MedicalXpress

Gene variant contributes to accumulation of necrotic debris in vessels

February 24 2014, by Tracie White

Think of it like a garbage strike. Due to a genetic defect, the body's ability to dispose of its daily tonnage of dead cells gets damaged, and as a result the body's garbage—in the form of old cells and debris—starts to build up in the walls of its blood vessels.

This is how Nicholas Leeper, MD, assistant professor of vascular surgery and of cardiovascular medicine, describes the findings of a recent study of which he was senior author.

The study was published Feb. 17 in the *Journal of Clinical Investigation*. Yoko Kojima, MD, PhD, senior research associate, was the lead author.

Normally, the body is extremely efficient at taking out the garbage. Two hundred billion cells die every day in our bodies, and most get cleared out within a matter of seconds. But when this process breaks down and garbage, in the form of necrotic cells, starts building up in the walls of blood vessels, it's not a good thing.

Leeper and his colleagues set out to discover why genetic variation at the chromosome 9p21 location has been repeatedly identified as the most important commonly inherited DNA sequence for a wide range of cardiovascular diseases, including stroke, heart attacks and aneurysms.

Conducting studies in mice with atherosclerosis, the researchers showed that loss of a candidate gene at this locus leads to impaired "efferocytosis"—from the Latin for "take to the grave"—the process by

which dead or necrotic cells are removed. Mice with this genetic variation showed an increase in buildup of these dead cells, further advancing their atherosclerosis, as opposed to those that did not have the genetic variation.

In other words, a commonly inherited genetic variant, which is found in 20 percent of the population, contributes to the development of coronary artery disease (also known as coronary atherosclerosis) by stimulating the accumulation of necrotic debris within the evolving plaque.

"If you were born with genetic variation at the 9p21 locus, your risk of heart disease is elevated, though we haven't understood why," Leeper said. "This research gets at that hidden risk. You can be a nonsmoker, be thin, have low blood pressure, and still be at risk for a heart attack if you were born with this variant. This work may help explain that inherited risk factor, and more importantly help develop a new therapy to prevent the heritable component of cardiovascular disease."

Provided by Stanford University Medical Center

Citation: Gene variant contributes to accumulation of necrotic debris in vessels (2014, February 24) retrieved 6 May 2024 from https://medicalxpress.com/news/2014-02-gene-variant-contributes-accumulation-necrotic.html