

# Metabolic study in mice could lead to 'good cholesterol' boosters

**Researchers have identified a new player in the control of so-called “good” cholesterol that circulates in the bloodstream and reduces heart attack risk, according to a report in the August issue of *Cell Metabolism*, a publication of Cell Press.**

Should the metabolic pathway uncovered in mice operate similarly in humans, the new discovery could point the way to therapies that protect against heart disease by boosting concentrations of the beneficial high-density lipoprotein cholesterol (HDL-C).

“By and large, the medicines now available lower levels of the ‘bad’ low-density lipoprotein cholesterol [LDL-C],” said Weijun Jin of the University of Pennsylvania School of Medicine. “There is a great need for methods to raise good cholesterol levels. Our findings suggest there may be multiple places to interrupt the metabolism of HDL-C.”

LDL-C can build up in blood vessel walls, increasing the risk of heart disease or stroke. By contrast, HDL-C tends to carry cholesterol away from the arteries to the liver—a process known as reverse cholesterol transport—where it is broken down and then eliminated from the body.

Existing LDL-C-lowering drugs such as statins can reduce the risk of heart attack by 20 to 35 percent, Jin said. However, treatment methods that would simultaneously lower bad cholesterol and increase good cholesterol have the potential to work even better. Indeed, researchers believe that increasing HDL-C while lowering LDL-C might cut heart attack risk by as much as 70 percent, he explained.

In the current study, the researchers found that treatments that partially block the activity of liver enzymes called proprotein convertases decreased plasma HDL-C levels in mice. They showed that the metabolic effect of the proprotein convertases depended on yet another factor, an enzyme called endothelial lipase (EL), which breaks down HDL-C. Proprotein convertases normally reduce EL function, they reported. Thus, the loss of proprotein convertase activity leads to an increase in EL and a decline in HDL-C.

Likewise, they showed that increased activity of proprotein convertases in the liver gives a significant boost to the protective HDL-C.

“Proprotein convertases are an unexpected new player in HDL-C metabolism,” Jin said. “By manipulating levels of the enzyme in both directions, we were able to reduce HDL-C to almost nothing or double it.” That wide range of effects suggests that it may be “theoretically possible to manipulate good cholesterol levels to whatever point you like.”

He emphasized, however, that the new findings represent basic research in animals. Further investigation will examine to what extent the pathway is preserved in humans, Jin said. The authors will also look for chemicals capable of modifying the pathway, which could hold promise as new good-cholesterol-boosting drugs.

Source: Cell Press

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