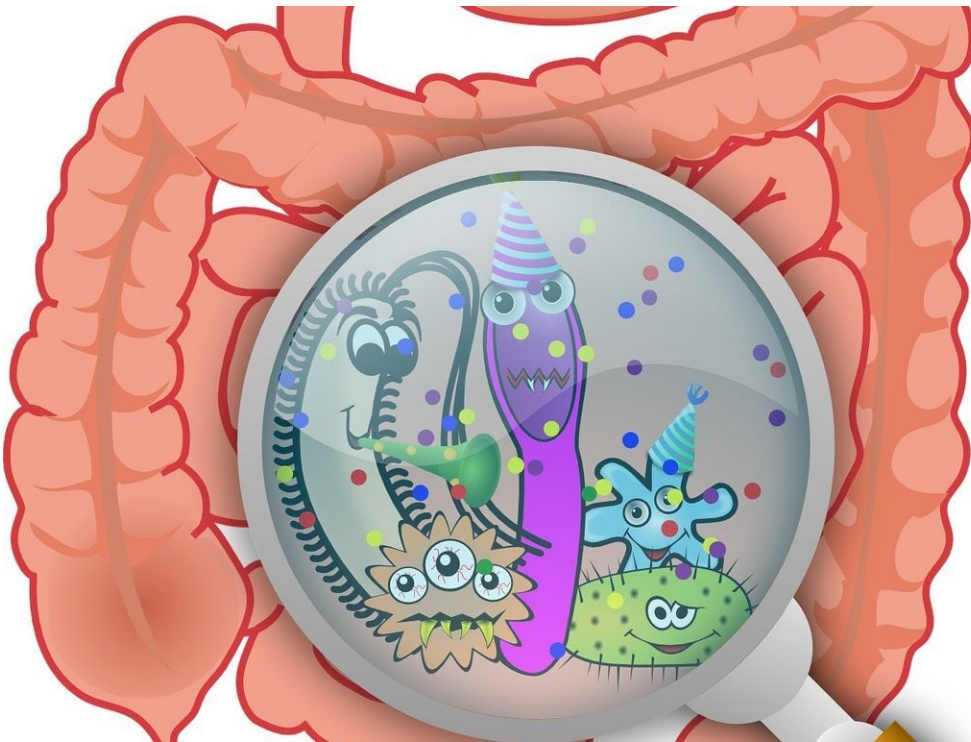


The gut may be involved in the development of multiple sclerosis

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The gut has long been suspected to play a role in autoimmune disease. A research team has now identified evidence of a potential mechanism.

It is incompletely understood which factors in patients with multiple sclerosis (MS) act as a trigger for the [immune system](#) to attack the brain

and spinal cord. A potential factor is described by a research team in the journal *Proceedings of the National Academy of Sciences, PNAS*. The [medical researchers](#) used an animal model to show that the protein Smad7 mobilizes immune cells in the intestines which, in turn, trigger inflammation in the central nervous system. Analyses of intestinal tissue samples taken from MS patients confirmed the results, which were published online on 4 December 2019.

The study was conducted at the Department of Neurology and the Centre of Neuroimmunology at St. Josef-Hospital, university hospital of Ruhr-Universität Bochum. The Bochum-based group with biologist Dr. Steffen Haupeltshofer and neurologists Professor Simon Faissner and Professor Ingo Kleiter, formerly at the Bochum university hospital, currently at Marianne-Strauß-Klinik in Berg, collaborated with other colleagues from Bochum, Bremen, Mainz, Düsseldorf, Jülich and Rome.

Protein Smad7 activates immune cells in the intestines

The research team initially analyzed the signal protein Smad7 in intestinal [immune cells](#) in mice, or more precisely: in T-cells. The researchers compared genetically modified mice with a normal and those with a particularly high quantity of Smad7 in T-cells as well as mice without any Smad7 in T-cells. They monitored if the animals developed opticospinal encephalomyelitis—a disease that mimics MS in humans.

The strongest clinical MS-like symptoms occurred in animals with an increased Smad7 level in T-cells. In their intestines, T-cells were more frequently activated, which then migrated into the central nervous system where they triggered inflammation. Moreover, the ratio of protective regulatory T-cells to pathogenic autoreactive T-cells had changed. In mice that didn't have any Smad7 protein, no clinical signs of

a MS-like disease occurred.

Results confirmed using tissue samples from patients

In the next step, the researchers analysed [tissue samples](#) taken from the intestines of 27 MS patients and compared them with samples taken from 27 healthy individuals. In the patients, they identified changes similar to those in the [animal model](#): the signal protein Smad7 occurred more frequently in intestinal mucosa samples of MS patients than in those of healthy individuals; in addition, an abnormal ratio of regulatory to pathogenic mechanisms was identified in intestinal mucosa samples in patients.

"For other [autoimmune diseases](#) such as Crohn's and other inflammatory bowel diseases, researchers are already aware that Smad7 offers a promising therapeutic target; our results suggest that the same is true for multiple sclerosis," says Ingo Kleiter. "Researchers are increasingly exploring intestinal involvement in the development and progression of MS," adds Simon Faissner.

More information: Steffen Haupeltshofer et al. Smad7 in intestinal CD4+ T cells determines autoimmunity in a spontaneous model of multiple sclerosis, *Proceedings of the National Academy of Sciences* (2019). [DOI: 10.1073/pnas.1905955116](https://doi.org/10.1073/pnas.1905955116)

Provided by Ruhr-Universität Bochum

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