Providing Context for Chemical Effects Through Compound Structure Similarity

B. Cook[1*], J. Abedini[1], S. Bell[1], J. Rooney[1], E. McAfee[2], J. Phillips[2], D. Allen[1], N. Kleinstreuer[3]

[1]ILS, RTP, NC, USA; [2]Sciome, RTP, NC, USA; [3]NIH/NIEHS/DNTP/NICEATM, RTP, NC, USA

The National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) recently expanded the Integrated Chemical Environment (ICE, https://ice.ntp.niehs.nih.gov/). ICE now provides structure-based searching capabilities of curated in vivo, in vitro, and in silico data and other computational tools to facilitate the safety assessment of chemicals. One ICE feature, Chemical Quest, allows users to take a structure-based approach to explore ICE's repository of over 800,000 chemicals, derived from the U.S. Environmental Protection Agency's (EPA's) DSSTox database, through a SMILES similarity search utilizing chemical fingerprints. Chemical Quest can be queried through chemical identifiers (CASRN, DTXSID, SMILES or InChiKey) or by drawing a 2D chemical representation. Chemicals identified as structurally similar can be filtered by Tanimoto score or SMART strings and then imported into any ICE tool. Such tools include "Chemical Characterization" which allows for chemical lists to be compared based on physicochemical properties. Results from queries can also be sent to NTP's Chemical Effects in Biological Systems and the EPA's Chemical and Products Database, providing further options to examine and compare chemicals based on physicochemical properties, bioactivity, and product use categories. ICE Search provides summary information, curated reference data, and bioactivity details for chemicals and mixtures. Concentration-response relationships from curated high-throughput assays can be examined using the Curve Surfer tool. ICE's In Vitro to In Vivo Extrapolation tool translates in vitro bioactivity profiles to estimated equivalent in vivo doses for different exposure routes, while the Physiologically Based Pharmacokinetics tool predicts tissue-level concentrations resulting from in vivo doses. This presentation will use case studies to provide an overview of ICE tools and features for chemical analyses and comparisons through structural similarity. This project was funded with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.