AOP-ExpoVis User Manual

Version Number: 1.0

AOP-ExpoVis: An Integrated Online Tool Combining Weighted Network Analysis and Adverse Outcome Pathways to Predict Molecular Mechanisms of Environmental Toxicity

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Introduction

Welcome to AOP-ExpoVis, an interactive web application designed to explore relationships between chemicals, diseases, and phenotypes. This manual provides detailed instructions on how to use the features of the online application.

If you use AOP-ExpoVis in your research, please cite our work as follows:

Author(s), Title, Journal/Conference, Year, DOI/URL (or other citation details).

Accessing the Application

You can access AOP-ExpoVis by navigating to the following URL in your web browser: *http://1.203.174.23:3675*

User Interface Overview

The application interface is divided into two main sections: the sidebar and the main panel.

Sidebar

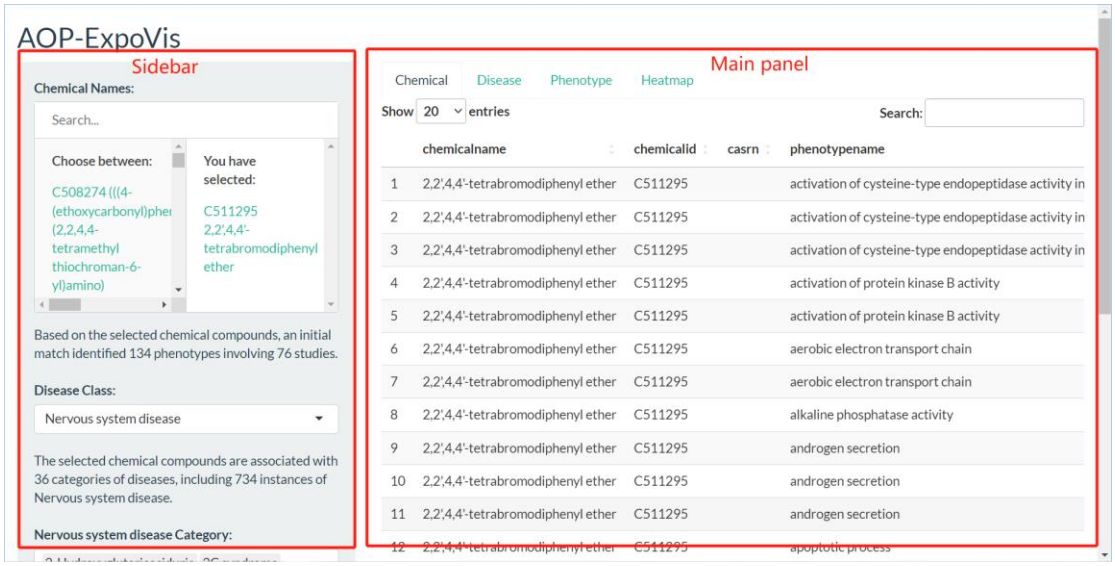
The sidebar contains input controls for selecting chemicals, disease classes, and categories. Here's a brief overview of each input:

1. Chemical Names: Multi-select input where you can choose from a list of chemical names.
2. Disease Class: Dropdown menu for selecting a disease class.
3. Disease Category: Dropdown menu for selecting specific disease names within the chosen disease class.

Main Panel

The main panel displays the results of your selections and is divided into multiple tabs:

1. Chemical: Displays a table of chemicals and their associated phenotypes.
2. Disease: Shows a table of diseases related to the selected chemicals.
3. Phenotype: Lists phenotypes associated with the selected diseases.
4. Heatmap: Provides interactive heatmaps of inferred phenotype coherence and phenotype cluster coherence.
5. AOP: Displays information about Adverse Outcome Pathways (AOP) and associated key events.

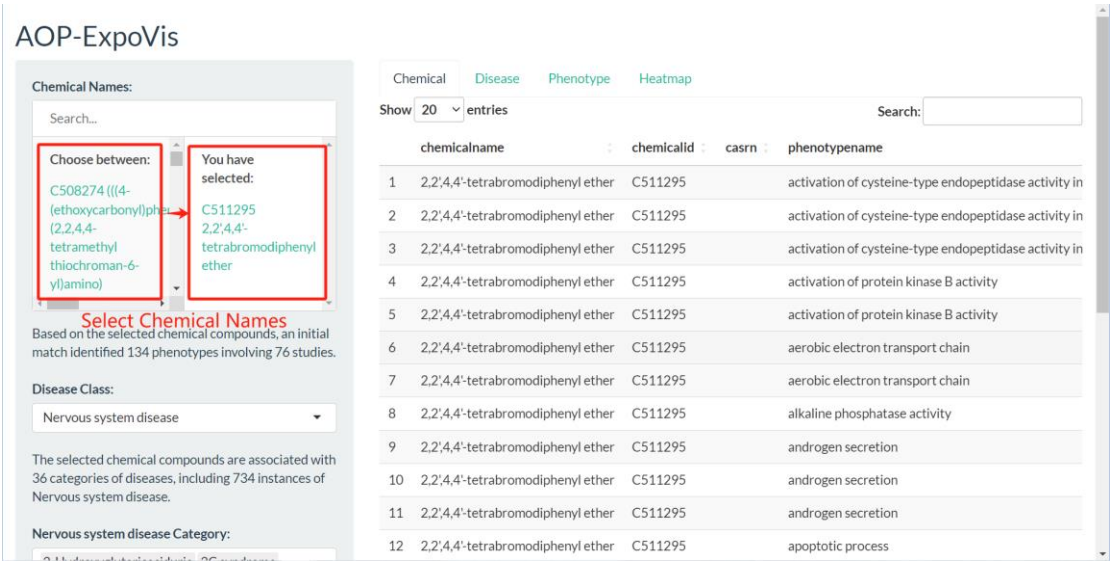

AOP-ExpoVis
Sidebar
Chemical Names:
Search...
Choose between:
C508274 (((4-(ethoxycarbonyl)phe (2,2,4,4-tetramethyl thiochroman-6-yl)amino)
You have selected:
C511295 2,2',4,4'-tetrabromodiphenyl ether
Based on the selected chemical compounds, an initial match identified 134 phenotypes involving 76 studies.
Disease Class:
Nervous system disease
The selected chemical compounds are associated with 36 categories of diseases, including 734 instances of Nervous system disease.
Nervous system disease Category:
Main panel
Chemical
Disease
Phenotype
Heatmap
Show 20 entries
Search:
chemicalname
chemicalid
casrn
phenotypename
1 2,2',4,4'-tetrabromodiphenyl ether C511295 activation of cysteine-type endopeptidase activity in
2 2,2',4,4'-tetrabromodiphenyl ether C511295 activation of cysteine-type endopeptidase activity in
3 2,2',4,4'-tetrabromodiphenyl ether C511295 activation of cysteine-type endopeptidase activity in
4 2,2',4,4'-tetrabromodiphenyl ether C511295 activation of protein kinase B activity
5 2,2',4,4'-tetrabromodiphenyl ether C511295 activation of protein kinase B activity
6 2,2',4,4'-tetrabromodiphenyl ether C511295 aerobic electron transport chain
7 2,2',4,4'-tetrabromodiphenyl ether C511295 aerobic electron transport chain
8 2,2',4,4'-tetrabromodiphenyl ether C511295 alkaline phosphatase activity
9 2,2',4,4'-tetrabromodiphenyl ether C511295 androgen secretion
10 2,2',4,4'-tetrabromodiphenyl ether C511295 androgen secretion
11 2,2',4,4'-tetrabromodiphenyl ether C511295 androgen secretion
12 2,2',4,4'-tetrabromodiphenyl ether C511295 apoptotic process

Using the Application

Step-by-Step Guide

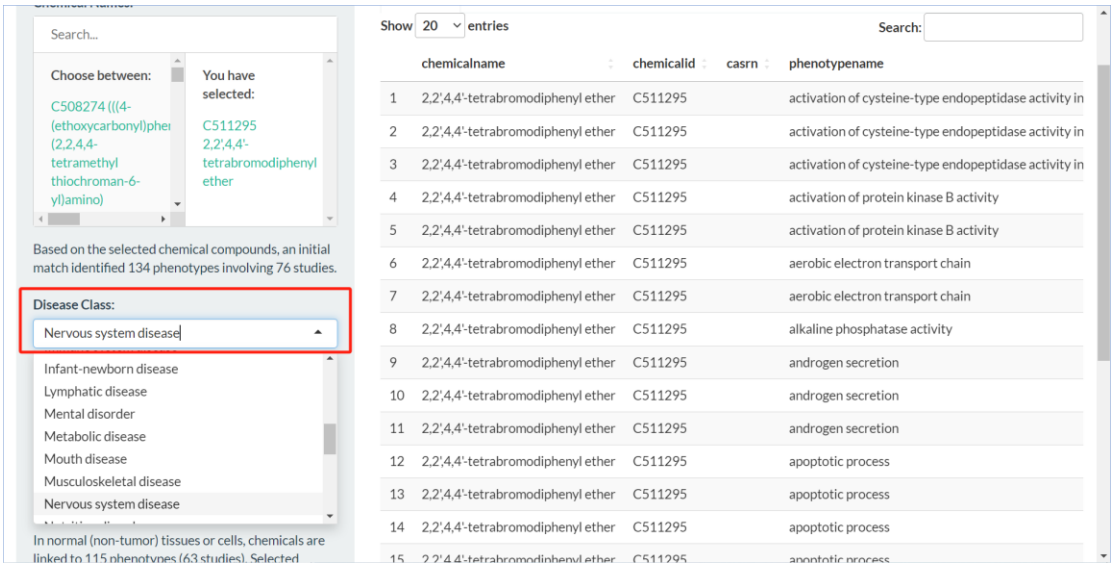
1. Select Chemical Names

- In the sidebar, use the Chemical Names input to select one or more chemical names. You can search and select from the provided list.
- The selected chemicals will be used to filter related diseases and phenotypes.



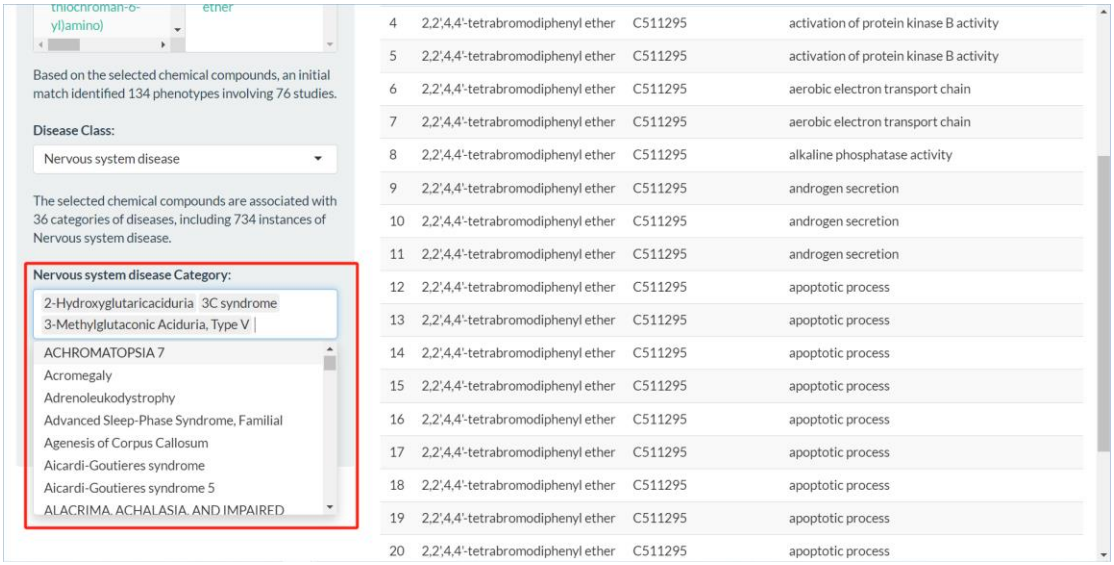
2. Select Disease Class

- Choose a disease class from the Disease Class dropdown. This will filter the related diseases and phenotypes.
- The available disease classes are dynamically populated based on the selected chemicals.



3. Select Disease Category

- After selecting a disease class, use the Disease Category dropdown to choose specific disease names within the selected disease class.
- This selection further refines the phenotypes related to the chosen diseases.



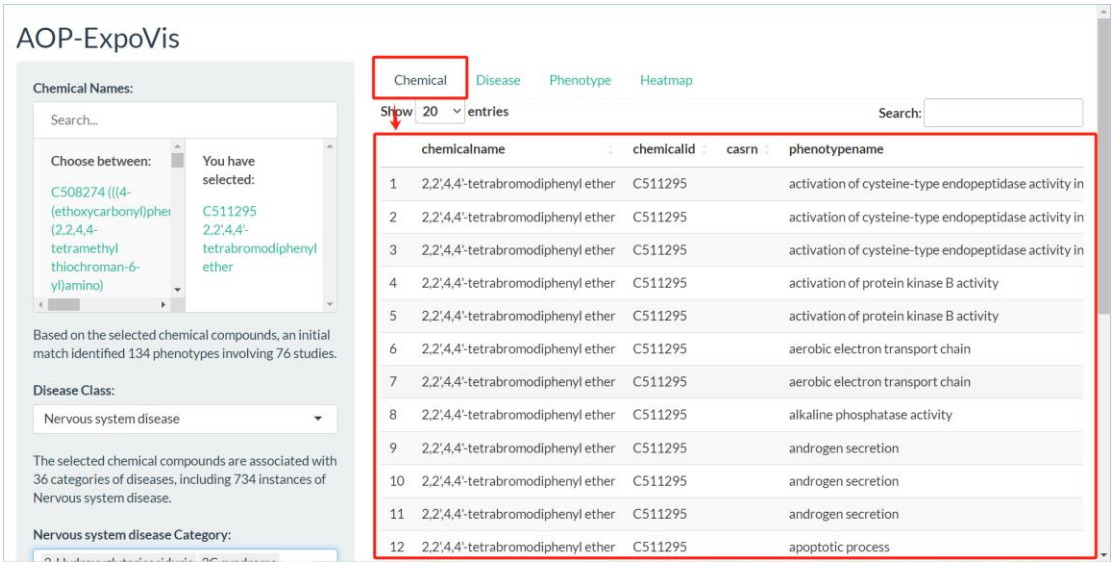
Viewing Results

Chemical Tab

- This tab displays a table of the selected chemicals and their associated phenotypes.
- You can view details such as chemical names, chemical IDs, phenotype names,

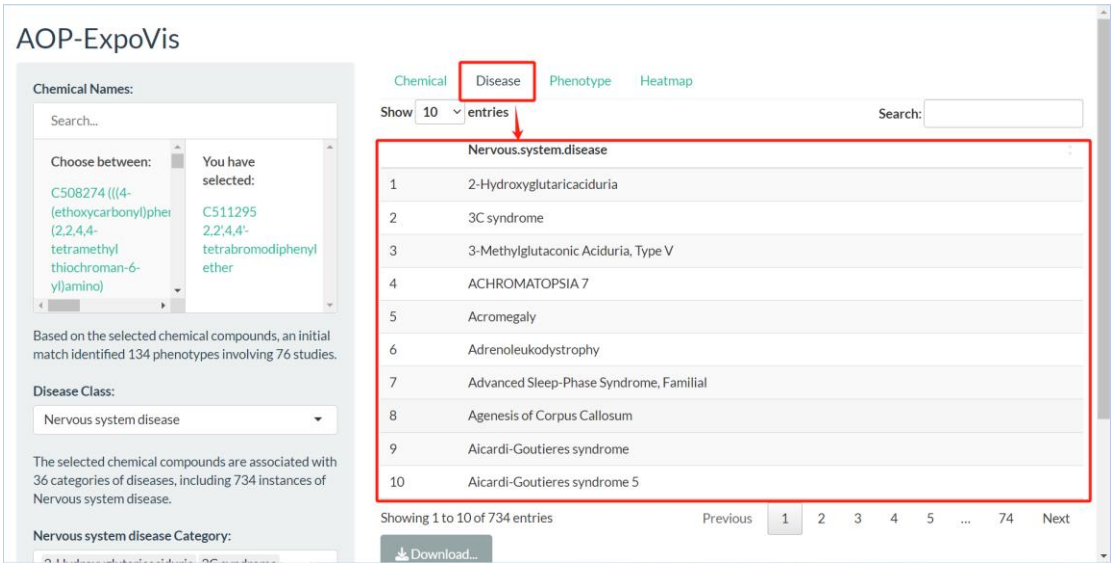
phenotype IDs, and related studies.

- Download the data table by clicking the **Download** button at the bottom of the tab.



Disease Tab

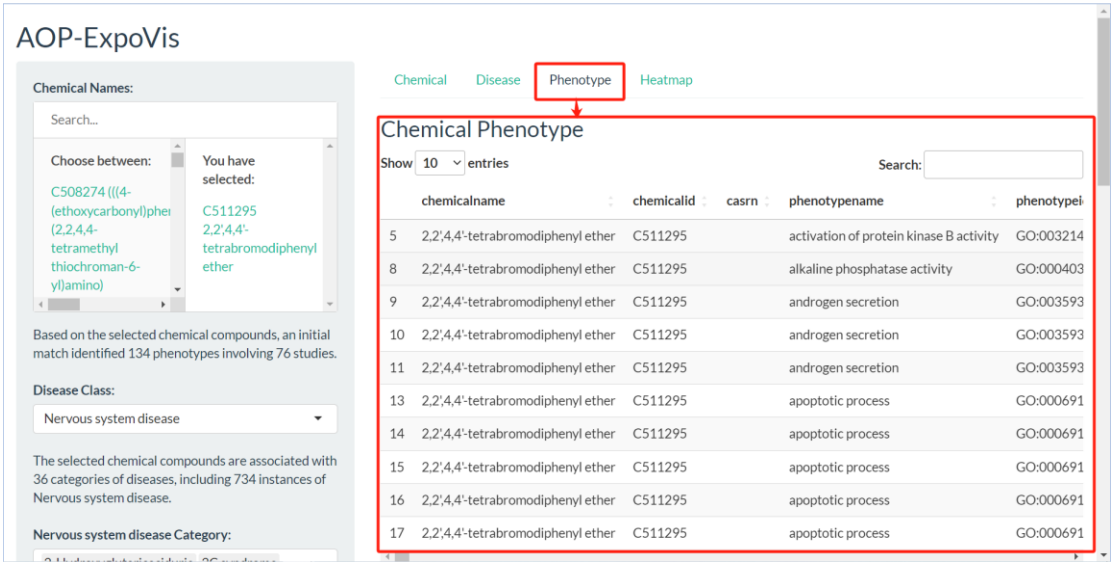
- Shows a table of diseases related to the selected chemicals.
- The table includes disease names.
- Download the data table by clicking the **Download** button at the bottom of the tab.



Phenotype Tab

- Lists phenotypes related to the selected diseases.

- Includes columns such as chemical phenotype and disease phenotype.
- Use the search and filter features to find specific phenotypes.
- Download the data table by clicking the **Download** button at the bottom of the tab.



Heatmap Tab

The Heatmap tab contains three sub-tabs: **Inferred Phenotype Coherence**, **Phenotype Cluster Coherence**, and **AOP**. Each sub-tab provides detailed visual and tabular representations of the data.

1. Inferred Phenotype Coherence

1.1 Results Table:

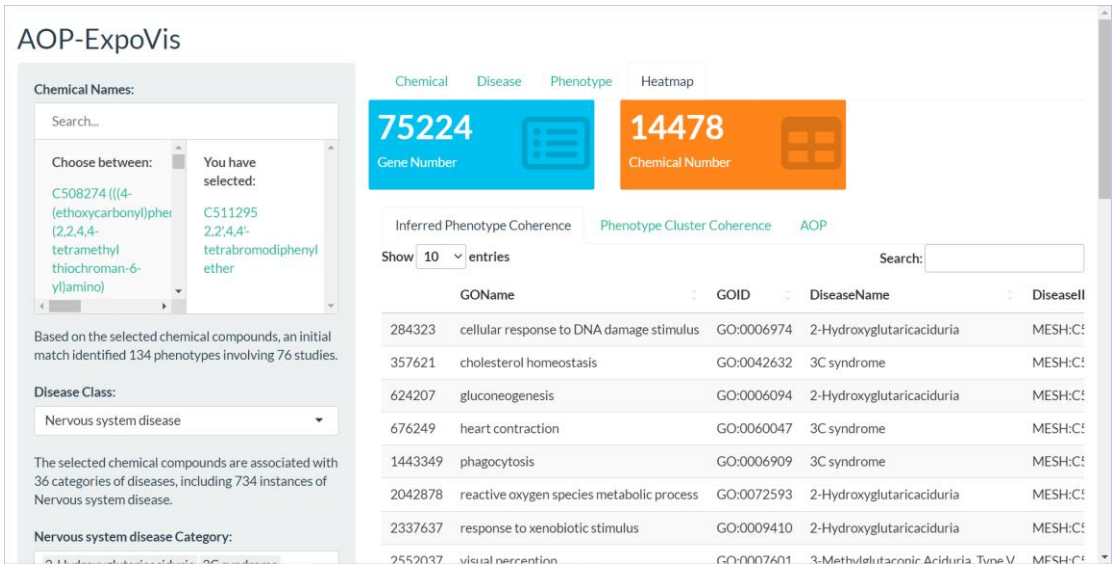
This table presents the results of the inferred phenotype coherence analysis, which measures the consistency of phenotypic effects across different studies and datasets. Columns include GOName, GOID, DiseaseName, DiseaseID, InferenceChemicalQty, InferenceGeneQty, ny_chemical, nx_chemical, ny_gene, nx_gene, p2_gene, p2_chemical, p1, chemical, log10_chemical, p1_gene, and log10_gene.

Columns Explained:

- **GOName**: The name of the Gene Ontology (GO) term representing a specific phenotype.
- **GOID**: The unique identifier for the GO term.
- **DiseaseName**: The name of the disease associated with the phenotype.

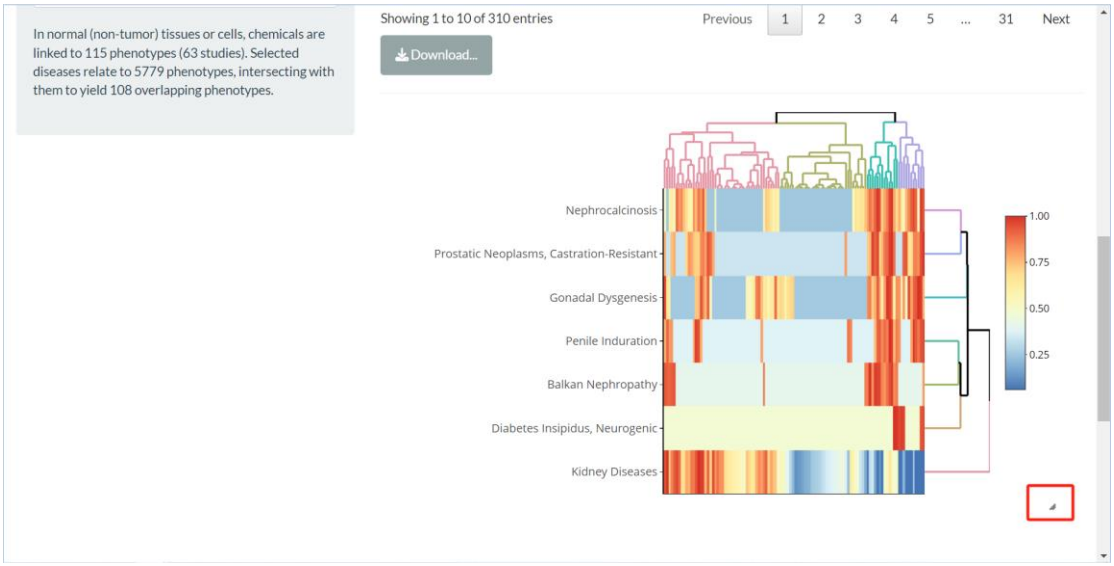
- **DiseaseID**: The unique identifier for the disease.
- **InferenceChemicalQty**: The number of chemicals inferred to be associated with the phenotype. This is based on data from the Comparative Toxicogenomics Database (CTD), which includes interactions and associations between chemicals and phenotypes.
- **InferenceGeneQty**: The number of genes inferred to be associated with the phenotype. This metric is derived from CTD data and reflects the associations between genes and phenotypes.
- **ny_chemical**: The number of occurrences of the phenotype in relation to chemicals. It represents the degree of the node in the network graph where the phenotype is connected to various chemicals.
- **nx_chemical**: The total number of chemicals analyzed in relation to the phenotype. This metric provides context for the ny_chemical value.
- **ny_gene**: The number of occurrences of the phenotype in relation to genes. It represents the degree of the node in the network graph where the phenotype is connected to various genes.
- **nx_gene**: The total number of genes analyzed in relation to the phenotype. This metric provides context for the ny_gene value.
- **p2_gene**: The probability of observing the gene-phenotype association by chance, calculated using the hypergeometric distribution. This value helps assess the significance of the association.
- **p2_chemical**: The probability of observing the chemical-phenotype association by chance, calculated similarly to p2_gene. This value helps assess the significance of the association.
- **p1_chemical**: The overall probability of the chemical-phenotype association. It combines direct connectivity and pathway significance using a weighted approach.
- **log10_chemical**: The logarithm (base 10) of the p1_chemical value, providing a more interpretable scale for the probability.

- **p1_gene**: The overall probability of the gene-phenotype association, calculated similarly to p1_chemical.
- **log10_gene**: The logarithm (base 10) of the p1_gene value, providing a more interpretable scale for the probability.



1.2 Heatmap:

- Visual representation of the inferred phenotype coherence.
- Allows you to explore the relationships between different phenotypes based on the inferred data.
- You can resize the heatmap using the triangle at the bottom right corner (highlighted in the red box in the image).
- Supports zooming and panning for detailed exploration.



1.3 Downloading Data:

- Click the **Download** button to export the results table as a CSV file.
- The heatmap data can also be downloaded for offline analysis.

2. Phenotype Cluster Coherence

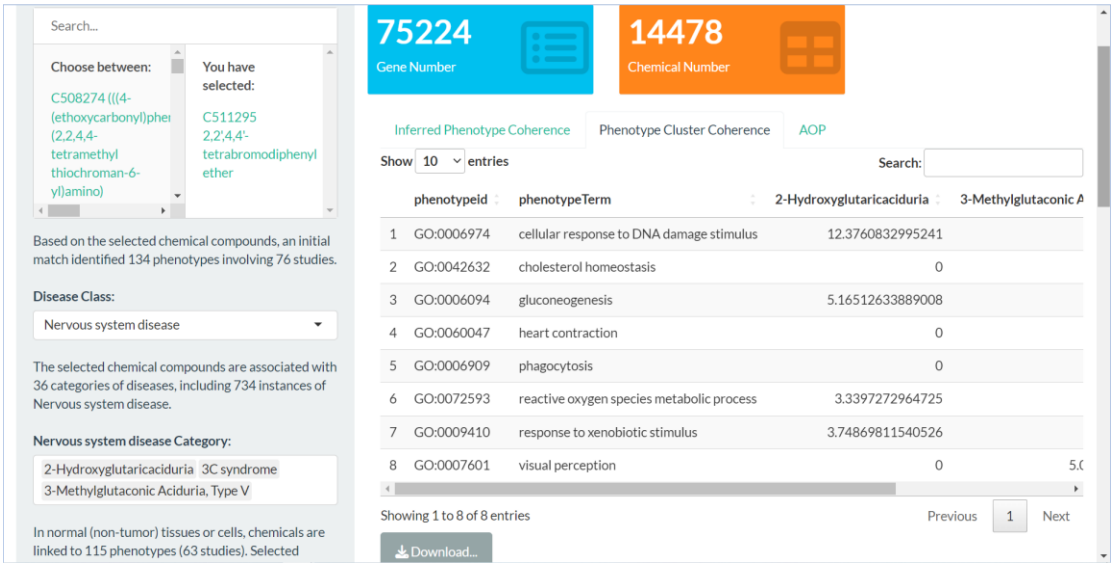
2.1 Results Table:

This table presents the results of the phenotype cluster coherence analysis, which examines the clustering of phenotypes associated with selected.

Columns Explained:

- **phenotypeid:** The unique identifier for the phenotype.
- **phenotypeTerm:** The name or description of the phenotype.
- **Disease Columns:** Each disease column represents a specific disease and contains values indicating the coherence of the phenotype with that disease.

Note: The disease columns dynamically change based on the diseases selected for the analysis. For example, if the analysis includes diseases such as Balkan Nephropathy, Diabetes Insipidus (Neurogenic), Gonadal Dysgenesis, Kidney Diseases, Nephrocalcinosis, Penile Induration, and Prostatic Neoplasms (Castration-Resistant), the table will display separate columns for each of these diseases. These columns provide insight into how phenotypes cluster in relation to the selected diseases.

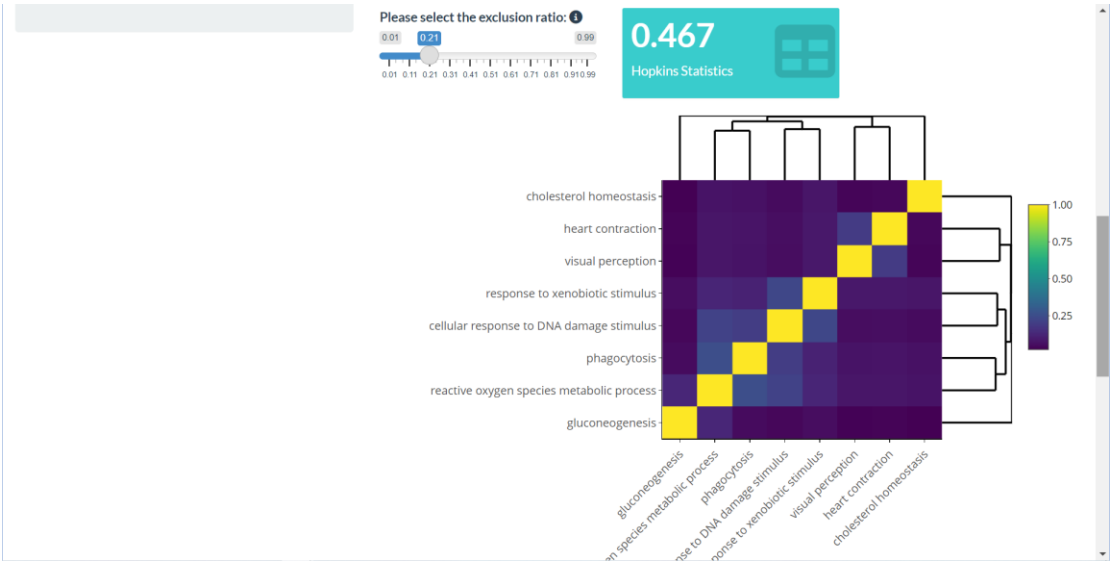


2.2 Heatmap:

- Visual representation of the phenotype cluster coherence.
- Shows how different phenotypes cluster together based on the analysis.
- You can resize the heatmap using the triangle at the bottom right corner (highlighted in the red box in the image).
- Supports zooming and panning for detailed exploration.

2.3 Customizing Heatmap:

- Use the **Threshold Slider** to adjust the exclusion ratio.
- The exclusion ratio determines the percentage of data points to exclude from the analysis, enhancing data clarity.



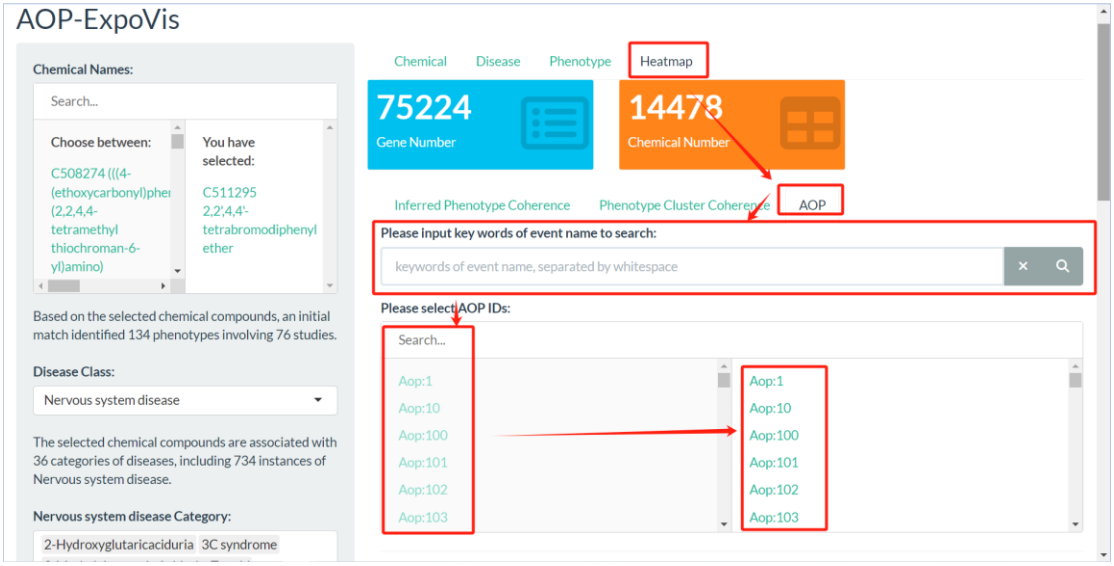
2.4 Downloading Data:

- Click the **Download** button to export the results table as a CSV file.
- The heatmap data can also be downloaded for offline analysis.

AOP Tab

1. Search and Select Key Events:

- Use the search input to find key events by keywords.
- Select AOP IDs from the dropdown menu to filter relevant key events.



2. Table Display: Displays key events related to the selected AOP IDs.

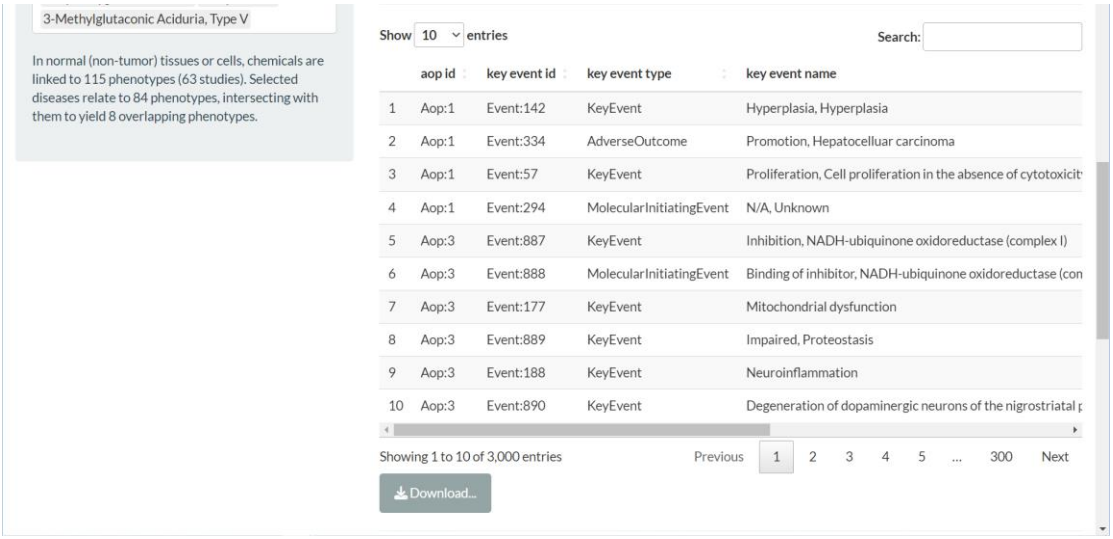
2.1 Key Events Table:

This table provides detailed information about key events related to selected AOPs.

Columns Explained:

- **aop id**: The unique identifier for the Adverse Outcome Pathway.
- **key event id**: The unique identifier for the key event within the AOP.
- **key event type**: The type of key event (e.g., Molecular Initiating Event, Key Event).
- **key event name**: The name or description of the key event.
- **event is in ctd**: Indicates whether the key event is present in the CTD.
- **event score**: The score representing the significance or impact of the key event.
- **event children**: The number of downstream key events or related entities.

- **max**: The maximum score among the key events.
- **event max score**: The maximum score considering all related key events.

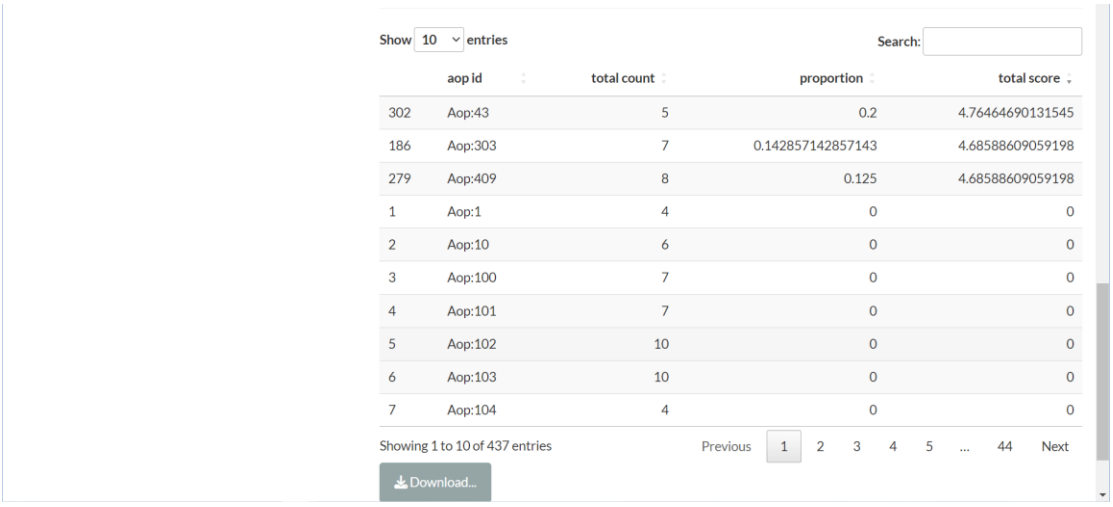


2.2 AOP Summary Table:

This table summarizes the overall statistics and importance of the selected AOPs.

Columns Explained:

- **aop id:** The unique identifier for the Adverse Outcome Pathway.
- **total count:** The total number of key events within the AOP.
- **proportion:** The proportion of key events that are present in the CTD, calculated as the number of key events in CTD divided by the total number of key events in the AOP.
- **total score:** The sum of the importance scores of all key events within the AOP, providing an overall measure of the pathway's significance.



3. Downloading Data:

- Click the Download button to export the table data as a CSV file.

Features and Functionalities

Interactive Data Tables

The application features interactive data tables that allow you to easily navigate and view detailed information. Each table can be sorted and filtered, enabling you to find specific data points quickly.

- **Sorting:** Click on the column headers to sort the data in ascending or descending order.
- **Filtering:** Use the search boxes at the top of each column to filter the data based on your criteria.
- **Pagination:** Navigate through pages of data using the pagination controls at the bottom of the table.
- **Download Options:** Export the entire table or the filtered results as a CSV file by clicking the **Download** button.

Interactive Heatmaps

The heatmaps in AOP-ExpoVis provide a visual representation of the data, allowing you to explore relationships between phenotypes, diseases, and chemicals.

- **Resizing**: Use the triangle at the bottom right corner of the heatmap to resize it according to your needs.
- **Zooming and Panning**: Use your mouse scroll wheel or touchpad gestures to zoom in and out. Click and drag to pan around the heatmap.
- **Customizable Settings**: Adjust the exclusion ratio using the **Threshold Slider** to refine the data displayed in the heatmap.
- **Download Options**: Export the heatmap as an image or the underlying data as a CSV file for further analysis.

AOP Analysis

The AOP tab provides insights into Adverse Outcome Pathways and their key events. This feature helps you understand the biological mechanisms underlying chemical exposures and their effects.

- Search and Filter: Use the search input to find key events by keywords. Select AOP IDs from the dropdown menu to filter relevant key events.
- Table Display: View detailed information about key events related to the selected AOP IDs.
- Download Options: Export the table data as a CSV file for offline analysis.

Troubleshooting and Support

If you encounter any issues or have questions about using AOP-ExpoVis, please contact our support team at ***pshi@cmu.edu.cn***. Provide details of the issue, including steps to reproduce it, and any error messages received.

Common Issues and Solutions

1. UI Elements Not Responding:

- **Issue:** Sometimes, UI elements may become unresponsive.
- **Solution:**

(1) Refresh the browser page to reload the application.

(2) Clear the browser cache and cookies, then try again.

(3) Ensure that your internet connection is stable.

(4) If the problem persists, try using a different web browser or device.

2. Data Not Displaying:

- **Issue:** Data may not load or display correctly in the tables or heatmaps.
- **Solution:**

(1) Ensure that you have made the necessary selections in the sidebar inputs.

(2) Refresh the browser page to reload the application.

(3) Clear the browser cache and cookies, then try again.

(4) Check if there are any error messages displayed, and follow any provided instructions.

3. Download Issues:

- **Issue:** Difficulty downloading data tables or heatmaps.
- **Solution:**

(1) Ensure that your browser allows downloads from the application.

(2) Check if your browser's pop-up blocker is preventing the download prompt. Disable the pop-up blocker temporarily if necessary.

(3) Try using a different web browser if the download does not start.

4. Heatmap Interaction Problems:

- **Issue:** Issues with resizing, zooming, or panning the heatmaps.
- **Solution:**

(1) Ensure that you are using the latest version of a supported web browser.

(2) Use the triangle at the bottom right corner to resize the heatmap.

(3) Use the mouse scroll wheel or touchpad gestures to zoom in and out.

(4) Click and drag to pan around the heatmap.

(5) Refresh the page if the heatmap becomes unresponsive.

5. Search Functionality Not Working:

- **Issue:** The search input for key events may not return expected results.
- **Solution:**

(1) Ensure that you are entering the correct keywords.

(2) Check for any typos or incorrect spellings.

(3) Clear the search input and try entering the keywords again.

(4) Refresh the page and attempt the search once more.

Conclusion

AOP-ExpoVis is a powerful tool for exploring the intricate relationships between chemicals, diseases, and phenotypes. By following this user manual, you can effectively utilize the application's features to conduct comprehensive analyses. For any further assistance, refer to the provided contact information. Enjoy your experience with AOP-ExpoVis!