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Muscular dystrophy: Repair the muscles, not the genetic defect

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A potential way to treat muscular dystrophy directly targets muscle repair instead of the underlying genetic defect that usually leads to the disease.

Muscular dystrophies are a group of muscle diseases characterized by skeletal muscle wasting and weakness. Mutations in certain proteins, most commonly the protein dystrophin, cause muscular dystrophy in humans and also in mice.

A University of Michigan team led by cell biologist Haoxing Xu, discovered that mice missing a critical calcium channel inside the cell, called TRPML1, showed similar muscle defects as those present in muscular dystrophy patients. Though these mice did not have the defect in dystrophin, they still developed muscular dystrophy-like muscle characteristics.

When researchers increased the activity of the calcium channel in the muscular dystrophic mice, it improved muscle membrane repair and restored muscle function.

"The hope is that the same calcium channel will work in people with muscular dystrophy," Xu said.

The long-term plan is to develop clinical trials of a drug that would provide the extra activity of TRPML1.

The findings are scheduled for advance online publication Sept. 14 in *Nature Medicine*. Xiping Cheng, U-M Department of Molecular, Cellular, and Developmental Biology, is first author on the paper.

While the treatment in mice using a gene therapy approach involved a viral carrier to insert extra TRPML1 channels in muscle, Xu says his team has recently discovered a drug that can activate this calcium channel. This drug might provide a similar boost to muscle membrane repair in human muscular dystrophy patients, but this requires further test in the laboratory.

More information: The intracellular Ca2+ channel MCOLN1 is required for sarcolemma repair to prevent muscular dystrophy, *Nature Medicine*, DOI: 10.1038/nm.3611

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