SEX DIFFERENCES IN ESTROGEN AND ANDROGEN SIGNALING IN THE MEDAKA BRAIN

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Introduction:

Sex differences in the mammalian and avian brain are organized early during development as a result of a combination of hormonal and genetic events [1-3, 9]. This is an irreversible process, and thus the sex of the brain is permanently fixed. In contrast, the phenotypic sex of teleosts, including sex-specific reproductive behavior, can be manipulated by treatment with exogenous steroid hormones, even after reaching sexual maturity [10]. Furthermore, quite a few teleost species can spontaneously change their phenotypic sex in response to social and physiological events, even in adulthood [7]. These phenomena suggest that teleosts have an unknown, unique mechanism of brain sexual differentiation, which enables them to hold remarkable sexual plasticity throughout their lifetime. To dissect the molecular basis of sexual differentiation of the teleost brain, we examined sex differences in estrogen and androgen signaling in the brain of medaka *Oryzias latipes*.

Methods:

We searched for genes differentially expressed between the sexes in the medaka brain. One of the genes identified in the screen was that encoding the brain-predominant form of aromatase, the rate-limiting enzyme in the conversion of androgen to estrogen [4-6, 8]. Since estrogen and androgen are known to exert profound influences on sexual differentiation of the mammalian and avian brain, the aromatase gene was selected for further analysis of expression in the medaka brain. We also examined sex differences in the expression of nuclear receptors for estrogen and androgen in the medaka brain to assess the possible involvement of these receptors in sexual differentiation of the teleost brain.

Results:

The medaka aromatase gene was found to be expressed at higher levels in the female than male brain. Estrogen and androgen receptors also exhibited sexual dimorphism in the medaka brain, with each receptor having a discrete pattern of sex-biased expression. Detailed expression studies led to the identification of sex-specific action sites of aromatase, estrogen, and androgen in the medaka brain. We also found that the expression of aromatase and estrogen and androgen receptors in the medaka brain was not under the direct control of sex chromosome genes but relies mostly, if not solely, on steroid hormones.

Conclusion:

Sex differences in the expression of aromatase, estrogen receptors, and androgen receptors in the brain and their steroid-dependent regulatory system supposedly contribute substantially to the mechanisms underlying sexual differentiation and plasticity of the teleost brain.

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