Gut bacteria may affect whether a statin drug lowers cholesterol

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Statins can be effective at lowering cholesterol, but they have a perplexing tendency to work for some people and not others. Gut bacteria may be the reason.

A research team led by a Duke University scientist has identified three bile acids produced by gut bacteria that were evident in people who responded well to a common cholesterol-lowering drug called simvastatin. The finding, published Oct. 13, 2011, in PLoS One, demonstrates how gut bacteria can cause inherent differences in the way people digest, metabolize and benefit from substances such as drugs.

The study represents the intersection of two emerging research interests: An analysis of the intestinal microflora, plus the use of a science called metabolomics, which examines the thousands of biochemical components involved in cellular metabolism and how they affect health.

"This is personalized medicine – the effects of drugs and how we respond," said lead author Rima Kaddurah-Daouk, Ph.D., an associate professor in Duke's Department of Psychiatry and leader of the Pharmacometabolomics Network. "We found that the benefit of statins could be partly related to the type of bacteria that lives in our guts. The reason we respond differently is not only our genetic makeup, but also our gut microbiome."

The researchers gathered data from a subset of participants enrolled in a large, national project called the Cholesterol and Pharmacogenetics

(CAP) study, which was led by co-author Ronald M. Krauss, M.D., of Children's Hospital Oakland Research Institute. In the smaller gut bacteria trial, Kaddurah-Daouk, Krauss and colleagues identified 100 people from the CAP study whose LDL cholesterol fell dramatically as a result of taking simvastatin; 24 who had a fairly good response on the drug; and 24 who showed little benefit.

They then analyzed the blood work from the participants before any had taken the drug, searching for known bile acids and fat-like substances called sterols that are involved in the body's break-down and use of cholesterol.

Among the group who had a strong response to the drug, three bile acids appeared to play a role. The bile acids are produced by certain gut bacteria, which are increasingly understood as factories for chemicals that can contribute to a state of health. Among the people who responded poorly to the statin, five different bile acids were commonly evident.

The researchers hypothesize that because bile acids and statins share transporter routes to the liver and intestines – they are basically in competition for a ride -- producing more or less of certain bile acids could improve or diminish the drug's effects.

A blood test that screens for these specific bile acids could provide a way for doctors to determine who would respond to simvastatin and who wouldn't. Additionally, new strategies could be developed to manipulate the gut microbiome using probiotics to spur different gut bacteria, which could then give the drugs a boost.

"We really need to partner with diagnostic and pharmaceutical companies to target drugs for subpopulations," Kaddurah-Daouk said. "It's no doubt that metabolites from bacteria are playing an important role in regulating our systems. We're at a very early stage of understating

this relationship, but eventually we could take a quick chemical assay and get a read on where we are metabolically."

Provided by Duke University Medical Center