

Track: Aquatic Toxicology and Ecology

Session: Quantitative adverse outcome models and in vitro - in vivo extrapolation

Title (150 characters including spaces)

Modeling a Molecular Initiating Event to Population Effects: A case study of aromatase inhibition in fathead minnows

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Abstract (2500 char including spaces)

An adverse outcome pathway (AOP) conceptually links a molecular initiating event with measureable key events at higher levels of biological organization that ultimately result in an adverse outcome. Development of an AOP requires experimental data and scientific expertise to identify key events that occur en route to an adverse outcome. However, realistic scenarios where an adverse outcome may be observed in the environment will not be limited to the test conditions that were used in experimental studies. As such, it would be useful to have a predictive, quantitative tool that can simulate a wide range of conditions to better understand how sensitive the adverse outcome is to different degrees of molecular initiation (e.g., competitive inhibition of an enzyme, or different ligand-receptor binding affinities) or key events. To illustrate some of these ideas and create a quantitative AOP model, we linked three computational models that represent different levels of biological organization: the hypothalamic-pituitary-gonadal (HPG) axis; oocyte growth dynamics; and a population dynamics model. We simulated aromatase inhibition in fathead minnows exposed to fadrozole, a model aromatase inhibitor with an HPG axis model that predicted plasma vitellogenin concentrations as a function of time. The time course of predicted plasma vitellogenin concentrations was input into the oocyte growth dynamics model to predict clutch sizes and spawning intervals which were then used as input into the population dynamics model. We then investigated the sensitivity of population dynamics to changes in aromatase inhibition by simulating exposure to different fadrozole concentrations that were tested experimentally. At the highest concentration of fadrozole tested experimentally, spawning was curtailed. The case study was able to explore how mild to severe reductions in fecundity affected population dynamics. *This abstract does not necessarily reflect US EPA policy.*