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Gut bacteria are protected by host during illness

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To protect their gut microbes during illness, sick mice produce specialized sugars in the gut that feed their microbiota and maintain a healthy microbial balance. This protective mechanism also appears to help resist or tolerate additional harmful pathogens, and its disruption may play a role in human diseases such as Crohn's disease, report scientists from the University of Chicago in *Nature* on Oct 1.

"Both hosts and their gut microbiota can suffer in the case of sickness, but this mutually beneficial relationship is guarded by the host," said study senior author Alexander Chervonsky, MD, PhD, chairman of the Committee on Immunology at the University of Chicago.

When faced with systemic illness, animals eat less to conserve energy instead of foraging for food and to deprive pathogens of nutrients. However, this can harm beneficial gut bacteria, which have an important role in health and disease.

To investigate how microbiota might be supported during illness, Chervonsky and his team focused on a potential internal resource produced by the host – L-fucose, a sugar which has been shown to affect gut microbes. A host cannot use L-fucose for energy, but when bound to proteins, it can be used by microbes as a food source. Under normal conditions, however, the small intestine of mice produces almost no L-fucose.

The team exposed different types of mice to a molecule that mimicked a

systemic infection. The mice became sick – eating less food, drinking less water and losing weight. Only a few hours after this induced sickness, the researchers observed that L-fucose was produced and present on almost every surface of the small intestine. This effect was seen only in response to illness.

The researchers then tested genetically engineered mice lacking Fut2, the gene responsible for L-fucose production. Healthy under normal conditions, mice without Fut2 regained weight after induced sickness – a measure of recovery – much slower than their normal counterparts. However, only mice with both intact gut microbiota and the ability to produce L-fucose recovered efficiently.

"Mice that can produce L-fucose recover better than those that can't," Chervonsky said. "If you remove bacteria the effect goes away."

The team used genetic analyses to confirm that gut microbes were affected metabolically by the production of L-fucose. As part of this analysis, they noted that sick mice without Fut2 had significantly greater expression of harmful microbial genes than normal mice. Hypothesizing that L-fucose production was somehow preventing opportunistic bacteria from expressing virulent genes, they exposed mice to a mild bacterial pathogen and then four days later induced sickness. Under this condition, mice without Fut2 lost significantly more weight than normal, suggesting that the production of L-fucose helps the host tolerate or resist additional harmful pathogens.

Interestingly, around 20 percent of humans lack a functional gene to produce L-fucose, a problem that has been associated with the inflammatory bowel ailment known as Crohn's disease.

"We speculate that without L-fucose, the activation of virulence genes cannot be blocked, and that's why bacteria play a role in Crohn's

disease," Chervonsky said. "Whether we can use this toward therapeutics in the future requires further study."

More information: "Rapid fucosylation of intestinal epithelium sustains host–commensal symbiosis in sickness," *Nature*, 2014. dx.doi.org/10.1038/nature13823

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