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New muscle repair gene discovered

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An international team of researchers from Leeds, London and Berlin has discovered more about the function of muscle stem cells, thanks to next-generation DNA sequencing techniques.

The work, which was co-led from the University of Leeds' School of Medicine and the Charité, Berlin, is published this week in the journal *Nature Genetics*.

The researchers investigated several families whose children suffered from a progressive muscle disease. The children developed severe weakness of the body's muscles and the diaphragm - the main breathing muscle - making them dependent on a wheelchair and continuous mechanical ventilation. The children also had to be tube-fed because the esophagus - a muscular tube that transports food from the mouth down into the stomach - did not work properly.

Using state-of the-art, next generation DNA sequencing technology, the scientists initially found a defect in the MEGF10 gene for a large family living in the UK. Further work found mutations in families with a similar condition from Europe and Asia.

Their work means that accurate genetic testing and diagnosis will now be possible for this devastating condition.

The MEGF10 gene normally plays an important function in muscle stem cells. These are also called 'satellite cells', because they are attached to the outer surface of the muscle fibres, where they normally remain

silent. If a muscle fibre becomes damaged, the satellite cells become active, start to divide and then fuse with the muscle fibre. MEGF10 has an important role in this fusion process because it provides the 'gluey' surface for the attachment of the satellite cell.

Since body muscles make up about 40% of our weight and are the largest organ in the body, the muscles need to be maintained during normal life. MEGF10 also has a role in this regeneration process; failure causes progressive muscle weakness in not only muscles of the body and limbs but also the muscle cells that can be found in the internal organs.

The project's joint directors, Professor Markus Schuelke from the NeuroCure Clinical Research Center and the Department of Neuropediatrics of the Charité, and Professor Colin A. Johnson from the Leeds Institute of Molecular Medicine, University Leeds, emphasized the relevance of the new methods for genomic analysis. They commented: "These methods enable us to sequence hundreds or even thousands of genes at the same time for an affordable price. This enables clinicians and researchers to discover novel genetic defects even in single patients. This is good news for families with unsolved rare genetic disorders. Many affected patients and their parents, who often have a "diagnostic Odyssey" behind them, may now hope that the cause of their disease will be found in the near future."

More information: The paper, Logan et al. Mutations in MEGF10, a regulator of satellite cell myogenesis, cause early onset myopathy, areflexia, respiratory distress and dysphagia (EMARDD) is published in *Nature Genetics* 2011 Nov 20, doi: 10.1038/ng.995

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