MedicalXpress

Gene variant reduces cholesterol by two mechanisms

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High levels of low-density lipoprotein (LDL) cholesterol increases the risk for coronary heart disease.

A variant in the human gene encoding the protein sortilin is associated with reduced plasma LDL levels and a decreased risk of heart attack.

This variant results in markedly higher sortilin protein expression in liver.

Dr. Daniel Rader and colleagues at the University of Pennsylvania in Philadelphia have uncovered a two-pronged mechanism for the change in LDL observed.

Using a mouse model system, the Rader team found that increased liver sortilin is responsible for reducing secretion of APOB, a protein that transports LDL to tissue, and also triggers LDL breakdown.

Both of these effects were dependent on a cellular process known as lysosomal targeting.

Their data provide functional evidence that genetically-increased hepatic sortilin in humans reduces LDL by increasing LDL degradation, thus removing LDL from circulation, as well as decreasing APOB.

More information: Hepatic sortilin regulates both apolipoprotein B secretion and LDL catabolism, *Journal of Clinical Investigation*.

Provided by Journal of Clinical Investigation