PRESS RELEASE

Instructions for building antibodies decoded

International research team finds piece of puzzle in the pathogenesis of the autoimmune disease MOGAD

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Bonn, December 18 – *MOG Antibody-associated Disease* (MOGAD) is a rare autoimmune disease of the central nervous system. The blood of patients contains antibodies against myelin oligodendrocyte glycoprotein (MOG), a protein in the myelin layer that surrounds the neurons in the brain. It is believed that these antibodies contribute to the destruction of this protective layer in the brain. Researchers at the University Hospital Bonn (UKB) and the Universities of Basel and Bonn, in collaboration with Yale School of Medicine and the German Center for Neurodegenerative Diseases (DZNE), have now deciphered the construction plan of the anti-MOG antibodies. The researchers see their findings on the misdirected immune response, which have now been published in the journal *Neurology® Neuroimmunology & Neuroinflammation*, as the basis for developing specific MOGAD therapies.

MOGAD is a disease in which the immune system mistakenly produces antibodies that target the MOG protein. This presumably damages the protective myelin layer around nerve cells, leading to inflammation in the central nervous system. However, until now, it has been difficult to study the mechanisms that cause the disease because the structure of the anti-MOG antibodies was unknown. In regard to therapy, it is important to distinguish the autoimmune disease MOGAD, that occurs in episodes and can affect the brain, optic nerve and spinal cord, from multiple sclerosis (MS).

Ihr Weg zu uns
auf dem UKB-Gelände:
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White blood cells contain instructions for building MOG antibodies

The international research team led by Prof. Anne-Katrin Pröbstel from the UKB and the Universities of Basel and Bonn succeeded in identifying MOG-reactive B cells, the antibody factories of the immune system, in patient blood. These contained the genetic instructions for the anti-MOG antibodies. "Based on this alone, we were able to determine that MOG reactivity is present in different B cell subtypes," says Dr. Nora Wetzel, and Dr. Laila Kulsvehagen adds: "For example, there are B cells that are specific to MOG from the outset, while other B cells only develop this reactivity as they mature." The two co-first authors of the study belong to Prof. Pröbstel's research group.

The genetic code also allowed the researchers to produce the antibodies in the laboratory and test their functions. This revealed that the antibodies use various mechanisms to

eliminate MOG-producing cells. "Interestingly, not all MOG antibodies were equally effective in using these different mechanisms. While this was partly due to the binding capacity of the antibodies, we suspect that the structural interaction between the MOG antigen and the antibody is relevant, especially for the activation of the immune cascade," says Prof. Pröbstel, director of the Center for Neurology at the University Hospital Bonn (UKB), member of the ImmunoSensation^2 Cluster of Excellence at the University of Bonn and research group leader at the German Center for Neurodegenerative Diseases (DZNE).

This study confirms previous work involving patient sera and brain autopsies, thus reinforcing the hypothesis that anti-MOG antibodies contribute to the development of the disease, known in technical terms as pathogenesis. Prof. Pröbstel emphasizes: "The new understanding of the origin of MOG-reactive B cells and antibody functions is important for developing tailored therapies."

Participating institutions and funding:
In addition to the University Hospital Bonn (UKB) and the Universities of Basel and Bonn, the Yale School of Medicine (New Haven, USA), the German Center for Neurodegenerative Diseases (DZNE), the Medical University of Lodz (Poland), the Medical Center of the University of Amsterdam (Netherlands), and the Mannheim Medical Faculty and the University of Heidelberg are also involved in the study. The research team at the University Hospital Basel and the University Hospital Bonn received funding for the study from the Propatient Foundation of the University Hospital Basel, the Fondation Pierre Mercier pour la Science, the Swiss Multiple Sclerosis Society, the National Multiple Sclerosis Society, the Swiss National Science Foundation, the State Secretariat for Education, Research and Innovation (SERI), and Horizon Europe.

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