org](#) elafin is also now known to be a marker that can be measured by a blood test to determine whether or not skin graft patients will be susceptible to graft-versus-host disease ([GVHD](#)).

In earlier studies the French and Canadian team of researchers had shown that mice genetically engineered to manufacture more elafin were afforded protection against a condition similar to human colitis. In the new study they aimed to find out if increasing the levels through the use of [probiotic bacteria](#) would also protect against inflammation.

The research team fed the bacteria to mice and found that the levels of elafin increased to greater levels than in [control mice](#) fed non-genetically engineered bacteria of the same strains. They induced IBD in the mice and found that those fed the bacteria with the elafin gene had greater resistance, and that there was less inflammation and cell damage. They also reported a reduction in the numbers of neutrophil and macrophage immune cells in the gut.

The researchers also added the bacteria to cultures of gut tissue from human IBD patients and reported that the key signs of [inflammation](#) were reduced in the presence of the elafin-manufacturing bacteria.

The study findings, reported this week in *Science Translational Medicine*, suggest that the bacteria could be of benefit to IBD patients, and could be given in pill form or alternatively, the food-grade bacteria could be added as live cultures to yogurts. More research is needed to ensure the best strains of bacteria are selected and to ensure the safety and efficacy of the treatment in human patients.

More information: Food-Grade Bacteria Expressing Elafin Protect Against Inflammation and Restore Colon Homeostasis, *Sci Transl Med* 31 October 2012: Vol. 4, Issue 158, p. 158ra144 [DOI: 10.1126/scitranslmed.3004212](#)

ABSTRACT

Elafin, a natural protease inhibitor expressed in healthy intestinal mucosa, has pleiotropic anti-inflammatory properties in vitro and in

animal models. We found that mucosal expression of Elafin is diminished in patients with inflammatory bowel disease (IBD). This defect is associated with increased elastolytic activity (elastase-like proteolysis) in colon tissue. We engineered two food-grade strains of lactic acid bacteria (LAB) to express and deliver Elafin to the site of inflammation in the colon to assess the potential therapeutic benefits of the Elafin-expressing LAB. In mouse models of acute and chronic colitis, oral administration of Elafin-expressing LAB decreased elastolytic activity and inflammation and restored intestinal homeostasis. Furthermore, when cultures of human intestinal epithelial cells were treated with LAB secreting Elafin, the inflamed epithelium was protected from increased intestinal permeability and from the release of cytokines and chemokines, both of which are characteristic of intestinal dysfunction associated with IBD. Together, these results suggest that oral delivery of LAB secreting Elafin may be useful for treating IBD in humans.

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