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Researchers find genetic cause of new type of muscular dystrophy

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A newly discovered mutation in the *INPP5K gene*, which leads to short stature, muscle weakness, intellectual disability, and cataracts, suggests a new type of congenital muscular dystrophy. The research was published in the *American Journal of Human Genetics* by researchers from the George Washington University (GW), St. George's University of London, and other institutions.

"The average pediatrician may only see one child with a rare disorder in his or her entire career. Even working with a team of specialists, it can sometimes take years for a child to be diagnosed with a specific rare disease," said Chiara Manzini, Ph.D., co-corresponding author for the study and assistant professor in the GW Institute for Neuroscience and in pharmacology & physiology at the GW School of Medicine and Health Sciences. "With a correct diagnosis, families have access to the best care and what to expect as far as the progression of the disease. From a research standpoint, we can develop new, targeted therapies to help these patients."

The research team found five individuals from four families presenting with variable clinical features, including muscular dystrophy, short stature, intellectual disability, and cataracts. While these indicators overlap with related syndromes, dystroglycanopathies and Marinesco-Sjögren syndrome, sequencing revealed a unique mutation in the gene *INPP5K* in the affected members of each family. This is what led the researchers to believe these individuals are presenting a new type of congenital muscular dystrophy.

Congenital muscular dystrophy is a group of muscular dystrophies characterized by muscle weakness, with its onset at or near birth. The cause is genetic mutations in genes responsible for making the proteins necessary to build and maintain muscles, and sometimes to correctly develop the eyes and the brain. However, the *INPP5K* gene is unique in that it has a different function than other genes associated with congenital muscular dystrophy. Most genes involved in congenital muscular dystrophy are responsible for maintaining contacts between muscle fibers, while this gene has a function inside the cell and regulates both signaling in response to factors like insulin, and protein trafficking.

"Now that we've identified the genetic mutation, we want to know why the disruption in the gene causes this disorder," said Manzini. "The unique mechanism of this gene could help us develop therapies we have not thought about before, and may move research in a different direction."

"Mutations in the inositol phosphatase INPP5K cause a congenital muscular dystrophy syndrome overlapping the dystroglycanopathies and Marinesco-Sjögren Syndrome" was published in *The American Journal of Human Genetics*.

Provided by George Washington University