

In lab research, scientists slow progression of a fatal form of muscular dystrophy

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Thomas Burris, Ph.D., chair of pharmacology and physiology at Saint Louis University and Colin Flaveny, Ph.D., assistant professor of pharmacology and physiology at SLU. Credit: Saint Louis University

In a paper published in the Nature journal *Scientific Reports*, Saint Louis

University (SLU) researchers report that a new drug reduces fibrosis (scarring) and prevents loss of muscle function in an animal model of Duchenne muscular dystrophy (DMD), providing a promising approach in designing new medications for those suffering from DMD.

DMD is a fatal form of a muscle wasting disorder that affects one out of every 5,000 to 10,000 boys. The illness is caused by mutations in a gene on the X chromosome. With treatment, those with DMD have an average lifespan of around 25 years. Boys with the illness typically need to use a wheelchair by age 12 and require mechanical ventilation to help with breathing. Many eventually suffer cardiac or respiratory failure.

Thomas Burris, Ph.D., chair of pharmacology and physiology at Saint Louis University and Colin Flaveny, Ph.D., assistant professor of pharmacology and physiology at SLU, study natural hormones that regulate nuclear receptors. By understanding how the body's natural hormones operate, they aim to develop synthetic compounds to target these receptors in order to create drugs to treat diseases.

In the course of this work, Burris and Flaveny have explored the roles of the nuclear receptor REV-ERB, which regulates key processes in the body, from sleep to cholesterol, and, most recently, [muscle regeneration](#).

"Recently, we found that REV-ERB appears to play unique roles for each stages of [muscle tissue](#) development," Flaveny said.

Muscle stem cells which help replace damaged muscle tissue produce myoblasts that will either reproduce (proliferate) or form muscle tissue (differentiate).

A decline in expression of REV-ERB leads to myoblast differentiation. Conversely, an increase in REV-ERB expression is involved in the regulation of mitochondrial and metabolic function in fully

differentiated skeletal muscle.

The team showed that REV-ERB is a regulator of muscle differentiation, and that a drug that inhibits this receptor, called SR8278, stimulates muscle regeneration after acute injury.

Following up on these promising results, they decided to explore whether the drug SR8278 could slow the progression of muscular dystrophy in an animal model.

DMD patients experience ongoing cycles of muscle destruction and regeneration that promote inflammation, fibrosis (scarring), and the loss of skeletal and cardiac [muscle function](#).

Validating their theory, the research team discovered that SR8278 increased lean mass and muscle function and decreased muscle fibrosis and [muscle](#) protein degradation in mice.

"These results suggest that REV-ERB is a potent target for the treatment of DMD," Burris said. "This is an encouraging finding as we search for better treatments for those with this debilitating illness."

More information: Ryan D. Welch et al, Pharmacological inhibition of REV-ERB stimulates differentiation, inhibits turnover and reduces fibrosis in dystrophic muscle, *Scientific Reports* (2017). [DOI: 10.1038/s41598-017-17496-7](#)

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