Gene behind rare muscle disease discovered

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Researchers at the Harry Perkins Institute of Medical Research and The University of Western Australia (UWA) have discovered the genetic cause of a rare muscle disease that causes muscle weakness, droopy eyelids and difficulty swallowing.

The disease known as oculopharyngodistal myopathy (OPDM) is an inherited muscle disease. Genes associated with OPDM had only been identified previously in Asian populations.

Perkins researchers in the Rare Disease Genetics and Functional Genomics Group, led by Associate Professor Gina Ravenscroft, and the Preventative Genetics Group, led by Emeritus Professor Nigel Laing AO, published findings from an international study that identified the genetic cause of OPDM in people of European descent in *Nature Communications*.

The researchers discovered that a specific type of mutation, an expansion of a repeat sequence, in the ABCD3 gene triggers a cascade of cellular issues that ultimately leads to muscle degeneration. These repeat expansions have been difficult to pinpoint, but new technologies and computer tools have enabled researchers to more easily find these repeat expansions that cause disease.

"It is so important to study genetic variations across different populations. Discovering that the ABCD3 gene was the cause of OPDM in Europeans adds to the understanding of this disease and opens the door for researchers to explore potential treatments for this and similar muscle diseases," Associate Professor Ravenscroft said.

"Identifying disease-causing genes for families is so rewarding, often families experience these life-changing symptoms and many never get answers about the cause of their disorder. For some families, this has ended a very long diagnostic odyssey, with DNA samples first received almost 30 years ago."

There are more than 10,000 distinct rare diseases, 70% of which start in childhood. Most of these diseases have a genetic origin, and families have to rely on medical researchers to find the disease-gene needle in

their DNA haystack.

"Rare diseases affect around 1 in 10 people and these families can go a lifetime without answers. By finding the genetic cause, we can give families a better understanding of the disease progression, their likelihood of passing it on, and importantly, it offers the possibility of finding new treatments or cures one day," Associate Professor Ravenscroft said.

More information: Andrea Cortese et al, A CCG expansion in ABCD3 causes oculopharyngodistal myopathy in individuals of European ancestry, *Nature Communications* (2024). DOI: 10.1038/s41467-024-49950-2

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