The Singapore Bioimaging Consortium (SBIC)
presents a seminar on

"Quantitative Imaging of Molecular Mechanisms Underlying Glucose-Regulated Hormone Secretion from Pancreatic Islets"

Speaker: **Prof David W. Piston**
Head, Department of Cell Biology & Physiology
Washington University

Host : **Dr Han Weiping**
Date : **Thursday, 25 July 2019**
Time : **2.00pm – 3.00pm**
Venue : **SBIC Seminar Room**
11 Biopolis Way
Level 2, Helios Building, Singapore 138667
(Please enter via Level 1)

Abstract

The islet of Langerhans is the functional unit responsible for glucose-regulate secretion of insulin from β-cells and glucagon from α-cells, and thus plays a key role in blood glucose homeostasis. Chronic imbalance in the insulin/glucagon output of the islet is the defining trait of diabetes. Over the last 25 years, we have been interested in understanding the multicellular mechanisms of islet function, and its role in the regulation of blood glucose under normal and pathological conditions. Using our unique quantitative optical imaging methods and novel microfluidic devices, the *dynamics* of these molecular mechanisms can be followed quantitatively in living cells within intact islets. We have shown that the neurotransmitter dopamine plays an important role in islet function through autocrine and paracrine signaling between islet cells, which fine tunes hormone output via tonic inhibition of secretory activity. The dopamine receptors D3 and D2 are present and active in islet cells, and we are characterizing the complex interplay between the dopamine receptors that are active in the various islet cell types. Preliminary data suggest that dopamine signaling cascades act on distinct pathways to differentially regulate insulin and glucagon. These experiments utilize in situ hybridization to test cell specific receptor expression in the islets, and adeno viruses to deliver genetically encoded fluorescent reporters to mouse. Two-photon excitation metabolic imaging and confocal microscopy are used to assay responses triggered by selective activation of D2 or D3 receptors. These experiments allow us to define a model for dopaminergic regulation of hormone secretion. To facilitate these experiments, we are developing new methods for fast, high-content quantitative imaging of islet functions. We have combined light-sheet fluorescence microscope (dual view inverted Selective Plane Illumination Microscopy–diSPIM) and hyperspectral imaging (Image Mapping Spectrometer–IMS) to provide rapid acquisition of three-dimensional data sets of multiple biosensors in whole islets. This has allowed us to utilize mouse models combining a glucagon-promoter calcium sensor (GCaMP6) in α-cells, a novel, orange cAMP sensor driven by adenovirus expression in 70% of islet cells, and a red calcium sensor driven by the rat insulin promoter in β-cells. This combination allows simultaneous monitoring of calcium activity in α- and β-cells, while measuring cAMP levels in both cell types.

Using the IMS-diSPIM system we can measure putative paracrine interactions between the two cell types' signaling pathways with isotropic spatial resolution and sub-second temporal resolution.

About the Speaker

Prof David W. Piston is the Edward J. Mallinckrodt Jr. Professor and Head of the Department of Cell Biology and Physiology, Professor of Physics, and Professor of Bioengineering at Washington University in St. Louis. Prof Piston received a Bachelor of Arts Degree with a major in Physics from Grinnell College in Grinnell, Iowa, followed by the M.S. and PhD degrees in physics at the University of Illinois. His doctoral dissertation work was done under the mentorship of Prof Enrico Gratton, and he subsequently completed a postdoctoral research fellowship in Applied Physics with Watt Webb at Cornell University. During his time at Cornell, two-photon excitation microscopy was invented, and this served as Prof Piston's entry into biomedical research. In 1992, Prof Piston joined the faculty at Vanderbilt University, where he remained until the end of 2014, when he moved to Washington University. He has received a number of honors including a Beckman Young Investigator Award (1993), NIH Study Section Chair (2004-2006), Searle Scholars Advisory Board (2006-20112) and election as a Fellow of the American Association for the Advancement of Science (2015). Prof Piston is currently serving as the President of the Biophysical Society. His diverse research group focuses on the understanding the molecular mechanisms that underlie hormone secretion from islets of Langerhans in the pancreas. Driven by this biomedical focus, the lab develops, optimizes, and applies novel fluorescence microscopies and probes, largely based on the Green Fluorescent Protein and its relatives. His lab combines these new approaches for measuring molecular mechanisms that underlie functional behaviors of constituent islet cell types *in situ* and *in vivo* at various points along both glucose-regulated and non- glucose-regulated signaling pathways.

--- Admission is free and all are welcome ---