MetaboAnalyst 5.0

A Web-based Tool for streamlined Metabolomics Data Analysis

2022.07.12

6. Network Explorer

Network analysis of multi-Omics data could enhance the interpretation on the biological sense with a intuitive way from the system level. The knowledge-based network exploration on the multiple omics data has been implemented since version 4. Network Explorer module of MetaboAnalyst has added support for data-driven network analysis from Version 5.

Highlights:

- Added the Debiased Sparse Partial Correlation (DSPC) algorithm to calculate a partial correlation network from user's uploaded data (Basu et al. 2017).

6.0 Knowledge & Background

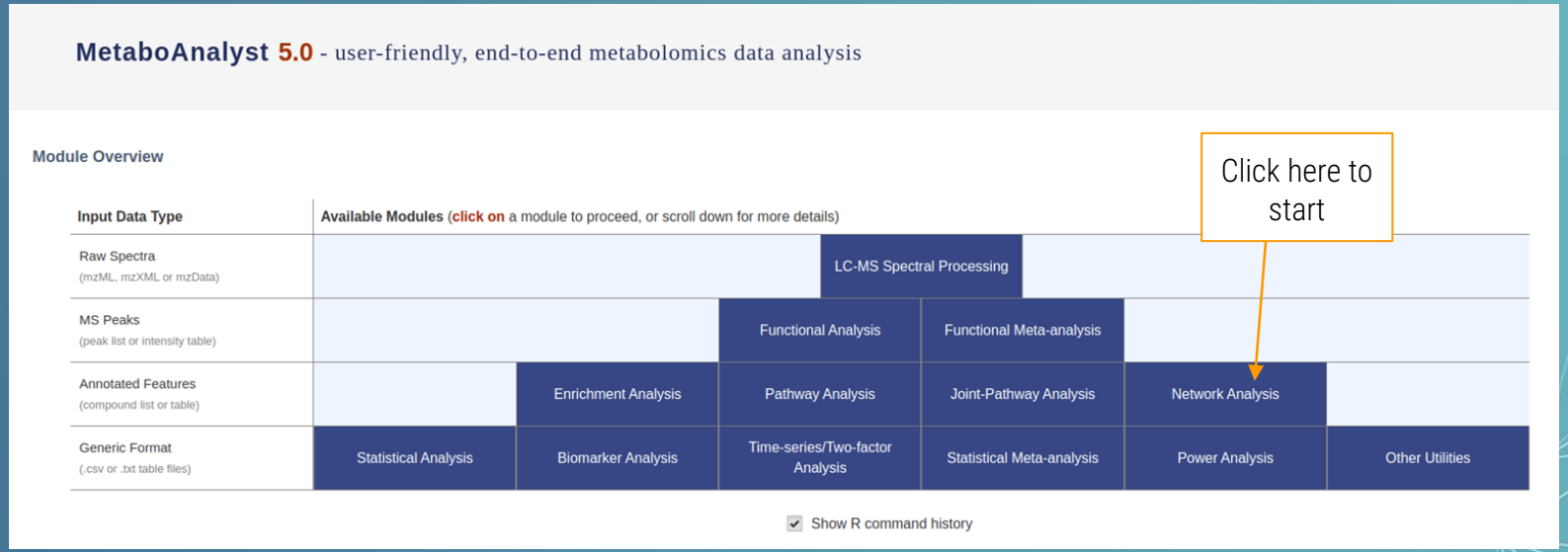
Knowledge-driven network

- The general concept of knowledge-driven network is to analyze each set of omics data individually and then map the significant features (e.g., metabolites, genes) into the context of our knowledge framework in the forms of networks in order to uncover meaningful links among them, as well as their associations with disease phenotypes (*Zhou et al., 2020*).

Data-driven network

- However, knowledge-driven approaches are limited due to an insufficient coverage of the metabolome and lack of knowledge of metabolite-metabolite interactions. Meanwhile, data-driven approaches that permit the inclusion of unknown compounds can overcome these limitations to construct biologically relevant networks and even aid in identifying unknown compounds (*Basu et al., 2017*). Therefore, to address concerns in incomplete knowledge of metabolic networks and infer the putative identity of unknown metabolites, we introduce a data-driven network feature in MetaboAnalyst 5.0.

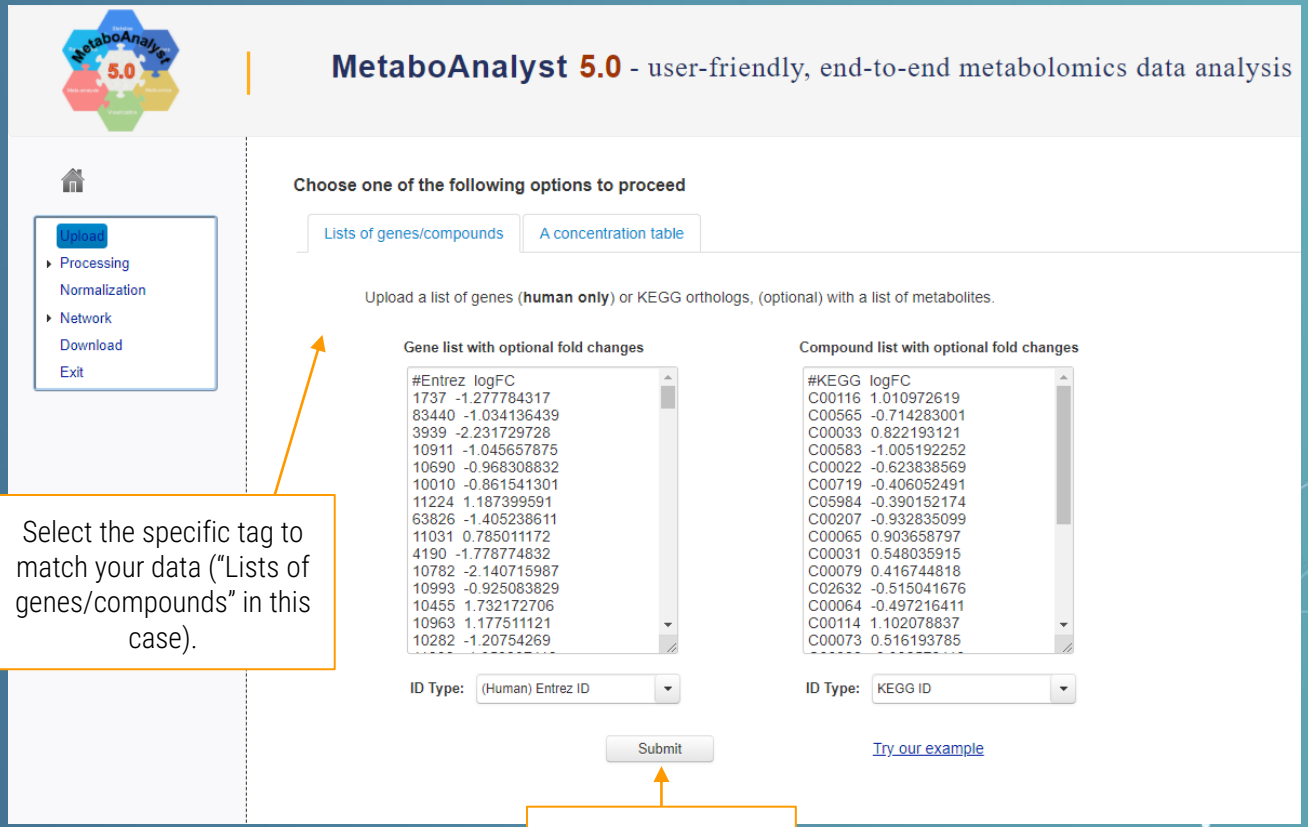
6.1 Start Network Explorer



6.2 Starting from a list

Knowledge-driven network analysis

6.2.1 Data Upload Page – list(s)

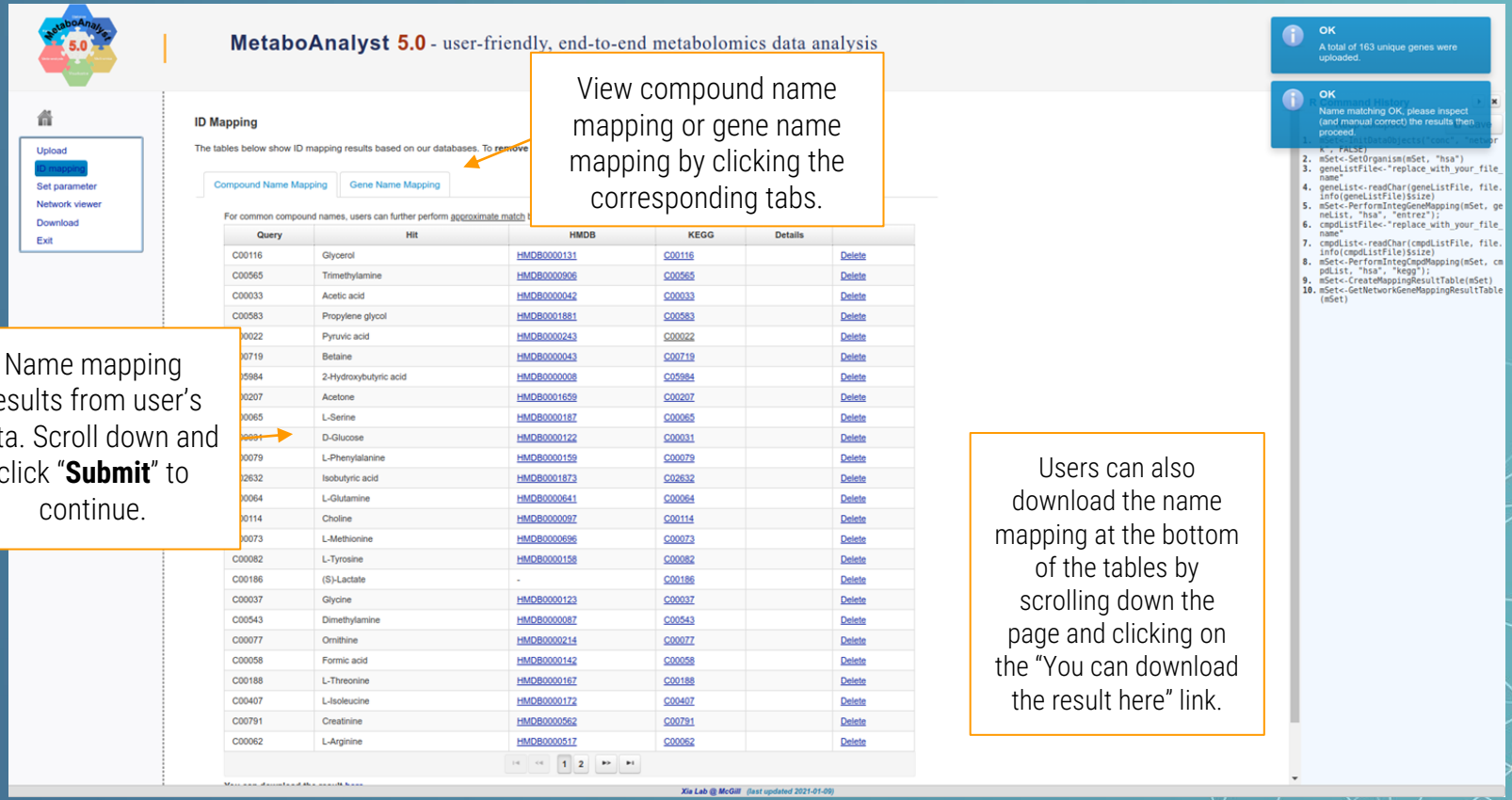


Select the specific tag to match your data ("Lists of genes/compounds" in this case).

Click "**Submit**" to continue.

TIP: The Fold change is optional. The titles of the 2 columns need to start with '#'.

6.2.2 Name Mapping

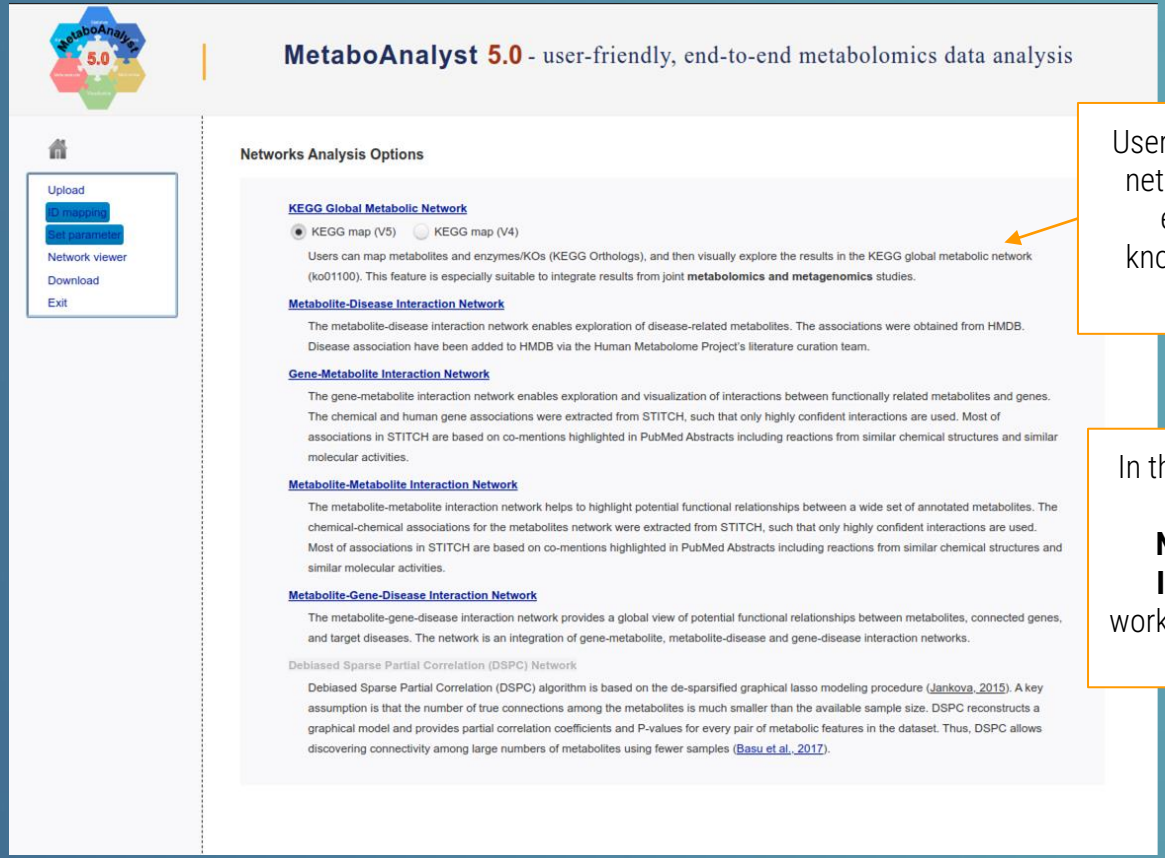


View compound name mapping or gene name mapping by clicking the corresponding tabs.

Name mapping results from user's data. Scroll down and click "**Submit**" to continue.

Users can also download the name mapping at the bottom of the tables by scrolling down the page and clicking on the "You can download the result here" link.

6.2.3 Network Selection

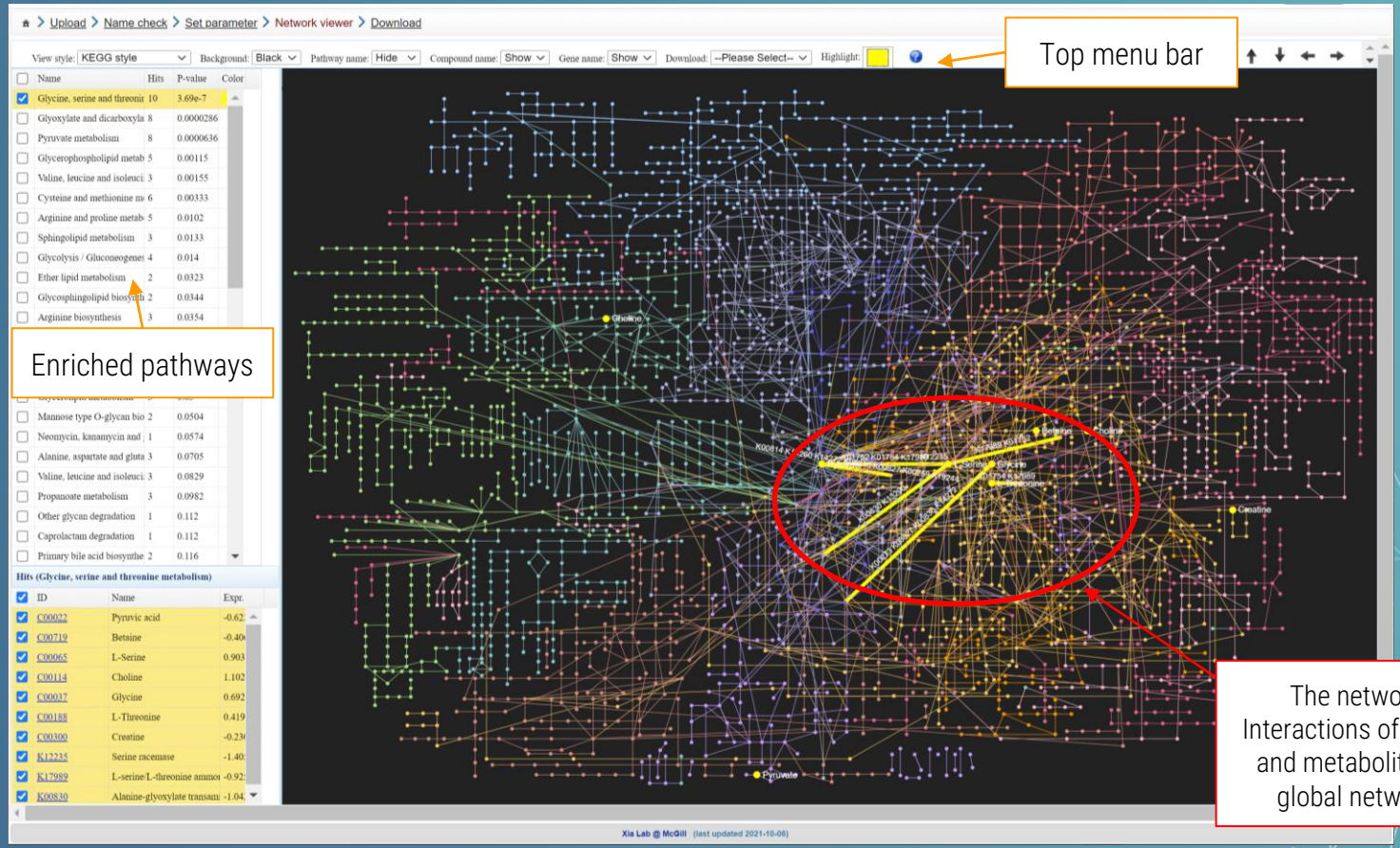


Users can choose a network option to explorer the knowledge-based network.

TIP: The KEGG global metabolic network has been updated to the latest version in MetaboAnalyst, but the old version is still being provided for reproducibility with the previous version. This option will be phased out in the future.

In this tutorial, we will mainly demonstrate using the "**KEGG Global Metabolic Network**" and the "**Gene-Metabolite Interaction Network**". Other parts is working with the same mechanism, and will be introduced briefly.

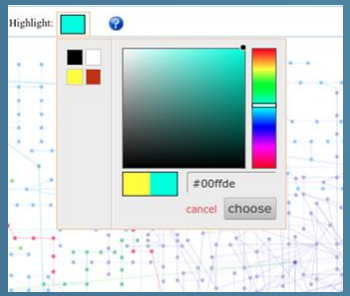
6.2.4 KEGG Global Metabolic Network



6.2.5 Highlight Enriched Pathways

1) Switch the background color to white

2) Choose a highlight color

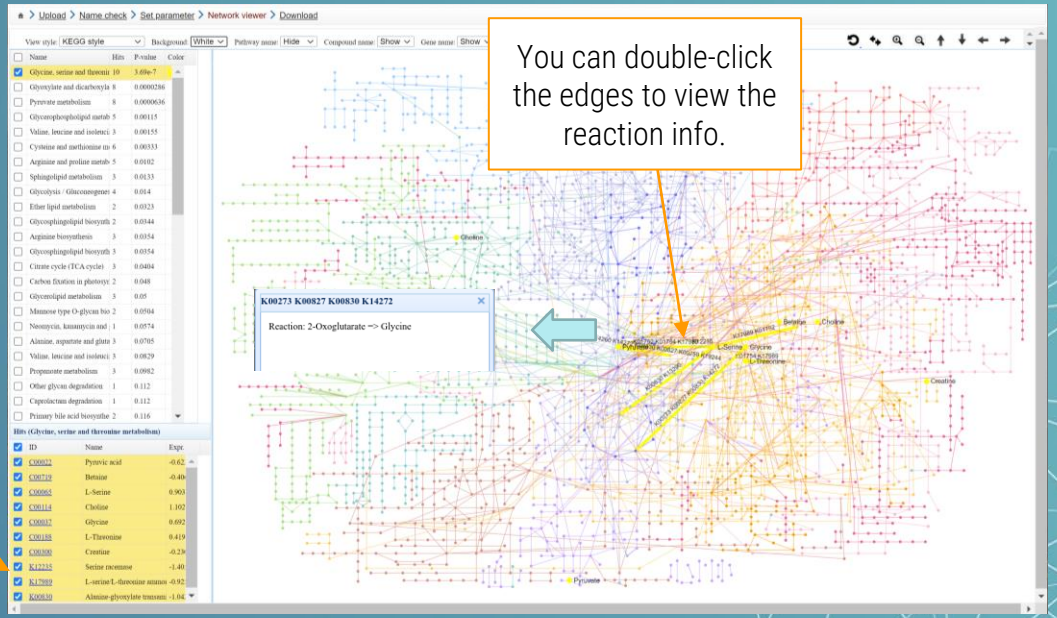


3) Click an enriched pathway to highlight

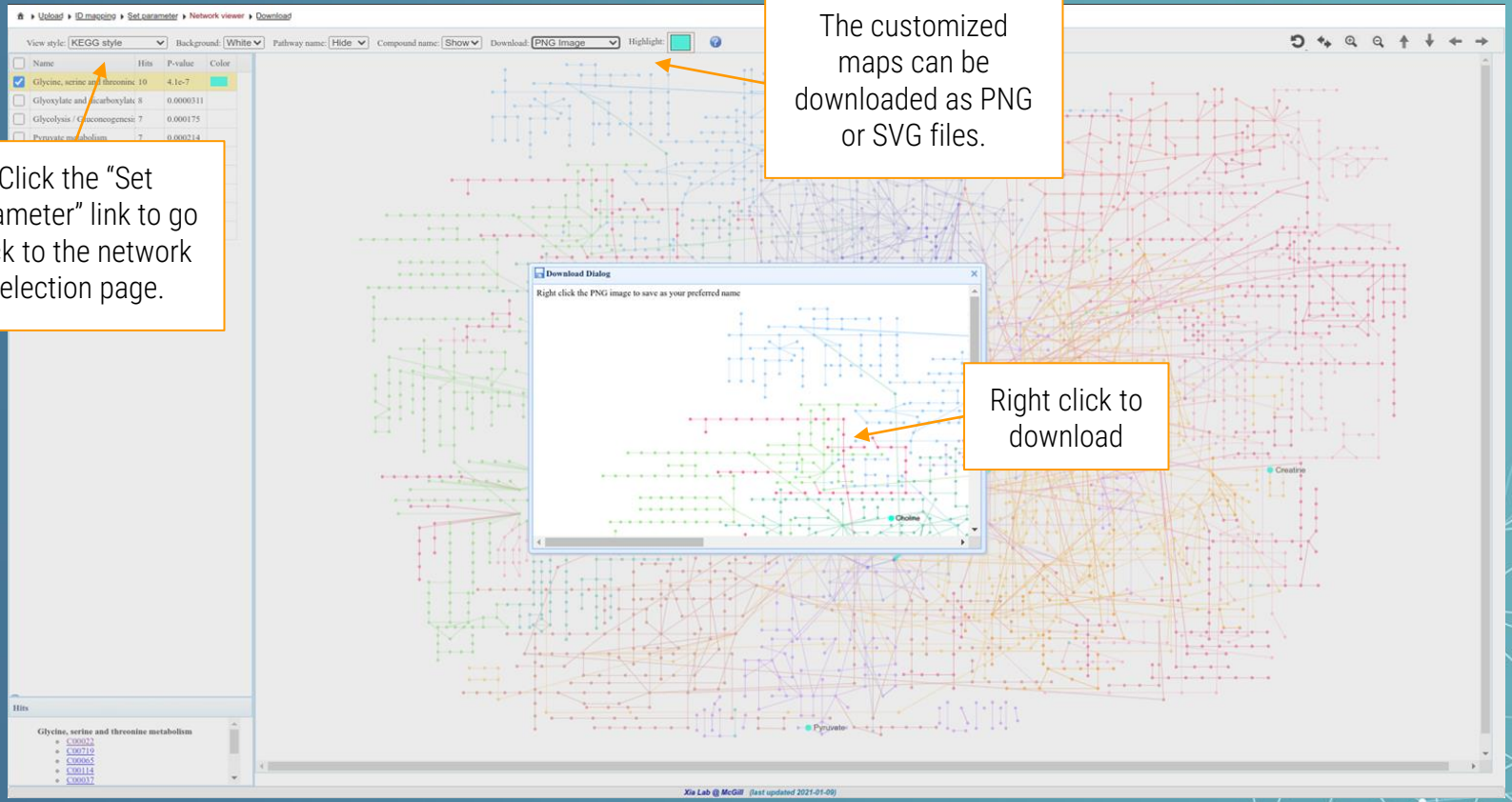
TIP 1: White background is better for publication or reports purposes. Please try to zoom in to find our more details of the interaction.

You can double-click the edges to view the reaction info.

You can click the link to get further details about the compound.



6.2.6 Download the Network

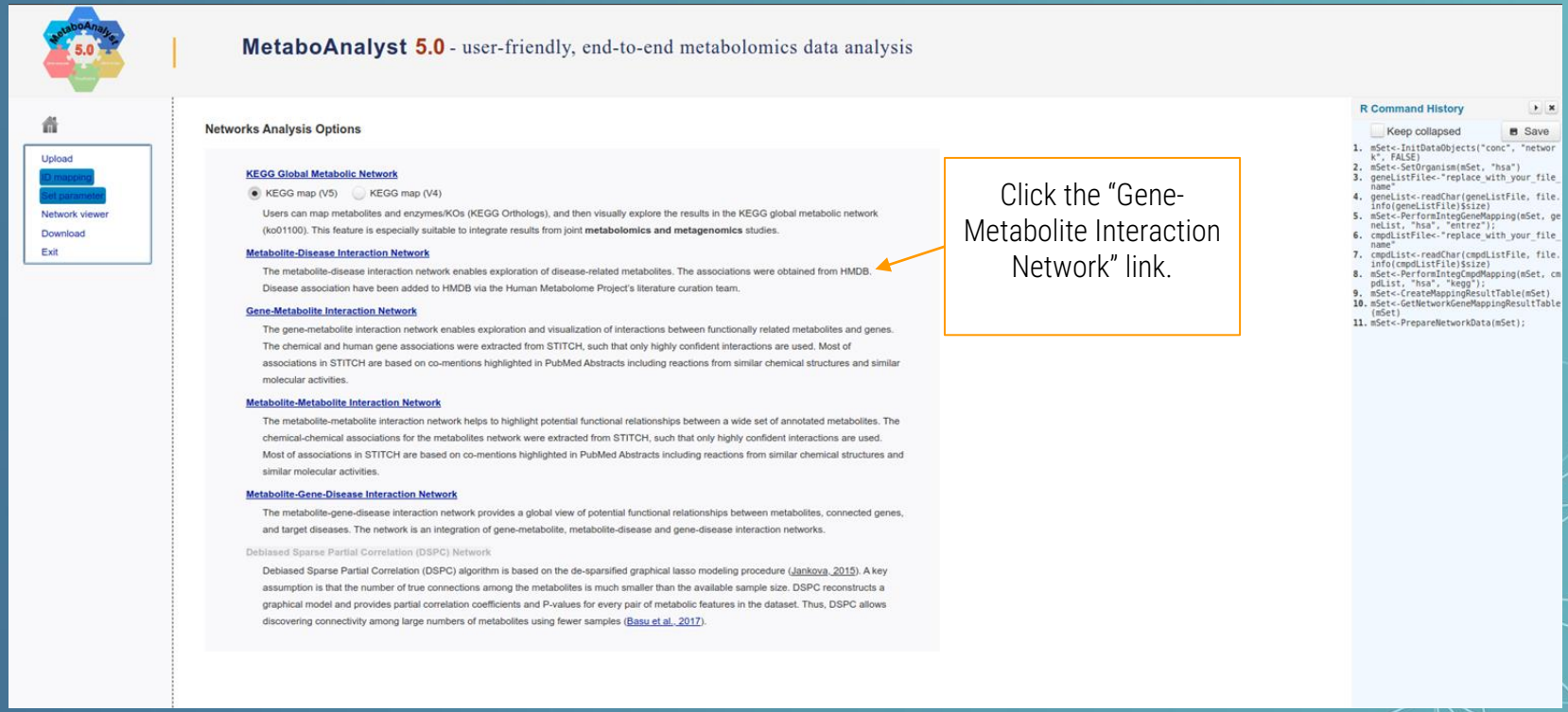


Click the “Set parameter” link to go back to the network selection page.

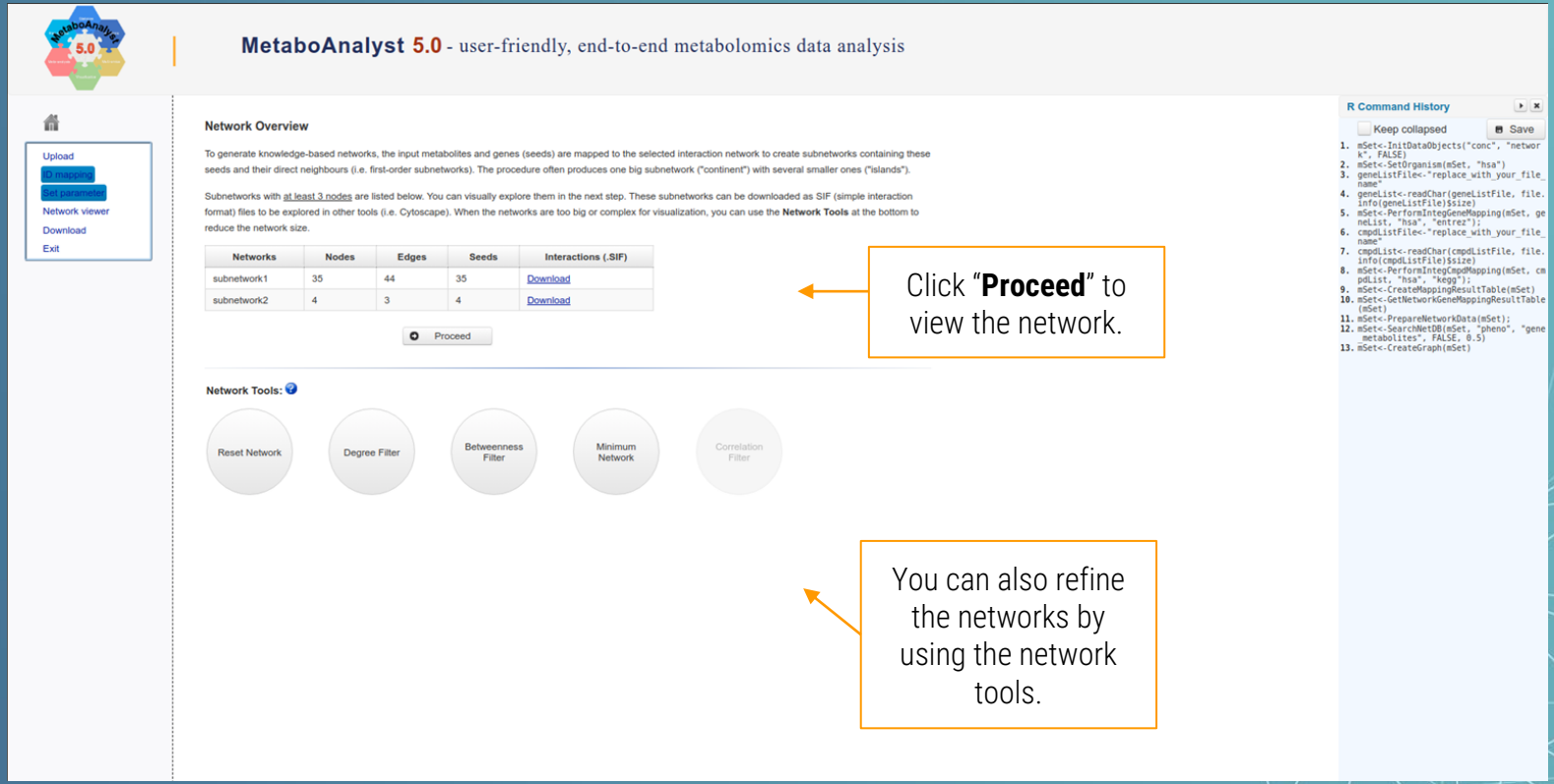
The customized maps can be downloaded as PNG or SVG files.

Right click to download

6.2.7 Gene-Metabolite Interaction Network



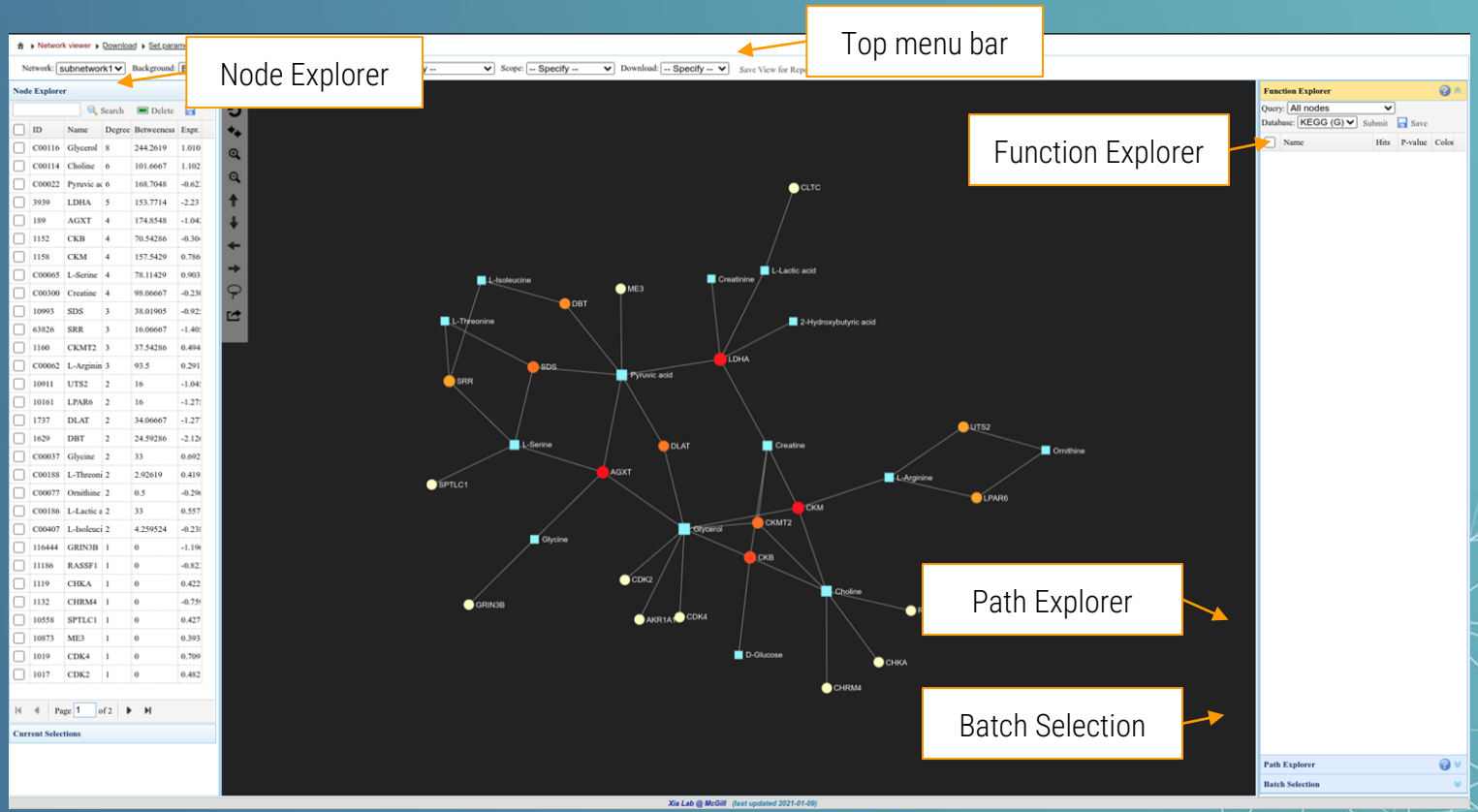
6.2.8 Network Overview



Click "**Proceed**" to view the network.

You can also refine the networks by using the network tools.

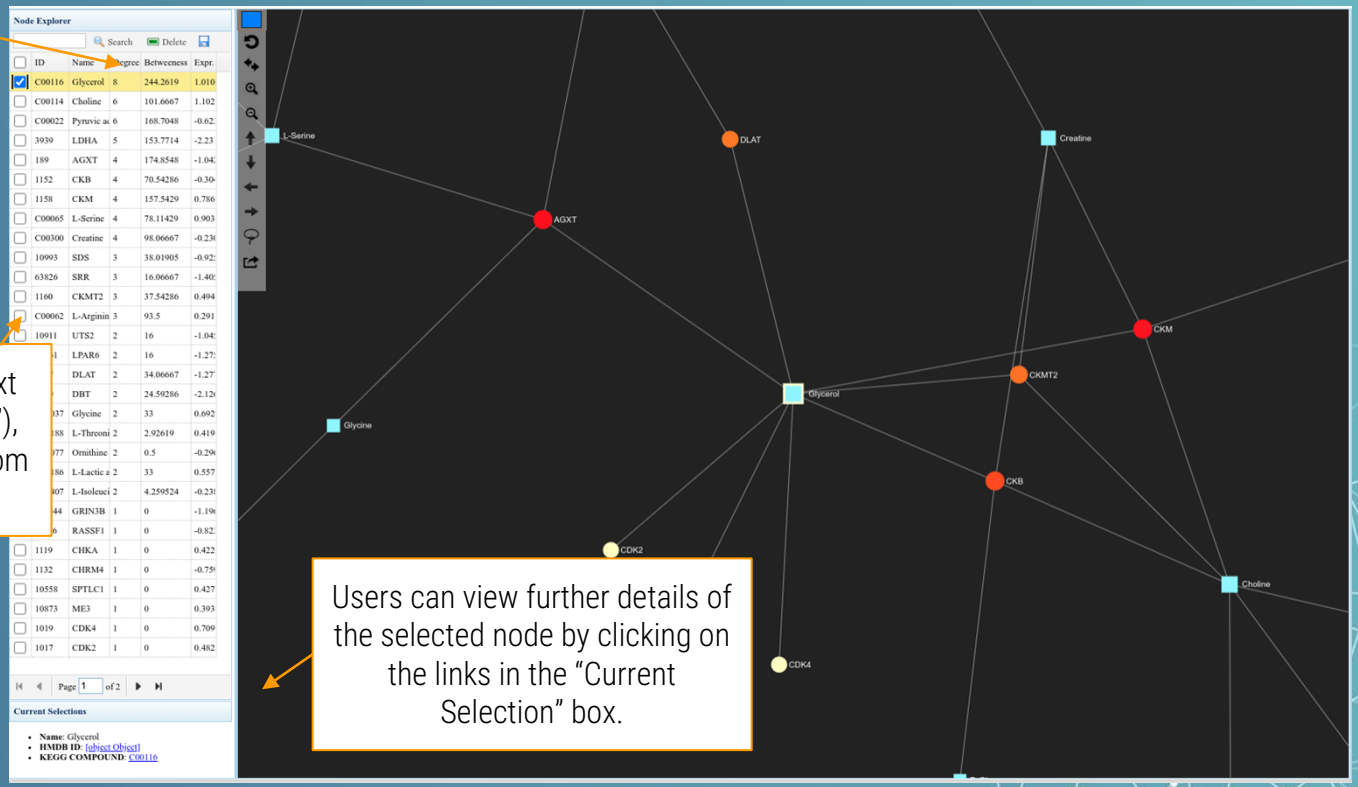
6.2.9 Network Viewer



6.2.10 Node Explorer

You can sort the node table by clicking the column header based on either degree or betweenness values.

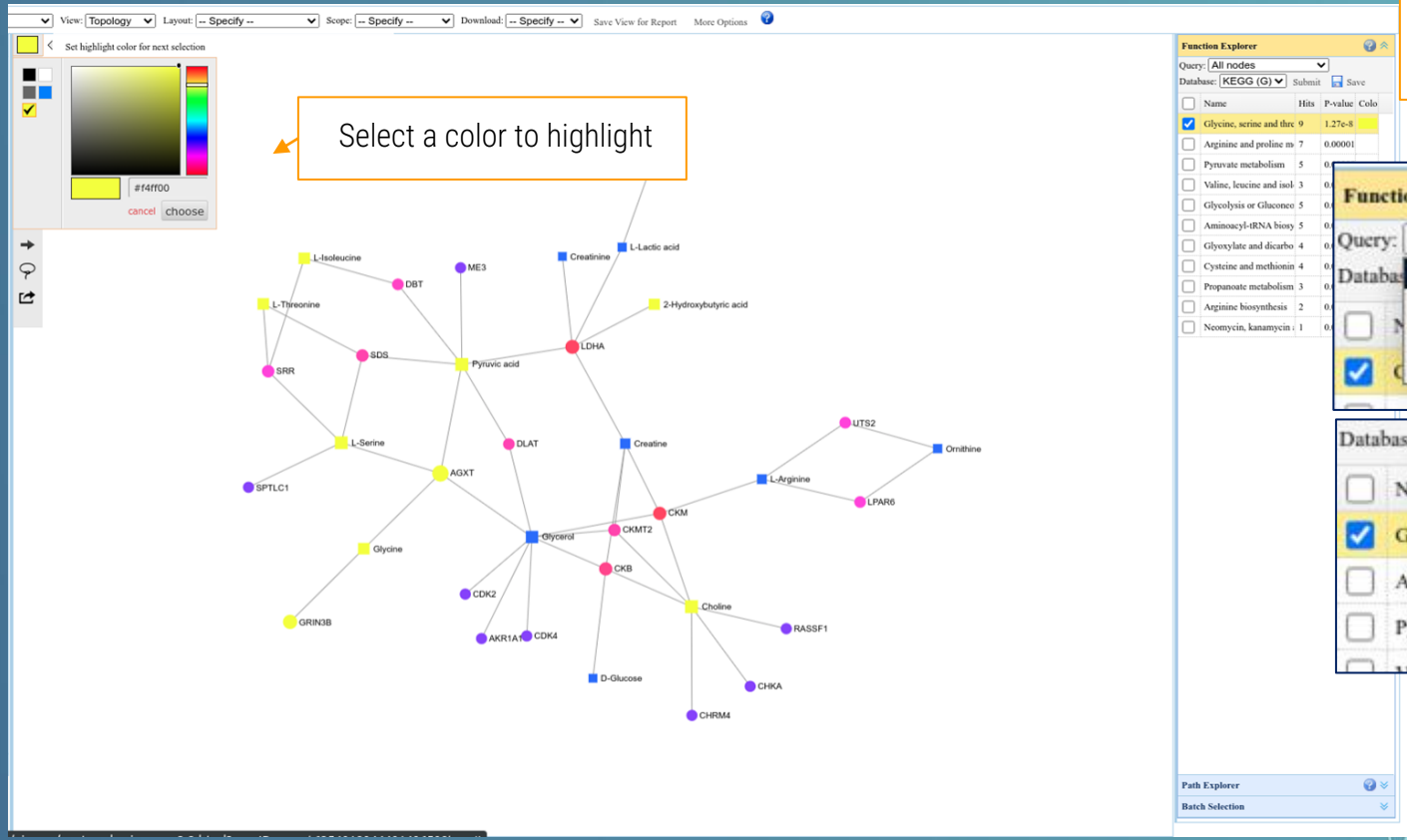
If you click on the empty box next to the ID (e.g., “C00116, Glycerol”), the network will automatically zoom into the selected node.



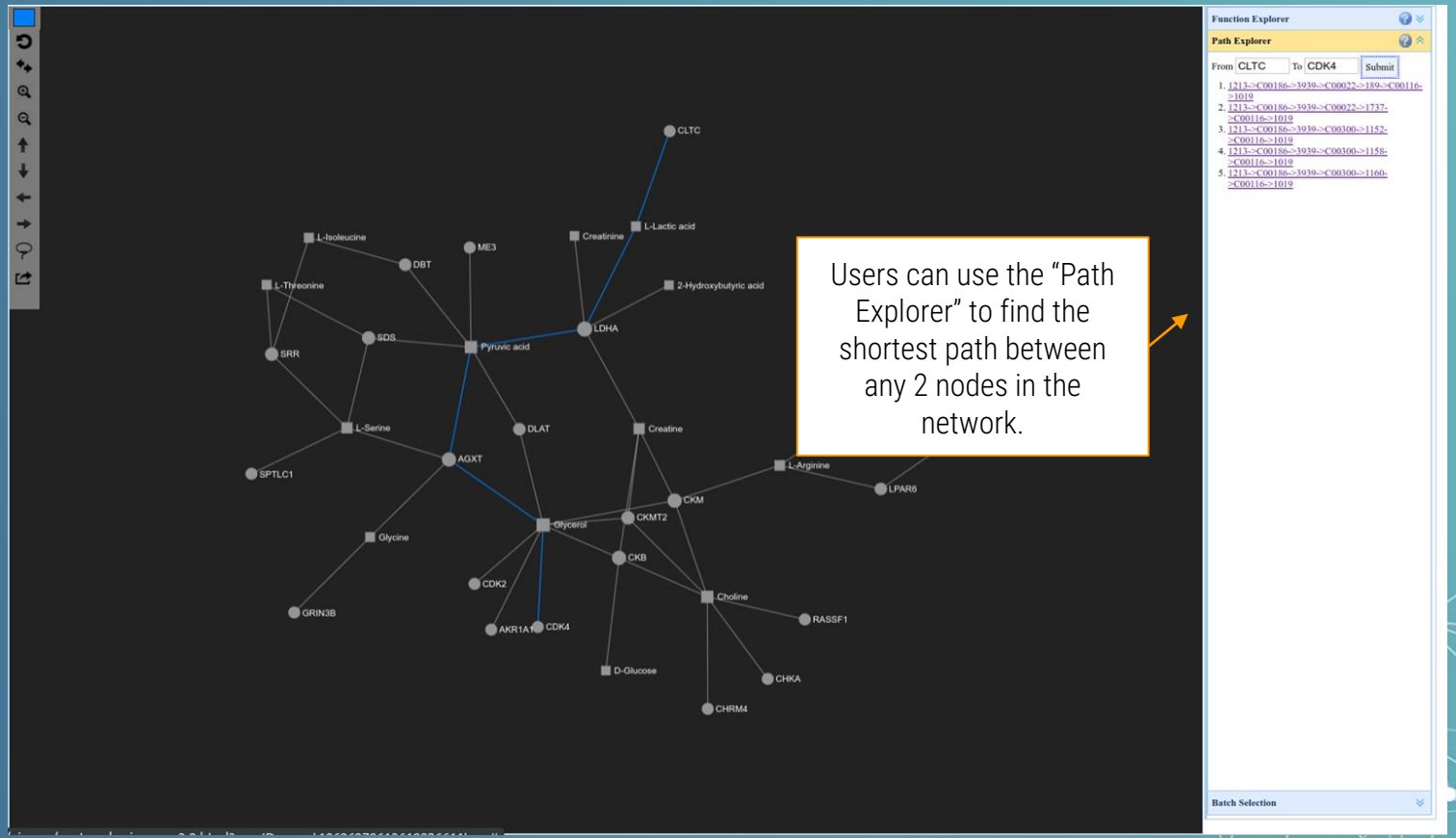
Users can view further details of the selected node by clicking on the links in the “Current Selection” box.

6.2.11 Function Explorer

Indicate the “Query” and “Database” type and then click the “Submit” to perform functional enrichment analysis

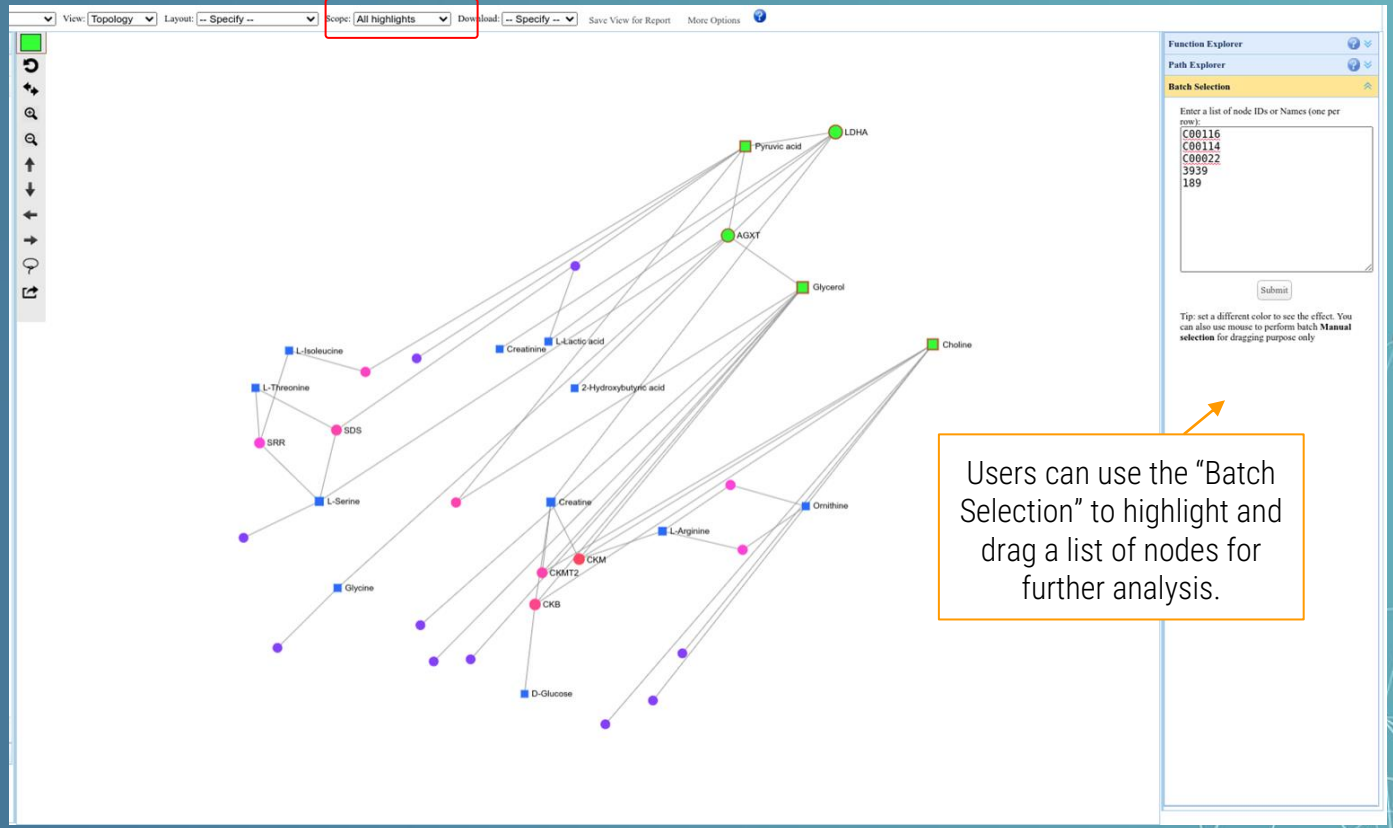


6.2.12 Path Explorer



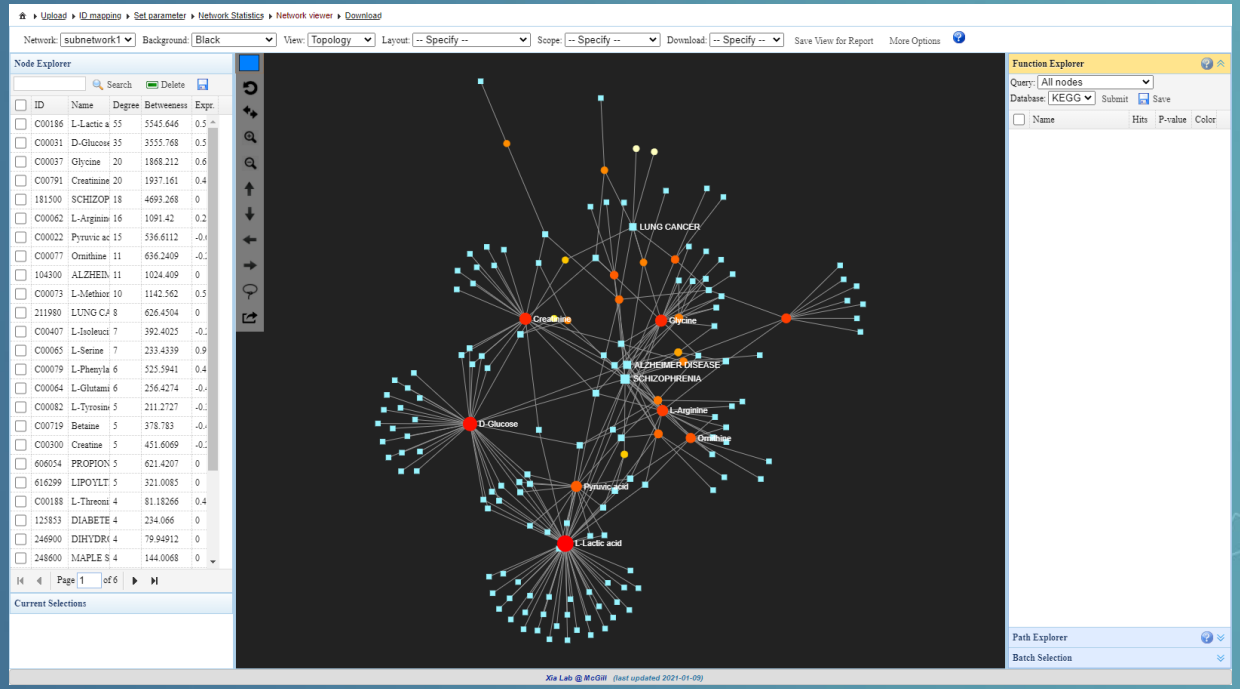
Users can use the “Path Explorer” to find the shortest path between any 2 nodes in the network.

6.2.13 Batch Selection



Users can use the “Batch Selection” to highlight and drag a list of nodes for further analysis.

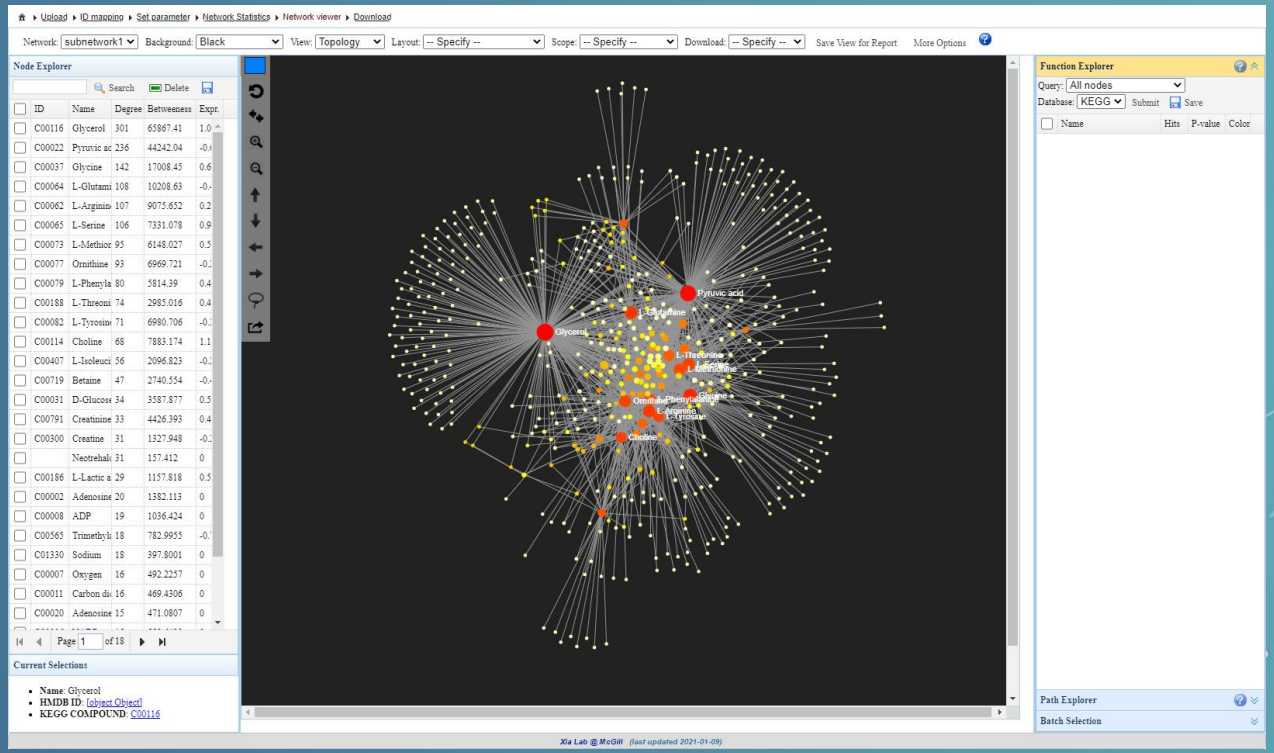
6.2.14 Metabolite-gene-disease interaction



TIP 1: This module is used to show the interactions among the metabolites and disease within a network. Most buttons of this module is working as the modules introduced above.

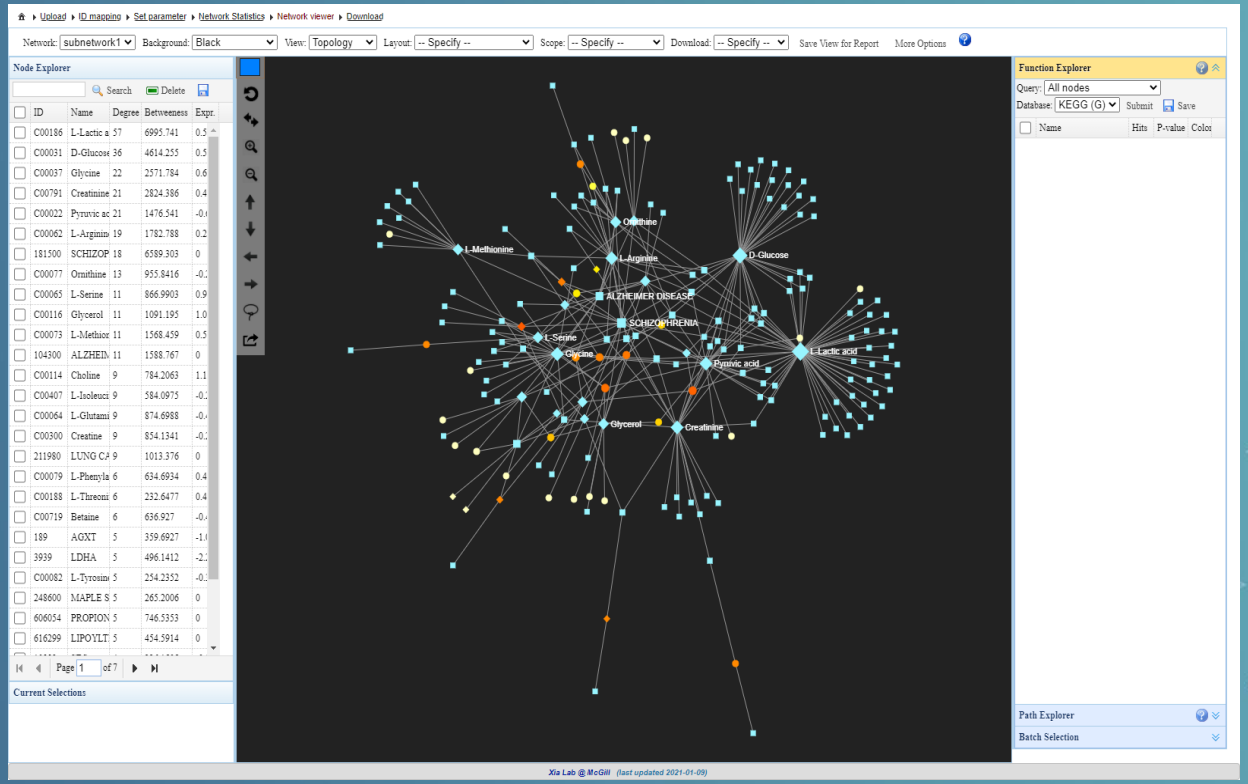
TIP 2: The topological characteristics of different nodes can be ranked by click the header in the 'Node Explorer'. Go and read the FAQs part to find out more about the introduction of topology.

6.2.15 Metabolite-metabolite interaction



TIP 1: This module is used to show the interactions among the metabolites within a network. Most buttons of this module is working as the modules introduced above.

6.2.16 Metabolite-gene-disease interaction

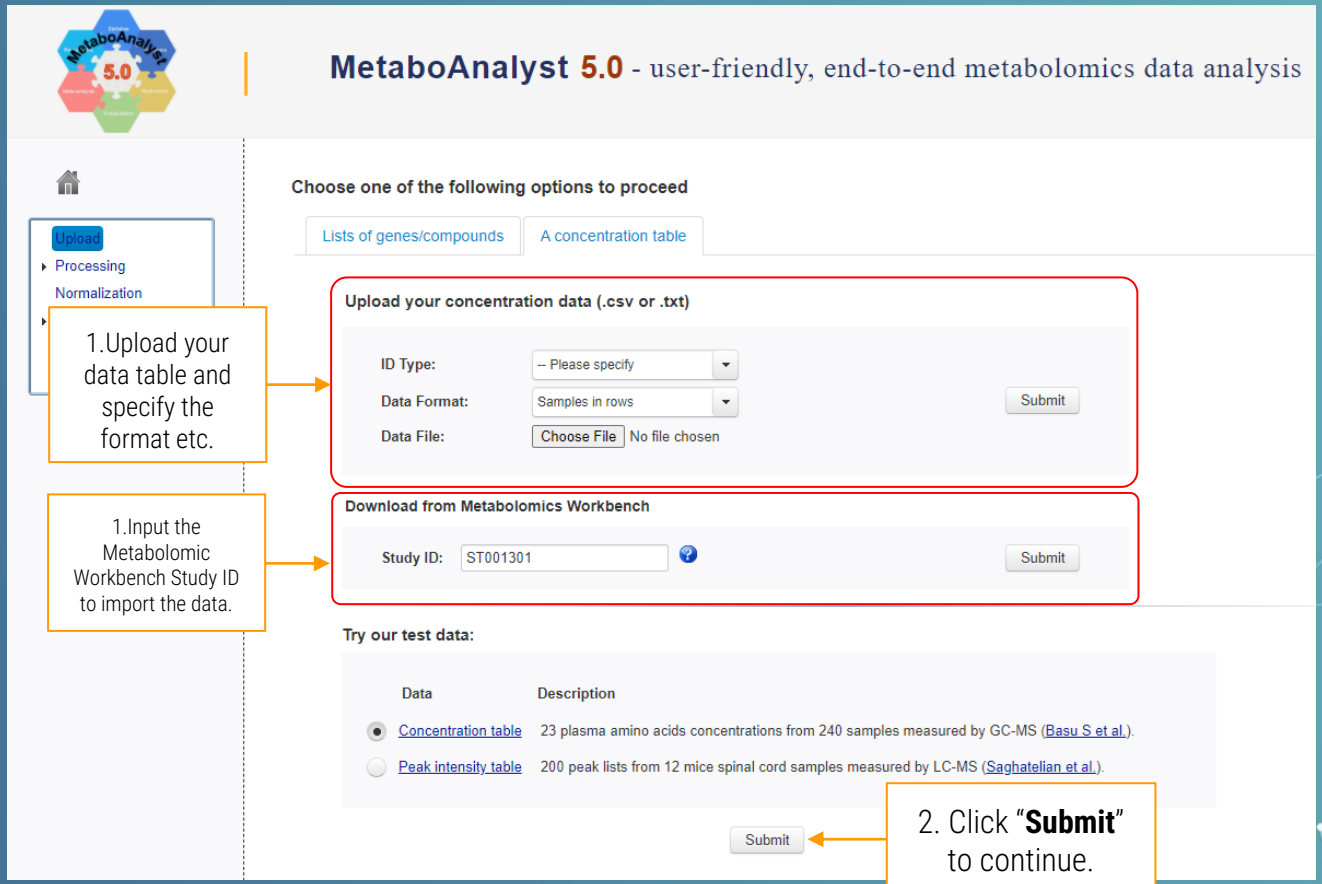


TIP 1: This module is used to show the interactions among the metabolites, genes and diseases within a network. Most buttons of this module is working as the modules introduced above.

6.3 Starting from a table

Data-driven network analysis

6.3.1 Data Upload Page – table(s)



1.Upload your data table and specify the format etc.

1.Input the Metabolomic Workbench Study ID to import the data.

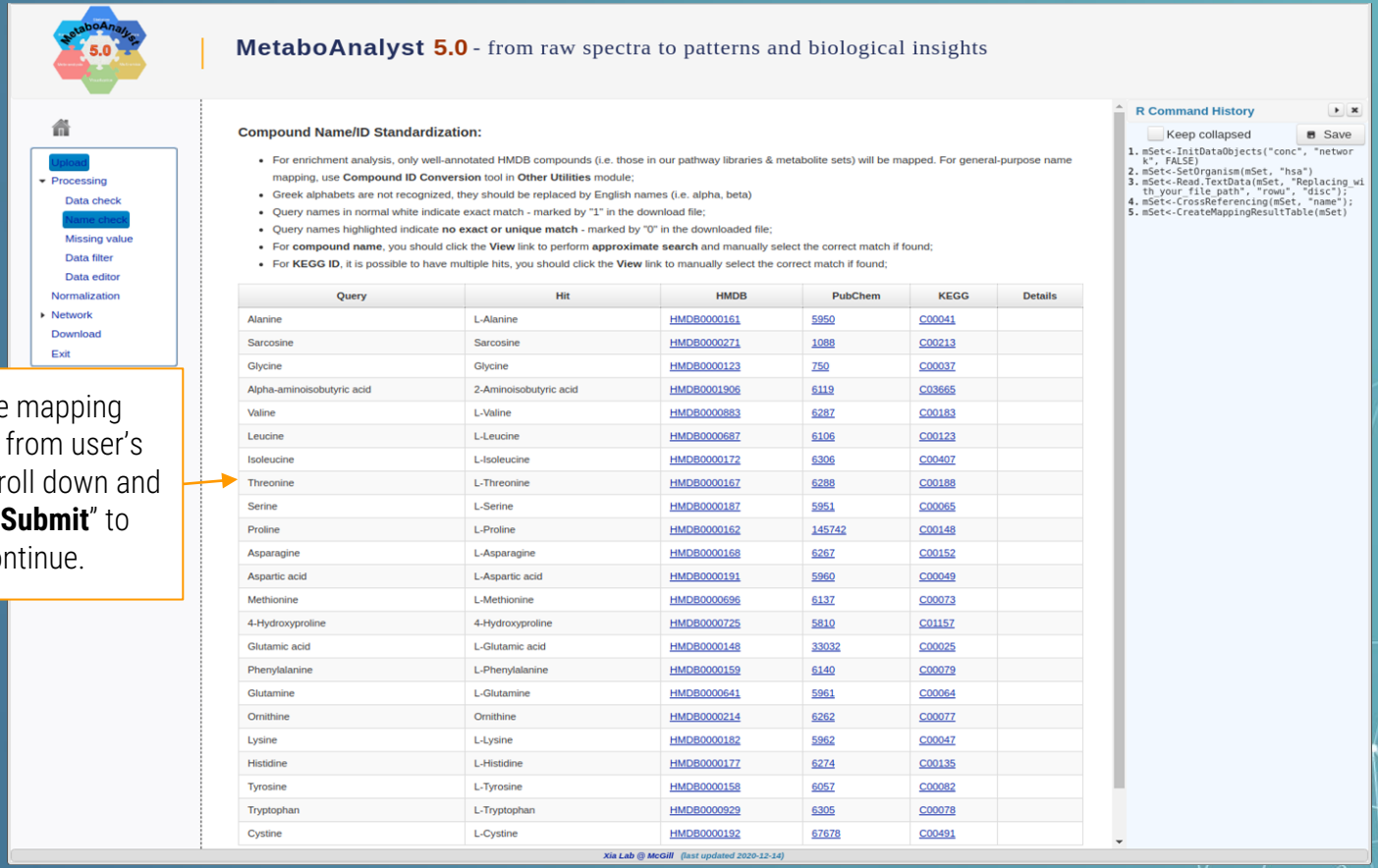
2. Click "**Submit**" to continue.

TIP1: To create a data-driven network, users must upload a concentration table.

TIP2: MetaboAnalyst now allows users to use the study results from Metabolomics Workbench directly by simply providing the STUDY ID.

TIP3: The data pre-processing steps, including data integrity check, ID standardization, and normalization need to be performed step by step.

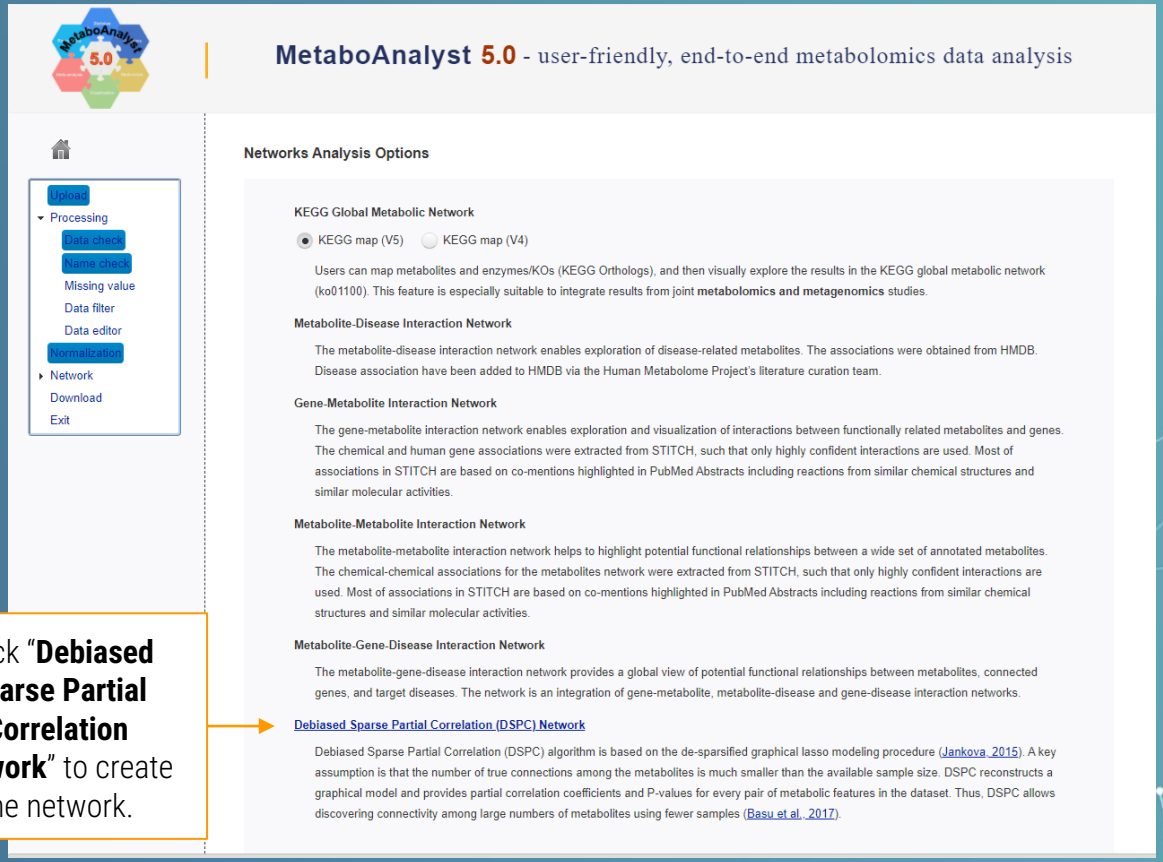
6.3.2 Name Mapping Page



Query	Hit	HMDB	PubChem	KEGG	Details
Alanine	L-Alanine	HMDB0000161	5950	C00041	
Sarcosine	Sarcosine	HMDB0000271	1088	C00213	
Glycine	Glycine	HMDB0000123	750	C00037	
Alpha-aminoisobutyric acid	2-Aminoisobutyric acid	HMDB0001906	6119	C03665	
Valine	L-Valine	HMDB0000883	6287	C00183	
Leucine	L-Leucine	HMDB0000687	6106	C00123	
Isoleucine	L-Isoleucine	HMDB0000172	6306	C00407	
Threonine	L-Threonine	HMDB0000167	6288	C00188	
Serine	L-Serine	HMDB0000187	5951	C00065	
Proline	L-Proline	HMDB0000162	145742	C00148	
Asparagine	L-Asparagine	HMDB0000168	6267	C00152	
Aspartic acid	L-Aspartic acid	HMDB0000191	5960	C00049	
Methionine	L-Methionine	HMDB0000696	6137	C00073	
4-Hydroxyproline	4-Hydroxyproline	HMDB0000725	5810	C01157	
Glutamic acid	L-Glutamic acid	HMDB0000148	33032	C00025	
Phenylalanine	L-Phenylalanine	HMDB0000159	6140	C00079	
Glutamine	L-Glutamine	HMDB0000641	5961	C00064	
Ornithine	Ornithine	HMDB0000214	6262	C00077	
Lysine	L-Lysine	HMDB0000182	5962	C00047	
Histidine	L-Histidine	HMDB0000177	6274	C00135	
Tyrosine	L-Tyrosine	HMDB0000158	6057	C00082	
Tryptophan	L-Tryptophan	HMDB0000929	6305	C00078	
Cystine	L-Cystine	HMDB0000192	67678	C00491	

Name mapping results from user's data. Scroll down and click "**Submit**" to continue.

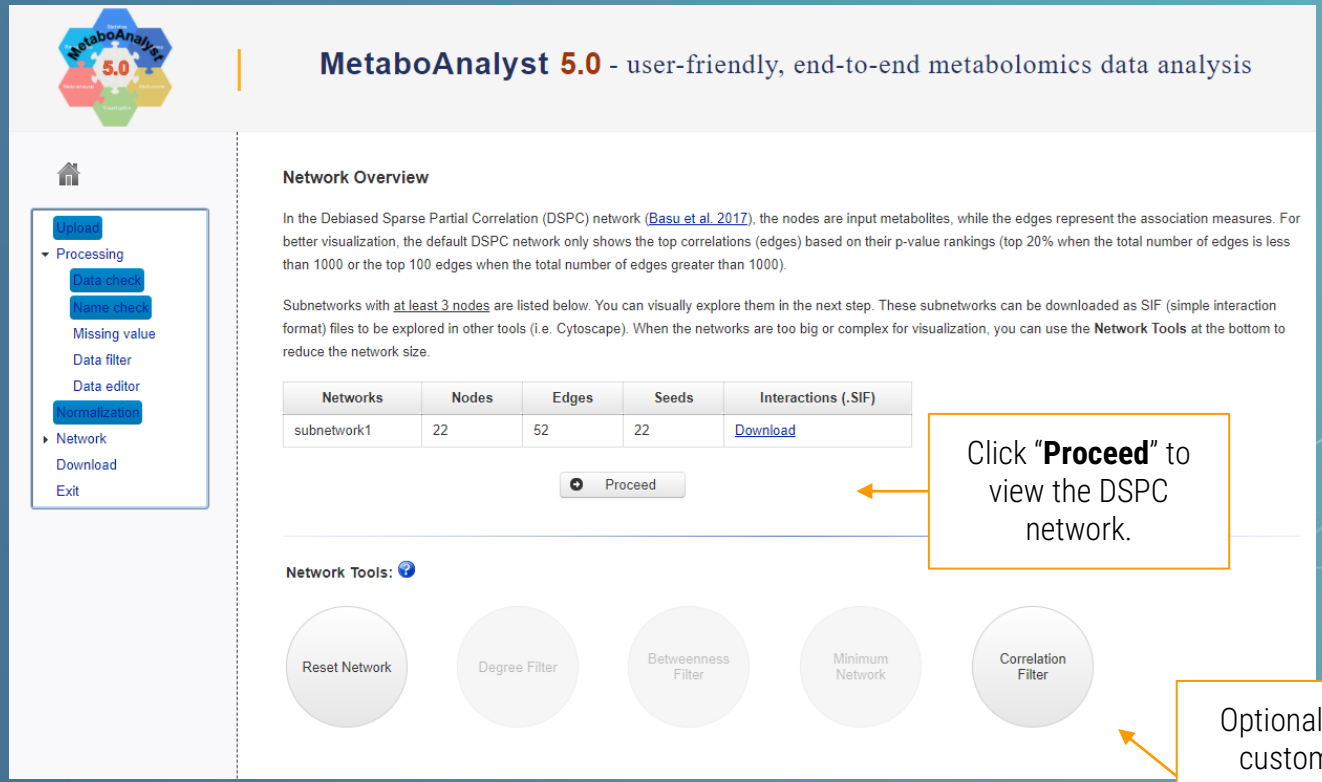
6.3.3 Network Parameters



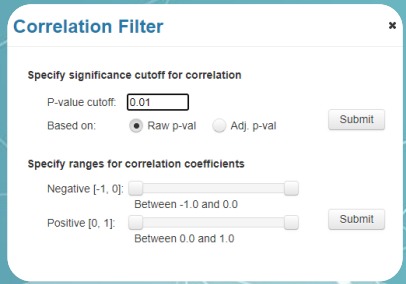
Click "**Debiased Sparse Partial Correlation Network**" to create the network.

TIP: If you are using table uploading option, DSPC will be enabled. Otherwise, the other options will be enabled.

6.3.4 Network Overview

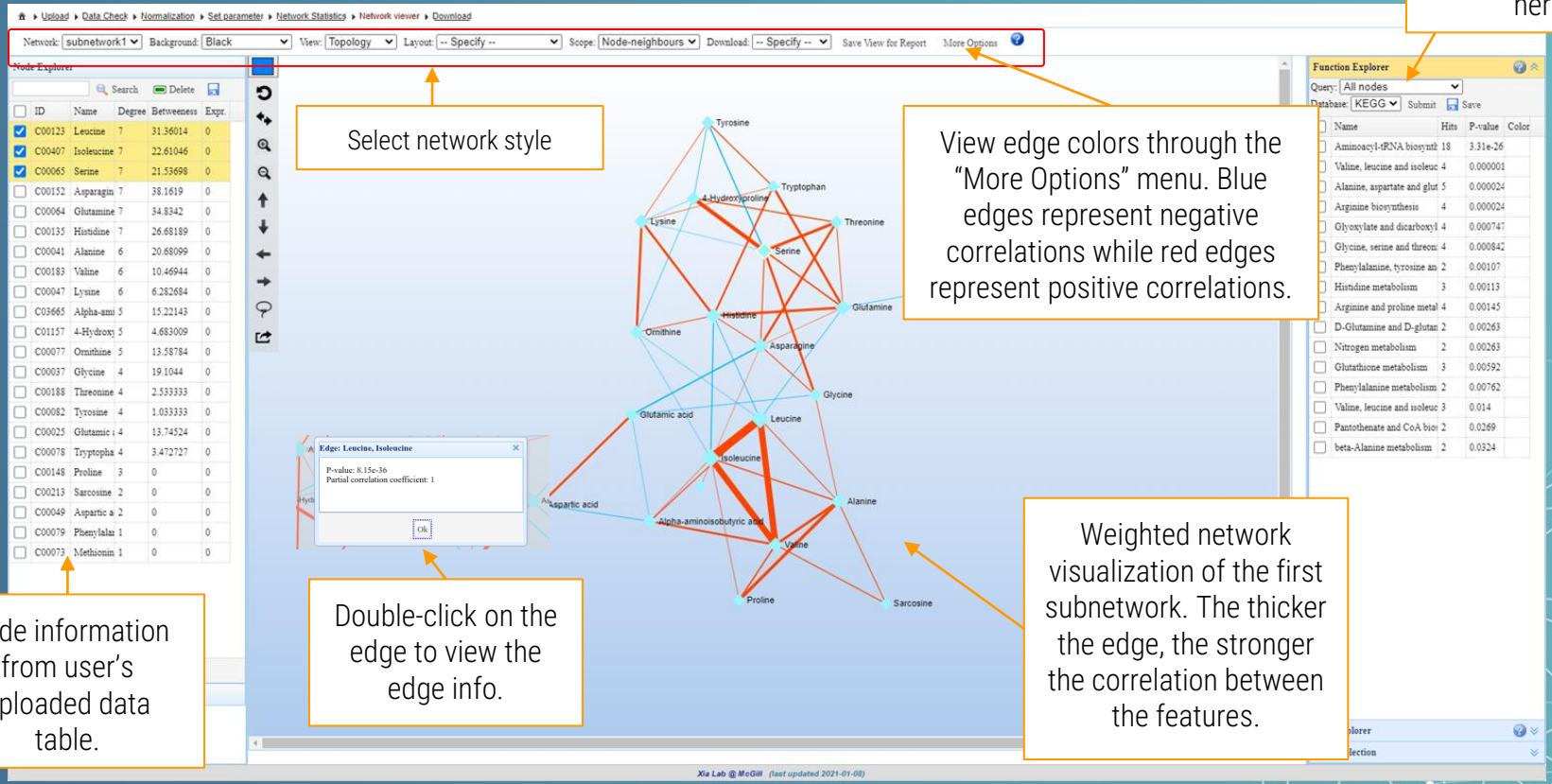


Click "**Proceed**" to view the DSPC network.



Optional filters to customize the network can be found here.

6.3.5 Network View



Perform enrichment analysis on selected nodes here.

Select network style

View edge colors through the “More Options” menu. Blue edges represent negative correlations while red edges represent positive correlations.

Node information from user’s uploaded data table.

Double-click on the edge to view the edge info.

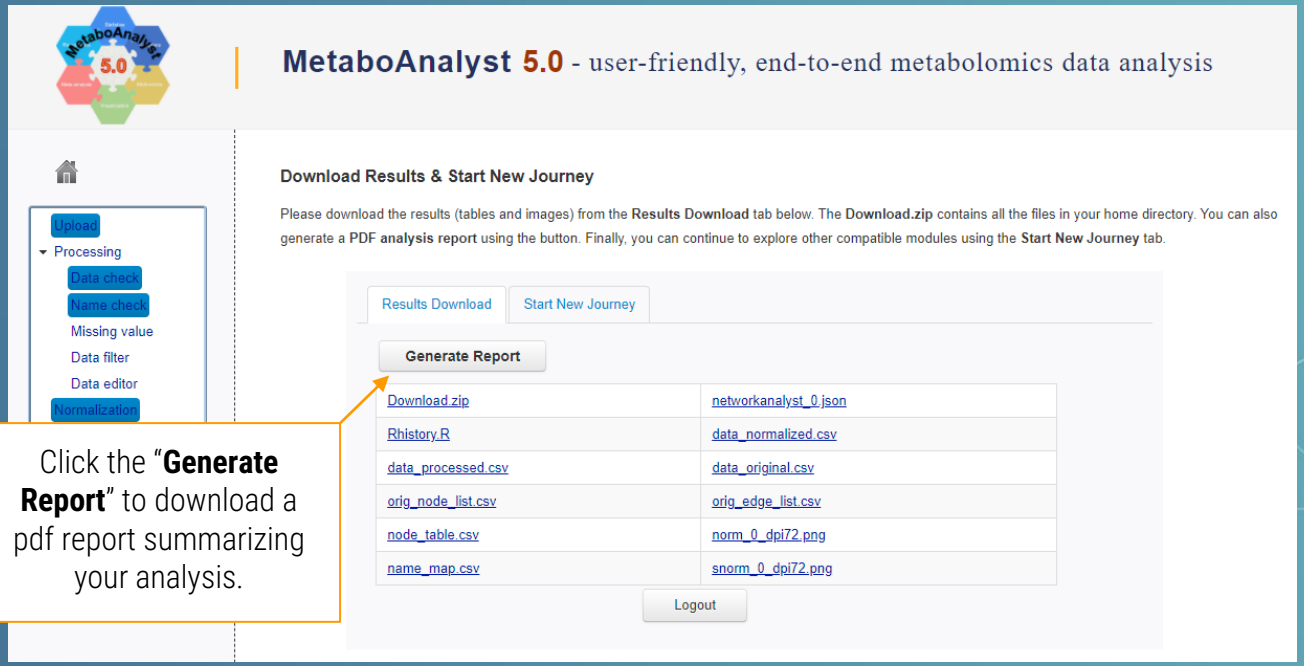
Weighted network visualization of the first subnetwork. The thicker the edge, the stronger the correlation between the features.

6.3.6 DSPC in Statistical Analysis module

Users can also perform DSPC network analysis in the **Statistical Analysis** module.

TIP: You can do DSPC analysis from network analysis module or statistics module.

6.4 Result Downloading



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