Medical Xpress

Curing arthritis in mice

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With a new therapeutic product, researchers have managed to cure arthritis in mice for the first time. The scientists are now planning to test the efficacy of the drug in humans.

Rheumatoid arthritis is a condition that causes painful inflammation of several joints in the body. The joint capsule becomes swollen, and the disease can also destroy cartilage and bone as it progresses. Rheumatoid

arthritis affects 0.5% to 1% of the world's population. Up to this point, doctors have used various drugs to slow or stop the progression of the disease. But now, ETH Zurich researchers have developed a therapy that takes the treatment of rheumatoid arthritis in mice to a new level: after receiving the medication, researchers consider the animals to be fully cured.

The drug is a biotechnologically produced active substance consisting of two fused components. One component is the body's own immune messenger interleukin 4 (IL-4); previous studies have shown that this messenger protects mice with rheumatoid arthritis against cartilage and bone damage. ETH scientists have coupled an antibody to IL-4 that, based on the key-lock principle, binds to a form of a protein that is found only in inflamed tissue in certain diseases (and in tumour tissue).

Localised drug delivery

"As a result of combination with the antibody, IL-4 reaches the site of the disease when the fusion molecule is injected into the body," says pharmacist Teresa Hemmerle, who has just completed her dissertation in the group of Dario Neri, a professor at the Institute of Pharmaceutical Sciences. Together with Fabia Doll, also a PhD pharmacist at ETH, she is the lead author of the study. "It allows us to concentrate the active substance at the site of the disease. The concentration in the rest of the body is minimal, which reduces side-effects," she says.

The researchers tested the new fusion molecule, which they refer to as an 'armed antibody', in a CTI project together with the ETH spin-off Philochem. They used a mouse model in which the animals developed swollen, inflamed toes and paws within a few days. Among other things, the researchers studied the fusion molecule in combination with dexamethasone, a cortisone-like anti-inflammatory drug that is already used to treat rheumatoid arthritis in humans. The researchers started

treating each mouse as soon as they began showing signs of the disease in the form of swollen extremities.

Clinical trials in the next year

When used separately, the new fusion molecule and dexamethasone managed only to slow the progression of the disease in the affected animals. In contrast, the typical signs of arthritis, such as swollen toes and paws, disappeared completely within a few days when both medications were administered at the same time. Concentrations of a whole range of immune messengers in blood and inflamed tissue, which are changed in rheumatoid arthritis, returned to their normal levels. "In our mouse model, this combined treatment creates a long-term cure," says Hemmerle, who, since completing her dissertation, has been working at Philochem, where she continues the project.

Based on the promising results from the animal model, Philochem is currently preparing to test the new drug in clinical trials on people suffering from rheumatoid arthritis. According to the researchers, these tests will begin in the next year.

More information: Hemmerle T, Doll F, Neri D: Antibody-based delivery of IL4 to the neovasculature cures mice with arthritis. *PNAS*, online publication 4 August 2014, DOI: 10.1073/pnas.1402783111

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