New device reduces scarring in damaged blood vessels

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When blood vessels are damaged through surgery, it can trigger an endless cycle of scarring and repair.

"Scar tissue will always form inside the blood vessel and, in many cases, eventually block blood flow," said Guillermo Ameer, professor of biomedical engineering at Northwestern University's McCormick School of Engineering. "Then surgeons have to go back in, eliminate the obstruction, or put in a new graft or stent to restore blood flow. In the case of a prosthetic vascular graft used for bypass surgery, it will scar again and ultimately fail."

Ameer, who is also professor of surgery at the Feinberg School of Medicine, has developed a new material that, when applied to damaged blood vessels, can prevent scarring and stop the cycle before it begins.

The soft, porous, and thin elastic material contains an acid form of vitamin A, called a retinoid, which is produced by the body to help cells develop and stay healthy. Synthetic retinoids have been formulated and traditionally used to treat acne and some types of cancer. Unfortunately, the oral dose needed to positively affect vessel healing and prevent scarring could never be administered to humans as it is toxic in very high doses.

"We solved this problem by using engineering and biomaterial science concepts," Ameer said. "We incorporated the retinoid into a biodegradable membrane that can be handled and implanted by a surgeon. That way, we can target the blood vessel and safely get the effect we want."

The research is described in the paper "Periadventitial atRA citrate-based polyester membranes reduce neointimal hyperplasia and restenosis after carotid injury in rats," which was published in the September 19 issue of the *American Journal of Physiology: Heart and Circulatory Physiology*. Elaine Gregory, research associate in surgery, and Antonio Webb, a former postdoctoral researcher in Ameer's lab and current professor at the University of Florida, were the paper's first authors.

Ameer started with an inherently antioxidant, citrate-based polymer previously developed in his laboratory. Then he added the all-trans retinoic acid (atRA), a vitamin A derivative. Ameer's longtime collaborator and co-senior author of the paper, Melina Kibbe, the Edward G. Elcock Professor of Surgical Research at Feinberg, evaluated the membrane in an animal model. When wrapped around the outside of a damaged blood vessel, it created a favorable environment for the healing process. Ameer and Kibbe noted a 50-60 percent reduction of scar formation compared to vessels without the membrane.

"We're putting something on the outside of the vessel that affects what happens inside the vessel," Ameer said. "It seems counterintuitive, but scarring also involves cells that are normally present on the outside layer of the blood vessel."

Damaged cells typically produce aggressive signals that cause their neighboring cells to become inflamed. Ameer said the material "keeps the cells quiet," so dangerous messages do not spread to the rest of the vessel. The membrane achieves local exposure to atRA, protecting the blood vessel and regulating how it responds to injury.

"Whether or not you employ a stent or attach a prosthetic graft to a blood vessel, you injure it," Ameer said. "The vessel's response to the injury can get out of control. With this fairly simple method, we are trying to control the inflammatory response and maintain adequate blood flow through the vessel."

Provided by Northwestern University

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