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Risk Assessment: New data initiatives and predictive approaches for mutagenicity and carcinogenicity
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New Chemical/Biological Profiling and Informatics Approaches for Exploring Mutagenicity & Carcinogenicity: Updates of EPA ToxCast™ and Tox21 Programs

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EPA's National Center for Computational Toxicology is building capabilities to support a new paradigm for toxicity screening and prediction through harnessing of legacy toxicity data, creation of data linkages, and generation of new in vitro screening data. In association with EPA's ToxCast™, ToxRef DB, and ACToR projects, the DSSTox project provides cheminformatics support and is improving public access to structure-annotated chemical toxicity information to facilitate modeling, data-mining and read-across approaches. Phase I of EPA's ToxCast™ research project is building on three rich data tiers: 309 unique, structurally diverse chemicals (predominantly pesticides), activity and concentration response data from approximately 500 in vitro (cell-based and cell-free) high-throughput screening (HTS) assays, and extensive in vivo rodent bioassay data extracted from EPA pesticide registration records (entered in EPA's ToxRefDB). Contained within these data tiers are chemicals with mutagenic and non-mutagenic mechanisms of carcinogenicity, target-specific bioassay data for multiple rodent species pertaining to tumorigenicity, and HTS assay results potentially relevant to, and informative of mutagenic and carcinogenic mechanisms in rodents and humans. Highlights of the first ToxCast™ Data Analysis Summit will be presented, along with some preliminary analysis of genetox HTS assays. A future course for broadening the chemical test space, HTS assay coverage, and reference genotoxicity studies contained within ToxRefDB will be described, in the context of both the ToxCast™ programs and the expanded multi-laboratory Tox21 research projects. These efforts, combined with progress in expanding public genotoxicity databases and integrating structure-activity relationship (SAR) approaches, point to exciting prospects for computational toxicology impacting the field of mutagenesis and carcinogenesis. *This work was reviewed by EPA and approved for publication, but does not necessarily reflect EPA policy, nor does mention of trade names constitute endorsement.*

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