Novel cytokine protects mice from colitis

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Inflammatory bowel disease (IBD), which affects more than 1 million patients in North America, results from an uncontrolled immune response triggered by environmental factors, such as bacteria, in people genetically predisposed to the disorder. Ulcerative colitis, or inflammation of the lining of the colon, is one such condition.

The aberrant immune response found in IBD is prompted by different cytokines - small signaling proteins secreted by various cells, including immune cells - that activate the immune system, causing chronic inflammation.

Now researchers led by Jesús Rivera-Nieves, MD, of the Inflammatory Bowel Disease Center, Division of Gastroenterology at the University of California, San Diego School of Medicine, have discovered that expression of a newly identified human cytokine - Interleukin 37 (IL-37) - protects mice from colitis. The study will be published this week in *Proceedings of the National Academy of Sciences* (*PNAS*).

IL-37 is a member of the IL-1 family and functions as an inhibitor of innate inflammation and immunity. While most molecules in the IL-1 family appear to promote an inflammatory response, IL-37 modulates or downgrades inflammation.

Charles A. Dinarello, MD, from the University of Colorado, recently expressed human IL-37 in lab mice, which do not have an orthologue, or similar molecule, for this particular cytokine. Nonetheless, IL-37 works the same in both mice and humans. The mice were then fed water containing dextran sulfate sodium (DSS), a substance that induces colitis, to see whether IL-37 provided protection from intestinal inflammation.

It did. "While we still don't understand its mechanism of action, our hope is that, in the future, scientists may be able to engineer cells to overproduce IL-37 and use it to treat or control an overactive immune system in humans," said Rivera-Nieves.

That would represent a major advance in treating IBD, particularly for the 30 to 50 percent of IBD patients for whom highly effective biological therapies - tumor necrosis factor inhibitors - don't work, or for an even larger percentage of patients whose symptoms eventually return.

Provided by University of California - San Diego