

## Plaque in arteries may not all be the same

May 14 2019



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A specific type of immune cell is more commonly found in arterial plaque from patients suffering from a recent stroke or mini-stroke, according to preliminary research presented at the American Heart Association's Vascular Discovery Scientific Sessions 2019.



The finding raises the possibility that targeted <u>immune therapy</u> might someday reduce the onset of <u>heart attack</u> and stroke in <u>high-risk patients</u>.

"Despite decades of research, we don't know how to predict and prevent plaque from rupturing in the arteries," said Chiara Giannarelli, M.D., Ph.D., senior author of the study and Assistant Professor in Medicine (Cardiology), and Genetics and Genome Sciences at the Icahn School of Medicine at Mt. Sinai Medical Center in New York. "Most of the research has involved looking at human tissue under the microscope. This has helped us better understand many features of ruptured plaque, but little is known about how and which individual cells types contribute the most to ruptures causing stroke or heart attack."

In two separate groups of patients, the researchers analyzed plaque from a total of 38 patients (average age 72 years, 40% female) who underwent a procedure to remove the plaque that narrows the carotid arteries decreasing blood supply to the brain. Some patients had no symptoms, while others had experienced a stroke or mini-stroke within the previous six months.

The researchers first used a technique called mass-cytometry to find the basic cellular make-up of plaque tissue from 15 patients.

"We found an unexpected dominance of T-cells in this plaque," said Dawn Fernandez, Ph.D., lead author of the study and Postdoctoral Fellow in Cardiology at the Icahn School of Medicine in New York. "These findings in the plaque were different and unrelated to T-cell levels found in the patients' <u>blood samples</u>."

The researchers expanded on these findings in a second mass-cytometry analysis to study the remaining 23 patients. They also used cutting-edge technologies to analyze gene expression in all the individual immune cells in the plaque to study their function.



## They found:

- T-cells dominate advanced plaques; and
- A subtype of T-cells, called CD4-positive effector memory cells, were more common in patients who previously had a stroke or mini-stroke.

"This analysis highlights that there is localized inflammation driven by T-cells in atherosclerotic plaque which is not related to any systemic immune response," said Giannarelli.

She said the findings are particularly intriguing in light of previous heart disease research targeting the immune system. In results that the American Heart Association considered one of the top advances of 2017, the multi-center CANTOS trial found that heart attacks and strokes could be reduced by giving a drug (canakinumab) that decreases inflammation by targeting the immune cell interleukin-1 beta. Interleukin-1 beta is part of the innate immune system which provides the body's first line of defense against bacteria or other foreign substances.

"This milestone study finally proved the inflammatory theory of heart disease," Giannarelli said. "Our study found that plaque from stroke patients is full of T-cells that are part of the adaptive immune system, a specialized second-line of defense in the body. This may help us eventually identify targets for new immune therapies for the late stages of atherosclerosis."

She said the study's small sample size does limit its power to detect additional differences in immune cell types in subsets of <u>patients</u>, such as smokers or those with high blood pressure.



## Provided by American Heart Association

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