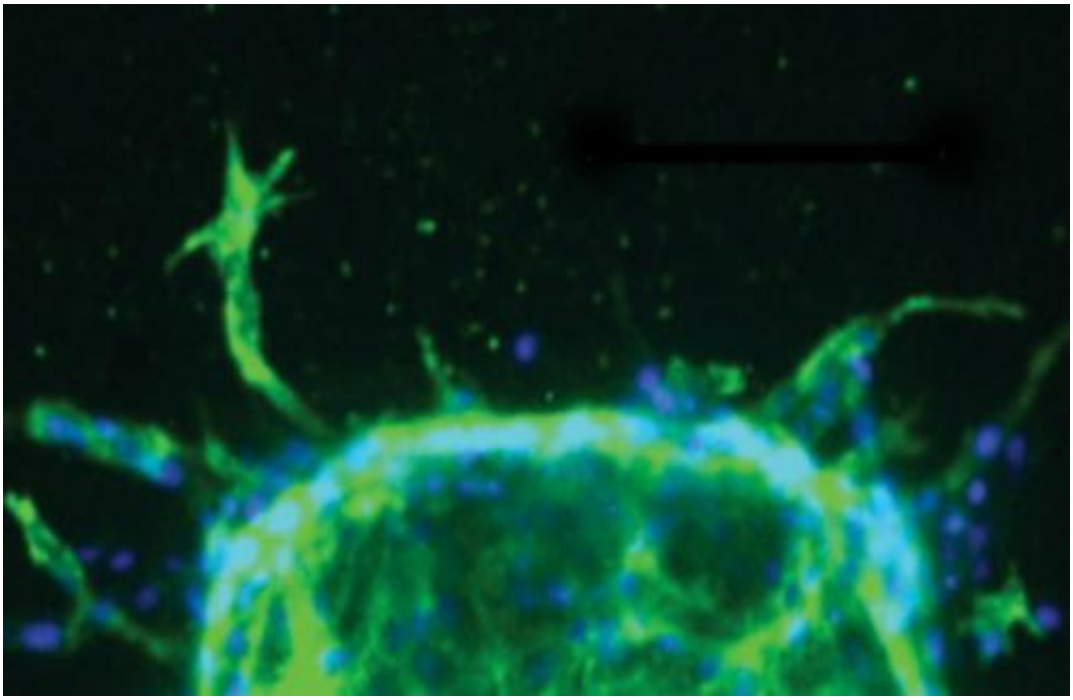
MedicalXpress

# Research lends new insights on conditions for new blood vessel formation

July 3 2014



With lifesaving applications possible in both inhibiting and accelerating the creation of new blood vessels, a more fundamental understanding of what regulates angiogenesis is needed. Now, researchers at the University of Pennsylvania, Boston University and Harvard University have uncovered the existence of a threshold above which fluid flowing through blood vessel walls causes new capillaries to sprout. Credit: Boston University

Angiogenesis, the sprouting of new blood vessels from pre-existing ones, is essential to the body's development. As organs grow, vascular

networks must grow with them to feed new cells and remove their waste. The same process, however, also plays a critical role in the onset and progression of many cancers, as it allows the rapid growth of tumors.

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This discovery could help pave the way for cancer-fighting drugs, treatments for the hardened blood vessels found in the cardiovascular disease arthrosclerosis or even growing synthetic organs in the lab.

The research was led by postdoctoral fellow Peter Galie of the Department of Bioengineering in Penn's School of Engineering and Applied Science and Christopher Chen, then a professor of bioengineering at Penn who is now at Boston University and an associate faculty member of the Wyss Institute for Biologically Inspired Engineering at Harvard University. They collaborated with Duc-Huy Nguyen, Colin Choi and Daniel Cohen, all members of Chen's lab, and professor Paul Janmey, also of the Department of Bioengineering, as well as the Department of Physiology in Penn's Perelman School of Medicine.

Their study was published in the *Proceedings of the National Academy of Sciences*.

The team's experiments incorporated "blood-vessel-on-a-chip" devices, which use microfluidic technology to simulate processes that normally occur deep within tissues. They found that cells lining each artificial vessel sprouted to form new vessels once the force exerted by fluid flow

through the vessel exceeded a certain threshold.

"These findings suggest that our blood vessels can sense when blood flow exceeds their carrying capacity and respond by producing additional vessels on demand," Chen explained. "Perhaps we could one day take advantage of this response to enhance vessel regrowth where the need is critical, such as after a heart attack."

During their experiments, the researchers controlled the fluid flow within the artificial vessel, and ultimately where new vessels would sprout, by changing the shape and orientation of thin needles deployed within a collagen gel containing each vessel. Using a mathematical model, they predicted the exact spots along the vessel where force exceeded the sprouting threshold, thereby pinpointing the location where new vessels would form.

Now the researchers aim to advance new experiments designed to figure out how cells sense this mechanical threshold.

"The logical next step is to determine the molecular mechanism behind this phenomenon," said Galie, "what proteins are involved and how might they be targeted in new drug therapies."

Provided by University of Pennsylvania