MedicalXpress

Researchers find new gene mutation associated with congenital myopathy

July 25 2012

University of Michigan researchers have discovered a new cause of congenital myopathy: a mutation in a previously uncharacterized gene, according to research published this month in the *American Journal of Human Genetics*.

About 50% of congenital myopathy cases currently do not have a known genetic basis, presenting a clear barrier to understanding disease and developing therapy, says James Dowling, M.D., Ph.D., the paper's co-senior author and assistant professor of Pediatric Neurology at the University of Michigan's C.S. Mott Children's Hospital. Finding a new myopathy gene opens the possibility of providing a genetic explanation for disease in these individuals where no genetic cause is currently known.

In addition, "the identification of a new myopathy gene is an essential first step towards understanding why this disease occurs and how we combat its effects." says Dowling, who worked with Margit Burmeister, Ph.D. and her team from the University of Michigan's Molecular and Behavioral Neuroscience Institute to study the new myopathy gene (CCDC78).

Dowling says the gene, which has not been studied previously, is an important potential regulator of muscle function and, in particular, part of an important muscle structure called the triad.

"Many myopathies and dystrophies have abnormal triad

structure/function, so finding a new gene product involved in its regulation will help researchers better understand the triad and its relationship to muscle disease," Dowling says.

Congenital myopathies are clinically and genetically heterogeneous diseases that typically become evident in childhood with hypotonia and weakness. They are associated with impaired mobility, progressive scoliosis, chronic respiratory failure and often early death.

Currently there are no known treatments or disease modifying therapies for congenital myopathies.

The researchers performed linkage analysis followed by whole exome capture and next generation sequencing in a family with congenital myopathy. They then validated the gene mutation and provided insights into the disease pathomechanisms using the zebrafish model system.

Dowling says the researchers' next step is to further model the disease using zebrafish, in the hopes that this knowledge can be translated into therapy development.

"The study provides the first descriptions of the zebrafish model, and gives insight into how we will use it," says Dowling, who also is director of the Pediatric Neuromuscular Disorders Clinic at C.S. Mott Children's Hospital.

"Once we develop and characterize a model of the disease, we can then use it as a platform for therapy development."

More information: Journal reference: AJHG-D-12-00101R4