New drug targets vascular inflammation, drastically improving the long-term effectiveness of vascular procedures

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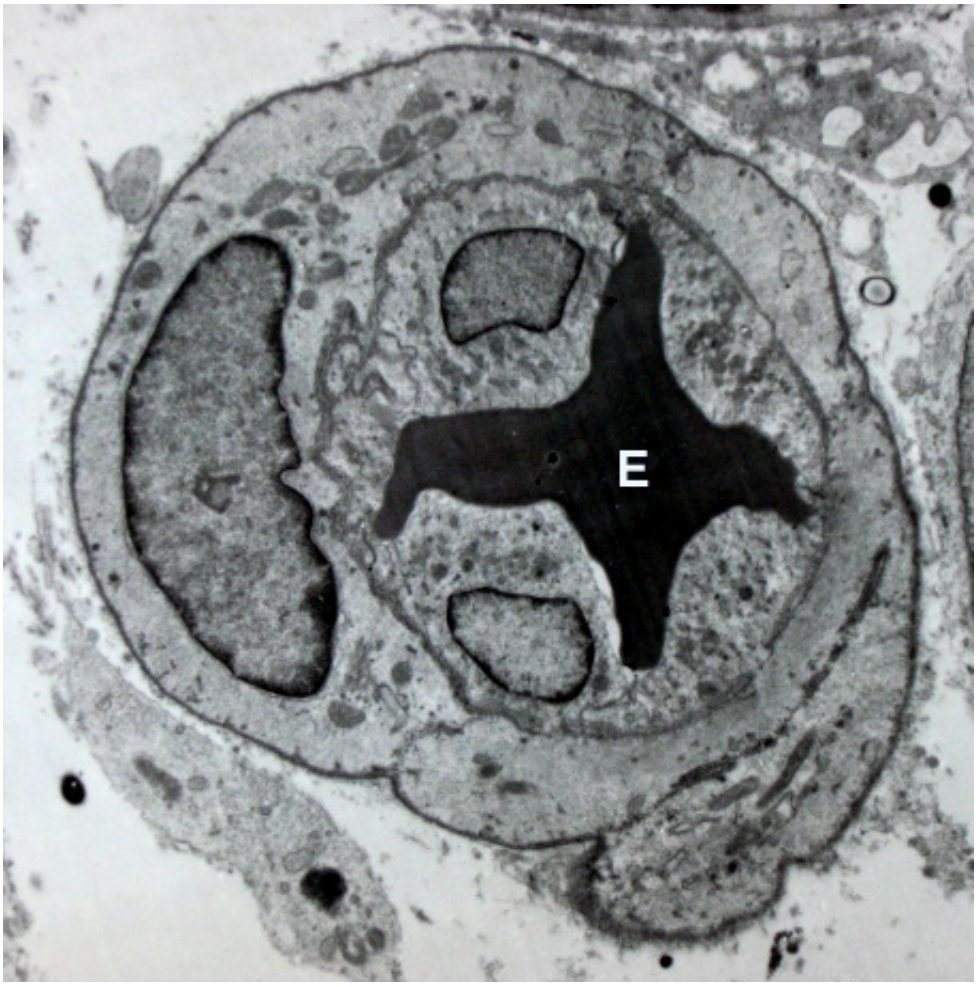

Blood vessel with an erythrocyte (red blood cell, E) within its lumen, endothelial cells forming its tunica intima (inner layer), and pericytes forming its tunica adventitia (outer layer) Credit: Robert M. Hunt/Wikipedia/CC BY 3.0

Cardiovascular procedures like bypass grafting and vessel stenting are some of the most common surgeries performed in the United States, but about half of them will require additional corrective measures, according to Craig Duvall, Cornelius Vanderbilt Chair and undergraduate director of biomedical engineering. The need for follow-up procedures is often due to intimal hyperplasia, a condition where blood vessels become re-blocked by abnormal growth or migration of smooth muscle cells in the wall of the blood vessel. A team of researchers led by Duvall has developed a nanomedicine to combat this condition.

A primary cause of IH is the response to injury by the vascular smooth muscle cells that reside in the wall of the surgically manipulated blood vessel. The physical manipulation of the vascular tissue by surgeons during lifesaving procedures injures the smooth muscle cells and causes them to undergo abnormally high rates of cell division. Duvall and his colleagues in bioengineering, molecular and cellular biology and the School of Medicine found that MK2i-NP, a long-lasting inhibitor of smooth muscle cell stress response, is an effective therapeutic for IH.

MK2i-NP is the first therapeutic of its kind because it focuses on the switch of cells from healthy behavior to the abnormal cell behavior that causes IH, instead of simply blocking cell division. "This phenotype switch is a superior target for IH therapeutics compared to targeting cell proliferation alone, which has proven to not be effective," Duvall said.

Why it matters

"MK2i-NP is a promising therapeutic because it blocks IH at the source," Duvall said. Other therapies for IH exist, but in addition to being ineffective, they can cause side effects such as blood clotting that threaten the function of the blood vessel.

The results of this study suggest that MK2i-NP is a compelling

alternative to available treatments because it can reduce vascular IH and improve the long-term performance of cardiovascular procedures. "MK2i-NP could significantly reduce the need for re-intervention after vascular procedures, reducing health care costs for additional procedures," Duvall said.

What's next

Collaboration with Colleen Brophy, vascular surgeon at Vanderbilt University Medical Center, and her lab members enabled Duvall's team to test MK2i-NP on human blood vessels, which supports the potential of this drug for clinical translation.

"Our longer-term goals are to take this MK2i-NP therapeutic and use it for in vivo delivery applications to extend beyond our recent work focused on delivery to explanted tissue during vascular transplant surgeries," Duvall said. In the short term, they plan on continuing to test the drug to prove its efficacy before moving on to patient trials.

More information: J. William Tierney et al, Therapeutic MK2 inhibition blocks pathological vascular smooth muscle cell phenotype switch, *JCI Insight* (2021). DOI: 10.1172/jci.insight.142339

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