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DSSTox Project Update: Supporting Improved Toxico-Chemoinformatics Capabilities

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Efforts to improve public access to chemical toxicity information resources and to systematize older toxicity studies, along with significant amounts of new data being generated from high throughput screening (HTS) technologies, have the potential to significantly improve predictive capabilities in toxicology. The EPA DSSTox project is contributing to these efforts on a number of fronts. Chemical structure annotation is effectively linking data across diverse study domains (e.g., 'omics, HTS, traditional toxicity studies), toxicity domains (carcinogenicity, developmental toxicity, immunotoxicity, etc) and database sources (EPA, NTP, FDA, GEO, etc.). In the past year, the DSSTox project has moved to structure annotate and publish a number of EPA priority chemical lists: IRIS, the High Production Volume Chemicals, Pesticide Actives and Inerts, etc. The DSSTox project has played a key role in producing chemical inventory files for new HTS programs within the NIEHS National Toxicology Program and the EPA ToxCast Program, and in interfacing these efforts to the NIH Chemical Genomics Center and PubChem. Structure annotation of diverse datasets has enabled us to "look across" these datasets in chemical space, generating chemical overlap matrices to identify those chemicals present in multiple databases of EPA and toxicological interest, and to use this information to aid in the selection and prioritization of chemicals for new HTS testing. DSSTox is serving as a source of high quality structure-annotated files for the new ACToR (Aggregated Computational Toxicology Resource) data repository, under development within the EPA NCCT, which will house in an integrated platform multiple domains of toxicologically relevant data. To further promote structure-searching of chemical information within EPA, a publicly available structure-browser is to be hosted on the DSSTox website to enable structure and similarity searching through DSSTox files, with remote searching of a particular DSSTox data file to be made accessible from off-site (e.g., NTP, IRIS, Ecotox). These efforts, in collaboration with a variety of EPA and external public efforts (e.g., ToxML, ILSI, NCI, PubChem), are broadly linking information across the chemical domain, while elaborating the "activity" portion of the SAR paradigm towards the goal of improved prediction capabilities. *This work does not necessarily reflect EPA policy.*