

Loss of gene expression may trigger cardiovascular disease, researchers find

November 30 2012, by Helen Dodson

(Medical Xpress)—A Yale-led team of researchers has uncovered a genetic malfunction that may lead to hardening of the arteries and other forms of cardiovascular disease. The study appears in the journal *Cell Reports*.

Fibroblast growth factors (FGFs), which spur the formation of new tissue and cells, have also recently emerged as key regulators of the vascular system. In studies of mice, the Yale team found that disruption of the FGF signaling process to the endothelium—the innermost lining of the heart and blood vessels—caused a state of FGF resistance and a cascade of other signaling malfunctions. Key among these malfunctions was a transition from endothelial to connective tissue, known as Endo-MT, which drove the formation of scar tissue build-up in the vessels—a condition called neointima.

Neointima formation underlies a number of common diseases, including narrowing of arteries and other valves after angioplasty or stent implantation, hypertension, atherosclerosis, and [transplant rejection](#).

The researchers also found that one cause of the reduction in expression and activation of the FGF signaling cascade was vessel wall inflammation, which leads to [graft rejection](#) in transplantation.

"Our research shows that the loss of FGF signaling, and resulting state of FGF resistance, is clearly associated with inflammation, and is caused by the expression of key [inflammatory mediators](#)," said senior author Dr.

Michael Simons, professor of cell biology at Yale School of Medicine and director of the Yale Cardiovascular Research Center. "This triggers the occurrence of Endo-MT, and buildup of scar tissue in the vessel wall, valves, and other tissues."

"Our results demonstrate that FGF signaling is required to maintain proper vascular homeostasis pathways, and suppression of formation of [scar tissue](#) in vessels and tissue. The loss of FGF signaling input may be the root cause of a number most common [cardiovascular illnesses](#)," explained Simons.

Provided by Yale University

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