

mGWAS-Explorer Tutorial

-- user list upload



Computer and Browser Requirements

- A personal computer with an Internet connection
- An up-to-date web browser that supports HTML5 with JavaScript enabled, such as Google Chrome (v50+), Firefox (3.0+), and Internet Explorer (9.0+)
- We recommend a ≥ 2 GHz CPU, 4 GB physical RAM with at least 2 GB free and a minimum of a 15-inch screen with a screen resolution of 1,280 × 800 or higher
- A mouse with scrolling support is required for network visualization

Starting up

- Go to the mGWAS-Explorer homepage (www.mgwas.ca).
- There are five modules corresponding to five different input types.
- For SNP list input, click the “SNPs” button to enter the data upload page.

mGWAS-Explorer -- linking SNPs, genes, metabolites and diseases for functional insights

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Click an icon below to start

- SNPs**
 - Connect SNPs to genes, metabolites or diseases
- Metabolites**
 - Connect metabolites to SNPs, genes or diseases
- Genes**
 - Connect genes to SNPs, metabolites or diseases
- Search**
 - Search significant SNP-metabolite associations within 65 mGWAS
- Browse**
 - Browse individual mGWAS in Manhattan plot or network

Comprehensive Library
Comprehensive collection and deep annotation of results from [65 mGWAS publications](#). Support for searching a single item, exploring individual studies, and uploading a list.
Integrating with protein-protein interaction, SNP to disease, and metabolite to gene associations based on well-established databases.

Interactive Visualization
Users can easily browse and analyze SNP-based, gene-based, and metabolite-based networks in a systems-biology context.
Cross-phenotype association analysis can be performed to dissect shared genetic architecture between metabolism and disease from the SNP module.

Functional Profiling
Users can perform various functional analysis including SNP set enrichment analysis, gene set enrichment analysis, and metabolite set enrichment analysis.
Other features including topology analysis, searching different paths connecting SNPs, genes, metabolites, and diseases for hypothesis generation.

News & Updates

- Added support for metabolite-disease and gene-disease network (05/23/2022). [NEW](#)
- Redesigned home page (05/20/2022). [NEW](#)
- Updated tutorials and FAQs (05/13/2022). [NEW](#)
- Fixed issues with table browsing and table statistics (05/10/2022). [NEW](#)

Data upload

Note 1: click on “Set parameters” will show the dialog window for SNP annotation. → slide 5

- Users can specify the type of biofluid, population, ID type, SNP annotation, and the network type
- Enter a list of SNPs with one entry per line
- In this case, we use the example dataset by clicking the “Try example” button
- Click the “Submit” button to upload and then “Proceed” button

Enter a list of SNPs below:

Biofluid	<input type="text" value="Unspecified"/>
Population	<input type="text" value="Unspecified"/>
ID type	<input type="text" value="rsID"/>
Network type	<input checked="" type="checkbox"/> SNP-Metabolite <small>Statistical associations based on curated mGWAS datasets</small>
	<input type="checkbox"/> SNP-Gene <small>Set parameters</small>
	<input type="checkbox"/> SNP-Disease <small>Curated and literature-based associations from DisGeNET</small>

SNP list
(one entry per line)

Note 2: the “Genes” and “Metabolites” modules have the similar interface in the upload page.

Data upload - SNP annotation

- We provide four options for SNP annotations.
- **HaploReg** support LD proxy search.
- For **VEP**, users can either choose a specific distance or the nearest few genes.
- Optionally, users can include PPI.

Enter a list of SNPs below:

Biofluid: Unspecified

Population: Unspecified

ID type: rsID

Network type:
 SNP-Metabolite
 SNP-Gene
 SNP-Disease

SNP list
(one entry per line)

```
rs35731912
rs13381043
rs10877786
rs2080811
rs7152677
rs12796811
rs114093749
rs2059266
rs911360
rs75558547
rs10091098
rs6970487
rs12610495
rs144582715
rs117438562
rs56122507
```

Submit

SNP to gene annotation

HaploReg: LD proxies None r^2 0.8

VEP: genes within 5 kb

VEP: top 1 nearest gene(s) within 50kb

PPI: include direct interactions [PPI Databases](#)

Submit

Network building

- The table results and network summaries will display on the page.
- Users can download/browse tables by clicking the associated icon.
- The networks will be available for visual analytics in the next step.

The screenshot shows the 'Network Builder' interface. At the top, there is a breadcrumb trail: Home > Upload > Network Builder. The main content is divided into two sections: 'Tables' and 'Networks'. The 'Tables' section contains a table with four rows, each representing a different data source with download and browse icons. The 'Networks' section contains a table with two rows, each representing a network with view icons. On the right side, there is a 'Network Tools' panel with several filter buttons. At the bottom, there are 'Previous' and 'Proceed' navigation buttons.

Tables

The pair-wise tables together with the supporting information are listed below. You can click the table name to download the complete table, or browse the tables (max. 1000 entries). Click the **Proceed** button at the bottom to directly explore the results in a network context.

snp2met	[SNP:12, Metabolite: 9]	Browse
snp2gene	[SNP:34, Gene: 2]	Browse
snp2dis	[SNP:34, Disease: 69]	Browse
protein2protein	[protein:8]	Browse

Networks

In some cases, multiple isolated networks will be generated, with a big 'continent' containing most of queries, and several small 'islands' containing one or a few queries. These networks will be available for visual analysis in the next step.

Networks	Queries	Nodes	Edges	Topology
mgwas1	1	117	274	View
mgwas2	1	4	4	View

Network Tools:

- Degree Filter
- Betweenness Filter
- Shortest Path Filter
- Manual Batch Filter
- Minimum Network
- Steiner Forest Network
- Reset Network

[Previous](#) [Proceed](#)

Table browsing

- Users can browse the table results and/or filter items by entering keywords in the search bar.
- Click “Proceed” to go back to the “Network Builder” page.


Home > Upload > Network Builder > Table

SNP ↑↓	EA ↑↓	Chr ↑↓	Position ↑↓	Metabolite ↑↓	Effect Size (β) ↑↓	P-value ↑↓	Literature ↑↓	Biofluid ↑↓	Population ↑↓
<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
rs505922	T	9	136149229	ADpSSEGDFXAEggGVR	-0.0432	7.760e-13	24816252	blood	European
rs505922	T	9	136149229	ADpSSEGDFXAEggGVR_X-14304--leucylalanine	-0.084	2.820e-18	24816252	blood	European
rs505922	T	9	136149229	ADsSEGDFXAEggGVR*_ADpSSEGDFXAEggGVR*	0.0701	4.520e-34	24816252	blood	European
rs505922	T	9	136149229	DSegGDFXAEggGVR*_ADpSSEGDFXAEggGVR*	0.0731	1.720e-31	24816252	blood	European
rs514659	A	9	136142203	ADpSSEGDFXAEggGVR	-0.0441	2.630e-13	24816252	blood	European
rs514659	A	9	136142203	ADpSSEGDFXAEggGVR_X-14304--leucylalanine	-0.0845	1.680e-18	24816252	blood	European
rs514659	A	9	136142203	ADsSEGDFXAEggGVR*_ADpSSEGDFXAEggGVR*	0.0709	9.540e-35	24816252	blood	European
rs514659	A	9	136142203	DSegGDFXAEggGVR*_ADpSSEGDFXAEggGVR*	0.0738	4.750e-32	24816252	blood	European
rs529565	T	9	136149500	ADpSSEGDFXAEggGVR	-0.0435	5.410e-13	24816252	blood	European
rs529565	T	9	136149500	ADpSSEGDFXAEggGVR_X-14304--leucylalanine	-0.0847	1.450e-18	24816252	blood	European
rs529565	T	9	136149500	ADsSEGDFXAEggGVR*_ADpSSEGDFXAEggGVR*	0.0708	1.150e-34	24816252	blood	European
rs529565	C	9	136149500	Citric acid	0.0277014	2.100e-10	Borges_UKBB_2020	blood	European
rs529565	T	9	136149500	DSegGDFXAEggGVR*_ADpSSEGDFXAEggGVR*	0.0731	1.740e-31	24816252	blood	European
rs545971	T	9	136143372	ADpSSEGDFXAEggGVR	0.0439	3.330e-13	24816252	blood	European
rs45971	T	9	136143372	ADpSSEGDFXAEggGVR_X-14304--leucylalanine	0.0843	2.020e-18	24816252	blood	European

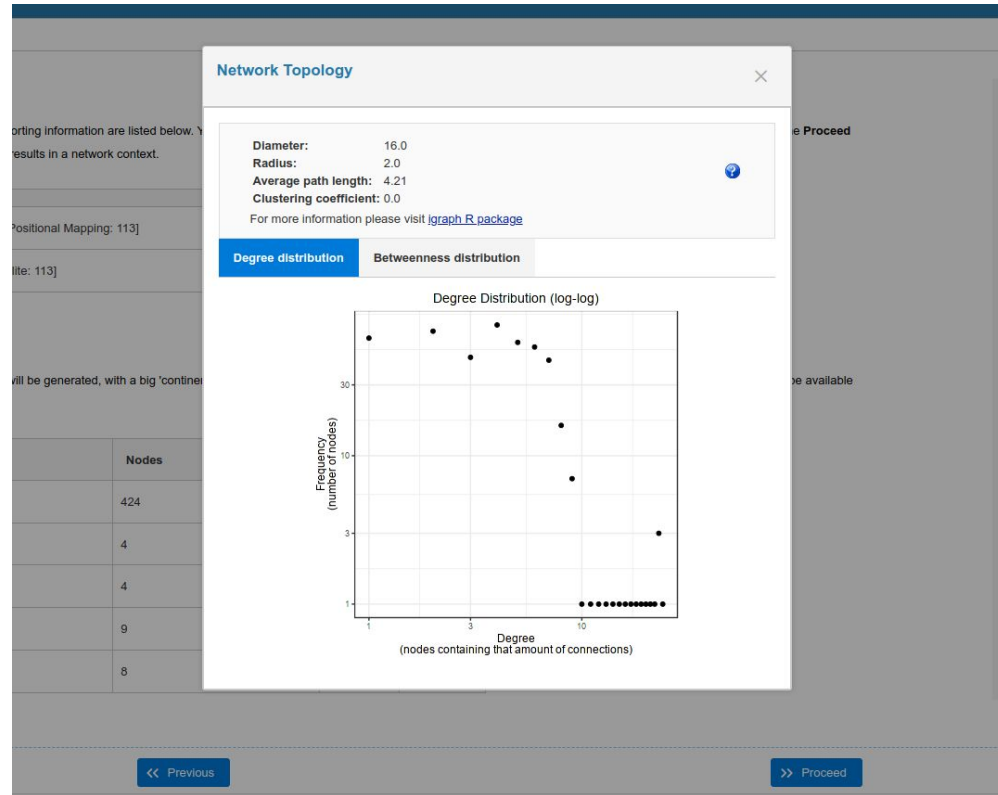
(1 of 4) << < 1 2 3 4 > >> 16 ▾

[Download](#) [Proceed](#)

Network topology measures

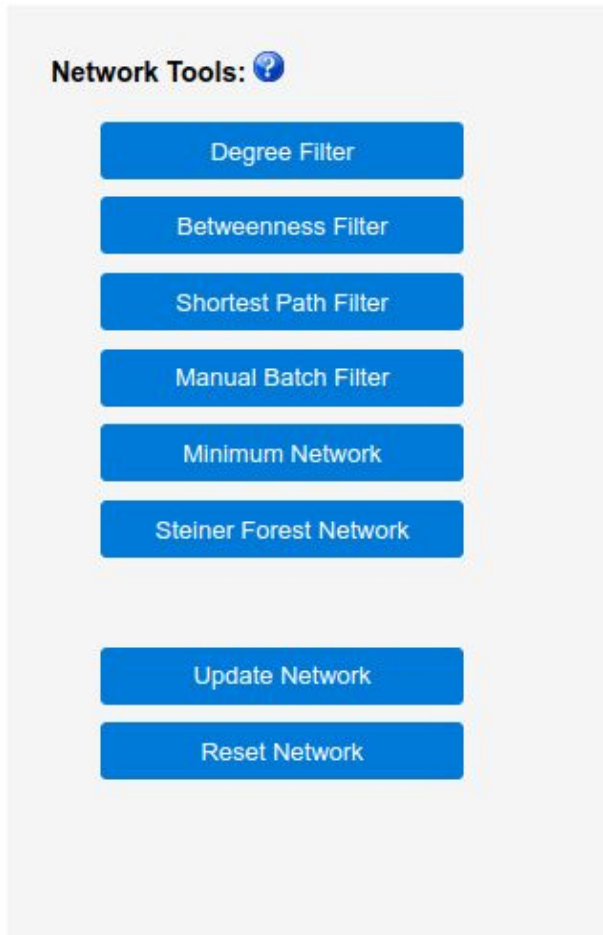
- Click the  View icon to inspect some common network topology measures

- ❑ *Diameter*: shortest distance between the two most distant nodes in the network.
- ❑ *Radius*: is the smallest eccentricity within a graph. Eccentricity of a node is calculated by measuring the shortest distance from (or to) the vertex, to (or from) all vertices in the graph, and taking the maximum.
- ❑ *Average path length*: average number of steps of shortest paths between all possible pairs of nodes.
- ❑ *Clustering coefficient (transitivity)*: measures the probability that the adjacent vertices of a vertex are connected. It is computed from the ratio of triangles and connected triplets in the graph.



Network filtering

- When the network is too large (i.e., > 2500 nodes), users can use “**Network Tools**” to reduce the size of the networks based on topological measures.
 - ❑ *Degree filter*: the degree of a node is the number of connections it has to other nodes.
 - ❑ *Betweenness filter*: the betweenness centrality measures the number of shortest paths going through the node.
 - ❑ *Shortest path filter*: If there are multiple paths that can link two nodes together, only one shortest path will be kept to reduce dense networks.
 - ❑ *Compute minimum network*: you can also use “Minimum Network” or “Steiner Forest Network” tools to construct a minimally connected network that contains all of the seed nodes.
 - ❑ *Manual batch filter*: you can manually filter the network by either excluding or including a given list.



Visual exploration of the network

The screenshot displays a network visualization tool interface. The central area shows a complex network graph with nodes of various colors (blue, pink, red, yellow) and sizes, connected by edges. The interface includes several panels and a top menu bar.

Top menu bar: Contains navigation and configuration options such as "Network: mgwas1", "Background: Gradient (light)", "View: Default", "Layout: -- Specify --", "Node: - Specify -", "Edge: - Specify -", "Scope: -- Specify --", "Download: -- Specify --", and "View Options".

Function explorer: Located on the right side, it features a search query "All SNPs" and a database selection "Variant Set (DisGeNET)". Below this is a table of results:

Name	Hits	Pval	Color
Diabetes Mellitus, Non-Insuli	32	8.41e-40	
Age related macular degenera	18	1.66e-28	
Venous Thrombosis	9	2.33e-16	
E-selectin Measurement	4	2.84e-13	
Waist Circumference	5	1.04e-8	
Venous Thromboembolism	6	1.31e-8	
Alkaline phosphatase measur	4	2.78e-8	
Low density lipoprotein chole	7	2.92e-7	
Serum total cholesterol meas	7	5.13e-7	
Body mass index	9	8.58e-7	
C-reactive protein measurem	5	0.00000438	
Paroxysmal nocturnal hemogi	2	0.00000931	
Protein measurement	4	0.0000219	
von Willebrand's factor (lab t	4	0.0000229	
Glucose tolerance test	2	0.0000531	
Blood Protein Measurement	7	0.0000568	
Fasting blood glucose measur	3	0.000077	
Hematocrit procedure	3	0.0000814	

Node explorer: Located on the left side, it displays a table of node properties:

Name	Degree	Betweenness	Input
rs2925979	105	34849.21	✓
rs635634	71	17707.77	✓
rs2519093	67	11179.63	
rs579459	56	7743.264	
rs495828	55	8795.038	
Citrulline	52	9990.848	
GLP2R	52	9990.848	
rs651007	51	7055.618	
rs649129	32	2220.576	
Diabetes Mellitu	32	56263.09	
rs532436	24	132.1149	
rs600038	24	85.61987	
PLEKHA1	19	3549.996	
Age related mac	18	3259.347	
rs507666	17	1711.728	
rs9271770	11	3977	
rs2820443	9	2312.944	
ABO	9	601.4287	

Module explorer: Located at the bottom right, it shows the "InfoMap" algorithm and a table for module exploration:

Module	Size	Pval	Color
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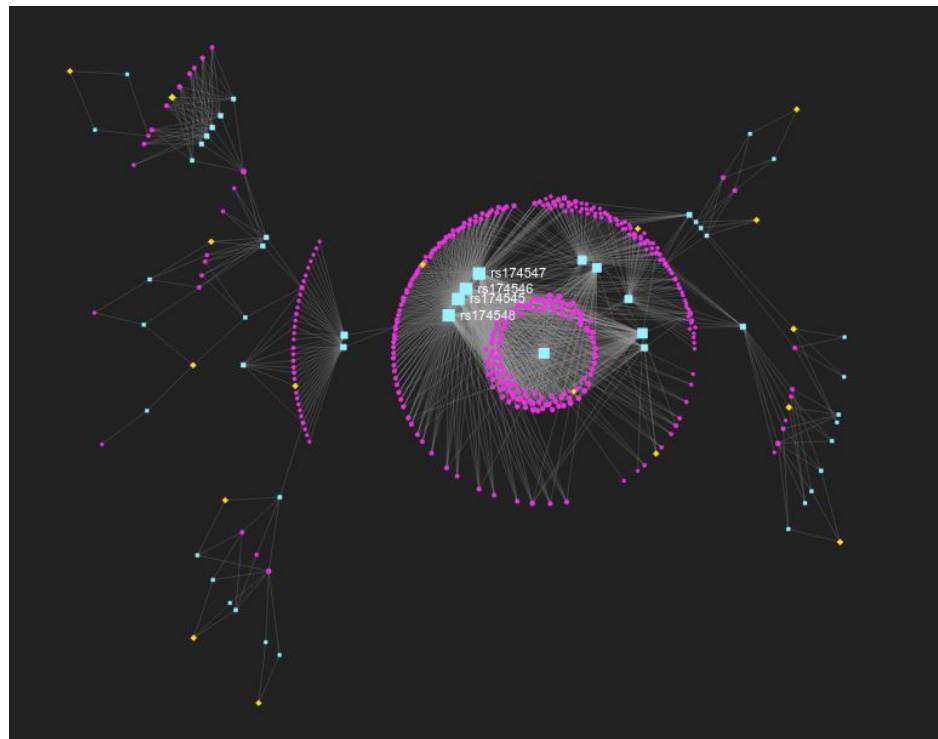
Current Selections: Located at the bottom left, it lists the selected node and links:

- Node: rs2820443
- Link: dbSNP
- Link: Ensembl

Customizing the network

Network: Background: View: Layout: Node: Edge: Scope: Download: [View Options](#)

- ❑ *Change background color:* users can change the background color to “black”, “white”, “gradient (light/dark)”, or customize the background to your preferred colors.
- ❑ *Change view style:* users can switch to “Topology” or “Grey” view.
- ❑ *Change layout:* the mGWAS-Explorer currently supports >10 types of network layout algorithms, including Force-Atlas, Fruchterman-Reingold, Circular, Graphopt, Large Graph, Random, Circular Bipartite/Tripartite, Linear Bipartite/Tripartite, Concentric and Backbone layout.
- ❑ *Change node styles:* users can customize node labels, color, size and shape.
- ❑ *Change edge styles:* the edge opacity, thickness and color can be modified.



==The End==