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Gene therapy protects mice from heart condition

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A new gene therapy developed by researchers at the University of Missouri School of Medicine has been shown to protect mice from a life-threatening heart condition caused by muscular dystrophy.

"This is a new therapeutic avenue," said Yi Lai, Ph.D., the leading author of the study and assistant research professor in the MU School of Medicine's Department of Molecular Microbiology and Immunology. "This is just a first step, but we hope this could lead to a treatment for people with this devastating heart condition, which is a leading cause of death for people with Duchenne muscular dystrophy."

About one in 3,500 children, mostly boys, are born with Duchenne muscular dystrophy (DMD). They experience a progressive wasting away of muscles, starting in the legs and pelvis. Children with DMD have difficulty walking, and most need wheelchairs by age 12.

As DMD depletes the skeletal muscles, it also causes the heart to decay. A weakened heart kills up to 40 percent of people with DMD, usually by their 20s or early 30s. DMD originates with mutations in a single gene. For more than two decades, researchers have explored using gene therapy, an experimental treatment, to replace the flawed gene with a healthy copy.

The recent MU study, however, did not try to replace the faulty gene. The researchers targeted a different gene—one involved with the heart's built-in system for responding to heart attacks and other emergencies.

This targeted gene expresses a protein called nNOS. During short-term stresses, nNOS activates briefly to help regulate the heart. The MU researchers altered the gene to enable more efficient transfer of the nNOS gene to mouse hearts.

Seven months after the gene therapy, the mice who received the treatment showed significantly improved overall heart health. On most disease indicators, the researchers found that the treatment protected their hearts from the damage of DMD.

"The study showed for the first time that a modified nNOS gene could be delivered through gene therapy to protect the hearts of mice from Duchenne muscular dystrophy," said Dongsheng Duan, Ph.D., co-author of the study and Margaret Proctor Mulligan Professor in Medical Research at the MU School of Medicine.

"Since nNOS protects against multiple heart diseases, this method could one day be extended to the treatment of other heart diseases, such as heart failure or a heart attack," Duan said.

The technique is in an early stage of development and will require more research before potential applications in humans are explored.

More information: The study, "Partial Restoration of Cardiac Function with ΔPDZ nNOS in Aged MDX Model of Duchenne Cardiomyopathy," was published in *Human Molecular Genetics*.

Provided by University of Missouri-Columbia