A novel pathway for prevention of heart attack and stroke

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A recent Finnish study could pave the way for preventing brain and cardiac ischemia induced by atherosclerosis. Finnish researchers have found that the low-expression variant of fatty acid-binding protein 4 (FABP4), which is particularly common among Finns, reduces the risk of heart attack and stroke. The finding revealed a promising new way to customise a potentially preventive drug for atherosclerosis.

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Led by Professor Perttu Lindsberg, the long-term research project of the Department of Neurology at the Hospital District of Helsinki and Uusimaa (HUS) focuses on carotid atherosclerosis. It is a joint effort involving the University of Helsinki, the Helsinki University Central Hospital, the Wihuri Research Institute and the National Institute for Health and Welfare. The findings were published in the highly esteemed scientific journal *Circulation: Cardiovascular Genetics*.

The research indicates that people who have inherited the genetic variant reducing the expression of FABP4 from both parents have eight-fold lower odds for myocardial infarction than the rest of the population.

The researchers also found that patients with carotid stenosis who

carried the protective gene variant suffered from brain ischemia three times less frequently than carotid stenosis patients without the gene variant.

"It could be that reduced cell stress in the stenosis, attenuated inflammation, as well as reduced accumulation of cholesterol and other lipids in the arteries help keep atherosclerosis asymptomatic among the gene carriers," explains Jani Saksi, a researcher in the Molecular Neurology Research Program at the University of Helsinki.

Tests on laboratory animals have previously shown that an orally ingested drug suppressing FABP4 activity effectively slows down the progression of atherosclerosis and even reduces existing stenoses. The phenomenon has not yet been studied in humans.

The Finnish study is the first to detect a link between the FABP4 variant and lower total cholesterol levels in the blood. The decrease in serum total cholesterol levels was the most pronounced in obese subjects who had inherited the gene variant from both parents. In fact, obese carriers of the gene variant show fewer clinical markers of early atherosclerosis and lower levels of stenosis than the rest of the population.

"These findings suggest that FABP4 could be a new potential target for drug development aiming to prevent lethal and disabling myocardial and cerebral infarctions induced by atherosclerosis," says Saksi. "The inhibition of FABP4 activity – especially among obese people in the risk group for atherosclerosis – may prove to be an important method for reducing these individuals' risk for cardiovascular diseases."

More information: Jani Saksi & al. "The Low-Expression Variant of Fatty Acid-Binding Protein 4 Favors Reduced Manifestations of Atherosclerotic Disease and Increased Plaque Stability." *Circulation: Cardiovascular Genetics.* Published online August 13, 2014.

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