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Scientists build a living patch for damaged hearts

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Duke University biomedical engineers have grown three-dimensional human heart muscle that acts just like natural tissue. This advancement could be important in treating heart attack patients or in serving as a platform for testing new heart disease medicines.

The "heart patch" grown in the laboratory from human cells overcomes two major obstacles facing cell-based therapies – the patch conducts electricity at about the same speed as natural heart cells and it "squeezes" appropriately. Earlier attempts to create functional heart patches have largely been unable to overcome those obstacles.

The source cells used by the Duke researchers were human embryonic stem cells. These cells are pluripotent, which means that when given the right chemical and physical signals, they can be coaxed by scientists to become any kind of cell – in this case heart muscle cells, known as cardiomyocytes.

"The structural and functional properties of these 3-D tissue patches surpass all previous reports for engineered human heart muscle," said Nenad Bursac, associate professor of biomedical engineering at Duke's Pratt School of Engineering. "This is the closest man-made approximation of native human heart tissue to date."

The results of Bursac's research, which is supported by the National Heart Lung and Blood Institute, were published on-line in the journal *Biomaterials*.

Bursac said this approach does not involve genetic manipulation of cells.

"In past studies, human stem cell-derived cardiomyocytes were not able to both rapidly conduct electrical activity and strongly contract as well as normal cardiomyocytes," Bursac said. "Through optimization of a three-dimensional environment for cell growth, we were able to 'push' cardiomyocytes to reach unprecedented levels of electrical and mechanical maturation."

The rate of functional maturation is an important element for the patch to become practical. In a developing human embryo, it takes about nine months for a neonatal functioning heart to develop and an additional few years to reach adult levels of function; however, advancing the functional properties of these bioengineered patches took a little more than a month, Bursac said. As technology advances, he said, the time should shorten.

"Currently, it would take us about five to six weeks starting from pluripotent stem cells to grow a highly functional heart patch," Bursac said.

"When someone has a heart attack, a portion of the heart muscle dies," Bursac said. "Our goal would be to implant a patch of new and functional heart tissue at the site of the injury as rapidly after heart attack as possible. Using a patient's own cells to generate pluripotent stem cells would add further advantage in that there would likely be no immune system reaction, since the cells in the patch would be recognized by the body as self."

In addition to a possible therapy for patients with heart disease, Bursac said that engineered heart tissues could also be used to effectively screen new drugs or therapies.

"Tests or trials of new drugs can be expensive and time-consuming," Bursac said. "Instead of, or along with testing drugs on animals, the ability to test on actual, functioning human tissue may be more predictive of the drugs' effects and help determine which drugs should go on to further studies."

Some drug tests are conducted on two-dimensional sheets of heart cells, but according to Bursac, the 3-D culture model provides a superior environment for functional maturation of cells. This is expected to better mimic real-world heart muscle responses to different drugs or toxins. Engineered heart tissues made with cells from patients with a cardiac genetic disease could be used as the model to study that disease and explore potential therapies.

The current experiments were conducted on one human pluripotent stem cell line. Bursac and his colleagues have reproduced their findings on two other cell lines and are testing additional lines. They are also planning to move to larger animal models to learn how the patch would become functionally integrated with its host and how the patch establishes connections with the circulatory system.

Provided by Duke University