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Gene therapy cures a severe paediatric neurodegenerative disease in animal models

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A single session of a gene therapy developed by the Universitat Autonoma de Barcelona (UAB) cures Sanfilippo Syndrome A in animal models. This syndrome is a neurodegenerative disease that affects between 1 and 9 out of every 100,000 children, and causes the death of the child on reaching adolescence. The study has been published in *The Journal of Clinical Investigation*.

Sanfilippo Syndrome type A, or Mucopolysaccharidosis type IIIA (MPSIIIA), is a neurodegenerative disease caused by mutations in the gene that encodes the enzyme sulfamidase. Mutations in this gene lead to deficiencies in the production of the enzyme, which is essential for the breakdown of substances known as glycosaminoglicans. If these substances are not broken down, they accumulate in the cells and cause neuroinflammation and organ dysfunction, mainly in the brain, but also in other parts of the body. Children born with this mutation are diagnosed from the age of 4 or 5. They suffer neurodegeneration, causing mental retardation, aggressiveness, hyperactivity, sleep alterations, loss of speech and motor coordination, and they die in adolescence.

A team of researchers headed by the director of the UAB's Centre for Animal Biotechnology and Gene Therapy (CBATEG), Fàtima Bosch, has developed a gene therapy treatment that cures this disease in animal models, with pre-clinical studies in mice and dogs. The treatment consists of a single surgical intervention in which an adenoassociated viral vector is injected into the cerebrospinal fluid, the liquid that

surrounds the brain and the spinal cord. The virus, which is completely harmless, genetically modifies the cells of the brain and the spinal cord so that they produce sulfamidase, and then spreads to other parts of the body, like the liver, where it continues to induce production of the enzyme.

Once the enzyme's activity is restored, glycosaminoglican levels return to normal for life, their accumulation in cells disappears, along with the neuroinflammation and dysfunctions of the brain and other affected organs, and the animal's behaviour and its life expectancy return to normal. While mice with the disease lived only up to 14 months, those given the treatment survived as long as healthy ones.

This is a joint project between the UAB and the pharmaceutical company Esteve. The study has been published in the online edition of *The Journal of Clinical Investigation*.

More information: Haurigot, V. et al. Whole body correction of mucopolyscaccharidosis IIIA by intracerebrospinal fluid gene therapy, *The Journal of Clinical Investigation* Vol 123, number 8, August 2013. www.jci.org/articles/view/66778

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