Dr. Milica Radisic (L) and
Dr. Sara Nunes de Vasconcelos (R)

PHOTO: CHRISTOPHER WAHL

REPAIRING DAMAGED HEARTS AND DEVELOPING SAFER DRUGS WITH

BIOWIRE TECHNOLOGY

THE newest brainchild of cardiac tissue engineering is to make possible the regeneration of heart tissue, and two HSRLCE members plan to turn that prospect into reality.

Dr. Milica Radisic, a scientist at the Institute of Biomaterials and Biomedical Engineering (IBBME), and Dr. Sara Nunes de Vasconcelos, an assistant scientist at the Toronto General Research Institute (TGRI), are pioneering a heart "patch kit" using human pluripotent stem cell–derived cardiomyocytes (hPSC-CMs) and coaxing them into becoming living, implantable cardiac tissue that can help to repair heart damage.

The work is a major triumph, since it addresses an inherent challenge in using stem cell–derived cardiac cells, in that they reflect very early human development. Dr. Radisic's team figured out how to make the cells mature so they act more like adult cells, findings that they reported in the journal *Nature Methods* in 2013. Other collaborators included stem cell scientist Dr. Gordon Keller (McEwan Centre for Regenerative Medicine) and Dr. Peter Backx, director of HSRLCE's Transgenic Physiology Lab.

The team developed an in vitro platform called biowires (because they are wire shaped and propagate electrical impulses) to create an optimal environment, using 3D cell culture that mimics the physiological and electrical cues of a real heart. After two to three weeks, the cells emerge as fully mature and functional adult cardiac cells.

The timing was right for this endeavour, suggests Dr. Radisic: "Ten or 15 years ago it wasn't possible to get human cardiomyocytes or develop these models in the labs, since post-natal human cardiomyocytes are terminally differentiated and it is not possible to propagate them. Using human pluripotent stem cells and differentiating cardiomyocytes from them enabled us to achieve this goal."

Dr. Nunes de Vasconcelos is now focusing on how to vascularize the cardiac tissue, which includes addressing the high cell death that typically occurs immediately after cell transplantation. Her lab is using an innovative technology to accelerate vascularization, using ready-made vessels obtained from fat tissue that can connect with host vessels and start carrying blood within the first days post-transplantation. Preliminary findings show significantly improved survival of the transplanted cardiac cells. Vascularization will also aid in generating more complex tissues for in vitro use such as drug screening.

> "Offering new ways to repair or replace damaged heart tissue"

Ultimately, biowires will offer new ways to repair or replace damaged heart tissue. The more immediate goal is using the novel technology as an in vitro drug-screening tool to assess cardiotoxicity before drugs reach the market. Using the bioengineered human heart tissue will offer more accurate information than animal models have offered to date. The Radisic lab is developing the proprietary drug-testing platform with U.S. partners at Columbia University and MIT through a start-up company called Tara Biosystems.