Fetal Gene Therapy Prevents Gaucher Disease

Using gene therapy on the brains of fetal mice and non-human primates, researchers have managed to prevent a fatal neurodegenerative condition known as Gaucher disease.

AsianScientist (Aug. 2, 2018) – Researchers have developed a fetal gene therapy that prevents Gaucher disease, a fatal neurodegenerative ailment. Their findings are published in Nature Medicine.

Gaucher disease is an irreversible, inherited genetic metabolic disorder that results from not having enough glucocerebrosidase—an enzyme that breaks down fatty chemicals called glucocerebrosides. Because individuals suffering from Gaucher
The present study showed that gene therapy during the fetal stages of development can prevent Gaucher disease in mice.

“Although the symptoms of some mild forms of Gaucher disease can be treated postnatally, more severe forms that cause early-onset, irreversible neurodegeneration are currently untreatable and are often fatal in infants. Being able to provide therapy at the earliest possible opportunity is vital in treating the brain which has a limited capacity to regenerate,” explained senior author Dr. Ahad Rahim of the UCL School of Pharmacy.

The researchers thus used a viral vector to deliver genetic material into the brains of fetal mice carrying neuropathic Gaucher disease, caused by mutations in GBA. Mice receiving the gene therapy exhibited less brain degeneration and survived considerably longer than untreated mice.

“We found that the mice that received an injection of adeno-associated virus vector were more able to break down fatty chemicals and re-express the gene encoding an enzyme that is deficient in Gaucher disease,” said corresponding author Dr. Simon Waddingdon of the UCL Institute for Women’s Health.

Mice receiving the injection in utero lived for at least 18 weeks after birth compared to just 15 days in control mice. They also displayed no signs of neurodegeneration, and were fertile and fully mobile. Neonatal intervention also alleviated disease severity in mice, but less effectively.
Given the promising results shown in mice, the team from Singapore performed the test in non-human primates during gestation, a period when a clinical diagnosis of genetic conditions can be made the immune system is more responsive to gene therapy. The team showed that the delivery of viral vectors to the developing brain is feasible.

“Macaques and humans share a very similar neurological, immunological and physiological developmental time-line in the womb, making them accurate models for pre-clinical investigations before clinical trials can proceed,” said Associate Professor Jerry Chan, a senior consultant at KK Women’s and Children’s Hospital and principal investigator at Duke-NUS Medical School.

“We have used a clinically relevant method to deliver the GBA gene using AAV vectors to the brain efficiently. This new approach will bring hope, not only for Gaucher disease, but also for other inborn errors of metabolism that can potentially be treated using fetal gene therapy,” he added.

The team is now engaged with Apollo Therapeutics in developing gene therapy for Gaucher disease.

The article can be found at: Massaro et al. (2018) Fetal Gene Therapy for Neurodegenerative Disease of Infants.

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