This Injectable Biomaterial Heals Tissues From the Inside Out

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Anew biomaterial that can be injected intravenously, reduces inflammation in tissue and promotes cell and tissue repair. The biomaterial was tested and proven effective in treating tissue damage caused by heart attacks in both rodent and large animal models. Researchers also provided proof of concept in a rodent model that the biomaterial could be beneficial to patients with traumatic brain injury and pulmonary arterial hypertension.

“This biomaterial allows for treating damaged tissue from the inside out,” said Karen Christman, a professor of bioengineering at the University of California San Diego, and the lead researcher on the team that developed the material. “It’s a new approach to regenerative engineering.”

A study on the safety and efficacy of the biomaterial in human subjects could start within one to two years, Christman added. The team, which brings together bioengineers and physicians, presented their findings in the Dec. 29 issue of Nature Biomedical Engineering.

There are an estimated 785,000 new heart attack cases in the United States each year, and there is no established treatment for repairing the resulting damage to cardiac tissue. After a heart attack, scar tissue develops, which diminishes muscle function and can lead to congestive heart failure.

“Coronary artery disease, acute myocardial infarction, and congestive heart failure continue to be the most burdensome public health problems affecting our society today,” said Dr. Ryan R. Reeves, a physician in theDivision of Cardiovascular Medicine at UC San Diego Health. “As an interventional cardiologist, who treats patients with coronary artery disease and congestive heart failure on a daily basis, I would love to have another therapy to improve patient outcomes and reduce debilitating symptoms.”

In previous studies, the team led by Christman developed a hydrogel made from the natural scaffolding of cardiac muscle tissue, also known as the extracellular matrix (ECM), that can be injected into damaged heart muscle tissue via a catheter. The gel forms a scaffold in damaged areas of the heart, encouraging new cell growth and repair. Results from a successful phase 1 human clinical trial were reported in fall 2019. But because it needs to be injected directly into heart muscle, it can only be used a week or more after a heart attack — sooner would risk causing damage because of the needle-based injection procedure.

The team wanted to develop a treatment that could be administered immediately after a heart attack. This meant developing a biomaterial that could be infused into a blood vessel in the heart at the same time as other treatments such as angioplasty or a stent, or injected intravenously.

“We sought to design a biomaterial therapy that could be delivered to difficult-to-access organs and tissues, and we came up with the method to take advantage of the bloodstream - the vessels that already supply blood to these organs and tissues,” said Martin Spang, the paper’s first author, who earned his Ph.D. in Christman’s group in the Shu Chien-Gene Lay Department of Bioengineering at the UC San Diego Jacobs School of Engineering.

One advantage of the new biomaterial is that it gets evenly distributed throughout damaged tissue, because it’s infused or injected intravenously. By contrast, hydrogel injected via a catheter remains in specific locations and doesn’t spread out.

How the biomaterial is made

Researchers in Christman’s lab started with the hydrogel they developed, which was proven to be compatible with blood injections as part of safety trials. But the particle size in the hydrogel was too big to target leaky blood vessels. Spang, then a Ph.D. student in Christman’s lab, solved this issue by putting the liquid precursor of the hydrogel through a centrifuge, which allowed for sifting out bigger particles and keeping only nano-sized particles. The resulting material was put through dialysis and sterile filtering before being freeze dried. Adding sterile water to the final powder results in a biomaterial that can be

injected intravenously or infused into a coronary artery in the heart.

How it works

Researchers then tested the biomaterial on a rodent model of heart attacks. They expected the material to pass through the blood vessels and into the tissue because gaps develop between endothelial cells in blood vessels after a heart attack.

But something else happened. The biomaterial bound to those cells, closing the gaps and accelerating healing of the blood vessels, reducing inflammation as a result. Researchers tested the biomaterial in a porcine model of heart attack as well, with similar results.

The team also successfully tested the hypothesis that the same biomaterial could help target other types of inflammation in rat models of traumatic brain injury and pulmonary arterial hypertension. Christman's lab will undertake several preclinical studies for these conditions.

Next steps

"While the majority of work in this study involved the heart, the possibilities of treating other difficult-to-access organs and tissues can open up the field of biomaterials/tissue engineering into treating new diseases," Spang said.

Meanwhile, Christman along with Ventrix Bio, Inc., a startup she cofounded, are planning to ask for authorization from the FDA to conduct a study in humans of the new biomaterial's applications for heart conditions. This means that human clinical trials begin in be one or two years.

The biomaterial is based on a hydrogel that Christman's lab developed.

“One major reason we treat severe coronary artery disease and myocardial infarction is to prevent left ventricular dysfunction and progression to congestive heart failure,” said Dr. Reeves. “This easy-to-administer therapy has the potential to play a significant role in our treatment approach.”

Read the original article on University of California San Diego.