

# Study explains how exercise helps patients with peripheral artery disease

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Peripheral artery disease (PAD) affects 5 million individuals in the U.S. and is the leading cause of limb amputations. Doctors have long considered exercise to be the single best therapy for PAD, and now a new study helps explain why. Led by researchers at Beth Israel Deaconess Medical Center and published in this week's Online Early Edition of the *Proceedings of the National Academy of Sciences (PNAS)*, the findings demonstrate that a protein called PGC-1alpha plays a key role in the process.

"[Exercise](#) is a staple of healthy living," notes senior author Zoltan Arany, MD, PhD, an investigator in BIDMC's Cardiovascular Institute and Assistant Professor of Medicine at Harvard Medical School. "One of the many benefits of exercise, endurance exercise in particular, is the generation of new blood vessels in leg muscles." Known as angiogenesis, this naturally occurring process comes to the rescue when an injury or artery blockage leaves normal tissue starved for blood.

PAD is a common circulatory problem in which narrowed arteries reduce blood flow to the limbs. The end result is leg pain primarily encountered while walking. More seriously, PAD is also likely to be a sign of widespread accumulation of [fatty deposits](#) in the arteries, which may be reducing blood flow to the heart and brain as well as to the legs.

The PGC-1alpha molecule was first identified more than 10 years ago. Last year, Arany was part of a research team that discovered that when body parts are jeopardized by poor circulation, PCG-1alpha senses

dangerously low levels of oxygen and nutrients and, in response, spurs the growth of new blood vessels. Knowing that muscle adapts to endurance-type exercise by triggering angiogenesis, Arany and his coauthors set out to better understand the mechanisms behind this orchestrated process, and to determine if PGC-1alpha had a hand in the outcome.

The researchers studied mice in cages equipped with electronically monitored running wheels. As predicted, voluntary exercise was found to lead to robust angiogenesis in mouse skeletal muscle. The investigators also found that the mice that were lacking PGC-1alpha failed to grow new blood vessels in response to exercise. Ultimately, their experiments demonstrated that exercise activates beta-adrenergic signaling, which leads to a robust induction of PGC-1alpha.

"Our data strongly suggest a new paradigm for the process of angiogenesis in response to exercise, demonstrating that upstream beta-adrenergic signaling, likely stemming from increased nerve activity, triggers angiogenesis," the authors write. (Interestingly, they add, this suggests that the use of beta blockers in patients with PAD might block some of the benefits of exercise. These medications are widely used to treat patients with coronary artery disease, and patients with PAD often have concurrent CAD.)

"With this study, we have found that the protein PGC-1 alpha can single-handedly transform muscle to be capable of greater endurance and increase the blood content of that muscle. Being able to increase [blood vessel density](#) could help wound healing and even prevent amputations in millions of patients with diabetes and vascular disease of the limbs," notes Arany. "Exercise remains one of the most effective interventions for a number of chronic diseases, including obesity, diabetes, atherosclerosis and neurodegenerative diseases. PAD is a leading cause of morbidity and the most common cause of limb amputation in the U.S.

and yet even the best medical therapy available is less effective than simply walking daily."

Source: Beth Israel Deaconess Medical Center

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