

GnRH secretion through kisspeptin signaling, and dynorphin (*Dyn*), which plays an inhibitory role in GnRH control, are frequently co-expressed with *KISS1* in *KNDY* neurons of the median eminence that project to GnRH neurons. This system is intimately involved in both estrogen and progesterone negative feedback regulation of GnRH secretion.

RFamide-related peptides (RFRPs) are the mammalian orthologues of gonadotropin inhibitory hormone (GnIH), which was initially discovered in the quail. While RFRP-1 and RFRP-3 neurons send axonal projections to GnRH neurons in humans and RFRPs are secreted into the pituitary portal system, further studies are required to determine their potential physiologic role in the human.

■ OVARIAN STEROIDS

Ovarian steroid-producing cells do not store hormones but produce them in response to FSH and LH during the normal menstrual cycle. The sequence of steps and the enzymes involved in the synthesis of steroid hormones are similar in the ovary, adrenal, and testis. However, the enzymes required to catalyze specific steps are compartmentalized and may not be abundant or even present in all cell types. Within the developing ovarian follicle, estrogen synthesis from cholesterol requires close integration between theca and granulosa cells—sometimes called the *two-cell model for steroidogenesis* (Fig. 392-6). FSH receptors are confined to the granulosa cells, whereas LH receptors are restricted to the theca cells until the late stages of follicular development, when they are also found on granulosa cells. The theca cells surrounding the follicle are highly vascularized and use cholesterol, derived primarily from circulating lipoproteins, as the starting point for the synthesis of androstenedione and testosterone under the control of LH. These steroid precursors cross the basal lamina to the granulosa cells, which receive no direct blood supply. The mural granulosa cells are particularly rich in aromatase and, under the control of FSH, produce estradiol, the primary steroid secreted from the follicular phase ovary and the most potent estrogen. Theca cell-produced androstenedione and, to a lesser extent, testosterone are also secreted into peripheral blood, where they can be converted to