

Mice fed tryptophan develop immune cells that foster a tolerant gut

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Credit: Martha Sexton/public domain

Immune cells patrol the gut to ensure that harmful microbes hidden in the food we eat don't sneak into the body. Cells that are capable of triggering inflammation are balanced by cells that promote tolerance, protecting the body without damaging sensitive tissues. When the balance tilts too far toward inflammation, inflammatory bowel disease

can result.

Now, researchers at Washington University School of Medicine in St. Louis have found that a kind of tolerance-promoting immune cell appears in mice that carry a specific bacterium in their guts. Further, the bacterium needs [tryptophan](#)—one of the building blocks of proteins—to trigger the cells' appearance.

"We established a link between one bacterial species—*Lactobacillus reuteri*—that is a normal part of the [gut microbiome](#), and the development of a population of cells that promote tolerance," said Marco Colonna, MD, the Robert Rock Belliveau MD Professor of Pathology and the study's senior author. "The more tryptophan the mice had in their diet, the more of these immune cells they had."

If such findings hold true for people, it would suggest that the combination of *L. reuteri* and a tryptophan-rich diet may foster a more tolerant, less inflammatory gut environment, which could mean relief for the million or more Americans living with the abdominal pain and diarrhea of [inflammatory bowel disease](#).

The study is published Aug. 3 in the journal *Science*.

Postdoctoral researcher Luisa Cervantes-Barragan, PhD, was studying a kind of immune cell that promotes tolerance when she discovered that one group of study mice had such cells, while a second group of study mice that were the same strain of mice but were housed far apart from the first group did not have such cells.

The mice were genetically identical but had been born and raised separately, indicating that an environmental factor influenced whether the immune cells developed.

She suspected the difference had to do with the mice's gut microbiomes—the community of bacteria, viruses and fungi that normally live within the gastrointestinal tract.

Cervantes-Barragan collaborated with Chyi-Song Hsieh, MD, PhD, the Alan A. and Edith L. Wolff Distinguished Professor of Medicine, to sequence DNA from the intestines of the two groups of mice. They found six bacterial species present in the mice with the immune cells but absent from the mice without them.

With the help of Jeffrey I. Gordon, MD, the Dr. Robert J. Glaser Distinguished University Professor, the researchers turned to mice that had lived under sterile conditions since birth to identify which of the six species was involved in inducing the immune cells. Such mice lack a gut microbiome and do not develop this kind of immune cell. When *L. reuteri* was introduced to the germ-free mice, the immune cells arose.

To understand how the bacteria affected the immune system, the researchers grew *L. reuteri* in liquid and then transferred small amounts of the liquid—without bacteria—to immature immune cells isolated from mice. The [immune cells](#) developed into the tolerance-promoting cells. When the active component was purified from the liquid, it turned out to be a byproduct of tryptophan metabolism known as indole-3-lactic acid.

Tryptophan—commonly associated with turkey—is a normal part of the mouse and the human diet. Protein-rich foods contain appreciable amounts: nuts, eggs, seeds, beans, poultry, yogurt, cheese, even chocolate.

When the researchers doubled the amount of tryptophan in the mice's feed, the number of such cells rose by about 50 percent. When tryptophan levels were halved, the number of cells dropped by half.

People have the same tolerance-promoting cells as mice, and most of us shelter *L. reuteri* in our gastrointestinal tracts. It is not known whether tryptophan byproducts from *L. reuteri* induce the cells to develop in people as they do in [mice](#), but defects in genes related to tryptophan have been found in people with inflammatory bowel disease.

"The development of these cells is probably something we want to encourage since these [cells](#) control inflammation on the inner surface of the intestines," Cervantes-Barragan said. "Potentially, high levels of tryptophan in the presence of *L. reuteri* may induce expansion of this population."

More information: "Lactobacillus reuteri induces gut intraepithelial CD4+CD8 α α + T cells" *Science* (2017). [science.sciencemag.org/lookup/.../1126/science.aah5825](https://www.sciencemag.org/lookup/.../1126/science.aah5825)

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