ANNOUNCEMENT

EDSP21 and ToxCast Dashboards To Be Discontinued
The Existing CompTox Portal
Two legacy dashboards to be discontinued
invitrodb version 3 data release

• When invitrodb version 3 data were released access was provided to the data via the CompTox Chemicals Dashboard only

• Legacy EDSP21 and ToxCast dashboards were not updated with new data and will be retired from service by end of August 2019

• New functionality supporting the bioactivity data associated with ToxCast, Tox21 and EDSP is available at https://comptox.epa.gov/dashboard

• This presentation provides an overview of bioactivity data in the dashboard
Bioactivity Sub-Tabs

Segregation of data
Bioactivity Data

- Summary view of data – tabular and graphical
- Navigate to the EDSP21 subset of assays
- Navigate to all Toxcast/Tox21 data
- Navigate to PubChem data widget
- ToxCast “Models” – now includes “COMPARA” data
ToxCast: Summary
Sub-Tab
ToxCast Summary Plot

Bisphenol A
80-05-7 | DTXSID7020182
Searched by Expert Validated Synonym.

Chemical Activity Summary

ToxCast Data

AC50 (uM): 40.39
Scaled top: 9.38
Assay Endpoint Name: ACEA_AR_agonist_80hr
Gene Symbol: AR
Organism: human
Tissue: prostate
Assay Format Type: cell-based
Biological Process Target: cell proliferation
Detection Technology: RT-CEC
Analysis Direction: NA
Intended Target Family: nuclear receptor

Description: 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 signalling function. To generalize the intended target to other relatable targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "steroidal".
The bioassay data displayed in this panel includes modeled AC50 values from multi-concentration data only. Single concentration data may also be available for some assay technologies. Single concentration data are included in the list of ‘tested’ assays endpoints if multi-concentration data are unavailable; this can be visualized by searching for a chemical, and clicking “All Tested” in the Assay pane in the Toxcast Dashboard. Raw, normalized, and interpreted single concentration data from level 0 to level 2 are fully available from the freely downloadable MySQL database, invitrodb. Internet Explorer may enable the best functionality to view the Toxcast Dashboard. The scaled response shown on the graph below is calculated by dividing the response values by the activity cutoff thereby enabling response comparisons across assay endpoints.
ToxCast Summary Plot

• Hover over target type and associated data points will “pulse”
• Click on target type to switch off all data points. Click again to switch them on.
• Download a copy of the Summary Plot by clicking on 

![download icon]
# ToxCast Summary Table

211 active of 989 assays

<table>
<thead>
<tr>
<th>Name</th>
<th>Modal</th>
<th>SeqAPASS</th>
<th>Gene Symbol</th>
<th>AOP</th>
<th>Event</th>
<th>Hit Call</th>
<th>Top</th>
<th>AC50</th>
<th>logAC50</th>
<th>Cutoff</th>
<th>ModIACc</th>
<th>Intended Target Family</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVS_ENZ_hTrkA</td>
<td>EAM52902.1</td>
<td>NTRK1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>43.6</td>
<td>21.0</td>
<td>1.32</td>
<td>20.0</td>
<td>1.28</td>
<td>kinase</td>
</tr>
<tr>
<td>BSK_HDFCGF_ColagenIII_down</td>
<td>NP_000081.1</td>
<td>COL3A1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>0.254</td>
<td>40.0</td>
<td>1.60</td>
<td>0.144</td>
<td>1.60</td>
<td>cell adhesion molecules</td>
</tr>
<tr>
<td>ACEA_ER_80hr</td>
<td>NP_000116.2</td>
<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
<td>112</td>
<td>0.373</td>
<td>-0.428</td>
<td>26.9</td>
<td>-0.666</td>
<td>1.32</td>
<td>nuclear receptor</td>
</tr>
<tr>
<td>ATG_ER_CIS_up</td>
<td>NP_000116.2</td>
<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
<td>2.41</td>
<td>9.81e-2</td>
<td>-1.01</td>
<td>0.503</td>
<td>-1.32</td>
<td>1.32</td>
<td>nuclear receptor</td>
</tr>
<tr>
<td>ATG_ERa_TRANS_up</td>
<td>NP_000116.2</td>
<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
<td>5.70</td>
<td>0.119</td>
<td>-0.923</td>
<td>1.15</td>
<td>-1.49</td>
<td>1.49</td>
<td>nuclear receptor</td>
</tr>
<tr>
<td>NVS_NRhER</td>
<td>NP_000116.2</td>
<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
<td>69.2</td>
<td>0.230</td>
<td>-0.639</td>
<td>24.4</td>
<td>-0.805</td>
<td>1.805</td>
<td>nuclear receptor</td>
</tr>
<tr>
<td>OT_ERaERa_0480</td>
<td>NP_000116.2</td>
<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
<td>175.5</td>
<td>5.73</td>
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<td>ACTIVE</td>
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<td>4.31</td>
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<td>2.15e-2</td>
<td>2.15e-2</td>
<td>nuclear receptor</td>
</tr>
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</tr>
<tr>
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<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
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<td>-0.200</td>
<td>20.0</td>
<td>-0.423</td>
<td>0.423</td>
<td>nuclear receptor</td>
</tr>
</tbody>
</table>
ToxCast Summary Table

- Select/change columns of data displayed in the table
- In the table hover over some column-headings for details
- Sort columns using up/down arrows
- Blue hyperlinks either download files or link out
<table>
<thead>
<tr>
<th>Name</th>
<th>Modal</th>
<th>SeqAPASS</th>
<th>Gene Symbol</th>
<th>AOP</th>
<th>Event</th>
<th>Hit Call</th>
<th>Top</th>
<th>AC50</th>
<th>logAC50</th>
<th>Cutoff</th>
<th>ModlAcc</th>
<th>Intended Target Family</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVS_ENZ_nTrkA</td>
<td></td>
<td>9AV529202.1</td>
<td>NTRK1</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>43.6</td>
<td>21.0</td>
<td>1.32</td>
<td>20.0</td>
<td>1.20</td>
<td>kinase</td>
</tr>
<tr>
<td>NVS_NR_nER</td>
<td></td>
<td>NP_000116.2</td>
<td>ESR1</td>
<td>200</td>
<td>1181</td>
<td>ACTIVE</td>
<td>69.2</td>
<td>0.230</td>
<td>-0.639</td>
<td>24.4</td>
<td>-0.805</td>
<td>nuclear receptor</td>
</tr>
<tr>
<td>NVS_NR_nGR</td>
<td></td>
<td>NP_00167.1</td>
<td>NR3C1</td>
<td>66</td>
<td>654</td>
<td>ACTIVE</td>
<td>100</td>
<td>5.04</td>
<td>0.702</td>
<td>28.9</td>
<td>0.286</td>
<td>nuclear receptor</td>
</tr>
<tr>
<td>NVS_ADME_hCYP1A1</td>
<td></td>
<td>NP_000490.1</td>
<td>CYP1A1</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>83.5</td>
<td>5.85</td>
<td>0.767</td>
<td>20.0</td>
<td>0.252</td>
<td>cyp</td>
</tr>
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<td>NVS_GPCR_hAdoRA1</td>
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<td>-</td>
<td>ACTIVE</td>
<td>76.2</td>
<td>2.04</td>
<td>0.311</td>
<td>29.3</td>
<td>-0.146</td>
<td>gpcr</td>
</tr>
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<td></td>
<td>NP_000675.1</td>
<td>ADRB1</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>28.0</td>
<td>22.3</td>
<td>1.35</td>
<td>20.0</td>
<td>1.67</td>
<td>gpcr</td>
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<td>NP_00758.1</td>
<td>CYP2B6</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>87.6</td>
<td>11.5</td>
<td>1.06</td>
<td>20.0</td>
<td>0.380</td>
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<tr>
<td>NVS_ADME_hCYP2C19_Activ</td>
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<td>CYP2C19</td>
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<td>-</td>
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<td>5.60</td>
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<td>20.0</td>
<td>-8.01e-2</td>
<td>cyp</td>
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<tr>
<td>NVS_ADME_hCYP2C9</td>
<td></td>
<td>NP_000762.2</td>
<td>CYP2C9</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>72.0</td>
<td>2.49</td>
<td>0.396</td>
<td>20.0</td>
<td>0.211</td>
<td>cyp</td>
</tr>
<tr>
<td>NVS_ADME_hCYP2C18</td>
<td></td>
<td>NP_00763.1</td>
<td>CYP2C18</td>
<td>-</td>
<td>-</td>
<td>ACTIVE</td>
<td>104</td>
<td>6.35</td>
<td>0.803</td>
<td>20.0</td>
<td>0.569</td>
<td>cyp</td>
</tr>
</tbody>
</table>
ToxCast Summary Table – Display Assay Modal

- Select modal icon to display assay details
  - Assay annotations
  - Citations re. the assay
  - tcpl processing details
  - Reagents used in assay
  - Links to Adverse Outcome Pathways
Endocrine Disruptor Screening Program (EDSP) Sub-Tab
EDSP21 Subset of Assays
### EDSP21 Subset of Assays

<table>
<thead>
<tr>
<th>Set</th>
<th>Selected Count</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ER</td>
<td>18 of 28</td>
<td></td>
</tr>
<tr>
<td>AR</td>
<td>7 of 19</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>7 of 14</td>
<td></td>
</tr>
<tr>
<td>Steroidogenesis</td>
<td>2 of 27</td>
<td></td>
</tr>
</tbody>
</table>

- The EDSP21 assays are segregated into ER (Estrogen Receptor), AR (Androgen Receptor), Thyroid and Steroidogenesis.

- Selecting the Active subset of hit calls displays all associated bioactivity curves.

- Use Filter Assays to filter by text string.
EDSP21 Subset of Assays

• Display bioactivity plots associated with an assay – default is “Representative Samples Only” – one chart per assay. Deselect to see all charts for an assay.

• Select to switch between multiple chart or single chart view

• Download a summary of bioactivity for a chemical as Excel or TSV
EDSP21 Subset of Assays

- For a summary description of an assay hover over the assay name.
- For full assay details select the associated assay modal icon.

Data from the assay component ATG_ERa_TRANS was analyzed into 1 assay endpoint. This assay endpoint, ATG_ERa_TRANS_up, was analyzed in the positive fitting direction relative to DMSO as the negative control and baseline of activity. Using a type of inducible reporter, measures of mRNA for gain-of-function activity can be used to understand the reporter gene at the transcription factor level as they relate to the gene ESR1. 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 reporter gene function.

To generalize the intended target to other related targets, this assay endpoint is annotated to the "nuclear receptor" intended target family, where the subfamily is "steroidal".
Associated Analytical QC data

• When analytical quality control data is available the Pass/Fail grade with purity information and annotations are displayed above the bioactivity charts

• The Analytical QC data are hyperlinked to the relevant data files
ToxCast/Tox21
Sub-Tab
ToxCast/Tox21 data

- Navigation of data under this sub-tab parallels the capabilities of the EDSP21 sub-tab except data are organized based on “assay vendor”
Filtering – Gene annotation added

- Using the filter assay box it is possible to find all assays associated with a particular gene. The example below shows filtering based on PPARA (PPAR-alpha)
Filtering

Search through list of assays by Gene Symbol – e.g. ESR1 returns set of assays
PubChem
Sub-Tab
### PubChem Biological Activities

#### BioAssay Results

<table>
<thead>
<tr>
<th>Activity</th>
<th>Activity Value, µM</th>
<th>Activity Type</th>
<th>Target Name</th>
<th>BioAssay Name</th>
<th>BioAssay AID</th>
<th>Substance SID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inconclusive</td>
<td>0.0014</td>
<td>Potency</td>
<td>Chain A, Crystal Structure Of Human Estrogen-Related Receptor Gamma Ligand Binding Domain Complex With Bisphenol A (human)</td>
<td>qHTS assay to identify small molecule agonists of the endoplasmic reticulum stress response signaling pathway - cell viability counter screen</td>
<td>1159517</td>
<td>144214049</td>
</tr>
<tr>
<td>Active</td>
<td>0.0055</td>
<td>Kd</td>
<td>ESRG - estrogen related receptor gamma (human)</td>
<td>Experimentally measured binding affinity data (Kd) for protein-ligand complexes derived from PDB</td>
<td>977611</td>
<td>87557090</td>
</tr>
<tr>
<td>Active</td>
<td>0.0055</td>
<td>Kd</td>
<td>THRB - thyroid hormone receptor beta (human)</td>
<td>Binding affinity to human ER alpha</td>
<td>1121409</td>
<td>103308477</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>0.0126</td>
<td>Potency</td>
<td></td>
<td>qHTS assay for small molecule antagonists of thyroid hormone receptor beta signaling</td>
<td>568547</td>
<td>26752849</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>0.1364</td>
<td>Potency</td>
<td></td>
<td>qHTS assay to identify small molecule antagonists of the peroxisome proliferator-activated receptor delta (PPARdelta) signaling pathway - cell viability counter screen</td>
<td>743213</td>
<td>144210190</td>
</tr>
</tbody>
</table>
ToxCast Models
Sub-Tab
PubChem – integrated view of bioassay data

- Prediction models associated with bioactivity are all assembled under the ToxCast:Models sub-tab - the Estrogen and Androgen Pathway Models and the CERAPP and COMPARA QSAR models.

- For Model details and links to papers etc. hover over the help icon.

CoMPARA is a larger scale collaboration between 35 international groups, using QSAR models to predict androgen receptor activity using a common training set of 1746 compounds provided by U.S. EPA. A key result is a consensus model of AR agonist and antagonist activity that is run against the DSS tox chemical library. These results are intended to be used in prioritization for compounds for follow-up testing. More details about the project are available on ResearchGate.
Lists of Chemicals
Lists of Chemicals

- Chemical List page – lots of lists added including segregation
  - LIST: Algal Toxins, Amino Acids, Bisphenol Compounds, PAHs, Synthetic Cannabinoids and Psychoactives, Vitamins, PCBs
  - WIKILIST: Additives in Cigarettes, Extremely Hazardous Substances
  - EPA: Chemical Contaminants, Pesticides Chemical Search
  - TOXCAST related chemicals lists
Lists of Chemicals

- Filter lists using text string – “what are all ToxCast lists?”

<table>
<thead>
<tr>
<th>List Acronym</th>
<th>List Name</th>
<th>Last Updated</th>
<th>Number of Chemicals</th>
<th>List Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEMINV</td>
<td>EPA CHEMINV: EPA Chemical Inventory for ToxCast</td>
<td>2017-02-23</td>
<td>5231</td>
<td>CHEMINV is full list of unique DSSTox substances mapped to historical chemical inventory of physical samples registered by EPA’s ToxCast Chemical Contractor (Evotec) since launch of ToxCast program in 2007.</td>
</tr>
<tr>
<td>CHEMINV_DMSOINSOLUBLES</td>
<td>EPA CHEMINV: EPA ToxCast Chemventory DMSO Insolubles</td>
<td>2016-02-10</td>
<td>558</td>
<td>Chemicals in EPA’s ToxCast physical sample library CHEMINV insoluble in DMSO</td>
</tr>
<tr>
<td>CHEMINV_REACTIVES</td>
<td>EPA CHEMINV: EPA ToxCast Chemventory List of Reactives</td>
<td>2016-02-10</td>
<td>24</td>
<td>ToxCast Chemical inventory (CHEMINV) physical sample library list of chemicals that were deemed too reactive to include in HTS testing.</td>
</tr>
<tr>
<td>CHEMINV_STABILITY</td>
<td>EPA CHEMINV: EPA ToxCast Chemventory chemicals with Stability problems</td>
<td>2016-02-10</td>
<td>34</td>
<td>ToxCast chemical inventory (CHEMINV) physical sample library list of chemicals that were determined to have stability problems such that they decompose over time in DMSO.</td>
</tr>
<tr>
<td>CHEMINV_VOLATILES</td>
<td>EPA CHEMINV: EPA ToxCast CHEMINV list of volatiles</td>
<td>2016-02-10</td>
<td>130</td>
<td>List of volatile chemicals in EPA ToxCast chemical inventory physical sample library CHEMINV</td>
</tr>
<tr>
<td>EPACHEMINV_AVAL</td>
<td>EPACHEMINV: ToxCast/Tox21 chemical inventory available as DMSO solutions (20181123)</td>
<td>2018-11-21</td>
<td>6408</td>
<td>EPACHEMINV_AVAL is list of unique DSSTox substances available as DMSO solutions for ToxCast and Tox21 partner projects, managed by EPA Chemical Contract Services.</td>
</tr>
<tr>
<td>EPAPFASINSOL</td>
<td>PFAS EPA: Chemical Inventory Insoluble in DMSO</td>
<td>2010-06-29</td>
<td>43</td>
<td>PFAS chemicals included in EPA’s expanded ToxCast chemical inventory found to be insoluble in DMSO above 5mM.</td>
</tr>
<tr>
<td>EPAPFASINV</td>
<td>PFAS EPA: ToxCast Chemical Inventory</td>
<td>2010-06-29</td>
<td>430</td>
<td>PFAS chemicals included in EPA’s expanded ToxCast chemical inventory and available for testing.</td>
</tr>
<tr>
<td>TOXCAST</td>
<td>TOXCAST: EPA ToxCast Screening Library</td>
<td>2017-04-11</td>
<td>4746</td>
<td>TOXCAST is the complete list of chemicals having undergone some level of screening in EPA’s ToxCast research program since 2007 (last updated 4/11/2017); sublists included.</td>
</tr>
<tr>
<td>TOXCAST_E1K</td>
<td>TOXCAST_e1k - EPA ToxCast Screening Library (e1k Subset)</td>
<td>2016-01-25</td>
<td>799</td>
<td>TOXCAST_e1k is the e1k subset of TOXCAST, selected for screening in endocrine-related assays.</td>
</tr>
</tbody>
</table>
Individual chemical lists with details

Download the file of chemicals in various formats
Lists of Assays
List of Assays - Filter by Vendor

- The modal icon opens up details regarding the individual assay
- The list of assays, or selected assays, can be downloaded as a file

<table>
<thead>
<tr>
<th>Assay Component Endpoint Name</th>
<th>Details</th>
<th>Multi Conc. Actives</th>
<th>Single Conc. Active</th>
<th>Description</th>
<th>Gene Symbols</th>
</tr>
</thead>
<tbody>
<tr>
<td>NVS_ADME_hCYP19A1</td>
<td></td>
<td>72 / 247</td>
<td>75 / 1879</td>
<td>Data from the assay component endpoint, NVS_ADME_hCYP19A1, the negative control and baseline were used to understand changes in enzyme activity. Furthermore, this assay endpoint produced multiple assay endpoints within the intended target family, where the subfamily is &quot;cytochrome P450.&quot;</td>
<td>CYP19A1</td>
</tr>
<tr>
<td>NVS_ADME_hCYP19A1 Activator</td>
<td></td>
<td>3 / 247</td>
<td>5 / 1879</td>
<td>Data from the assay component endpoint, NVS_ADME_hCYP19A1, the negative control and baseline were used to understand changes in enzyme activity. Furthermore, this assay endpoint has produced multiple assay endpoints within the intended target family, where the subfamily is &quot;cytochrome P450.&quot;</td>
<td>CYP19A1</td>
</tr>
<tr>
<td>NVS_ADME_hCYP19A1</td>
<td></td>
<td>72 / 180</td>
<td>111 / 1124</td>
<td>Data from the assay component endpoint, NVS_ADME_hCYP19A1, was analyzed in the positive fitting direction relative to Acetaminophen as the negative control and baseline of activity. Using a type of enzyme reporter, loss-of-signal activity can be used to understand changes in the enzymatic activity as they relate to the gene CYP19A1. Furthermore, this assay endpoint can be referred to as a primary readout, because this assay has produced multiple assay endpoints where this one serves an enzymatic activity function. To generalize the intended target to other related targets, this assay endpoint is annotated to the &quot;cytochrome P450&quot; intended target family, where the subfamily is &quot;cytochrome P450.&quot;</td>
<td>CYP19A1</td>
</tr>
</tbody>
</table>
Single Concentration Data (**August 2019 release**)

- Some assays have single concentration screening data. Select modal to view data
- Sort data based on various parameters
- Filter through the data using name substrings
- Download the data as a file
Histogram Views of Data for Assays

- The modal icon opens up details regarding the individual assay
- ACTIVE hits shown by default. Delete INACTIVE filter to see all data
Interactive histogram summary view
Interactive histogram summary view

• Display specific subset of data from histogram by selecting individual bars
New Search Capability
Search Assay or Gene from Home Page
Searching Gene or Assay from the Home Page

• Switch to Assay/Gene Search tab and use the type-ahead search
Select hit based on **Assay**

Opens associated list of chemicals for an assay
Select hit based on **Gene Symbol**

Opens list of assays associated with that Gene
Future CompTox Portal
Feedback Welcomed

• Send comments to us via the web page at

http://comptox.epa.gov/dashboard/contact_us