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Quantitative linkages between in vitro assays, molecular biomarkers and traditional toxicity endpoints using the inland silverside *Menidia beryllina*

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Abstract

In vitro cell assays are a rapid and efficient way to screen for chemicals based on their ability to interact with specific cell receptors (e.g. estrogen receptor). The results of these assays could be used to predict toxicity *in vivo*. To do so, it is important to understand the quantitative relationship between *in vitro* responses and adverse effects observed *in vivo*. This study examined the estrogenic potency of four environmental chemicals frequently detected in wastewater effluent, estrone, bisphenol A, p-nonylphenol and galaxolide. *In vitro* assays were conducted using a transactivation estrogen receptor (ER) reporter assay. As expected, estrone was the most potent test chemical while the others had weak estrogenic effects. Two *in vivo* tests were performed using the inland silverside *Menidia beryllina*: a 7-day toxicity test with Menidia larvae developed by the USEPA and a 21-day toxicity test with juveniles developed at the University of Florida. Both tests were conducted using the same four concentrations for each chemical. The toxicity of these chemicals was investigated using traditional endpoints (growth and survival) as well as molecular analyses by qPCR. Responses of the *in vitro* and qPCR assays were observed at lower concentrations compared with traditional endpoints. Our findings highlight the importance of characterizing the relationship between in vitro and *in vivo* assays in order to better estimate the toxicity of chemicals in the environment.