Muscular dystrophy mystery solved; scientists move closer to MD solution

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Muscular dystrophy, which affects approximately 250,000 people in the United States, occurs when damaged muscle tissue is replaced with fibrous, bony or fatty tissue and loses function. While scientists have identified one protein, dystrophin, as an important piece to curing the disease, another part of the mystery has eluded scientists for the past 14 years. Now, one University of Missouri scientist and his team have identified the location of the genetic material responsible for a molecular compound that is vital to curing the disease.

Duchenne muscular dystrophy (DMD), predominantly affecting males, is the most common type of muscular dystrophy. Patients with Duchenne muscular dystrophy have a gene mutation that disrupts the production of dystrophin. Absence of dystrophin starts a chain reaction that eventually leads to muscle cell degeneration and death. A previous study by Dongsheng Duan, associate professor of molecular microbiology and immunology, discovered a potential delivery method to replace the mutated genes with healthy genes. Following the replacement of these genes, Duan observed that dystrophin production was restarted in animals with muscular dystrophy.

However, while dystrophin is vital for muscle development, the protein also needs several "helpers" to maintain the muscle tissue. One of these "helper" molecular compounds is nNOS, which produces nitric oxide. This is important for muscles that are in use during high intensity movements, such as exercise.

"When you exercise, not only does the muscle contract, but the blood vessels are constricted," Duan said. "nNOS is important because it produces nitric oxide that relaxes the blood vessels, helping to maintain the muscle with a healthy blood supply. If no blood reaches the muscle cells, they will eventually die. In DMD patients, this means the disease will progress as the muscle cells are replaced by the fibrous, bony or fatty tissue."

Since 1994, researchers have known about the importance of nNOS, but have not been able to determine how to produce nNOS in a dystrophic muscle, or a muscle lacking dystrophin. Many scientists have tried to solve this mystery without success. In his most recent study, published Monday in *The Journal of Clinical Investigation*, Duan and his team identified the location of genetic material responsible for the production of nNOS.

Following the identification of the genetic material, Duan and his team created a series of new dystrophin genes. In their study, they used dystrophic mice to test the efficacy of these new genes. After genetically correcting the mice with the new dystrophin gene, Duan's team discovered that the missing nNOS was now restored in the dystrophic muscle. The mice that received the new gene did not experience muscle damage or fatigue following exercise.

"With this new discovery, we've solved a longstanding mystery of Duchenne Muscular Dystrophy," Duan said. "This will change the way we approach gene therapy for DMD patients in the future. With this study, we have finally found the genetic material that can fully restore all the functions required for correcting a dystrophic muscle and turning it into a normal muscle."

Source: University of Missouri-Columbia