Antimicrobial found to calm inflamed gut in mice

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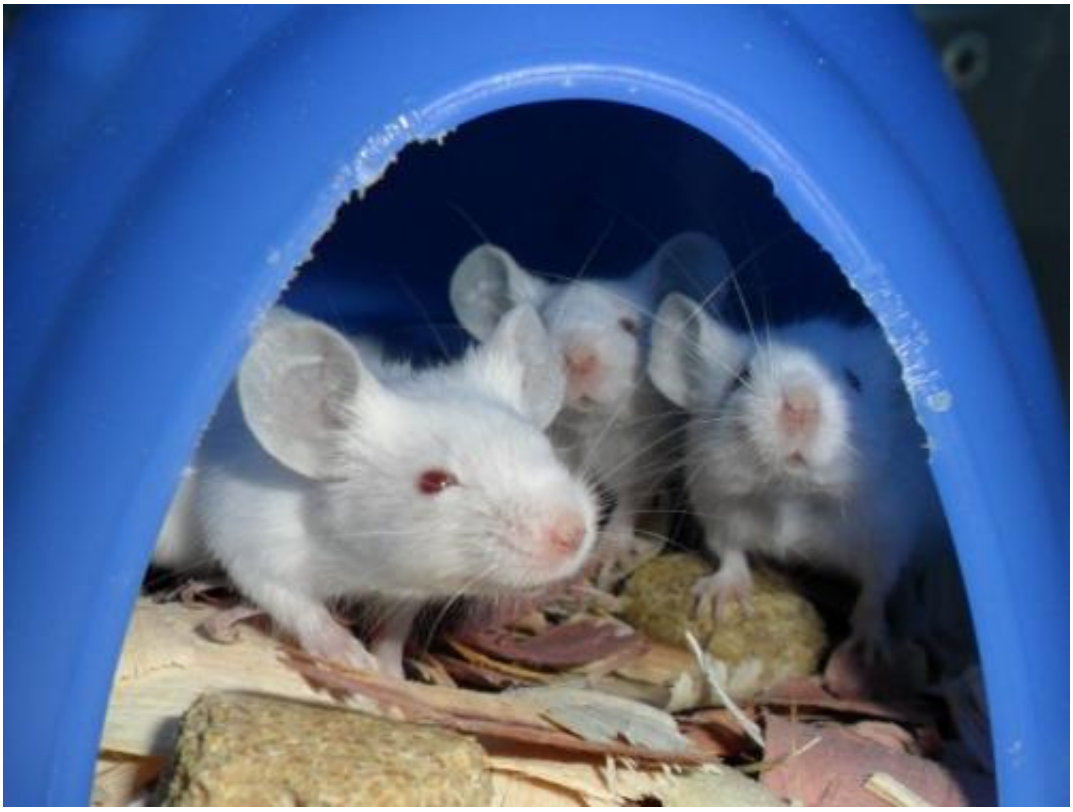

Credit: Martha Sexton/public domain

(Medical Xpress)—A team of researchers with the University of California has found that introducing a type of antimicrobial protein called a microcin into the guts of mice with inflamed bowels caused a reduction in the degree of inflammation. In their paper published in the journal *Nature*, the team describes their study of the use of the protein in

mice and their evidence that microcins intercede in the relationship between different types of bacteria in the gut.

Over the past several decades, scientists have made a lot of progress in better understanding the factors that lead to irritable bowel syndrome which covers a host of gut ailments, from Crohn's disease to colitis. Most of them, they believe, are due to harmful gut bacteria multiplying and pushing out beneficial bacteria. In this new effort, the team of researchers was studying small proteins called microcins, which are secreted by probiotic bacteria and serve as a means for striking back when pushed by harmful bacteria. They conducted a study to determine if introducing the protein into the guts of mice with IBS would have a positive impact—prior work in the lab had suggested it might.

In the study, the researchers caused several mice to have IBS, then separated them into groups—some received doses of a type of E. coli that produces microcin, another group received another strain of E. coli that does not produce the protein while a third group got a dose of diarrhea-producing Salmonella enterica and a fourth got a dose of E. coli that is suspected to play a role in causing Crohn's disease in humans.

After waiting to see what might happen, the team found that the E. coli with the probiotic reproduced rapidly enough to push out the harmful bacteria that was causing the IBS in the mice—that in turn led to a reduction in inflammation. The team also found that the antimicrobial also caused a reduction in Salmonella enterica numbers in infected mice.

The researchers suggest that introducing microcin-producing bacteria to the gut of people suffering from IBS might someday be a realistic treatment for those afflicted, noting that such therapies could offer a way forward in overcoming problems associated with antibiotic resistance.

More information: Martina Sassone-Corsi et al. Microcins mediate competition among Enterobacteriaceae in the inflamed gut, *Nature* (2016). DOI: 10.1038/nature20557

Abstract

The Enterobacteriaceae are Gram-negative bacteria and include commensal organisms as well as primary and opportunistic pathogens that are among the leading causes of morbidity and mortality worldwide. Although Enterobacteriaceae often comprise less than 1% of a healthy intestine's microbiota1, some of these organisms can bloom in the inflamed gut2,3,4,5; indeed, expansion of enterobacteria is a hallmark of microbial imbalance known as "dysbiosis"6. Microcins are small secreted proteins that possess antimicrobial activity in vitro7,8, but whose role in vivo has been unclear. Here we demonstrate that microcins enable the probiotic bacterium Escherichia coli Nissle 1917 (EcN) to limit expansion of competing Enterobacteriaceae (including pathogens and pathobionts) during intestinal inflammation. Microcin-producing EcN limited growth of competitors in the inflamed intestine, including commensal E. coli, adherent-invasive E. coli, and the related pathogen Salmonella enterica. Moreover, only therapeutic administration of the wild-type, microcin-producing EcN to mice previously infected with S. enterica substantially reduced intestinal colonization of the pathogen. Our work provides the first evidence that microcins mediate inter- and intra-species competition among the Enterobacteriaceae in the inflamed gut. Moreover, we show that microcins can be narrow-spectrum therapeutics to inhibit enteric pathogens and reduce enterobacterial blooms.