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Why the "gut brain" plays a central role for allergies

An international research team led by scientists from Bern and Charité – Universitätsmedizin Berlin has identified a previously unknown function of the intestinal nervous system. The study reveals that the intestinal nervous system plays a key role in regulating both the composition and stability of the intestinal barrier. Disruption of this protective mechanism can lead to the development of allergies. These findings open new avenues for advancing therapies for allergies, chronic inflammatory bowel diseases and irritable bowel syndrome.

The intestinal nervous system, often referred to as the "gut brain", is essential in controlling digestion and maintaining the intestinal barrier. This protective layer, made up of the intestinal mucosa, immune cells and the microbiome, shields the body from contents of the gut. Its effectiveness depends on the delicate balance among these components. If this balance is disrupted, inflammation, allergies or chronic intestinal diseases can arise. The intestinal mucosa serves as the body's primary defense against pathogens. While previous studies have shown that the intestinal nervous system is involved in immune responses in addition to digestion, its role in the development of intestinal epithelial cells has remained largely unclear until now.

An international research team led by the University of Bern, Inselspital Bern, Bern University Hospital and Charité, has now shown for the first time that the intestinal nervous system acts as a central regulator of the intestinal barrier. By releasing a specific molecule, it directs the development of different cell types in the intestinal wall and in this way shapes immune responses in the intestine that can promote allergies. The results of this study were recently published in *Nature Immunology*.

The intestinal nervous system as a "conductor" between stem cells and immune cells

In their study, the researchers investigated in the mouse model how specific nerve cells in the gut interact with intestinal stem cells. They focused on the vasoactive intestinal peptide (VIP), a messenger molecule produced by the intestinal nervous system. The findings show for the first time that intestinal nerve cells use VIP to communicate directly with intestinal stem cells, ensuring that these cells do not multiply too rapidly nor develop excessively into certain cell types. When this regulatory mechanism breaks down and VIP is absent, an excess of so-called tuft cells occurs. These cells then release signals that activate an allergy-like response in the intestine.

"Our findings show that the intestinal nervous system is a decisive factor in preserving a healthy intestinal mucosa, regulating immune responses, and ultimately maintaining an intact intestinal barrier," explains Dr. Manuel Jakob from the Department of Visceral Surgery and Medicine at

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Inselspital, research associate at the Department for BioMedical Research (DBMR) at the University of Bern and scientist at Charité. The study's first author adds: "Our 'gut brain' is far more than a facilitator of digestion. It acts as a central hub for health, immunity and potentially for conditions that affect large parts of the population. Interestingly, the results suggest that the effect may be shaped by the diet, i.e. the formulation of the food".

New approaches for inflammatory and allergic gut diseases

A healthy gut microbiome and a balanced immune response are vital for protecting the body from disease, making research on the intestinal nervous system increasingly significant. "The mechanism we have uncovered may help explain why some individuals are particularly sensitive in the gut and how we might intervene more precisely in the future," explains Prof. Christoph Klose, head of the Neuroimmune Interaction research group at Charité's Institute of Microbiology, Infectious Diseases and Immunology and senior author of the study. "By deepening our understanding of how nerves, cells and immune responses interact in the gut, we can develop more targeted and personalized therapies - for example for allergies, irritable bowel syndrome or chronic inflammatory bowel diseases." The findings also suggest that these reactions might be directly influenced through diet. As a next step, the team plans to investigate how nutrition can be strategically used to support the nerve-gut axis and support intestinal health.

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Department for BioMedical Research (DBMR)

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-centered clinical research. The DBMR is also committed to the promotion of young scientists.

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