

## KISSPEPTIN NEURONS AS A MASTER REGULATOR OF MAMMALIAN REPRODUCTION

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Kisspeptin encoded by *Kiss1* gene and its receptor, GPR54, have been considered as a reigning neuropeptide that controls the hypothalamus-pituitary-gonadal axis in mammals. Loss-of-function mutation in *Gpr54* causes severe hypogonadotropic hypogonadism in human and mice, and *Kiss1* KO rats show absolute loss of gonadotropin secretion. There are two major populations kisspeptin neurons located in the rat hypothalamus; namely, the anteroventral periventricular nucleus (AVPV) and the arcuate nucleus (ARC). A mainstream hypothesis is that the AVPV kisspeptin neurons are responsible for the induction of GnRH/gonadotropin surge and the subsequent ovulation, while the ARC kisspeptin neurons are the intrinsic source of pulsatile activity of GnRH neurons, and therefore, the center for the follicular development.

The ARC kisspeptin neurons are characterized by co-expression of other two neuropeptides, such as neurokinin B and dynorphin, and these kisspeptin neurons are recently referred to as KNDy neurons. Neurokinin B and dynorphin have stimulatory and inhibitory effect, respectively, on the periodic activity of KNDy neurons and GnRH/gonadotropin pulsatile secretion. Our recent studies suggest that KNDy neurons are the hub to integrate the signaling induced by the change in physiological statuses in animals, such as puberty and lactation.

Here, we discuss how kisspeptin neurons control reproductive functions via GnRH and gonadotropin secretion under various physiological conditions. We also discuss the possible upstream regulators with implications of our recent studies.