Characterization of Chemical Interactions with the Estrogen and Androgen Steroid Hormone Receptors

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Environmental chemicals capable of interacting with the estrogen and androgen steroid hormone receptors represent a wide range of chemical structures all capable of inducing unique conformational changes in the receptor with which they interact. The unique steroid hormone receptor conformations induced by these chemicals are likely to manifest unique biological activity. In addition, many chemicals are capable of interacting with more than one steroid hormone receptor. The biological and toxicological result of multiple steroid receptor interactions together with the unique receptor activities induced by a chemical remains to be determined. The proposed studies use a mechanism-based approach to determine the steroid hormone-responsive activities of environmental chemicals and to correlate activity with biological response. We will use a series of in vitro assays as well as in vivo studies to link chemical interaction with estrogen receptor (ER)α, ERβ, and androgen receptor (AR) steroid receptors with changes in gene expression regulation and the ultimate biological response. Reporter gene assays will be used to isolate high affinity peptides specific for chemically liganded estrogen and androgen receptors. These peptides will be used as highly specific steroid receptor antagonists. Human estrogen-responsive ECC-1 endometrial carcinoma cells will be analyzed for unique differences in gene expression following treatment with estradiol, bisphenol A, HPTE, or genistein. In vivo experiments will utilize both male and female pups from exposed mothers to identify estrogenic and antiandrogenic responses. Together, these studies will provide a mechanistic-based understanding of endocrine-active chemicals, linking receptor conformation with gene expression regulation and biological response.


Presentation(s):


Gaido, K. W. (2001). Altered gene profiles in fetal rat testes exposed to di(n-butyl)phthalate in utero. Invited presentation at Texas A & M University, College Station, TX, March 5.

Gaido, K. W. (2001). Identifying the molecular basis for di(n-butyl)phthalate’s effects on the developing male rat reproductive tract. Invited presentation at West Virginia University Medical Center, Morgantown, WV, October 8.


Peer-reviewed publication(s):


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This abstract was prepared by the principal investigator for the project. Please see www.USLRI.org for more information about the LRI.


Other publication(s):


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