

Attacking aortic aneurysms before they grow

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A new study investigates a genetic culprit behind abdominal aortic aneurysm, a serious condition that puts people at risk of their aorta rupturing—a potentially deadly event.

Finding a viable genetic target for AAA could change the game, says senior author Katherine Gallagher, M.D., a <u>vascular surgeon</u> and an associate professor of surgery and microbiology and immunology at Michigan Medicine, the academic medical center of the University of Michigan.

That's because there are no medications to directly treat the condition and prevent an aneurysm from growing. Current options include things like addressing blood pressure to lower the stress on the arteries and veins running through the body, and making lifestyle changes like quitting smoking. Most people monitor their aneurysm to see if it grows enough to eventually require endovascular or open surgical repair.

For this study, a team of Michigan Medicine researchers investigated the role of an epigenetic enzyme called JMJD3 in the development of AAAs.

They found the gene was turned on in both people and mice who had an AAA and that the gene promoted inflammation in monocyte/macrophages. When they blocked the enzyme, it prevented an aneurysm from forming.

"Targeting the JMJD3 pathway in a cell specificmanner offers the opportunity to limit AAA progression and rupture," says lead author Frank Davis, M.D., a vascular surgery resident at the Frankel Cardiovascular Center.

"We are the first to perform an extensive single-cell RNA sequencing and gene expression analysis on human AAAs and non-aneurysmal aortic control samples," Gallagher adds.

More information: Frank M. Davis et al, Inhibition of macrophage histone demethylase JMJD3 protects against abdominal aortic aneurysms, *Journal of Experimental Medicine* (2021). DOI: 10.1084/jem.20201839

Provided by University of Michigan

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