molecular informatics
models – molecules – systems

Supporting Information

Tox21 Enricher

User's Manual

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http://hurlab.med.und.edu/Tox21Enricher

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Introduction to Tox21 Enricher

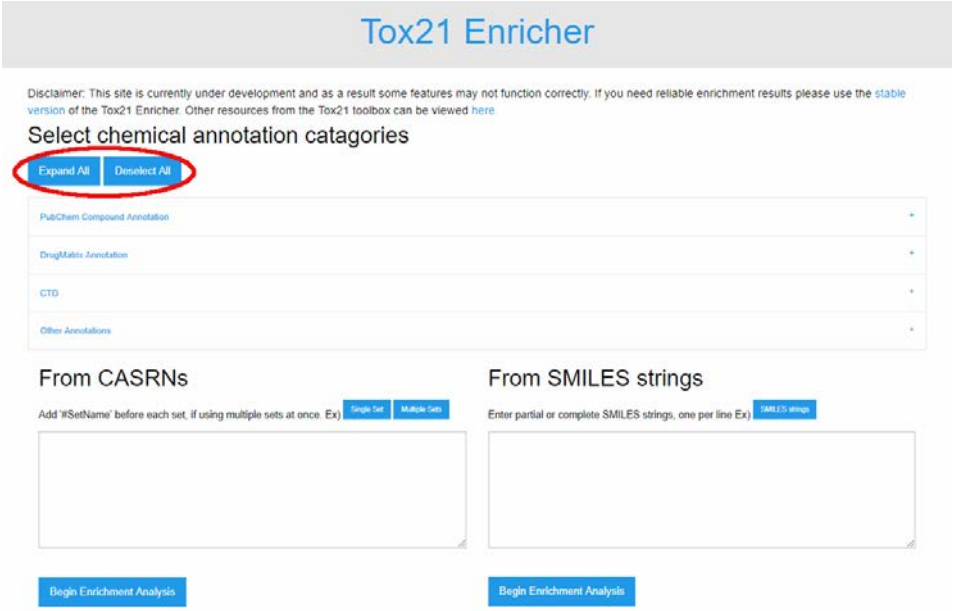
Humans are exposed to tens of thousands of chemicals that are used in our daily life, some at levels that may pose a health risk. For many of these chemicals, there limited toxicological information which makes risk assessment impossible. The United States Toxicology Testing in the 21st Century (Tox21) program was established to develop more efficient and human relevant toxicity assessment methods. The Tox21 program is currently screening over 10,000 chemicals, the Tox21 10K library, using quantitative high-throughput screening (qHTS) of assays that measure effects on toxicity pathways. To date, more than 70 assays have yielded >12 million concentration-response curves by Tox21 researchers. To efficiently apply these data for identifying potential hazardous compounds and for informing further toxicological testing, the United States National Toxicology Program (NTP) has developed several web applications (Tox21 Toolbox: http://ntp.niehs.nih.gov/tbox/), including tools for data visualization (Tox21 Curve Browser) and exploration (Tox21 Activity Profiler).

One critical usage of this dataset is to perform chemical-relational analysis based on the patterns of activity across the Tox21 assays and then to use nearest neighbor based prediction to infer the toxicological properties of untested chemicals via their association with tested chemicals. One approach to inferring the specific properties is to perform chemical annotation enrichment of chemical neighborhoods.

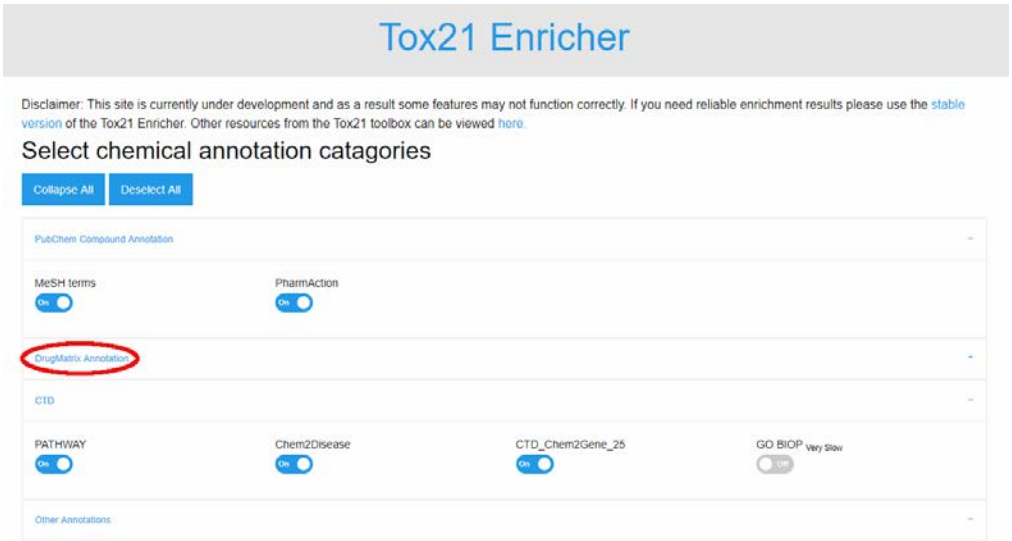
Here, we present Tox21 Enricher, a web-based chemical annotation enrichment tool for Tox21 assay data. Tox21 Enricher identifies significantly over-represented chemical biological annotations among sets of chemicals (neighborhoods), which facilitates the identification of the toxicological properties and mechanisms in the chemical sets.

Landing Page

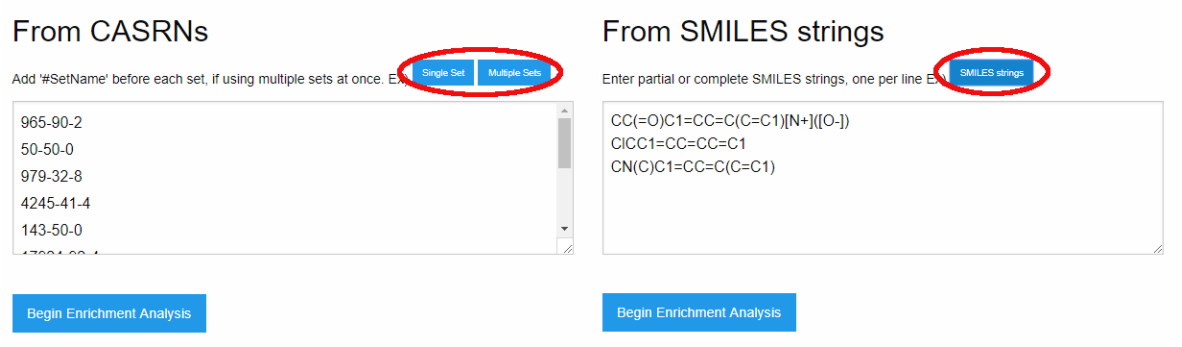
Upon visiting the Tox21 Enricher's web page, you will see the landing page. This page has buttons for expanding the annotation category group accordions and deselecting/selecting all enrichment categories. These buttons are circled in the image below.



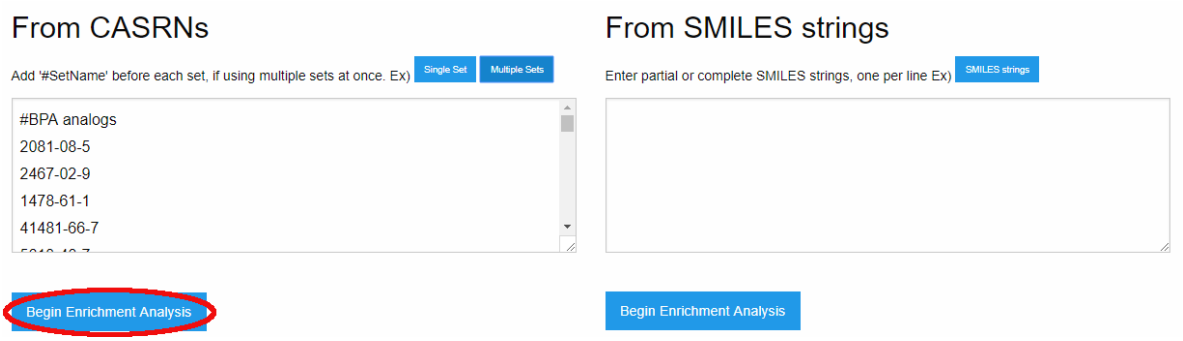
Once the "Expand All" button is clicked, each of the annotation category accordions will expand to show the categories they contain. **Each accordion may also be expanded/collapsed individually as shown below.**



After selecting the appropriate annotation categories, the next step is providing input for the enrichment analysis. This input can take the form of either CASRNs or SMILES strings. Each option has a text area for input. Each option also has buttons above their respective text areas that will populate example input.

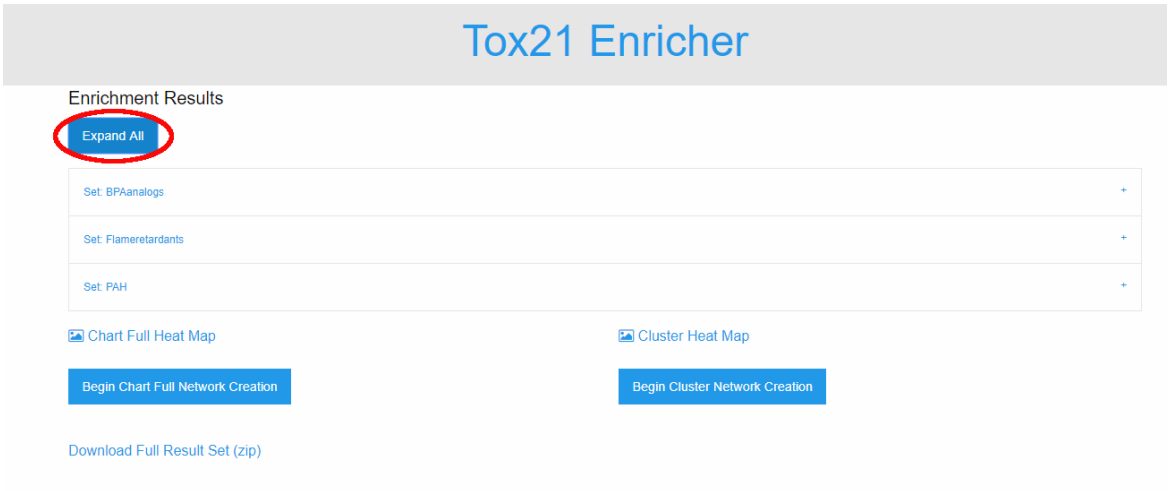


After input has been entered, it is time to begin enrichment. This can be done by clicking on the appropriate “Begin Enrichment Analysis” button for whichever input you are using. The button that is clicked will use the data in its respective text area, so you must ensure you are using the right button. This can be seen using the multi-set CASRN example input below.

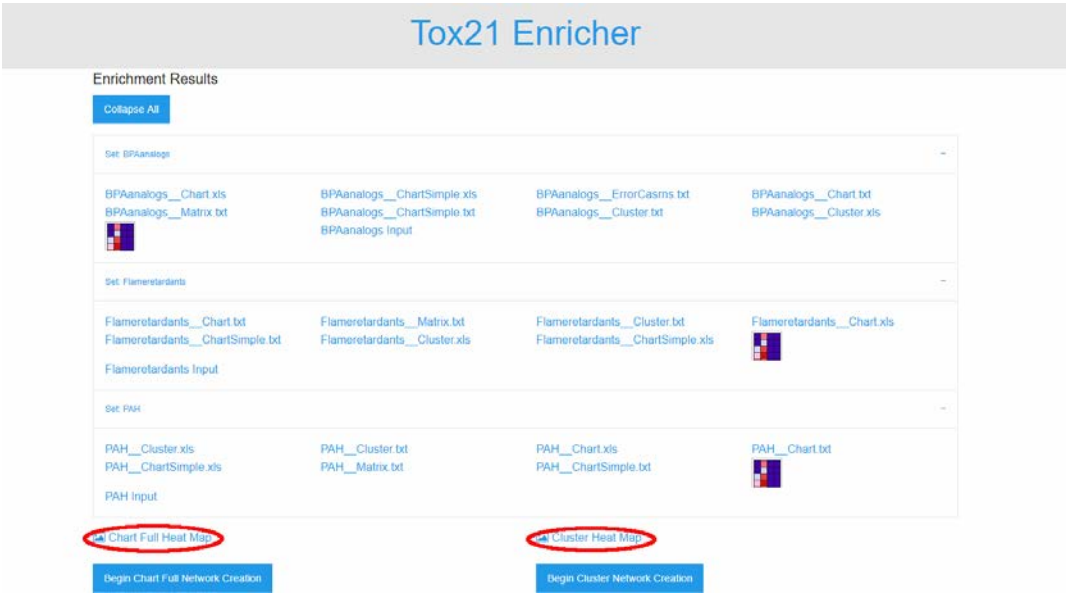


Results Page

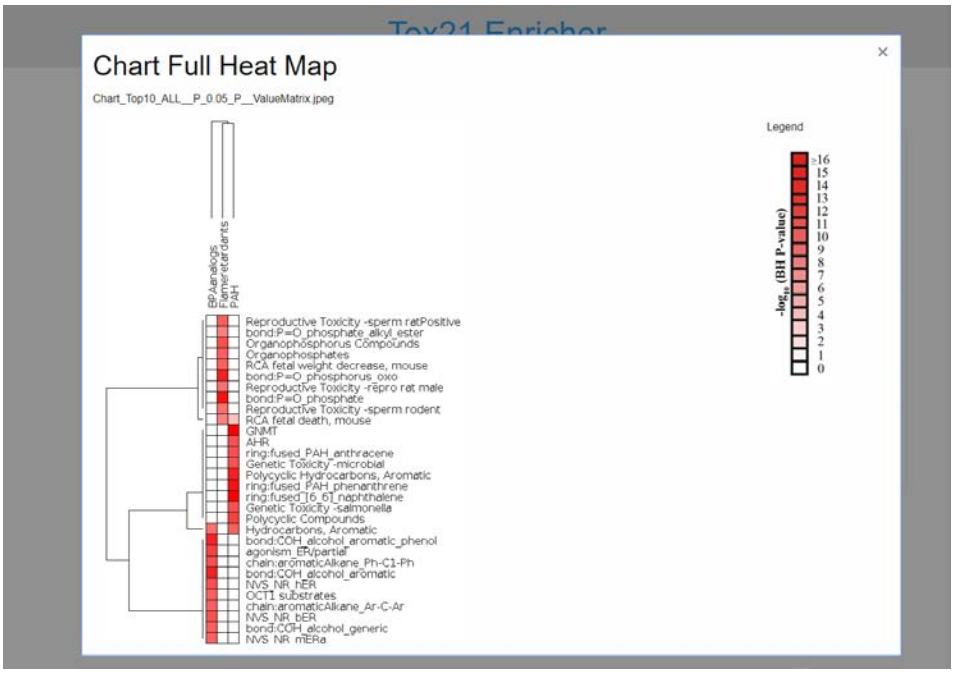
Once enrichment is complete, a results page will be loaded. Like the landing page, results on this page will be placed in collapsed accordions. This accordion can be clicked on to expand it, or the “Expand” button may be used, as on the landing page. This button is highlighted in the screenshot below.



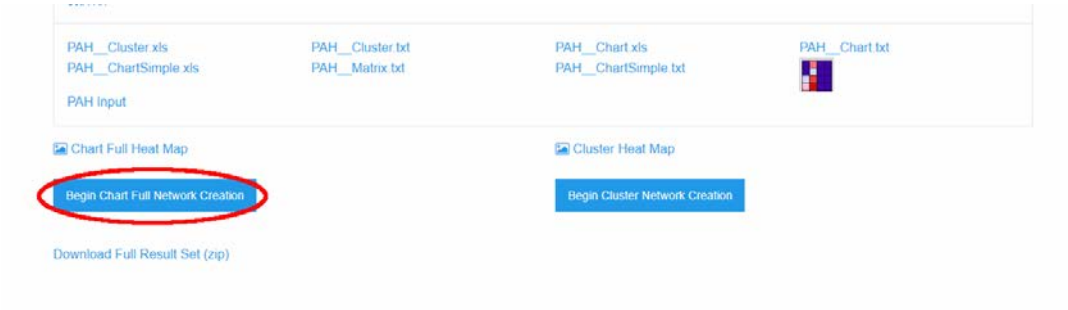
The results shown above are of our multi-set input that we submitted in our last landing page example. In the screenshot below, we can see the results for each set expanded. The cluster and chart full heat map image links can also be seen highlighted.



Clicking on the one of the heat map image links will display as seen in the screenshot below.

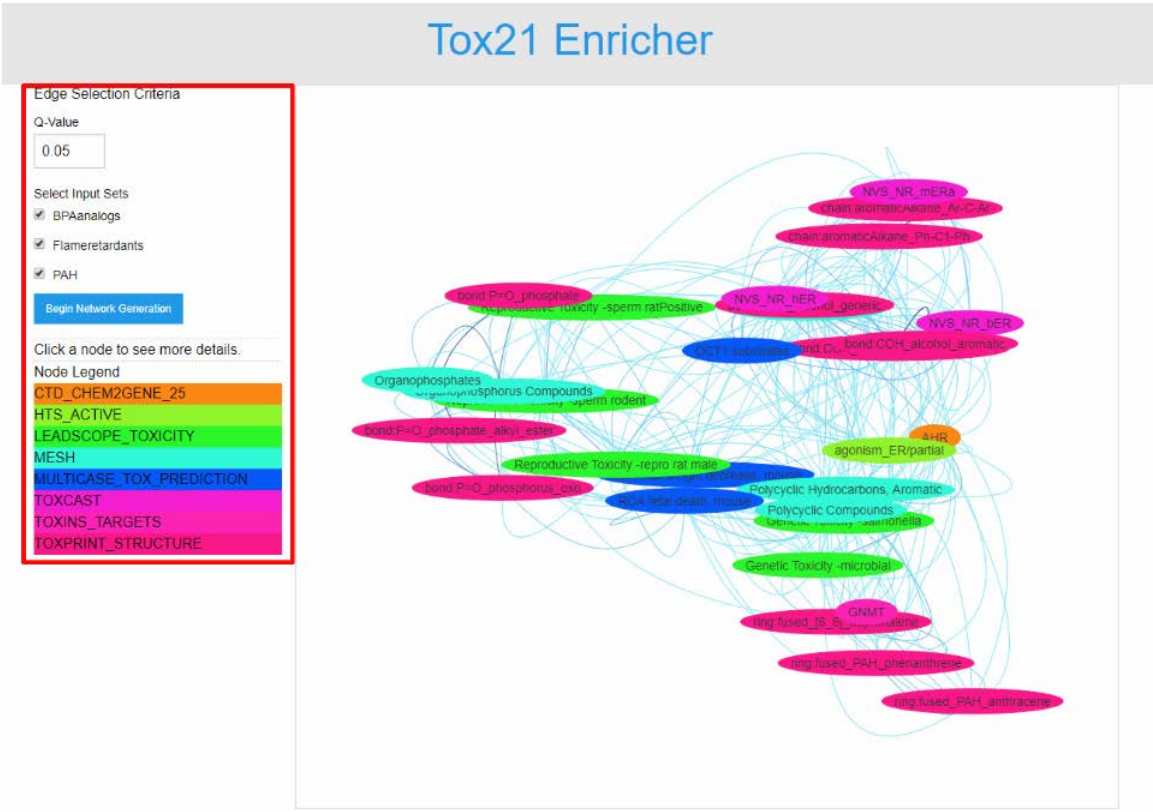


Next, we can click either the “Begin Chart Full Network Creation” button or the “Begin Cluster Network Creation” button. These buttons can be seen highlighted below.



Network Page

After clicking either of the network creation buttons, you will see the network page as shown below. The left side of this page is where we have edge selection criteria, input set select for node data to visualize, and the color key for the current network. In the screenshot below, we are using the Chart Full data for our network. The nodes correspond to significantly enriched annotations and the edges indicates that there are significant overlap between the two annotations in terms of chemical contents. The edge color gradient indicates the degree of overlap based on Jaccard index.



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