

## NRP Endocrine Disruptors

### Final Summary

Original project title
<b>Mechanisms of action of (xeno)estrogens on the early development and differentiation of brain and gonads in zebrafish</b>
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<b>4050-066552</b>

#### **Influence of (xeno)estrogens on the sexual development in zebrafish**

*This project was mainly focused on the role of aromatases in the sexual development and the differentiation of sensory neurons in zebrafish. The enzyme CYP19-aromatase (zebrafish has two different ones) converts in a single step androgens into estrogens. Hence expression and precisely regulated presence and activity of aromatases are expected to play a prominent role in sexual and neuronal development.*

#### **Research questions**

- 1) When in the development and in which tissues is the enzyme aromatase active in the zebrafish?
- 2) Do environmental pollutants with endocrine activity disturb the normal aromatase activity patterns and what consequences does that have?
- 3) What is the role of aromatases during embryonic zebrafish development?
- 4) How is synthesis of aromatase regulated, how disregulated by pollutants?

#### **Results**

- 1) Zebrafish have two aromatases which are expressed in the gonads (Cyp19a1) and in the brain (Cyp19a2). We have identified the specific sites in the brain where Cyp19a2 is present. These sites give a hint towards the possible function the aromatases have. Presence and activities of the aromatases get disturbed (in time and total activity) in the presence of (xeno)-estrogens.
- 2) Contrary to what was expected we could not assign a role to the brain-located aromatase in the sexual development. The sexual development in zebrafish is most probably a multifactorial process.
- 3) We could show for the first time that aromatases play a role in the differentiation of neuromasts (lateral line organ).

- 4) Aromatases are not multi-chemical target genes. Only a selection of environmental pollutants may disturb their activities and by that influence developmental processes.
- 5) We now understand and can explain the contradictory results in the literature in which both estrogenic and anti-estrogenic activities have been assigned to dioxins.

### Perspectives

We have identified that aromatases play a major role in developmental processes. Future activities are directed to better understand these processes and the key factors involved.

We have learned that sexual differentiation is most probably a multi-factorial process in zebrafish. Research projects will be directed to identify the key factors in sexual development.