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New gene mutation will help better diagnosis of myopathy

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A new gene mutation which will help doctors give a more accurate diagnosis of a particular type of brain and muscle disease in children has been discovered for the first time by University of Leeds experts.

Mitochondrial myopathy, as it is known, causes muscle weakness, movement problems and learning difficulties and affects more than 70,000 people in the UK.

For the first time, mutations in a particular gene, MICU1, have been linked to myopathy. The discovery gives a better understanding of the genetic causes of the condition.

Working with colleagues from University College London and Great Ormond Street Hospital, as well as colleagues from the Netherlands and Italy, Dr Eamonn Sheridan's team identified two mutations in the gene using a technique called exome sequencing – an alternative to whole genome sequencing.

Mitochondria are the batteries of the body's cells where energy is produced. They are found in large numbers in nerve and muscle cells, which have high energy demands. To function properly, mitochondria need a certain amount of calcium. If calcium levels are either too high or too low, they stop working properly.

MICU1 carries instructions for a protein which is essential for mitochondrial function.

Researchers found that mutations in the MICU1 gene caused less protein to be produced which led to an increase in calcium in the mitochondria. This resulted in damage to the mitochondria and changes in calcium levels in the rest of the cell.

Dr Sheridan, of the Institute of Biomedical and Clinical Sciences at the University of Leeds, said: "This research will enable clinicians to give individuals a more precise diagnosis, and information on how the condition might progress, as well as helping families to make better-informed decisions."

Professor Michael Duchen, of University College London, said: "Mitochondrial calcium signalling has long been thought to be important in regulating cellular energy supply, and defects in these pathways have been thought to be important in many conditions. However, this is the first time that a human condition has been directly linked to a gene defect in this pathway, so this is very exciting for us."

Although it is not known precisely how changes in the cell lead to myopathy, the findings will help provide useful information about the causes of myopathy and how to develop future therapies.

More information: The paper, "Loss-of-function mutations in MICU1 cause a brain and muscle disorder linked to primary alterations in mitochondrial calcium signaling", by Logan et al, is available at dx.doi.org/10.1038/ng.2851

Provided by University of Leeds