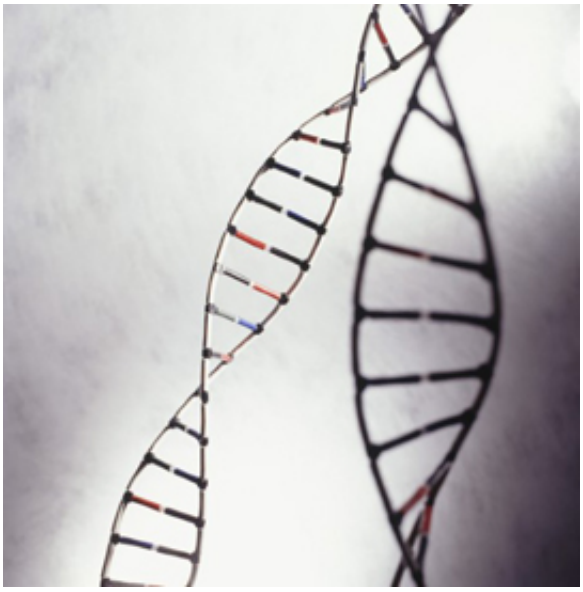
Huntington's disease gene dispensable in adult mice

March 7 2016



Credit: NIH

Adult mice don't need the gene that, when mutated in humans, causes the inherited neurodegenerative disorder Huntington's disease.

The finding suggests that treatment strategies for Huntington's that aim to shut off the huntingtin gene in adults—now in early clinical stages—could be safe.

The results are scheduled for publication Monday, March 7 in *PNAS*.

Huntington's disease is caused by a gene encoding a toxic protein (mutant huntingtin) that causes brain cells to die. Symptoms commonly appear in mid-life and include uncontrolled movements, balance problems, mood swings and cognitive decline. A juvenile form of Huntington's disease also can appear during the teenage years.

Researchers led by Xiao-Jiang Li, MD, PhD and Shihua Li, MD, at Emory University School of Medicine, used genetically engineered mice in which the huntingtin gene can be deleted, triggered only when the mice are given the drug tamoxifen.

When the huntingtin gene is deleted at an age older than four months, these mice appeared to stay healthy, despite having lost their huntingtin genes in cells all over their bodies. They maintained their body weight and could complete tests of movement and grip strength as well as control mice.

In contrast with adults, engineered mice younger than four months old whose huntingtin gene was deleted developed lethal pancreatitis. The huntingtin gene encodes a large scaffold protein, with many interaction partners, which is thought to be involved in intracellular trafficking. The huntingtin gene is essential for embryonic development, and scientists have already shown that if mouse embryos don't have it at conception, they die in utero.

"When it comes to gene suppression or editing strategies for Huntington's disease, a major concern has been possible side effects because of huntingtin's essential function," says Xiao-Jiang Li, who is professor of human genetics at Emory University School of Medicine. "Our studies suggest that such concerns may be allayed if deletion of huntingtin occurs only in the adult brain or in older adults."

However, it is possible that other more subtle alterations of behavior or

memory are present in the huntingtin-deleted mice, he adds.

The strategy of lowering huntingtin expression is widely believed to be promising in treating Huntington's disease, Li says. Additional research could make clear whether the post-natal role of huntingtin tapers off with age in humans in the same way that it does in mice.

More information: Ablation of huntingtin in adult neurons is nondeleterious but its depletion in young mice causes acute pancreatitis, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1524575113

Provided by Emory University

Citation: Huntington's disease gene dispensable in adult mice (2016, March 7) retrieved 24 April 2024 from https://medicalxpress.com/news/2016-03-huntington-disease-gene-adult-mice.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.