

**Computational Modeling of Steroidogenesis
to Predict Molecular Responses to Endocrine Disruptors**

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There is increasing evidence that exposure to endocrine disrupting chemicals (EDCs) can induce adverse effects on reproduction and development in both humans and wildlife. Some of these adverse effects elicited via disturbances to tightly regulated endocrine pathways, can be mediated through inhibition of the enzymes involved in steroidogenesis. We are developing a mechanistic mathematical model of the intratesticular and intraovarian metabolic network of steroid synthesis, and the kinetics for enzyme inhibition by EDCs, in order to predict the molecular response. The deterministic model describes the biosynthetic pathways for the conversion of cholesterol to the steroid sex hormones and the gamete maturation inducing hormones secreted by the gonads in fish. The model includes intermediate metabolites and enzymatic reactions for the pathways involved in steroidogenesis. Computer simulations were performed to compare the model-predicted responses with experimental data. Preliminary results show that model-predicted plasma concentrations of sex steroids are comparable to *in vivo* baseline data. Application of the model should improve our understanding of the dynamic dose-response behavior at the molecular level, and aid the identification of biomarkers that are indicative of potential adverse effects at the individual and population levels. *This work was reviewed by the U.S. EPA and approved for publication but does not necessarily reflect Agency policy.*