Researchers prove the gene responsible for Duchenne muscular dystrophy can be repaired

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Researchers from Université Laval's Faculty of Medicine and the CHUQ Research Center have proven that it is possible to repair the defective gene responsible for Duchenne muscular dystrophy. The team, led by Professor Jacques P. Tremblay, is presenting its new therapeutic approach in an article published today in the online version of the scientific journal *Gene Therapy*.

Duchenne muscular dystrophy is a hereditary disease affecting one in 3,500 males. It causes progressive muscle degeneration that begins in early childhood and causes death by age 25 in most people afflicted. The disease is caused by mutations that affect a protein called "dystrophin." The mutations alter the normal nucleotide sequences of this protein's gene and stop its synthesis.

Professor Tremblay's team partnered with Cellectis, a French firm specializing in genome engineering, in order to design enzymes—called meganucleases—with the ability to correct the dystrophin gene. During in vitro testing, the researchers inserted genes coding for a variety of meganucleases into human muscle cells. They repeated the experiment in vivo with mice carrying the mutation that causes the illness. Both series of testing showed that the meganucleases can lead to a restoration of the normal nucleotide sequences of the dystrophin gene and its expression in muscle cells.

A number of hurdles must be overcome before this approach can be tested in humans, cautions Dr. Tremblay. "It must first be proven in laboratory animals that it is possible to insert a meganuclease targeting the dystrophin gene directly into muscle cells, and that this will induce the synthesis of dystrophin able to attach to the muscle fiber membrane," explains the researcher. "We're still two to three years away from this stage," he estimates. "Subsequent stages, including human trials, could take even longer," adds Dr. Tremblay.

Provided by Université Laval