

Timeline: the role of kisspeptins in reproductive biology

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Although the focus of this issue is on contributions published over the past three to four years, the discovery of the kisspeptins was hailed as an important breakthrough by our advisors so frequently that we had to include it. Manuel Tena-Sempere guides us on a tour of the key findings that have shaped this blossoming field.

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KISS1 is found to be a metastasis suppressor in melanoma cell lines with different invasive capacities¹.

GPR54, an orphan receptor related to galanin receptors, is cloned from rat brain³.

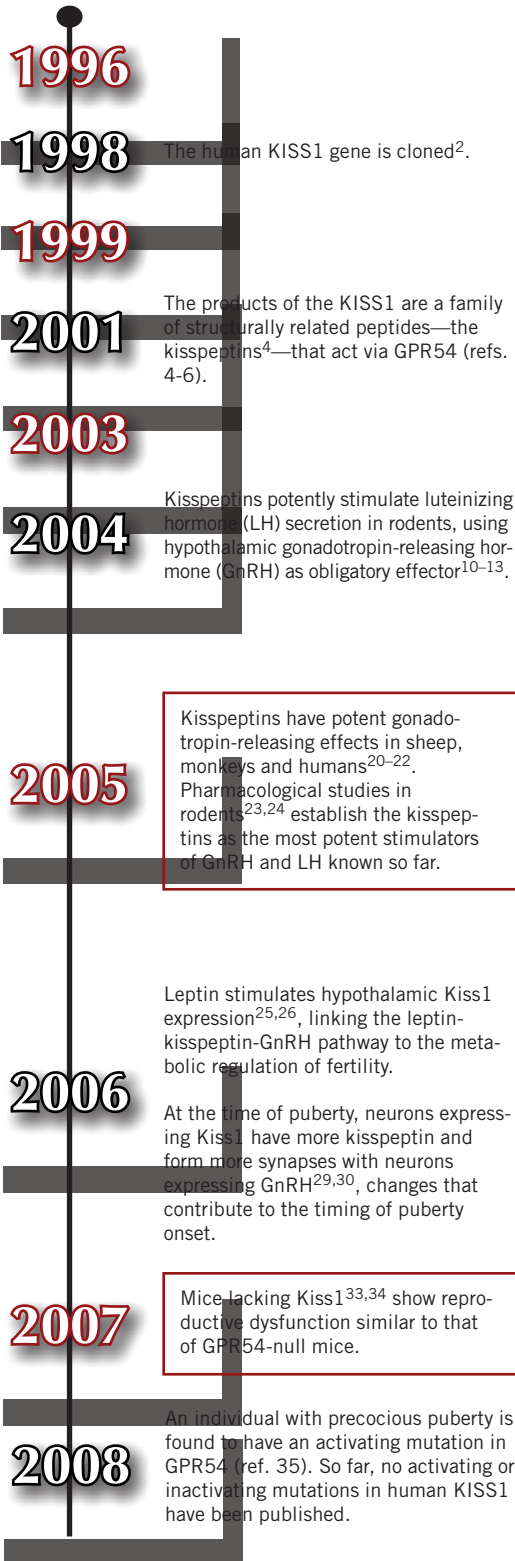
Mutations of GPR54 cause idiopathic hypogonadotropic hypogonadism in humans^{7,8}. Mice that lack GPR54 phenocopy the human disease^{8,9}.

Neurons expressing Kiss1 in the arcuate nucleus of the hypothalamus are suggested to mediate the inhibitory effects of sex steroids on gonadotropin secretion in rodents^{14,15}, a phenomenon later shown in sheep, monkeys and humans^{16–18}.

Adverse metabolic conditions such as fasting depress the hypothalamic expression of Kiss1, an effect linked to suppressed puberty¹⁹. Kisspeptin treatment rescues delayed puberty induced by chronic malnutrition in rats¹⁹.

A subset of hypothalamic neurons expressing Kiss1 in the anteroventral periventricular nucleus is crucial for the stimulatory effects of estrogen and for the preovulatory surge of gonadotropins^{27,28}—the hormonal trigger of ovulation.

Neurons expressing Kiss1 are sexually dimorphic, a feature that involves the effects of sex steroids during early key periods of brain sex differentiation^{31,32}.



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