New technology offers insight into cholesterol

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New technology offers insight into cholesterol regulation

With new advanced techniques developed by the Copenhagen Center for Glycomics at the University of Copenhagen it is possible to study cells in greater detail than ever before. The findings have just been published in the *Journal of Biological Chemistry* and may, in the long term, improve the treatment of high cholesterol.

Researchers from the Copenhagen Center for Glycomics at the University of Copenhagen have studied an important receptor protein called LDLR using new, groundbreaking techniques. The protein plays an important role in the absorption of the bad cholesterol, LDL.

The findings have just been published in the *Journal of Biological Chemistry*.

The key to major discoveries within the fields of health and diseases is not just hidden in the human DNA code. The proteins encoded by the

genes also play an important role, not least the attached sugar chains which give the proteins an identity and handle important functions in the human organism. Researchers have now studied how LDLR is decorated with sugar molecules, so-called glycosylation modifications.

"We have not previously had a simple method for studying where glycosylation modifications are located on proteins in the body, because the sugars are very complicated and appear in different combinations. By removing the Cosmc protein, which is necessary for extending the sugar modifications, we have created cells with simplified glycosylations, which we call SimpleCells. The technique has enabled us to see 20 times as many sugar modifications on our proteins as were previously known," says PhD Nis Borbye Pedersen, formerly postdoc at the Copenhagen Center for Glycomics, now postdoc at the Department of Biology, University of Copenhagen.

A surprising finding

An interesting finding of the study, characterised as a regular breakthrough by Nis Borbye Pedersen, is the discovery of which of the 20 almost identical enzymes is responsible for the so-called O-glycosylation, where the GalNAc sugar molecule is bound to the amino acids serine and threonine.

"So far, we have not really understood why the body has produced 20 more or less identical enzymes. We have now found out that only one of them seems to be involved in precisely these sugar modifications: GalNAc-T11. So the study provides us with an understanding of which tasks the 20 enzymes perform," he says.

Sugar the key to cholesterol

The researchers from the Copenhagen Center for Glycomics are now conducting new studies which indicate that the presence or not of sugar modifications on the receptor protein LDLR does have a functional impact. The new results may play a role in the future treatment of cholesterol.

"We are currently studying whether glycosylation affects the receptor protein's ability to bind and remove cholesterol from the blood. It has long been known that the receptor protein LDLR plays a key role, at the molecular level, to getting rid of the bad cholesterol and thus improving our health, and so understanding the regulation of this important receptor protein is very valuable. At best, it may improve the strategy for treating high blood cholesterol levels," says Nis Borbye Pedersen.

More information: *Journal of Biological Chemistry*, www.jbc.org/content/289/25/17312.long

Provided by University of Copenhagen