Diet has an impact on multiple sclerosis disease course

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Intestinal bacteria influence the course of multiple sclerosis. Credit: RUB, Kramer

Intestinal bacteria operate as a self-sufficient organ: they influence the immune system and the brain via their metabolites.

The short-chain fatty acid propionic acid influences the intestine-mediated immune regulation in people with multiple sclerosis (MS). This has been shown by a team from the Department of Neurology of Ruhr-Universität Bochum (RUB) at St. Josef-Hospital in an international study headed by Professor Aiden Haghikia. The application of propionic acid in addition to MS medication reduced the relapse rate and the risk of disability progression in the long term. Moreover, initial Magnetic Resonance Imaging studies indicated that propionic acid may reduce brain atrophy as a sign of neuronal cell death. The results were published in the journal *Cell*.

Self-sufficient organ within the gut

The gut microbiome, i.e. the entire bacterial colonisation of the intestine, plays an important role not only for the healthy organism, but its association with chronic diseases, such as multiple sclerosis has been recently appreciated. Within the gut, the interaction between dietary components, microbiota, their metabolites, and the immune system takes place in the intestinal wall. "This is how intestinal bacteria can directly and indirectly affect anatomically distant structures such as the brain," explains Aiden Haghikia. "Accordingly, the gut microbiome acts like an self-sufficient endocrine organ that interacts with the environment."

Short chain fatty acids can suppress inflammatory reactions

In the current study, the researchers successfully transferred the results previously shown in the cell culture dish and the experimental model to their MS patients: short-chain fatty acids such as propionic acid or its salt propionate increased the differentiation and function of regulatory T cells in the gut. "These cells stop excessive inflammatory processes and reduce auto-immune cells in autoimmune diseases like MS," says Professor Ralf Gold, Director of the Department of Neurology at St. Josef Hospital.

In their study, the researchers showed that the microbiome composition is altered in MS patients. Moreover, they demonstrated a deficiency of propionic acid in the feces and serum of MS patients, which was most pronounced in the earliest phases of the disease. These data were obtained in collaboration with the Max Delbrück Center Berlin and the Institute of Nutritional Sciences at Martin Luther University Halle-Wittenberg.

Intestinal bacteria and the power plants of the cells of paramount importance

In collaboration with researchers from the Bar-Ilan University in Israel, who had developed an intestinal model for the functional analysis of the microbiome, it emerged that propionate associated changes of the gut microbiome play a crucial role in

the differentiation of regulatory cells. The increased function of these cells was due to their improved energy utilization through an altered function of the mitochondria, as the research team demonstrated in collaboration with the Molecular Cell Biology research group at the RUB Faculty of Medicine.

The intestine as target for future therapeutic approaches

The short-chain fatty acids represent only a fraction of the metabolites of intestinal bacteria that are generated from the diet. "Further research into this largely unknown organ and the knowledge gained from it will enable us to develop innovative dietary measures to complement the known therapeutics in the future," says Aiden Haghikia.

More information: Alexander Duscha et al. Propionic Acid Shapes the Multiple Sclerosis Disease Course by an Immunomodulatory Mechanism, *Cell* (2020). DOI: 10.1016/j.cell.2020.02.035

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