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Scientists discover genetic switch that can prevent peripheral vascular disease in mice

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Millions of people in the United States have a circulatory problem of the legs called peripheral vascular disease. It can be painful and may even require surgery in serious cases. This disease can lead to severe skeletal muscle wasting and, in turn, limb amputation.

At The University of Texas Health Science Center at Houston (UTHealth) Medical School, scientists tested a non-surgical preventative treatment in a mouse model of the disease and it was associated with increased blood circulation. Their proof-of-concept study appears in the journal *Cell Reports*.

Unlike previous studies in which other investigators used individual stimulatory factors to grow blood vessels, Vihang Narkar, Ph.D., senior author and assistant professor in the Department of Integrative Biology and Pharmacology at the UTHealth Medical School, identified and turned off a genetic switch that stifles blood vessel development.

"We discovered an inhibitory switch that degrades blood vessels," said Narkar, whose laboratory is in the UTHealth Center for Metabolic and Degenerative Diseases at The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases. "We were able to genetically turn it off to prevent peripheral vascular disease in a preclinical study."

Added Narkar, "Our next step will be to test this targeted treatment in models of other conditions that dramatically decrease circulation like

diabetes and atherosclerosis."

Narkar said using individual growth factors to stimulate blood vessel growth often leads to the formation of leaky and non-functional blood vessels. "By turning off a genetic switch that acts as a roadblock for blood vessel growth, we were able to trigger and accelerate the natural process of blood vessel regeneration that involves a battery of growth factors," he said.

The switch is called peroxisome proliferator-activated receptor gamma co-activator 1 beta (PGC1beta) and could be a key to future treatments for additional conditions like cardiac myopathies, cancer and retinopathy.

Provided by University of Texas Health Science Center at Houston