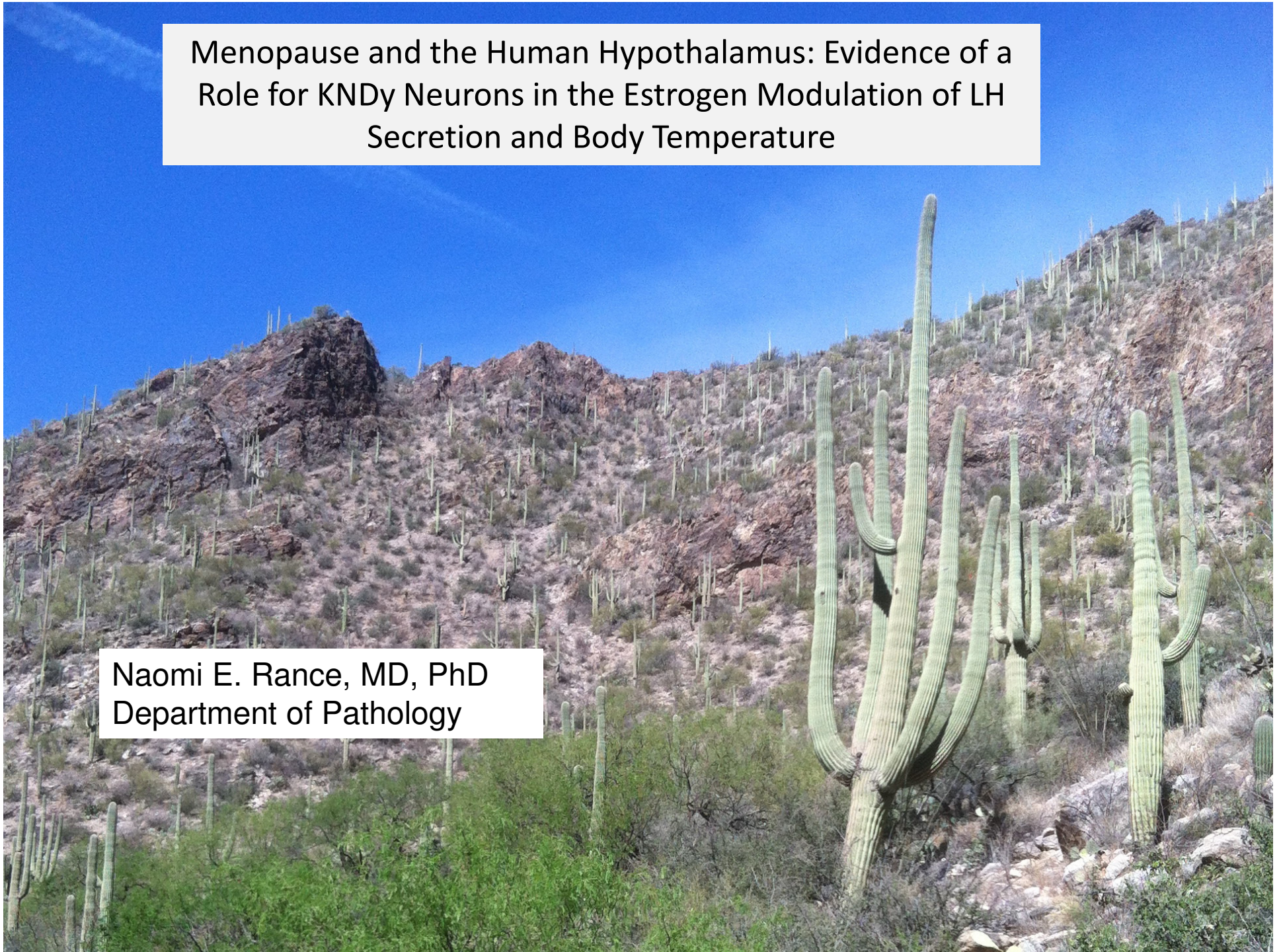
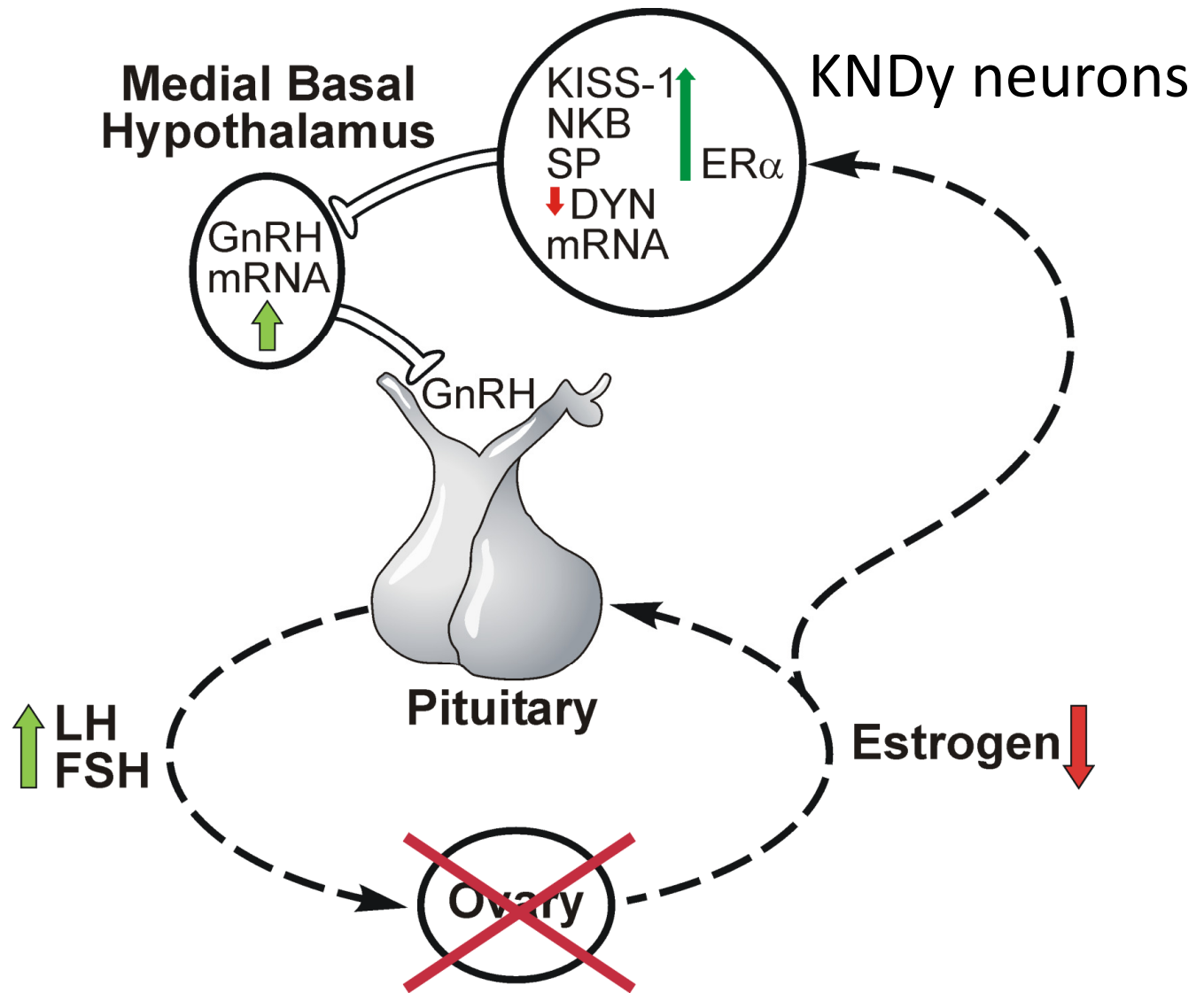


Menopause and the Human Hypothalamus: Evidence of a
Role for KNDy Neurons in the Estrogen Modulation of LH
Secretion and Body Temperature

Naomi E. Rance, MD, PhD
Department of Pathology

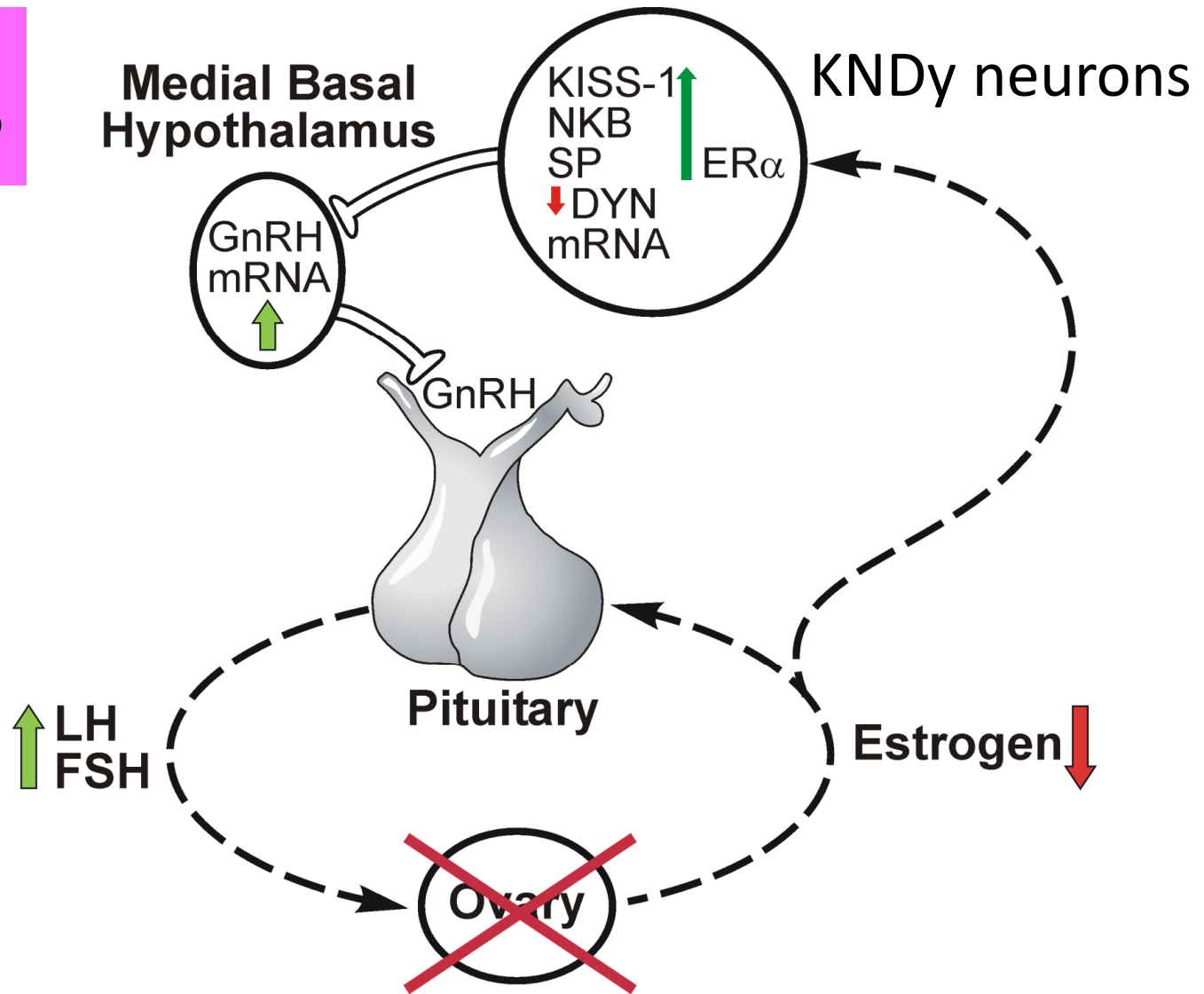


Neuroendocrine regulation in postmenopausal women



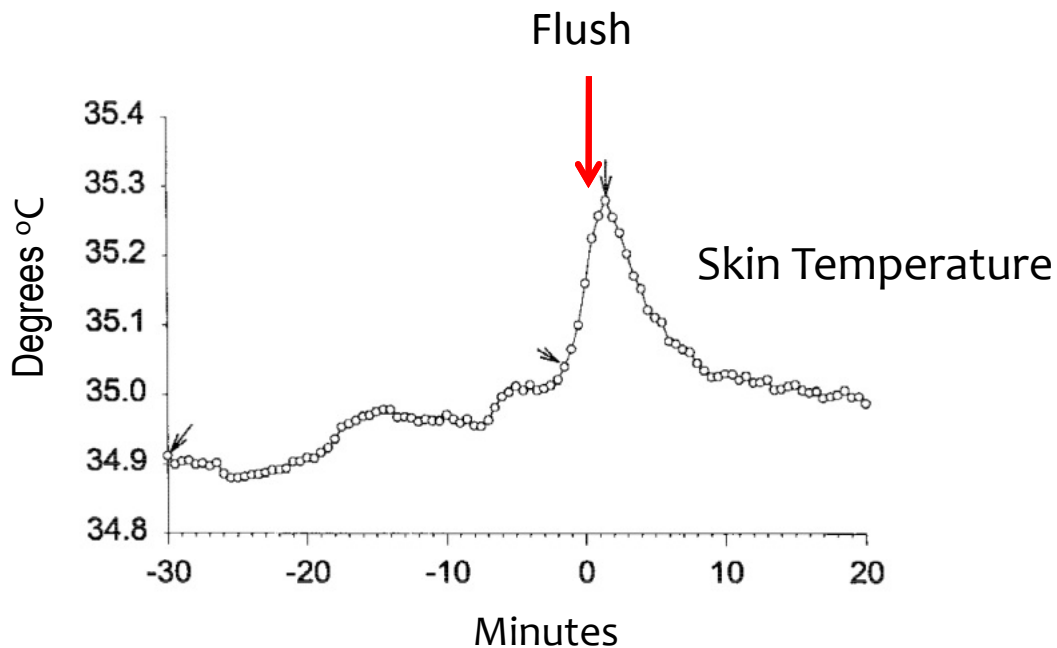
Neuroendocrine regulation in postmenopausal women

**HOT
FLUSHES???**

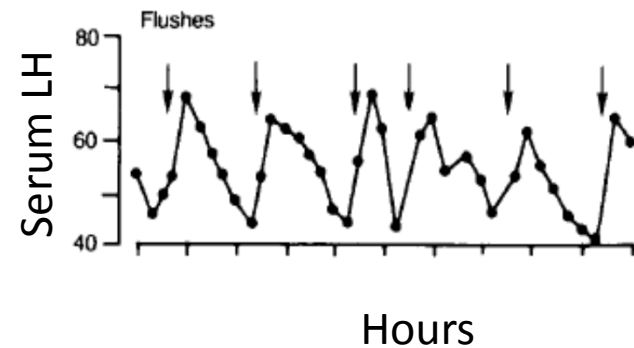


The Hot Flush

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

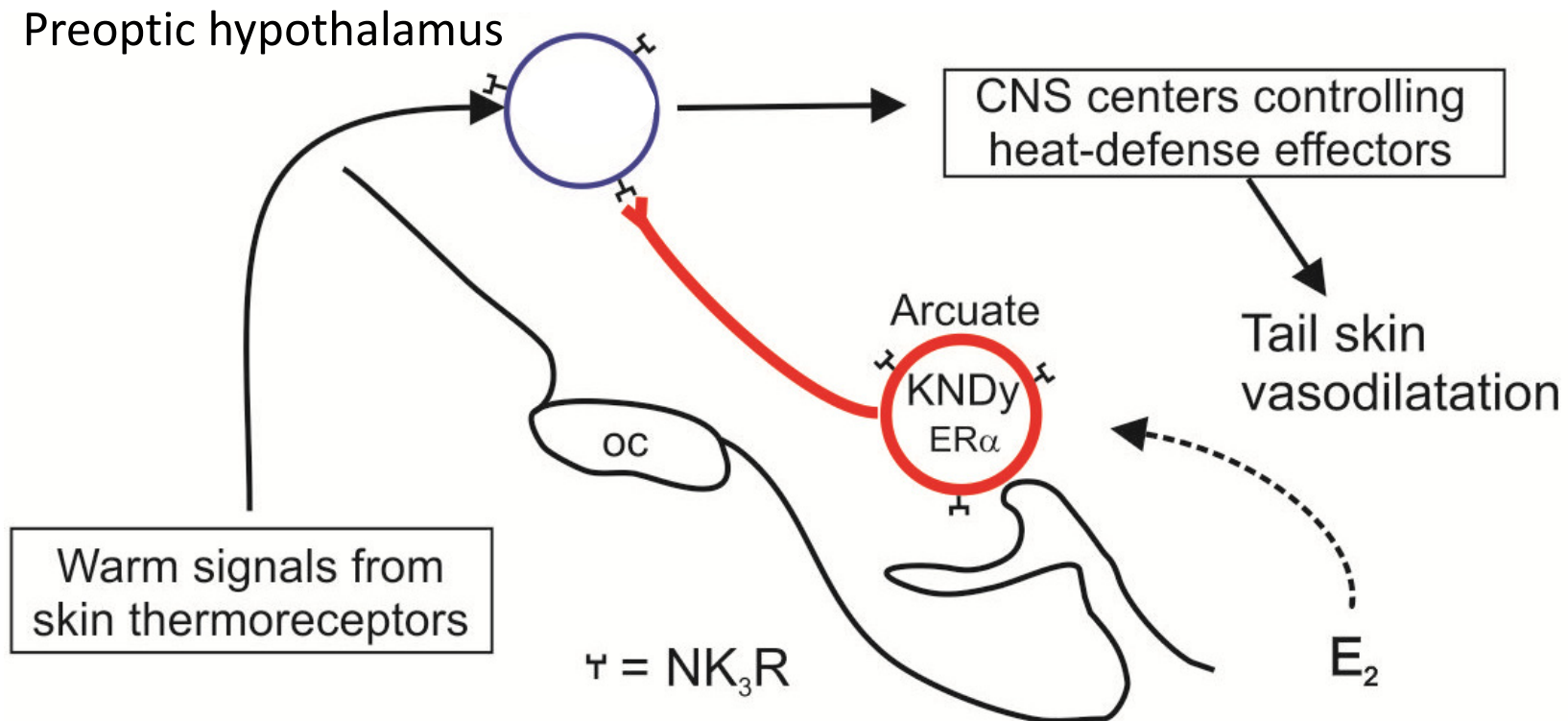


Hot flushes are linked to pulsatile LH secretion!



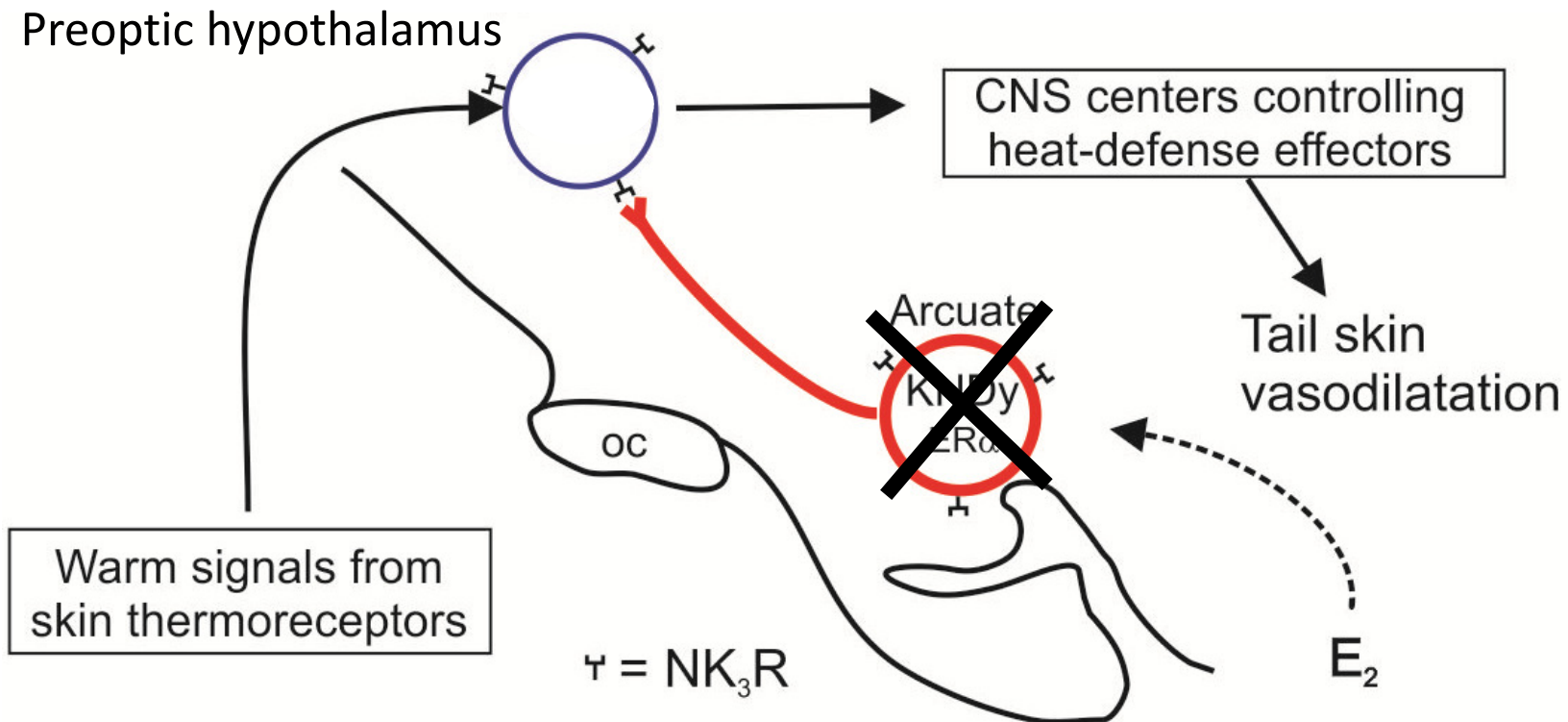
Freedman Am. J. Hum. Biol. 2001, Casper and Yen, Science 1978

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



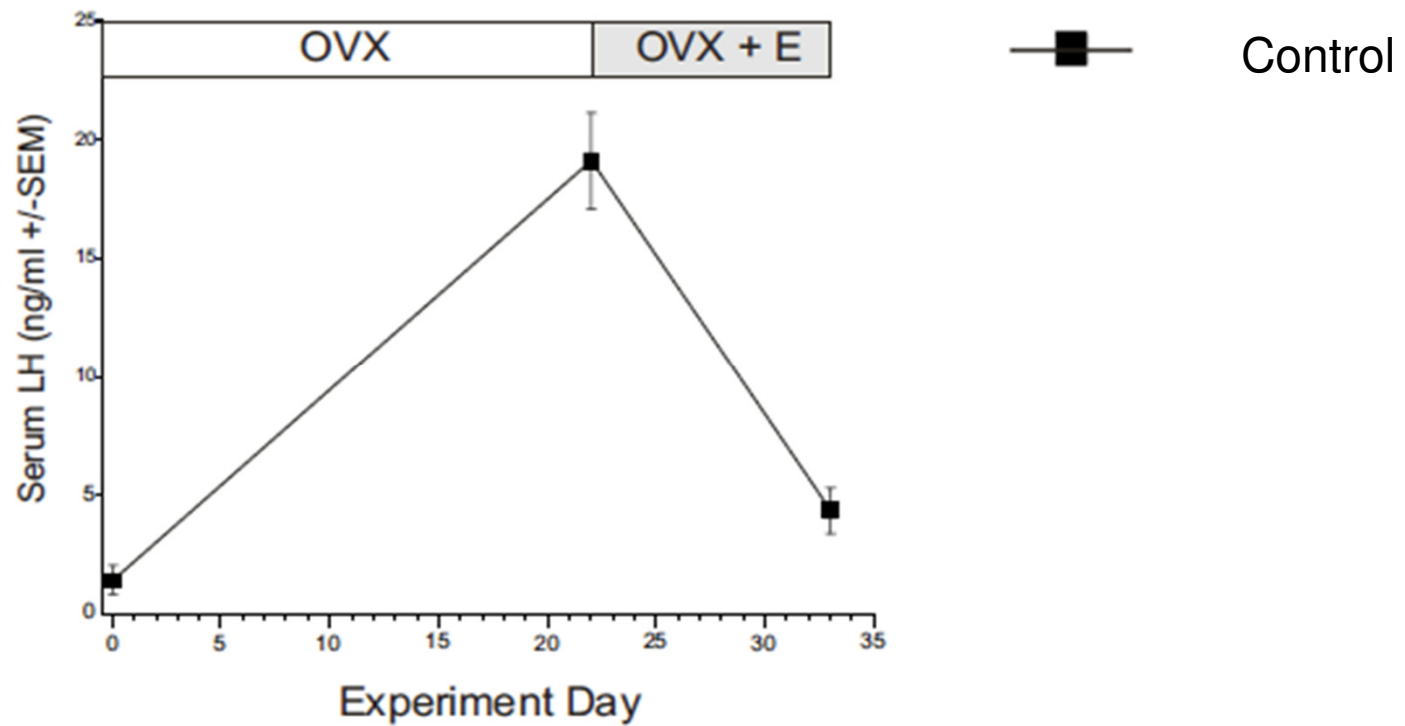
Krajewski et al, Neuroscience 2010, Dacks et al., Endocrinology 2011

Do KNDy neurons modulate body temperature and LH secretion?



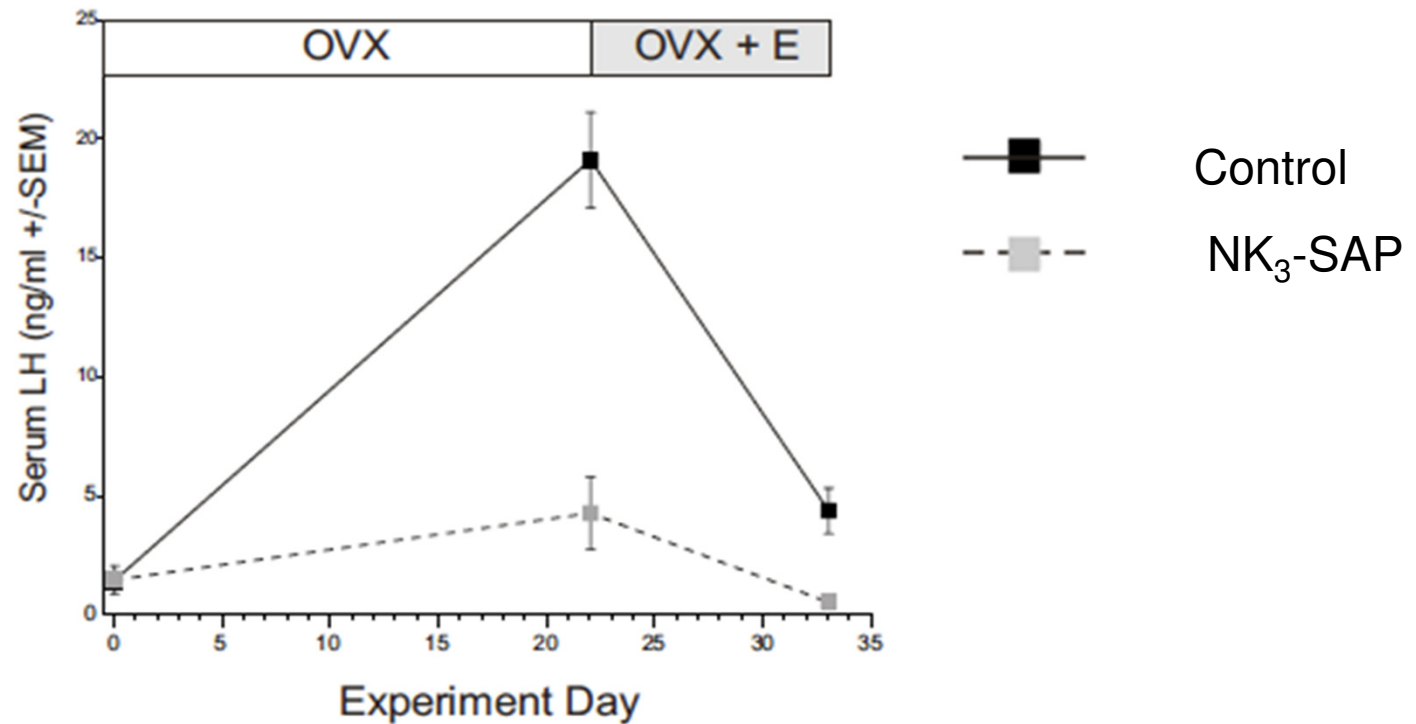
Krajewski et al, Neuroscience 2010, Dacks et al., Endocrinology 2011

Effect of KNDy neuron ablation on LH secretion



Mittelman-Smith et al., Endocrinology. 2012

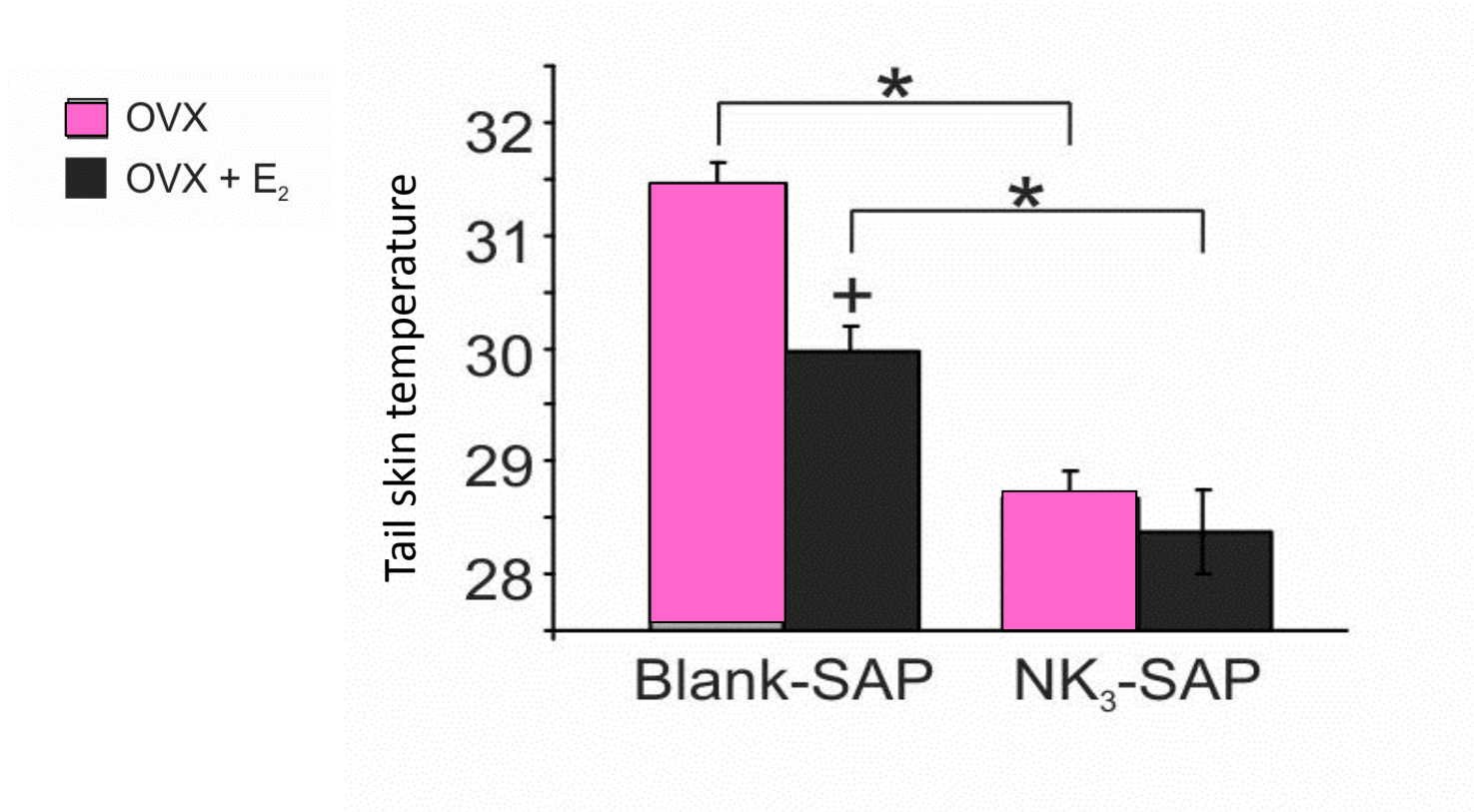
Effect of KNDy neuron ablation on LH secretion



Mittelman-Smith et al., Endocrinology. 2012

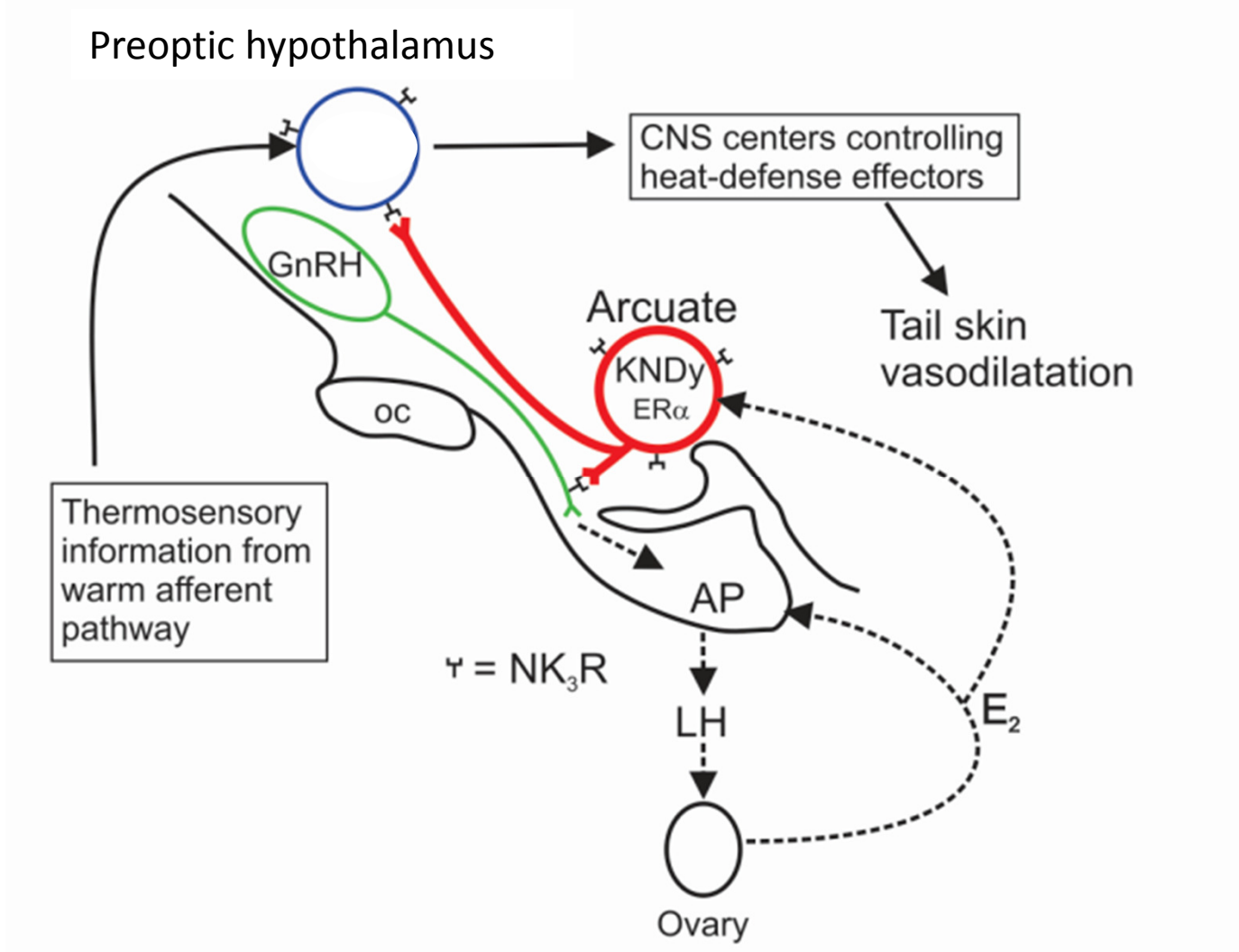
Ablation of KNDy neurons results reduced tail skin temperature.

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



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