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Major Professor: Ei Terasawa

Degree Objective: Ph.D. Endocrinology and Reproductive Physiology

Background: BS Molecular Biology Univ Wisconsin-Madison, Madison, WI

Current Research Project:

17-beta estradiol (E2) has recently been demonstrated to have rapid neuromodulatory function in primate GnRH neurons. E2 stimulates firing rate within a minute, the frequency of intracellular calcium ([Ca2+]i) oscillations and their synchronization, and release of the GnRH decapeptide within 10 min. Moreover a recent study suggests that GPR30, in part, mediates rapid E2 action: The E2-induced rapid stimulation of [Ca2+]i oscillations is abrogated by GPR30 specific siRNA transfection and the GPR30 agonist, G1, causes effects similar to those with E2. However, the mechanism of E2 action through GPR30 in GnRH neurons is still unknown. It has been reported in breast cancer cells that GPR30 activates adenylyl cyclase (AC) and PKA through Gαs, trans-activates EGFR and downstream MAPK and PI3K/AKT pathways through Gβ/γ, matrix metallo-protease, and heparin-bound EGF pathway. Although these findings in cancer cells may be applicable to GnRH neurons, there are cell type specific differences in the intracellular mechanisms involved in GPR30 mediated [Ca2+]i changes by either IP3 receptor (IP3-R) or ryanodine receptor (RyR) mediated [Ca2+]i stores. Moreover, extracellular calcium ([Ca2+]e) through voltage gated calcium channel (VGCC) and RyR mechanisms are essential for GnRH neurosecretion. Therefore, the goal of this study is to investigate intracellular mechanisms of rapid E2 resulting in GnRH neurosecretion. The hypothesis for this study is that rapid E2 action in primate GnRH neurons is mediated through a GPR30 signaling pathway resulting in stimulation of [Ca2+]i changes by coordination of extracellular and intracellular [Ca2+] stores and culminates in the rapid neurosecretion of GnRH.

Honors:

Grants Received:

Publications:

Terasawa E, Kurian JR, Guerriero KA, Kenealy BP, Hutz ED, Keen KL. Recent discoveries on the control of gonadotrophin-releasing hormone neurones in nonhuman primates. J Neuroendocrinol 2010: 22; 630-8.

National Presentations:

Kenealy BP, Keen KL, Ronnekleiv OK, Terasawa E. STX, a novel non-steroidal estrogenic compound, induces rapid action, calcium signaling and decapeptide release in primate GnRH

neurons. SRC summer Research Conferences FASEB; The physiology of integrated nuclear and extranuclear steroid signaling, Aug 8-13, Snowmass CO, 2010.

Kenealy BP, Lehman JR, Keen KL, Terasawa E. Role of GPR30 in rapid estrogen action in primate gonadotropin releasing hormone (GnRH) neurons: Interaction with EGF receptors. Abstracts for the 40th Annual Meeting of the Society for Neuroscience, held at San Diego, CA, 2010; No. 87.16.

Other Presentations:

Kenealy BP, Keen KL, Lehman JR, and Terasawa E. Involvement of epidermal growth factor-receptor (EGF-R) in rapid estrogen action mediated by GPR30 in primate luteinizing hormone releasing hormone (LHRH) neurons. ERP Annual Symposium 2009.

Kenealy BP, Keen KL, Terasawa E. Involvement of Mitogen Activated Protein Kinase (MAPK) in rapid estrogen action mediated by GPR30 in LHRH neurons. ERP Annual Symposium 2010.

ERP Service:

ERP recruitment focus group 2008-present,

ERP symposium committee 2009-2010, 2010-2011