TITLE: CHEMICAL PRIORITIZATION FOR DEVELOPMENTAL TOXICITY USING LITERATURE MINING-BASED WEIGHTING OF TOXCAST ASSAYS

PRESENTERS: Singh[2] AV, Shah[1] I, Sipes NS[1], Reif[1] D and Knudsen[1] TB

INSTITUTIONS: [1]National Center for Computational Toxicology, US EPA Office of Research and Development and [2]Lockheed Martin.

ABSTRACT: Defining a predictive model of developmental toxicity from in vitro and high-throughput screening (HTS) assays can be limited by the availability of developmental defects data. ToxRefDB (www.epa.gov/ncct/todrefdb) was built from animal studies on data-rich environmental chemicals, and has been used as an anchor for predictive modeling of ToxCast™ data. Scaling to thousands of untested chemicals requires another approach. ToxPlorer™ was developed as a tool to query and extract specific facts about defined biological entities from the open scientific literature and to coherently synthesize relevant knowledge about relationships, pathways and processes in toxicity. Here, we investigated the specific application of ToxPlorer to weighting HTS assay targets for relevance to developmental defects as defined in the literature. First, we systemically analyzed 88,193 Pubmed abstracts selected by bulk query using harmonized terminology for 862 developmental endpoints (www.devtox.net) and 364,334 dictionary term entities in our VT-KB (virtual tissues knowledgebase). We specifically focused on entities corresponding to genes/proteins mapped across of >500 ToxCast HTS assays. The 88,193 devtox abstracts mentioned 244 gene/protein entities in an aggregated total of ~8,000 occurrences. Each of the 244 assays was scored and weighted by the number of devtox articles and relevance to developmental processes. This score was used as a feature for chemical prioritization by Toxicity Prioritization Index (ToxPi), along with ToxCast AC50 values (concentration at half maximal activity). We compared the ToxPi ranking of chemicals anchored to devtox literature with other anchors including ToxRefDB, Zebrafish embryogenesis, and murine Embryonic Stem cell endpoints. Preliminary analysis showed various degrees of correlation among the different anchoring methods.[This abstract does not necessarily reflect EPA policy].