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Study unravels genetics behind debilitating inflammatory disease Takayasu arteritis

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Researchers have uncovered the genetics behind what makes some people susceptible to Takayasu arteritis, a debilitating disease that can lead to poor circulation, easy tiredness in the legs and arms, organ damage and stroke.

A study led by the University of Michigan has identified five genes tied to Takayasu arteritis, an inflammation that damages the aorta and can lead to narrowed arteries, aneurysms, high blood pressure, and heart failure. The findings appear in the August issue of The *American Journal of Human Genetics*.

"Discovering the genetic makeup of Takayasu arteritis is a pivotal step that will lead to fundamental understanding of the disease mechanisms and developing therapies to more effectively treat it," says senior author Amr Sawalha, M.D., associate professor of internal medicine in the division of rheumatology at the U-M Medical School. "This disease can be devastating but is understudied and poorly understood."

Takayasu arteritis mainly causes inflammation in the aorta – the large artery that carries blood from the heart to body– and other major blood vessels. This inflammation can also affect the heart valves, reduce blood flow to the legs and arms, and cause a stroke. Other symptoms include weight loss, fever, night sweats, fatigue and joint and muscle pain.

The disease is most common among women and typically occurs between the ages 20 and 40.

The new findings increase the number of genes linked to susceptibility to the disease to five risk areas both in the HLA (an inherited group of genes known as human leukocyte antigen) and outside the HLA. In addition to the previously established genetic association in HLA-B for Takayasu arteritis, researchers discovered and carefully localized novel genetic risk areas in HLA-DQB1/HLA-DRB1, FCGR2A/FCGR3A, and PSMG1.

"We have established and localized the genetic association with IL12B, which encodes the P40 subunit of the interleukin-12 (IL-12) and IL-23," says Güher Saruhan-Direskeneli, M.D., professor of physiology at Istanbul University and co-author of the study.

"Therapies to inhibit the IL12/IL23 pathway have been successful in other inflammatory diseases, and these recent findings support investigating this pathway closer in Takayasu arteritis as a potential therapeutic target," Sawalha adds.

More information: "Identification of Multiple Genetic Susceptibility Loci in Takayasu Arteritis," *American Journal of Human Genetics*, August, 2013, dx.doi.org/10.1016/j.ajhg.2013.05.026.

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