KISSPEPTINS REGULATE FISH REPRODUCTION

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Gonadotropin-releasing hormone (GnRH) is the primary regulator of vertebrate reproductive functions. We have cloned novel genes that are emerging as important regulators of GnRH and the reproductive axis, kiss1 (encoding Kisspeptin-1), kiss2 and their G-protein coupled Kisspeptin receptors (kissr1 and kissr2), in non-mammalian vertebrates, the teleost. In the zebrafish, kiss1 mRNA expression was observed in the ventral habenula, and kiss2 mRNA expression was observed in the posterior tuberal nucleus and the periventricular hypothalamic nucleus. Laser capture microdissection coupled with real-time PCR showed kissr1 mRNA expression in the ventral habenula, while kissr2 mRNA expression was seen throughout the brain. Luciferase-reporter assay showed higher response of zebrafish Kiss-R1 to Kiss1 and that of zebrafish Kiss-R2 to Kiss2. The expression pattern of kiss1, kiss2, gnrh2 and gnrh3 mRNA levels were significantly increased at the start of the pubertal phase, suggesting regulatory roles of kisspeptins on GnRH neuron types during sexual maturation, which is supported by the expression of Kiss-R2 in the three GnRH neuron types (GnRH1, GnRH2 and GnRH3) in the tilapia. Using double-label in situ hybridization, we showed co-expression of kissr1 and kiss1 mRNAs in the ventral habenula. Further, central administration of Kiss1 significantly decreased the amount of kiss1 mRNA, while increased kissr1 and c-fos mRNA in the ventral habenula. These observations suggest that Kiss1 is autoregulated through Kiss-R1 in the habenula. In sexually mature female zebrafish, Kiss2 but not Kiss1 administration significantly increased β-subunit of gonadotropins mRNA levels in the pituitary, which suggests that hypothalamic Kiss2 is the predominant regulator of gonadotropin synthesis in teleosts. Hence the regulation of reproduction by the hypothalamic Kisspeptin-Kiss receptor-GnRH system is well conserved in vertebrates.