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Researchers identify 'master coordinator' for aortic rupture

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Every year, more than 16,000 Americans die as a result of what's known as an "aortic dissection"—a catastrophic rupture of the aorta, the body's largest artery. Once thought to be a simple structural failure, aortic dissection is now understood to be caused by an inflammatory process that weakens the artery's walls.

University of Texas Medical Branch at Galveston researchers have been at the forefront of understanding this process. In earlier studies they linked the blood-pressure-regulating molecule, angiotensin II, to the immune signaling protein IL6, which they determined played a major role in producing aortic dissections. Exactly how IL6 generated the inflammation leading to aortic dissection remained unknown, however.

Now the UTMB researchers have found what they believe is the missing piece of the puzzle in a group of cells called Th17 lymphocytes. Part of the body's adaptive immune system, these cells normally serve a protective function; they generate a protein called IL17 to bring other cells to support immune defenses. But in laboratory mouse experiments, the scientists found that locally produced vascular IL6 promotes Th17 formation and accumulation in the vessel wall. There, Th17 lymphocytes instigate a misguided immune attack on the aorta.

"In our study, we compared the effects of angiotensin II on normal mice and mice deficient in Th17 cells, either genetically or by blocking its action," said UTMB professor Allan Brasier, senior author of a paper on the discovery now online in the journal *Arteriosclerosis, Thrombosis, and*

Vascular Biology. "The results showed us that interfering with the Th17 lymphocyte significantly reduces dissections. These data suggest that Th17 lymphocyte is the master coordinator of cellular inflammation in the vessel wall."

To establish the clinical relevance of their findings, the scientists examined tissue samples from patients with a genetic mutation that predisposed them to aortic dissections. The samples, which were derived from a bank maintained by University of Texas Health Science Center at Houston professor and paper author Dianna Milewicz, showed clear signs of Th17 cell accumulation.

"The idea here is that the immune system has evolved to protect us against viruses and bacteria, these sorts of things," Brasier said. "But under certain pathological conditions, the immune system can actually produce disease through chronic inflammation."

Provided by University of Texas Medical Branch at Galveston