pdn
Department of Physiology, Development and Neuroscience

Neural Regulation of Fertility
or "What's going on in the Herbison lab?"

wellcome

Did you know that the brain controls fertility in all mammals including humans?

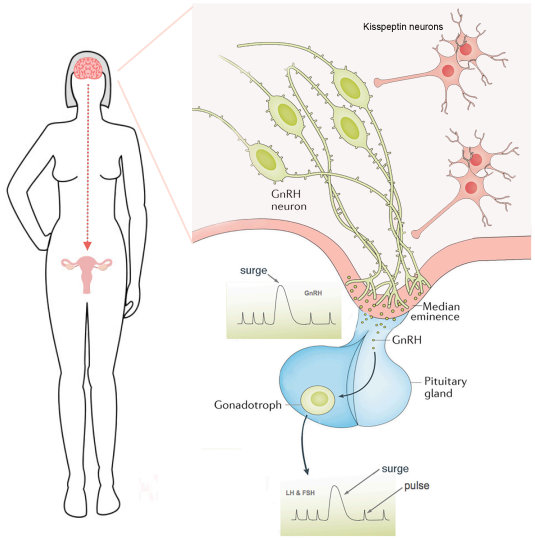
The primary goal of the laboratory is to understand precisely how the brain controls reproductive hormone secretion so that new treatments can be brought forward for the beneficial regulation of fertility in the clinic.

In Western societies, 15-25% of couples suffer from infertility – in about a third of cases this results from a problem in communication between the brain and ovary. This includes conditions like –

Polycystic Ovary Syndrome (PCOS); a condition affecting 5% of reproductive-aged women in which the pulses coming from the brain can occur too fast for the ovary to function correctly.

Hypothalamic amenorrhea; a situation where excessive stress results in abnormal hormone pulses leading to a loss of periods and infertility.

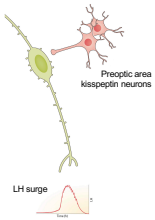
Control of fertility by kisspeptin and GnRH neurons



Our Questions

1. How do the preoptic area kisspeptin neurons control the GnRH surge that initiates ovulation?

It is very likely that a sub-population of preoptic area (POA) kisspeptin neurons play a key role in activating the GnRH neurons once every cycle to generate the GnRH and LH surge that triggers ovulation[1].



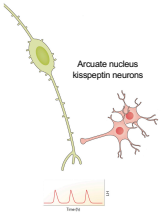
We are trying to understand -

1. The molecular and electrical characteristics of the sub-population of kisspeptin neurons in the POA responsible for activating the GnRH neurons.
2. How hormones and circadian inputs modulate the activity of these POA kisspeptin neurons.

1. Herbison *Nature Rev Endo* 2016

2. How do the arcuate nucleus kisspeptin neurons control the pulses of GnRH and LH?

It is now clear that the arcuate nucleus (ARN) kisspeptin neurons represent the pulse generator that drives pulsatile GnRH and LH secretion in mammals[2,3].



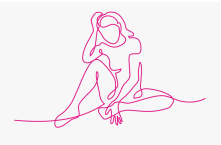
We are trying to understand -

1. What is the mechanism through which the ARN kisspeptin neurons are synchronized to episodically activate the GnRH neurons?
2. What are the key inputs to ARN kisspeptin neurons that regulate their frequency of episodic synchronization?
3. How gonadal steroids modulate the activity of the ARN kisspeptin neurons?

2. Clarkson, Han et al. , *PNAS* 2017
3. Herbison *Endocrinology* 2019

3. What goes wrong with the brain control of fertility at times of metabolic stress and in PCOS?

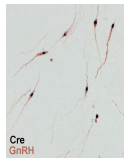
Excessive stress resulting from improper nutrition, over-exercising and/or psychological factors results in a slowing or absence of LH pulses and blocks the LH surge. Conversely, women with PCOS have LH pulses that occur too quickly.



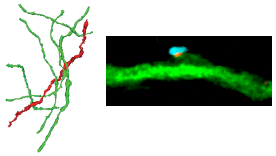
We are using animal models of under-nutrition and PCOS to try and understand -

1. How these conditions impact upon the GnRH pulse and surge generators,
2. What pathways are activated within the brain in these conditions to modualte the activity of the pulse and surge generators.
3. How we might be able to reverse these alterations in pulse generator activity to restore fertility.

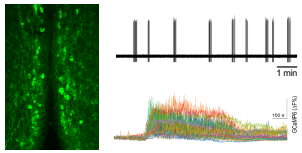
Techniques we use to explore how the brain controls fertility



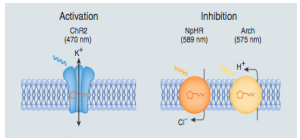
Genetically-modified rodents



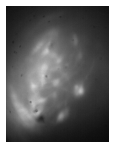
Morphology with tissue clearing and expansion microscopy



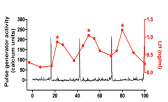
In vitro acute brain slice electrophysiology and GCaMP imaging



In vivo optogenetics and chemogenetics



In vivo GCaMP fiber photometry and GRIN lens monitoring



In vivo hormone profiling

In vivo targeted gene deletion with CRISPR