

Computational Model of Steroidogenic Pathways in Fish Gonads

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Exposure to endocrine disrupting compounds (EDC) can induce adverse effects on reproduction mediated through alterations in the enzymes involved in steroidogenesis. We are developing a computational model of the intratesticular and intraovarian metabolic network that mediates steroidogenesis to identify and link new molecular biomarkers of exposure to effects for EDCs. The mathematical model describes the biosynthetic pathways for the conversion of cholesterol to the primary steroid hormones (testosterone, estradiol, and 11-ketotestosterone) secreted by the testes and ovaries in fish. The model includes the intermediate molecules and reactions for the multiple pathways involved in the biosynthesis of the primary steroid hormones. The initial concentrations and enzyme kinetic reaction rates were taken from the literature or set to biologically reasonable values. Computer simulations were performed to examine the predicted time-varying steroid concentrations, and compared with the limited amount of available, relevant experimental data. This model allows for an improved understanding of the source-to-outcome linkages necessary for effective use of molecular biomarkers for risk assessments with EDCs. Since the biosynthetic pathways for steroid hormones are to a significant extent evolutionarily conserved, this computational model is likely to also be relevant for mammalian species. *This work was reviewed by the U.S. EPA and approved for publication but does not necessarily reflect Agency policy.*