

The Use of MS-based Metabolomics to Determine Markers Associated with Endocrine Disruption in Small Fish Species

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Endocrine disrupting chemicals (EDCs) are exogenous substances that disrupt the physiological function of endogenous hormones. In fish, these xenobiotics are capable of interfering with the dynamic equilibrium of the hypothalamic-pituitary-gonadal (HPG) axis resulting in adverse effects on the reproductive system such as impaired gonadal development, decreased fecundity, and reduction in fry survival. In order to assess the impacts of EDCs on the reproductive function of exposed fish species, we selected the fathead minnow (*Pimephales promelas*) (FHM) as a model organism. Gonadal tissues collected from male and female FHMs were prepared for mass spectrometry-based metabolomic analyses where specific molecules that have previously been shown to be impacted by EDCs were targeted for detection, identification, and quantification. These molecules included estradiol, estrone, estriol, testosterone, progesterone, pregnenolone, and cholesterol. Additionally, a discovery-based mass spectrometry (MS) approach was developed in order to identify differentially expressed metabolomic profiles specific to EDC exposures. Overall, this research demonstrates the use of an MS-based approach for assessing classes of metabolites in FHM that are not readily measured using other analytical platforms. In particular, the sensitivity afforded by an MS-based approach will allow for the detection of endogenous steroids that are often crucial to understanding the mode of action (MOA) of a particular EDC. This information will be used to link molecular responses to whole animal outcomes for use in the refinement and development of predictive models of toxicity. Use of such models should improve the efficiency of current testing of EDCs, thus streamlining the risk assessment process used in making regulatory decisions.

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