THE UNIVERSITY OF BRITISH COLUMBIA

Cellular and Physiological Sciences Seminar Series

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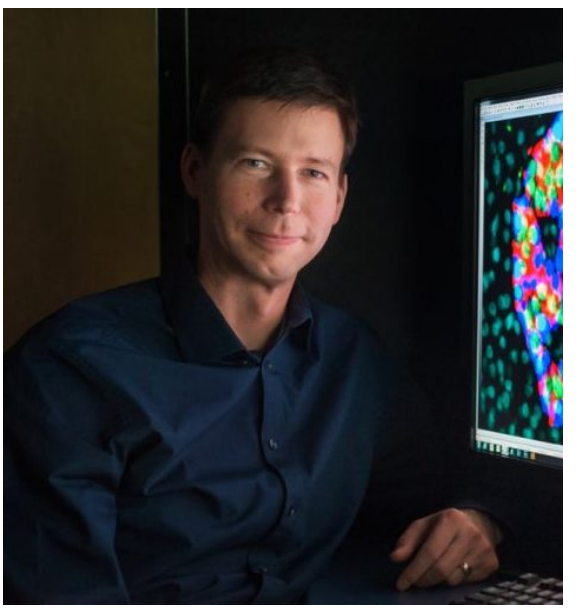

Thursday, September 12, 2019
12:45 - 1:45 (LSC 3)
Host: Drs. Rideout/Kopp

"Cell Therapy for Diabetes Using Differentiated Stem Cells – from Bench to Clinical Trials"

Diabetes results from insufficient production of the hormone insulin from beta cells in pancreatic islets. Pancreas and islet transplantation can replace the lost beta cells in patients but are limited by the scarcity of available donor organs. Our aim is to differentiate pluripotent stem cells into functional beta cells that can serve as an unlimited source for transplantation to treat diabetes. We have investigated the therapeutic potential of pancreatic progenitor cells derived from human embryonic stem cells. Several months following implant into diabetic rodents, these Stage 4 cells mature and secrete sufficient human insulin, in a regulated manner, to reverse diabetes. The maturation and function does not appear to be adversely affected by high fat diet, and implanted cells can improve glucose homeostasis in a mouse model of type 2 diabetes, particularly when combined with low doses of various diabetes drugs. Moreover, this combination therapy can promote significant weight loss in this animal model. However, we discovered that cell maturation and function are compromised in mice with hypothyroidism, and the cells mature faster in immunodeficient nude rats compared to SCID mice. Moreover, we have observed that Stage 4 cells appear to mature faster in female mice than in male mice. Therefore, the cell environment in the host can impact the maturation and ultimately the function of stem cell derived pancreatic progenitor cells. For this reason, we seek to develop culture methods to produce fully functional beta cells prior to implant. An extended differentiation protocol was produced to generate more mature cells (Stage 7) that have greater insulin content and mild glucose-responsiveness, mimicking immature beta cells. These cells are able to reverse diabetes in rodents significantly faster and with lower doses of cells as compared to Stage 4 cells. Moreover, we have found that these cells can function within macroencapsulation devices implanted subcutaneously, designed to protect cells from immune attack. The cells also perform similarly in male and female recipients. Glucose responsiveness has also been improved by further protocol refinements. These cells may provide a useful model system for studying disease mechanisms and for screening for new drugs to improve beta cell function, in addition to providing an unlimited source of cells for transplant to treat diabetes.

Join us for coffee and cookies at 12:15 in LSC 1410
Contact Drs. Rideout/Kopp<elizabeth.rideout@ubc.ca><janel.kopp@ubc.ca>