

CompTox Chemicals Dashboard & Bioactivity Data



Introduction: Scarlett VanDyke

CompTox Chemicals Dashboard; Bioactivity Intro: Dr. Nisha Sipes

High throughput transcriptomics (HTTr) &

High throughput phenotypic profiling (HTPP): Dr. Logan Everett

ToxCast: Madison Feshuk, MPHTM

Outline & Disclaimer

- Introduction
- High throughput transcriptomics (HTTr)
 - CCD Demo: *Bioactivity: HTTr*
- High-throughput phenotypic profiling (HTPP)
 - CCD Demo: *Bioactivity: HTPP*
- Toxicity Forecasting (ToxCast)
 - CCD Demo: *Bioactivity: ToxCast*

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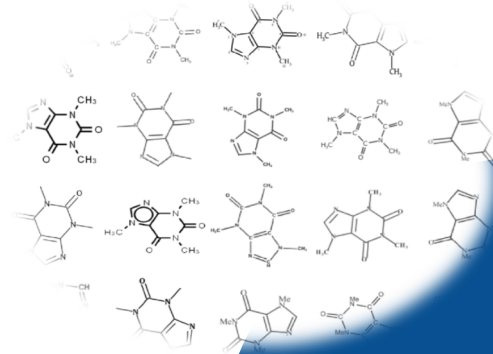
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Bioactivity Introduction

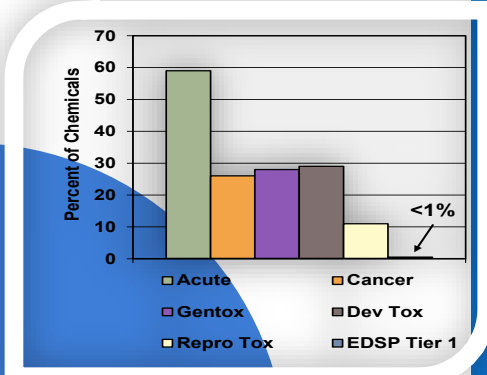
Nisha Sipes

Need for Alternative Approaches for Next-Gen Risk Assessment

- Several limitations to traditional *in vivo* toxicology testing
- EPA needs rapid and efficient methods to prioritize, evaluate, and regulate thousands of chemicals in commerce
- New Approach Methods (NAMs) can provide information on hazard + exposure to inform research and decisions



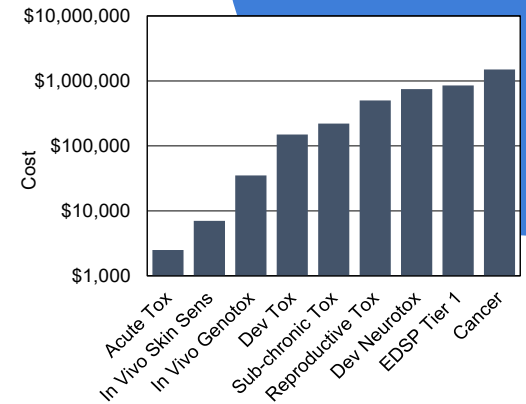
Too Many Chemicals



Time

Modified from Judson et al., EHP 2010

Cost

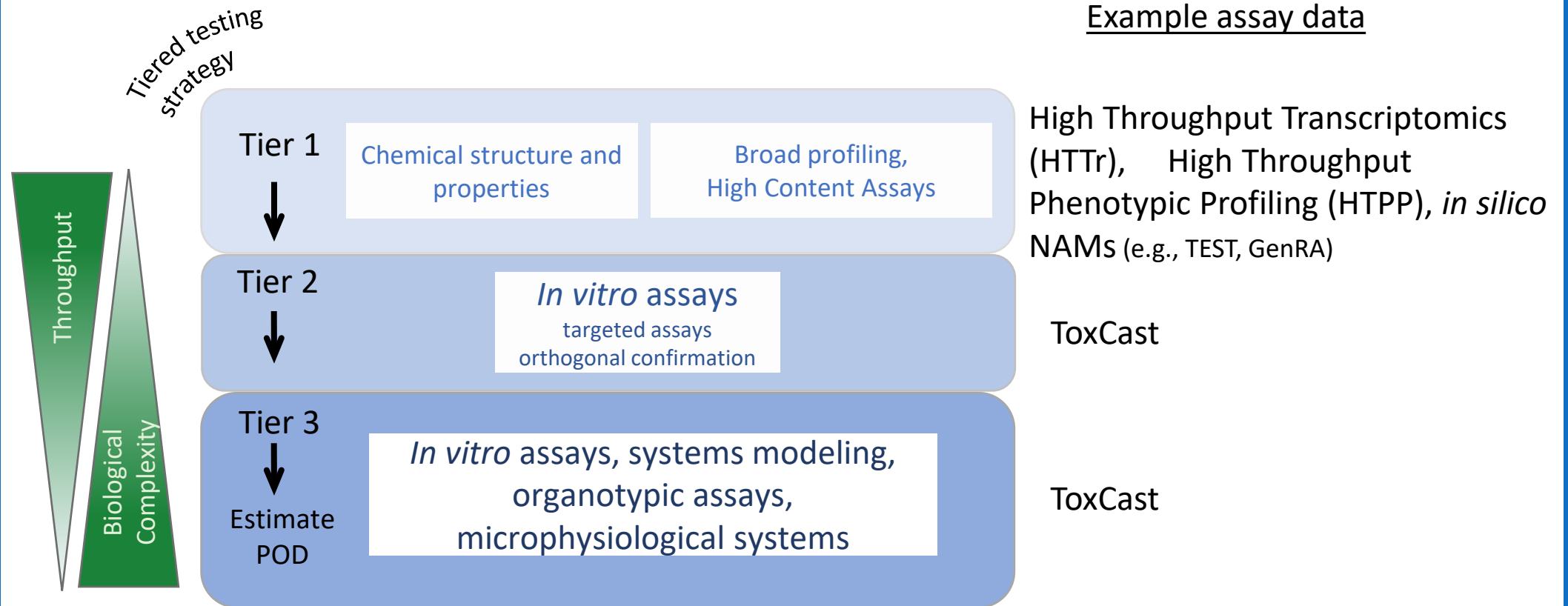


Ethics



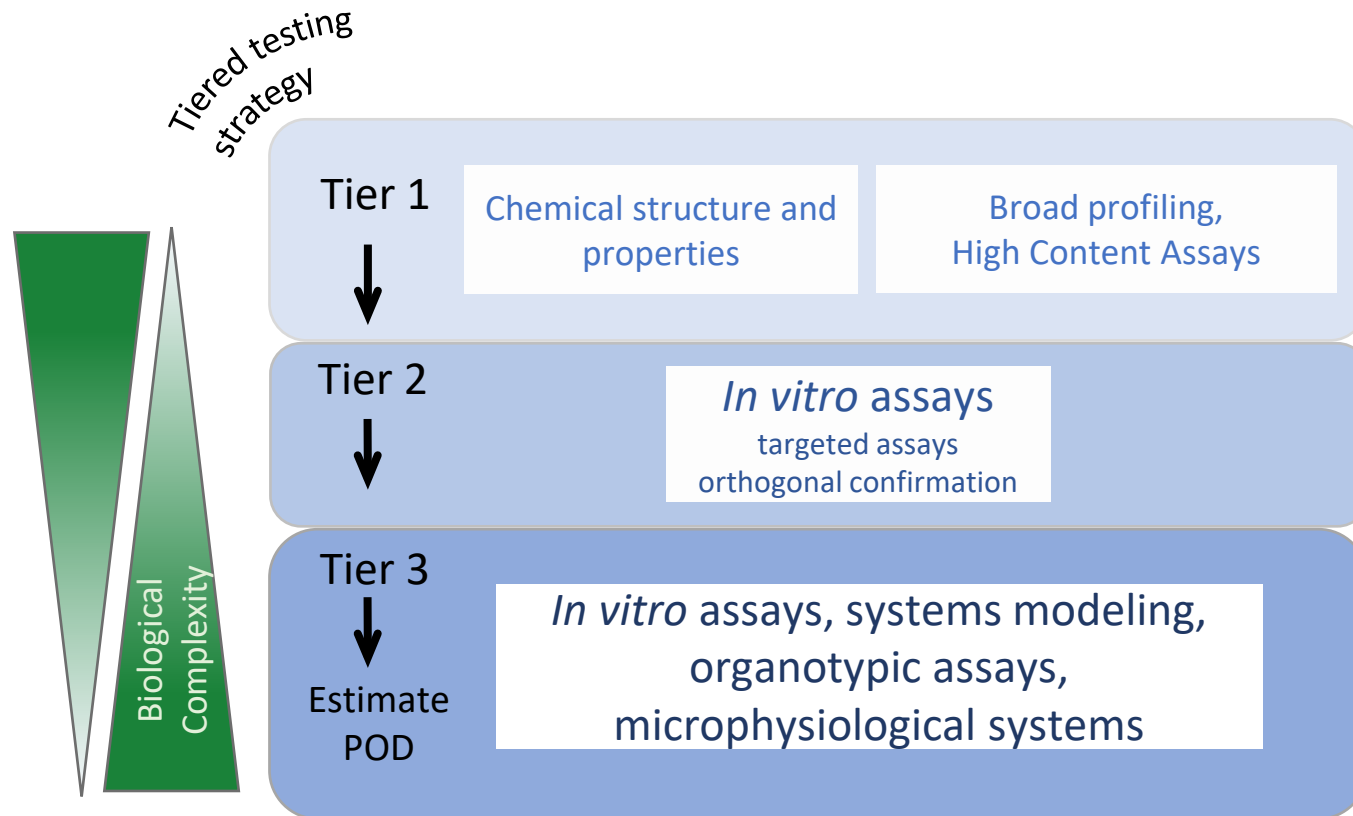
NAMs for hazard include broad profiling and targeted approaches

Adapted from the US EPA's NexGen Blueprint of Computational Toxicology



NAMs for hazard include broad profiling and targeted approaches

Adapted from the US EPA's NexGen Blueprint of Computational Toxicology



How to make data comparable between tiers?

A single curve-fitting approach (*tcplfit2 R package*) enables

- Comparison
- Interoperability

CompTox Chemicals Dashboard: Bioactivity Tab

CompTox Chemicals Dashboard v2.4.1 Home Search Lists About Tools Submit Comments Atrazine DTXSID9020112

Atrazine
1912
Search

Advanced Search
Batch Search
Structure Search (BETA)

Bioactivity - TOXCAS

Chemical Details
Executive Summary
Physchem Prop.
Env. Fate/Transport
Hazard Data
Safety > GHS Data
ADME > IVIVE
Exposure
Bioactivity
ToxCast: Summary
HTTr: Summary
HTPP: Summary
PubChem
ToxCast: Models
Comments

Enhanced Data Sheets

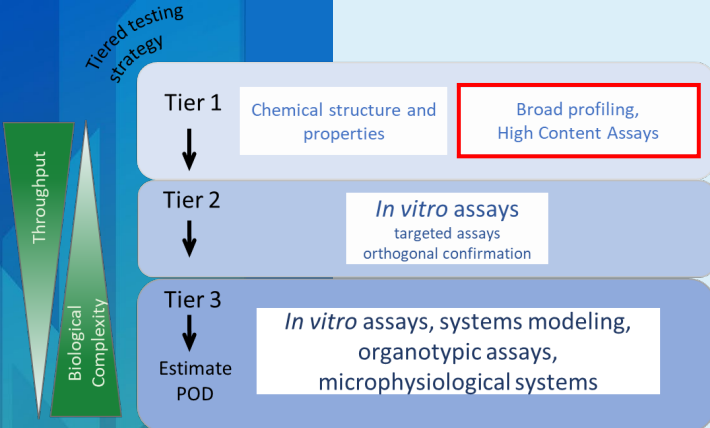
- MetFrag Input File (Beta)
- Abstract Sifter Input File
- Synonyms and Identifiers
- Related Substance relationships
- ToxCast Assays: AC50
- ToxValDB Details
- ToxRefDB Details
- Physicochemical Property Values

linear

Scaled Top

Cytotox Lower Bound In µM (1000,000)

- cell adhesion molecules
- cyp
- cytokine
- deiodinase



High-Throughput Transcriptomics (HTTr)

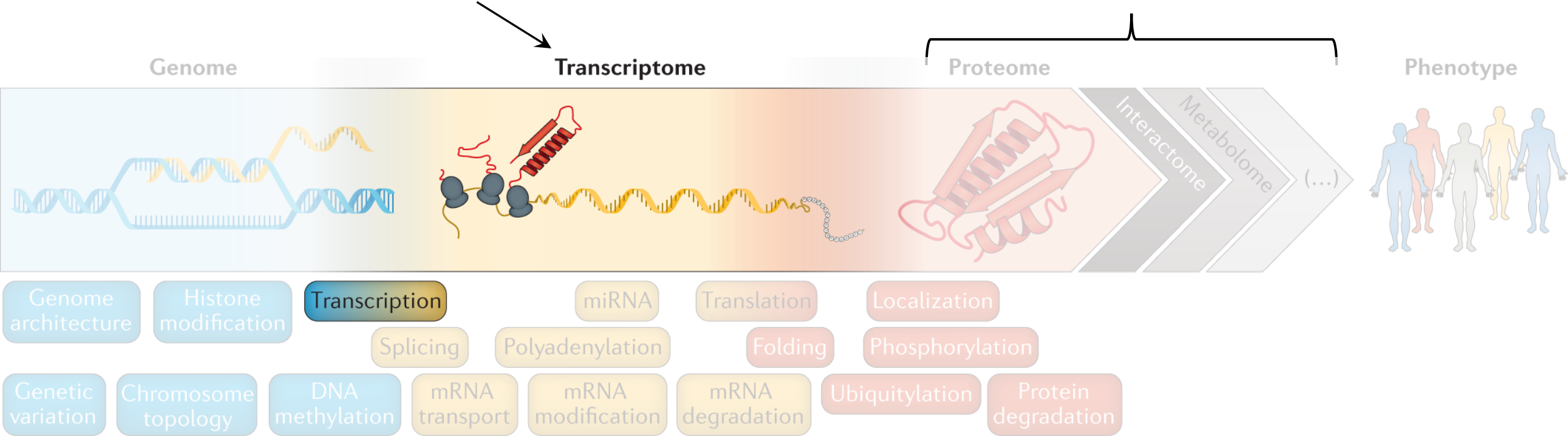
Logan Everett

(with contributions from Joshua Harrill and Richard Judson)

Why Transcriptomics?

Highly dynamic in response to environmental stimuli,
Well-established, cost-effective, high-throughput methods

Broad profiling methods are newer
or less cost-effective

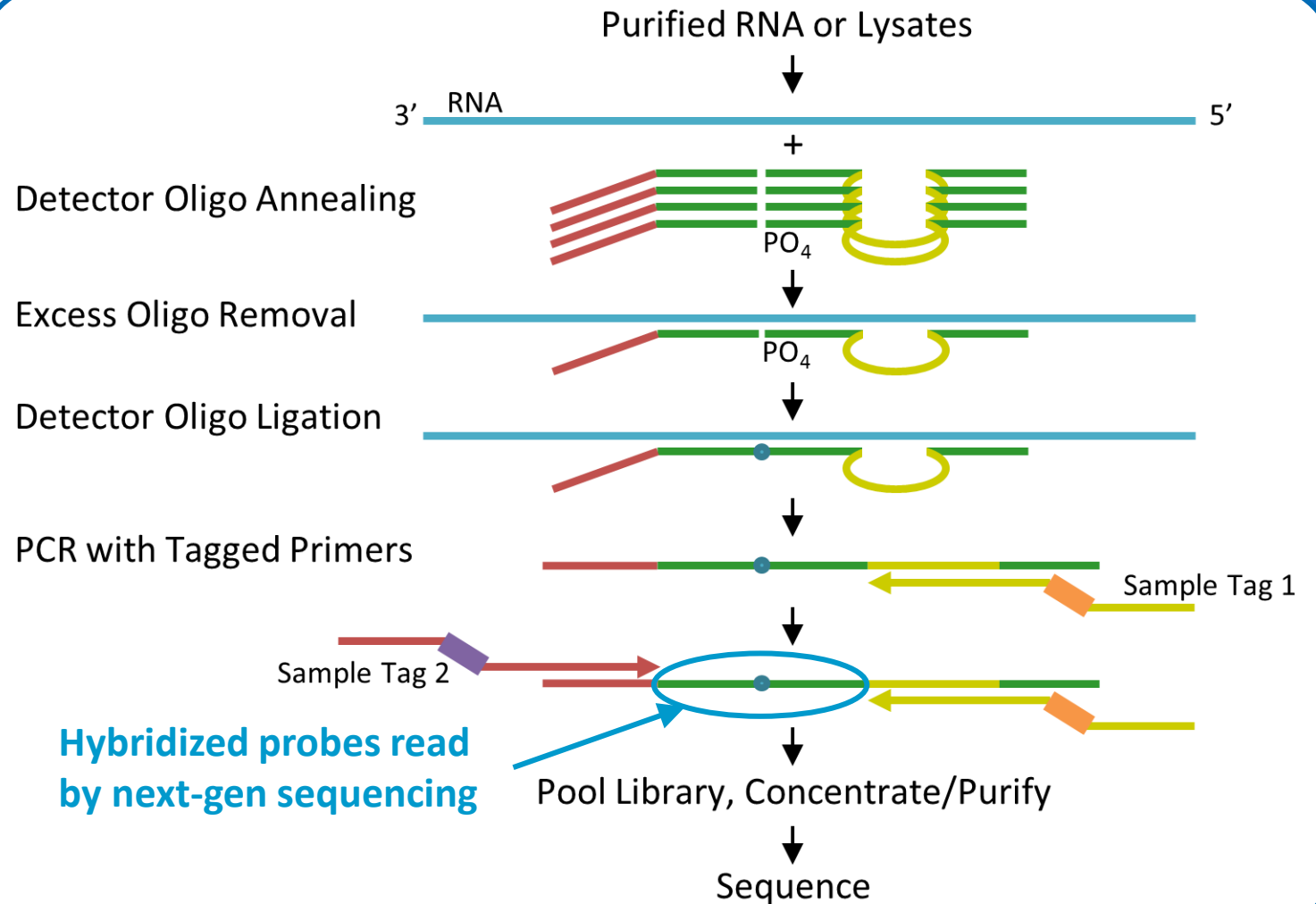


Hazardous exposures can cause perturbations
at multiple levels of gene regulation



Targeted RNA-seq Assay (TempO-seq)

- Next-Gen sequencing of targeted probes hybridized to expressed transcripts
- Whole transcriptome coverage (>20,000 genes)
- Captures gene expression at lower cost than RNA-seq or microarrays
- Compatible with raw cell lysates – *ideal for large-scale screening*



Automated *in vitro* Chemical Screening Strategy

Cryopreserved
Cell Stocks



Cell
Expansion



Cell Plating



BioTek
MultiFlo™ FX

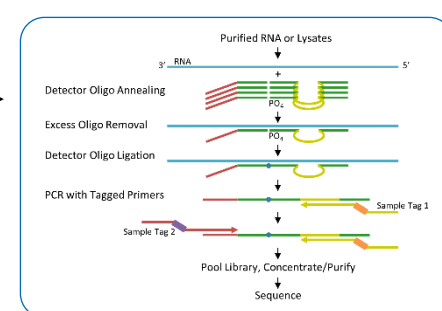
Dispensing Test
Chemicals



LabCyte Echo® 550
Liquid Handler

6 - 24 hr exposures

TempO-seq:
Human Whole Transcriptome



Yeakley, et al. PLoS ONE (2017)

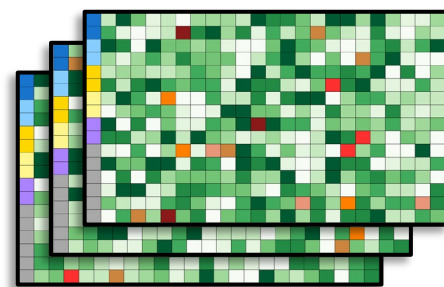
DOI: [10.1371/journal.pone.0178302](https://doi.org/10.1371/journal.pone.0178302)

Cell Line Examples:

MCF-7 Breast cancer

U-2 OS Bone cancer

HepaRG Liver metabolism



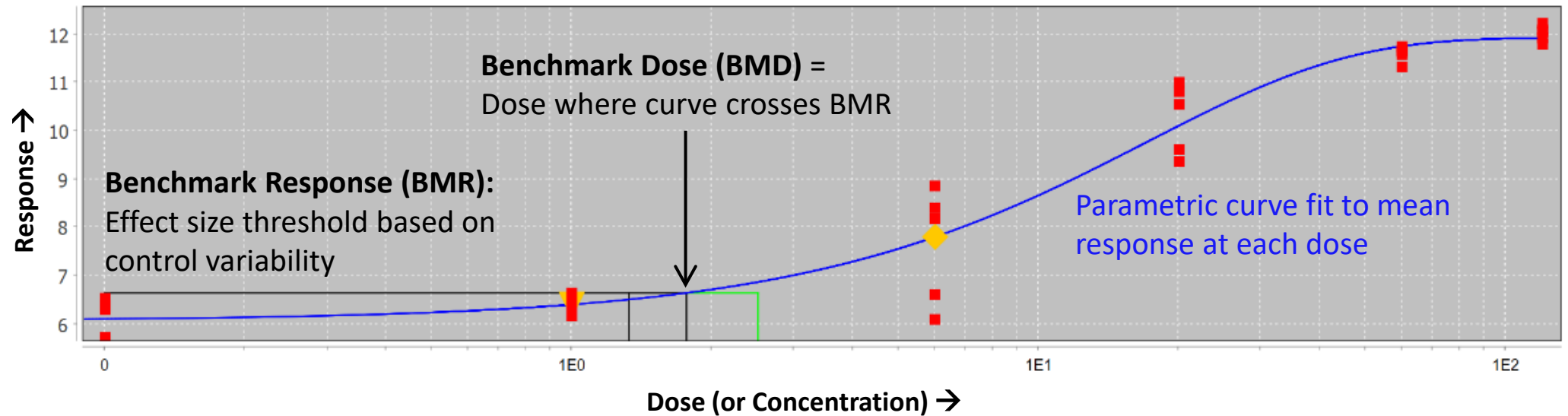
384-well test plates run in triplicate with:

- ~40 test chemicals x 8 concentrations (half-log spacing)
- Multiple vehicle controls, reference chemicals & QC samples on every plate to track assay performance
- Treatment positions randomized on each plate
- Independent culture batch on each plate

See Harrill, et al. Tox Sci 2021

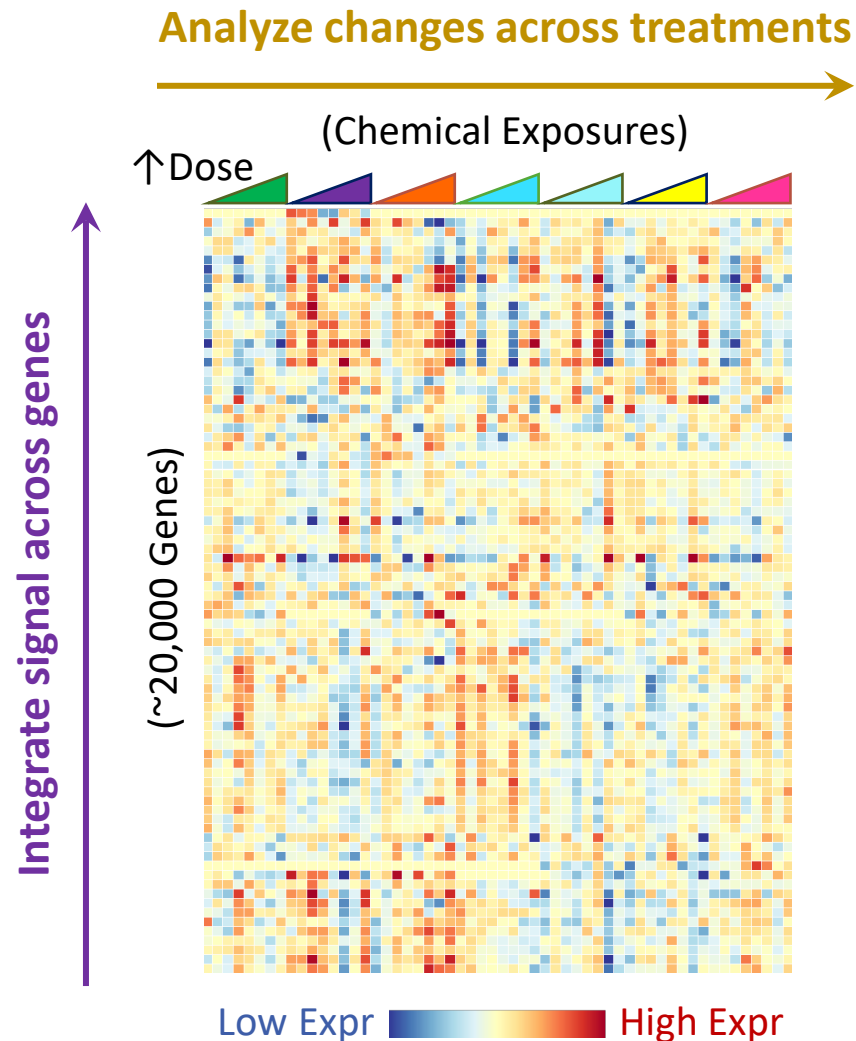
DOI: [10.1093/toxsci/kfab009](https://doi.org/10.1093/toxsci/kfab009)

Benchmark Dose



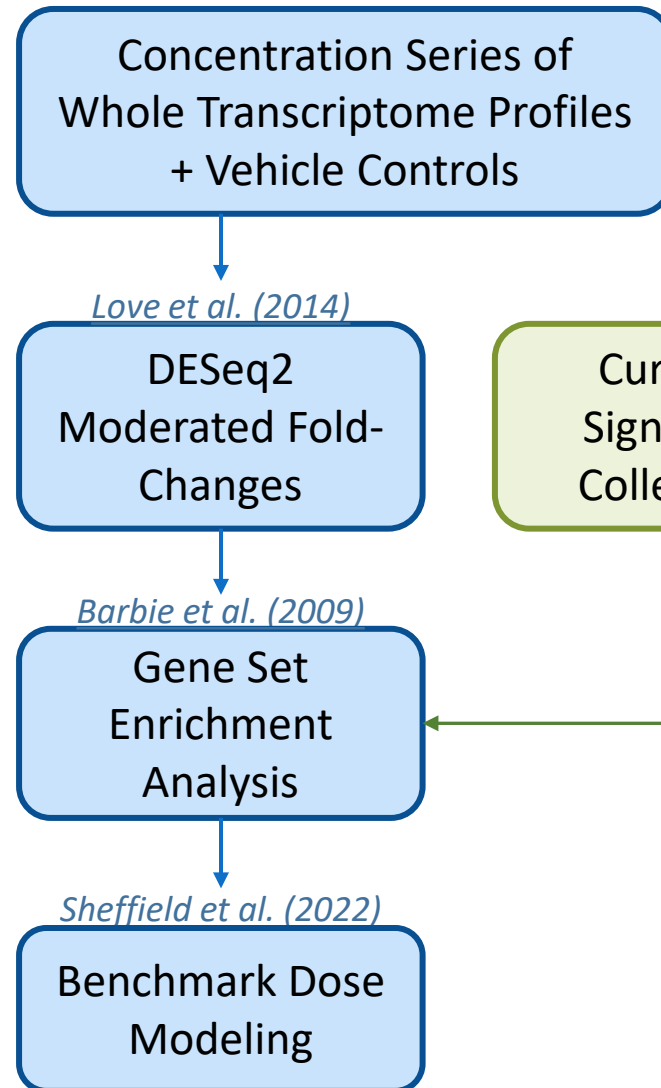
- Widely used approach for apical endpoint data
- EPA Benchmark Dose Software (BMDS): www.epa.gov/bmds

Transcriptomic Dose-Response Models



- Different genes may respond at different doses of a given exposure!
- Need to analyze both:
 - Dose-responsive trends
 - Coordinated changes in gene expression
- Gene-level data noisier in transcriptomics than targeted measurements (e.g. RT-qPCR)
- Dose-response modeling thousands of features (e.g. mRNA levels) leads to computational & statistical challenges

Dose-Response Modeling of Gene Sets/Signatures



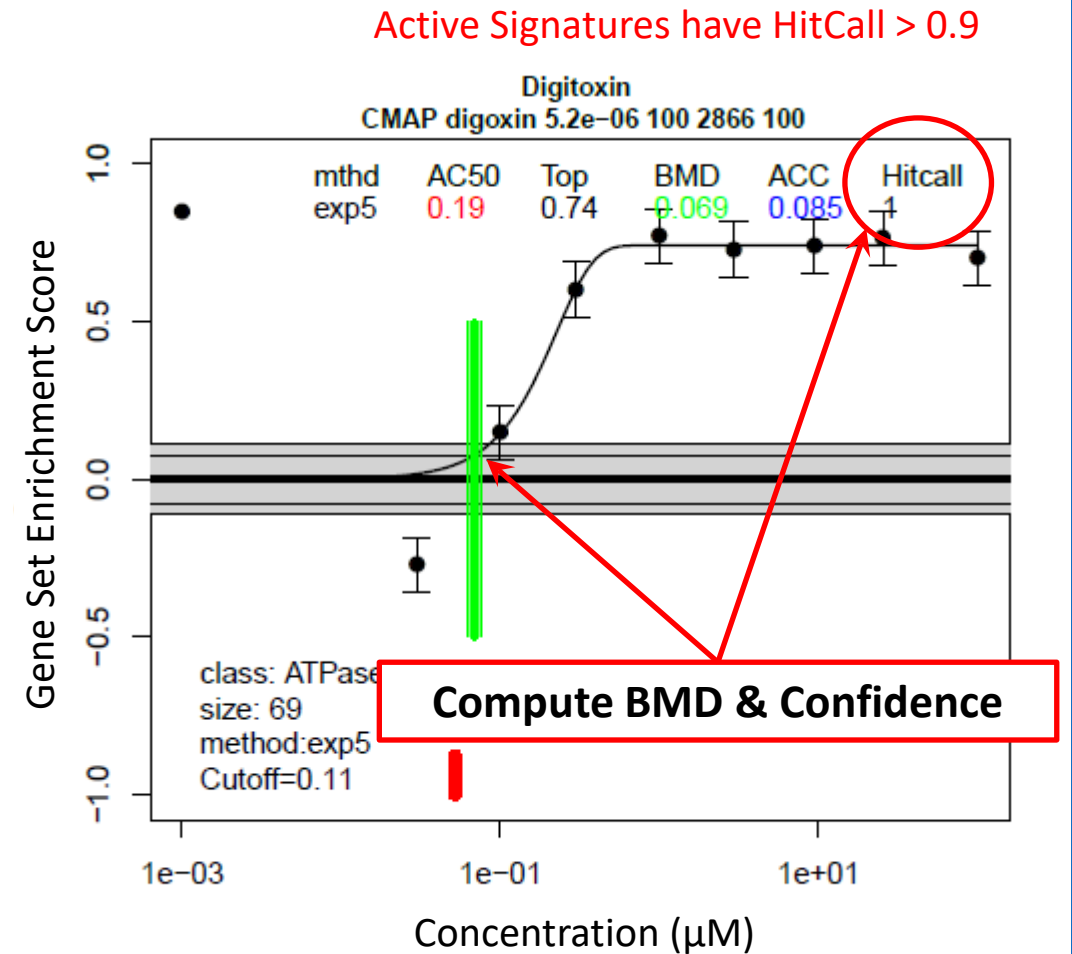
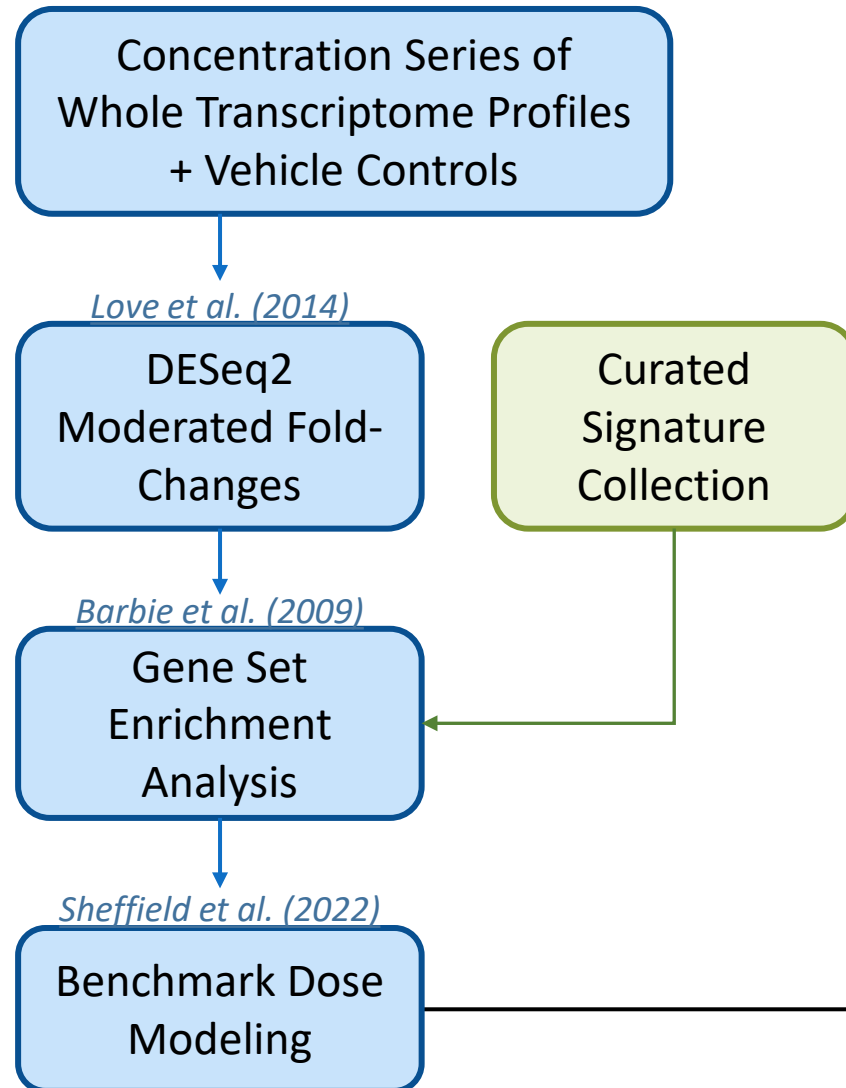
Catalog of gene set signatures with toxicological relevance, annotated for known molecular targets

- Bioplanet (Huang, et al. *Front Pharmacol* 2019)
- CMap (Subramanian, et al. *Cell* 2017)
- DisGeNET (Piñero, et al. *Database* 2015)
- MSigDB (Liberzon, et al. *Cell Syst* 2015)

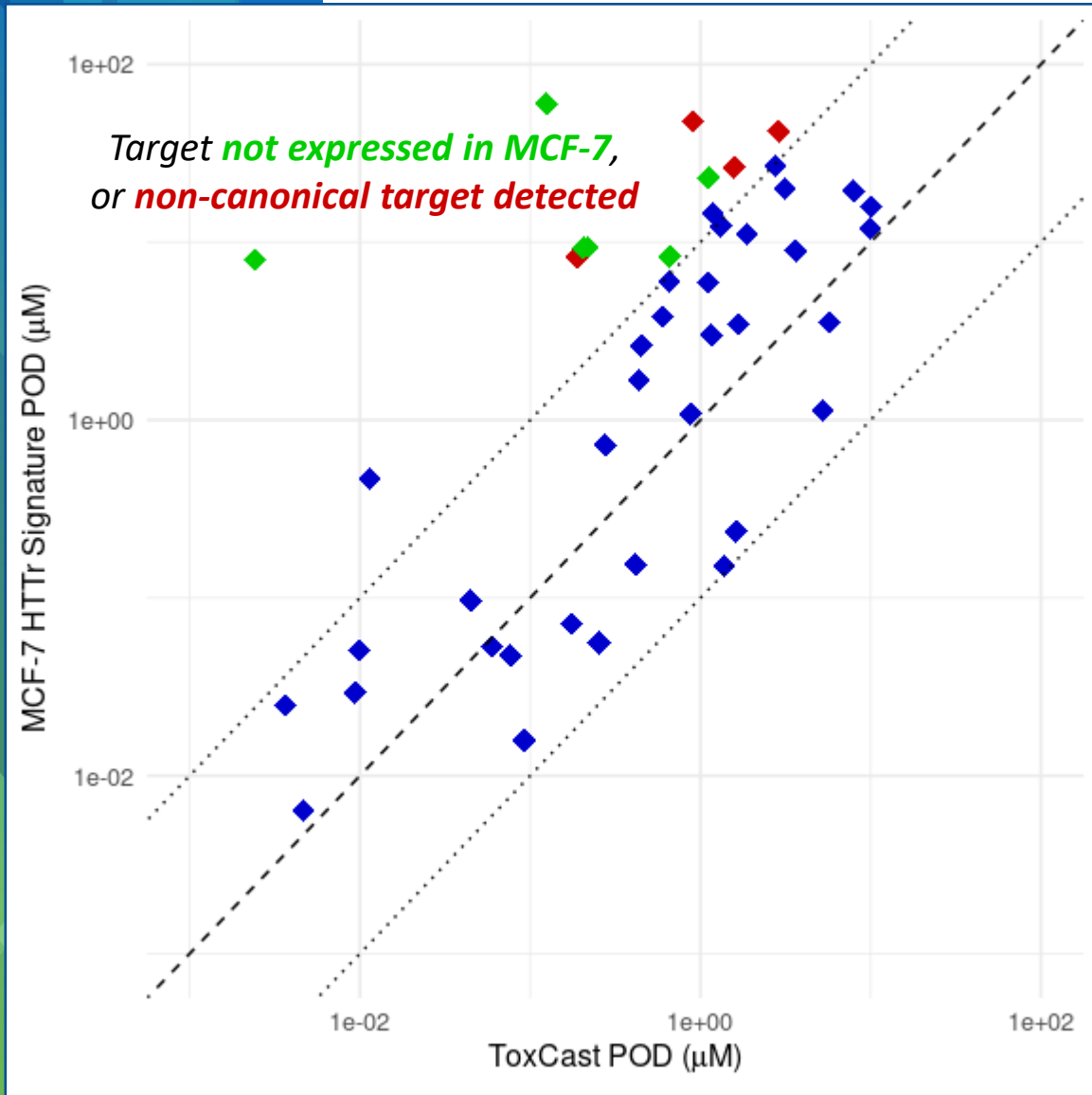
Open Source: github.com/USEPA/CompTox-httrpathway

- EPA/CCTE method for summarizing large-scale transcriptomic screening studies
- Integrates signal across known gene set (a.k.a. signature) **before** dose-response modeling

Dose-Response Modeling of Gene Sets/Signatures



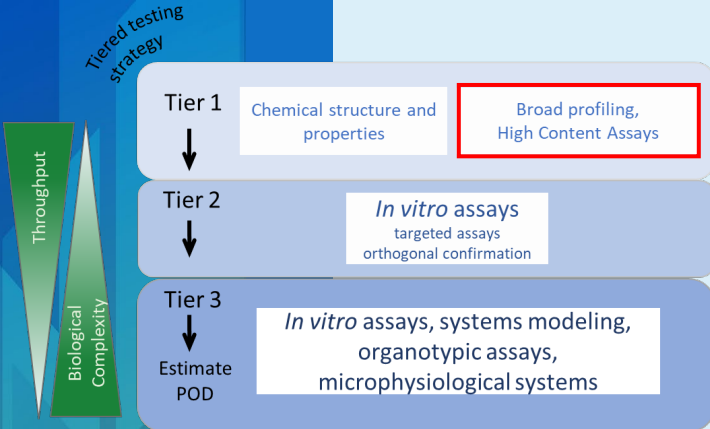
tPODs Are Concordant With ToxCast



- Computed 5th percentile of active signature/assay PODs from:
 - Pilot study of 44 well-characterized chemicals in MCF-7 cells, 6h exposure
Harrill, et al. *Toxicol Sci* (2021)
DOI: [10.1093/toxsci/kfab009](https://doi.org/10.1093/toxsci/kfab009)
 - ToxCast targeted assay results (*multiple cell types, assays, and exposure lengths*)
Paul-Friedman, et al. *Toxicol Sci* (2020)
DOI: [10.1093/toxsci/kfz201](https://doi.org/10.1093/toxsci/kfz201)
- Signature-based PODs are highly concordant with ToxCast results for the majority of chemicals in pilot study



Demo



High-Throughput Phenotypic Profiling (HTPP)

Logan Everett

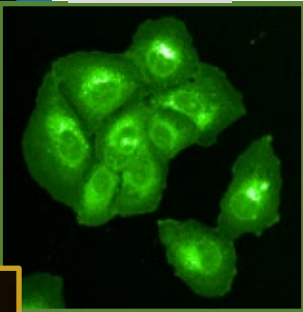
(with contributions from Joshua Harrill and Jo Nyffeler)

Cell Painting with Multiple Markers

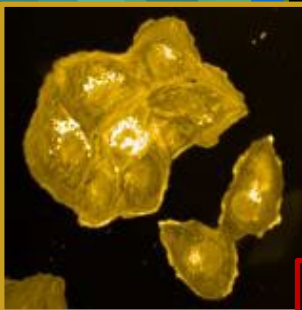
DNA



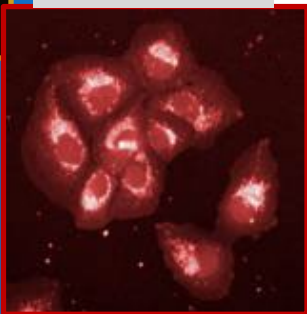
RNA + ER



Golgi + membrane
+ actin skeleton



Mitochondria



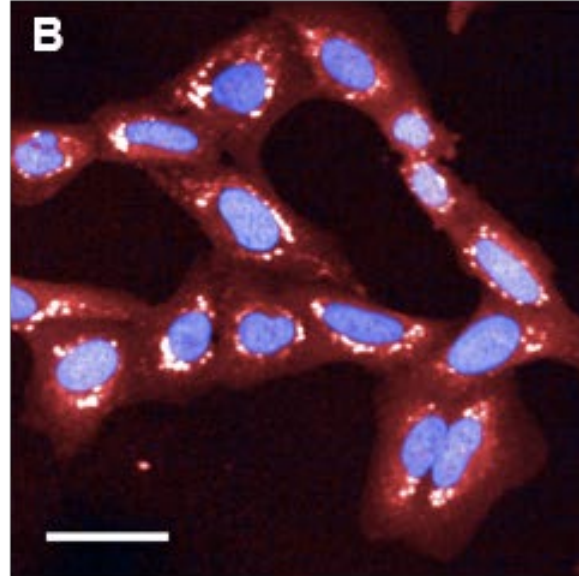
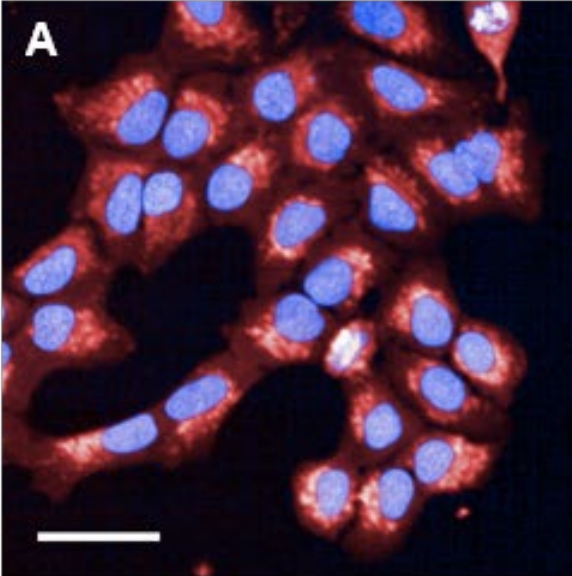
- Measures a large variety of phenotypic features in fluoroprobe labeled cells *in vitro*.
- Method based on Bray, et al. *Nat Protoc* (2016) DOI: [10.1038/nprot.2016.105](https://doi.org/10.1038/nprot.2016.105)

Marker	Cellular Component	Labeling Chemistry
Hoechst 33342	Nucleus	Bisbenzamide probe that binds to dsDNA
Concanavalin A – AlexaFluor 488	Endoplasmic reticulum	Lectin that selectively binds to α -mannopyranosyl and α -glucopyranosyl residues enriched in rough endoplasmic reticulum
SYTO 14 nucleic acid stain	Nucleoli	Cyanine probe that binds to ssRNA
Wheat germ agglutinin (WGA) – AlexaFluor 555	Golgi Apparatus and Plasma Membrane	Lectin that selectively binds to sialic acid and N-acetylglucosaminyl residues enriched in the trans-Golgi network and plasma membrane
Phalloidin – AlexaFluor 568	F-actin (cytoskeleton)	Phallotoxin (bicyclic heptapeptide) that binds filamentous actin
MitoTracker Deep Red	Mitochondria	Accumulates in active mitochondria

Example Chemicals

Solvent control (0.5% DMSO)

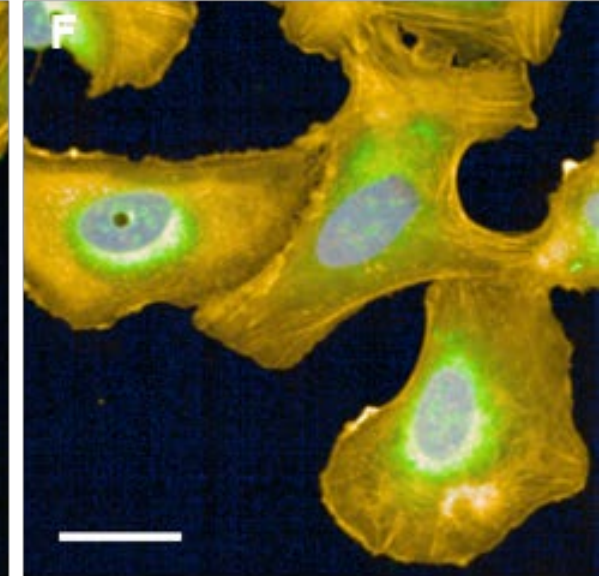
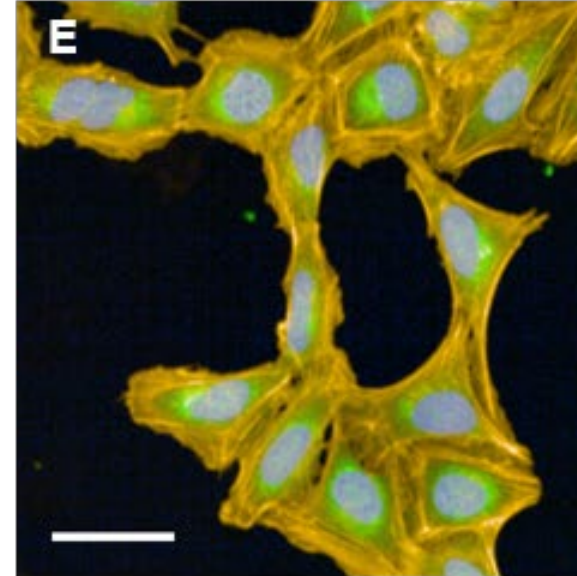
Berberine chloride (10 μ M)



→ Mitochondrial compactness/texture

Solvent control (0.5% DMSO)

Etoposide (3 μ M)

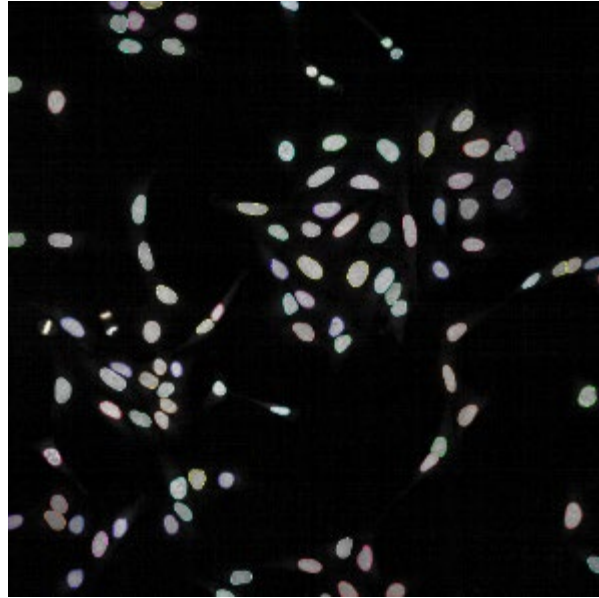
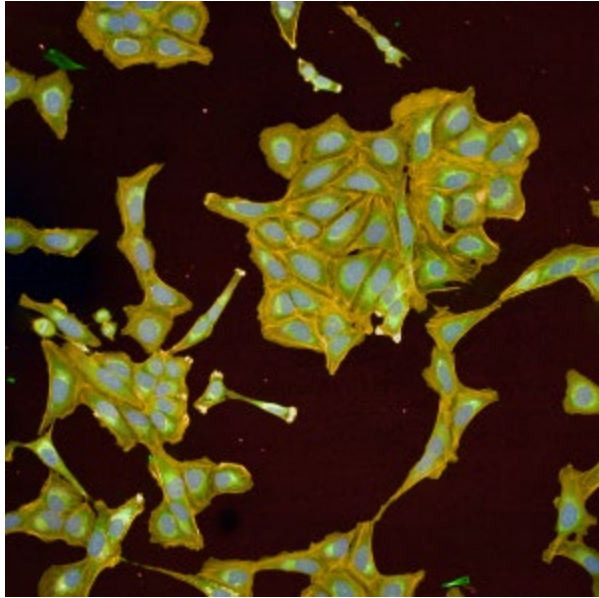


→ Cells are larger

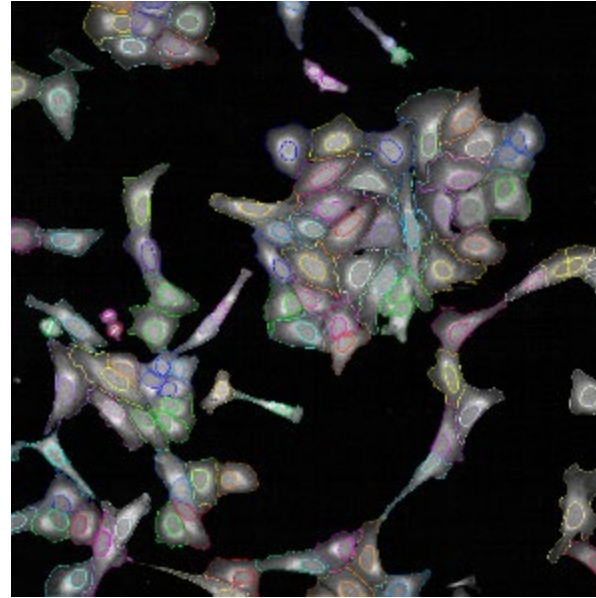
Strong phenotypes are observable qualitatively and can be measured quantitatively using imaging processing software

Image Segmentation

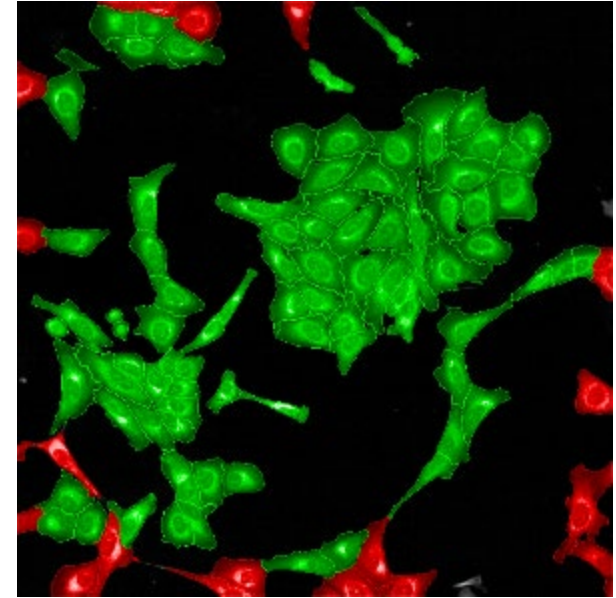
1. find nuclei



2. find cell outline

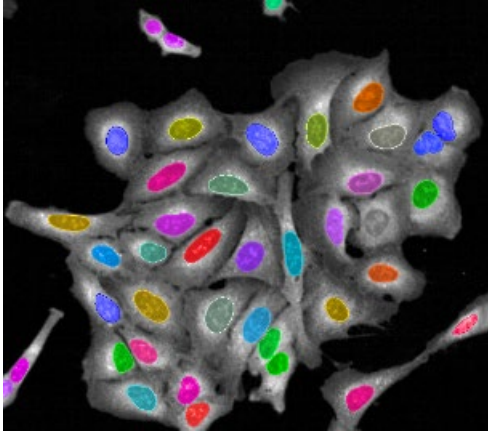


3. reject border objects

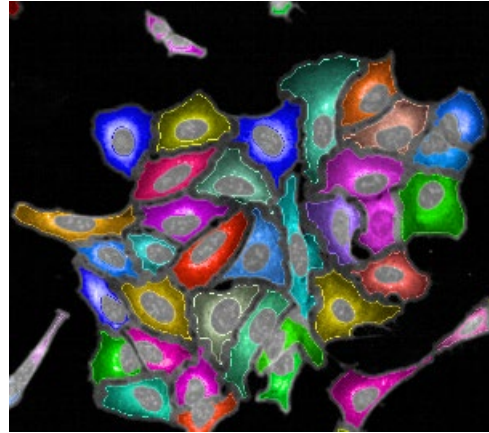


Define Cellular Compartments

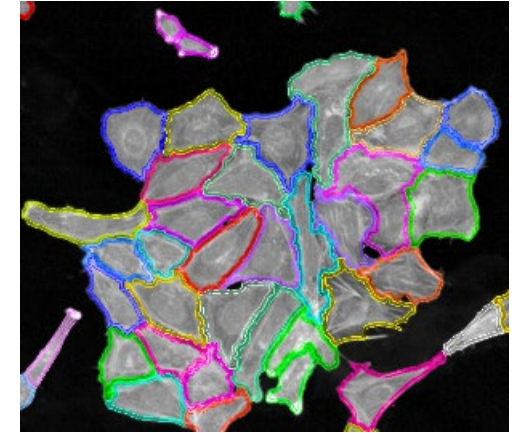
nuclei



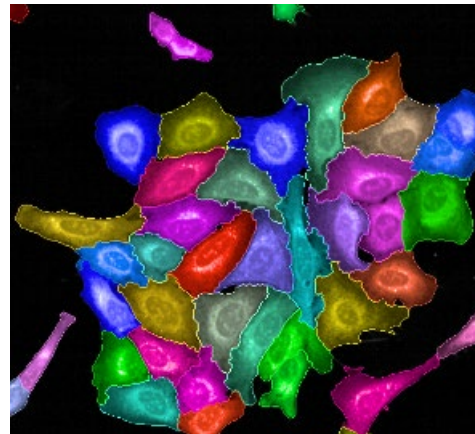
cytoplasm



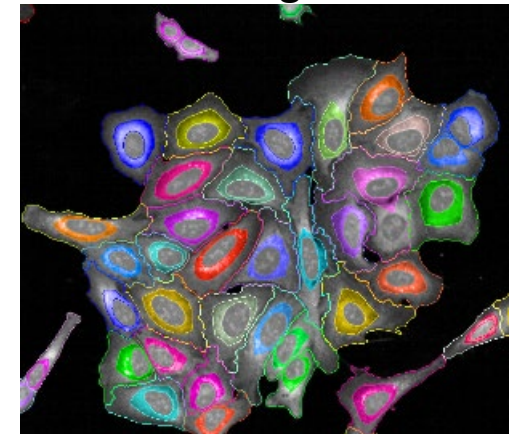
membrane



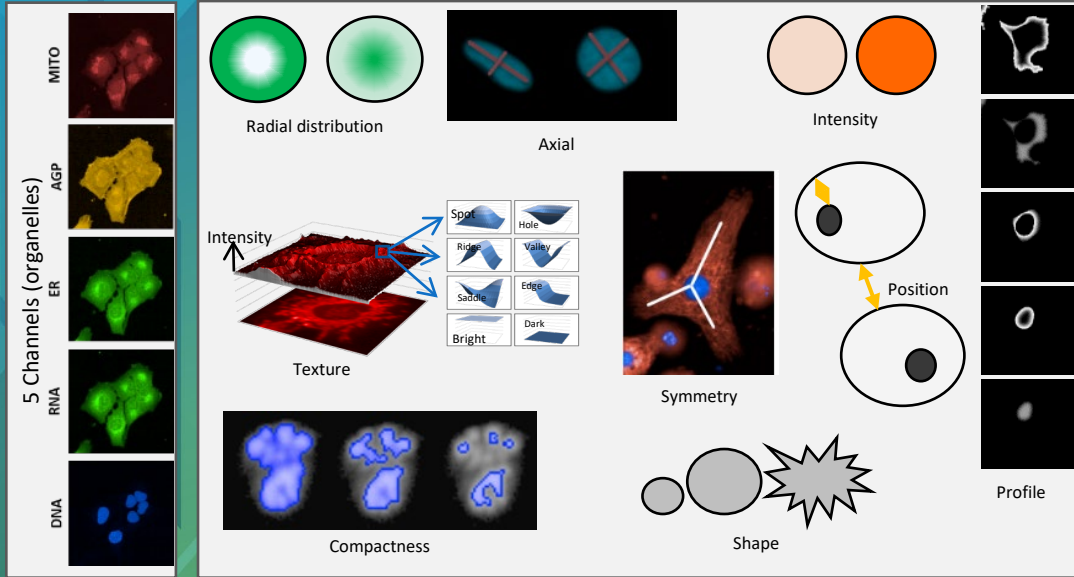
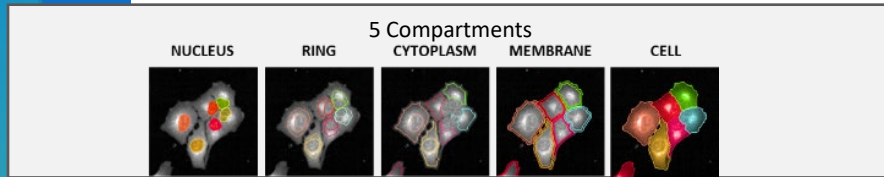
cell



ring



Phenotypic Feature Extraction



49 Feature Categories
(ex. MITO_Texture_Cytoplasm)

1300 features / cell

		Module								
		Position [7]	Basic morphology [5]	SCARP morphology					Intensity [9]	Texture [14]
				Symmetry [80]	Compactness [40]	Axial [20]	Radial [28]	Profile [20-30]		
Channel	DNA			Nuclei	Nuclei	Nuclei	Nuclei Cell	Nuclei Cytoplasm	Nuclei	Nuclei
	RNA			Nuclei	Nuclei	Nuclei	Nuclei	Nuclei	Nuclei	Nuclei
	ER			Cell	Cell	Cell	Cell	Cytoplasm	Ring Cytoplasm	Ring Cytoplasm
	AGP			Cell	Cell	Cell	Cell	Nuclei Cytoplasm	Ring Cytoplasm Membrane	Ring Cytoplasm Membrane
	Mito			Cell	Cell	Cell	Cell	Nuclei Cytoplasm	Ring Cytoplasm	Ring Cytoplasm
	Not associated with a channel	Nuclei Cell	Nuclei Cell							

PerkinElmer Opera Phenix

Modality: Confocal (single z)

Objective: 20X Water

Plate: CellCarrier-384 Ultra

Fields: 5 or 9

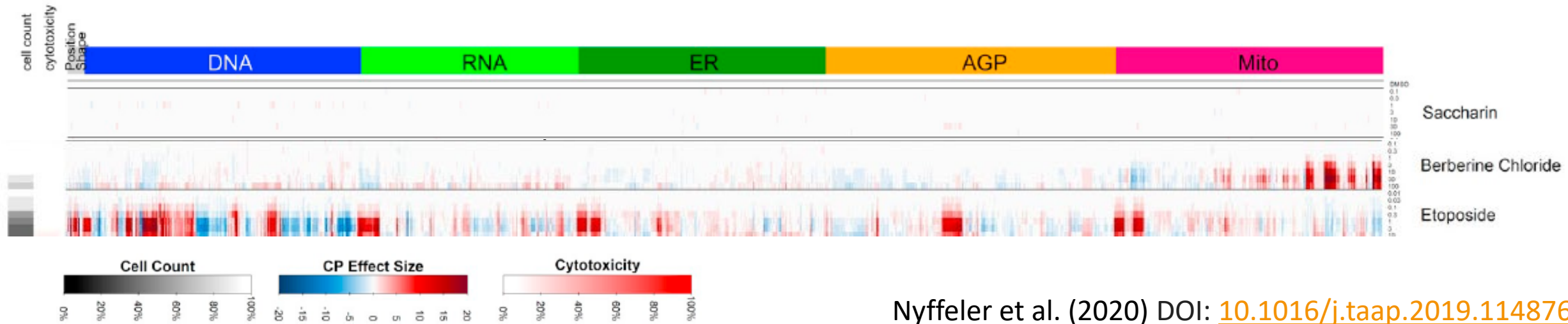
Harmony software performs feature extraction

Slide by Joshua Harrill

Illustrations from Perkin Elmer

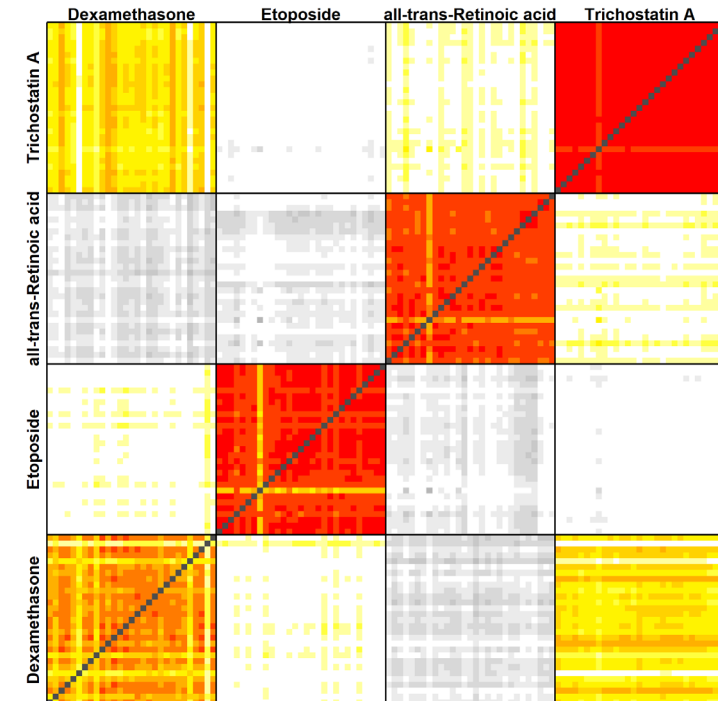
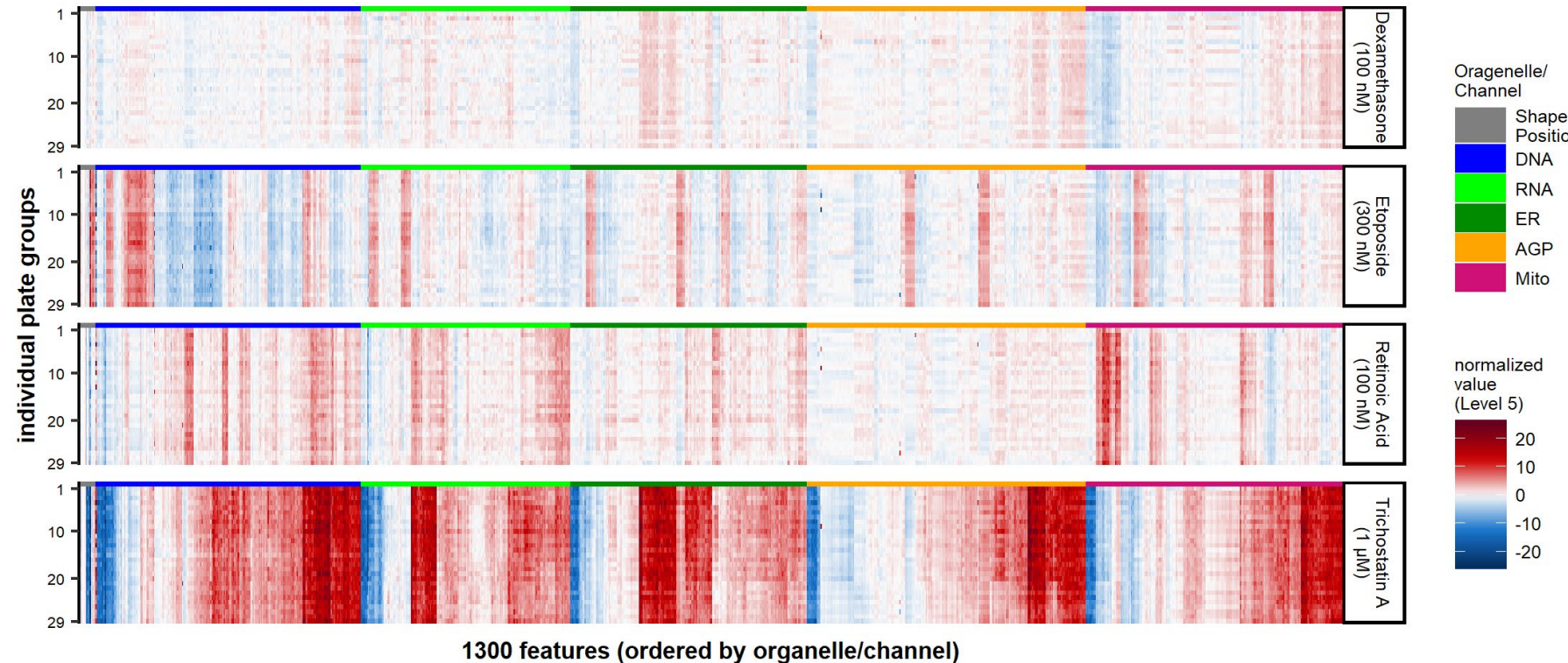


Quantification of Cellular Features



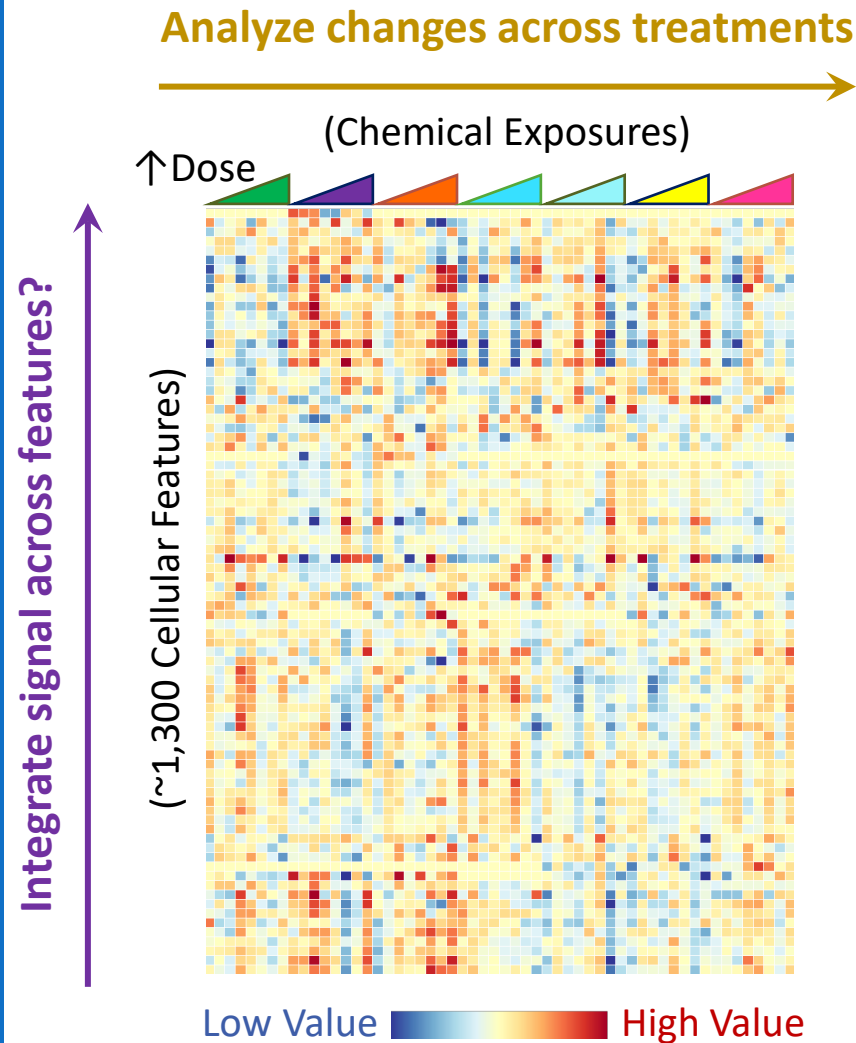
- Cell-level features are summarized per well & normalized to controls
- Different chemicals induce distinct, dose-responsive profiles

Assay Performance / Reproducibility



⇒ Reference chemicals produce reproducible and distinct profiles.

High-Dimensional Dose-Response Models



- Different features may respond at different doses of a given exposure!
- Need to analyze both:
 - Dose-responsive trends
 - Coordinated changes across features
- Differences from transcriptomics:
 - Lack knowledgebases linking features to biological processes
 - Certain features are highly correlated

Cell Painting Dose-Response Models

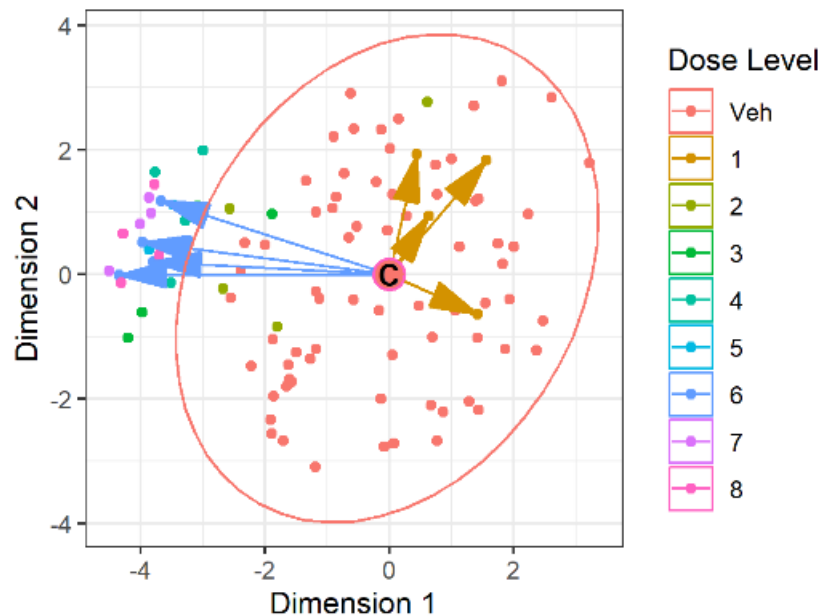
Global Mahalanobis

derive a Mahalanobis distance
(relative to control wells)

1300 features

Feature-level
fitting

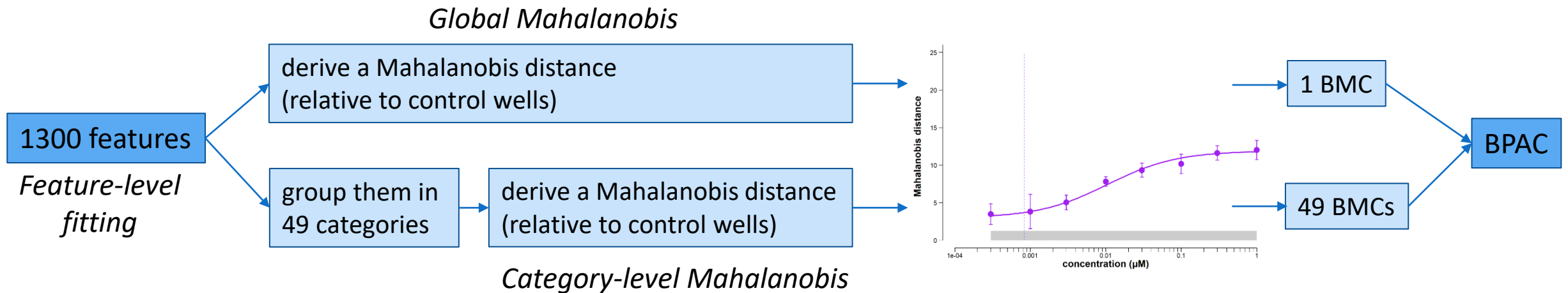
*This figure is for illustrative
purposes, actual calculations
involve higher number of
dimensions.*



Mahalanobis Distance (D_M):

- A multivariate distance metric that measures the distance between a point (vector) and a distribution
- Essentially measures how much an overall cell painting profile differs from control wells
- Considers the variability of control wells in each dimension

Cell Painting Dose-Response Models



- Chemicals where a BMC can be determined using either the global or category D_M approach are considered active.
- The minimum of the global or most sensitive category BMC is the **Biological Phenotype Altering Concentration (BPAC)**

Acknowledgements



Questions?

everett.logan@epa.gov

CCTE Leadership

Rusty Thomas

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Katie Paul Friedman

Kimberly Slentz-Kesler

HTTr Team

Joshua Harrill

Richard Judson

Imran Shah

Derik Haggard

Joseph Bundy

Beena Vallanat

Jesse Rogers

Bryant Chambers

Laura Word

Jacob Fredenburg

Sarah Davidson-Fritz

James Johnson

Felix Harris

Khan Inan

Joshua Witten

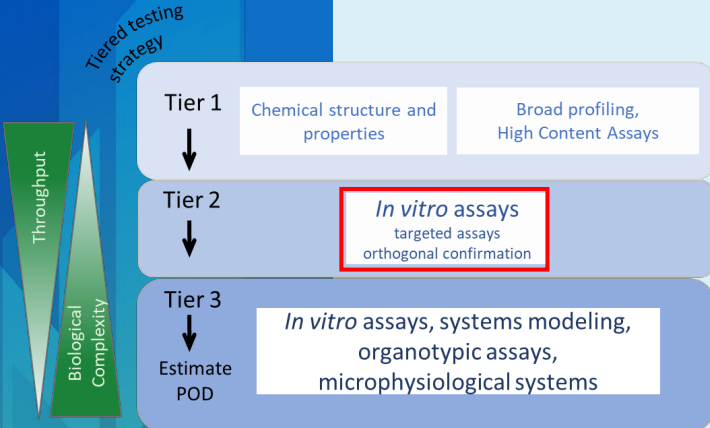
Woody Setzer

Clinton Willis

Thomas Sheffield



Demo



Toxicity Forecasting (ToxCast)

Madison Feshuk

(with contributions from Katie Paul Friedman)

ToxCast Database Coverage

The Toxicity Forecaster (ToxCast) program curates and makes publicly available targeted bioactivity screening data. Latest database release (v4.1) includes:

26 Assay Sources

623 Unique Assays

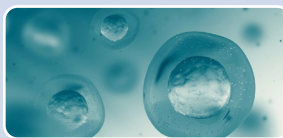
1496 Unique Endpoints

9559 Chemicals

Including a TOX21 assay source for data generated by the TOX21 program



Diverse biology with **over 500 mapped gene targets**, including:



Endocrine-Related: Estrogen Receptor, Androgen Receptor, Thyroid, Steroidogenesis



Cellular Signaling Pathways: Cytotoxicity, Proliferation, Stress, Mitochondrial Toxicity

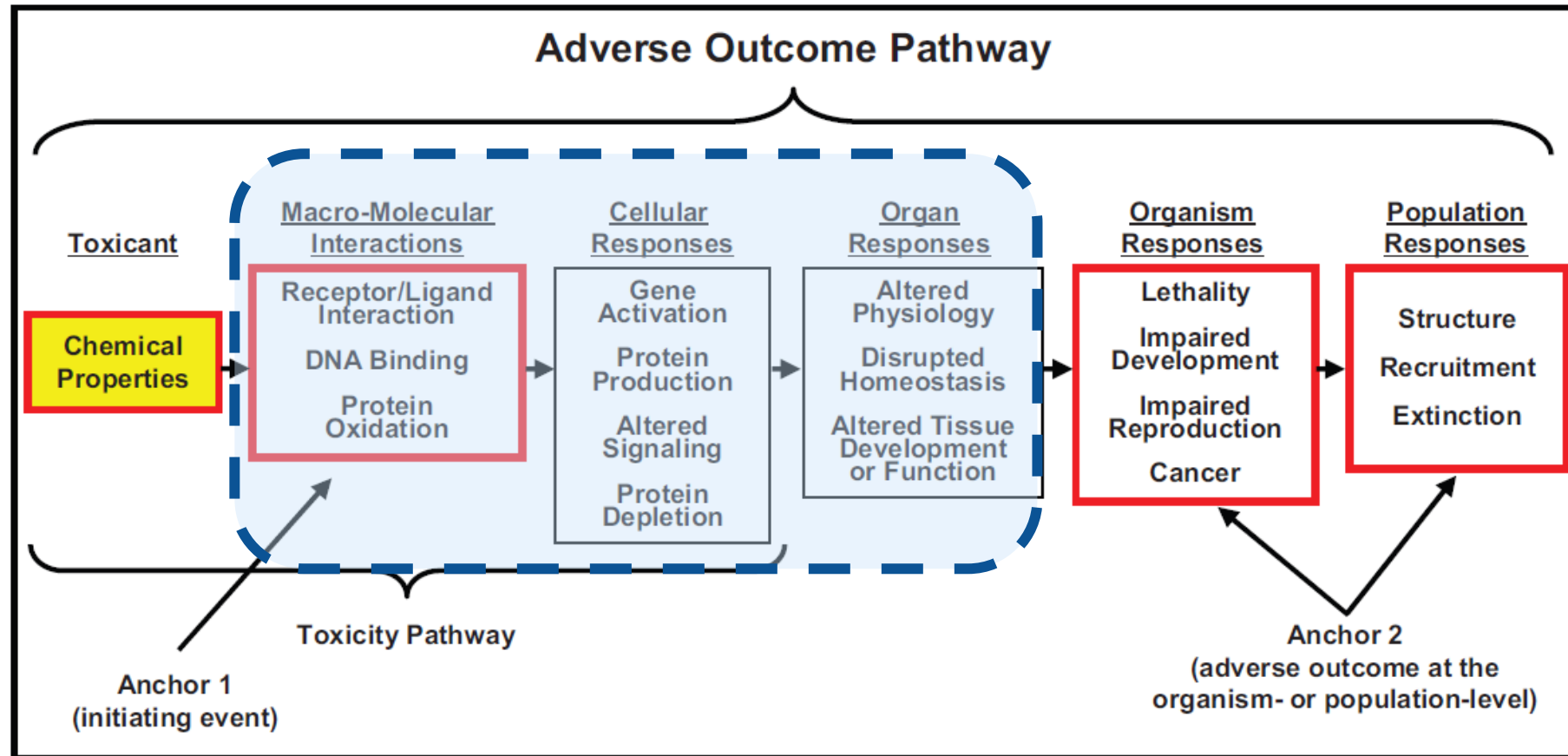


Protein Interactions: Receptors, Transporters, Ion Channels, Enzymes



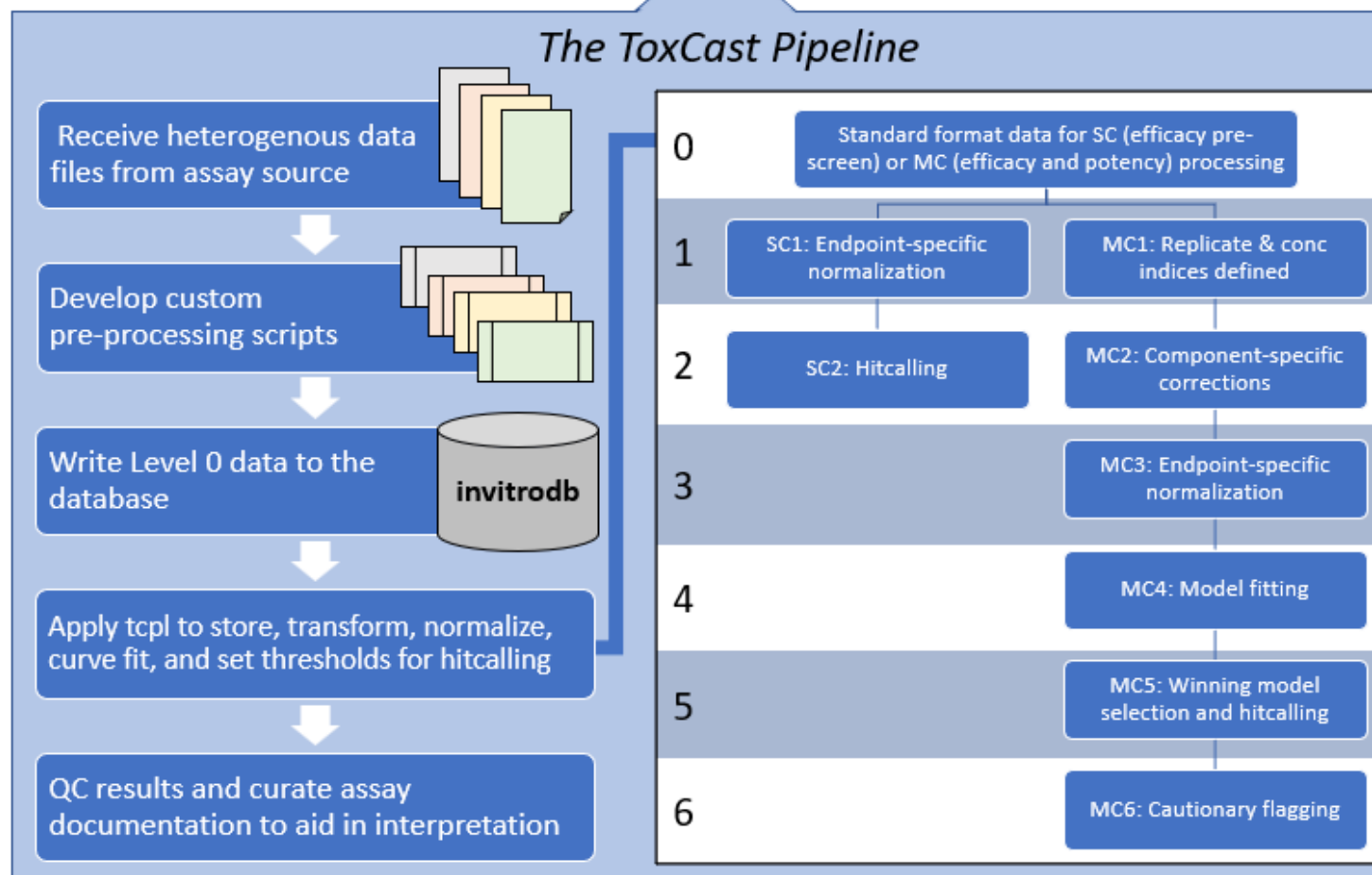
Complex Responses, e.g. Immune Response, Development, Neurotoxicity, etc.

Heterogeneous targeted NAMs in ToxCast address a range of event types in the AOP framework



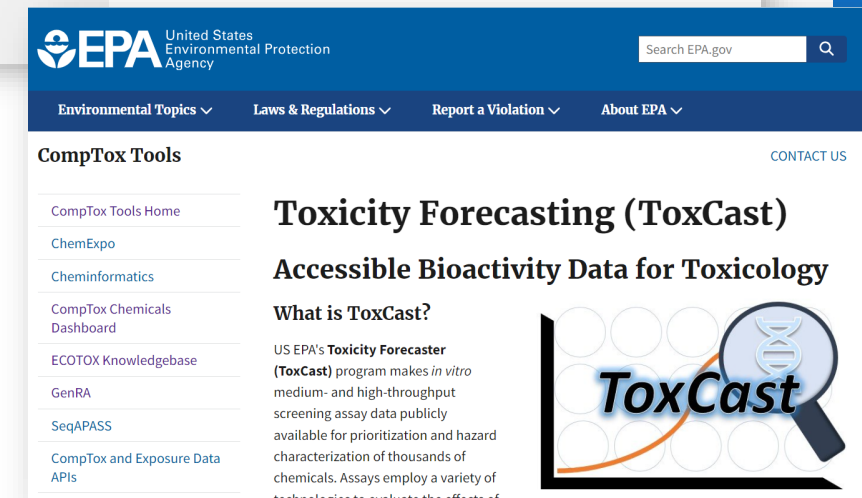
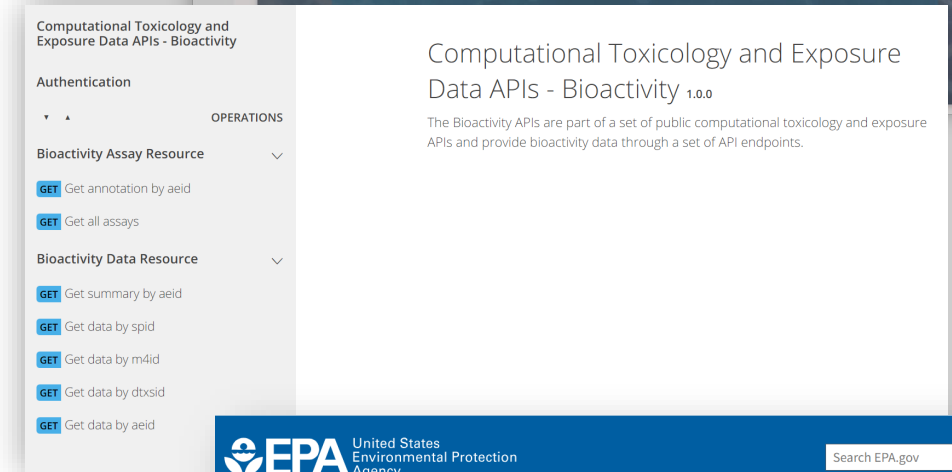
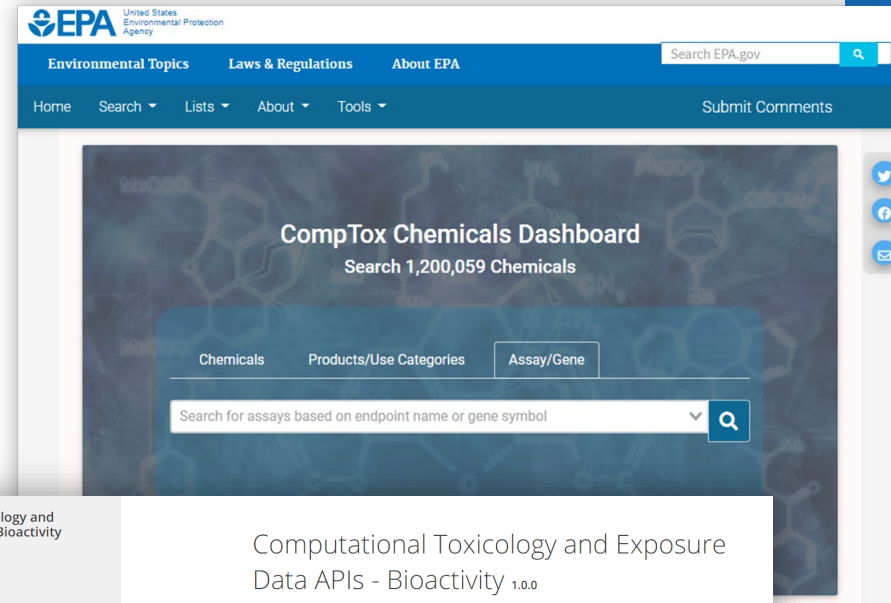
ToxCast Pipeline and Database

Process Overview



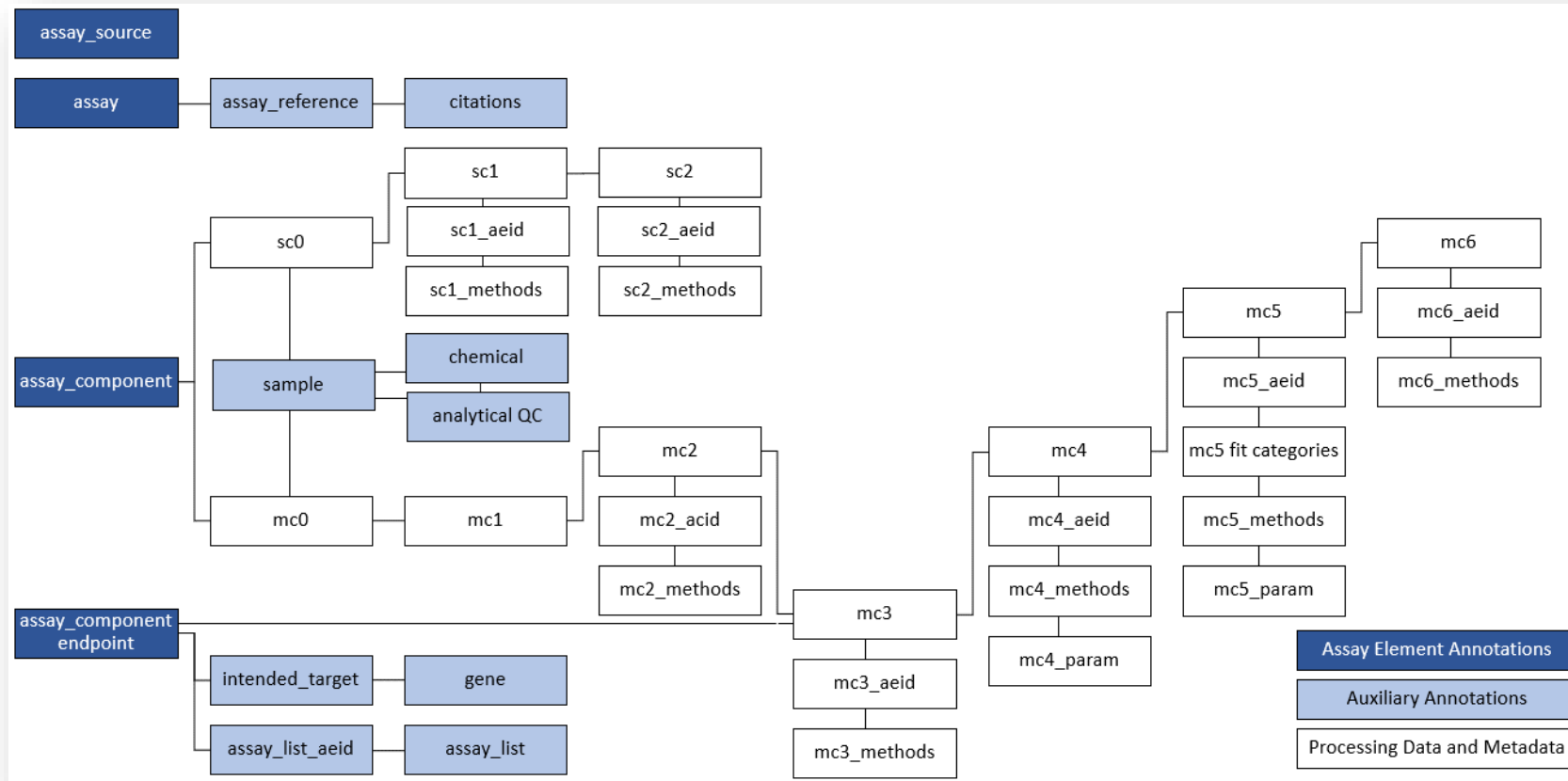
Exploring ToxCast

- Ongoing work has also focused on augmenting and diversifying how ToxCast data can be accessed for our users.
- ToxCast data is accessible via:
 - [CompTox Chemicals Dashboard](#)
 - [Computational Toxicology and Exposure Bioactivity APIs](#)
 - [Downloadable Data Pages](#)



Database Structure

- ToxCast covers diverse biological space and annotations help us flexibly aggregate and differentiate processed ToxCast data for user needs
- The ToxCast database (invitrodb) captures the following types of information:
 - Assay Element Annotations
 - Auxiliary Annotations
 - Processing Data and Metadata



Assay Element Annotations

- Each annotation is assigned as a feature to an assay element level:
 - **Assay Source:** *Who* conducted the assay
 - **Assay:** *What* assay platform was used
 - **Assay Component:** “Raw” readout of *what* was measured
 - **Assay (component) Endpoint:** *How* the measurement is interpreted (i.e. normalized component data)

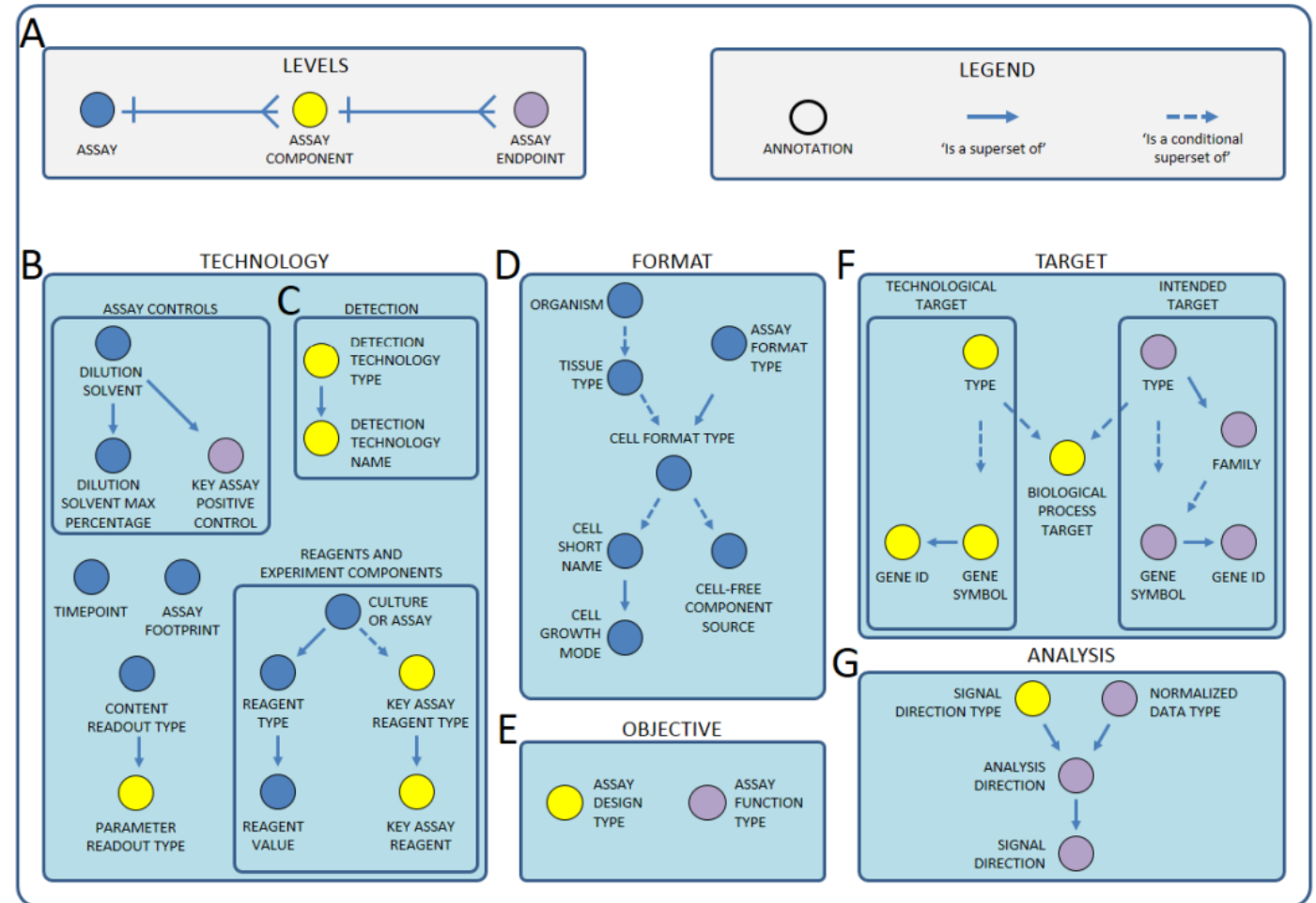


Note: All processing with tcpl occurs at the assay component or assay endpoint, depending on the processing type (single-concentration or multiple-concentration) and level. **No data is stored at the assay or assay source level.**

Assay Element Annotations

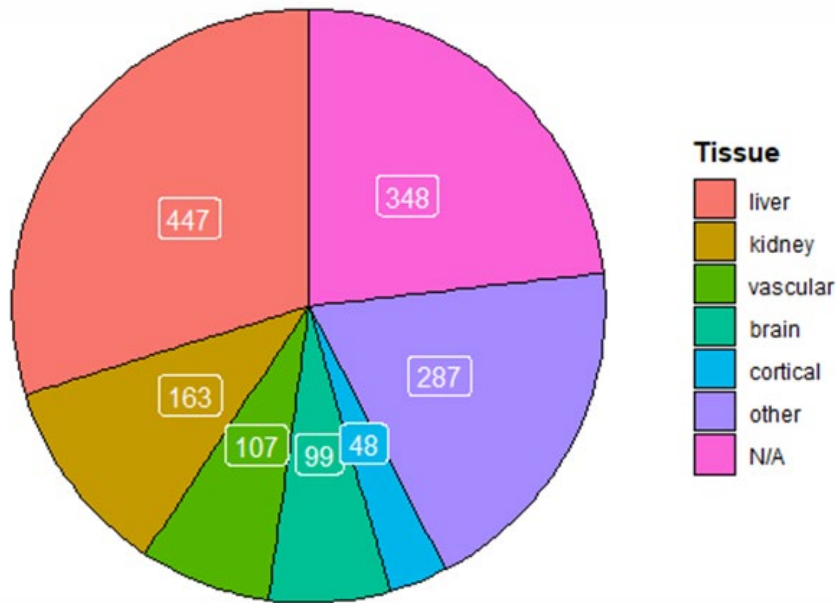
- Annotations follow Bioassay Ontology (BAO) framework capture four types of information:

- Identification (A)
 - Design (B-E)
 - Technology
 - Format
 - Objective
 - Target (F)
 - Technological target
 - Intended target
 - Biological process
 - Analysis (G)



Assay Element Annotations

- Most annotations employ controlled vocabulary within the database
- Some annotations are hierarchical
- e.g., general 'intended_target_family' and more specific 'intended_target_family_sub'



Tissue of origin across all assays



Intended_target_family frequency across all endpoints

Auxiliary Annotations

- Capture additional information, including:
 - Assay list presence
 - Linkages to relevant Adverse Outcome Pathways (AOPs) and Key Events (KEs)
 - Relevant gene identifier(s) from National Center for Biotechnology Information (NCBI)
 - Reagents or experimental conditions
 - Publications describing assay design or results

The screenshot displays a database management interface. On the left, a 'SCHEMAS' panel shows a tree view of the 'invitrodb' database, listing various tables such as 'assay', 'assay_component', 'assay_component_descriptions', 'assay_component_endpoint', 'assay_component_endpoint_descriptions', 'assay_component_map', 'assay_descriptions', 'assay_list', 'assay_list_aeid', 'assay_reagent', 'assay_reagent_armitage', 'assay_reference', 'assay_source', 'chemical', 'chemical_assay_count', 'chemical_library', 'citations', 'class', 'cytotox', 'etl_metadata', 'flyway_schema_history', 'gene', and 'intended_target'. The main window shows a SQL query: `1 • select * from invitrodb.assay_component_endpoint;` The 'Result Grid' below the query displays the following data:

aeid	acid	assay_component_endpoint_name	export_ready	internal_ready	assay_component_endpoint_desc	assay_function_type	normalized_data_t
2	1	ACEA_ER_80hr	1	1	Data from the assay component ACEA_ER_80h...	signaling	percent_activity
4	2	APR_HepG2_CellCycleArrest_1hr	1	1	Data from the assay component APR_HepG2_C...	signaling	log2_fold_induction
6	3	APR_HepG2_CellLoss_1hr	1	1	Data from the assay component APR_HepG2_C...	viability	log2_fold_induction
8	4	APR_HepG2_MicrotubuleCSK_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
10	5	APR_HepG2_MitoMass_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
12	6	APR_HepG2_MitoMembPot_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
14	7	APR_HepG2_MitoticArrest_1hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
16	8	APR_HepG2_NuclearSize_1hr	1	1	Data from the assay component APR_HepG2_N...	signaling	log2_fold_induction
18	9	APR_HepG2_P-H2AX_1hr	1	1	Data from the assay component APR_HepG2_P...	signaling	log2_fold_induction
20	10	APR_HepG2_p53Act_1hr	1	1	Data from the assay component APR_HepG2_p...	signaling	log2_fold_induction
22	11	APR_HepG2_StressKinase_1hr	1	1	Data from the assay component APR_HepG2_S...	signaling	log2_fold_induction
24	12	APR_HepG2_CellCycleArrest_24hr	1	1	Data from the assay component APR_HepG2_C...	signaling	log2_fold_induction
26	13	APR_HepG2_CellLoss_24hr	1	1	Data from the assay component APR_HepG2_C...	viability	log2_fold_induction
28	14	APR_HepG2_MicrotubuleCSK_24hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction
30	15	APR_HepG2_MitoMass_24hr	1	1	Data from the assay component APR_HepG2_M...	signaling	log2_fold_induction



Demo

Demo

- Toxicity Forecasting (ToxCast) home page <https://www.epa.gov/comptox-tools/toxicity-forecasting-toxcast>
 - Exploring ToxCast Data → Download Database Package
- Tcpl CRAN: <https://cran.r-project.org/web/packages/tcpl/index.html>
- Tcpl GitHub: <https://github.com/USEPA/CompTox-ToxCast-tcpl>
- CCD: <https://comptox.epa.gov/dashboard/>
 - Single Chemical Search "BPA" > Navigate to ToxCast tab >
 - ToxCast Summary plot (AC50 vs Scaled Top (max modeled response/cutoff), cytotoxicity burst median and lower bounds)
 - Bioactivity grid (Adding additional fields like Annotations, Inspecting plots)
 - Search by gene "estrogen"
 - Search by assay "ACEA_ER_80hr"
 - Lists of Assay vs Chemicals > Send to Batch
 - Batch Search Export of ToxCast AC50 values
- CCTE APIs home <https://api-ccte.epa.gov/docs/> (Must request API key to access)
- Bioactivity APIs <https://api-ccte.epa.gov/docs/bioactivity.html>
 - Overview of different request types
- ccdR for accessing APIs <https://cran.r-project.org/web/packages/ccdR/index.html>

CompTox Chemicals Dashboard (CCD)

<https://comptox.epa.gov/dashboard>

- CCD's ToxCast bioactivity module presents a view of potency and relative efficacy metrics across ToxCast endpoints for chemicals of interest
- Users can easily sort, filter, and export ToxCast results and assay descriptions
- Notable updates in the CCD v2.3 release (December 2023) include:
 - Data was refreshed to invitrodb v4.1
 - ToxCast Summary tab is now a single tab that combines the previous ToxCast Summary and ToxCast Conc. Response tabs
 - Bioactivity Summary Grid includes v4.1 information in new columns, including benchmark dose (BMD), benchmark response (BMR), and Continuous Hitcall

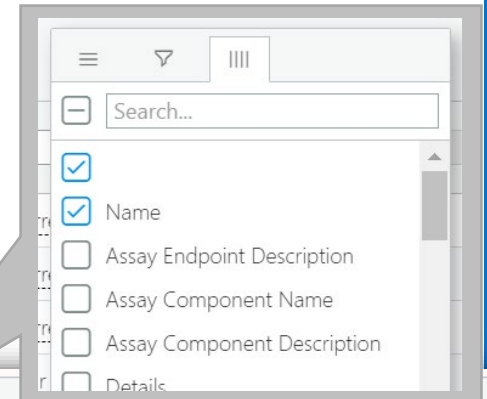
• *Example on right: Bisphenol A*

<https://comptox.epa.gov/dashboard/chemical/invitrodb/DTXSID7020182>



Filtering ToxCast Data on the CCD CompTox Chemicals Dashboard: <https://comptox.epa.gov/dashboard>

- CCD's ToxCast bioactivity module presents a view of potency and relative efficacy metrics across ToxCast endpoints for chemicals of interest
- Users can easily sort, filter, and export ToxCast results and assay descriptions
- Example: Consider BPA [DTXSID7020182](#)
 - Select ☰ in Bioactivity Summary Grid column headers to add additional annotation columns ☰☰☰
 - Explore!
 - Below shows results filtered to **EDSP ER Assay List** (assays used in the ToxCast ER pathway model)



<input type="checkbox"/>	Name ↑	Hit Call ↓↑	Assay Lists ▾ ↓↑	Gene Symbol ↓↑ ☰	Organism ↓↑	Tissue ↓↑	Cell Format ↓↑	Intended Target Family ↓↑
<input type="checkbox"/>			(1) EDSP ER					
<input type="checkbox"/>	ACEA_ER_80hr	Active	EDSP_ER	ESR1	human	breast	cell line	nuclear receptor
<input type="checkbox"/>	ACEA_ER_AUC_viability	Inactive	cytotoxicity burst EDSP_ER		human	breast	cell line	cell cycle
<input type="checkbox"/>	ATG_ERE_CIS	Active	EDSP_ER	ESR1	human	liver	cell line	nuclear receptor
<input type="checkbox"/>	ATG_ERa_TRANS	Active	EDSP_ER	ESR1	human	liver	cell line	nuclear receptor
<input type="checkbox"/>	NVS_NR_bER	Active	EDSP_ER	ESR1	bovine	uterus	tissue-based d cell-free	nuclear receptor

Filtering ToxCast Data on the CCD CompTox Chemicals Dashboard:

<https://comptox.epa.gov/dashboard>

- CCD's ToxCast bioactivity module presents a view of potency and relative efficacy metrics across ToxCast endpoints for chemicals of interest
- Users can easily sort, filter, and export ToxCast results and assay descriptions
- Example: Consider BPA [DTXSID7020182](#)
 - Select ☰ in Bioactivity Summary Grid column headers to add additional annotation columns ☰☰☰
 - Explore!
 - Below shows results filtered to **Actives in human ESR1 cell-based assays**

<input type="checkbox"/>	Name ↑	Hit Call ↓↑	Assay Lists ▾ ↓↑	Gene Symbol ▾ ↓↑ ☰	Organism ▾ ↓↑	Tissue ↓↑	Cell Format ▾ ↓↑	Intended Target Family ↓↑
	<input type="text"/>	<input type="text"/>	▾ (1) EDSP ER ▾	ESR1	human	<input type="text"/>	cell line	<input type="text"/>
<input type="checkbox"/>	ACEA_ER_80hr	Active	EDSP ER	ESR1	human	breast	cell line	nuclear receptor
<input type="checkbox"/>	ATG_ERE_CIS	Active	EDSP ER	ESR1	human	liver	cell line	nuclear receptor
<input type="checkbox"/>	ATG_ERa_TRANS	Active	EDSP ER	ESR1	human	liver	cell line	nuclear receptor
<input type="checkbox"/>	OT_ER_ERaERa_0480	Active	EDSP ER	ESR1	human	kidney	cell line	nuclear receptor
<input type="checkbox"/>	OT_ER_ERaERa_1440	Active	EDSP ER	ESR1	human	kidney	cell line	nuclear receptor
<input type="checkbox"/>	OT_ER_ERaERb_0480	Active	EDSP ER	ESR1 ESR2	human	kidney	cell line	nuclear receptor

ToxCast data are publicly accessible from the CompTox Chemicals Dashboard

Search by gene, vendor name, etc.

CompTox Chemicals Dashboard v2.2.1 Home Search Lists About Tools Submit Comments Search all data

Assay Endpoints List

Search Assay Lists

Showing 2205 of 2205 Records

Assay Component Endpoint Name	Details	Multi Conc. Actives	Single Conc. Active	Description	Gene Symbols
ACEA_AR_agonist_80hr		161/1830 (8.80%)	-	Data from the assay component ACEA_AR_agonist_80hr was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, measures of the cells for gain-of-signal activity can be used to understand the signaling at the pathway-level as they relate to the gene AR. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a signaling function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "steroidal".	AR
ACEA_AR_agonist_AUC_viability		609/1830 (33.28%)	-	Data from the assay component ACEA_AR_AUC_viability was analyzed in the negative fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, loss-of-signal activity can be used to understand changes in the viability. Furthermore, this assay endpoint can be referred to as a secondary readout, because this assay has produced multiple assay endpoints where this one serves a viability function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "cell cycle" intended target family, where the subfamily is "cytotoxicity".	
ACEA_AR_antagonist_80hr		743/1835 (40.49%)	-	Data from the assay component ACEA_AR_antagonist_80hr was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, measures of the cells for loss-of-signal activity can be used to understand the signaling at the pathway-level as they relate to the gene AR. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves a signaling function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "steroidal".	AR
ACEA_AR_antagonist_AUC_viability		707/1835 (38.53%)	-	Data from the assay component ACEA_AR_antagonist_AUC_viability was analyzed in the negative fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of growth reporter, loss-of-signal activity can be used to understand changes in the viability. Furthermore, this assay endpoint can be referred to as a secondary readout, because this assay has produced multiple assay endpoints where this one serves a viability function. To generalize the intended target to other reliable targets, this assay endpoint is annotated to the "cell cycle" intended target family, where the subfamily is "cytotoxicity".	

Rows: 2,205 Total Rows: 2,205

Many users are accustomed to viewing data per substance (as identified by a DSSTox identifier, or DTXSID), but you can also identify assay endpoint data by entering from Lists > Lists of Assays. These data can be exported after loading the data for the assay.

<https://comptox.epa.gov/dashboard/assay-endpoints>

Application Programming Interfaces (APIs)

<https://api-ccte.epa.gov/docs/bioactivity.html>

Computational Toxicology and Exposure Data APIs - Bioactivity

Authentication

OPERATIONS

Bioactivity Assay Resource

- GET Get annotation by aeid
- GET Get all assays

Bioactivity Data Resource

- GET Get summary by aeid
- GET Get data by spid
- GET Get data by m4id
- GET Get data by dtxid
- GET Get data by aeid

BIOACTIVITY DATA RESOURCE

Get summary by aeid

GET /bioactivity/data/summary/search/by-aeid/{aeid}

REQUEST

PATH PARAMETERS

* aeid int32 1386

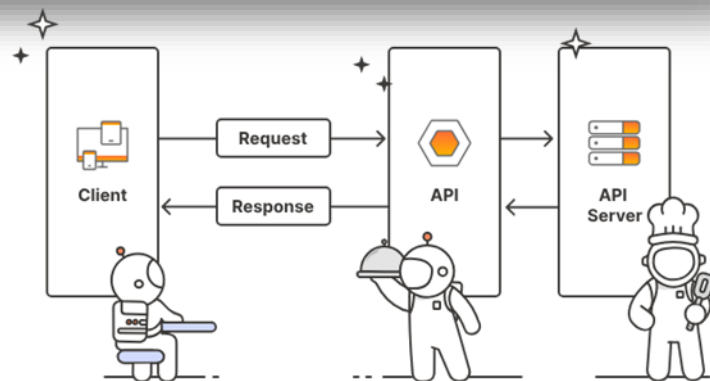
Numeric assay endpoint identifier
Examples: 1386

API Server <https://api-ccte.epa.gov>
Authentication Required (None Applied)

FILL EXAMPLE CLEAR TRY

```
curl -X GET "https://api-ccte.epa.gov/bioactivity/data/summary/search/by-aeid/1386" -H "accept: application/hal+json" Copy
```

- APIs provide data for various use cases, including research and applications with user interfaces
- Users can avoid large data downloads by accessing invitrodb programmatically via an API
- This is a great read-only solution for users who require more flexibility than the CCD can provide
- For additional documentation, check out the [CCTE API Home Page](#) or [ccdR R package](#). More integration with tcpl is coming soon



ToxCast Data Downloads

<https://www.epa.gov/comptox-tools/exploring-toxcast-data>

- Data downloads allow users to set up their own personal instance of the invitrodb MySQL database and interact with the data directly via the tcpl R package
- This is a preferred option for more customized or programmatic ToxCast data needs, or if users want to do their own data processing

tcpl: ToxCast Data Analysis Pipeline

A set of tools for processing and modeling high-throughput and high-content chemical screening data. The package was developed for the chemical screening data generated by the US EPA ToxCast program, but can be used for diverse chemical screening efforts.

Version: 3.1.0
Depends: R (≥ 3.5.0)
Imports: [data.table](#) (≥ 1.9.4), [DBI](#), [RMariaDB](#), [numDeriv](#), [RColorBrewer](#), [utils](#), [stats](#), [methods](#), [graphics](#), [grDevices](#), [sqldf](#), [dplyr](#), [tidyr](#), [plotly](#), [tcplfit2](#), [ggplot2](#), [gridExtra](#), [stringr](#)
Suggests: [roxygen2](#), [knitr](#), [prettydoc](#), [rmarkdown](#), [htmlTable](#), [testthat](#) (≥ 3.0.0), [reshape2](#), [viridis](#), [kableExtra](#), [colorspace](#), [magrittr](#), [vdiffr](#)
Published: 2023-10-06
Author: Richard S Judson [ctb, [ths](#)], Dayne L Filer [aut], Jason Brown [cre], Sarah E Davidson-Fritz [ORCID](#) [ctb], Madison Feshuk [ORCID](#) [ctb], Lori Kolaczowski [ctb], Kurt Dunham [ctb], Carter Thunes [ctb], Ashley Ko [ctb], Todd Zurlinden [ctb], Parth Kothiyia [ctb], Woodrow R Setzer [ctb], Matthew T Martin [ctb, [ths](#)], Katie Paul Friedman [ORCID](#) [ctb]
Maintainer: Jason Brown <brown.jason@epa.gov>
License: [MIT](#) + file [LICENSE](#)
URL: <https://github.com/USEPA/CompTox-ToxCast-tcpl>
NeedsCompilation: no
Materials: [NEWS](#)
CRAN checks: [tcpl results](#)

CompTox Tools

[CompTox Tools Home](#)

[ChemExpo](#)

[Cheminformatics](#)

[CompTox Chemicals Dashboard](#)

[ECOTOX Knowledgebase](#)

[GenRA](#)

[SeqAPASS](#)

[CompTox and Exposure Data APIs](#)

[Downloadable Computational Toxicology Data](#)

[CONTACT US](#)

Exploring ToxCast Data

On this page:

[Download ToxCast Data](#) | [ToxCast Results and Processing](#) | [Explore Use of ToxCast Data](#) | [Citations](#)

ToxCast data, once generated by labs and processed by EPA through the pipeline, can be downloaded from our website and is also available in the CompTox Chemicals Dashboard. The most recent ToxCast data is available in the [invitroDBv4.1 database](#). The database was released in September 2023. Data files from previously published ToxCast data releases are still [available for download](#). This page provides links to all relevant ToxCast chemical and assay data.

[ToxCast Chemicals](#) | [ToxCast Assays](#)

Resources

[About ToxCast](#)

[ToxCast Publications](#)

[Downloadable Computational Toxicology Data](#)

[Example Use Cases](#)

Download ToxCast Data

- **Most Recent InVitro Database Release (invitroDBv4.1) and Data Processing Package:** EPA's analysis of chemicals screened through high-throughput screening assays. The database release includes a MySQL database, release notes, summary files, assay information and concentration response plots. In conjunction, the ToxCast Pipeline for storing, transforming, normalizing, curve-fitting, and activity hit-calling is available as an R package, library(tcpl). Tcpl and invitrodb provide a standard for consistent and reproducible curve-fitting and data management for diverse, targeted in vitro assay data with readily available documentation, thus enabling sharing and use of these data in myriad toxicology applications.
 - [Download Database Package](#)
 - Download the tcpl R package:
 - [GitHub](#)
 - [CRAN](#)

Conclusions

- Hazard NAMs are being developed as alternatives to traditional hazard methods
- Many hazard NAM data are available in the CompTox Chemicals Dashboard, download or API
- Each assay technology may have specific limitations, which may require user discretion for more complex interpretations of the data
- Hazard NAM data may be qualitatively and quantitatively informative in different contexts