Pulsatile luteinizing hormone (LH) secretion in female mice across pubertal development

Y. Wan,[1] F.J. Steyn,[1] J.D. Veldhuis[2] and C. Chen,[1] [1]School of Biomedical Science, University of Queensland, St Lucia, QLD 4072, Australia and [2]Endocrine Research Unit, Mayo Clinic College of Medicine, Centre for Translational Science Activities, Mayo Clinic, Rochester, MN, USA.

The hypothalamic-pituitary-gonadal (HPG) axis is the main pathway that modulates the release of pituitary hormones that regulate ovarian function in females. Luteinizing hormone (LH) regulates both ovarian steroid (estradiol) synthesis and ovulation. Dynamic changes in LH release that occur with age and reproductive status may predict reproductive capacity. In this regard, transgenic mouse models may provide critical information to define the mechanisms that prime LH release for optimal reproductive function. Historically, assessment of pulsatile LH release in mice was problematic, and comparative measures of pulsatile LH in pubertal and/or early adult female mice do not exist. To address this, we monitored pulsatile LH release in female wild-type C57BL/6J mice over the estrous cycle, determining age-associated changes between the first ovulatory cycle (5 weeks old) and established adult cycles (10 weeks old). Blood sampling and analysis was completed following established methodologies (Steyn *et al.*, 2013; Veldhuis & Johnson, 1992). Observations demonstrate significant changes in the pattern of LH release across the estrous cycle. We observed a significant rise in pulse number and approximate entropy (measure of irregularity) of LH pulses from estrus to diestrus. This coincided with a gradual rise in basal, total and pulsatile LH release. Altered pulse dynamics were matched with a decrease in the mass of LH secreted per burst. Pulse dynamics between the first and adult ovulatory cycles were well conserved and defined by a significant rise in pulse number and irregularity, specific to diestrus only. Of interest, the onset of the preovulatory LH surge between the first and adult ovulatory cycles varied only in the timing of onset. To further define mechanisms of LH release relative to the ovarian cycle, pulse profiles were matched with hypothalamic expression of GnRH mRNA, pituitary LH content and circulating measures of estradiol. These measures provide additional insights to define dynamic changes in hypothalamic and systemic regulators of LH that predict the release of LH throughout the estrous cycle and with age. Observations provide data to further establish the mouse as a critical model for the assessment of mechanisms that regulate reproductive function.

Steyn FJ, Wan Y, Clarkson J, Veldhuis JD, Herbison AE, Chen C. (2013) *Endocrinology* **154:** 4939-45.
Veldhuis JD, Johnson ML. (1992) *Methods in Enzymology* **210:** 539-75.

This work was supported by the University of Queensland and Otago University. Y Wan receives a postgraduate scholarship from the University of Queensland.