Poster #28

Response Element Sequence Determines Xenoestrogen Activation of Estrogen Regulated Reporter Genes

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Environmental estrogens are natural or synthetic compounds in the environment that can mimic the activity of endogenous estrogens in exposed animals. These xenoestrogens specifically bind and activate the estrogen receptor (ER) resulting in the transcription enhancement of estrogen regulated genes. This process involves receptor dimers interacting with specific estrogen response elements (EREs) in the promoter of genes. All EREs are derivatives of the 13-mer palindromic consensus ERE originally identified from the xenopus and chicken vitellogenin genes with the sequence of GGTCAnnnTGACC. While the estrogen activity of many environmental chemicals has been evaluated in a wide range of *in vivo* and *in vitro* assays, the capacity for xenoestrogens to differentially activate genes regulated by nonconsensus EREs has not been well characterized. In this report, we describe the ability of known xenoestrogens to activate reporter genes controlled by consensus and nonconsensus ERE sequences. Transient transfection assays utilizing the luciferase reporter gene controlled by either the vitellogenin ERE or the pS2 ERE (GGTCAnnnTGGCC) were carried out in MCF-7 cells that are known to express wild type human ER-_. Evaluations were performed in the presence of either estradiol-17_ or the xenoestrogens diethylstilbestrol, bisphenol A, o,p'-DDT, p,p'-DDT, p-octylphenol, kepone, methoxychlor or the methoxychlor metabolite HPTE over the dose range of 1 nM to 10000 nM. The dose response activity of estradiol-17_ was found to be similar in both reporter gene systems. All xenoestrogens were able to induce measurable activity in the vitellogenin ERE reporter gene system. However, environmental estrogens induced luciferase activity in the reporter system controlled by the pS2 ERE were higher or lower than that of the consensus ERE reporter system. We conclude that xenoestrogen activity may depend on the specific ERE sequence contained in the promoter of estrogen regulated genes and that the response element specificity of xenoestrogens should be characterized in more detail.