Naomi E. Rance, MD, PhD Department of Pathology

Menopause and the Human Hypothalamus: Evidence of a Role for KNDy Neurons in the Estrogen Modulation of LH Secretion and Body Temperature
Neuroendocrine regulation in postmenopausal women

KNDy neurons

Medial Basal Hypothalamus

KISS-1
NKB
SP
DYN
mRNA

ERα

GnRH mRNA

GnRH

Pituitary

Estrogen

Ovary

LH
FSH

Rance, Peptides, 2009
Neuroendocrine regulation in postmenopausal women

HOT FLUSHES???

Rance, Peptides, 2009
The Hot Flush

- Caused by estrogen withdrawal
- Consists of activation of heat defense effectors
  - Skin vasodilatation, sweating and behavior

Hot flushes are linked to pulsatile LH secretion!

Tract-tracing studies in the rat show KNDy neurons project to preoptic thermoregulatory nuclei.

Krajewski et al, Neuroscience 2010, Dacks et al., Endocrinology 2011
Do KNDy neurons modulate body temperature and LH secretion?

Krajewski et al, Neuroscience 2010, Dacks et al., Endocrinology 2011
Effect of KNDy neuron ablation on LH secretion

Mittelman-Smith et al., Endocrinology. 2012
Effect of KNDy neuron ablation on LH secretion

*Mittelman-Smith et al., Endocrinology. 2012*
Ablation of KNDy neurons results in reduced tail skin temperature.

Evidence that KNDy neurons facilitate cutaneous vasodilatation!

*Mittelman-Smith et al. *PNAS*, 2012*
Modulation of LH secretion and the Heat Defense Pathway by KNDy neurons

Preoptic hypothalamus

Mittelman-Smith et al. *PNAS*, 2012
Alignment with Neuroscience  
Area of Excellence

• Research laboratory focusing on understanding the effects of estrogen withdrawal (menopause) on hypothalamic structure and function

• Neuropathologist, University of Arizona Medical Center

• Evelyn F. McNight Brain Institute

• Interdisciplinary Graduate Program in Neuroscience, Active Member
Current Collaborators

- Graduate Students of Neuroscience and Physiological Sciences IDPs
- Nathaniel McMullen, Department of Cellular and Molecular Medicine
- Ralph Fergosi and Richard Levine, Departments of Physiology and Neuroscience
- Andrej Romanovsky, Barrow Institute, Phoenix

Funding by NIH, National Institutes on Aging, Evelyn McNight Brain Institute, Arizona Biomedical Research Commission