Gonadal sex steroids provide feedback signals to the brain-pituitary axis to maintain gonadotropin secretion within homeostatic boundaries, which supports normal gonadal function, stimulation of Leidig cells and spermatogenesis in males and follicular growth, ovulation and corpus luteum formation in the female. Emerging evidence supports the idea that Kisspeptins and their receptor are part of the hypothalamic circuitry that governs the neuroendocrine reproductive network. KiSS-1 peptide, the natural ligand of GPR54 is a potent secretagogue that governs GnRH pulse amplitude and frequency governing LH and FSH secretion. The Kiss1 gene is a target for regulation by gonadal steroids as well as to changes in energetic resources or signals of energy availability (e.g. leptin) and allows for adjustments of the kisspeptin in response to real-time changes in energy availability. Kiss1 neurons in the arcuate nucleus are implicated in the sex steroid-dependent negative feedback control of gonadotropin secretion, whereas Kiss1 neurons in the anteroventral periventricular nucleus may be involved by positive feedback in generating the preovulatory GnRH/LH surge. In human volunteers, the acute intravenous administration of kisspeptin increases plasma LH and FSH levels. In infertility due to hypothalamic amenorrhea, acute administration of kisspeptin results in stimulation of reproductive hormones.