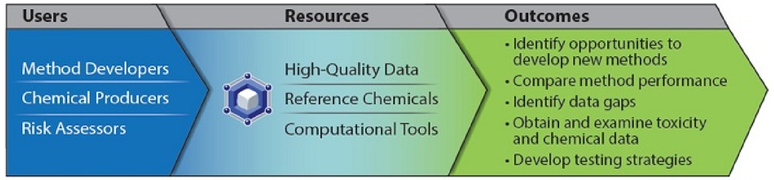
The Integrated Chemical Environment: Tools and Data to Support Toxicity Assessments

S Bell[1], J Phillips[2], J Abedini[1], X Chang[1], F Hermes[1], AL Karmaus[1], K Mansouri[1], R Rai[1], D Allen[1], W Casey[3], N Kleinstreuer[3]

[1]ILS, RTP, NC, USA; [2]Sciome LLC, RTP, NC, USA; [3]NIH/NIEHS/DNTP/NICEATM, RTP, NC, USA

The Integrated Chemical Environment



ICE provides free online access to:
- Curated in vivo and in vitro data related to toxicity testing
- In silico toxicity predictions and chemical property data
- Curated lists of chemicals with well-characterized toxic effects (reference chemical lists)
- Computational tools for chemical characterization and predicting toxicity

ICE supports:
- Data integration: brings together available data, including data on formulations
- Results exploration: enables dynamic, graphical exploration with publication-quality graphics
- Data analysis: allows characterization of data using online workflows
- FAIR (findable, accessible, interoperable and reusable) data access

ICE 2.0

New Features in ICE 2.0:

- Expand your search by adding chemicals in ICE with the same QSAR-ready structures as your chemicals
- Simplified assay selection
- Updated tools

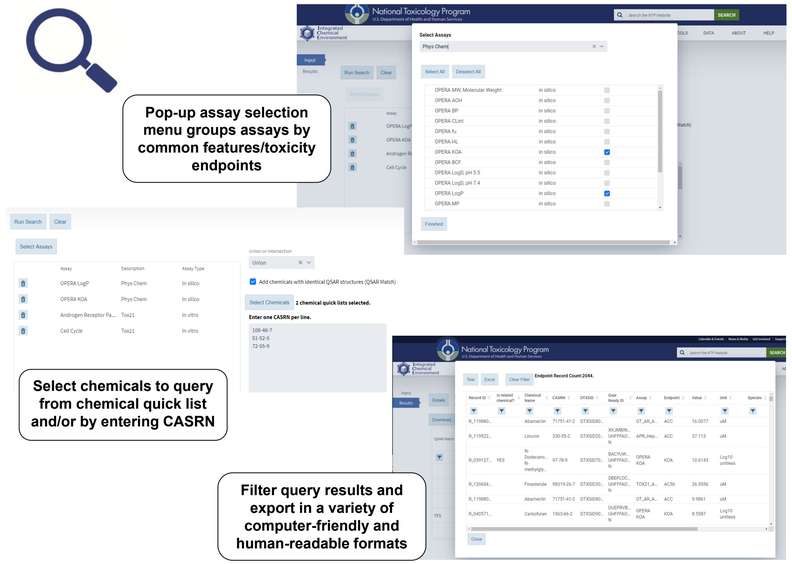
Contact Us

To get announcements of ICE updates and other NICEATM activities, visit the NIH mailing list page for NICEATM News at https://list.nih.gov/cgi-bin/wa.exe?SUBED1=niceatm-l&A=1 and click "Subscribe."

Visit ICE

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

ICE Search



Machine Learning

Use the Machine Learning tool to generate hypotheses and explore different machine learning approaches using ICE data. Selected endpoints and algorithms are available through ICE to facilitate use by those with limited backgrounds in computational toxicology. Users can build both classification and regression models.

Predicts endpoints for in vivo assays:
- Local lymph node assay (skin sensitization)
- Uterotrophic (estrogenic activity)
- Human skin sensitization potency

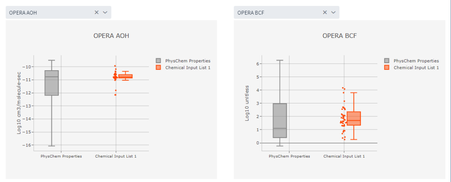
Machine learning methods available:
- cforest: conditional random forest
- rpart: recursive partitioning
- knn: k-nearest neighbor
- svmRadial: support vector machine with a radial kernel
- pls: partial least squares regression

Stand-alone version available for use with custom datasets: https://github.com/NIEHS/Machine-Learning-Pipeline

Chemical Characterization

The Chemical Characterization tool leverages ICE models to characterize a user-supplied chemical list. The output provides information on the chemical space covered based on different physicochemical properties.

Future plans for the Chemical Characterization tool:
- Chemical use category using EPA's Chemical and Products Database, CPDat
- Integration with ChemMaps (http://www.chemmaps.com)

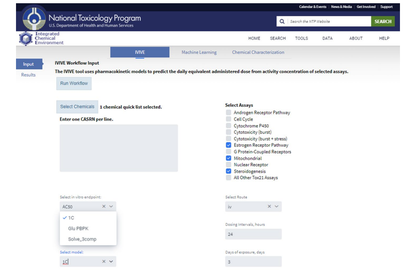


In Vitro to In Vivo Extrapolation

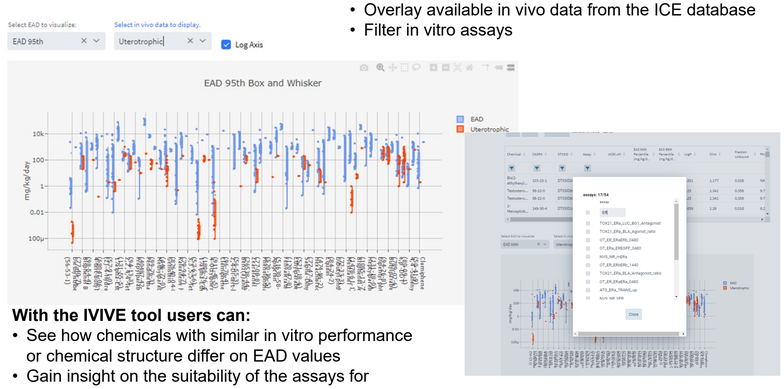
$$C_{ss} = \frac{Dose}{CL_r + CL_h}$$

The In Vitro to In Vivo Extrapolation (IVIVE) tool uses high-throughput in vitro data available from ICE to estimate an in vivo equivalent administered dose (EAD).

Choose from:
- One-compartment pharmacokinetic (1C PK) model including population simulation
- Two 3-compartment physiologically based pharmacokinetic (PBPK) models:
  - 3C Glu: incorporates gut glucuronidation for BPA-family compounds
  - Solve_3comp: uses EPA's httk package model
- Three-compartment models include gut, liver, and kidney in addition to rest of body
- Rat and human predictions
- IV and oral dosing route



Tool allows dynamic exploration of the IVIVE analysis
- Overlay available in vivo data from the ICE database
- Filter in vitro assays



With the IVIVE tool users can:
- See how chemicals with similar in vitro performance or chemical structure differ on EAD values
- Gain insight on the suitability of the assays for predicting the effect level for an in vivo endpoint

Stand-alone version available for use with custom datasets: https://github.com/NIEHS/

References

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