

## **Applications of High Throughput Screening to Identify Profiles of Biological Activity**

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ToxCast, the United States Environmental Protection Agency's chemical prioritization research program, is developing methods for utilizing computational chemistry and bioactivity profiling to predict potential for toxicity and prioritize limited testing resources ([www.epa.gov/toxcast](http://www.epa.gov/toxcast)). This presentation will provide an overview of the rationale, design and status of ToxCast. In Phase I, our proof-of-concept component, we have focused upon evaluating chemicals with an existing, rich toxicological database in order to provide an interpretive context for the high throughput screening data. This set of 320 reference chemicals, largely food use pesticides, and represents numerous structural classes and phenotypic outcomes. The in vivo datasets include chronic cancer bioassays in the rat and mouse, multigenerational studies in the rat and developmental toxicity studies for the rat and the rabbit. Bioactivity data is derived from a broad spectrum of nearly 500 readouts from biochemical assays, cell-based phenotypic assays, and model organisms. A variety of supervised and unsupervised computational tools are being used to derive signatures of bioactivity in the in vitro data that are predictive of phenotypic outcomes in the whole animal bioassays. Examples of resulting models will be presented. ToxCast is part of a larger government effort (Tox21) being conducted jointly by EPA, the National Toxicology Program of NIEHS, and the NCGC that is obtaining high throughput screening data on more than 2000 chemicals, with plans to expand to nearly 10000 chemicals in 2009. *This is an abstract of a proposed presentation.*