

Engineered probiotic developed to treat multiple sclerosis

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Researchers from Brigham and Women's Hospital, a founding member

of the Mass General Brigham health care system, have designed a probiotic to suppress autoimmunity in the brain, which occurs when the immune system attacks the cells of the central nervous system.

Autoimmunity in the brain is at the core of several diseases, including multiple sclerosis (MS).

In a new study, researchers demonstrated the treatment's potential using preclinical models of these diseases, finding that the technique offered a more precise way target [brain](#) inflammation with reduced [negative side effects](#) compared to standard therapies. The results are published in *Nature*.

"Engineered probiotics could revolutionize the way we treat [chronic diseases](#)," said lead author Francisco Quintana, Ph.D., of the Ann Romney Center for Neurologic Diseases at Brigham and Women's Hospital. "When a drug is taken, its concentration in the bloodstream peaks after the initial dose, but then its levels go down. However, if we can use living microbes to produce medicine from within the body, they can keep producing the active compound as its needed, which is essential when we consider lifelong diseases that require constant treatment."

Autoimmune diseases affect approximately 5%–8% of the U.S. population. Despite their widespread prevalence, there are limited treatment options for most of these diseases. Autoimmune diseases that affect the brain, such as MS, are particularly challenging to treat due to their location—many pharmacological therapies can't effectively access the brain due to the [blood-brain barrier](#), a protective mechanism that separates the brain from the [circulatory system](#).

To look for new ways to treat [autoimmune diseases](#), the researchers studied dendritic cells, a type of immune cell that is abundant in the gastrointestinal tract and in the spaces around the brain. These cells help control the rest of the immune system, but scientists don't yet know their

role in autoimmune diseases. By analyzing dendritic cells in the central nervous system of mice, they were able to identify a [biochemical pathway](#) that [dendritic cells](#) use to stop other [immune cells](#) from attacking the body.

"The mechanism we found is like a brake for the immune system," said Quintana. "In most of us, it's activated, but in people with autoimmune diseases, there are problems with this brake system, which means the body has no way to protect itself from its own [immune system](#)."

The researchers found that this biochemical brake can be activated with lactate, a molecule involved in many metabolic processes. The researchers were then able to genetically engineer probiotic bacteria to produce lactate.

"Probiotics are nothing new—we've all seen them sold as supplements and marketed as a way to promote health," said Quintana. "By using [synthetic biology](#) to get [probiotic bacteria](#) to produce specific compounds relevant to diseases, we can take the benefits probiotics and amp them up to the max."

They tested their probiotic in mice with a disease closely resembling MS, and they found that even though the bacteria live in the gut, they were able to reduce the effects of the disease in the brain. They did not find the bacteria in the bloodstream of the mice, suggesting that the effect they observed was a result of biochemical signaling between cells in the gut and in the brain.

"We've learned in recent decades that the microbes of the gut have a significant impact on the central nervous system," said Quintana. "One of the reasons we focused on multiple sclerosis in this study was to determine whether we can leverage this effect in treating autoimmune diseases of the brain. The results suggest we can."

While the current study only examined the effect of the probiotic in mice, the researchers are optimistic that the approach could be readily translated into the clinic because the strain of bacteria they used to create their probiotic has already been tested in humans. The researchers are also working to modify their approach for autoimmune diseases that affect other parts of the body, particularly gut diseases like inflammatory bowel syndrome.

Quintana and colleagues are working to launch a company in collaboration with Mass General Brigham Ventures.

"The ability to use living cells as a source of medicine in the body has tremendous potential to make more personalized and precise therapies," said Quintana. "If these microbes living in the gut are powerful enough to influence inflammation in the brain, we're confident we'll be able to harness their power elsewhere as well."

More information: Francisco Quintana, Lactate limits CNS autoimmunity by stabilizing HIF-1 α in dendritic cells, *Nature* (2023).
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