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Strengths and limits of transgenic zebra fish models to study the expression and the perturbation of steroidogenic genes by endocrine disrupting chemicals.

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Small fish species such as zebrafish (Danio rerio) are well-recognized models to identify Endocrine Disrupting Chemicals (EDCs), quantify their effects and explore their modes of action. Transgenic zebrafish models can provide reliable and suitable tools to assess EDCs while reducing the costs and the number of animals. The present work intends to review data recently obtained on new transgenic models that we developed to study the expression and the perturbation of several target genes involved in the biosynthesis of hormones and known to be affected by EDCs. These new transgenic lines express either fluorescent (Green or Red Fluorescent Protein) or luminescent (luciferase) proteins under the control of zebrafish promoters of steroidogenic genes coding for Cyp11c1 (11β-hydroxylase), Cyp19a1a (Aromatase A) or Cyp19a1b (Aromatase B). These genes are known to be expressed in various steroidogenic tissues and to play critical roles in the biosynthesis of glucocorticoids, androgens and estrogens. Using in vivo fluorescence imaging techniques on whole organisms, tissue sections and immunostaining with specific antibodies, transgenes were fully characterized at the cellular and tissue levels demonstrating that the fluorescent reporters perfectly mimic the endogenous protein expressions. At embryo-larval stages, cyp19a1b is expressed in radial glial cells of developing brain while no expression of cyp19a1a and cyp11c1 was found in brain. At these stages, GFP under the control of cyp11c1 promoter was detected in the inter-renal cells. In adults, cyp11c1, cyp19a1a and cyp19a1ab were expressed in gonads of males and females. Exposures of these lines to different compounds revealed a differential regulation depending on the promoter. Given the high auto-fluorescence of some tissues and/or some cells, recoding the reporter fluorescence can be difficult to perform but can be overcome by using luciferase reporter. These newly developed transgenic lines provide relevant models that allowed us to acquire new data on the expression of key steroidogenic genes in zebrafish and their perturbation by endocrine active compounds.

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