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Applications of High-Information Content Technology in Reproductive and Developmental Toxicology Workshop:

Cheminformatic Approaches in Predictive Toxicology

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High-information content and high throughput screening technologies, along with efforts to improve public access to chemical toxicity information resources and to systematize older toxicity studies, have the potential to significantly improve predictive capabilities in toxicology, including developmental toxicology. Important developments include: 1) large and growing public resources that link chemical structures to biological activity and toxicity data in searchable format, and that offer more nuanced and varied representations of activity; 2) standardized relational data models that capture relevant details of chemical treatment and effects of in vivo experiments; and 3) the generation of large amounts of new data from public efforts that are employing high-throughput screening (HTS) technologies to probe a wide range of bioactivity and cellular processes across large swaths of chemical space. By annotating toxicity data with associated chemical structure information, these efforts link data across diverse study domains (e.g., 'omics, HTS, traditional toxicity studies), toxicity domains (carcinogenicity, developmental toxicity, neurotoxicity, immunotoxicity, etc) and database sources (EPA, FDA, NCI, DSSTox, PubChem, GEO, ArrayExpress, etc.). Public initiatives, such as ToxML and the ILSI Developmental Toxicity Database Workgroup, are developing systematized data models of toxicity study areas and introducing standardized templates, controlled vocabularies, hierarchical organization, and powerful relational searching capability across captured data. Cheminformatics and data models, in turn, are providing the underpinning for the large public HTS efforts of the NIH Molecular Libraries Initiative, as well as new toxicity-targeted HTS programs within the EPA and the NIEHS National Toxicology Program. These initiatives are turning the structure-activity paradigm on its head, using chemicals to probe biological space and generating "biological profiles" of chemicals that, along with chemical structure considerations, offer the promise of providing richer, and more relevant and predictive associations to in vivo responses. *This work was reviewed by EPA and approved for publication, but does not necessarily reflect EPA policy.*