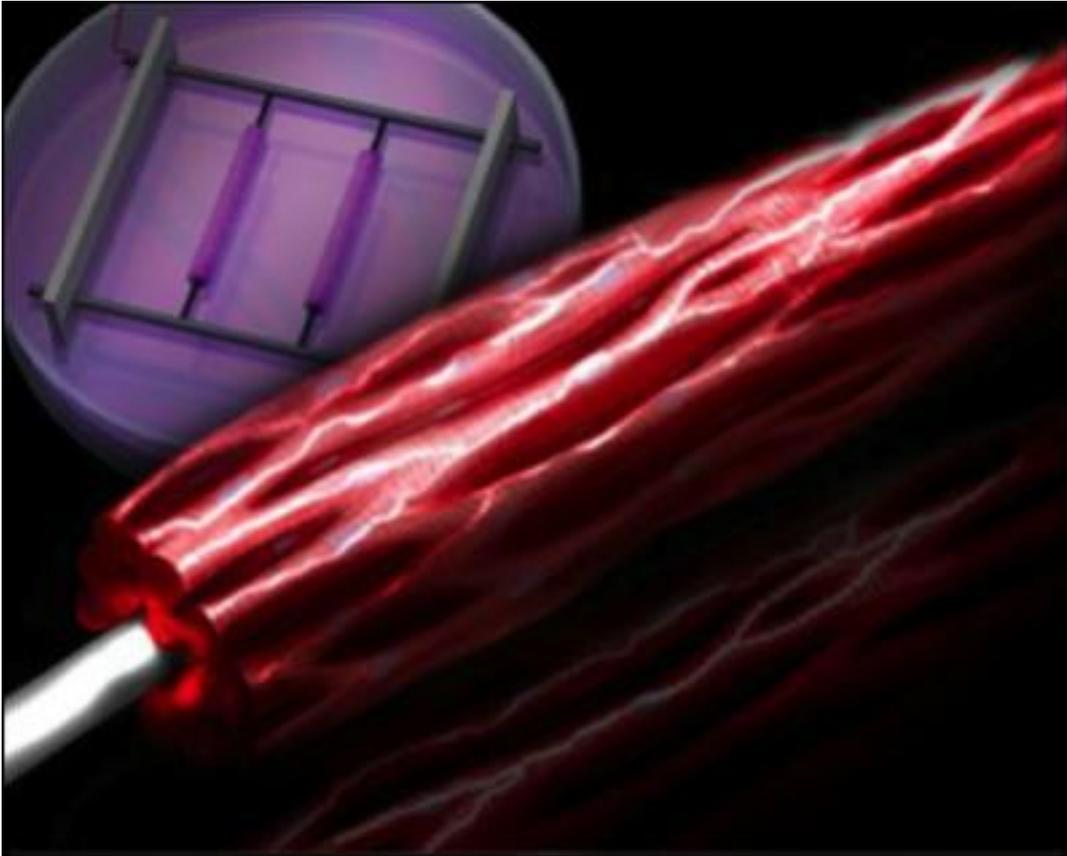


## **New 'Biowire' Technology Matures Human Heart by Mimicking Fetal Heart Rate**

University of Toronto Faculty of Applied Science & Engineering



A new method of maturing human heart cells that simulates the natural growth environment of heart cells while applying electrical pulses to mimic the heart rate of fetal humans has led researchers at the University of Toronto to an electrifying step forward for cardiac research.

The discovery, announced this week in the scientific journal *Nature Methods*, offers cardiac researchers a fast and reliable method of creating mature human cardiac patches in a range of sizes.

"You cannot obtain human cardiomyocytes (heart cells) from human patients," explains Milica Radisic, Canada Research Chair in Functional Cardiovascular Tissue Engineering and Associate Professor at the Institute of Biomaterials & Biomedical Engineering (IBBME) and the Department of Chemical Engineering. Because human heart cells - integral for studying the efficacy of cardiac drugs, for instance - do not naturally proliferate in large numbers, to date researchers have been using heart cells derived from reprogrammed human induced pluripotent stem cells (hiPSC's), which tend to be too immature to use effectively in research or transplantation.

"The question is: if you want to test drugs or treat adult patients, do you want to

use cells and look like and function like fetal cardiomyocytes?" asks Radisic, who was named a "Top Innovator Under 35" by MIT Technology Review and more recently was awarded the Order of Ontario and the Young Engineers of Canada 2012 Achievement Award. "Can we mature these cells to become more like adult cells?"

In response to the challenge, Radisic and her team, which includes graduate student Jason Miklas and Dr. Sara Nunes, a scientist at the University Health Network (UHN) in Toronto, created a 'biowire'. Stem-cells derived human cardiomyocytes are seeded along a silk suture typical to medical applications. The suture allows the cells to grow along its length, close to their natural growth pattern.

Like a scene lifted from Frankenstein, the cells are then treated to cycles of electric pulses, like a mild version of a pacemaker, which have been show to stimulate the cells to increase in size, connect and beat like a real heart tissue.

But the key to successfully and rapidly maturing the cells turns out to be the way the pulses are applied.

Mimicking the conditions that occur naturally in cardiac biological development – in essence, simulating the way fetal heart rates escalates prior to birth, the team ramped up the rate at which the cells were being stimulated, from zero to 180 and 360 beats per minute.

"We found that pushing the cells to their limits over the course of a week derived the best effect," reports Radisic.

Grown on sutures that can be sewn directly into a patient, the biowires are designed to be fully transplantable. The use of biodegradable sutures, important in surgical patches that will remain in the body, is also a viable option.

Miklas argues that the research has practical implications for health care. "With this discovery we can reduce costs on the health care system by creating more accurate drug screening."

According to Nunes, the development takes cardiac research just one step closer to viable cardiac patches.

"One of the greatest challenges of transplanting these patches is getting the cells to survive," says Nunes, who is both a cardiac and a vascularization specialist, "and for that they need the blood vessels. Our next challenge is to put the vascularization together with cardiac cells."

Radisic, who calls the new method a "game changer," points out just how far the field has come in a very short time.

"In 2006 science saw the first derivation of induced pluripotent stem cells from mice," she explains. "Now we can turn stem cells into cardiac cells and make

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relatively mature tissue from human samples, without ethical concerns."

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