

Cellular self-digestion process triggers autoimmune disease

December 13 2017

Autophagy refers to a fundamental recycling process of cells that occurs in yeast, fungi, plants, as well as animals and humans. This process allows cells to degrade their own components and thus activate energy resources to be able to adapt to nutritional needs. In addition, autophagy plays a central role in steering an organism's immune response.

Autoimmune diseases arise from an abnormal immune response to a normal body part such as the central nervous system in patients with multiple sclerosis.

No autoimmune reaction without autophagy proteins

Led by Jan Lünemann from the Institute of Experimental Immunology at the University of Zurich, a team of neuroimmunologists has now found evidence for another aspect of this cellular "self-digestion": Autophagy proteins are responsible for triggering autoimmune processes in a mouse model of multiple sclerosis. Upon genetically switching off the autophagy protein ATG5 in certain [immune cells](#), the researchers observed significantly lower levels of pathological T cells in the central nervous system of the mice. As a consequence, the animals failed to develop inflammation in the brain and spinal cord comparable with inflammation that develops in multiple sclerosis.

Immune cells target nerve cells

The researchers have now demonstrated that the autophagy protein

ATG5 has an essential function when myelin antigens are presented to immune cells during inflammation processes in the central nervous system. "This reactivation process is thought to play a decisive role in the development of autoimmune neuroinflammation," says Christian Keller, lead author of the study. In multiple sclerosis – one of the most common [autoimmune diseases](#) – T cells attack the myelin sheaths of the body's own nerve fibers. The immune cells are activated as soon as they come into contact with antigen-presenting cells. Dendritic cells are responsible for antigen presentation. When the myelin sheath becomes defective, the [dendritic cells](#) digest the isolation membrane through autophagy and present parts of it to pathological T cells entering the site of the inflammation. "This means they promote the progression of the disease," explains Keller.

The team plans to use the latest findings as a basis for investigating tissue samples of patients suffering from multiple sclerosis to find out whether [autophagy](#) is particularly active in certain immune cells. "In the long run, we want to see whether these new immunopathology findings can be used to develop new treatments for [multiple sclerosis](#)," says Jan Lünemann.

More information: Christian W. Keller et al. ATG-dependent phagocytosis in dendritic cells drives myelin-specific CD4+T cell pathogenicity during CNS inflammation, *Proceedings of the National Academy of Sciences* (2017). [DOI: 10.1073/pnas.1713664114](https://doi.org/10.1073/pnas.1713664114)

Provided by University of Zurich

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