

 MULTIPLE SCLEROSIS

A possible link between multiple sclerosis and gut microbiota

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The gut microbiota may have a role in the progression of multiple sclerosis (MS), according to two new studies. This finding could prompt novel strategies to treat MS by modifying the gut microbiota.

MS is an autoimmune disorder characterized by the destruction of the myelin sheath that surrounds nerve cells of the CNS. The exact causes are unknown, but the risk of developing MS is thought to comprise a combination of genetic and environmental factors. “The fact that only 30–35% of monozygotic twins are concordant for MS suggests that environmental factors must contribute a significant proportion of the remaining risk,” explains Sergio Baranzini, the corresponding author for one of the new studies.

Baranzini and colleagues used 16S ribosomal RNA gene sequencing to compare the microbiota of 71 untreated patients with MS and 71 healthy controls. The patients with MS had higher levels of *Akkermansia muciniphila* and *Acinetobacter calcoaceticus* and lower levels of *Parabacteroides distasonis* in the gut compared with the healthy controls.

Next, the researchers carried out *in vitro* and *in vivo* tests to determine the effects of these bacterial species on the immune response. They found that bacterial extracts from the gut microbiota of patients with MS strengthened the proinflammatory T-cell response in an *in vitro* model.

Finally, the researchers transplanted gut bacteria from patients with MS and healthy controls into germ-free mice and assessed the progression of experimental autoimmune encephalomyelitis (EAE), an artificially induced mouse model of MS. “The most significant finding is that the MS microbiota makes EAE worse,” comments Baranzini. The worsening of this condition was reflected in a weakening of the IL-10⁺ regulatory T-cell response, which modulates the development of EAE.

Several of these findings were corroborated in another study, to which Baranzini also contributed. “First, our clinical group compiled a cohort of monozygotic (genetically identical) twins discordant for MS — that is, one twin healthy, the other with MS,” say corresponding authors Hartmut Wekerle and Gurumoorthy Krishnamoorthy. Although the authors reported no substantial differences between the microbiota of the two groups overall, they did see a marked increase in the levels

of *A. muciniphila* and certain other bacterial species in untreated patients with MS.

The researchers performed fecal transplants to transfer the microbiota of the twin pairs into germ-free mice. Consistent with the results of the other study, microbial transplants from patients with MS were associated with exacerbation of EAE symptoms and reduced IL-10 production. Wekerle and Krishnamoorthy identify this loss of IL-10 production as a possible underlying mechanism, adding that “the difference in disease-promoting capacity is not so much explained by an overabundance of disease-promoting bacteria but, rather, a lack of protective microbes.”

These findings are likely to lead to further efforts to investigate which microorganisms regulate the pathogenesis of MS, their mechanisms of action, and which pathways are affected. “We have created an international consortium, the International MS Microbiome Study, with the goal of recruiting 2,000 patients,” says Baranzini, who hopes to replicate these findings. Further studies could explore modification of the gut microbiota, perhaps involving dietary changes, as a potential treatment for MS.

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ORIGINAL ARTICLES Baranzini, S. E. et al. Gut bacteria from multiple sclerosis patients modulate human T cells and exacerbate symptoms in mouse models. *Proc. Natl Acad. Sci. USA* <http://dx.doi.org/10.1073/pnas.1711235114> (2017) | Wekerle, H. et al. Gut microbiota from multiple sclerosis patients enables spontaneous autoimmune encephalomyelitis in mice. *Proc. Natl Acad. Sci. USA* <http://dx.doi.org/10.1073/pnas.1711233114> (2017)

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