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RESEARCH NEWS

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Loss of Arterial Elasticity May Accelerate Heart Disease

A protein that provides elasticity to blood vessels may also play a central role in hardening of the arteries, say HHMI researchers at the University of Utah.

Researchers had thought that atherosclerosis erodes the natural suppleness of the protein elastin, thereby hardening arteries. Now, however, the HHMI research team suspects that the signal that causes cells in the arterial wall to divide and grow thereby narrowing arteries comes from elastin itself.

"We theorize that elastin may be a key to understanding vascular disease," said Hughes investigator Mark Keating of the University of Utah. "In addition to acting like a big rubber band for arteries, elastin also has an important regulatory role in controlling proliferation of smooth muscle cells."

If follow-up studies support that hypothesis, it may be possible to design a drug that prevents destructive cell growth within artery walls. Such a drug could reduce the incidence of both heart attacks and strokes, which kill more than 750,000 Americans each year, Keating says.

Keating's research team, which includes colleagues at the University of Texas Southwestern Medical Center and Washington University School of Medicine, published their findings in the May 21 issue of the journal *Nature.*

In humans, elastin is ubiquitous. Its elasticity provides the lungs and skin with resilience. In the arterial system, where the protein is most abundant, elastin forms an elastic mortar between the arrays of cells that line the arteries. There, the protein provides the stability that allows the vessels to expand and contract continuously as blood pulses along.

Keating, who has long been interested in elastin's role in the vascular system, had previously found that mutations in the elastin gene contribute to supravalvular aortic stenosis, an obstructive disease of the vascular system.

To clarify the protein's role in the vasculature, Keating's team produced mice that have no functional elastin protein. These mice lived for only four days before their arteries turned into tendons, Keating says. "The cells no longer

recognized that they were part of an artery and instead formed a solid cylinder of cells," he said. "The arteries were completely obstructed through a process similar to hardening of the arteries in humans."

Keating says that these results suggest that elastin is essential for normal arterial development. Any disruption of the protein may lead to atherosclerosis by causing growth of smooth muscle cells beneath the arterial wall, Keating notes. Such "disruptions" could be caused by the stress of high blood pressure or the buildup of cholesterol-rich plaques, which cause inflammation within blood vessels. These injuries might damage elastin to the point where it can no longer prevent cell growth.

"Although we have learned a great deal about factors that increase the risk of vascular diseasesuch as hypertension, elevated cholesterol and cigarette smokingwe have not elucidated the pathogenic mechanisms that link these factors to a common pathology," Keating says. "It is possible that the destruction of elastic fibers in the arterial wall is that mechanistic link."