PMI Precision Medicine in Chronic Inflammation

Press Release

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How the intestinal fungus *Candida albicans* shapes our immune system

Members of the Cluster of Excellence "Precision Medicine in Chronic Inflammation" (PMI) have decoded a mechanism, how specific intestinal microbiota exacerbate inflammatory diseases at other body sites, such as the lungs.

The composition of the microorganisms living in and on our body - the so-called microbiome - has an enormous influence on human health. So far, it has not been possible to use this influence therapeutically, as the underlying mechanisms are largely unknown. In the Cluster of Excellence "Precision Medicine in Chronic Inflammation" various research groups are working on deciphering these interactions between humans and the microbiome. A team from the Institute of Immunology and the Institute of Clinical Molecular Biology at Kiel University (CAU) and the University Medical Center Schleswig-Holstein (UKSH) has now made a ground-breaking discovery. "We have discovered a mechanism how certain microbiota exacerbate inflammatory reactions in the lungs," said study leader Professor Petra Bacher. "The results now published in the scientific journal *Cell* offer new opportunities to better identify such disease processes and to provide targeted treatment," adds Professor Alexander Scheffold, head of the Institute of Immunology.

Humans live in close symbiosis with their microbiome, the countless bacteria, fungi and viruses that colonise the body surfaces, the skin, the intestines and the lungs. This coexistence is finely balanced and offers many benefits, such as protection against infections or help with the utilisation of nutrients. A disturbed microbiome is associated with a wide variety of diseases. These include chronic inflammatory bowel diseases, allergies, metabolic diseases, autoimmune diseases, cancer or even depression. Thus the microbiome recently attracted much attention, considering that influencing the microbiome could treat almost all major diseases in industrialized countries. In theory - but specific approaches are still lacking. The enormous diversity of the microbiome masks the essential components and the definition of cause and effect, preventing specific therapies.

The interaction with the microbiome is mainly controlled by the immune system. Cells of the immune system recognise specific microbes, and ensure a healthy balance. The key question is: how and by which microbes are the various effects on body functions triggered? A team of scientists from the Charité - Universitätsmedizin Berlin, the University Hospital Cologne, the RUB University Clinic in Bochum and the Leibniz Institute for Natural Product Research and Infection Biology and the University Jena, under the leadership of Petra Bacher and Alexander Scheffold from the CAU and the UKSH, has achieved a breakthrough. "We have identified the typically harmless fungus, *Candida albicans*, which colonises the intestine, skin and mucous membranes, as a central modulator of our immune system," explains Alexander Scheffold. "*Candida albicans* stimulates the immune system to produce certain immune cells, so-called Th17 cells. These enable a peaceful co-existence with the fungus." For the study, the researchers developed a sensitive method to isolate the Th17 cells that target *Candida albicans* from the blood. Further analysis revealed that some of these Th17 cells also recognise other fungi, such as the mould fungus *Aspergillus fumigatus*. This phenomenon is known as cross-reactivity.

Mould spores are inhaled daily with the breathing air, but are harmless for healthy people. On the other hand, moulds can colonize the lungs of people suffering from chronic lung diseases such as cystic fibrosis, chronic obstructive pulmonary disease or asthma. This is suspected of worsening the disease. "Surprisingly, we found that this group of patients has an increased population of cross-reactive Th17 cells in the lungs, which correlated with disease exacerbation. The protective Th17 response in the intestine seems to increase the disease-causing immune processes in the lungs," adds lead author Petra Bacher.

The researchers were thus able to show how a single member of the microbiome, *Candida albicans*, influences the specific immune reaction against a larger group of microbes at other body sites. Scheffold: "However, cross-reactivity is probably a common immune mechanism by which the microbiome manipulates the immune system, with protective or harmful effects. The ability to measure such specific effects of individual microbes now enables to develop targeted treatments."

Original publication

Petra Bacher, ... Alexander Schefold, et al. Human anti-fungal Th17 immunity and pathology rely on cross-reactivity against *Candida albicans*. *Cell,* published on Februar 21, 2019.
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Photos are available to download:

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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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Petra Bacher, Cluster of Excellence "Precision Medicine in Chronic Inflammation", Professor of Immunology and Immunogenetics 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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