

## Researchers use ASC secreted factors to create therapeutic factor concentrate for critical limb ischemia

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"Critical limb ischemia" (CLI) describes an advanced stage of peripheral artery disease characterized by obstruction of the arteries and a markedly reduced blood flow to the extremities. CLI identifies patients at high-risk for major amputation. The estimated annual incidence of CLI ranges between 500 and 1000 new cases out of one million people per year, with the highest rates among the elderly, smokers, and those with diabetes. CLI is considered to be a critical public health issue. Attempts at revascularization are often unsuccessful.

In an effort to develop an effective treatment for CLI, a team of researchers in the Czech Republic, Poland and the U.S. developed a potential therapy using adipose-derived stem cells (ASCs), taking advantage of ASC secreted factors to create a therapeutic factor concentrate (TFC) for promoting blood vessel growth (angiogenesis) and revascularization. The researchers created the TFC using beneficial growth factors secreted from adipose-derived stem cells and cytokines (a broad category of small proteins with signaling capabilities), all of which were filtered, concentrated and frozen.

"Recognition that the functional component of adult stem cells can be attributed to secreted factors led us to explore the therapeutic benefit of delivering these factors," said study co-author Dr. Vaclav Prochazak of the University Hospital Ostrava. "The purpose of our study was to test the efficacy of a single intramuscular administration of human TFC using laboratory animals modeled with subacute CLI."

Twenty-seven adult rabbits were surgically modeled with CLI and five additional used as controls. The CLI rabbits received either placebo, low dose TFC, or high dose TFC by injection into their left hind legs. One week after surgery, limb perfusion was tested using a Doppler probe and blood samples were analyzed for growth factors and cytokines.

A tissue assessment of the CLI-modeled animals after 35 days revealed that the tissue reperfusion in the high dose group was double that of the placebo group.

"Our results demonstrate that TFC represents a potent therapeutic combination for patients with CLI, many of whom are at-risk for amputation of their affected limb," wrote the authors. "We envision having an off-the-shelf product that would be immediately available for administration with little preparation and that would improve quality of life and reduce morbidity, such as amputation, for a significant patient population."

Their study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line as an unedited early e-pub at: [http://ingentaconnect.com/content/cog/ct/pre-prints/content-CT-1472\\_Prochazka\\_et\\_al](http://ingentaconnect.com/content/cog/ct/pre-prints/content-CT-1472_Prochazka_et_al)

The researchers are currently planning a clinical trial with patients who are not candidates for conventional revascularization.

"The therapeutic effects of stem cells may be due to secretion of several factors, including a phenomena called 'paracrine effects,' rather than stem cells directly replacing damaged or dead cells," said Dr. Amit Patel, director of Cardiovascular Regenerative Medicine, associate professor of surgery in the Division of Cardiothoracic Surgery of the University of Utah and section editor for *Cell Transplantation*. "The results of this study indicate that it may be highly beneficial to directly inject these factors because it cuts down on the processing time associated with stem cell preparation and also avoids the problem of stem cells becoming trapped in organs and tissues other than the target site. It will be very exciting to see the outcome of the clinical trial that is currently being planned, as this method may be beneficial for people with CLI as well as other conditions."

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