Department of Biomedical Sciences and
School of Veterinary Medicine
present a seminar on

The secret lives of gonadotropes: the interface between GnRH and ATP signaling in the pituitary

by

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Date: **7 October 2015 (Wednesday)**
Time: **10:00–11:15 am**
Venue: **Room 2-130, 1/F, Block 2**
To Yuen Building
City University of Hong Kong
Tat Chee Avenue, Kowloon Tong

Abstract: Successful reproduction requires integration of the neuroendocrine hypothalamic-pituitary-gonadal axis. Gonadotropin releasing hormone (GnRH) receptor within the anterior pituitary gonadotrope is a required conduit for this neuroendocrine integration of pituitary gonadotropin production. The GnRHR is a unique member of the G protein-coupled receptor superfamily; a GPCR that does not have an intracellular carboxyl-terminal tail resulting in altered signaling kinetics and desensitization properties. The GnRHR is localized to discrete membrane micro-domains (membrane rafts) within the gonadotrope necessary for productive signaling to MAPK pathways including the extracellular signal-regulated kinase (ERK) pathway. GnRH-induced ERK signaling in the gonadotrope is absolutely required for normal reproduction. Mouse models of conditional ERK1 and 2 gene deletions reveal a gender-specific anovulatory infertility. Proteomic analyses of the raft compartment identified co-localization of the GnRHR with the F_0F_1 ATP synthase complex at the plasma membrane. Immuno-fluorescence, flow cytometry and cell surface biotinylation studies provide evidence for membrane localization and the F_1 catalytic face of the synthase facing the extracellular space. Consistent with these finding, living pituitary cells are capable of synthesizing copious amounts of extracellular ATP when presented with appropriate substrates. Cannulation of the hypothalamic-pituitary portal vasculature suggests that extracellular ATP may be delivered to the pituitary gland from the hypothalamus via the median eminence. Disruption of extracellular ATP metabolism at the surface of the gonadotrope alters GnRH-induced secretion of luteinizing hormone. Our studies suggest that signaling through extracellular ATP modulates GnRH-induced secretion of gonadotropins.

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~ All are welcome ~