NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM): Assessing the Biological Relevance of \textit{In Vitro} Data: A Case Study Using Estrogen Pathway Signaling

\textbf{Background Material:}

- Using \textit{in vitro} high throughput screening assays to identify potential endocrine-disrupting chemicals. \textit{Environ Health Perspect.} 2013 Jan;121(1):7-14
- Network Model of the Estrogen Receptor Pathway: Integrating a Battery of \textit{In Vitro} HTS Assays (poster)

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Advances in high throughput screening (HTS) and computational toxicology provide the opportunity to evaluate thousands of chemicals for the purposes of screening for bioactivity and risk assessment. NICEATM has been working with U.S. Environmental Protection Agency (EPA) to evaluate the performance of a mathematical model of HTS data from 16 \textit{in vitro} assays that measure estrogen receptor (ER)-mediated bioactivity.

Our efforts have focused on establishing the reliability and biological relevance of this approach as measured against outcomes in the rodent uterotrophic assay, an animal model validated by U.S. EPA and Organisation for Economic Co-operation and Development (OECD) for assessing ER-mediated bioactivity. This evaluation necessitated the development of a database of high-quality uterotrophic test results against which the model output could be compared.

A comprehensive literature search of uterotrophic studies was performed for all 1886 chemicals run in the HTS assays. The search yielded >1000 papers, of which 670 were deemed potentially relevant. These papers were subjected to a quality control review based on six minimum criteria that derived from the EPA OCSPP 890.1600 and OECD 440 Test Guidelines that must be met for a study to be considered “guideline-like” (GL). Model predictions of ER-bioactivity were compared to outcomes of uterotrophic assays, and those results will be presented to the BSC.