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News release, September 24, 2015

Vaccination on the horizon for severe viral infection of the brain

Researchers from the University of Zurich and the University Hospital Zurich reveal possible new treatment methods for a rare, usually fatal brain disease. Thanks to their discovery that specific antibodies play a key role in combating the viral infection, a vaccine against the disease «progressive multifocal leukoencephalopathy» could now be developed.

Humans carry a multitude of viruses and bacteria in their gut, on their skin and in other organs. Often, these are involved in important bodily functions. Under certain conditions, however, some can also cause diseases. The JC virus, a member of the polyoma tumor virus family, is a prime example. This pathogen was first isolated from the brain of a patient who was suffering from a rare brain disease known as progressive multifocal leukoencephalopathy (PML). The virus, which more than 60 percent of the global population are infected with, normally resides in the kidneys and certain other organs. JC virus can trigger the PML infection in the brain, which, in most cases, is fatal.

Weak immune system facilitates brain infection

Two studies conducted by an international team of researchers from the University of Zurich, the University Hospital Zurich, the National Institutes of Health in the USA, San Raffaele Hospital in Milan, the University of Tübingen, and the UZH spin-off Neurimmune now reveal that the antibodies in PML patients often fail to recognize the JC virus they are infected with. «In healthy people, the disease never breaks out as the immune system keeps it well under control. Once the immune system is compromised, however, such as in patients with tumors, leukemia, AIDS, autoimmune diseases and certain immunosuppressive treatments, the JC virus is able to alter its genetic information and infect the brain,» explains Roland Martin, professor of neurology at the University of Zurich.

In multiple sclerosis (MS) patients, for instance, the treatment with a particular antibody, Tysabri™, prevents immune cells from reaching the brain – but at the same time, also inhibits the brain's immunosurveillance. If JC viruses enter the brain during the treatment, they go undetected, which can cause PML, the most significant side effect of the highly effective Tysabri™. Over 560 MS patients worldwide have already developed the PML brain infection. Over 20 percent of them died from the disease as there is no effective treatment to date. Only if the immune system function is completely restored can the JC virus be removed from the brain.

Active vaccination method and therapeutic antibodies developed in Zurich

The researchers now reveal potential ways to vaccinate against PML preventatively or, if the brain has already been infected, treat it with virus-specific human antibodies. By vaccinating mice and a PML patient with the virus' coating protein, the international groups were able to demonstrate that the antibody response was so strong that the patient was soon able to eliminate the JC virus. The so-called active vaccination method was developed at the University of Zurich and the University Hospital Zurich, and has already been used successfully on two more patients. The JC-virus-specific antibodies that are of interest for the treatment of the existing brain infection were developed by the group at the University of Zurich and the University Hospital Zurich together with colleagues from the University of Tübingen and the biotechnology company Neurimmune in Schlieren.

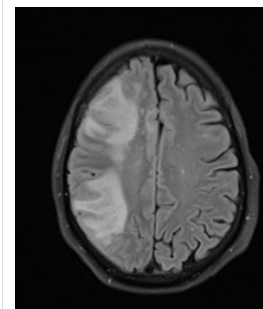
«We made a major breakthrough,» says Martin. «We managed to isolate antibody-producing cells from a patient who survived PML and use them to produce neutralizing antibodies against the JC virus. These human antibodies have a major advantage: they recognize the most important mutants of the JC virus that can cause PML. They now make promising candidates for the development of a treatment for PML.»

Literatur:

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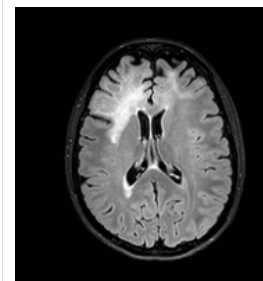
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Infection (light zone) in the brain of multiple sclerosis patients suffering from progressive multifocal leukoencephalopathy (PML). (Image: Neuroradiology, USZ).



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Infection (light zone) in the brain of multiple sclerosis patients suffering from progressive multifocal leukoencephalopathy (PML). (Image: Neuroradiology, USZ).

Jelcic I, Combaluzier B Jelcic I, Faigle W, Senn L, Reinhart BJ, Ströh L, Nitsch RM, Stehle T, Sospedra M, Grimm J, Martin R. Broadly neutralizing human monoclonal JC polyomavirus VP1-specific antibodies as candidate therapeutics for progressive multifocal leukoencephalopathy. Science Translational Medicine. September 23, 2015. Doi: 10.1126/scitranslmed.aac8691

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