McGill

DEPARTMENT OF PHYSIOLOGY

Dr. F.C. MacIntosh Lectureship Seminar

GUEST SPEAKER

Dr. Michael Laflamme

Professor, Laboratory Medicine & Pathobiology, University of Toronto

FRIDAY, SEPTEMBER 22, 2023
11:00AM

MCINTYRE MEDICAL SCIENCES BUILDING ROOM 1034

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"Heart Regeneration with Human Pluripotent Stem Cells"

Human pluripotent stem cells (hPSCs) have a number of attractive properties for myocardial infarct (MI) repair, including a tremendous capacity for expansion in the undifferentiated state and the ability to differentiate into phenotypically unambiguous cardiomyocytes. Our group has contributed reliable methods for the scaled generation of hPSC-derived cardiomyocytes (hPSC-CMs), and we have shown that hPSC-CMs can partially remuscularize the infarct scar and mediate beneficial effects on contractile function in multiple preclinical MI models. In recent work in the translationally relevant porcine MI model, we have shown that hPSC-CM transplantation results in large (cubic centimeters-scale) human myocardial implants that show progressive maturation over time, form vascular networks with the host, and evoke minimal cellular rejection. That said, a number of important barriers to translation remain, including concerns about the immature and heterogeneous phenotype of hPSC-derived cardiomyocytes, incomplete host-graft integration following transplantation, and the occurrence of frequent graft-related tachyarrhythmias. In this presentation, I will summarize our recent efforts to overcome these hurdles via the delivery of more mature cardiomyocyte populations, and I will describe an efficient, economic protocol for the large-scale manufacturing of mature ventricular hPSC-CMs. In transplantation studies comparing in vitro matured hPSC-CMs to conventional immature populations, we have found that both exhibit comparable levels of engraftment in injured hearts, but the matured cells form graft tissue with profoundly enhanced cardiac structure and alignment. Most importantly, hearts with mature hPSC-CM grafts exhibit better functional outcomes, including greatly improved electromechanical integration, reduced pro-arrhythmic behavior, and a greater increment of contractile recovery.