Role of Steroid Ligand Transformation in Chemical-Caused Alterations of Endocrine Functions

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Normal reproductive development depends on the interplay of steroid hormones with their receptors at specific tissue sites. Agents interfering with this process can elicit malformation or malfunction in the reproductive tract or other organs that rely on steroids to maintain normal physiology. Altered steroid biotransformation is a possible mechanism for chemical-induced developmental toxicity. The objective of this project is to evaluate the impact of steroid ligand modification by chemicals that change biotransformation enzymes. Studies are conducted to test the hypothesis that metabolism of endogenous steroid hormones can be altered following exposure to exogenous chemicals and that perturbed hormone bioavailability can lead to impaired reproductive development. We have demonstrated that many exogenous compounds are able to alter the expression of enzymes that are involved in hydroxylizing and conjugating steroid hormones. Such enzyme effects are frequently mediated by xenobiotics-inducible transcriptional factors such as the nuclear receptors constitutive androstane receptor (CAR) and pregnane X receptor (PXR). While our research has provided some important linkage between xenobiotic exposure, enzyme induction, and steroid elimination from the body, it has also suggested that there are likely many adaptive responses the body utilizes to maintain the bioavailability of steroid hormones at their target sites.

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Presentations:


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