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Biosensor zebrafish comes to the rescue to study effects of steroids and endocrine disruptors on brain development

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Unlike other vertebrates, fishes exhibit a remarkable sexual plasticity supported by a unique feature, the presence of two aromatase genes: *cyp19a1a* encodes ovarian aromatase that plays a crucial role in gonadal differentiation, while the cyp19a1b gene encodes brain aromatase, which provides brain plasticity. We showed that, in zebrafish, cyp19a1b is strongly expressed in a unique brain cell type, the radial glial cells (RGC) that persist throughout life and act as progenitors, allowing the brain to constantly keep growing. The link between the two aromatase genes is provided by the fact the cyp19a1b gene is extremely sensitive to estrogens, and thus aromatizable androgens, through a mechanism that requires a well conserved ERE. This feature not only makes cyp19a1b sensitive to circulating steroids, but also allows to use zebrafish tg (cyp19a1b-GFP) to monitor the presence of xenoestrogens in a very robust and sensitive way (EC50 estradiol 0.48 nM). By quantifying GFP expression in live fish, we show that short-term exposure of tg (cyp19a1b-GFP) embryos from 0 to 120 hpf to estrogenic compounds turns on cyp19a1b driven GFP expression. Some, but not all, androgens and progestagens also up regulate GFP expression, demonstrating the capacity of the brain to metabolize these compounds into estrogens. We have also evidenced that estrogens modulate the neurogenic activity in adult, probably allowing remarkable brain plasticity, but also indicating that abnormal exposure of fish embryos to any estrogenic endocrine disruptors is likely to affect the neurogenic process.

Biography

Olivier Kah received his Doctor in Sciences Degree at the University of Bordeaux in 1983 and is a Research Director at the French National Centre for Scientific Research (CNRS). For 35 years, he has been interested in the central regulation of reproduction, working mainly in fish. More recently, his team focuses on the roles of sex steroids and endocrine disruptors in the development and plasticity of the brain in zebrafish. He has published around 180 papers cited more than 6500 times (h index 48) and has given over 100 invited lectures. He is the current President of the International Federation for Fish Endocrinology and of the French Research Network in Animal and Human Reproduction. He serves as an Editor for *Endocrinology and Frontiers in Neuroendocrine Sciences*.

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