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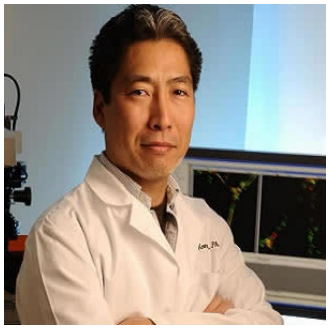
# Scientists find key to regenerating blood vessels



Researchers at Sanford Burnham Prebys Medical Discovery Institute (SBP) have identified a signalling pathway that is essential for angiogenesis, or the growth of new blood vessels from pre-existing vessels. The discovery may lead to improvement in current strategies to increase blood flow in ischaemic tissue, according to a study published in Nature Communications.

Previous efforts to treat ischemia by creating new blood vessels have focused on delivering angiogenic growth factors like vascular endothelial growth factor (VEGF) to ischaemic sites. But all of these studies, including more than 25 phase II and III clinical trials, have failed to offer significant benefit to patients.

In the new study, researchers used a combination of 3D cell culture and living tissue to show that VEGF promotes vascularisation, but the vessel structures formed are chaotic, unstable and non-functional. "Functional vessels need to have a lumen, a pipe-like opening that allows oxygenated blood and nutrients to travel through the body," explains Masanobu Komatsu, PhD, associate professor at SBP's Lake Nona campus.

As the study findings show, the formation of fully functional blood vessels requires activation of protein kinase Akt by a protein called R-Ras, and this mechanism is necessary for the formation of the lumen.

"Generating new blood vessels is similar to the way trees grow; sprouts develop from existing vessels and then branch out further and further to restore vascularity, says Fangfei Li, PhD, postdoctoral associate in Komatsu's lab and lead author of the paper. "This study shows that there are distinct steps and signals that control the process.

"First, VEGF activates Akt to induce endothelial cells to sprout. Then, R-Ras activates Akt to induce lumen formation," explains Li. "The second step involving Akt activation by R-Ras stabilises the microtubule cytoskeleton in endothelial cells, creating a steady architecture that promotes lumen formation," says Li.

The next step for the research team is to work toward promoting the combined signalling of Akt in clinical studies, i.e., prompting R-Ras activation through either gene therapy or pharmacologically in parallel with VEGF therapy, according to Komatsu.

Source: Sanford-Burnham Prebys Medical Discovery Institute
Image Credit: SBP

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