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NRP Endocrine Disruptors

Intermediate Summary

Mechanisms of action of (xeno)estrogens on the early development and differentiation of brain and gonads in zebrafish (XEBRA)
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English Summary

Mechanisms of endocrine disruption in zebrafish

Alterations in sexual development have been observed in fish as effects of exposure to chemical compounds which interfere with the endogenous hormone system by mimicking natural hormones (e.g. (xeno)estrogens) or by imbalancing the hormone synthesis. The mechanisms underlying these effects are not well understood and are studied in this project using zebrafish as a model.

Project description:

Research questions
In this project we focus on the two aromatase isoforms of zebrafish, cyp19A1 and cyp19A2, which are mainly expressed in the gonad and the liver, respectively. These cyp19 genes are (xeno)estrogen target genes and are major players in maintaining the correct hormone balance in time and in the various tissues. In the first period of the project we have adressed the following main scientific questions:
1) Where, when and to what extend are the two cyp19 genes expressed in brain and gonads during normal development?
2) What is the effect of (xeno)estrgens exposure on their developmentally-related expression?

Results
In order to be able to answer the questions, we first developed and implemented methods which would allow us to quantify cyp19 expression in time and in the various tissues and localize cyp19 expression in the tissues. Because of high homology between the two cyp19 genes, and their encoded proteins, this was a difficult task. During the first period of this project we have developed gene-specific tools. Using these tools, we were able to localize CYP19A2 protein in the brain. CYP19A2 expression was found in the telencephalon and the olfactory bulb; the staining was localized not in neurons but in radial glial cells. We do not have indications that the localization of cyp19A2 expression is changed upon exposure to estrogens. We and others expect that Cyp19A1 is mainly expressed in the follicle cell layer in

the gonads, we are currently confirming this. Surprisingly, we also found CYP19A1 expression in neuromasts. Function of CYP19A1 in neuromasts and influence of disturbed expression is currently investigated.
During this first project period, we also have determined the time windows which are important for sexual differentiation and which represent potential xeno-estrogen sensitive developmental periods. This allows us to focuss our work on these periods during development.

Perspectives
Having the tools and baseline knowledge on the ontogeny of sexual differentiation and of the aromatase system in zebrafish, our follow-up project will take advantage of this progress and focus on the physiological role of the two cyp19 genes during sexual differentiation, on the role of these two genes during (xeno)-estrogen exposure, how the expression of these genes is regulated and what the function of the different estrogen receptors is in these pathways.