Mutated gene safeguards against heart attacks

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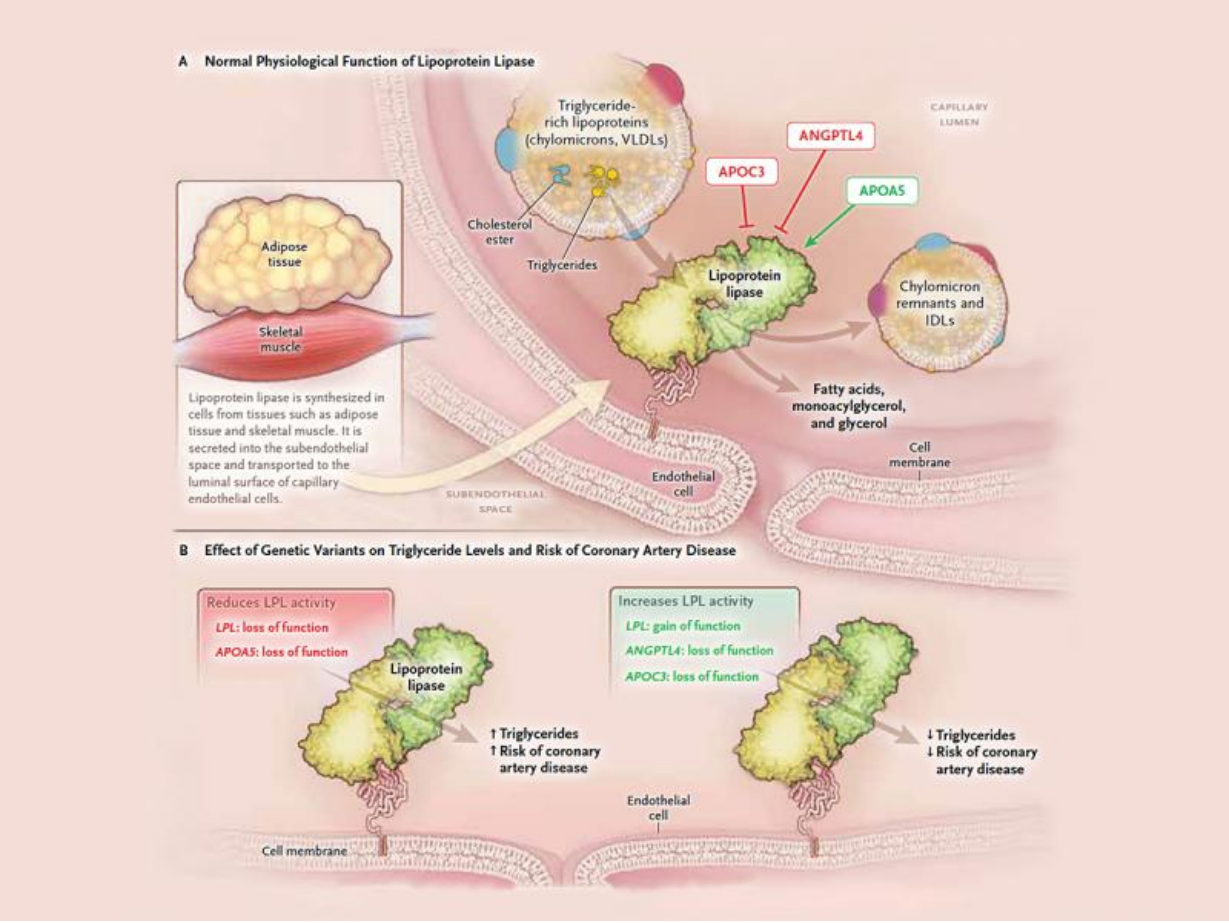

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An international research group headed by the cardiologist Prof. Heribert Schunkert, medical director of the German Heart Center at TU Munich, has discovered a gene mutation that may significantly reduce the probability of suffering a heart attack. "This discovery makes it considerably easier to develop new medications that simulate the effect of this mutation," explains Prof. Schunkert. "This gives follow-on research aiming at reducing heart attacks in the future a concrete goal."

Fighting heart attacks with big data

For the large-scale study at hand, the scientists analyzed 13,000 different genes from a pool of 200,000 participants - both heart attack patients and healthy control persons. They were on the lookout for correlations between gene mutations and coronary artery disease.

For a number of genes, the researchers registered a correlation, including the ANGPTL4 (angiopoietin-like 4) gene. In addition, subjects with the mutated ANGPTL4 gene had significantly lower triglyceride values in their blood.

"The blood fat triglyceride serves as an energy store for the body.

However, as with LDL cholesterol, elevated values lead to an increased risk of cardiovascular disease. Low values, by contrast, lower the risk," explains Prof. Jeanette Erdmann, director of the Institute of Integrative and Experimental Genomics at the University of Lübeck, who also collaborated on the work.

Importance of triglycerides underestimated

According to professor Schunkert the significance of triglycerides for human health hitherto has been underestimated: "For most patients the focus still lies on cholesterol. A differentiation is always made between the healthy HDL and the harmful LDL cholesterol variants. However, in the mean time we know that the HDL values always run inversely proportional to those of the triglycerides and that HDL itself actually tends to behave in a neutral manner."

"The triglycerides, on the other hand, are the second important blood fat, alongside the harmful LDL cholesterol. We published this in the Lancet two years ago," explains Prof. Schunkert. "The only reason HDL blood values are still measured is because, together with HDL and triglyceride values, they can be used to derive the LDL values, which cannot be measured directly."

The current study now shows that the concentration of triglycerides in the blood are influenced not only by nutrition and predisposition, but also by the ANGPTL4 gene. "At the core of our data is the lipoprotein lipase (LPL) enzyme. It causes the decomposition of triglycerides in the blood," explains Prof. Erdmann

Normally, ANGPTL4 hems the LPL enzyme, causing blood fat values to rise. The mutations identified by the researchers disable the function of this gene and thereby ensure that the triglyceride value drops significantly.

New approach to fighting coronary disease

"At the same time," says Jeanette Erdmann, "we discovered that the body does not even need the ANGPTL4 gene and manages wonderfully without it. It seems to be superfluous." Shutting down the gene or inhibiting the LPL enzyme in another manner may ultimately protect against coronary disease.

"Based on our results, medications now need to be developed that neutralize the effect of the ANGPTL4 gene, thereby reducing the risk of a heart attack," says the study leader, Prof. Schuinkert. "Other researchers have already done this successfully in animal tests. They drastically reduced the blood fat levels in monkeys that received a neutralizing antibody against ANGPTL4. This feeds the hope that antibody preparations with a similar effect can soon be used successfully in humans."

More information: N. Stitziel, ..., H. Schunkert; Coding Variation in ANGPTL4, LPL, and SVEP1 and Risk of Coronary Disease; New England Journal of Medicine, March 3, 2016 – DOI: 10.1056/NEJMoa1507652

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