Medical Xpress

# Building heart tissue that beats

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When a heart gets damaged, such as during a major heart attack, there's no easy fix. But scientists working on a way to repair the vital organ have now engineered tissue that closely mimics natural heart muscle that beats, not only in a lab dish but also when implanted into animals. They presented their latest results at the 247th National Meeting & Exposition of the American Chemical Society (ACS).

"Repairing damaged hearts could help millions of people around the world live longer, healthier lives," said Nasim Annabi, Ph.D. Right now, the best treatment option for patients with major heart damage—which can be caused by severe heart failure, for example—is an organ transplant. But there are far more patients on waitlists for a transplant than there are donated hearts. Even if a patient receives a new heart, complications can arise.

The ideal solution would be to somehow repair the tissue, which can get damaged over time when arteries are clogged and starve a part of the heart of oxygen. Scientists have been searching for years for the best fix. The quest has been confounded by a number of factors that come into play when designing a complex organ or tissue.

Simple applications, such as engineered skin, are already in use or in clinical trials. But building tissue for an organ as complicated as the heart requires a lot more research. To address this challenge and engineer complex 3-D tissues, researchers at the Brigham and Women's Hospital and Harvard Medical School in Boston and the University of Sydney in Australia were able to combine a novel elastic hydrogel with microscale technologies to create an artificial cardiac tissue that mimics the mechanical and biological properties of the native heart.

"Our hearts are more than just a pile of cells," said Ali Khademhosseini, Ph.D., who is at Harvard Medical School. "They're very organized in their architecture."

To tackle the challenge of engineering heart muscle, Khademhosseini and Annabi have been working with natural proteins that form gelatin-like materials called hydrogels.

"The reason we like these materials is because in many ways they mimic aspects of our own body's matrix," Khademhosseini said. They're soft and contain a lot of water, like many human tissues.

His group has found that they can tune these hydrogels to have the chemical, biological, mechanical and electrical properties they want for the regeneration of various tissues in the body. But there was one way in which the materials didn't resemble human tissue. Like gelatin, early versions of the hydrogels would fall apart, whereas human hearts are elastic. The elasticity of the heart tissue plays a key role for the proper function of heart muscles such as contractile activity during beating. So, the researchers developed a new family of gels using a stretchy human protein aptly called tropoelastin. That did the trick, giving the materials much needed resilience and strength.

But building tissue is not just about developing the right materials. Making the right hydrogels is only the first step. They serve as the tissue scaffold. On it, the researchers grow actual heart cells. To make sure the cells form the right structure, Khademhosseini's lab uses 3-D printing and microengineering techniques to create patterns in the gels. These patterns coax the cells to grow the way the researchers want them to. The result: small patches of heart muscle cells neatly lined up that beat in synchrony within the grooves formed on these elastic substrates. These micropatterned elastic hydrogels can one day be used as cardiac patches. Khademhosseini's group is now moving into tests with large animals. They are also using these elastic natural hydrogels for the regeneration of other tissues such as blood vessels, skeletal muscle, heart valves and vascularized skin.

**More information:** Talk: Microengineered hydrogels for stem cell bioengineering and tissue regeneration:

**Abstract**
Micro- and nanoscale technologies are emerging as powerful tools for controlling the interaction between cells and their surroundings for biological studies, tissue engineering, and cell-based screening. In addition, hydrogel biomaterials have been increasingly used in various tissue engineering applications since they provide cells with a hydrated 3D microenvironment that mimics the native extracellular matrix. In our lab we have developed various approaches to merge microscale techniques with hydrogel biomaterials for directing stem cell differentiation and generating complex 3D tissues. In this talk, I will outline our work in controlling the cell-microenvironment interactions by using patterned hydrogels to direct the differentiation of stem cells. In addition, I will describe the fabrication and the use of microscale hydrogels for tissue engineering by using a 'bottom-up' and a 'top-down' approach. Top-down approaches for fabricating complex engineered tissues involve the use of miniaturization techniques to control cell-cell interactions or to recreate biomimetic microvascular networks. Our group has also pioneered bottom-up approaches to generate tissues by the assembly of shape-controlled cell-laden microgels (i.e. tissue building blocks), that resemble functional tissue units. In this approach, microgels were fabricated and induced to self assemble to generate 3D tissue structures with controlled microarchitecture and cell-cell interactions.