MedicalXpress

Researcher closes in on pathways involved in ALS disease

December 4 2017, by Jeff Sossamon

It is estimated that between 14,000 and 15,000 Americans have amyotrophic lateral sclerosis (ALS), according to the National Institutes of Health. Symptoms of ALS, also known as Lou Gehrig's disease, may be subtle at first but develop into more obvious muscle weakness and paralysis. Recently, a University of Missouri researcher identified a potential target for therapeutics that may help to lessen the severity and progression of ALS. Researchers suggest that this same enzyme pathway also could help in the recovery of patients who have suffered strokes and other disorders.

"ALS is a motor neuron disease. It begins with the degeneration of upper and lower motor neurons, and leads to muscle atrophy, paralysis and eventually death," said Shinghua Ding, an associate professor of bioengineering and an investigator in the Dalton Cardiovascular Research Center. "Our previous studies indicated that an enzyme known as NAMPT (nicotinamide phosphoribosyltransferase) is primarily expressed in the neurons in mouse models, and overexpression of NAMPT can protect against further brain injury following a stroke. For these reasons, NAMPT became a good target of study."

Ding and his team first observed that mice lacking the NAMPT enzyme led to progressive loss of weight, hypothermia, motor neuron degeneration, and motor function deficits. Most of these symptoms also are observed in humans with ALS.

Then the team treated the mice with a product that regulates NAMPT

activity. The molecule is called nicotinamide mononucleotide (NMN) and serves as a substitute for the missing enzymatic product. Mice treated with the NMN molecule exhibited enhanced motor neuron function and overall improved health. Importantly, they demonstrated that NAMPT levels were significantly reduced in the spinal cord. Their discovery indicates that NAMPT is involved in ALS pathogenesis.

"What we've shown is that NAMPT is essential to neuronal function and viability," Ding said. "Remarkably, NMN improved health span, restored motor function and extended the lifespan in NAMPT-deficient mice. Based on our findings, it is an ideal candidate for further study, and the possible development of drugs in the diagnosis and treatment of ALS and stroke victims."

The study, "Deletion of NAMPT in Projection Neurons of Adult Mice Leads to Motor Dysfunction, Neurodegeneration, and Death," recently was published in *Cell Reports*.

Provided by University of Missouri-Columbia