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INNOVATIVE RESEARCH FOR A SUSTAINABLE FUTURE

Computational Toxicology Research Program

Fast, Automated Chemical Screening for Assessing Exposure, Hazard and Risk

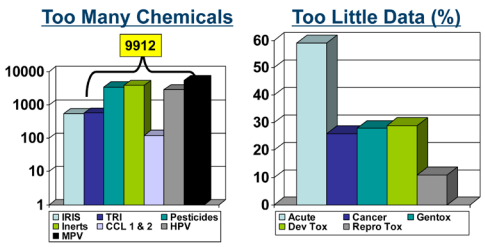
Tens of thousands of chemicals are currently in commerce, and hundreds more are introduced every year. Because current chemical testing is expensive and time consuming, only a small fraction of chemicals have been assessed adequately for potential risk.

The U.S. Environmental Protection Agency is working to change the current approach to chemical toxicity risk assessment through its Computational Toxicology Research Program (CompTox). The program uses innovative research that integrates advances in molecular biology, chemistry, and computer science to more effectively and efficiently rank chemicals based on potential risks. Using CompTox methods and tools, a large number of chemicals can be screened effectively for risks at a small cost in a very short amount of time.

CompTox Methods and Tools

ACToR and ToxRefDB (Aggregated Computational Toxicology Resource and Toxicity Reference Database)

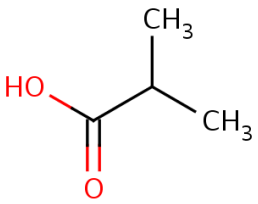
These publically available databases enable scientists and the interested public to search and download thousands of toxicity testing results on hundreds of chemicals. ACToR aggregates data from more than 500 public sources on over 500,000 chemicals, and ToxRefDB captures more than 30 years and $2 billion worth of animal testing results. ACToR is the umbrella data warehouse that provides linkages to all available CompTox chemical toxicity databases including ToxRefDB, Distributed Structure-Searchable Database (DSSTox) and the ToxCast Database (ToxCastDB).



EPA's Need for Toxicity Data

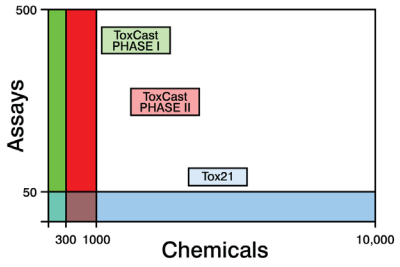
DSSTox (Distributed Structure-Searchable Toxicity Database)

The website provides a public forum for publishing downloadable, structure-searchable, standardized chemical structure files associated with toxicity data.



ToxCast™ (Toxicity Forecaster)

Chemical Type	ToxCast Phase I	ToxCast Phase II	Tox21
Pesticides/ Environmental	329	320	2200
Manufactured/ Industrial	42	230	2800
Highly Toxic	73	150	500
Pharmaceuticals	0	100	2500
Consumer Products/ Food additives	0	0	1500
Green	4	60	500
Total Unique	309	~700	~10000

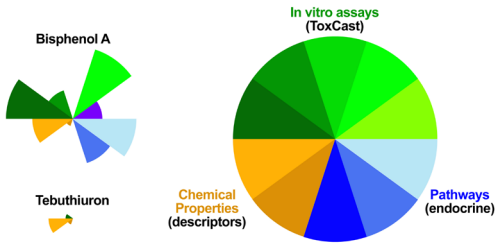


Computational Toxicology Research Program

A multiyear, multimillion dollar effort that uses advanced science tools to help understand how human biology is impacted by exposure to chemicals and to determine which exposures are the most likely to lead to adverse health effects. ToxCast™ currently includes over 500 fast, automated chemical screening tests that are assessing more than 1000 environmental chemicals. All available ToxCast chemical screening data can be queried and downloaded from the ToxCast database (ToxCastDB). ToxCastDB provides all ToxCast data with links to chemicals, assays, genes, pathways and endpoints.

A large contributor to ToxCast™ is the Tox21 collaboration. Tox21 pools chemical research, data and screening tools from multiple federal agencies, including the Food and Drug Administration (FDA), the National Toxicology Program/ National Institute of Environmental Health Sciences and the National Institutes of Health (NIH) Chemical Genomics Center.

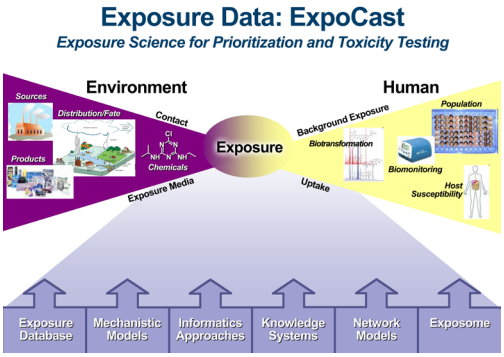
ToxPi
(Toxicological Priority Index)



A flexible prioritization support software tool that incorporates profiles, inferred toxicity pathways, dose estimates and chemical structural descriptors to calculate a potential toxicity score.

ExpoCast
(Exposure Forecaster)

Works with ToxCast™ to determine priority chemicals that may need further screening and develops novel approaches for evaluating chemicals based on potential



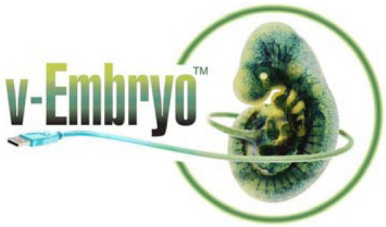
for biologically relevant human exposure.

Virtual Tissues

This research includes advanced

v-LIVER
VIRTUAL LIVER PROJECT

computer models of the liver and embryo that will be used to predict the effects of chemicals in humans. Virtual Liver (v-Liver™) will use fast, automated chemical screening data from ToxCast™ and other data to simulate how chemicals could cause liver disease and cancer in people. Virtual Embryo (v-Embryo™) will use ToxCast™ data to develop predictions for what chemical interactions will most likely lead to toxicity and birth defects.



Collaboration Opportunities

The CompTox Research Program partners and collaborates with EPA regions and program offices, industry, academia, trade associations, other federal agencies, state and local government agencies and non-governmental organizations with an interest in revolutionizing the current approach to assessing chemical toxicity risk to humans and the environment. Collaboration opportunities include a Communities of Practice group and different types of agreements that facilitate the sharing of research data and studies.

The CompTox program goal is to provide fast, automated tests for screening and assessing chemical exposure, hazard and risk. Housed within EPA's Office of Research and Development, CompTox is composed of three main elements. The largest component is the National Center for Computational Toxicology (NCCT), which was established in 2005 to coordinate research on chemical screening and prioritization, informatics and systems modeling.

The second element consists of research in EPA's National Health and Environmental Effects Research Laboratory (NHEERL) and National Exposure Research Laboratory (NERL). The final components are the academic centers working on various aspects of computational toxicology funded by EPA's Science to Achieve Results (STAR) program.

More information at:
www.epa.gov/comptox

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