Molecular Mechanisms of Zebrafish Sex Differentiation and Sexual Behavior

av

Ajay Pradhan

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Opponent: Prof. Svante Winberg
Institutionen för neurovetenskap
Uppsala Universitet

Örebro universitet
Institutionen för naturvetenskap och teknik
Fakultetsgatan 1
701 82 Örebro
Abstract


The master regulator gene Sry on Y chromosome in mammals controls the switch for initiating the male differentiation pathway. In some species, apart from genetic intervention, environmental factors also play a crucial role in sex determination whereas in other species like zebrafish, the presence of sex chromosomes is not reported and sex differentiation relies on a multitude of genetic cues. Zebrafish gonadal differentiation initiates with the onset of a juvenile ovary stage and depending on the influence of unknown genetic factors either maintains oocyte development or undergoes apoptotic processes to override the female differentiation pathway. Induction of survival signals through heat-killed bacteria (HK) activated NF-κB and prostaglandin synthase 2a (ptgs2a) whereas male specific genes like sox9a and amh were down-regulated. Long term exposure of HK resulted in a female biased sex ratio. Exposure studies with a NF-κB activator, sodium deoxycholate (DOC), also resulted in higher female sex ratio. Apoptotic signal induction by NF-κB inhibitor NAI resulted in male biased sex ratio suggesting that survival signal is crucial for maintaining juvenile ovarian stage. Up-regulation of ptgs2a in response to survival signal suggested a role of prostaglandin synthases and prostaglandins in sex differentiation. The inhibition of PtgS2 by meloxicam resulted in a male biased sex ratio. On further evaluation, the prostaglandin PGE2 was found to be involved in ovarian differentiation while PGD2 was involved in testis differentiation. Primordial germ cell (PGC) number can determine the ovarian fate in zebrafish and Retinoic acid (RA) is an important regulator of PGC. Inhibition of RA biosynthesis by WIN 18,446 disrupted spermatogenesis and fecundity which indicates that RA is involved in maintenance of gonadal germ cells. Gonadal hormones and the brain have interlinked circuits to regulate secondary sexual characters including sexual behavior. Prostaglandins are known to influence sexual behavior which led us to investigate the effects of hormones and prostaglandins. Estradiol treatment resulted in suppression of sexual behavior in males while it had no noticeable effect on females. Androgen (11-KT) treatment resulted in male typical behavior in females without affecting behavior in males. However, PGE2 and PGD2 did not to alter behavior in both males and females.

Keywords: NFκB, prostaglandin, retinoic acid, gonads, gene regulation, brain

Ajay Pradhan, School of Science and Technology, Örebro University, SE-701 82 Örebro, Sweden, e-mail: ajay.pradhan@oru.se