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Human genetic research uncovers how omega-6 fatty acids lower bad cholesterol

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Supplementing the diet with omega-6 polyunsaturated fatty acids has beneficial effects on heart health by lowering "bad" LDL cholesterol and raising "good" HDL cholesterol, but the underlying mechanisms involved are poorly understood. Now research based on the genetic information from over 100,000 individuals of European ancestry has uncovered a gene that affects blood cholesterol levels through the generation of a compound from omega-6 polyunsaturated fatty acids, called lipoxins. The study, publishing online October 16 in the Cell Press journal *Cell Metabolism*, also provides additional evidence that aspirin assists in preventing heart attacks by promoting lipoxin production. These insights could change the way doctors care for patients at increased risk for heart disease.

"Our findings could help pave the way for novel therapeutic approaches to prevent cardiovascular disease and its associated clinical sequelae, including heart attacks and stroke," says senior author Dr. Ivan Tancevski, of the Innsbruck Medical University, in Austria.

In assessing the genetic information from the study participants of European descent, Dr. Tancevski and his colleagues identified one gene, called Alox5, that codes for an enzyme that generates lipoxins from omega-6 polyunsaturated fatty acids to help the body get rid of bad cholesterol. Lipoxins have anti-inflammatory properties.

The team found that aspirin, which is widely used to prevent heart attacks and stroke, also acts on this pathway. In experiments conducted

in mice, aspirin stimulated production of lipoxins that then promoted the transport of excess cholesterol to the liver, where it is excreted through bile. Treating mice that had atherosclerotic plaques in their blood vessels with aspirin even caused the plaques to regress. "Aspirin is known to prevent cardiovascular disease due to its antithrombotic and anti-inflammatory effects. We now identified a third mechanism by which aspirin may confer protection," says Dr. Tancevski.

The researchers went a step further in generating and testing chemically modified lipoxins mimetics that were even more effective at lowering LDL cholesterol, suggesting that new lipoxin-based specific drugs could provide greater benefits for patients.

More information: *Cell Metabolism* www.cell.com/cell-metabolism/a… 1550-4131(14)00401-X

Provided by Cell Press

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