Presentation Type:
Platform Preferred

Track:

Session:

Abstract Title:

A compendium of transcriptomic effects of endocrine disrupting chemicals on the fathead minnow ovary

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Abstract:

Understanding potential hazards of chemicals released into the environment is challenging not only due to the large and growing number of chemicals and materials that need to be screened, but also to the bioavailability, exposure conditions, and species differences among others. Examining effects on critical pathways resulting in adverse outcomes of interest such as reduced reproduction provides a broader measure of the potential hazards of a chemical. Effective mining of complex relationships, effects and potential impacts can be gained through meta-network analyses derived from expression data. The Hypothalamus-Pituitary-Gonadal (HPG) Axis is an evolutionarily conserved endocrine pathway principally responsible for the control of reproduction. Measuring impacts of chemicals on the HPG axis provides a functional measure of the chemical's reproductive hazards. Therefore, analysis of steroidogenesis and the biological elements controlling it can be used to understand chemical effects and key events leading to adverse reproductive outcomes. Here, we used network inference approach to investigate the impacts of chemicals on steroidogenesis. Fathead minnows (*Pimephales promelas*) were exposed to known endocrine disruptors and impacts on steroidogenesis were examined through network analysis of a large compendium of ovarian gene expression and hormone data sets. The compendium contained 1,472 microarrays, with data from twenty-three different in vivo exposure experiments encompassing 13 different chemicals, 1 complex mixture, 5 ovary stages, multiple time points, and multiple chemicals doses. Transcriptional networks were obtained from two different sources: 1) all 23 exposures and 2) seven individual chemicals (fadrozole, flutamide, prochloraz, trenbolone, vinclozolin, trilostane, and ketoconazole). Gene networks inferred by both approaches were consistent with minor differences and both were able to detect important interactions from genes involved in reproduction and development pathways (such as

estrogen and progesterone signaling). Common interactions between the combined and individual networks can offer insights about the common mechanism whereas the difference in the interactions can provide the specific chemical effect.