

Polypeptide May Help Trigger Ovulation

➤ Gonadotropin-releasing hormone (GnRH) neurons form the final neural pathway regulating reproduction. As the follicular phase of the female reproductive cycle ends, feedback by estradiol on the GnRH neuronal system switches from negative to positive, leading to a surge in GnRH release. This surge boosts luteinizing hormone (LH) release by the gonadotropes of the anterior pituitary, inducing ovulation.

In addition to estradiol, a circadian timing signal also appears to be critical for the surge in some species, but the nature of this signal is unknown. The most likely source is

the central mammalian circadian pacemaker in the suprachiasmatic nuclei. One candidate neuromodulator that may mediate this signaling is vasoactive intestinal polypeptide (VIP).

Suzanne M. Moenter, Ph.D., and Catherine A. Christian, Ph.D, both at the University of Virginia in Charlottesville, examined VIP's effects on the firing activity of GnRH neurons in mouse brain slices at different times of day. They used an ovariectomized, estradiol-treated mouse model that exhibits daily LH surges timed to the late afternoon. Cells from animals not treated with estradiol did not respond to VIP, regardless of time of day. With estradiol

treatment, VIP's effect on GnRH neurons was time-of-day-dependent. VIP increased firing in cells during surge onset, but this response was reduced at surge peak; in separate experiments, introducing a VIP receptor antagonist decreased GnRH neuron firing during the surge peak.

These findings indicate that both estradiol and time of day influence GnRH neuron response to

VIP, the researchers say in a paper to be published soon in *Endocrinology*.^{*} They suggest that VIP might produce an excitatory signal from the circadian clock that helps time the GnRH surge. ■

* Christian CA, Moenter SM. Vasoactive intestinal polypeptide can excite gonadotropin-releasing hormone neurons in a manner dependent on estradiol and gated by time of day. *Endocrinology*, in press.

