

Gut-residing bacteria trigger arthritis in genetically susceptible individuals

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A single species of bacteria that lives in the gut is able to trigger a cascade of immune responses that can ultimately result in the development of arthritis.

Our gut, like that of most mammals, is filled with thousands of species of bacteria, many of which are helpful and aid in the development of a normal, healthy immune system. Gut-residing bacteria can also play a role in disorders of the immune system, especially [autoimmune disorders](#) in which the body attacks its own cells.

It turns out that [rheumatoid arthritis](#) is one such disorder. Researchers in the laboratories of Christophe Benoist and Diane Mathis at Harvard Medical School and Dan Littman at New York University made this discovery while working in mice prone to arthritis.

"In the absence of all bacteria, these mice didn't develop arthritis, but the introduction of a single [bacterium](#) was enough to jump-start the immune process that leads to development of the disease," says Mathis, an HMS professor of pathology.

The findings appear in the June 25 issue of the journal *Immunity*.

The researchers began by raising arthritis-prone mice in a germ-free environment. The mice had much lower levels of arthritis-causing autoantibodies than mice raised in a non-germ-free facility. The germ-free mice also showed strong attenuation in the onset and severity of

clinical arthritis.

At three weeks of age, some mice were transferred to a non-germ-free facility and the researchers introduced segmented filamentous bacteria into their systems. When they introduced this normally-occurring bacteria into the mice, the animals rapidly began producing autoantibodies and developed arthritis within four days.

First author Hsin-Jung Wu emphasizes that these bacteria do not cause the mice to "catch" arthritis. "It's more that they have the [genetic susceptibility](#), and this bacterium creates an environment that allows this genetic susceptibility to play out," says Wu, a postdoctoral researcher at Harvard Medical School. "It's an interaction between genetics and the environment."

The team mapped out the complex chain of events leading to arthritis. The segmented filamentous bacteria cause the animals to produce more of a particular subset of T cells. The immune system reacts to the activity of the T cells as if to a foreign threat and produces autoantibodies that trigger the devastating disease.

One surprising finding was that bacteria in the gut could influence the development of an autoimmune disease affecting tissues distant from the gut. Diseases such as irritable bowel syndrome have been linked to gut-residing bacteria, but this study is unique in showing the mechanism by which a bacterium in the gut can influence the development of an autoimmune response that ends in inflammation and pain in the joints.

The team will continue to use this mouse model of arthritis to answer questions about the link between the disease and autoimmune response. Next, they plan on tackling the molecular explanation of how these bacteria promote the development of this particular subset of T cells and to explore connections with other autoimmune diseases, in particular

type-1 diabetes.

Provided by Harvard Medical School

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