MetaboAnalyst 5.0

A Web-based Tool for streamlined Metabolomics Data Analysis

2022.07.12

3. Meta-Analysis (MS Peaks)

The Meta-Analysis of MS Peaks modules extends the mummichog algorithm (Li et al. 2013) implemented in the MS Peaks to Paths module to perform biological-interpretation based meta-analysis.

Highlights:

- Support for meta-analysis of untargeted metabolomics data integration at pathway level;
- Support for meta-analysis of multiple untargeted metabolomics data by pooling their peaks.

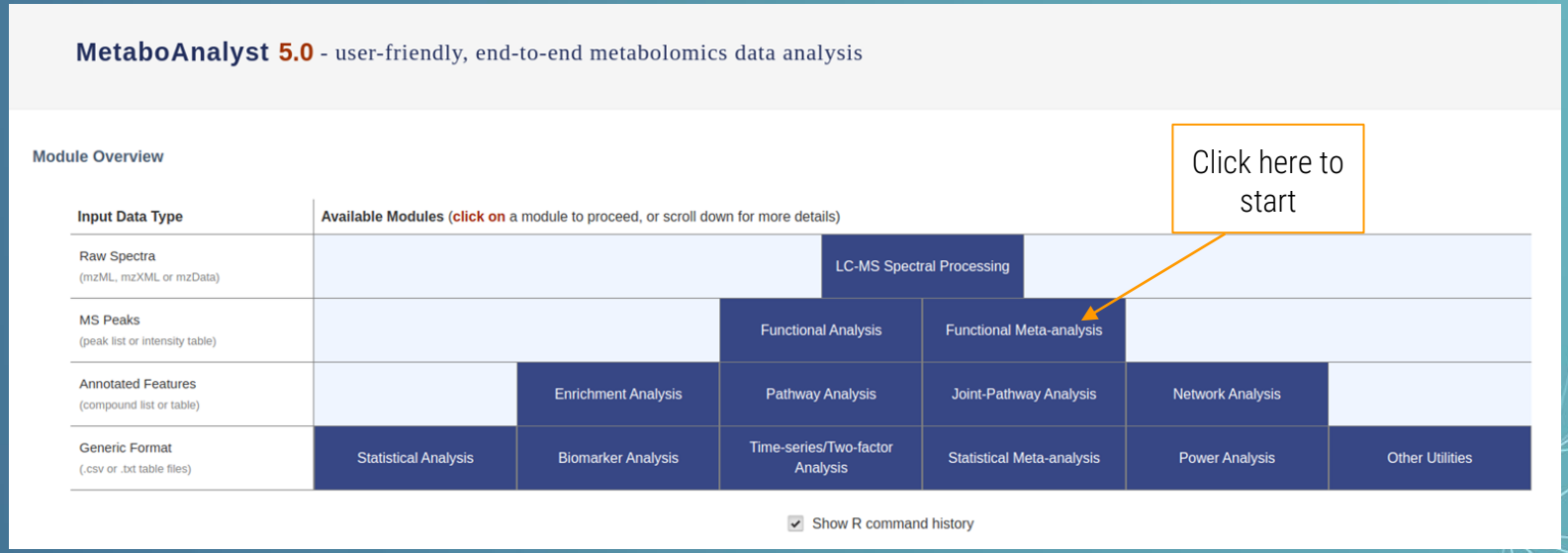
3.0 Knowledge & Background

Why meta-analysis?

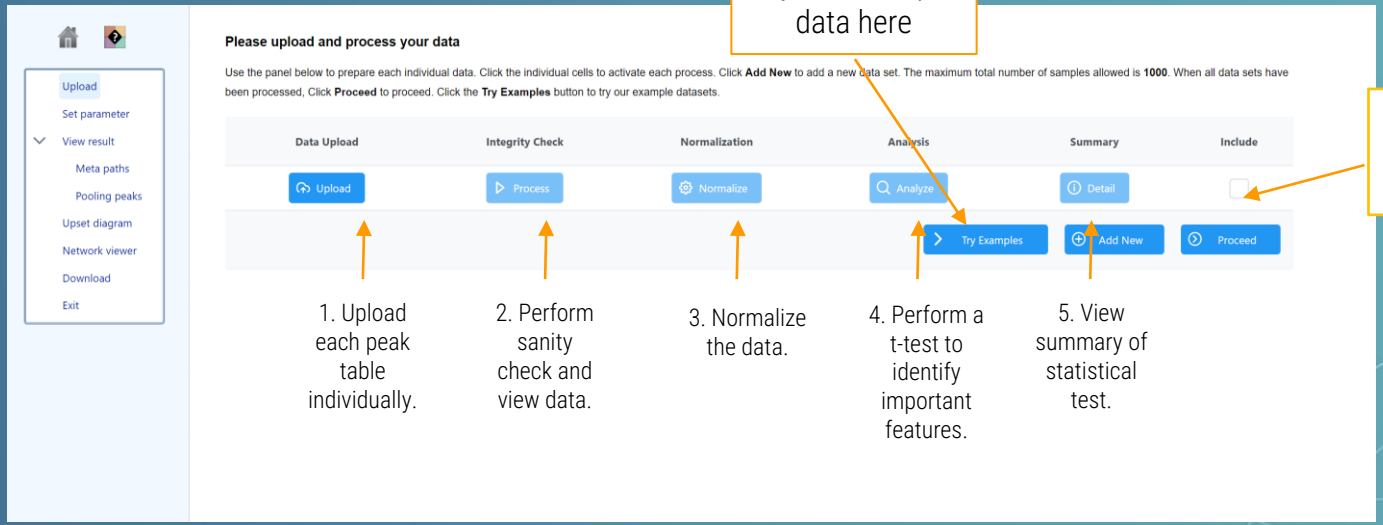
While individual studies may identify certain results, such results may not be reproducible in other independent studies of the same biological questions due to low sample size, sample heterogeneity, the type of LC-MS platform used, or metrics used for interpreting results. Meta-analysis, which is the combination of findings from independent studies - can be used to overcome such limitations and ultimately increase the power, precision, and generalizability of a study.

The Meta-Analysis (MS Peaks) module of MetaboAnalyst now permits users to perform meta-analysis of untargeted metabolomics data. The method implemented in this module also reduces the bias individual studies may carry towards specific sample processing protocols or LC-MS instruments.

3.2 Start Meta-Analysis (MS Peaks)



3.3.1 Meta-Analysis MS Peaks Upload

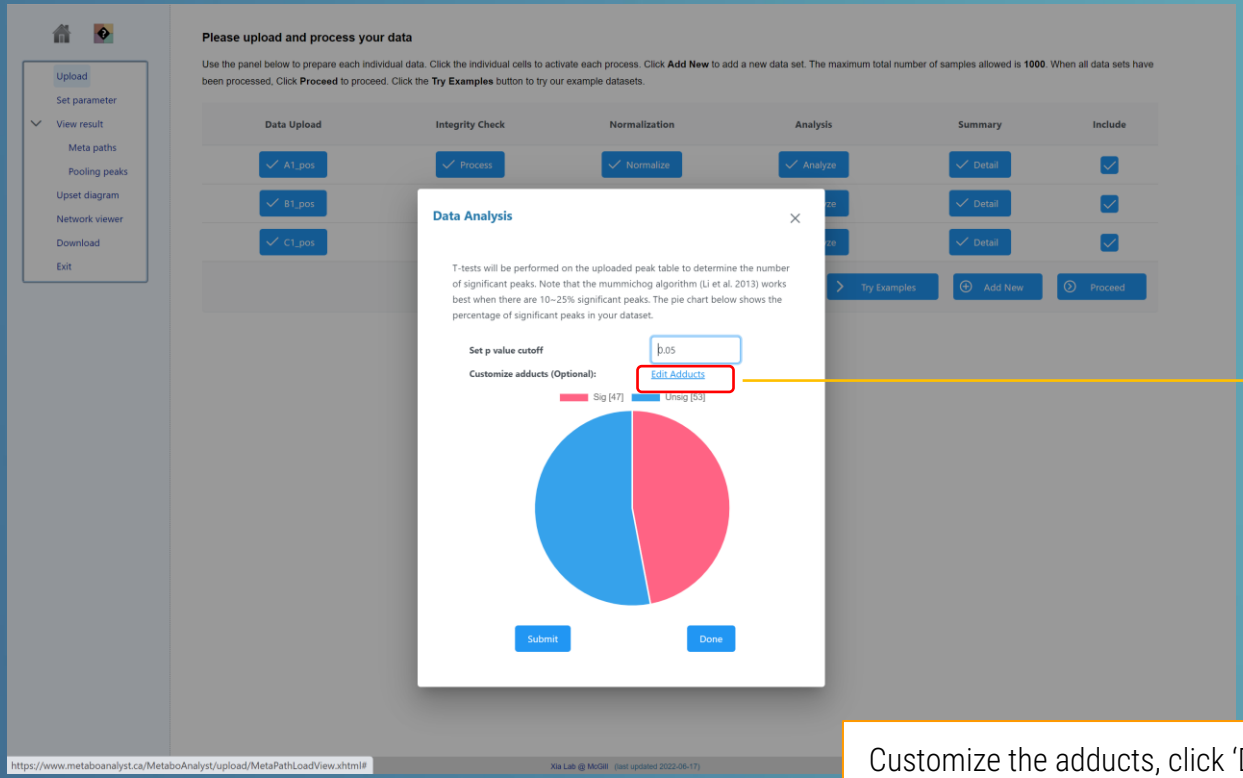


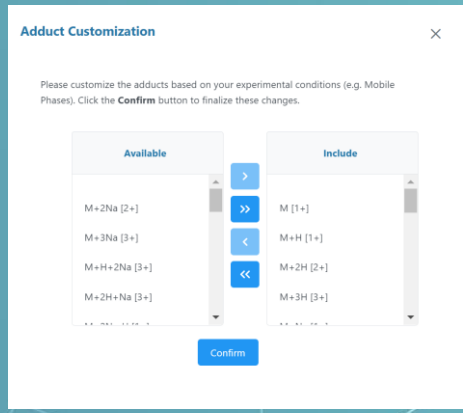
TIP 1: The uploading table should include all peaksafter processing rather than several interested peaks.

TIP 2: The mummichog algorithm (Li et al. 2013) works best when there are 10~25% significant peaks. Please try to adjust the percentage of significant features by changing the p value cutoff.

TIP 3: After performing the uplaoding and analyzing. Users could optionally define the potential adducts for more accurate mapping in the coming steps.

3.3.2 Meta-Analysis MS Peaks Adducts Customization

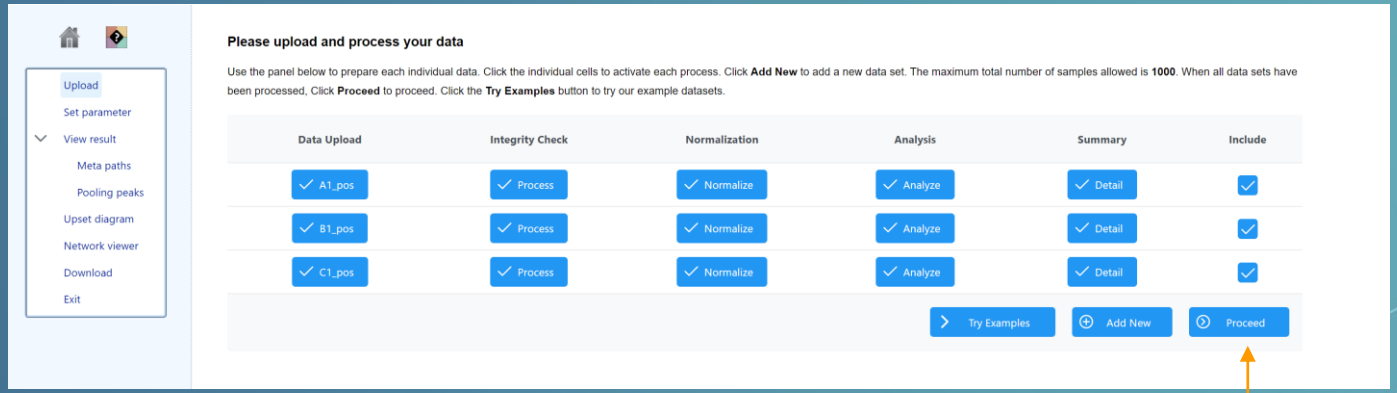




Customize the adducts, click ‘Done’ to finish the setting.

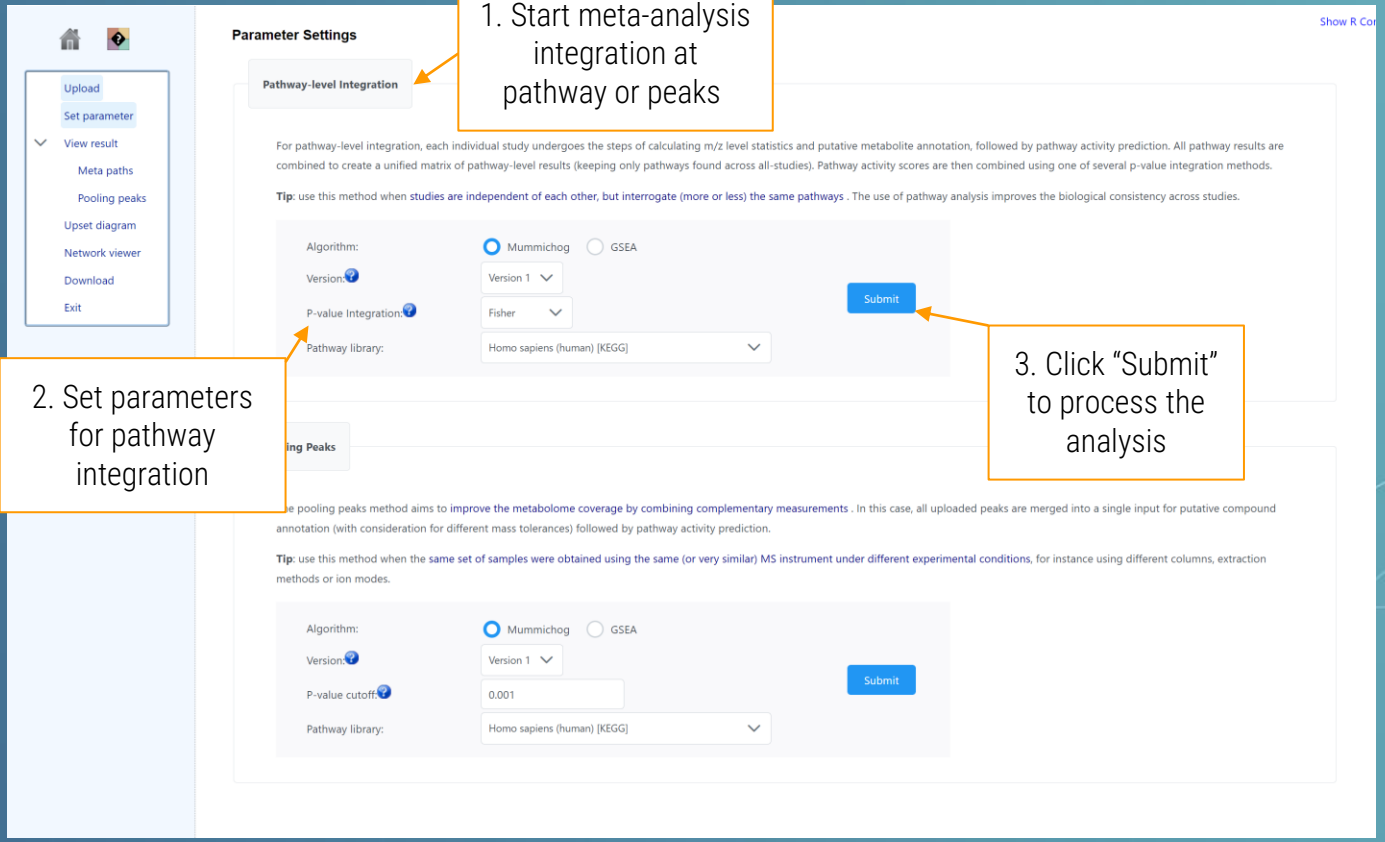
3.4 Upload Using Example Data

TIP: Users can either upload a single ion mode table as a dataset, or tables from both ion modes together by choosing the appropriate 'Ion Mode'.



Click "**Proceed**" to move forward with the meta-analysis

3.5.1 Parameter Setting : Pathway-level Integration



1. Start meta-analysis integration at pathway or peaks

2. Set parameters for pathway integration

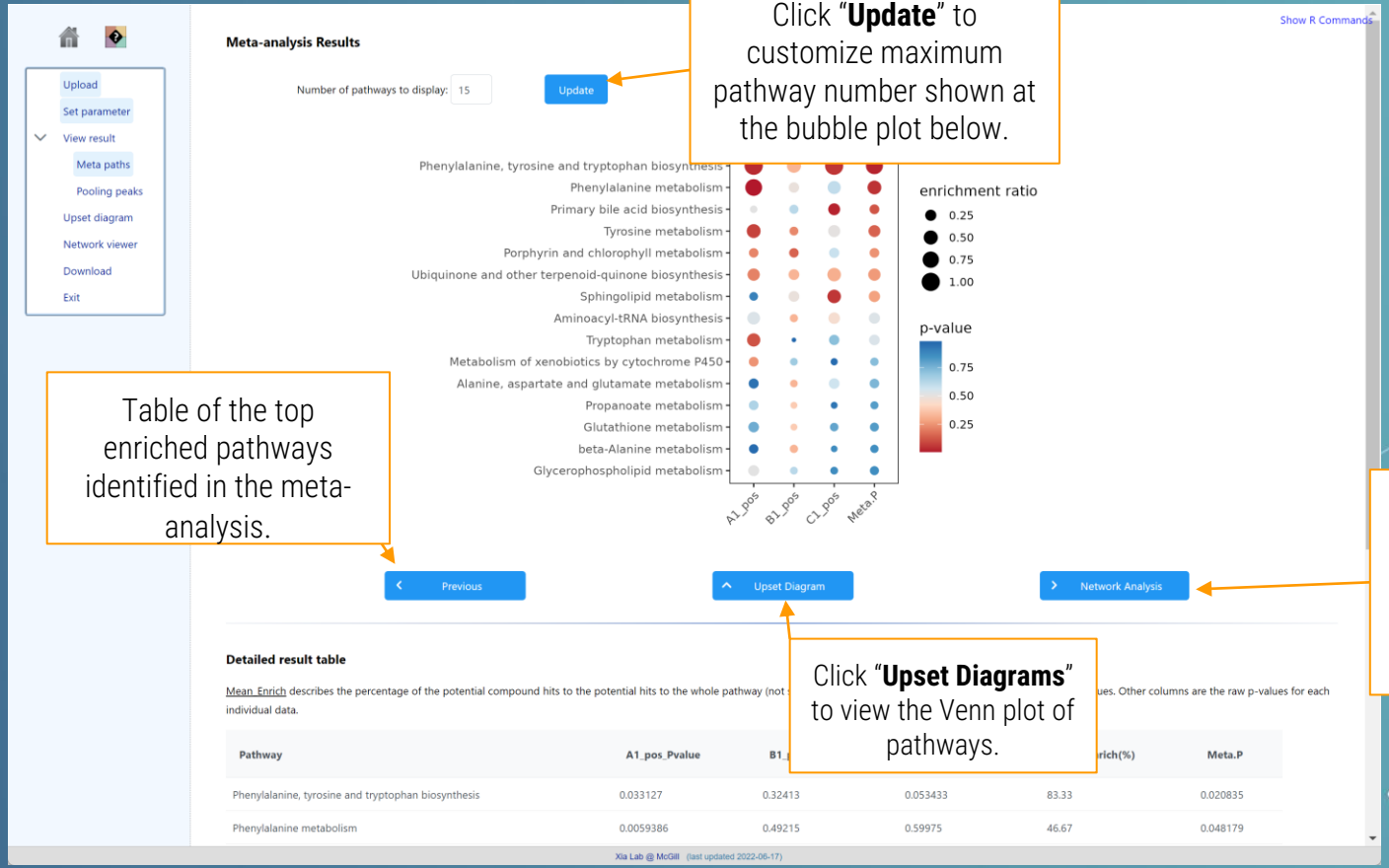
3. Click "Submit" to process the analysis

TIP1: Users could select to perform the meta-analysis at pathway level (by integrating p values) or at peaks level from pooling peaks together.

TIP2: *p* value integration provide 6 approaches here. Briefly, **Fisher** is sensitive to small p values and not recommended for 6 or more datasets. **Min** and **Max** are mathematically the minimum or maximum p values. **Stouffer** is used for data following gaussian curve, while **Edgington** bests fits circular data and sensitive to large p value. **Vote-counting** weight all datasets same and give a vote if there is a study meet the confidence interval ($p < 0.05$), at least 5 datasets are required to reach the significant level (meta.p < 0.05) for vote-counting.

>>Read More<<

3.5.2 Results (Pathway Level integration)



Click "**Update**" to customize maximum pathway number shown at the bubble plot below.

TIP: Pathway integration results are shown as a bubble plot. The node size is positively correlated with the enrichment ratio of the corresponding pathway. *Meta.P* is the integrated P values.

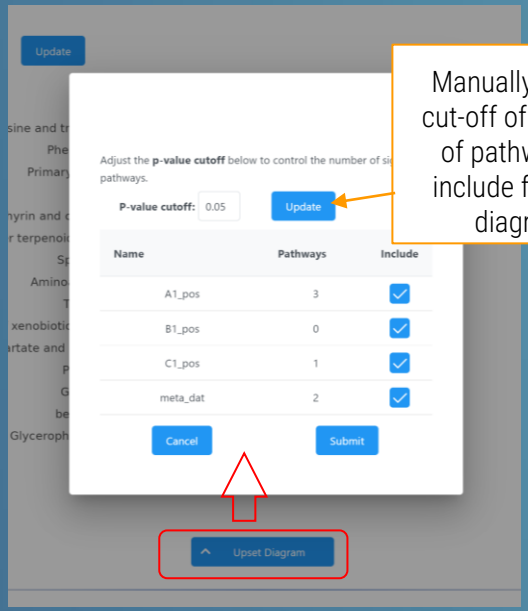
Table of the top enriched pathways identified in the meta-analysis.

Click "**Network Analysis**" to explore the data in the context of a KEGG metabolic network.

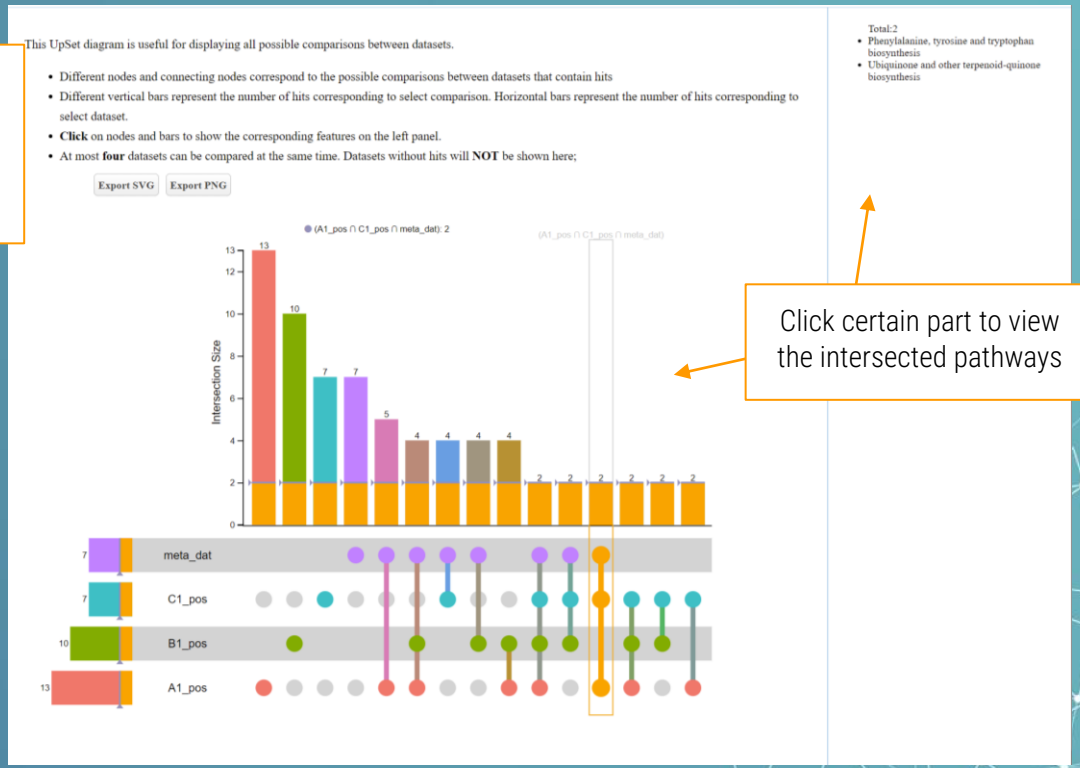
Click "**Upset Diagrams**" to view the Venn plot of pathways.

3.5.3 Results (Upset Diagram)

TIP: Venn diagram is providing the intersection results of different datasets.

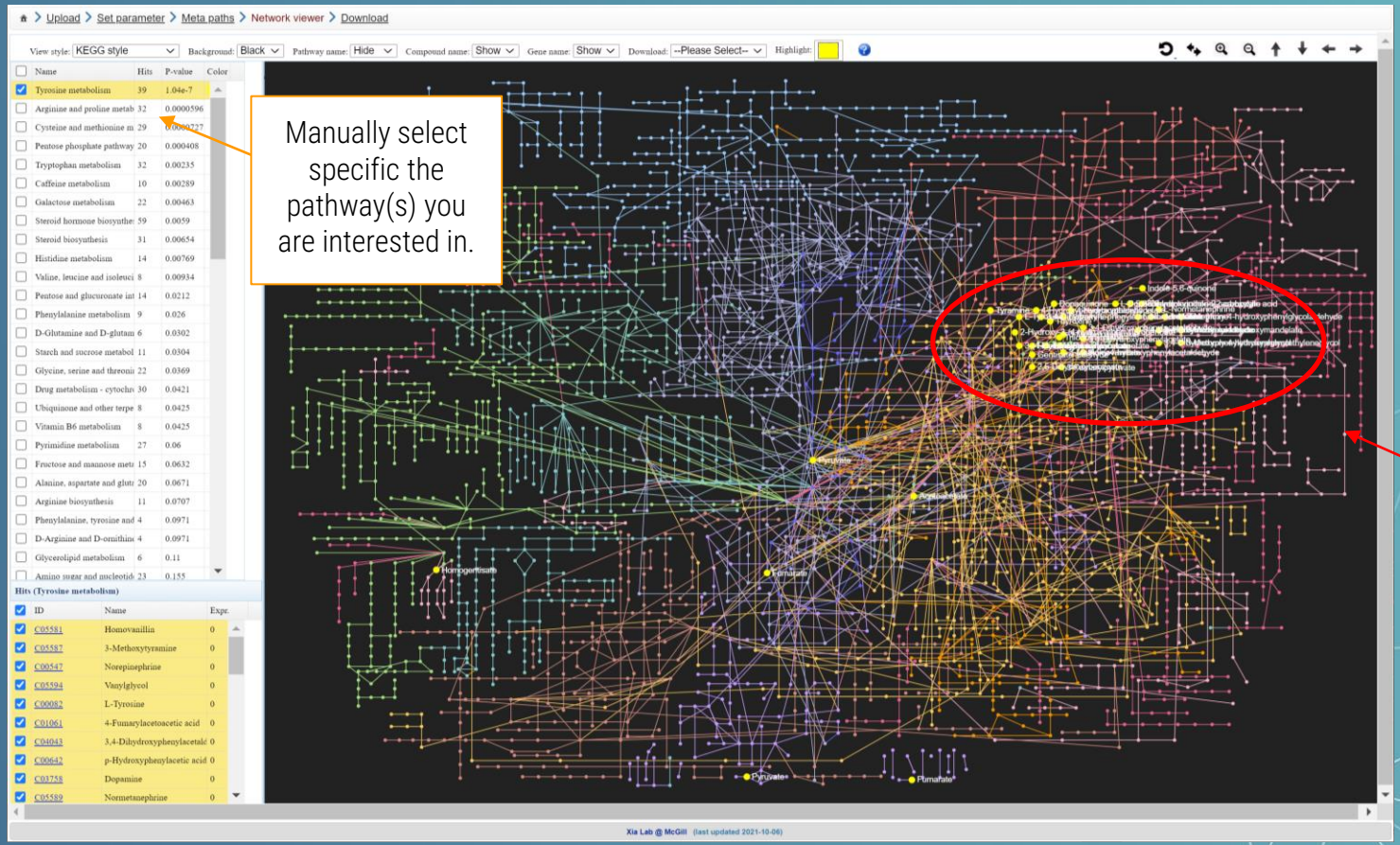


Manually set the cut-off of p values of pathways to include for Venn diagram.

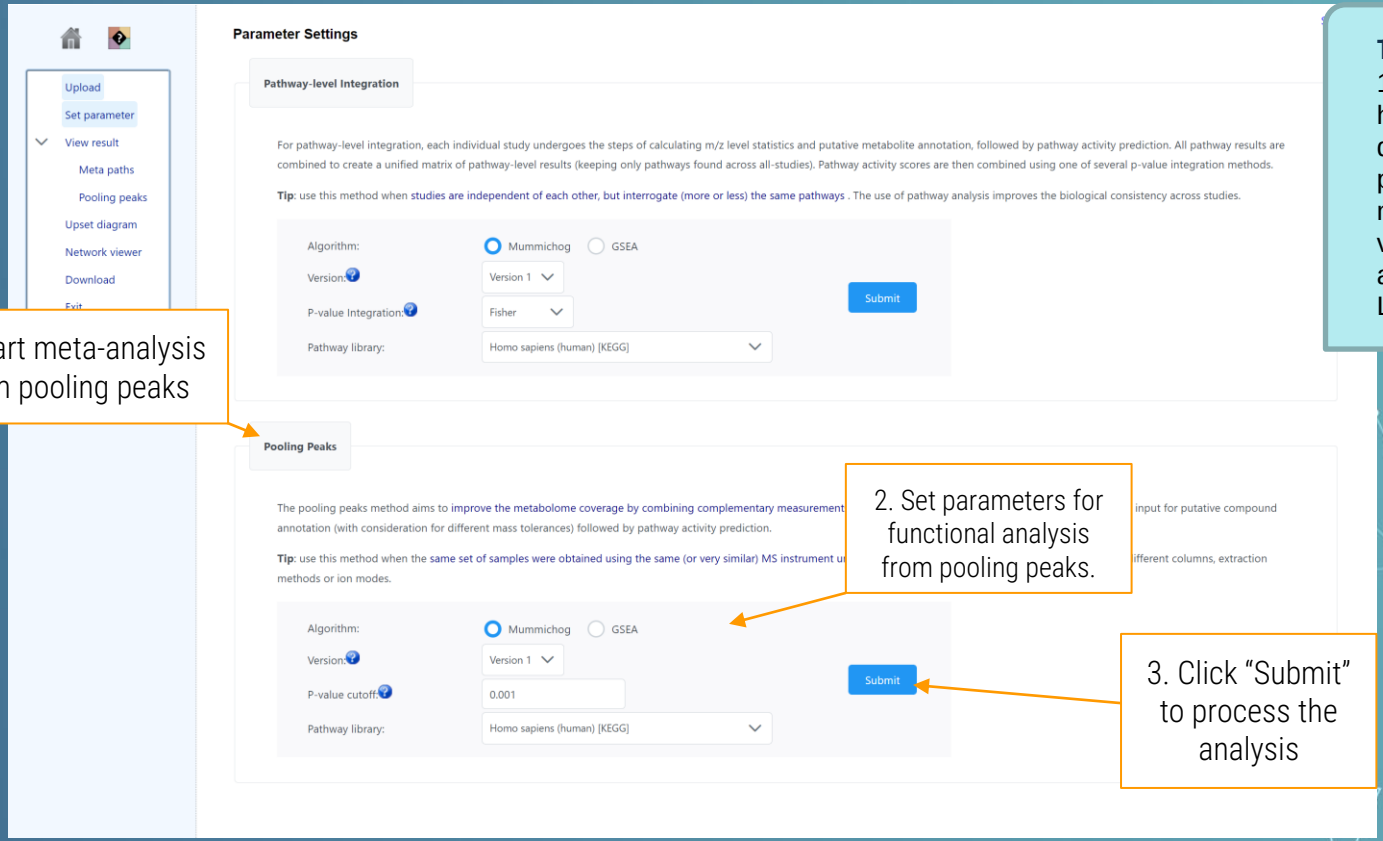


Click certain part to view the intersected pathways

3.5.4 Results (Network Exploration)



3.6.1 Parameter Setting – Pooling peaks



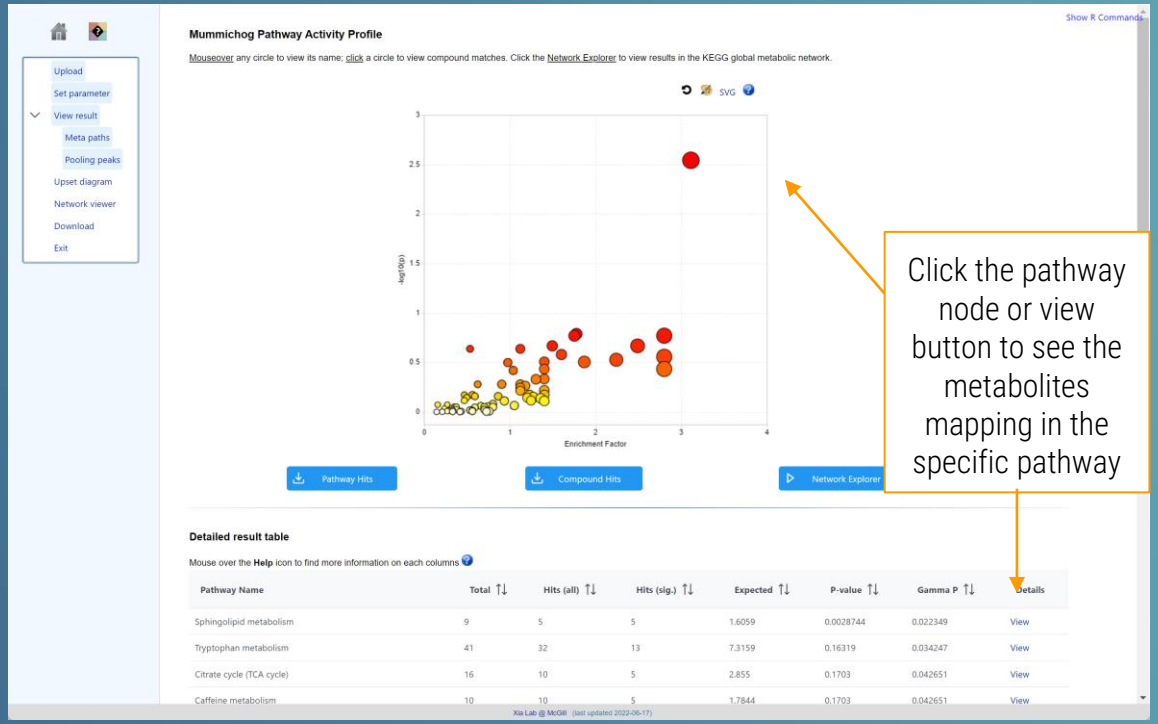
1. Start meta-analysis from pooling peaks

2. Set parameters for functional analysis from pooling peaks.

3. Click "Submit" to process the analysis

TIP: Mummichog version 1 is more compatible for heterogenous data (like different LC-MS platforms/ extraction method etc.), while the version 2 is only applicable for the same LC-MS condition.

3.6.2 Results (Pooling peaks)

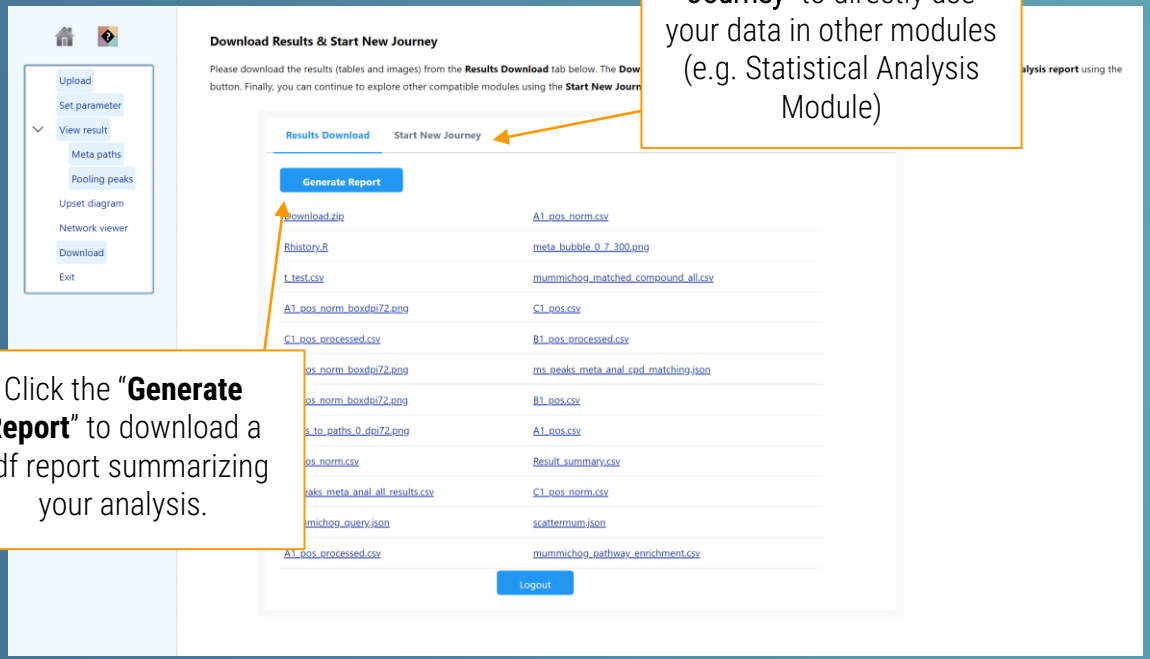


Click the pathway node or view button to see the metabolites mapping in the specific pathway

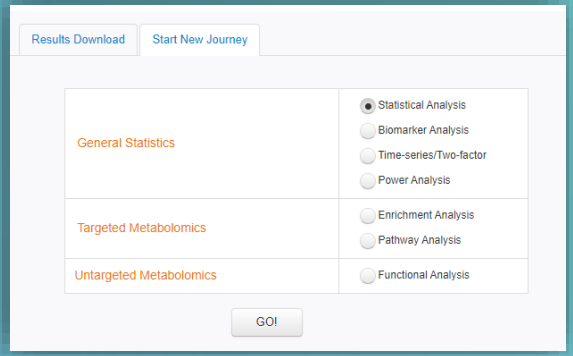
TIP: Click the network explorer at the bottom of this page to start the exploration of network analysis. You can also download the pathway or compound hits by clicking the corresponding buttons.

3.7 Result Downloading & New Journey

Click the "**Start New Journey**" to directly use your data in other modules (e.g. Statistical Analysis Module)



Click the "**Generate Report**" to download a pdf report summarizing your analysis.



Thanks

If you have any questions please read through the FAQs or contact us at Zhiqiang.pang[at]xialab.ca or Jeff.xia[at]xialab.ca