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**Major Professor:** Ei Terasawa

**Degree Objective:** Ph.D. Endocrinology and Reproductive Physiology

**Background:** BS Biology, University of Pittsburgh, PA

**Current Research Project:**

An increase in pulsatile gonadotropin hormone-releasing hormone (GnRH) is critical and triggers the initiation of puberty in primates. Recent clinical studies in patients with hypogonadotropic hypogonadism (HH), which results in a delay or absence of puberty, have shown that the kisspeptin/kisspeptin-1 receptor (KP/Kiss1R) signaling pathway may be involved in regulating the pubertal increase in GnRH release. Therefore, four experiments have been proposed to examine the hypothesis that KP is critical for triggering the pubertal increase in GnRH release from the hypothalamus in primates. Experiment 1: To assess the developmental pattern of KP release in the intact prepubertal and pubertal female rhesus monkey from the basal hypothalamus using an in vivo microdialysis method. Results demonstrate that there is a pubertal increase in mean KP release and that this increase is characterized by an increase in pulse frequency, but not pulse amplitude. Furthermore, a nocturnal increase in mean KP release becomes prominent only after puberty is triggered. Experiment 2: To examine the hypothesis that the pubertal increase in KP release is independent of ovarian steroid feedback by verifying whether there is a pubertal increase in KP release in ovariectomized (OVX) monkeys, and if this increase in KP release still occurs in the presence of the ovarian steroid estradiol. The results suggest that the pubertal increase in KP release appears independent of ovarian steroid feedback. Experiment 3: To assess the effects of a KP agonist (human KP-10) and antagonist (peptide 234) on GnRH release in prepubertal and pubertal monkeys in order to determine if developmental changes in Kiss1R function occur. A summary of the data demonstrates that 1) the KP agonist stimulates, while the KP antagonist suppresses GnRH release in ovarian-intact prepubertal and pubertal monkeys, 2) there is a dose-dependent to the KP agonist in prepubertal, but not pubertal, monkeys, and 3) ovarian steroid feedback modulates KP/Kiss1R signaling to GnRH neurons only after puberty is triggered. Experiment 4: To determine if long-term infusion of a KP antagonist can delay the onset of puberty in prepubertal monkeys. Results from this experiment are currently being analyzed. Experiments 1-3 have thoroughly examined KP release and KP/Kiss1R activity mechanism on GnRH neurons. However, completion of Experiment 4 will be necessary to fully test the hypothesis that KP is critical for triggering the pubertal increase in GnRH release from the hypothalamus in primates.

**Honors:**

2010: Henry Vilas Conference Presentation Travel Grant, UW-Madison



2010 : International Neuroendocrine Federation, 7th International Congress of Neuroendocrinology Young Investigator Travel Award, July 10-15, 2010, Rouen, France

2009: Annual Research Symposium: Endocrinology and Reproductive Physiology Symposium, Best Oral Presentation

2008: National Science Foundation 2008 Graduate Research Fellowship, Honorable Mention

## **Grants Received:**

NIH T32 Trainee; NIH Ruth L. Kirschstein National Research Service Award NIH T32-HD041921 2008-2010.

## **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 Jul;22(7):630-8. Epub 2010 May 8. Review. PMID: 20456608

Roseweir AK, Kauffman AS, Smith JT, Guerriero KA, Morgan K, Pielecka-Fortuna J, Pineda R, Gottsch ML, Tena-Sempere M, Moenter SM, Terasawa E, Clarke IJ, Steiner RA, Millar RP. Discovery of potent kisspeptin antagonists delineate physiological mechanisms of gonadotropin regulation. *J Neurosci.* 2009 Mar 25;29(12):3920-9. PMID: 19321788

Ramaswamy S, Guerriero KA, Gibbs RB, Plant TM. Structural interactions between kisspeptin and GnRH neurons in the mediobasal hypothalamus of the male rhesus monkey (*Macaca mulatta*) as revealed by double immunofluorescence and confocal microscopy. *Endocrinology.* 2008 Sep;149(9):4387-95. Epub 2008 May 29.

## **National Presentations:**

Guerriero KA, Keen KL, Terasawa E. Striking developmental changes in kisspeptin-Gpr54 signaling to GnRH neurons in female monkeys: Modification by estrogen feedback. 7th International Congress of Neuroendocrinology. July 10-15, 2010. Rouen, France. Abstract P1-36.

Guerriero KA, Keen KL, Terasawa E. The effects of ovariectomy on kisspeptin-54 release in vivo in the female rhesus monkey. 39<sup>th</sup> Annual Society for Neuroscience Meeting. October 17-21, 2009. Chicago, Ill. Abstract #703.7. Oral Presentation:

Guerriero KA, Keen KL, Roseweir AK, Millar RP, Terasawa E. Effects of a kisspeptin agonist and antagonist on the release of luteinizing hormone-releasing hormone-1 (LHRH-1) in female rhesus monkeys in vivo. 38<sup>th</sup> Annual Society for Neuroscience Meeting. November 15-19, 2008. Washington, DC Abstract #618.1. Oral Presentation



## **Other Presentations:**

Guerriero KA, Keen KL, Terasawa E. Developmental Changes in the Release Pattern of Kisspeptin-54 from the Stalk-Median Eminence of the Hypothalamus of Intact and Ovariectomized Female Rhesus Monkeys. ERP Annual Symposium 2009. Oral presentation.

Guerriero KA, Keen KL, Terasawa E. Striking developmental changes in kisspeptin-Gpr54 signaling to GnRH neurons in female monkeys: Modification by estrogen feedback. ERP Annual Symposium 2009. Oral presentation

Guerriero KA, Terasawa E, Keen KL. The role of kisspeptin in the pubertal increase of LHRH from the monkey hypothalamus: Agonist and antagonist effects. Abstract #P17. 4<sup>th</sup> Biennial Neuroscience Research Symposium. August 22, 2008. BioPharmaceutical Technology Center Institute, Madison, WI.

## **ERP Service:**

May 2010-Present: Curriculum Committee

August 2009-May 2010: Seminar Committee

August 2008-Present: Focus Group Committee