OmicsNet Tutorial: Network building

Computer Requirement

- Modern browser supporting **WebGL**
- Chrome 50+, Firefox 47+, Safari 10.1+ and Edge 12+
- Please make sure WebGL is enabled in your browser
  - Please consult this web page to verify: https://get.webgl.org/
- If not enabled, please consult our **FAQ** page for instructions
- For best performance and visualization, use:
- Latest version of **Google Chrome**
- A modern computer with at least 4GB of physical RAM
- A 15-inch screen or bigger (larger is better)
- Retina Display is supported

Motivation

- Explore the different interacting partners of lists of molecules.

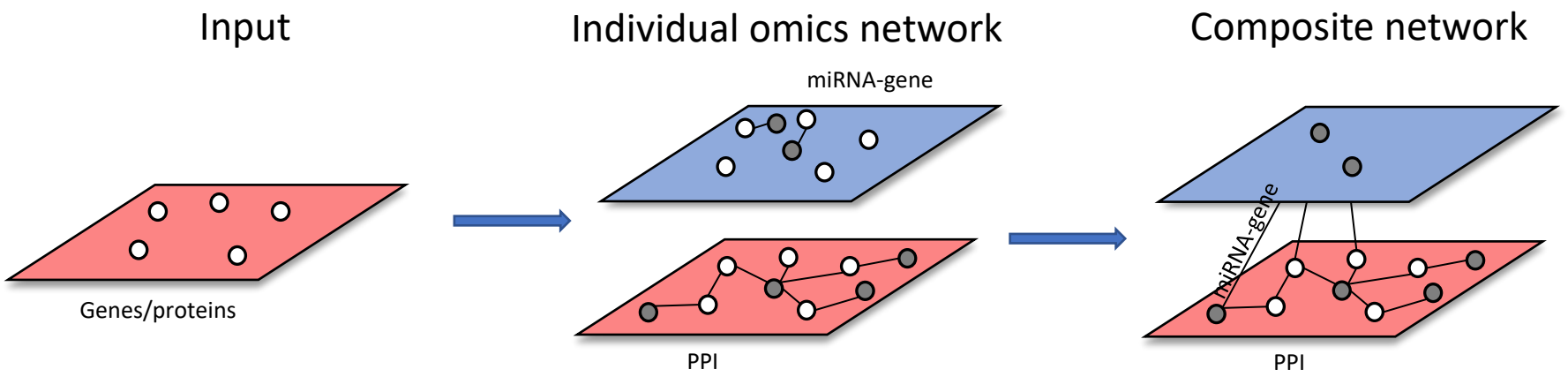
- Approach:
  - Single input list: search for interacting partners of seed molecules and expand to other omics types
  - Multiple input lists: build interaction networks from each individual input list and merge them to form composite network

- This tutorial will showcase examples of different network building processes.

Network building for single list

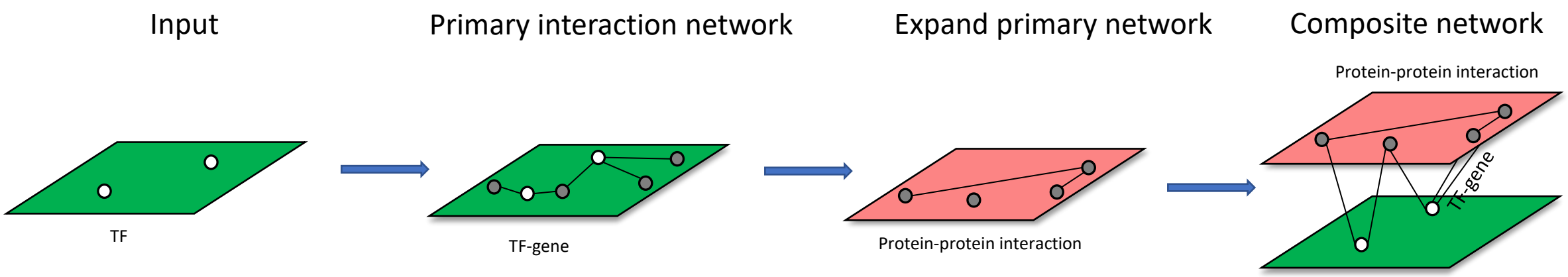
- If gene/protein list is uploaded, the seed gene/proteins can be used to query one or multiple interaction networks based on interaction type and database selected.

- The interaction networks will be merged into connected multi-omics subnetworks



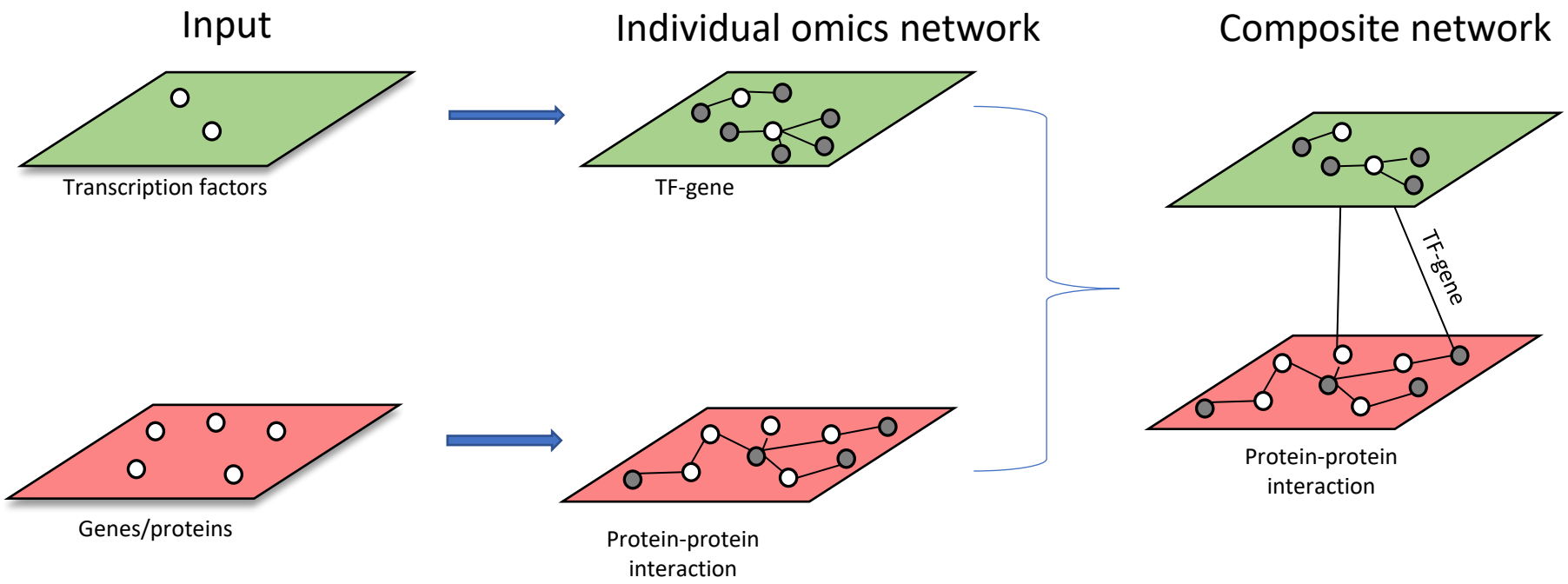
Network building for single list (2)

- If features from omics type other than gene/protein are uploaded, network building is an iterative process where primary interaction network is used to expand the composite network
- Primary interaction network is composed of seeds and its immediate interacting partners.
- Secondary interactions will query for interactions against molecules contained in the primary network, not only seeds.
  - **Add edges :** PPI as secondary or tertiary interaction will add edges to existing gene/proteins in the network by default.
  - **Add nodes and edges:** All other interaction types.

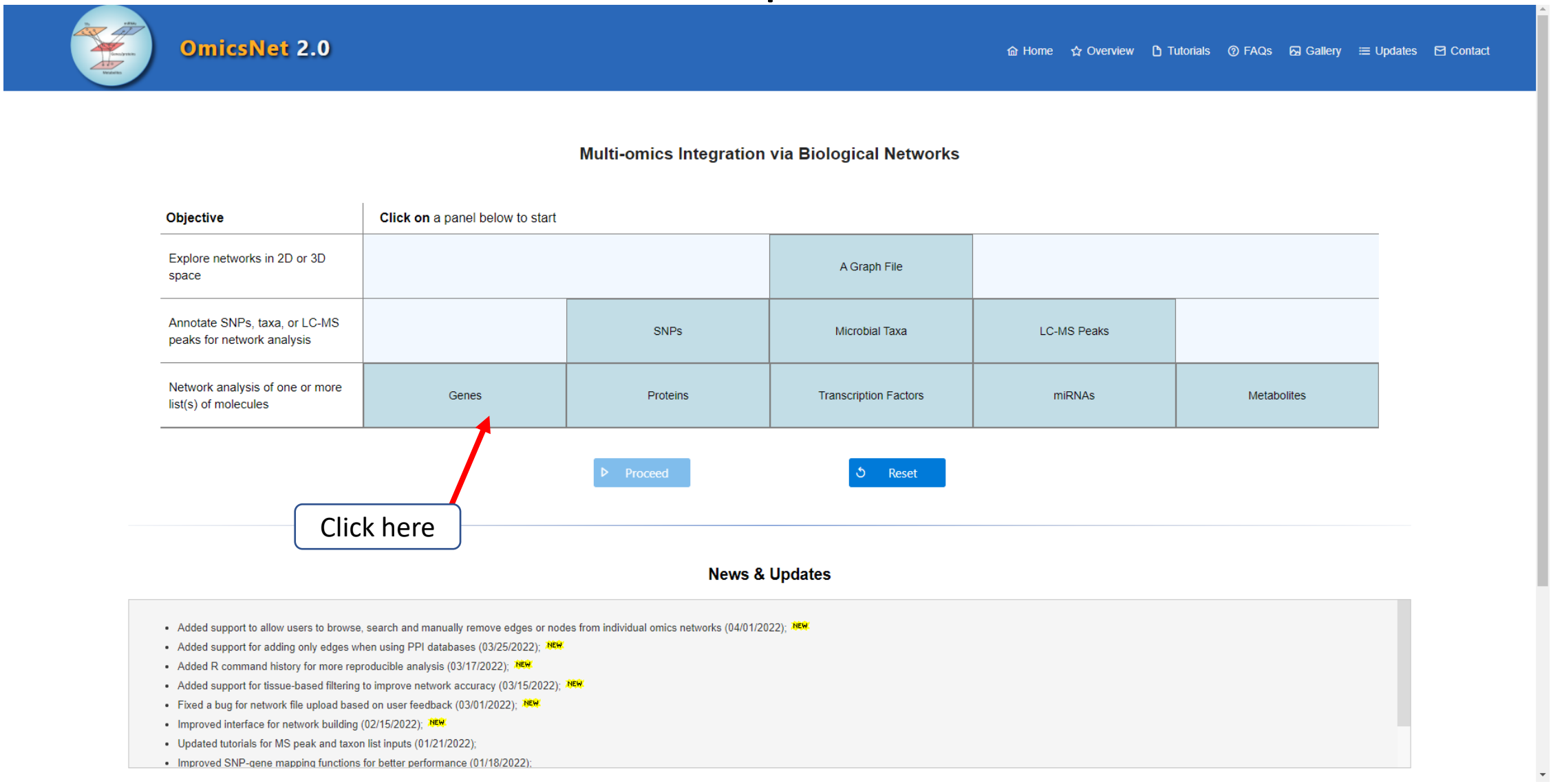


Network building for multiple lists

- Each list of molecules are used to build individual omics interaction network
- The individual omics networks are merged to form composite network through shared nodes.



Data upload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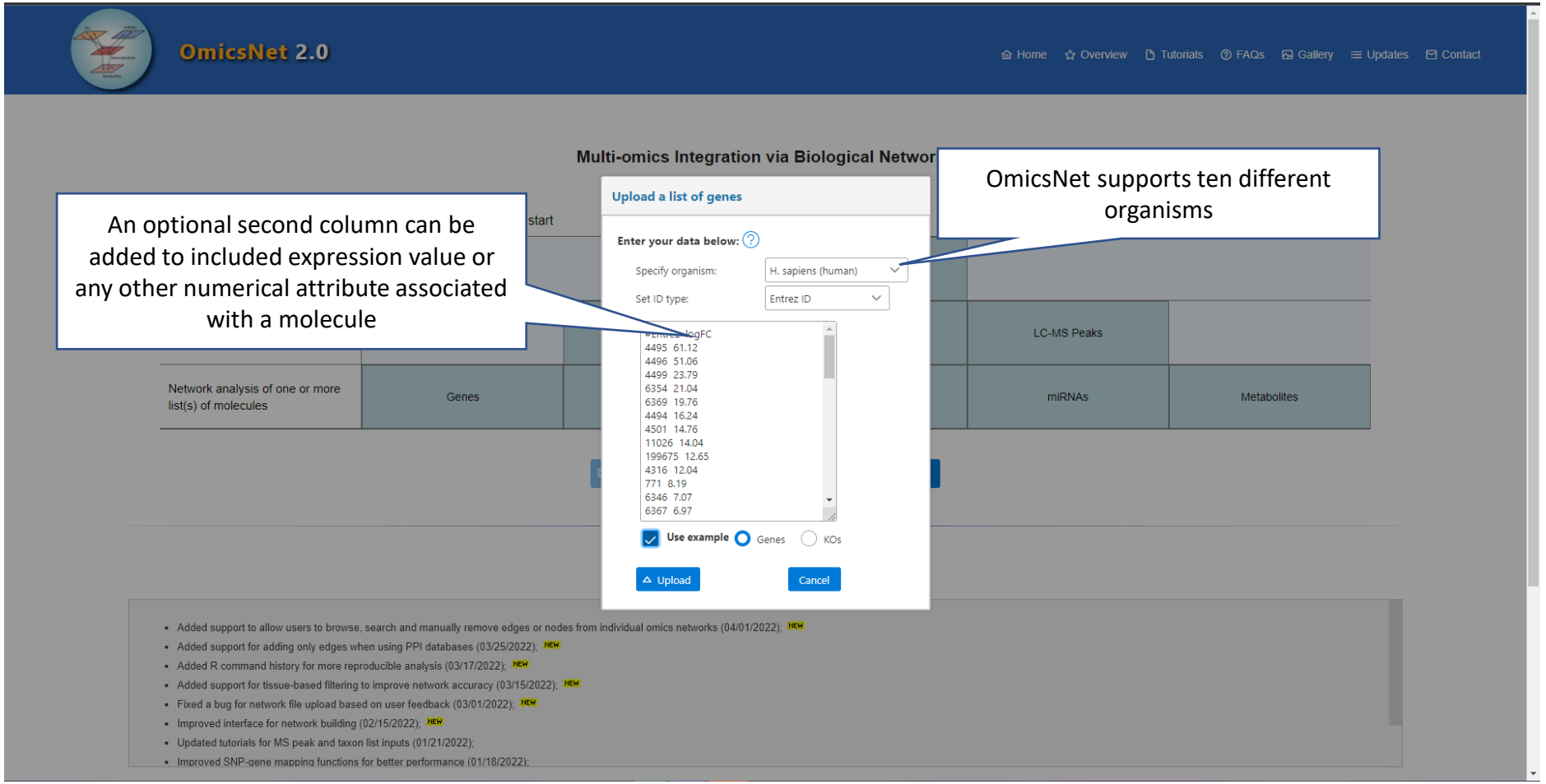
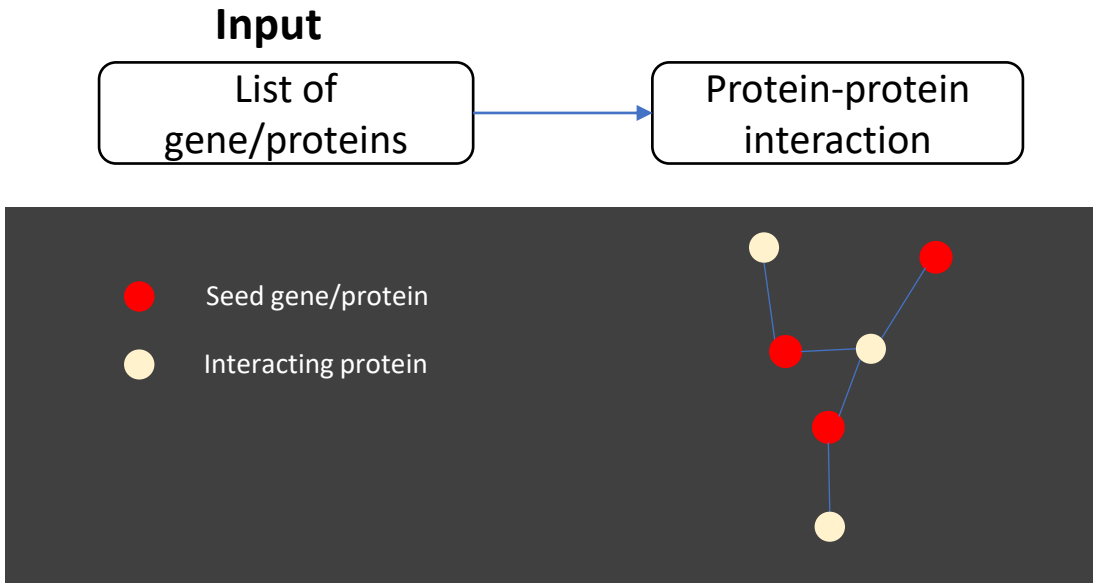
Multi-omics Integration via Biological Networks
Objective
Click on a panel below to start
Explore networks in 2D or 3D space
A Graph File
Annotate SNPs, taxa, or LC-MS peaks for network analysis
SNPs
Microbial Taxa
LC-MS Peaks
Network analysis of one or more list(s) of molecules
Genes
Proteins
Transcription Factors
miRNAs
Metabolites
Proceed
Reset
Click here
News & Updates
Added support to allow users to browse, search and manually remove edges or nodes from individual omics networks (04/01/2022);
Added support for adding only edges when using PPI databases (03/25/2022);
Added R command history for more reproducible analysis (03/17/2022);
Added support for tissue-based filtering to improve network accuracy (03/15/2022);
Fixed a bug for network file upload based on user feedback (03/01/2022);
Improved interface for network building (02/15/2022);
Updated tutorials for MS peak and taxon list inputs (01/21/2022);
Improved SNP-gene mapping functions for better performance (01/18/2022);

Data Upload(2)



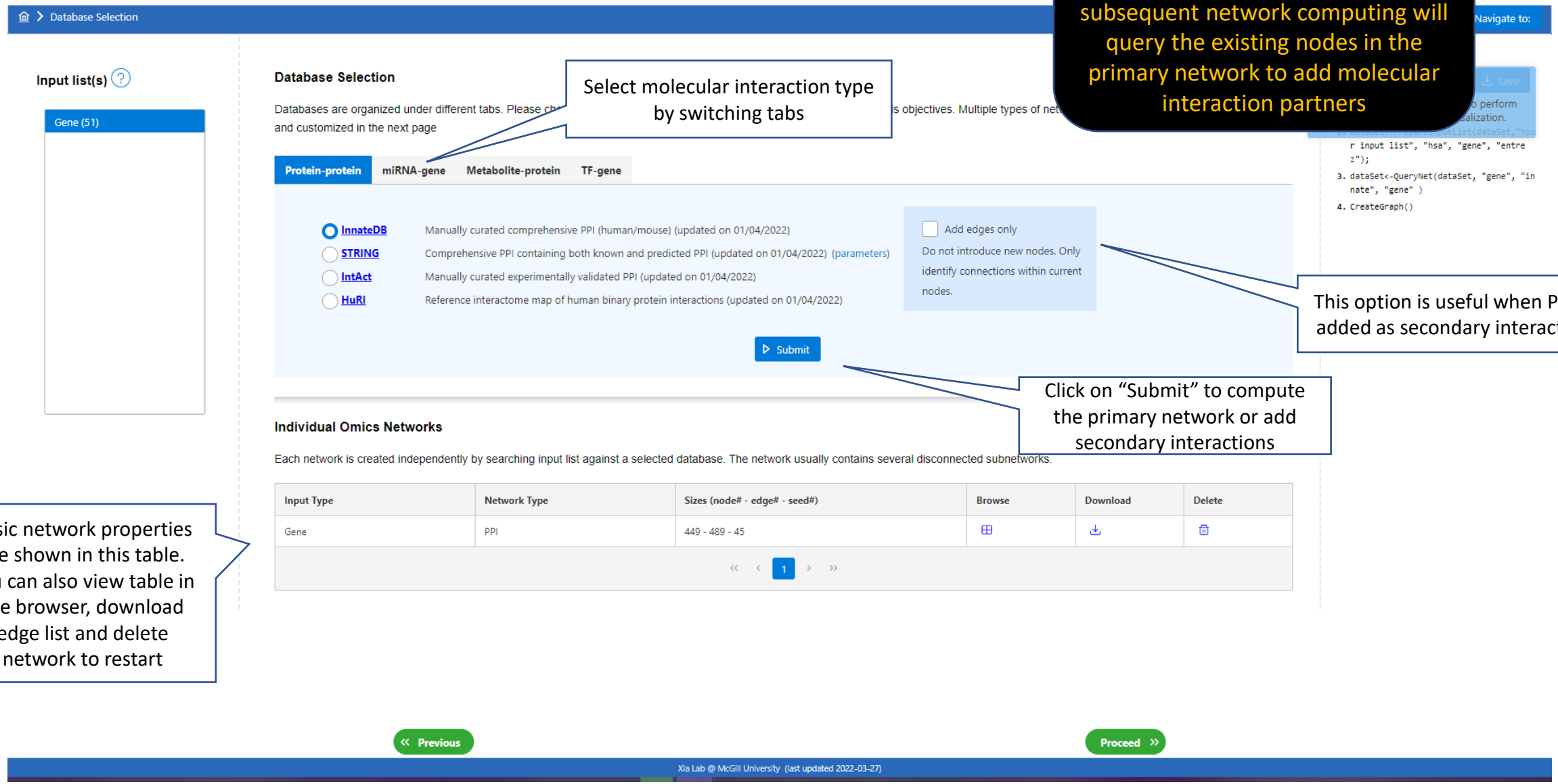
Case 1: Build PPI network from list of gene/proteins



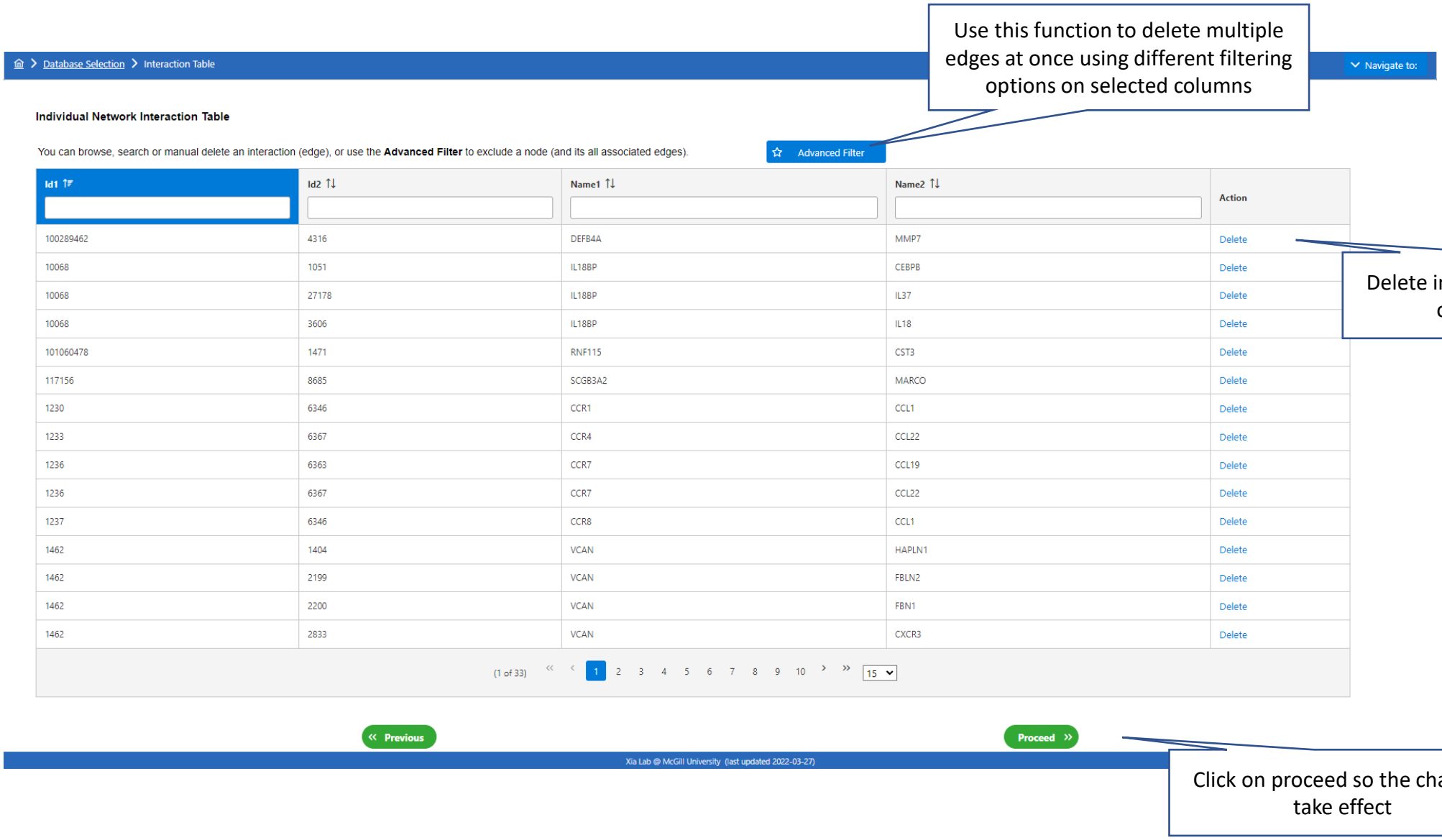
This procedure identifies which proteins directly interact with seed proteins from the molecular interaction database

Network Building

Network building for single input list is a sequential process. The first molecular interaction selected will become the primary network. The subsequent network computing will query the existing nodes in the primary network to add molecular interaction partners



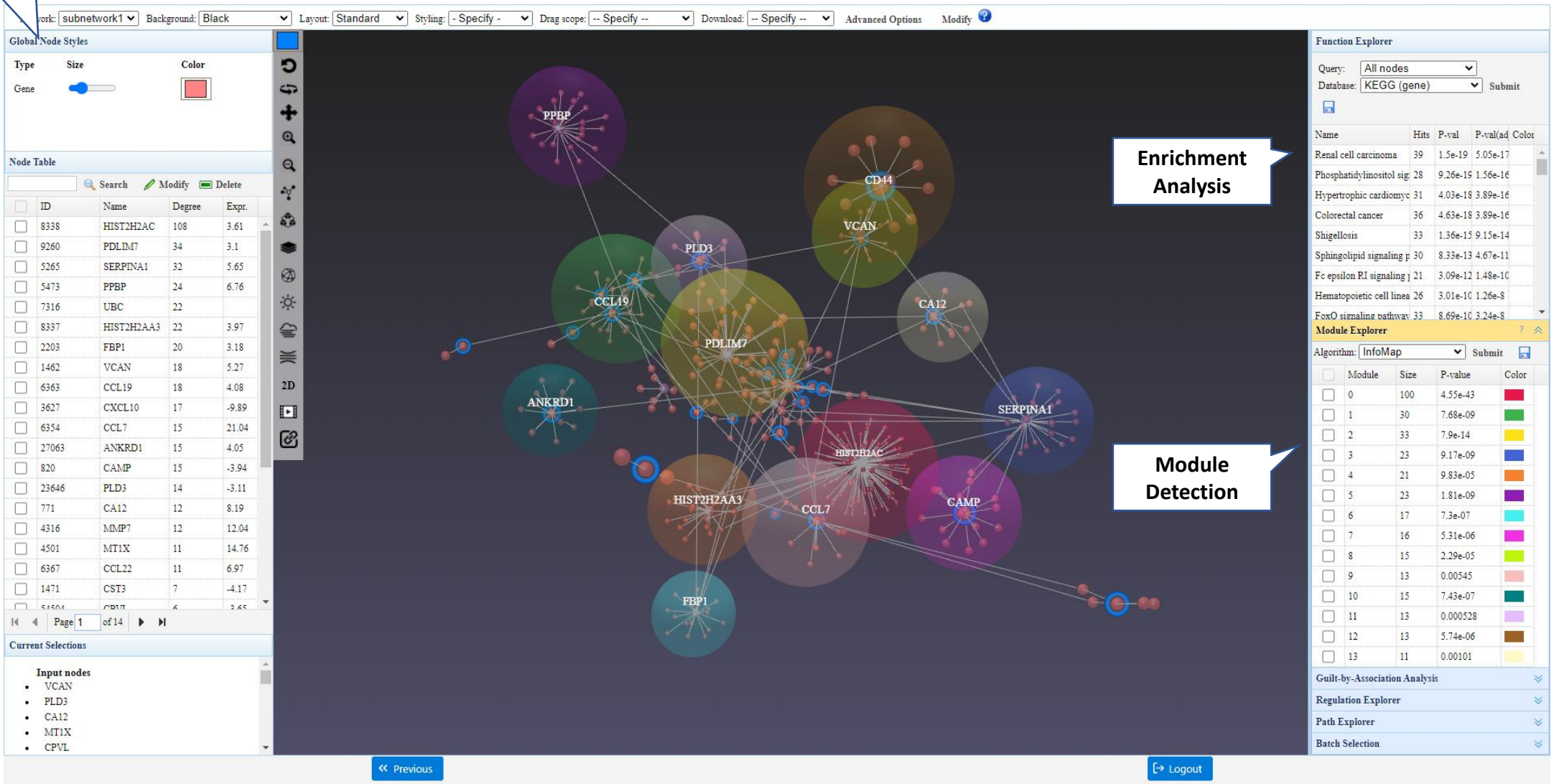
Browse View


Use this function to delete multiple edges at once using different filtering options on selected columns
Database Selection
Interaction Table
Navigate to:
Individual Network Interaction Table
You can browse, search or manual delete an interaction (edge), or use the Advanced Filter to exclude a node (and its all associated edges).
Advanced Filter
Id1
Id2
Name1
Name2
Action
100289462 4316 DEFB4A MMP7 Delete
10068 1051 IL18BP CEBPB Delete
10068 27178 IL18BP IL37 Delete
10068 3606 IL18BP IL18 Delete
101060478 1471 RNF115 CST3 Delete
117156 8685 SCGB3A2 MARCO Delete
1230 6346 CCR1 CCL1 Delete
1233 6367 CCR4 CCL22 Delete
1236 6363 CCR7 CCL19 Delete
1236 6367 CCR7 CCL22 Delete
1237 6346 CCR8 CCL1 Delete
1462 1404 VCAN HAPLN1 Delete
1462 2199 VCAN FBLN2 Delete
1462 2200 VCAN FBN1 Delete
1462 2833 VCAN CXCR3 Delete
(1 of 33) 1 2 3 4 5 6 7 8 9 10 15
Delete individual row by clicking on these buttons
Previous
Proceed
Xia Lab @ McGill University (last updated 2022-03-27)
Click on proceed so the changes take effect

Network Visualization

Node coloring and size

By default, seed nodes are highlighted by blue "halo" effect around the nodes.

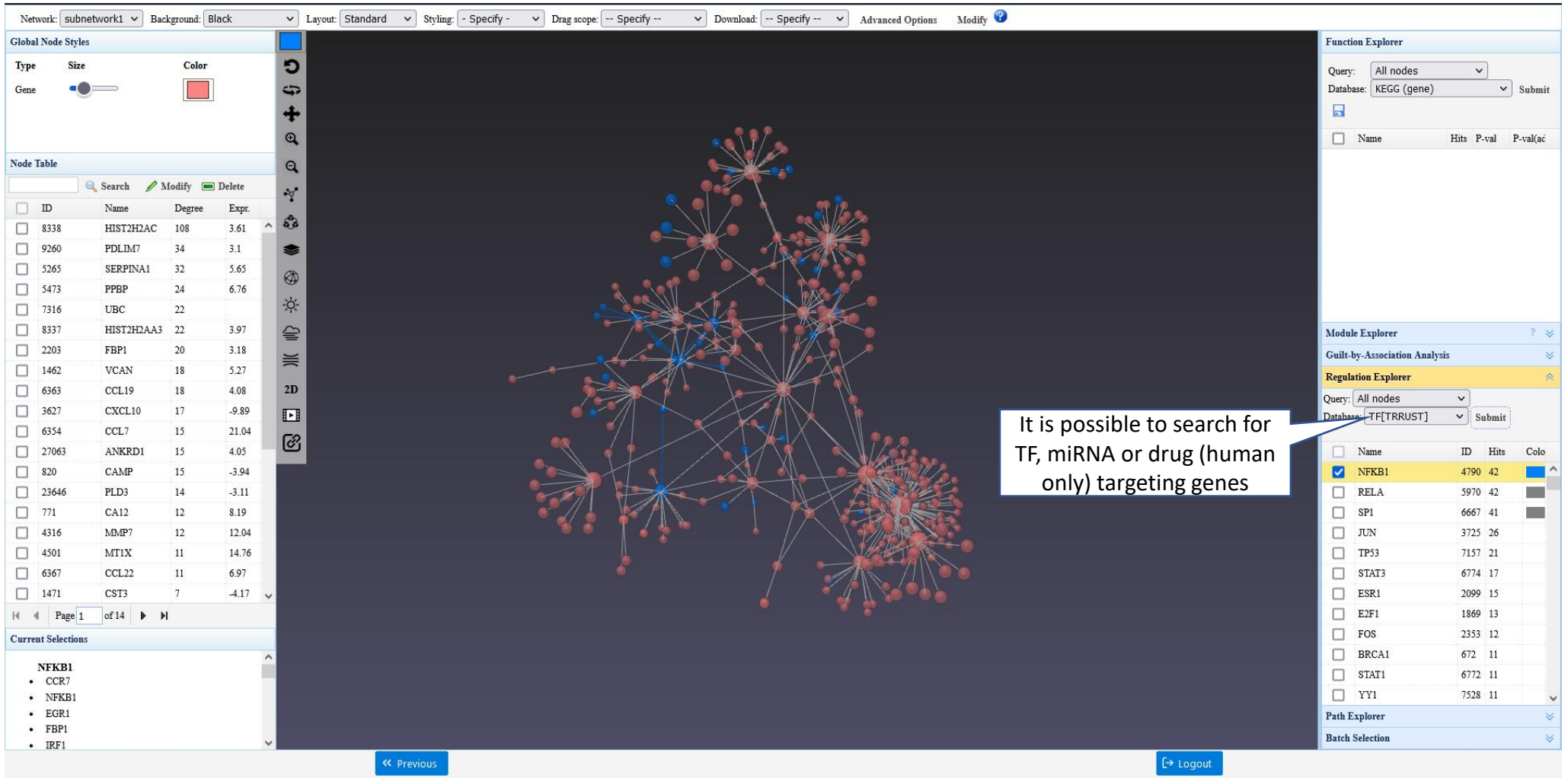


Enrichment Analysis

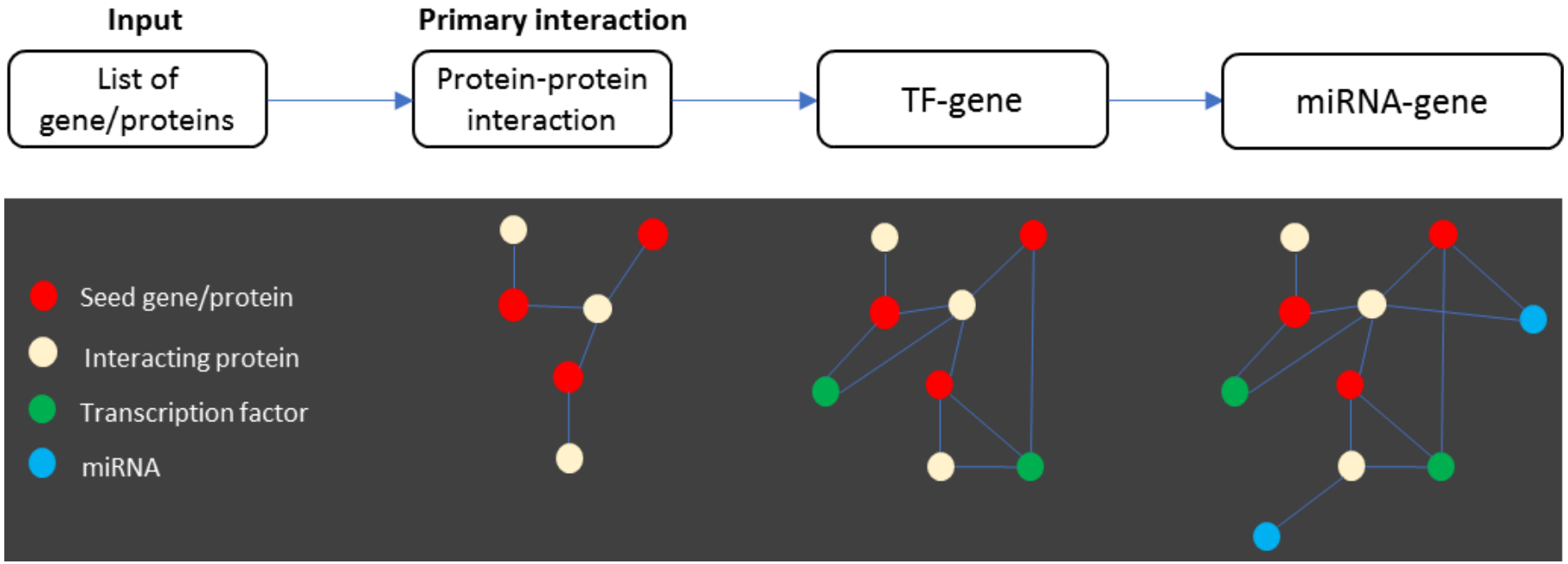
Module Detection

Module-based force-directed layout

Regulation explorer identifies gene regulators

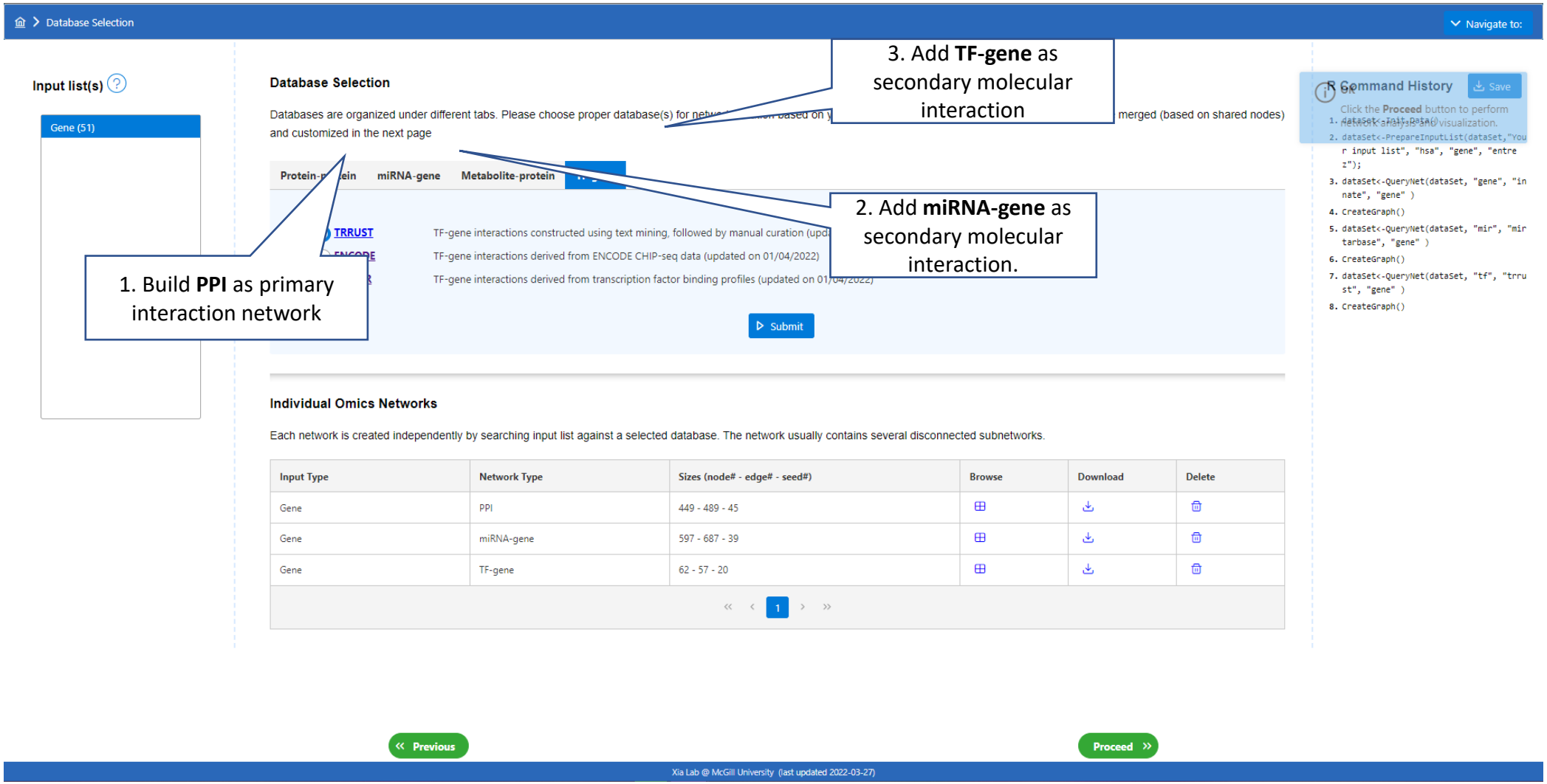


Case 2: Build regulatory network

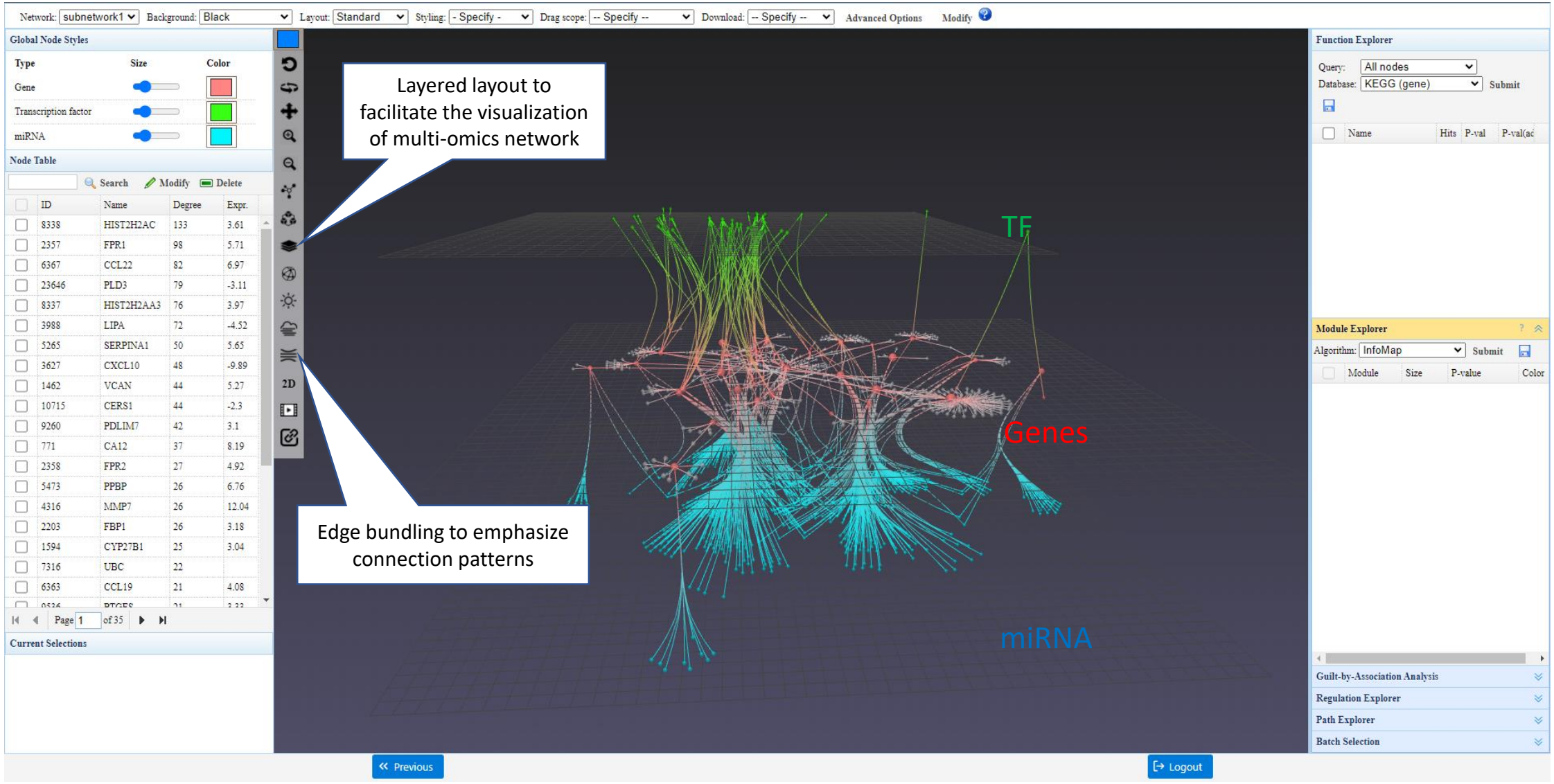


This procedure identifies which enzymes are interacting the metabolites and the PPI of these enzymes.

Network Building

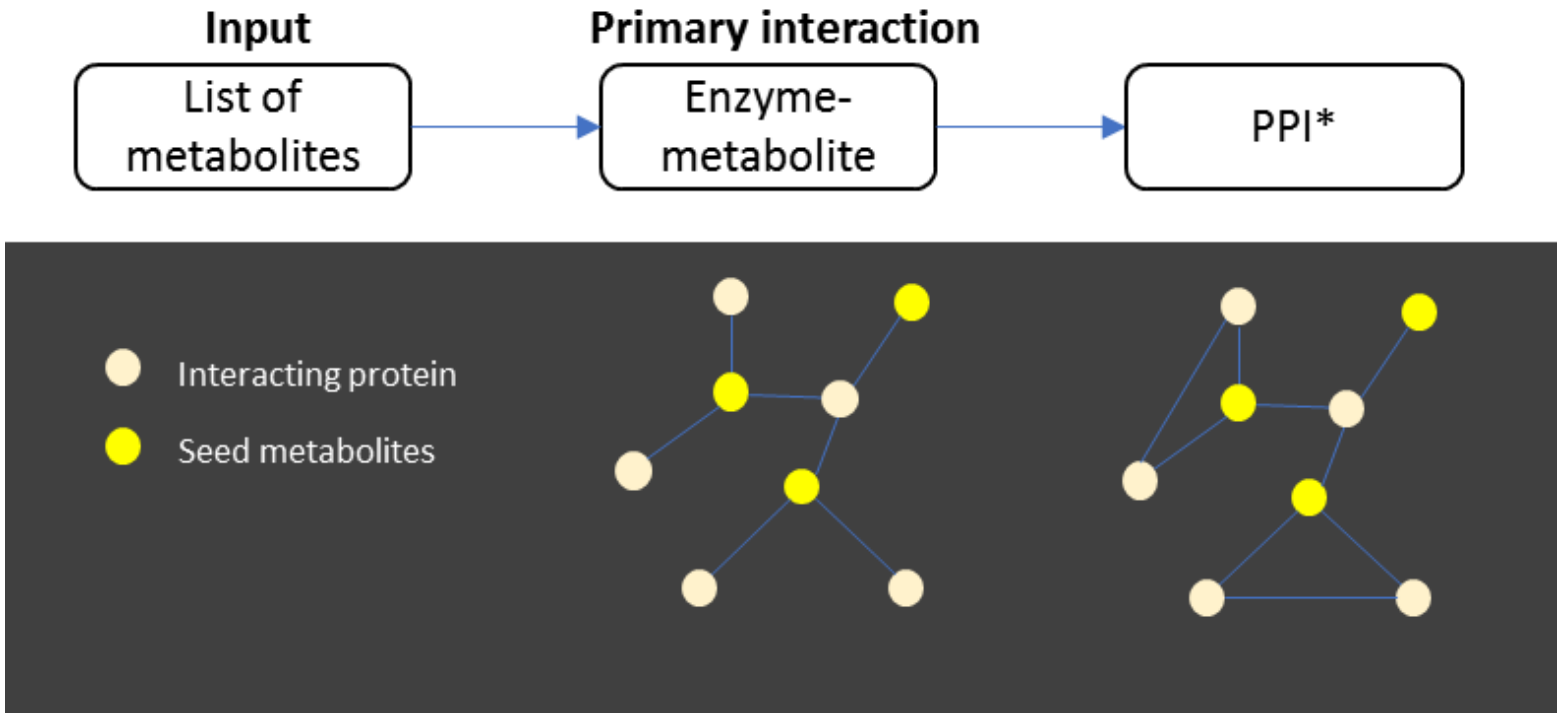


Network Visualization



Layered layout

Case 3: Build metabolite-enzyme network



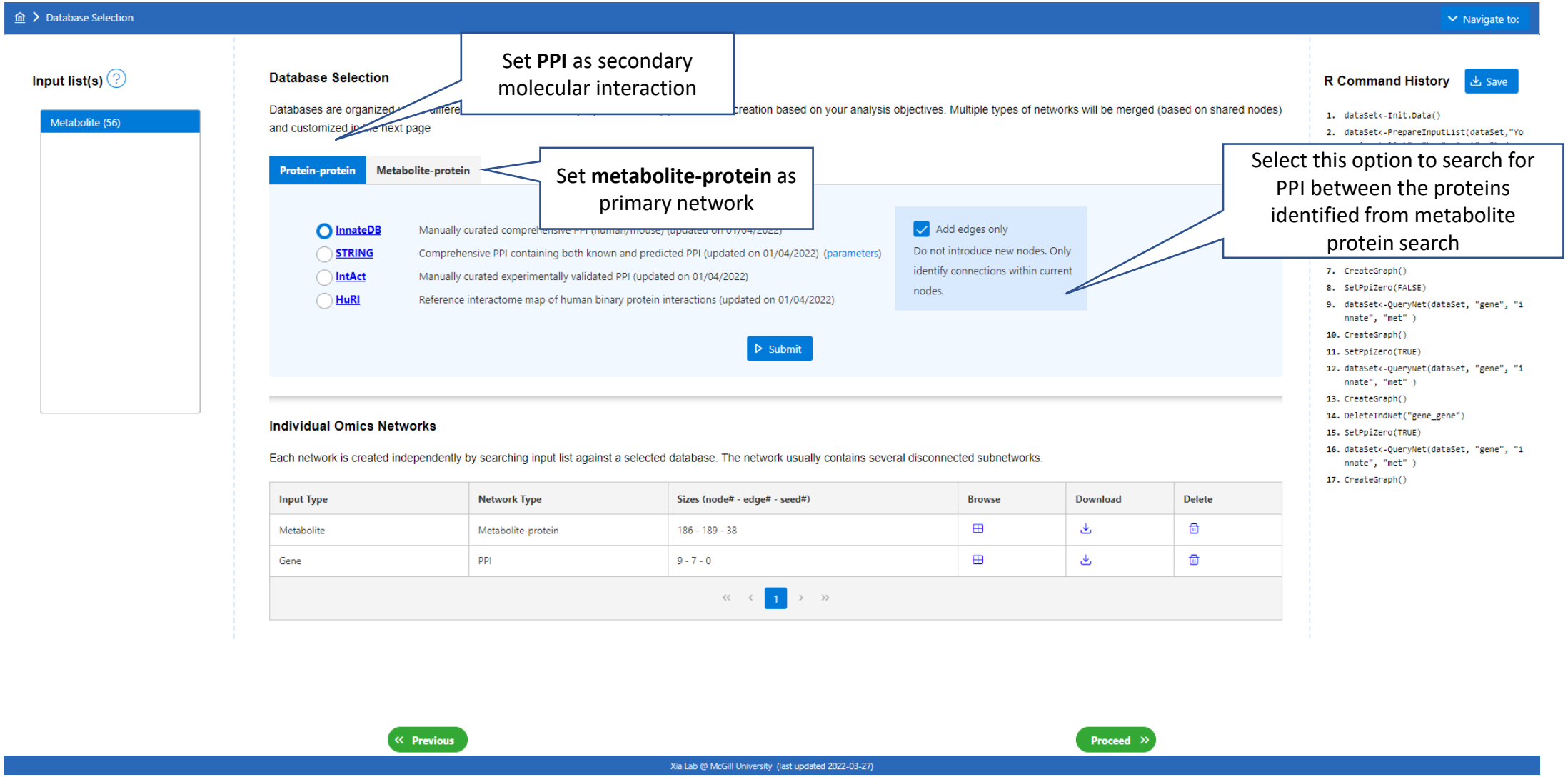
*PPI as secondary interaction **only adds connections** between existing protein/gene nodes.

This procedure identifies which enzymes are interacting the metabolites and the PPI of these enzymes.

PPI as secondary interaction

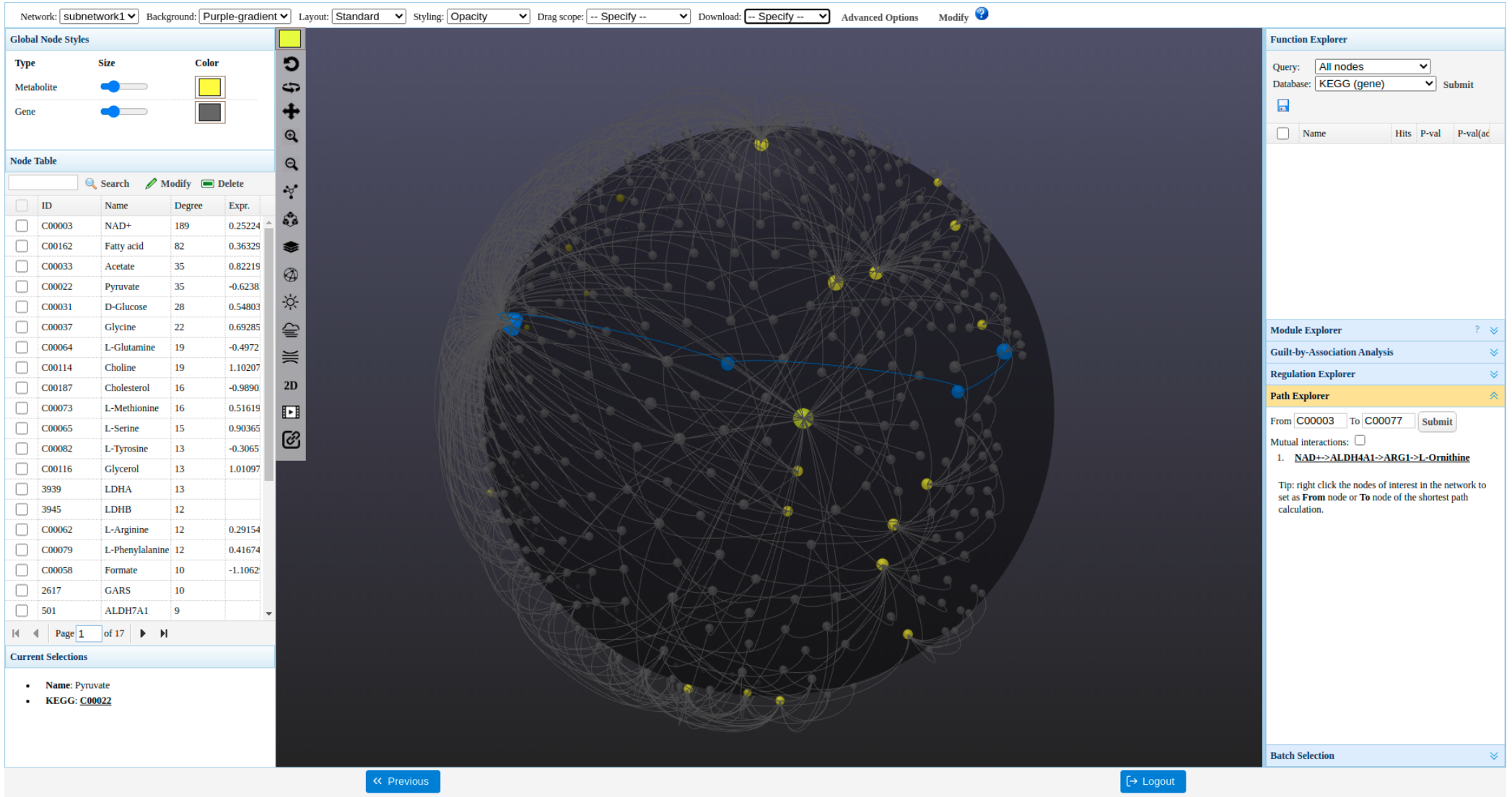
- By default, this process does not add new nodes targeting existing proteins in the network.
- Adding new nodes will dilute the focus on the molecules of interest.
- It will query for interactions between the existing protein nodes in the network, enriching the network with PPI information.

Network Building



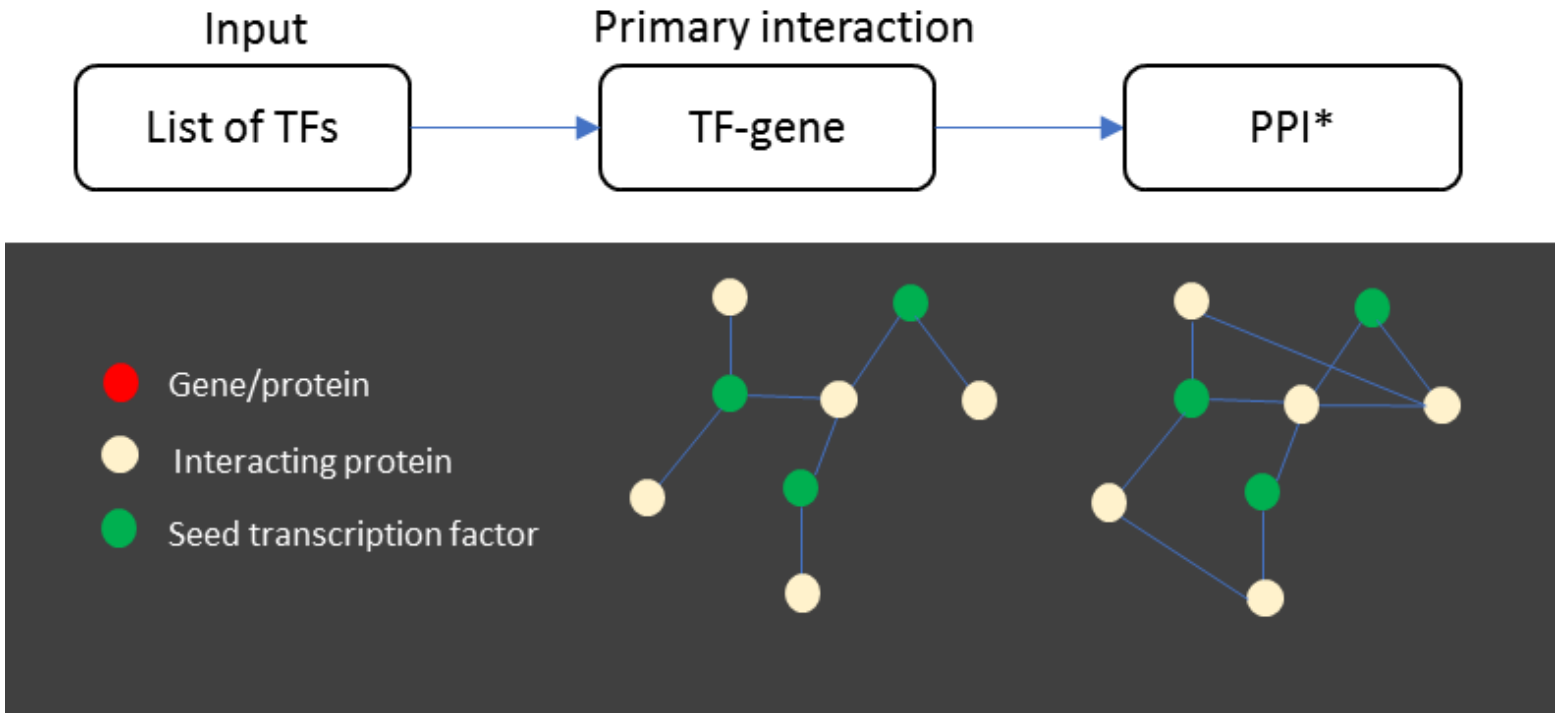
Network Visualization

Path explorer enables quick identification of the shortest path connecting two nodes within the subnetwork



Spherical layout

Case 4: Build transcriptional regulatory network



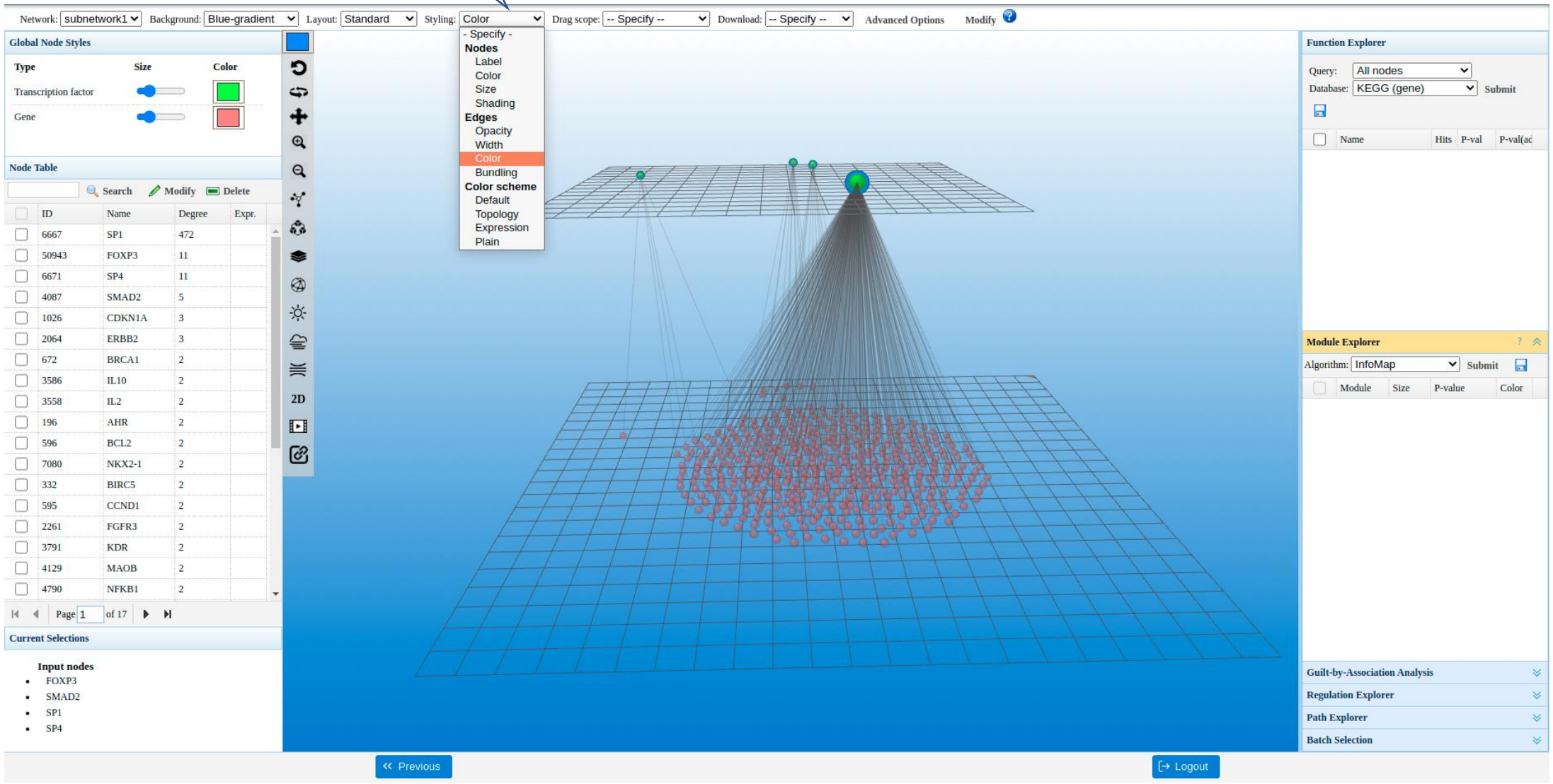
*PPI as secondary interaction only adds connections between existing protein/gene nodes.
This procedure identifies which genes are targeted by the TF and the PPI of these genes.

Change background color and select layout options here

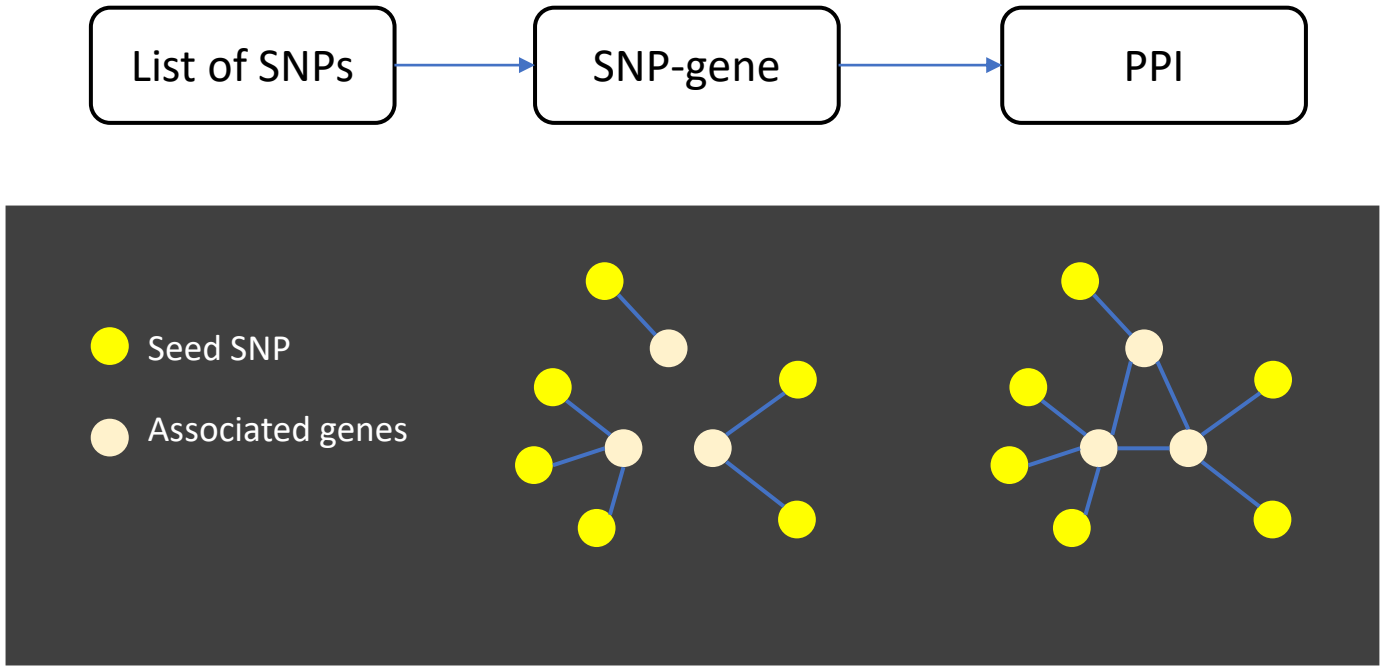
Styling options to customize nodes and edges appearance

Network Visualization

Edge occlusion is an issue that particularly affects negatively network visualization, decrease edge opacity or/and apply edge bundling to alleviate the issue.

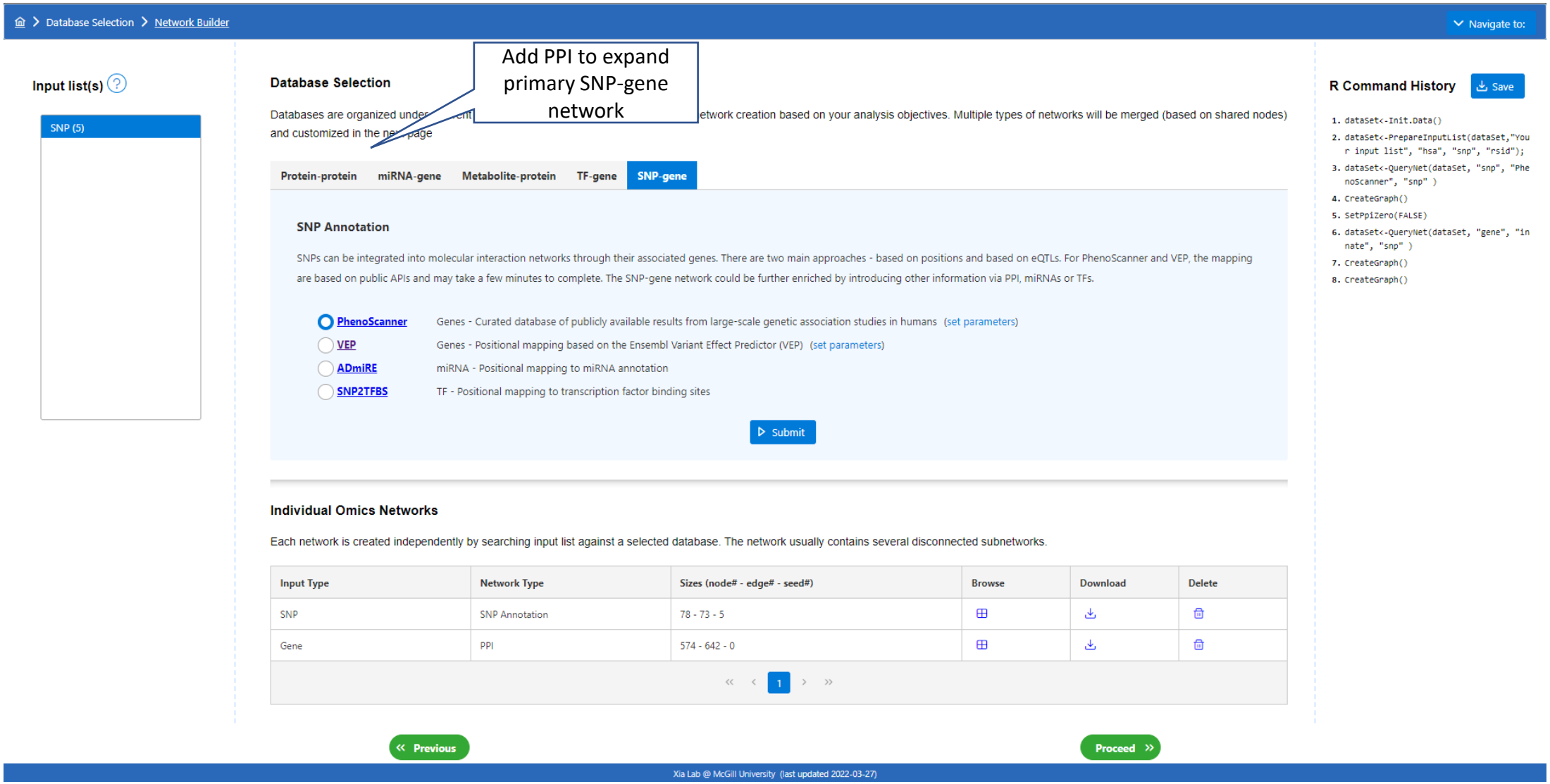


Case 5: Integrate SNPs in PPI network

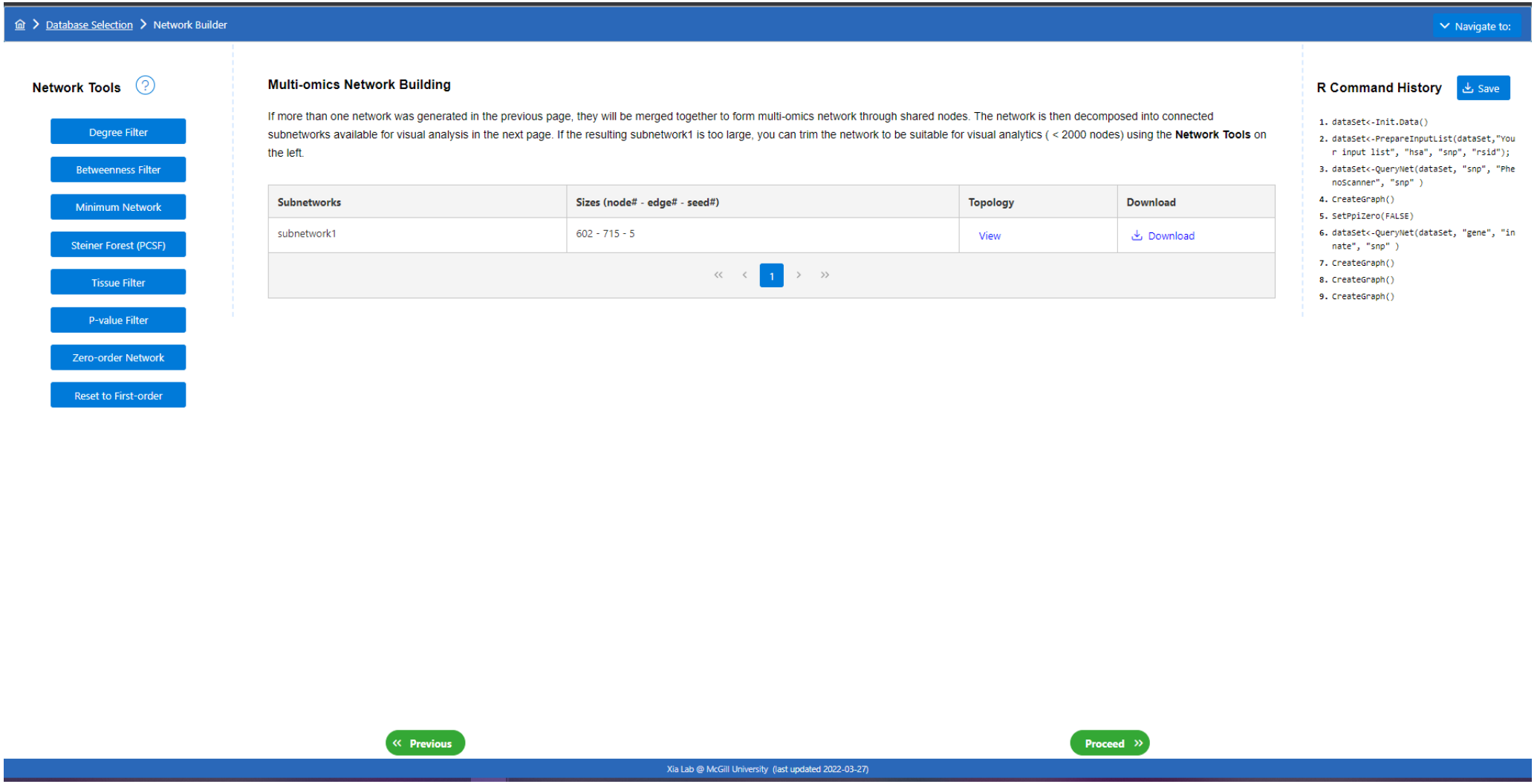


*PPI as secondary interaction only adds connections between existing protein/gene nodes.
This procedure identifies which genes associated with uploaded SNPs and link their protein products through PPI.

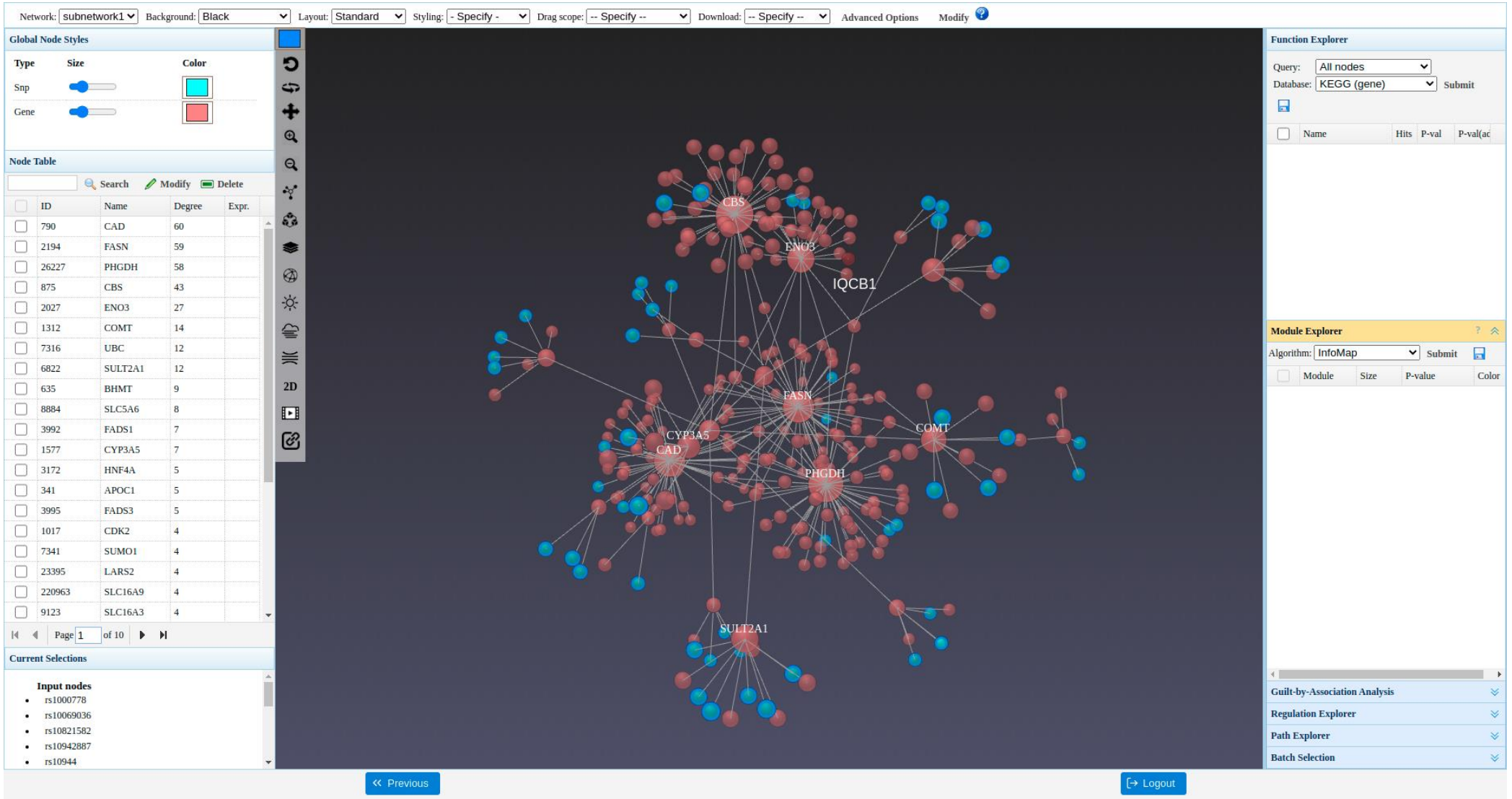
Network building



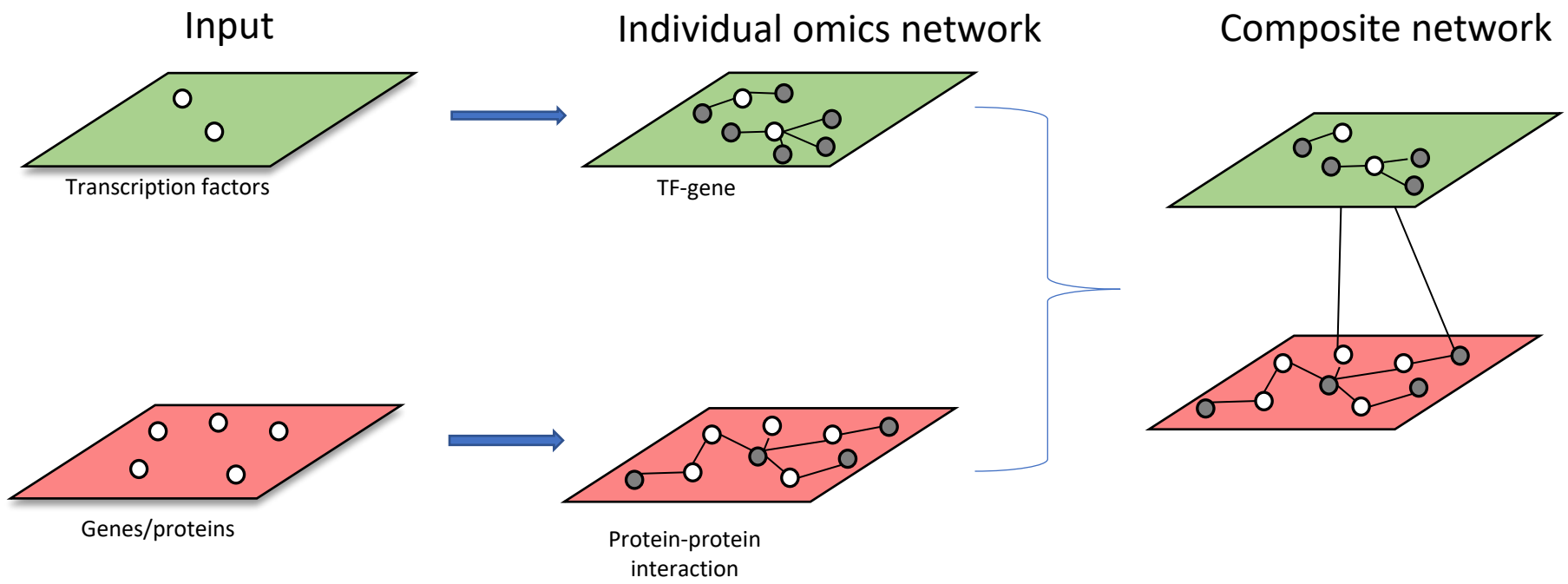
Network building (2)



Network Visualization

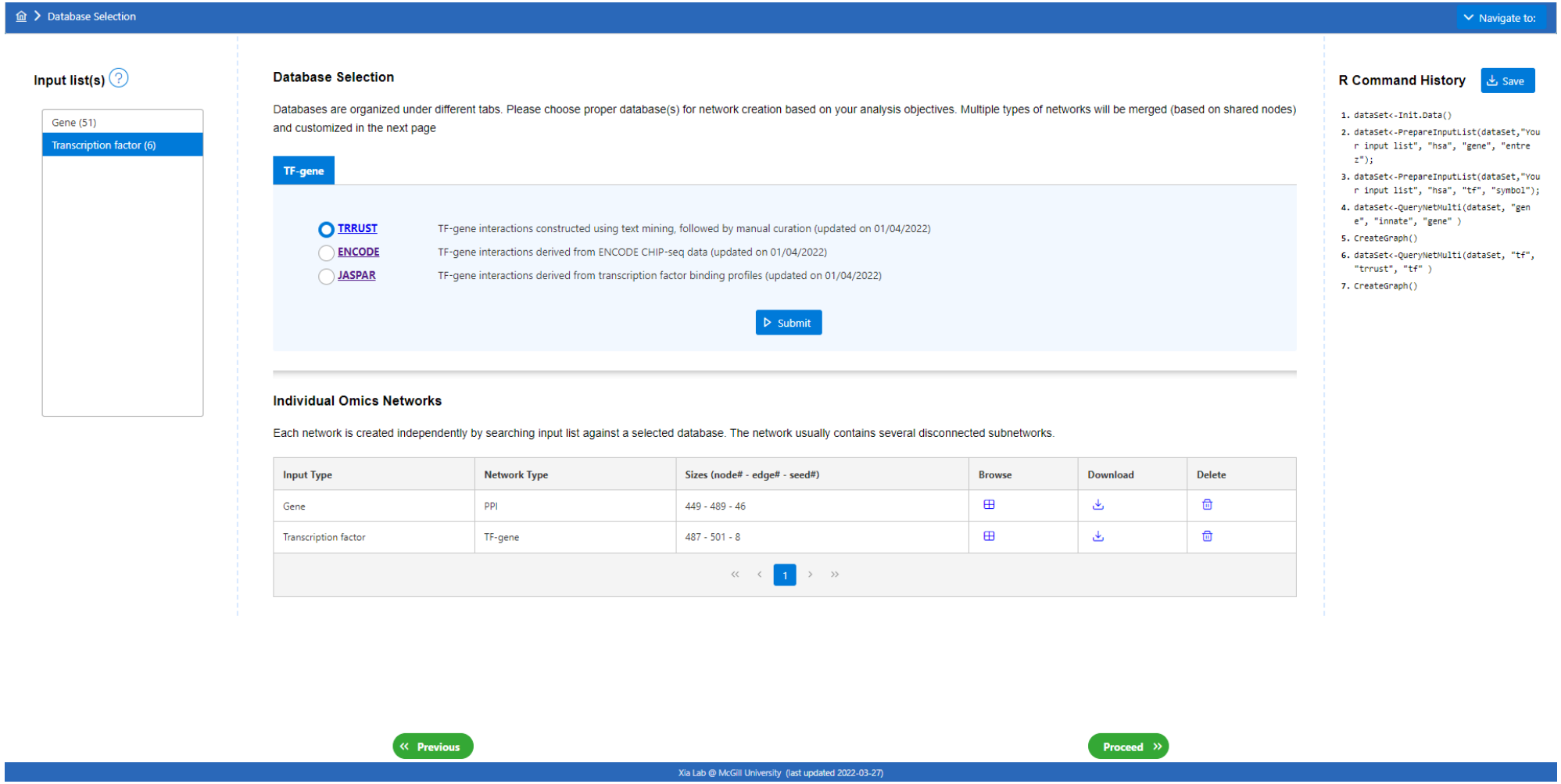


Case 6: Build transcriptional regulatory network from list of TFs and genes



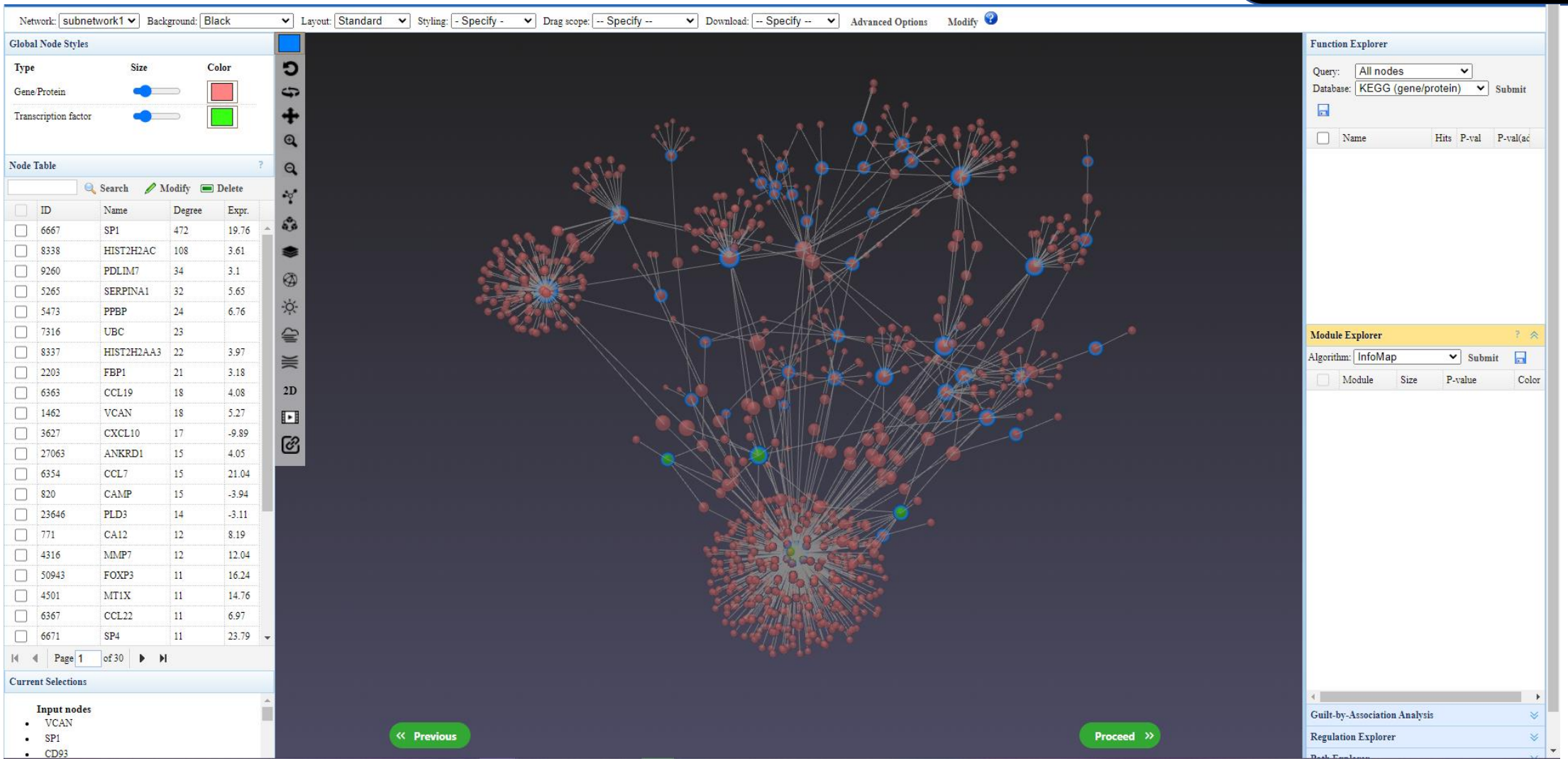
The composite network is build by merging the individual omics network through shared nodes (gene/protein node in this case)

Network Building



Network Visualization

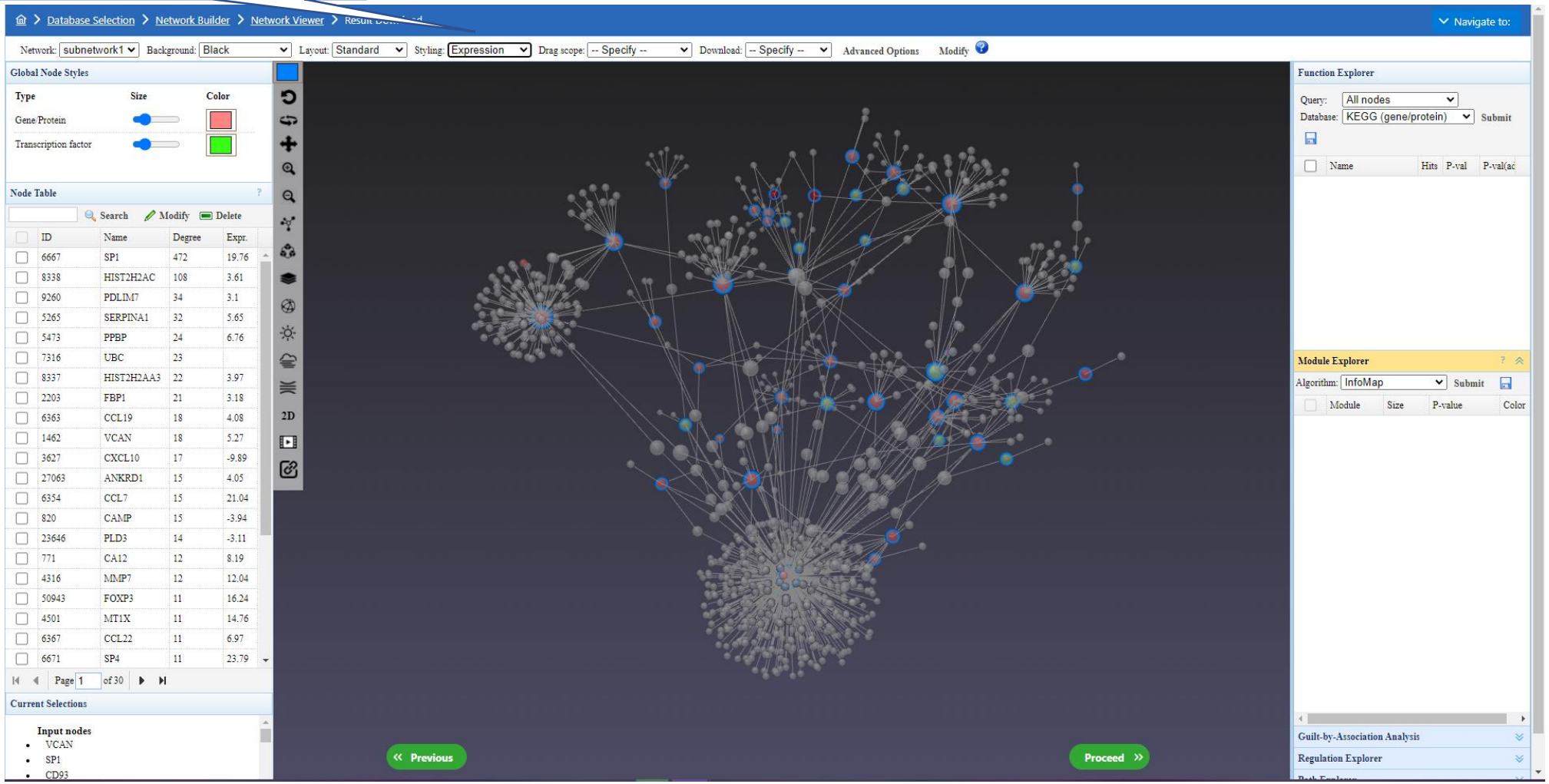
By default, nodes are colored by their omics types and seed nodes are highlighted in blue halos



Color nodes by expression values

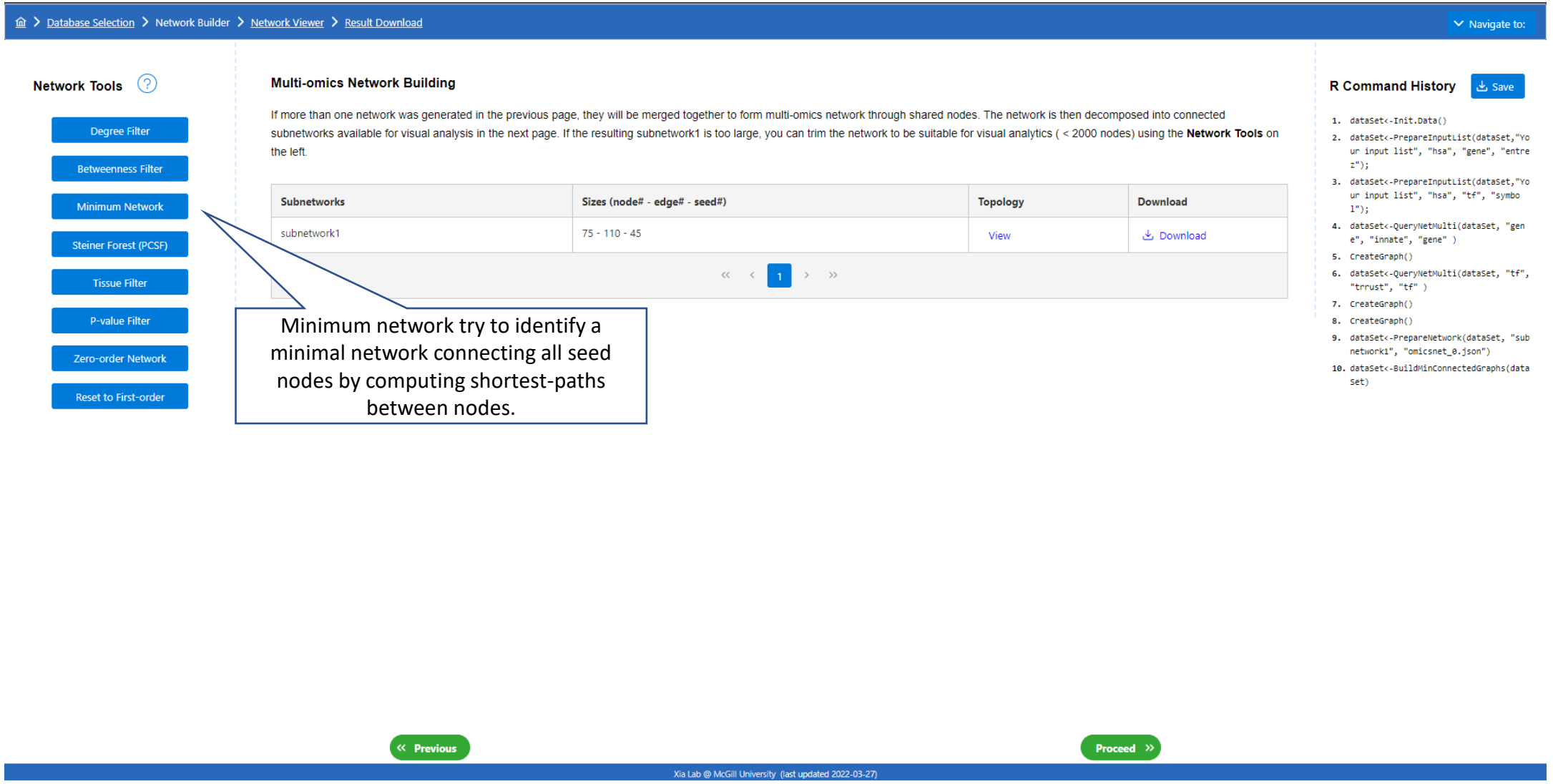
Click on this drop-down menu and select “Expression” at the bottom

Coloring by expression values facilitate the visualization of expression pattern of seed nodes.



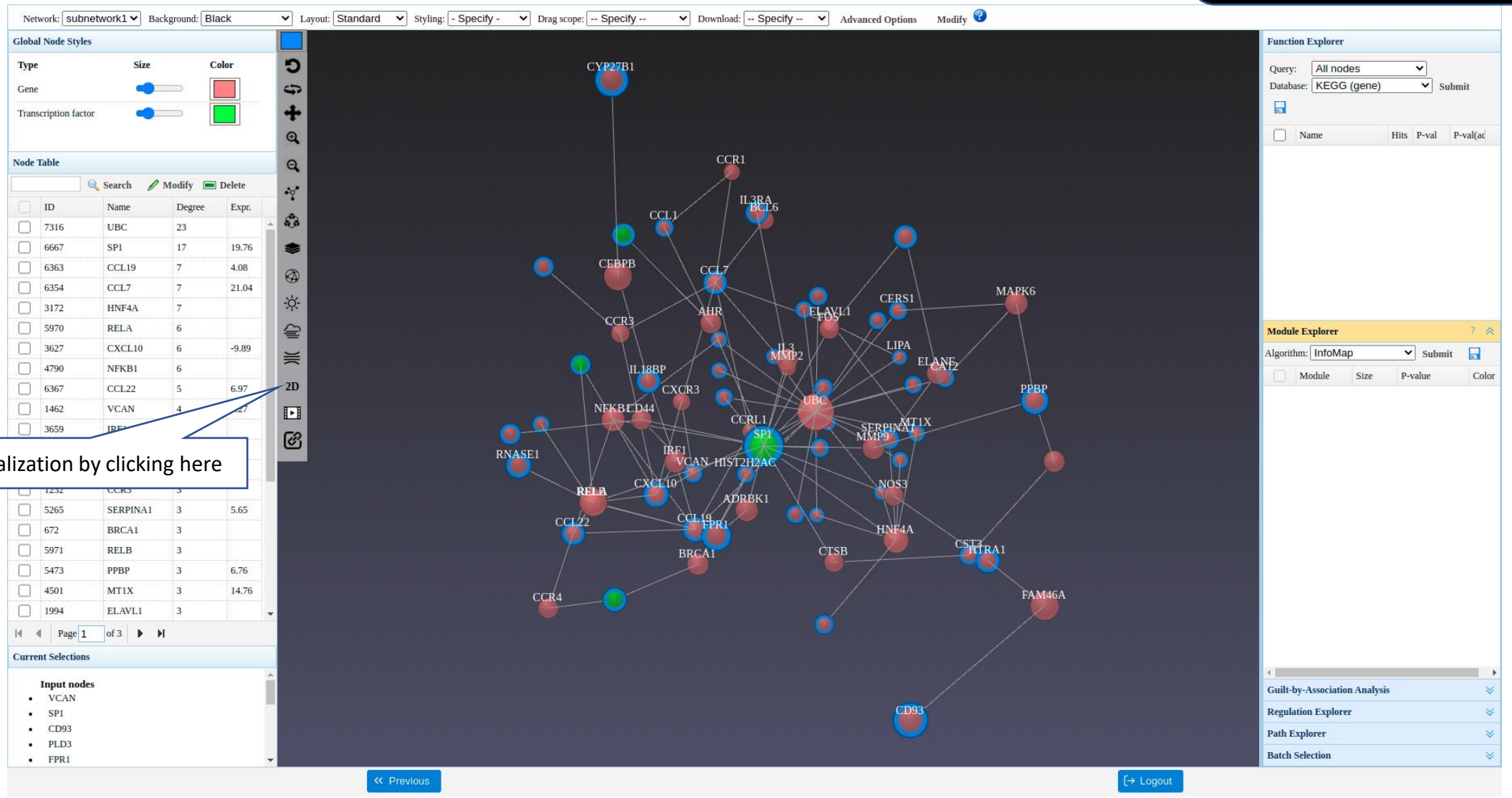
Trimming network

Use Network Tools to trim current network to reduce network size and focus on more relevant nodes.



Network visualization

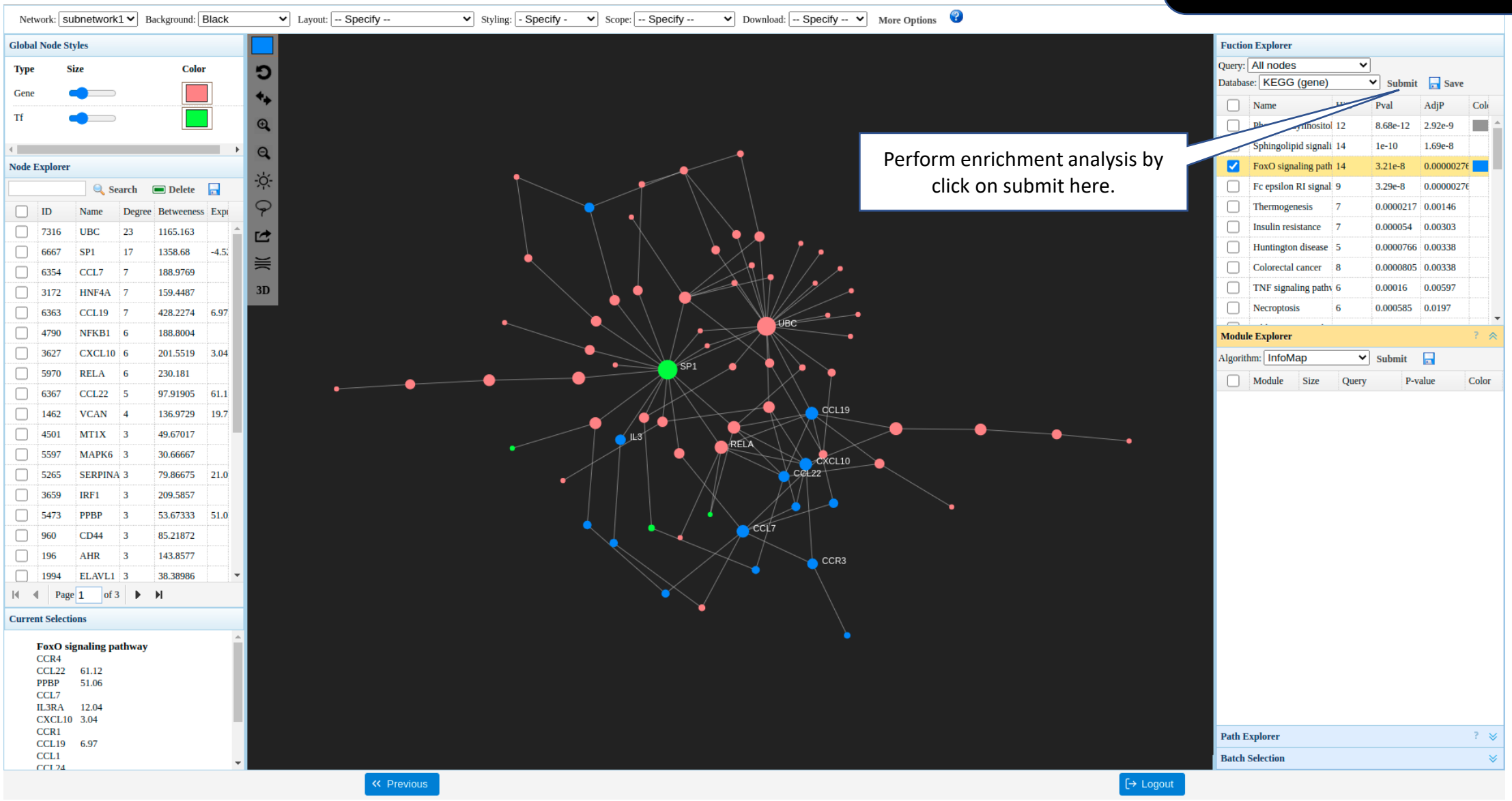
Notice that the network is composed mostly of seed nodes and has a minimum amount of interacting nodes that are necessary to form subnetwork



Try 2D visualization by clicking here

Enrichment analysis uncovers involved pathways

Selecting enriched pathways will highlight corresponding genes in the network.

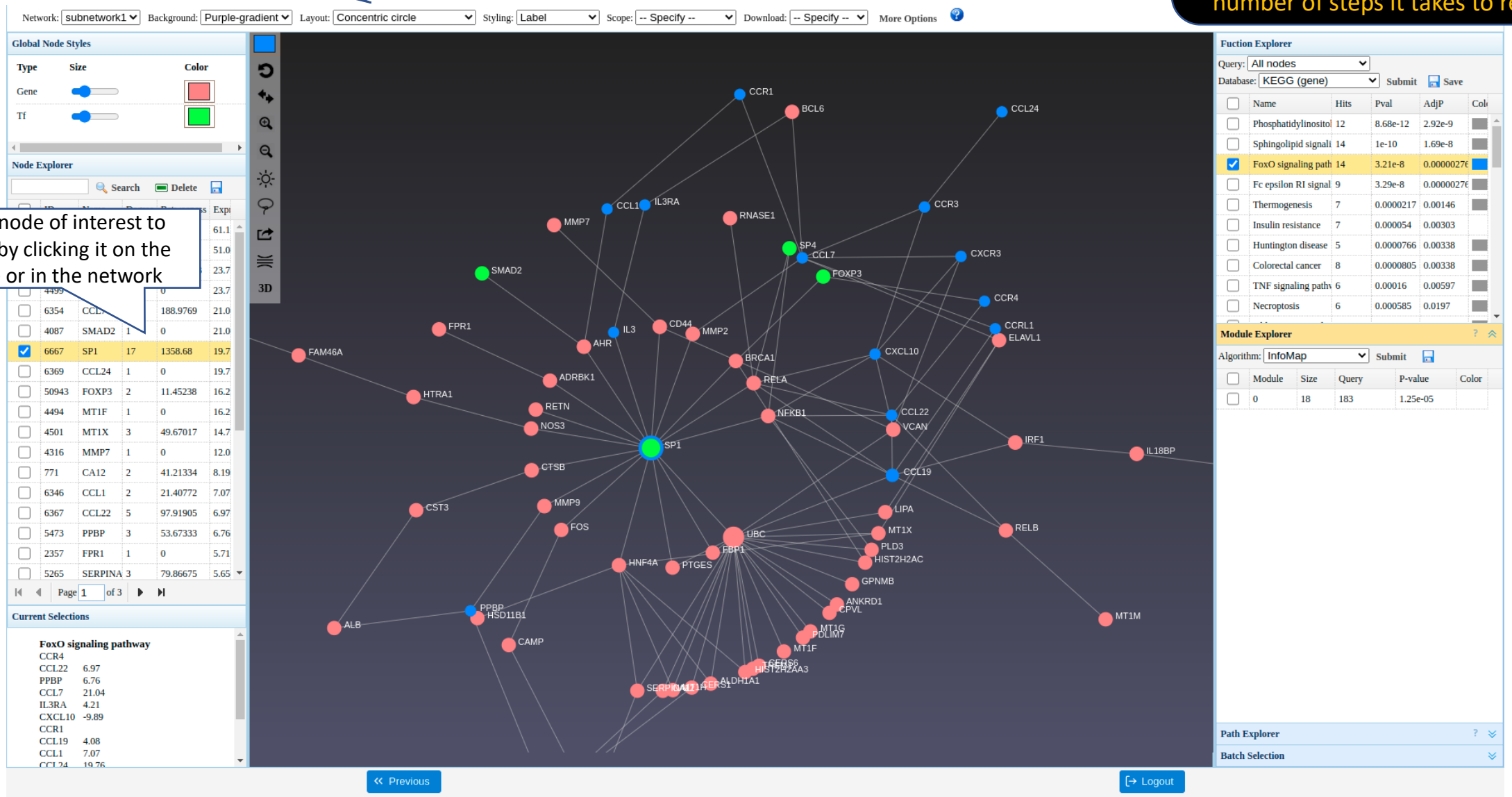


Concentric circle layout

2. Select concentric circle layout option here

Concentric circle layout reveals the connection patterns of a focal node to the rest of the network. The further a node is to the focal node, the greater number of steps it takes to reach it.

1. Select a node of interest to investigate by clicking it on the node table or in the network



The End