Providing Context for Chemical Effects Through Bioactivity and Consumer Use

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Abstract 2541

New Approach Methodologies

- New approach methodologies (NAMs) include in vitro and in silico techniques used to query a specific toxicity endpoint.
- NAMs are often developed for a specific set of regulatory needs, using chemicals with established bioactivity. The finite set of chemicals used for validation may not provide insight into an assay's structure-based limitations.
- Availability of structure-based information both for chemicals used to validate NAMs and for candidates for testing in NAMs is important for advancing and implementing these methods.
- This poster describes a freely available web tool for exploring, comparing, and visualizing structure-based chemical information.

The Integrated Chemical Environment (ICE)

- To provide free access to data, predictions, and structure-based information, the National Toxicology Program (NTP) developed and maintains the Integrated Chemical Environment (ICE): https://ice.ntp.niehs.nih.gov/
- ICE provides resources and tools to examine chemical activity and properties that are accessible to users with a broad range of chemistry expertise, with a focus on non-animal approaches.

Integrated Chemical Environment

Search

Data

$$C_{ss} = \frac{Dose}{CL_r + CL_h}$$

IVIVE

Chemical Characterization

Key features of ICE:

- Contains data and information for over 800,000 chemicals.
- Allows users to construct queries with curated chemical quick lists or user-specified CASRNs.
- Includes computational workflows for chemical characterization and predictive toxicology.

ICE supports:

- FAIR (findable, accessible, interoperable and reusable) data principles.
- Data integration: bringing together data from different endpoints and experiments for comparison.
- Results exploration: dynamic, graphical exploration of query results with capability to refine.
- Graphical display and data analysis of chemical characterization through computational tools.

More Information

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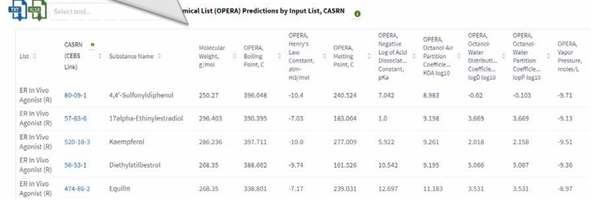
Visit ICE
https://ice.ntp.niehs.nih.gov/

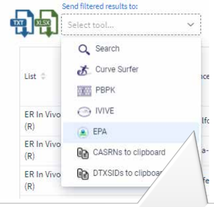
Data Exploration Through Chemical Characterization

How do chemical properties differ between my two chemical lists?

The ICE Chemical Characterization tool provides a comprehensive list and statistical summary of predicted chemical properties for quantitative assessments.

Chemical properties are reported based on measured values and quantitative structure-activity/property relationship (QSAR) model predictions.



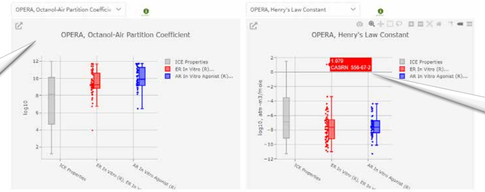


Queried and filtered chemicals can be sent to other tools within ICE or to the U.S. Environmental Protection Agency's (EPA) CompTox Chemicals Dashboard.

How does ICE characterize results based on chemical properties?

The ICE Chemical Characterization tool provides box-and-whisker plots for visualization and investigation of chemical property distributions.

Visual comparison of properties highlights differences between one or two lists of chemicals, and all chemicals in ICE.



Chemical that appear as outliers may be incompatible with desired assay platform.

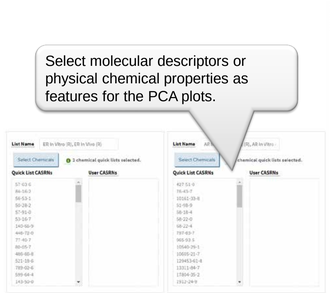
How diverse are my chemical lists?

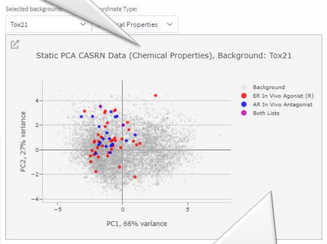
The ICE Chemical Characterization tool provides static and dynamic principal component analysis (PCA) plots to compare chemical properties, molecular descriptors, or bioactivity.

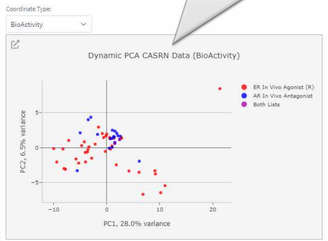
Chemical lists are plotted similarly (clustered together) or differently (scattered) based on selected attributes.

View direct spatial comparisons between two user-defined chemical lists for bioactivity, chemical properties, or molecular descriptors.

Select molecular descriptors or physical chemical properties as features for the PCA plots.







Examine chemical diversity relative to large reference datasets such as DSSToxDB (~800k) or Tox21(~1k).

Additional Resources to Add Context

Adding in data and links to other resources expands information available to users. ICE users can query CEBS and the EPA Dashboard directly from search to access data beyond what is available in ICE.

NTP Chemical Effects in Biological Systems (CEBS)

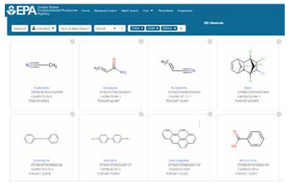
- CEBS provides detailed testing information from NTP studies.

EPA's CompTox Chemical Dashboard

- The EPA Dashboard provides individual chemical information ranging from toxicity values to exposure and usage.

EPA Chemical and Products Database (CPDat)

- CPDat offers functionality based-mapping for ~50,000 chemicals on categories such as consumer use.
- ICE leverages the CPDat data through the Consumer Use Explorer in the Chemical Characterization tool, allowing users to explore where chemicals are found in consumer products.



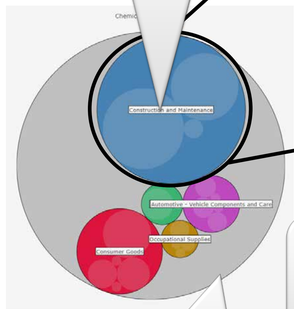
Combining ICE data, users can leverage their own workflows to provide additional insight.

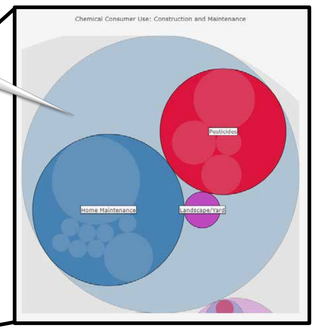
Batch Search on CompTox Chemical Dashboard

Carcinogenicity Data from ICE Grouped by CPDat Categories

Users can click on categories of interest to magnify the number of chemicals located in each subcategory.

Product use categories have several subcategories for target-specific analysis based on chemical list and use.





Users can view a detailed list of chemicals and chemical characteristics such as bioactivity.

User-defined chemical lists are plotted based on product use as classified in the CPDat Database.