Possible approach discovered for treating multiple sclerosis

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Possible approach discovered for treating multiple sclerosis. Credit: Medical University of Vienna

Around 2.5 million people are affected by the autoimmune disease multiple sclerosis (MS), the most common central nervous system

disease among young adults. There are around 12,500 MS sufferers in Austria and 400 new cases every year. There is currently no cure for MS but, with appropriate treatment, it is possible to delay the typical progression of the disease. In collaboration with national and international groups in Japan, Germany and Switzerland, researchers from MedUni Vienna, led by Wilfried Ellmeier from MedUni Vienna's Institute of Immunology, have now discovered in an animal model that the family of histone deacetylases (HDACs) plays a major role in the development of this type of autoimmune disease. After the necessary follow-up studies, this could lead to a new approach to treating multiple sclerosis in the future.

The human immune system is based on a lively exchange of information between the cells, allowing for a coordinated response to germs or pathologically modified cells. This process requires the DNA information contained in the cells to be read and this is often regulated by so-called "epigenetic" processes (i.e. via the "degree of packaging" of the DNA). Special enzymes, the family of so-called histone deacetylases (HDACs), play an important role in this process. In total there are 18 different HDACs. They determine the "degree of packaging", that is to say how efficiently the information can be read.

If the "degree of packaging" is lessened, it is easier to read the DNA, and this controls the expression of a large number of proteins. In addition to this, HDACs can also regulate the activity and function of proteins. This then leads to an increase in cell activity and boosts communication between the immune cells. In the immune system, increased cell activity during an immune response is primarily manifested by an increase in the number of special immune defence cells, T-cells (or T-lymphocytes). The extent of an immune response is thereby regulated by the HDAC family.

In a study funded by the EU and FWF, researchers from MedUni

Vienna – who came not only from the Division of Immunobiology at the Institute of Immunology (Wilfried Ellmeier) but also the Department of Medicine III (Rheumatology/lead author Lisa Göschl, and Michael Bonelli and Günter Steiner), Center for Anatomy and Cell Biology (Christian Seiser's group) and CeMM (Christoph Bock's group) – have shown that mice who have had HDAC1 switched off in the T-cells using a "molecular trick", do not develop experimental autoimmune encephalomyelitis (EAE) , even when the disease is artificially provoked. EAE is an autoimmune disease which can be regarded as similar to MS in the animal model – even though there are certain differences. The results of the study have now been published in the "Journal of Autoimmunity". "However, we still do not know the underlying mechanism responsible for this protective effect," explains Wilfried Ellmeier, "We now want to conduct follow-on studies to discover the molecular details."

Certain broad-spectrum HDAC molecule inhibitors are used in the treatment of patients with certain types of cancer. They are used to directly attack the tumour – and in most cases the tumour shrinks. Many preclinical studies using an animal model suggest that HDAC inhibitors could also be effective in diseases of the immune system, like autoimmune diseases, but the potential therapeutic effects of broad-spectrum inhibitors are to some extent counterbalanced by serious side effects. "Our study indicates that the development and use of HDAC1-specific inhibitors, with potentially fewer side-effects than broad-spectrum inhibitors, could be a possible approach for treating MS," says lead author Lisa Göschl, who conducted this study as part of her doctoral thesis at the Institute of Immunology and the Division of Rheumatology at MedUni Vienna. "However, a few more detailed studies are still required to clarify that," adds Ellmeier.

More information: Lisa Göschl et al. A T cell-specific deletion of HDAC1 protects against experimental autoimmune encephalomyelitis,

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