Researchers discover target that could ease spinal muscular atrophy symptoms

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is no cure for spinal muscular atrophy (SMA), a genetic disorder that causes the weakening of muscles and is the leading genetic cause of infant death, but University of Missouri researchers have discovered a new therapeutic target that improves deteriorating skeletal muscle tissue caused by SMA. The new therapy enhanced muscle strength, improved gross motor skills and increased the lifespan in a SMA model.

"This therapy does not directly target the disease-causing gene; instead it targets the pathways that affect muscle maintenance and growth," said Chris Lorson, investigator in the Christopher S. Bond Life Sciences Center and associate professor of veterinary pathobiology in the MU College of Veterinary Medicine. "We administered a particular protein, follistatin, to SMA mouse models to determine if enhanced muscle mass impacts the symptoms of SMA. After treatment, the mice had increased muscle mass, gross motor function improvement and an increase in average life span of 30 percent."

With the therapy, MU researchers inhibited myostatin, a protein that limits muscle tissue growth. Myostatin activity can be reduced significantly by enabling several proteins that bind to myostatin, including follistatin. When myostatin is inhibited, muscle mass and strength increase.

SMA is caused by the loss of survival motor neuron-1(SMN1). Humans have a nearly identical copy gene called SMN2. Because of a single molecular difference, SMN2 alone cannot compensate for the loss of SMN1.

"While most work in the SMA field has logically focused on targeting the SMN2 gene, the results of this study suggest that skeletal muscle is a viable therapeutic target that may reduce the severity of some SMA symptoms," said Lorson, who also is the scientific director for FightSMA, a private spinal muscular atrophy research foundation in Richmond, Va. "Because follistatin does not alter the expression level of SMN protein, the most effective treatment would combine strategies that directly address the genetic defect in SMA as well as SMN-independent strategies that enhance skeletal muscle."

The study, "Delivery of recombinant follistatin lessens disease severity in a mouse model of Spinal Muscular Atrophy," was published online in the December issue of *Human Molecular Genetics*.

Source: University of Missouri-Columbia