New knowledge about serious muscle disease

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About 3,000 people in Denmark suffer from one of the serious muscle-related diseases that come under the heading of muscular dystrophy. Some patients diagnosed with muscular dystrophy die shortly after birth, others become severely retarded and develop eye problems, while certain groups are confined to life in a wheelchair. Common to all muscular dystrophy sufferers is the difficulty of their muscle cells to attach themselves to each other and to the surrounding tissue. However, little is actually known about the root causes of the disease.

New basic research from University of Copenhagen now offers insight into previously unknown facts about muscular dystrophy that may improve future diagnosis and treatment of the disease. The findings have just been published in the scientific journal *PNAS* (*Proceedings of the National Academy of Science*).

"Our new research findings may shed light on some of the cellular processes that take place in connection with, for example, muscular dystrophy. This is important information because it is crucial for us to gain as detailed an understanding as possible about the individual cell components. Although the journey from the current basic research to any potential treatment options or diagnostic tools is a long one, our discoveries give grounds for optimism," says postdoc Malene Bech Vester-Christensen – who carried out the new experiments from her base at the Faculty of Health and Medical Sciences, University of Copenhagen, and has since taken up a research position at Novo Nordisk.

Sugar molecules central to our organism

The new method developed by researchers makes it easier to map the proteins that The protein previously associated with muscular dystrophy is a so-called glycoprotein – a protein with chains of sugar molecules attached. The special kind of sugar attached to these glycoproteins is called mannose. A functional pathway for binding mannose to the proteins is key to the functioning of the human organism, and genetic defects in the process that attaches mannose to the proteins – known as O-mannosylation – can lead to diseases such as muscular dystrophy.

"To date, only one single protein has been identified and characterised where the mannose deficiency on the protein leads to muscular dystrophy, but our method enables us to faster identify many new proteins that have mannose attached and therefore potentially play a key role for the disease," says Adnan Halim, who is associated with the research project and a postdoc with the Danish National Research Foundation, Copenhagen Center for Glycomics.

Facts about muscular dystrophy

Muscular dystrophy is a collective term for a range of neuromuscular disorders. There are roughly 100 different known muscular dystrophy diagnoses, which manifest themselves as various functional impairments/disabilities. The individual diagnoses vary greatly, as does the manner in which they develop. Some people experience only a few symptoms, while others suffer extensive functional impairment. About 3,000 people in Denmark suffer from one of the muscle-related diseases classified as muscular dystrophy. Muscular dystrophy cannot be cured, but much can be done to relieve and treat the consequences of the diseases. Source: The Danish Muscular Dystrophy Foundation.

Facts about the research

The researchers used cells with a functional pathway to attach mannose to proteins, but then simplified the proteins' sugar chains by removing the gene responsible for lengthening the chains and making them more complex. The proteins carrying the 'sugar chain', which now consists solely of mannose, were then isolated, enabling the researchers to determine which proteins carried mannose and where the mannose was situated.

Facts about mannose

For many years researchers believed that O-linked mannose on proteins was found only in yeast, but recent studies have showed that the mannose sugar molecule also binds to some of the proteins in human cells. Mannose plays a key role in the binding of muscle cells in tissue, and the lack of mannose on certain proteins can lead to muscular dystrophy. The variations in the degree of severity of the defects in the process known as O-mannosylation that attaches mannose to proteins – and probably also which proteins carry mannose – are key in determining how the disease manifests itself and its severity.

Provided by University of Copenhagen