Abstract

Ontogeny of steroid and thyroid hormone metabolism gene transcription during zebrafish embryo-larval development

Jelena Periz-Stanaćev¹, Evelyn Stinckens¹, Ellen D. G. Michiels¹, Isabelle J. Gabriëls¹, Casper Pype², Evy Verbueken², Steven J. Van Cruchten², Alexander L. N. van Nuijs³, Lucia Vergauwen^{1,4}, Dries Knapen¹

 ¹ Zebrafishlab, Veterinary Physiology and Biochemistry, Department of Veterinary Sciences, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium
² Applied Veterinary Morphology, Department of Veterinary Sciences, University of Antwerp, Universiteitsplein 1, 2610 Wilrijk, Belgium

³ Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Universiteitsplein 1, 2610, Wilrijk, Belgium

⁴ Systemic Physiological and Ecotoxicological Research (SPHERE), Department of Biology, University of Antwerp, Groenenborgerlaan 171, 2020 Antwerp, Belgium

The zebrafish is a valuable vertebrate model to study development as well as impairment of normal development. Studies have shown that steroid and thyroid hormones have a role in early development, but available information is still limited and fragmented.

In this study we describe the normal embryonic and larval transcriptional profiles of the thyroid and steroid hormone synthesis machinery and associated receptors, which has never been done so far. We isolated RNA at 25 time points between 0 and 32 days post fertilisation of zebrafish development covering the most important events during the embryonic and larval stages. We quantified mRNA levels of 21 genes involved in the steroidogenic pathway and 9 genes important for the thyroid system using QPCR.

Our results show that some of the enzymes and receptors, like $hmgcr\beta$, cyp17a1, *cyp11a1, hsd17b3, hsd20b2, esr2a, ar, thrb* and *thraa* are maternally transferred. This suggests an important role of steroid and thyroid hormones in programming the earliest stages of zebrafish development before the embryo's genome is activated around 3hpf (hours post fertilisation). Further, we observed distinct transcriptional patterns for different nuclear estrogen receptors during development. *Esr1* is abundantly transcribed from the time of embryonic genome activation, transcription of *esr2b* increases during the formation of the immature gonad and transcription of esr2a increases during gonad differentiation. Interestingly, the relative transcript levels of isozymes *hmgcr/hmgcrβ and cyp11a1/cyp11a2* change during development. Possibly one is required for early development, whereas the other is important for later development. *Dio3b* has the highest expression of all deiodinases during the first 12 days. Transcription of *dio1* increases at 120hpf and this level is maintained during the entire larval period. This may be related to inflation of the swim bladder around this time point.

These results will improve our fundamental understanding of the role of steroid and thyroid hormones during early life stages of the zebrafish and will be broadly applicable to the zebrafish research community.