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Nutrition in early life shapes intestinal immunity

Researchers from the University of Bern, Inselspital, Bern University Hospital and Charité – Universitätsmedizin Berlin have discovered that the composition of our diet in early life can strengthen the immune system. Using a mouse model, the researchers showed that certain food components increase the production and diversity of antibodies in the intestine, regardless of the existing intestinal microbiota. The results could fundamentally improve the prevention and treatment of diseases in the future.

Our digestive system is home to trillions of bacteria. These are not only essential for our digestion, but also for a healthy immune system. The significance of our diet in terms of immune system function is a growing focus in both research and public awareness. In 2020 already, a study showed that the microorganisms in the gut, the gut microbiota, can influence the antibody repertoire in the entire body. In particular, antibodies of the immunoglobulin A (IgA) type are crucial for intestinal mucosal immunity and play a central role in defense against pathogens by preventing their penetration and multiplication in the intestine. Lipopolysaccharides (LPS) are components of the bacterial cell wall. They are produced naturally by intestinal bacteria, but they can also be found in our food, particularly in fermented and minimally processed foods such as yoghurt, fruit and vegetables. The present study investigated the influence of these LPS molecules on the immune response in the intestine in detail.

A team of researchers led by Prof. Dr. Stephanie Ganal-Vonarburg and Prof. Dr. Andrew Macpherson from the Department for Biomedical Research (DBMR), University of Bern, and the Department of Visceral Surgery and Medicine at Inselspital, Bern University Hospital, in collaboration with Charité, was able to show that LPS-rich, balanced diets increase the diversity of the antibody repertoire in the mouse gut, particularly in the early phase of life. The results, recently published in the journal *Cell Press Immunity*, offer new insights into the complex mechanisms by which diet influences the immune system.

Bernese Clean Mouse Facility crucial for success

To investigate the effects of different diets on the immune system, the researchers used two types of mice: germ-free mice, which grow up without any microorganisms (including intestinal bacteria); and mice, whose intestines were colonized with bacteria. "The Clean Mouse Facility at the University and Inselspital is one of the largest gnotobiotic animal facilities in Europe and was crucial for conducting the study," explains Stephanie Ganal-Vonarburg, co-lead author of the study. The mice were fed either an LPS-rich, balanced standard diet or an LPS-poor, high-fat, high-carbohydrate diet. The latter is similar to a typical Western diet, which is high in fat and carbohydrates and low in fiber or plant-based

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components. "By using germ-free mice, we were able to observe the direct effect of diet and food components on the immune system in isolation, allowing us to more clearly define the role of LPS in immune modulation," says Prof. Dr. Francesca Ronchi, one of the first authors of the study, who began her work at the DBMR as a postdoctoral researcher and now works at the Institute of Microbiology and Infection Immunology at the Charité. She explains further: "We examined the production of IgA in gut-associated lymph nodes and determined the antibody levels. The antibody repertoire was characterized using modern sequencing techniques. Altogether this allowed us to analyze the immune response in detail."

LPS-rich diet boosts intestinal immunity

The study shows that an LPS-rich, balanced diet stimulates the production and diversification of immunoglobulin A (IgA) antibodies in the intestine, which is crucial for the defense against pathogens. "Diets that are not well balanced or varied contain lower quantities of such bacterial molecules as LPS and thus stimulate the mucosal immune system correspondingly less," says Ganal-Vonarburg. The influence of diet is particularly crucial in the early phase of life, as it leads to a long-term promotion of antibody diversity in the gut. To their surprise, the team of researchers was able to observe the nutrition-related effect in both germ-free and colonized mice. Ganal-Vonarburg states: "In other words, early life nutrition shapes gut immunity, even in the absence of gut bacteria." The study results also indicate that LPS can have different immunological effects depending on whether it derives from food or is produced by living intestinal bacteria. This distinction had not been described adequately before.

Health effects and future research

The research strengthens the University of Bern's position as an internationally recognized center for microbiome research and mucosal immunology. "The findings expand our understanding of how nutrition and microbial signals shape the immune system, especially in early life. They show that not only the composition of the microbiota, but also the type of food ingested can influence how the body responds to pathogens or vaccines in the long term," says Prof. Dr. Andrew Macpherson, co-last author of the study and Professor Emeritus of Gastroenterology. Ganal-Vonarburg adds: "We are currently investigating which other dietary components can influence the immune system. And, of course, whether these effects can also be observed in humans". The findings could contribute to the development of new nutritional guidelines that optimize immune function, as well as to the development of new approaches for the prevention and treatment of diseases.

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The Department for BioMedical Research (DBMR) of the Faculty of Medicine of the University of Bern was founded in 1994 by the University of Bern and the Inselspital, University Hospital Bern. The DBMR is divided into 13 research programmes with around 100 participating individual laboratories and several independent research laboratories whose research spans all biomedical areas. To bridge the gap between the laboratory and the bedside, the DBMR promotes clinical research with a strong emphasis on the development of translational approaches, the use of "omics" and other cutting-edge technologies, and extensive collaboration between laboratory-based and patient-centred clinical research. The DBMR is also committed to the promotion of young scientists.
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