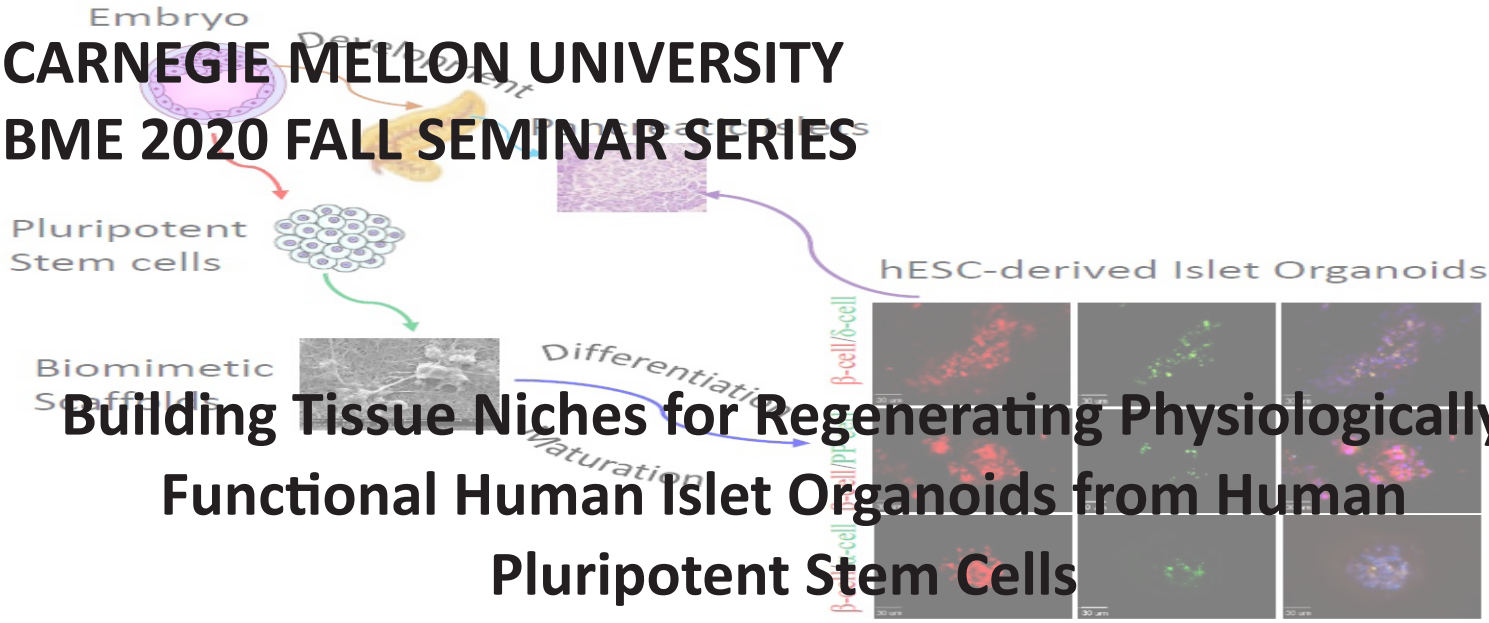
CARNEGIE MELLON UNIVERSITY
BME 2020 FALL SEMINAR SERIES



Building Tissue Niches for Regenerating Physiologically Functional Human Islet Organoids from Human Pluripotent Stem Cells

PRESENTED BY

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SCHEDULE

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(10:00 AM-11:00AM)

Creation of highly organized multicellular constructs, including tissues and organoids, will revolutionize tissue engineering and regenerative medicine. The development of these technologies will enable the production of individualized organs for patient-tailored organ transplantation or individualized tissues for cell-based therapy. These lab-produced high order tissues and organs can serve as disease models for pathophysiological study and drug screening. We have developed an innovative tissue assembly technologies for generating pancreatic islets from human pluripotent stem cells (HPSCs). These islets exhibited a tissue architecture similar to human pancreatic islets, consisting of pancreatic α, β, d, and pancreatic polypeptide (PP) cells. We discovered that tissue scaffolding and inspiring are critical to the generation of pancreatic endoderm and the assembly of islet architectures. The organoids formed consisted of A high level co-expression of PDX1, NKX6.1, and NGN3, suggests the characteristics of pancreatic β cells. More importantly, most insulin-secreting cells generated did not express glucagon, somatostatin, or PP. The expression of mature β cell marker genes such as Pdx1, Ngn3, Insulin, MafA, and Glut2 was detected in generated islet organoids. A high level expression of C-peptide confirmed the de novo endogenous insulin production in these organoids. Insulin-secretory granules, an indication of β cell maturity, were detected. Glucose challenging experiments suggested that these organoids are sensitive to glucose levels due to their elevated maturity. Exposing the organoids to a high concentration of glucose induced a sharp increase in insulin secretion, whereas glucagon is released when they are exposed to a low glucose, indicating the glucose-responsive insulin release and glucagon secretion, a characteristic physiological metabolism of the human islets. Our recent bioinformatics study revealed tissue specific niches essential for islet maturation. Thee discoveries are one-step closer to generate physiological functional human islets for diabetes treatment and drug discovery.

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