

mGWAS-Explorer Tutorial

-- how to perform network analysis



Understanding the network viewer

The screenshot displays a network viewer interface with the following components:

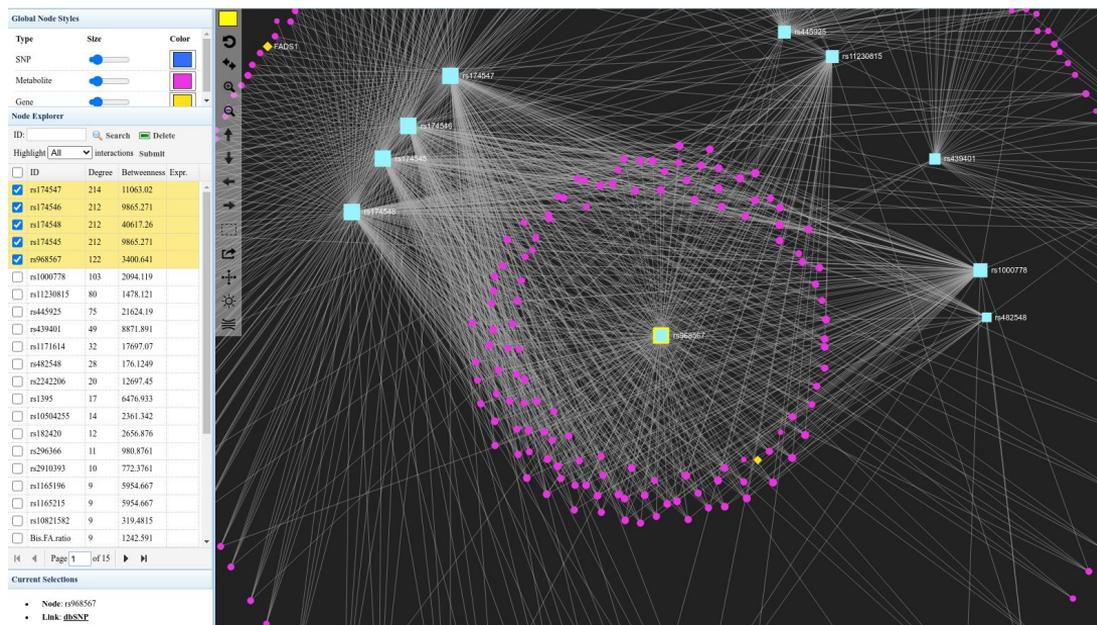
- Top menu bar:** Contains navigation and configuration options such as Network (mgwas1), Background (Gradient (light)), View (Default), Layout, Node, Edge, Scope, Download, and View Options.
- Global Node Styles:** Allows customization of node appearance by Type (SNP, Metabolite, Gene), Size, and Color.
- Node Explorer:** A table listing nodes with columns for Name, Degree, Betweenness, and Input. It includes search and delete functions.
- Function Explorer:** A table showing query results with columns for Name, Hits, Pval, and Color. The database is set to Variant Set (DisGeNET).
- Module Explorer:** A table for exploring modules with columns for Module, Size, Pval, and Color.
- Current Selections:** A list of selected nodes, including rs2820443, dbSNP, and Ensembl.

The central network visualization shows a complex graph of nodes (colored circles) and edges (colored lines) representing relationships between genetic variants and other entities. Callouts identify the Top menu bar, Node explorer, Function explorer, and Module explorer.

Node visualization and manipulation

The “Node Explorer” table on the left panel displays all the nodes in the current network, including node IDs, degree and betweenness values.

- *Node viewing*: click a node ID to view it in the network
- *Node search*: enter a node ID and click “Search” to locate it in the network
- *Node deletion*: select a node to be deleted and then click the “Delete” button



Node visualization and manipulation con't

Network: **mgwas1** Background: **Black** View: **Topology** Layout: **Concentric circle** Node: **- Specify -** Edge: **- Specify -** Scope: **Node-neighbours** Download: **-- Specify --** View Options

Global Node Styles

Type	Size	Color
SNP	<input type="range"/>	<input type="color" value="#0000FF"/>
Metabolite	<input type="range"/>	<input type="color" value="#FF0000"/>
Gene	<input type="range"/>	<input type="color" value="#FFFF00"/>

Node Explorer

ID: Search

Highlight **All** interactions Submit

<input type="checkbox"/> ID	Degree	Betweenness	Exp.
<input type="checkbox"/> rs1171614	32	17697.07	
<input type="checkbox"/> rs482548	28	176.1249	
<input type="checkbox"/> rs2242206	20	12697.45	
<input type="checkbox"/> rs1395	17	6476.933	
<input type="checkbox"/> rs10504255	14	2361.342	
<input type="checkbox"/> rs182420	12	2656.876	
<input type="checkbox"/> rs296366	11	980.8761	
<input type="checkbox"/> rs2910393	10	772.3761	
<input type="checkbox"/> rs1165196	9	5954.667	
<input type="checkbox"/> rs1165215	9	5954.667	
<input type="checkbox"/> rs10821582	9	319.4815	
<input type="checkbox"/> Bis.FA.ratio	9	1242.591	
<input type="checkbox"/> CH2.DB.ratio	9	1242.591	
<input type="checkbox"/> DB.in.FA	9	1242.591	
<input checked="" type="checkbox"/> Phosphatidylcho	9	976.2206	
<input type="checkbox"/> rs296365	8	564.6615	
<input type="checkbox"/> arachidonate (20	8	36.89805	
<input type="checkbox"/> l-arachidonoylg	8	36.89805	
<input type="checkbox"/> 4-androsten-3be	8	8067.631	
<input type="checkbox"/> Bis.DB.ratio	8	36.89805	
<input type="checkbox"/> CH2.in.FA	8	1190.269	

Page 1 of 15

Current Selections

- Node: Phosphatidylcholine diacyl C38:5

1) Select node of interest

2) Choose "Concentric circle" layout

3) Change the scope to "Node neighbours"

4) Double-click the node of interest to highlight the direct neighbours

We can easily dissect the pleiotropic and polygenicity effects of SNP-metabolite associations by performing this type of analysis.

For example, if a gene has a high degree value, it could be prioritized as potential master metabolic regulator genes.

Node visualization and manipulation con't

Network: **mgwas1** Background: **Gradient (light)** View: **Default** Layout: **-- Specify --** Node: **- Specify -** Edge: **- Specify -** Scope: **-- Specify --** Download: **-- Specify --** View Options

Global Node Styles

Type	Size	Color
SNP	<input type="range"/>	<input type="color" value="#0000FF"/>
Metabolite	<input type="range"/>	<input type="color" value="#FF00FF"/>
Gene	<input type="range"/>	<input type="color" value="#FFFF00"/>

Node Explorer

ID: Search

Highlight: **Shared** interactions

<input type="checkbox"/>	Name	Degree	Betweenness	Input
<input type="checkbox"/>	rs2925979	105	34849.21	<input checked="" type="checkbox"/>
<input type="checkbox"/>	rs635634	71	17707.77	<input checked="" type="checkbox"/>
<input type="checkbox"/>	rs2519093	67	11179.63	<input type="checkbox"/>
<input type="checkbox"/>	rs579459	56	7743.264	<input type="checkbox"/>
<input type="checkbox"/>	rs495828	55	8795.038	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Citrulline	52	9990.848	<input type="checkbox"/>
<input type="checkbox"/>	GLP2R	52	9990.848	<input type="checkbox"/>
<input type="checkbox"/>	rs651007	51	7055.618	<input type="checkbox"/>
<input type="checkbox"/>	rs649129	32	2220.576	<input type="checkbox"/>
<input checked="" type="checkbox"/>	Diabetes Mellitu	32	56263.09	<input type="checkbox"/>
<input type="checkbox"/>	rs532436	24	132.1149	<input type="checkbox"/>
<input type="checkbox"/>	rs600038	24	85.61987	<input type="checkbox"/>
<input type="checkbox"/>	PLEKHA1	19	3549.996	<input type="checkbox"/>
<input type="checkbox"/>	Age related mac	18	3259.347	<input type="checkbox"/>
<input type="checkbox"/>	rs507666	17	1711.728	<input type="checkbox"/>
<input type="checkbox"/>	rs9271770	11	3977	<input type="checkbox"/>
<input type="checkbox"/>	rs2820443	9	2312.944	<input type="checkbox"/>
<input type="checkbox"/>	ABO	9	601.4287	<input type="checkbox"/>
<input type="checkbox"/>	Body mass inde:	9	2026.139	<input type="checkbox"/>

Page 1 of 15

Current Selections

- Node: Diabetes Mellitus, Non-Insulin-Dependent

We can identify shared SNPs between metabolite (e.g., citrulline) and disease (diabetes).

Edge visualization and manipulation

Home > Upload > Network Builder > Network View

Network: **mgwas1** Background: **Gradient (light)** View: **Default** Layout: **-- Specify --** Node: **- Specify -** Edge: **Opacity** Scope: **-- Specify --** Download: **-- Specify --** View Options

Global Node Styles

Type: SNP Size: Color:

You can customize edge opacity, thickness or color.

t: -- Specify -- Node: - Specify - Edge: Opacity Scope: -- Specify -- Download: -- Specify -- View Options

Advanced View Options

Nodes scope: **All nodes** Submit
size: **Increase ++**

Edges shape: **Line** Submit
width: **Default**

Highlight other nodes: **Keep same** Submit

You can further customize nodes/edges using the advanced options.

Edge (rs78761021 - Citrulline)

P-value	PMID
1.053e-16	33414548

rs4951007 rs579451007 rs579451007 rs579451007

Double clicking an edge will show the edge evidence.

Functional enrichment analysis

- The “Function Explorer” at the top right panel supports functional enrichment analysis.
- In this case, select “All SNPs” and “Variant Set” library.
- Click the “Submit” button to perform the enrichment analysis.
- The enriched functional sets are displayed in the resulting table ranked by their P values.
- Click any functional set to view its nodes highlighted in the currently selected color.
- Extract modules by clicking the “Extract” icon in the vertical toolbar.

1) Specify “Query” type and “Database”, then click “Submit”

2) Select a color

3) Click and the SNPs belonging to this variant set will be highlighted to the selected color

4) Extract modules

SNPs in this functional set

Name	Hits	Pval	Color
Gen	9	1.54e-11	Blue
Arthritis, Gouty	9	1.55e-11	Blue
Serum albumin measurement	9	2.86e-10	Green
Phospholipid measurement	5	6.24e-10	Green
Hormone measurement	4	3.3e-9	Red
Chronic Kidney Diseases	4	9.05e-8	Red
Kidney Failure, Chronic	4	3.35e-7	Red
Uric acid measurement (proc)	5	0.0000144	Red
Polycystic kidney disease, ty	2	0.0000143	Red
Low density lipoprotein meas	4	0.0000165	Red
Serum total cholesterol meas	4	0.000023	Red
Triglycerides measurement	4	0.0000383	Red
High density lipoprotein meas	4	0.0000497	Red
Coronary Artery Disease	4	0.0000578	Red
Serum LDL cholesterol meas	3	0.000587	Red
Serum HDL cholesterol meas	3	0.000106	Red
Coronary heart disease	3	0.000533	Red
Arachidonic acid measurement	1	0.000539	Red
Acylcarnitines measurement	1	0.00162	Red
Lipase, Multispecific	1	0.00316	Red

ID	Deg
rs174547	214
rs174546	212
rs174548	212
rs174545	212
rs998567	122
rs1000778	103
rs11230815	80
rs445925	75
rs193401	49
rs1171614	32
rs482548	28
rs2342206	20
rs1395	17
rs10504255	14
rs182420	12
rs296366	11
rs2910393	10
rs1165196	9
rs1165215	9
rs10821582	9

Module detection and extraction

- Modules are tightly clustered subnetworks with more internal connections than expected based on chance.
- Select “InfoMap” algorithm and click “Submit”.
- A list of modules will be listed together with summary statistics about their sizes and P values.
- Click any module to view its nodes highlighted in the currently selected color.
- Extract modules by clicking the “Extract” icon.

2) Extract modules

1) Specify “Algorithm” type and then click “Submit”

ID	Degree	Betweenness	Expr.
rs174547	214	11063.02	
rs174546	212	9865.271	
rs174548	212	40617.26	
rs174545	212	9865.271	
rs98567	122	3400.641	
rs1000778	103	2094.119	
rs1238815	80	1478.121	

Module	Size	Pval	Color
0	228	7.68e-82	
1	74	1.75e-21	
2	35	6.9e-13	
3	17	2.2e-07	
4	15	6.62e-06	
5	9	1	

Path finder

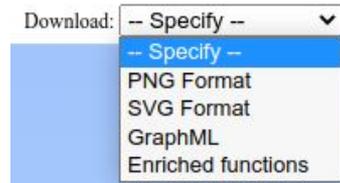
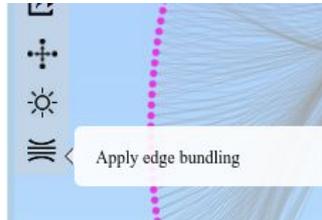
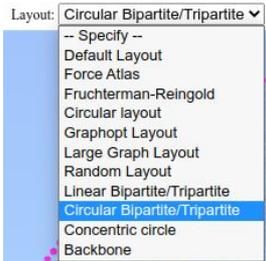
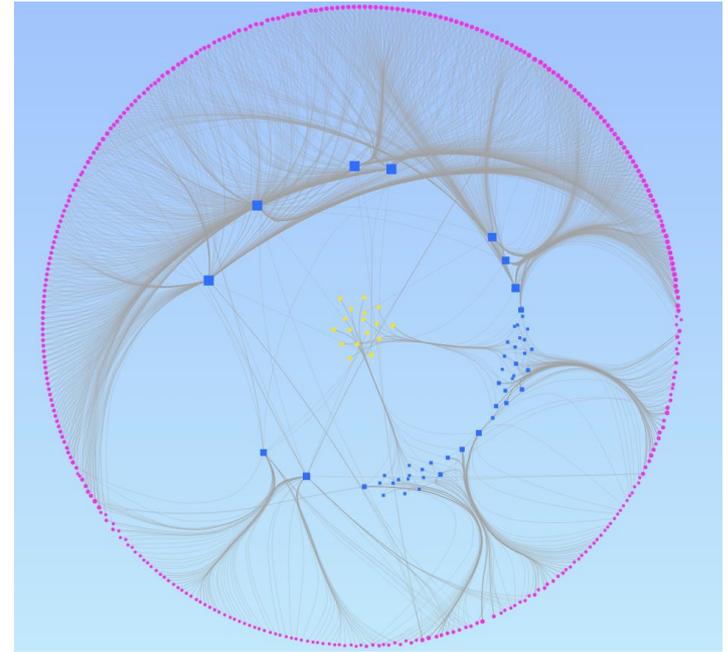
- You can use “Path Finder” to view the connections between any two nodes in the network.
- Click the “Path Finder” at the bottom right to open the sub-panel.
- You can either right click on the node of interest to select it as “Source” (e.g., malate) or “Target” (e.g., Hexanoylcarnitine), or manually enter the node IDs in “From” and “To” textbox.
- After clicking the “Submit” button, all shortest paths between these two nodes will be displayed in the resulting table.
- Click any path to highlight it in the network.

The screenshot displays the Path Finder interface. The main area shows a network graph with nodes and edges. The 'Path Finder' sub-panel is open, showing the 'From' node as 'malate' and the 'To' node as 'Hexanoylcarnitine'. The 'Submit' button is visible. Below the graph, the 'Path Finder' table lists the shortest paths between the two nodes.

Path
1. malate->rs944198->Alamine->rs445924->20a,FA,AcCoA->rs17458->Hexadecanoylcarnitine->rs1171614->Hexanoylcarnitine
2. malate->rs9882132->Alamine->rs445924->20a,FA,AcCoA->rs17458->Hexadecanoylcarnitine->rs1171614->Hexanoylcarnitine
3. malate->rs974720->Alamine->rs445924->20a,FA,AcCoA->rs17458->Hexadecanoylcarnitine->rs1171614->Hexanoylcarnitine
4. malate->rs944198->Alamine->rs445924-

Network customization & export

- To change the network layout, click the “Layout” drop-down menu at the top menu bar. Select “Circular Bipartite/Tripartite” layout to rearrange the nodes in a three-layered layout.
- To reduce edge crossing in the network, click the “Apply edge bundling” icon at the vertical toolbar
- To export the network, users can simply click the option under the “Download” drop-down menu at the top menu bar.



==The End==