



Joint Press Release of the Cluster of Excellence PMI at Kiel University and the Charité – Universitätsmedizin Berlin

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Balancing the gut – how the immune system maintains a healthy gut microbiota

Researchers from the Cluster of Excellence “Precision Medicine in Chronic Inflammation” and Charité - Universitätsmedizin Berlin have uncovered a critical mechanism that controls immune reactions against microorganisms in the intestine. The results of the international study may contribute to the development of new therapies for chronic inflammatory bowel disease. They have been published in the journal *Nature Immunology*.

The immune system protects against the spread of pathogenic germs in the intestine. At the same time, it allows the colonisation of beneficial microorganisms. Conversely, the composition of the microorganisms in the intestine, the so-called microbiota, has an influence on the quality of the immune reaction. An international research group led by Professor Alexander Scheffold of Kiel University (CAU) and the Cluster of Excellence Precision Medicine in Chronic Inflammation has uncovered a critical mechanism that establishes the balance between immune system and microbiota.

The researchers Dr. Christian Neumann (Charité), Dr. Sascha Rutz (Genentech, San Francisco), Professor Axel Kallies (University of Melbourne and Walter and Eliza Hall Institute of Medical Research, Melbourne), Professor Scheffold and colleagues studied molecular regulators of immune-microbiome-interactions in mice. The team focused on so-called regulatory T cells. These are immune cells that prevent harmless or even useful microorganisms in the intestine from being attacked by the immune system. "We have identified a molecule, c-Maf, which is critical for the development and function of specific regulatory T cells in the gut," explains Scheffold. C-Maf prevents the immune system from attacking the microbiota. "If this molecule is missing, the gut's immune system overreacts and the microbiota composition changes considerably," added first author Dr. Christian Neumann of Charité's Institute of Microbiology, Infectious Diseases and Immunology. This change in composition proved remarkably stable. When the researchers transferred the altered microbiota to mice with intact c-Maf-dependent regulatory T cells, they also developed an overreaction of the intestinal immune system.

"These results show that both the immune system and the microbiota mutually contribute to establishing and maintaining the balance in the gut," emphasises Prof. Scheffold. "This could explain how a microbial imbalance can contribute to chronic inflammatory bowel disease and why the treatment often fails". These findings could lead to new therapeutic approaches that, for example in the case of inflammatory bowel disease, aim to influence and harmonise both immune response and microbiota. In the future, the team would like to study how an established pathological interaction between intestinal bacteria and the immune system can be destabilized in patients and restored to its original state.

Original publication

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Photos are available to download:

https://precisionmedicine.de/pm/material/20190221_AlexanderScheffold_HaacksCAU.jpg



Alexander Scheffold, Cluster of Excellence "Precision Medicine in Chronic Inflammation", Professor of Immunology at Kiel University, Faculty of Medicine, and the University Medical Center Schleswig-Holstein, Campus Kiel. Photo: Jürgen Haacks, Kiel University

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The Cluster of Excellence "Precision Medicine in Chronic Inflammation" (PMI) has won funding from 2019 to 2025 through the German Excellence Strategy (ExStra). It succeeds the "Inflammation at Interfaces" Cluster, which had already won funding in two periods of the Excellence Initiative (2007-2018). Around 300 members from eight institutes at five locations are involved: Kiel (Kiel University, University Medical Center Schleswig-Holstein (UKSH), Muthesius University, Kiel Institute for the World Economy (IfW), Leibniz Institute for Science and Mathematics Education (IPN)), Lübeck (University of Lübeck, UKSH), Plön (Max Planck Institute for Evolutionary Biology), Borstel (Research Center Borstel - Leibniz Lung Center) and Großhansdorf (Lungenclinic Grosshansdorf). The aim is to draw on the multifaceted research approach to chronic inflammatory diseases of barrier organs, and transfer this interdisciplinarity to healthcare more intensively, as well as to fulfil previously unsatisfied needs of those affected. Three points are important in the context of a successful treatment, and are therefore at the centre of the PMI research: the early detection of chronic inflammatory diseases, the prediction of disease progression and complications, and the prediction of the individual response to treatment.

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