A Computational Framework for Systems-based Analysis of Developmental Toxicity

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   EPA is building capacity for multi-dimensional evaluation of toxicity using information about chemical properties, genome-wide responses, and cell-based assays (www.epa.gov/comptox/). The ToxRefDB database is making toxicity data accessible for correlation with bioactivity profiling data from the ToxCast[TM] research program. Proof-of-concept is underway (Phase I) to test the hypothesis that bioactivity signatures correlated with endpoints from traditional animal testing can be used to predict adverse outcome. Here we describe a new database module for developmental toxicology. Our first objective is to implement a semi-automated data-capture routine that reaches out to databases and resources using a thesaurus of metadata terms. This identifies study records / publications and uses a string of semi-automated steps to fetch, parse, and format associated data. Manual curation is applied for tracking provenance and to confirm categorization on an initial set of Data Evaluation Records from EPA's Office of Pesticide Programs. Our second objective is to develop a Natural Language Processing (NLP) lexicon that flags records holding developmental data and extracts content with logic-based text mining rules. It will be tested on records for the 320 reference chemicals (mostly pesticides) in over 400 high-throughput screening assays for the Phase-I ToxCast project. Traditional developmental toxicity data are fairly complete for these chemicals, and this NLP approach could accelerate and enhance curation of data into ToxRefDB. Correlation of effects in ToxRefDB will be used to identify appropriate phenotypic triggers for a prenatal developmental toxicity study in rats, based upon results from developmental studies in rabbits and reproductive studies in rats. *[This work has been reviewed by EPA and approved for publication but does not necessarily reflect official Agency policy].*