

The background features three overlapping circles in a medium blue color, arranged horizontally. The circles overlap in the center, creating a darker blue area. A white horizontal bar is positioned across the middle of the circles, containing the text.

# OmicNet Tutorial: Network building

# Computer Requirement

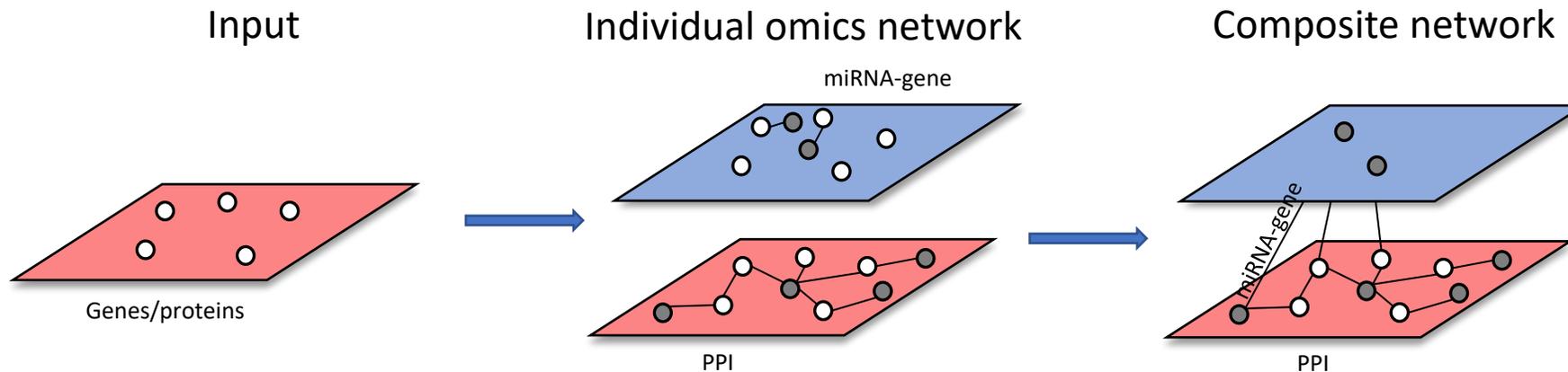
- Modern browser supporting **WebGL**
- Chrome 50+, Firefox 47+, Safari 10.1+ and Edge 12+
- Please make sure WebGL is enabled in your browser
  - Please consult this web page to verify: <https://get.webgl.org/>
- If not enabled, please consult our **FAQ** page for instructions
- For best performance 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.

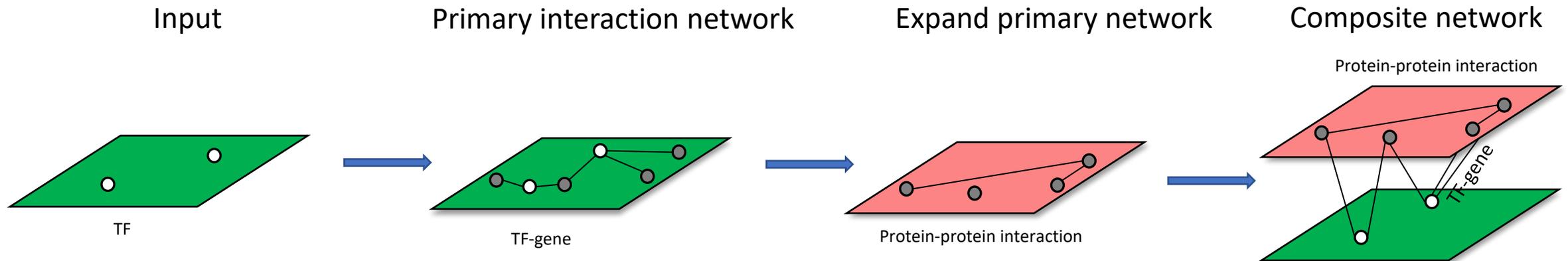
# Network building for single list

- 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



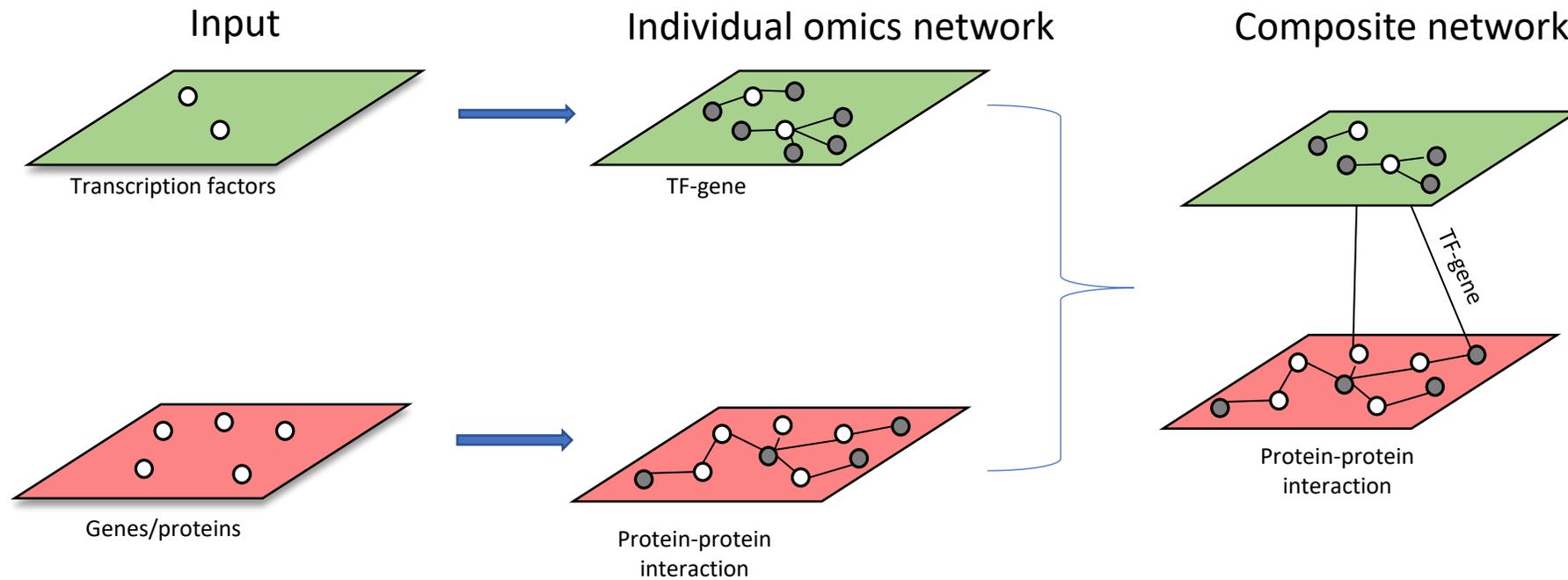
# Network building for single list (2)

- 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.

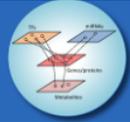


# Network building for multiple lists

- 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



## 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); **NEW**
- Added support for adding only edges when using PPI databases (03/25/2022); **NEW**
- Added R command history for more reproducible analysis (03/17/2022); **NEW**
- Added support for tissue-based filtering to improve network accuracy (03/15/2022); **NEW**
- Fixed a bug for network file upload based on user feedback (03/01/2022); **NEW**
- Improved interface for network building (02/15/2022); **NEW**
- 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)

**OmicsNet 2.0**

Home Overview Tutorials FAQs Gallery Updates Contact

### Multi-omics Integration via Biological Network

start

Network analysis of one or more list(s) of molecules

Genes	LC-MS Peaks	miRNAs	Metabolites

**Upload a list of genes**

Enter your data below: ?

Specify organism:

Set ID type:

Entrez ID	Gene Name	logFC
4495	61.12	
4496	51.06	
4499	23.79	
6354	21.04	
6369	19.76	
4494	16.24	
4501	14.76	
11026	14.04	
199675	12.65	
4316	12.04	
771	8.19	
6346	7.07	
6367	6.97	

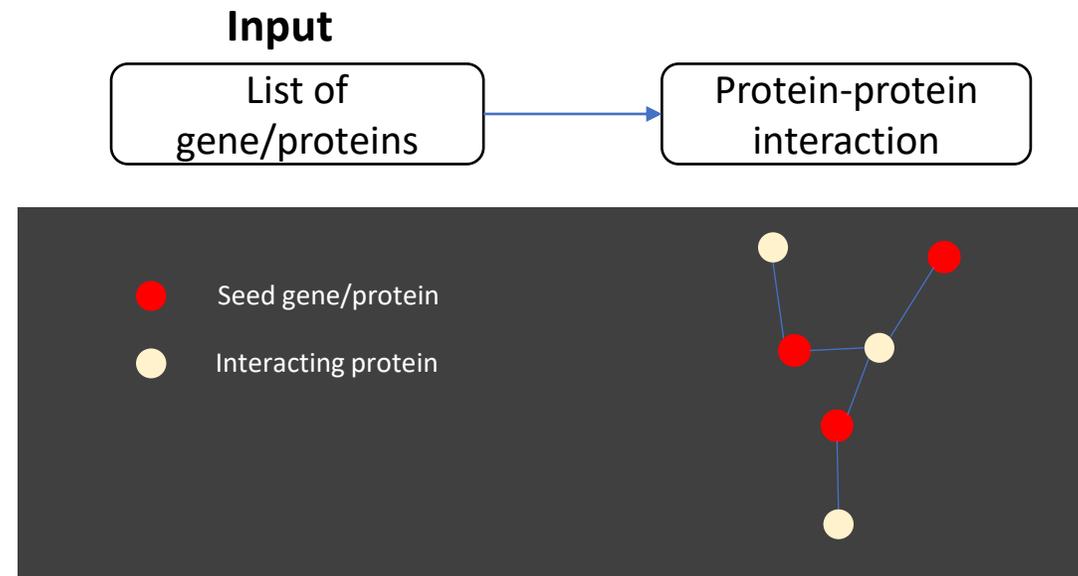
Use example  Genes  KOs

OmicsNet supports ten different organisms

An optional second column can be added to included expression value or any other numerical attribute associated with a molecule

- Added support to allow users to browse, search and manually remove edges or nodes from individual omics networks (04/01/2022); **NEW**
- Added support for adding only edges when using PPI databases (03/25/2022); **NEW**
- Added R command history for more reproducible analysis (03/17/2022); **NEW**
- Added support for tissue-based filtering to improve network accuracy (03/15/2022); **NEW**
- Fixed a bug for network file upload based on user feedback (03/01/2022); **NEW**
- Improved interface for network building (02/15/2022); **NEW**
- Updated tutorials for MS peak and taxon list inputs (01/21/2022);
- Improved SNP-gene mapping functions for better performance (01/18/2022);

# 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

Database Selection

Input list(s) ?

Gene (51)

Database Selection

Databases are organized under different tabs. Please choose a database and customized in the next page

Select molecular interaction type by switching tabs

Protein-protein miRNA-gene Metabolite-protein TF-gene

InnateDB Manually curated comprehensive PPI (human/mouse) (updated on 01/04/2022)

STRING Comprehensive PPI containing both known and predicted PPI (updated on 01/04/2022) (parameters)

IntAct Manually curated experimentally validated PPI (updated on 01/04/2022)

HuRI Reference interactome map of human binary protein interactions (updated on 01/04/2022)

Add edges only Do not introduce new nodes. Only identify connections within current nodes.

Submit

This option is useful when PPI is added as secondary interaction

Click on "Submit" to compute the primary network or add secondary interactions

Individual Omics Networks

Each network is created independently by searching input list against a selected database. The network usually contains several disconnected subnetworks.

Input Type	Network Type	Sizes (node# - edge# - seed#)	Browse	Download	Delete
Gene	PPI	449 - 489 - 45			

Basic network properties are shown in this table. You can also view table in the browser, download edge list and delete network to restart

Navigation: << Previous Proceed >>

# Browse View

Database Selection > Interaction Table

Navigate to:

Use this function to delete multiple edges at once using different filtering options on selected columns

## 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 >>

Click on proceed so the changes take effect

# Network Visualization

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

Node coloring and size

**Global Node Styles**

Type: Gene  
Size: [Slider]  
Color: [Color Picker]

**Node Table**

ID	Name	Degree	Expr.
<input type="checkbox"/>	8338 HIST2H2AC	108	3.61
<input type="checkbox"/>	9260 PDLIM7	34	3.1
<input type="checkbox"/>	5265 SERPINA1	32	5.65
<input type="checkbox"/>	5473 PPBP	24	6.76
<input type="checkbox"/>	7316 UBC	22	
<input type="checkbox"/>	8337 HIST2H2AA3	22	3.97
<input type="checkbox"/>	2203 FBP1	20	3.18
<input type="checkbox"/>	1462 VCAN	18	5.27
<input type="checkbox"/>	6363 CCL19	18	4.08
<input type="checkbox"/>	3627 CXCL10	17	-9.89
<input type="checkbox"/>	6354 CCL7	15	21.04
<input type="checkbox"/>	27063 ANKRD1	15	4.05
<input type="checkbox"/>	820 CAMP	15	-3.94
<input type="checkbox"/>	23646 PLD3	14	-3.11
<input type="checkbox"/>	771 CA12	12	8.19
<input type="checkbox"/>	4316 MMP7	12	12.04
<input type="checkbox"/>	4501 MT1X	11	14.76
<input type="checkbox"/>	6367 CCL22	11	6.97
<input type="checkbox"/>	1471 CST3	7	-4.17
<input type="checkbox"/>	84504 CD137	6	2.65

**Function Explorer**

Query: All nodes  
Database: KEGG (gene)

Name	Hits	P-val	P-val(ad)	Color
Renal cell carcinoma	39	1.5e-19	5.05e-17	
Phosphatidylinositol sig	28	9.26e-19	1.56e-16	
Hypertrophic cardiomyo	31	4.03e-18	3.89e-16	
Colorectal cancer	36	4.63e-18	3.89e-16	
Shigellosis	33	1.36e-15	9.15e-14	
Sphingolipid signaling p	30	8.33e-13	4.67e-11	
Fc epsilon RI signaling i	21	3.09e-12	1.48e-10	
Hematopoietic cell linea	26	3.01e-10	1.26e-8	
FoxO signaling pathway	33	8.69e-10	3.24e-8	

**Module Explorer**

Algorithm: InfoMap

Module	Size	P-value	Color	
<input type="checkbox"/>	0	100	4.55e-43	Red
<input type="checkbox"/>	1	30	7.68e-09	Green
<input type="checkbox"/>	2	33	7.9e-14	Yellow
<input type="checkbox"/>	3	23	9.17e-09	Blue
<input type="checkbox"/>	4	21	9.83e-05	Orange
<input type="checkbox"/>	5	23	1.81e-09	Purple
<input type="checkbox"/>	6	17	7.3e-07	Cyan
<input type="checkbox"/>	7	16	5.31e-06	Magenta
<input type="checkbox"/>	8	15	2.29e-05	Light Green
<input type="checkbox"/>	9	13	0.00545	Pink
<input type="checkbox"/>	10	15	7.43e-07	Dark Green
<input type="checkbox"/>	11	13	0.000528	Purple
<input type="checkbox"/>	12	13	5.74e-06	Brown
<input type="checkbox"/>	13	11	0.00101	Yellow

**Current Selections**

Input nodes

- VCAN
- PLD3
- CA12
- MT1X
- CPVL

**Enrichment Analysis**

**Module Detection**

Module-based force-directed layout

# Regulation explorer identifies gene regulators

Network: subnetwork1 Background: Black Layout: Standard Styling: - Specify - Drag scope: -- Specify -- Download: -- Specify -- Advanced Options Modify ?

**Global Node Styles**

Type	Size	Color
Gene	<input type="range"/>	<input type="color" value="red"/>

**Node Table**

ID	Name	Degree	Expr.
8338	HIST2H2AC	108	3.61
9260	PDLIM7	34	3.1
5265	SERPINA1	32	5.65
5473	PPBP	24	6.76
7316	UBC	22	
8337	HIST2H2AA3	22	3.97
2203	FBP1	20	3.18
1462	VCAN	18	5.27
6363	CCL19	18	4.08
3627	CXCL10	17	-9.89
6354	CCL7	15	21.04
27063	ANKRD1	15	4.05
820	CAMP	15	-3.94
23646	PLD3	14	-3.11
771	CA12	12	8.19
4316	MMP7	12	12.04
4501	MT1X	11	14.76
6367	CCL22	11	6.97
1471	CST3	7	-4.17

Page 1 of 14

**Current Selections**

- NFKB1
  - CCR7
  - NFKB1
  - EGR1
  - FBP1
  - IRF1

**Function Explorer**

Query: All nodes Database: KEGG (gene) Submit

Name	Hits	P-val	P-val(ac)
------	------	-------	-----------

**Module Explorer**

Guilt-by-Association Analysis

**Regulation Explorer**

Query: All nodes Database: TF[TRRUST] Submit

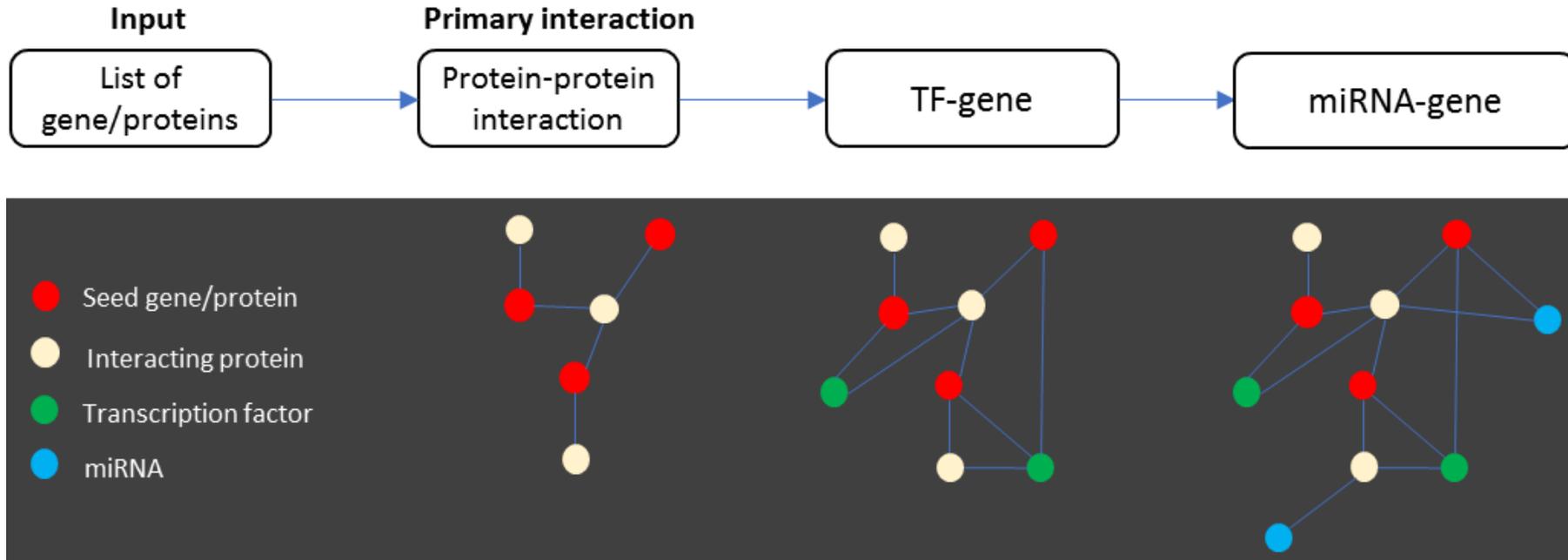
Name	ID	Hits	Color
<input checked="" type="checkbox"/> NFKB1		4790 42	Blue
<input type="checkbox"/> RELA		5970 42	Grey
<input type="checkbox"/> SP1		6667 41	Grey
<input type="checkbox"/> JUN		3725 26	
<input type="checkbox"/> TP53		7157 21	
<input type="checkbox"/> STAT3		6774 17	
<input type="checkbox"/> ESR1		2099 15	
<input type="checkbox"/> E2F1		1869 13	
<input type="checkbox"/> FOS		2353 12	
<input type="checkbox"/> BRCA1		672 11	
<input type="checkbox"/> STAT1		6772 11	
<input type="checkbox"/> YY1		7528 11	

Path Explorer Batch Selection

It is possible to search for TF, miRNA or drug (human only) targeting genes

Previous Logout

## Case 2: Build regulatory network



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

# Network Building

Database Selection

Input list(s) ?

Gene (51)

**1. Build PPI as primary interaction network**

**2. Add miRNA-gene as secondary molecular interaction.**

**3. Add TF-gene as secondary molecular interaction**

Database Selection

Databases are organized under different tabs. Please choose proper database(s) for network construction based on your input list and customized in the next page

Protein-protein   miRNA-gene   Metabolite-protein

TRRUST  
ENCODE

TF-gene interactions constructed using text mining, followed by manual curation (updated on 01/04/2022)  
TF-gene interactions derived from ENCODE CHIP-seq data (updated on 01/04/2022)  
TF-gene interactions derived from transcription factor binding profiles (updated on 01/04/2022)

Submit

Command History Save

Click the Proceed button to perform network analysis and visualization.

- dataset<-PrepareInputList(dataset,"Your input list", "hsa", "gene", "entrez");
- dataset<-QueryNet(dataset, "gene", "input list", "gene")
- CreateGraph()
- dataset<-QueryNet(dataset, "mir", "mir tarbase", "gene")
- CreateGraph()
- dataset<-QueryNet(dataset, "tf", "trrurst", "gene")
- CreateGraph()

Individual Omics Networks

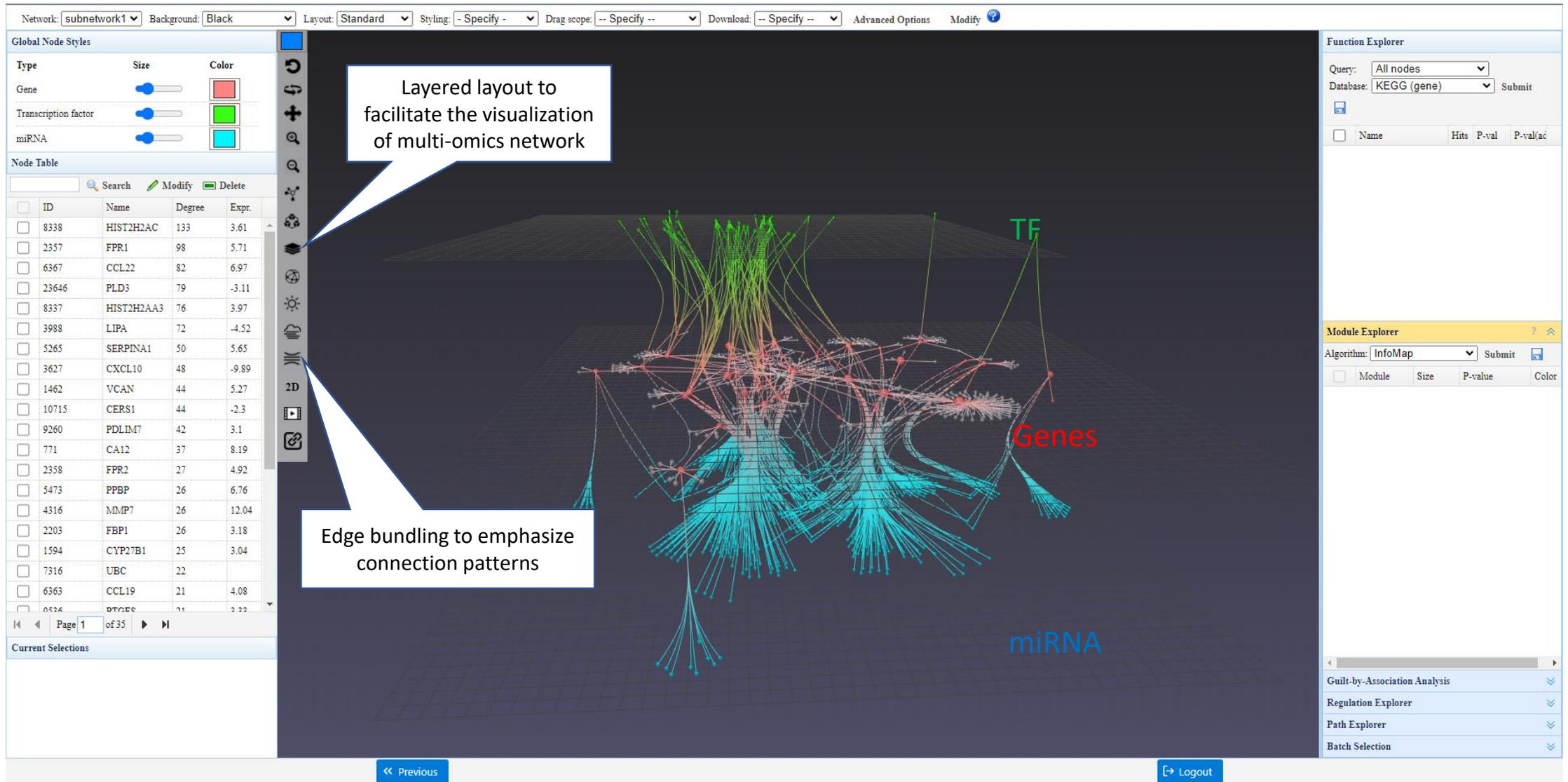
Each network is created independently by searching input list against a selected database. The network usually contains several disconnected subnetworks.

Input Type	Network Type	Sizes (node# - edge# - seed#)	Browse	Download	Delete
Gene	PPI	449 - 489 - 45			
Gene	miRNA-gene	597 - 687 - 39			
Gene	TF-gene	62 - 57 - 20			

Navigation: << < 1 > >>

Navigation: << Previous Proceed >>

# Network Visualization

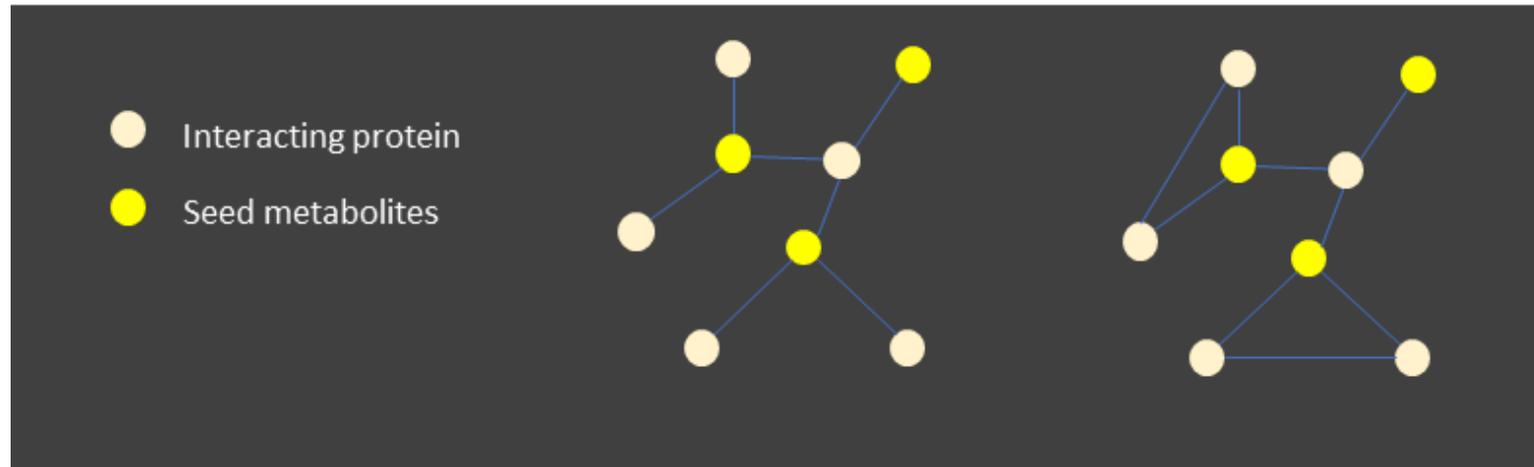
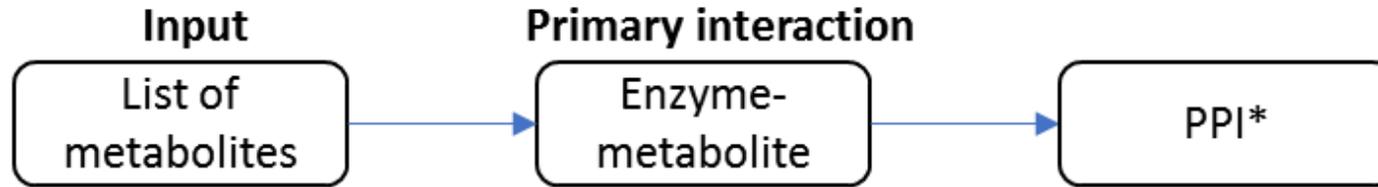


Layered layout to facilitate the visualization of multi-omics network

Edge bundling to emphasize connection patterns

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

Input list(s) ?

Metabolite (56)

## Database Selection

Databases are organized by database type and creation based on your analysis objectives. Multiple types of networks will be merged (based on shared nodes) and customized in the next page.

Set PPI as secondary molecular interaction

**Protein-protein** Metabolite-protein

Set metabolite-protein as primary network

- InnateDB** Manually curated comprehensive PPI (human/mouse) (updated on 01/04/2022)
- STRING** Comprehensive PPI containing both known and predicted PPI (updated on 01/04/2022) (parameters)
- IntAct** Manually curated experimentally validated PPI (updated on 01/04/2022)
- HuRI** Reference interactome map of human binary protein interactions (updated on 01/04/2022)

Add edges only  
Do not introduce new nodes. Only identify connections within current nodes.

Submit

Select this option to search for PPI between the proteins identified from metabolite protein search

## R Command History

Save

```

1. dataSet<-Init.Data()
2. dataSet<-PrepareInputList(dataSet,"Yo
3.
4.
5.
6.
7. CreateGraph()
8. SetPpiZero(FALSE)
9. dataSet<-QueryNet(dataSet, "gene", "innate", "met" )
10. CreateGraph()
11. SetPpiZero(TRUE)
12. dataSet<-QueryNet(dataSet, "gene", "innate", "met" )
13. CreateGraph()
14. DeleteIndNet("gene_gene")
15. SetPpiZero(TRUE)
16. dataSet<-QueryNet(dataSet, "gene", "innate", "met" )
17. CreateGraph()
    
```

## Individual Omics Networks

Each network is created independently by searching input list against a selected database. The network usually contains several disconnected subnetworks.

Input Type	Network Type	Sizes (node# - edge# - seed#)	Browse	Download	Delete
Metabolite	Metabolite-protein	186 - 189 - 38			
Gene	PPI	9 - 7 - 0			

<< < 1 > >>

<< Previous

Proceed >>

# Network Visualization

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

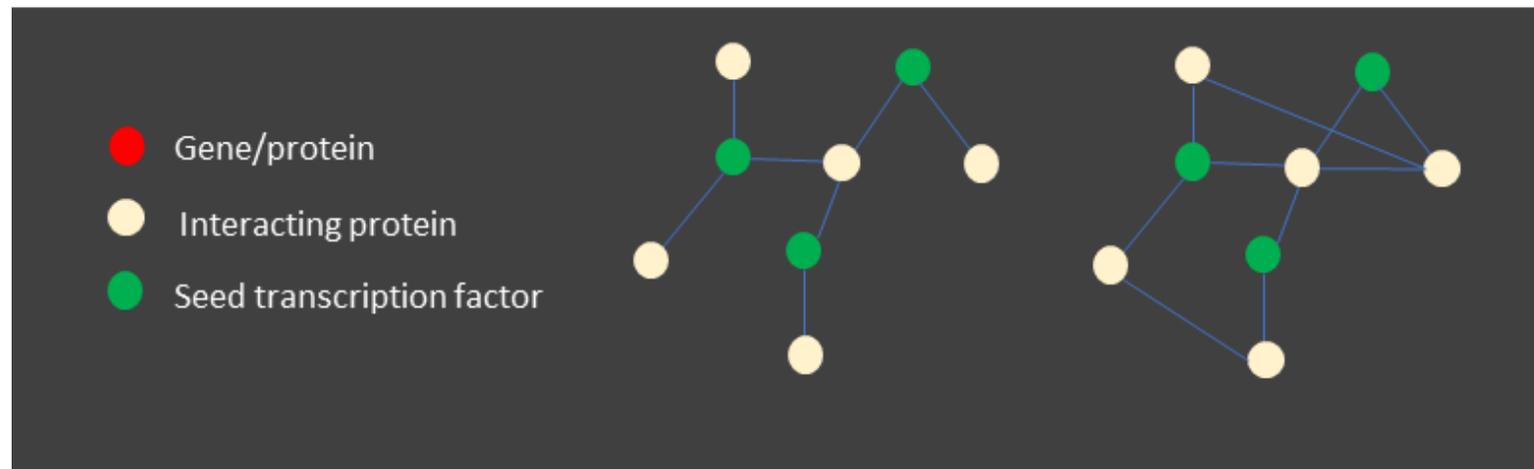
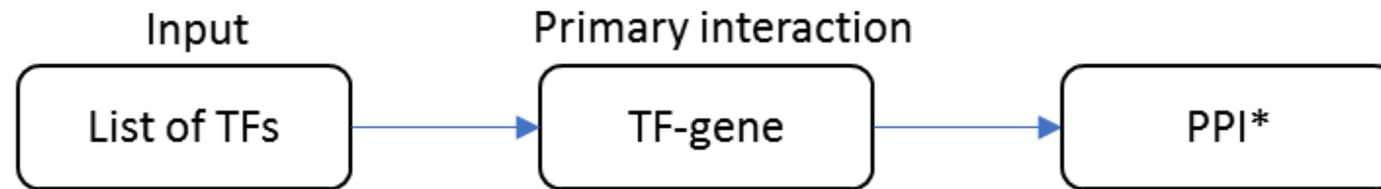
The screenshot displays a network visualization tool interface. At the top, there are settings for Network (subnetwork1), Background (Purple-gradient), Layout (Standard), Styling (Opacity), Drag scope (-- Specify --), and Download (-- Specify --). The main area shows a spherical network layout with nodes and edges. A path is highlighted in blue, connecting two nodes. The interface includes several panels:

- Global Node Styles:** Controls for Type (Metabolite, Gene), Size, and Color.
- Node Table:** A table listing nodes with columns for ID, Name, Degree, and Expr. The table is currently on page 1 of 17.
- Function Explorer:** A search interface with a Query field (All nodes) and a Database dropdown (KEGG (gene)).
- Module Explorer:** A section for exploring modules.
- Regulation Explorer:** A section for exploring regulations.
- Path Explorer:** A section for exploring paths, showing a path from C00003 to C00077. The path is: **NAD+ -> ALDH4A1 -> ARG1 -> L-Ornithine**.

At the bottom, there are buttons for "Previous" and "Logout".

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.

The screenshot displays a network visualization application interface. At the top, there are control panels for Network (subnetwork1), Background (Blue-gradient), Layout (Standard), and Styling (Color). A central 3D visualization shows a network graph with a central node (green and blue) and a large cluster of red nodes below it, connected by edges. A styling menu is open over the graph, listing options for Nodes (Label, Color, Size, Shading) and Edges (Opacity, Width, Color, Bundling, Color scheme, Default, Topology, Expression, Plain). On the left, a 'Node Table' lists various genes with their IDs, names, and degrees. On the right, there are panels for 'Function Explorer' and 'Module Explorer'. At the bottom, there are navigation buttons for 'Previous' and 'Logout'.

**Global Node Styles**

Type	Size	Color
Transcription factor	<input type="range"/>	<input type="color" value="green"/>
Gene	<input type="range"/>	<input type="color" value="red"/>

**Node Table**

ID	Name	Degree	Expr.
<input type="checkbox"/>	6667	SP1	472
<input type="checkbox"/>	50943	FOXP3	11
<input type="checkbox"/>	6671	SP4	11
<input type="checkbox"/>	4087	SMAD2	5
<input type="checkbox"/>	1026	CDKN1A	3
<input type="checkbox"/>	2064	ERBB2	3
<input type="checkbox"/>	672	BRCA1	2
<input type="checkbox"/>	3586	IL10	2
<input type="checkbox"/>	3558	IL2	2
<input type="checkbox"/>	196	AHR	2
<input type="checkbox"/>	596	BCL2	2
<input type="checkbox"/>	7080	NKX2-1	2
<input type="checkbox"/>	332	BIRC5	2
<input type="checkbox"/>	595	CCND1	2
<input type="checkbox"/>	2261	FGFR3	2
<input type="checkbox"/>	3791	KDR	2
<input type="checkbox"/>	4129	MAOB	2
<input type="checkbox"/>	4790	NFKB1	2

**Current Selections**

**Input nodes**

- FOXP3
- SMAD2
- SP1
- SP4

**Function Explorer**

Query: All nodes  
Database: KEGG (gene) Submit

<input type="checkbox"/>	Name	Hits	P-val	P-val(ac)
--------------------------	------	------	-------	-----------

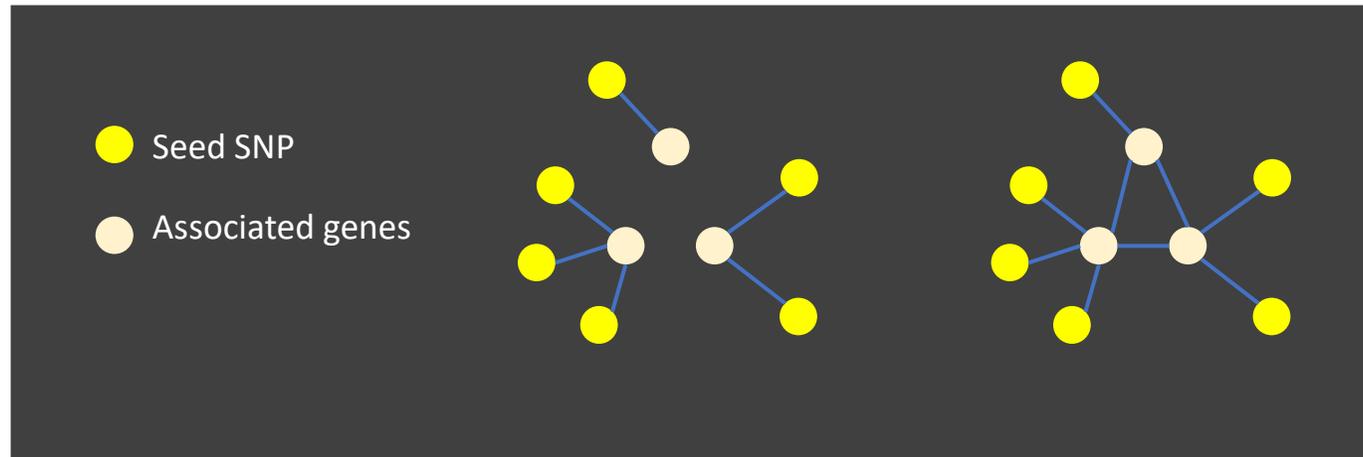
**Module Explorer**

Algorithm: InfoMap Submit

<input type="checkbox"/>	Module	Size	P-value	Color
--------------------------	--------	------	---------	-------

Navigation: << Previous | Logout >>

# 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

## Input list(s) ?

SNP (5)

## Database Selection

Databases are organized under different categories and customized in the next page

Add PPI to expand primary SNP-gene network

network creation based on your analysis objectives. Multiple types of networks will be merged (based on shared nodes)

Protein-protein miRNA-gene Metabolite-protein TF-gene **SNP-gene**

### SNP Annotation

SNPs can be integrated into molecular interaction networks through their associated genes. There are two main approaches - based on positions and based on eQTLs. For PhenoScanner and VEP, the mapping are based on public APIs and may take a few minutes to complete. The SNP-gene network could be further enriched by introducing other information via PPI, miRNAs or TFs.

- PhenoScanner** Genes - Curated database of publicly available results from large-scale genetic association studies in humans ([set parameters](#))
- VEP** Genes - Positional mapping based on the Ensembl Variant Effect Predictor (VEP) ([set parameters](#))
- ADmiRE** miRNA - Positional mapping to miRNA annotation
- SNP2TFBS** TF - Positional mapping to transcription factor binding sites

Submit

## R Command History

Save

```
1. dataSet<-Init.Data()
2. dataSet<-PrepareInputList(dataSet,"Your input list", "hsa", "snp", "rsid");
3. dataSet<-QueryNet(dataSet, "snp", "PhenoScanner", "snp" )
4. CreateGraph()
5. SetPpiZero(FALSE)
6. dataSet<-QueryNet(dataSet, "gene", "input list", "snp" )
7. CreateGraph()
8. CreateGraph()
```

## Individual Omics Networks

Each network is created independently by searching input list against a selected database. The network usually contains several disconnected subnetworks.

Input Type	Network Type	Sizes (node# - edge# - seed#)	Browse	Download	Delete
SNP	SNP Annotation	78 - 73 - 5			
Gene	PPI	574 - 642 - 0			

<< < 1 > >>

<< Previous

Proceed >>

# Network building (2)

## Network Tools ?

Degree Filter

Betweenness Filter

Minimum Network

Steiner Forest (PCSF)

Tissue Filter

P-value Filter

Zero-order Network

Reset to First-order

## Multi-omics Network Building

If more than one network was generated in the previous page, they will be merged together to form multi-omics network through shared nodes. The network is then decomposed into connected subnetworks available for visual analysis in the next page. If the resulting subnetwork1 is too large, you can trim the network to be suitable for visual analytics (< 2000 nodes) using the **Network Tools** on the left.

Subnetworks	Sizes (node# - edge# - seed#)	Topology	Download
subnetwork1	602 - 715 - 5	<a href="#">View</a>	<a href="#">Download</a>

<< < 1 > >>

## R Command History Save

```
1. dataSet<-Init.Data()
2. dataSet<-PrepareInputList(dataSet,"Your input list", "hsa", "snp", "rsid");
3. dataSet<-QueryNet(dataSet, "snp", "Phe noScanner", "snp" )
4. CreateGraph()
5. SetPpiZero(FALSE)
6. dataSet<-QueryNet(dataSet, "gene", "in nate", "snp" )
7. CreateGraph()
8. CreateGraph()
9. CreateGraph()
```

# Network Visualization

Network: subnetwork1 Background: Black Layout: Standard Styling: - Specify - Drag scope: -- Specify -- Download: -- Specify -- Advanced Options Modify

### Global Node Styles

Type	Size	Color
Snp	<input type="range"/>	<input type="checkbox"/>
Gene	<input type="range"/>	<input type="checkbox"/>

### Node Table

ID	Name	Degree	Expr.	
<input type="checkbox"/>	790	CAD	60	
<input type="checkbox"/>	2194	FASN	59	
<input type="checkbox"/>	26227	PHGDH	58	
<input type="checkbox"/>	875	CBS	43	
<input type="checkbox"/>	2027	ENO3	27	
<input type="checkbox"/>	1312	COMT	14	
<input type="checkbox"/>	7316	UBC	12	
<input type="checkbox"/>	6822	SULT2A1	12	
<input type="checkbox"/>	635	BHMT	9	
<input type="checkbox"/>	8884	SLC5A6	8	
<input type="checkbox"/>	3992	FADS1	7	
<input type="checkbox"/>	1577	CYP3A5	7	
<input type="checkbox"/>	3172	HNF4A	5	
<input type="checkbox"/>	341	APOC1	5	
<input type="checkbox"/>	3995	FADS3	5	
<input type="checkbox"/>	1017	CDK2	4	
<input type="checkbox"/>	7341	SUMO1	4	
<input type="checkbox"/>	23395	LARS2	4	
<input type="checkbox"/>	220963	SLC16A9	4	
<input type="checkbox"/>	9123	SLC16A3	4	

### Function Explorer

Query: All nodes Database: KEGG (gene) Submit

Name	Hits	P-val	P-val(ac)
------	------	-------	-----------

### Module Explorer

Algorithm: InfoMap Submit

Module	Size	P-value	Color
--------	------	---------	-------

### Current Selections

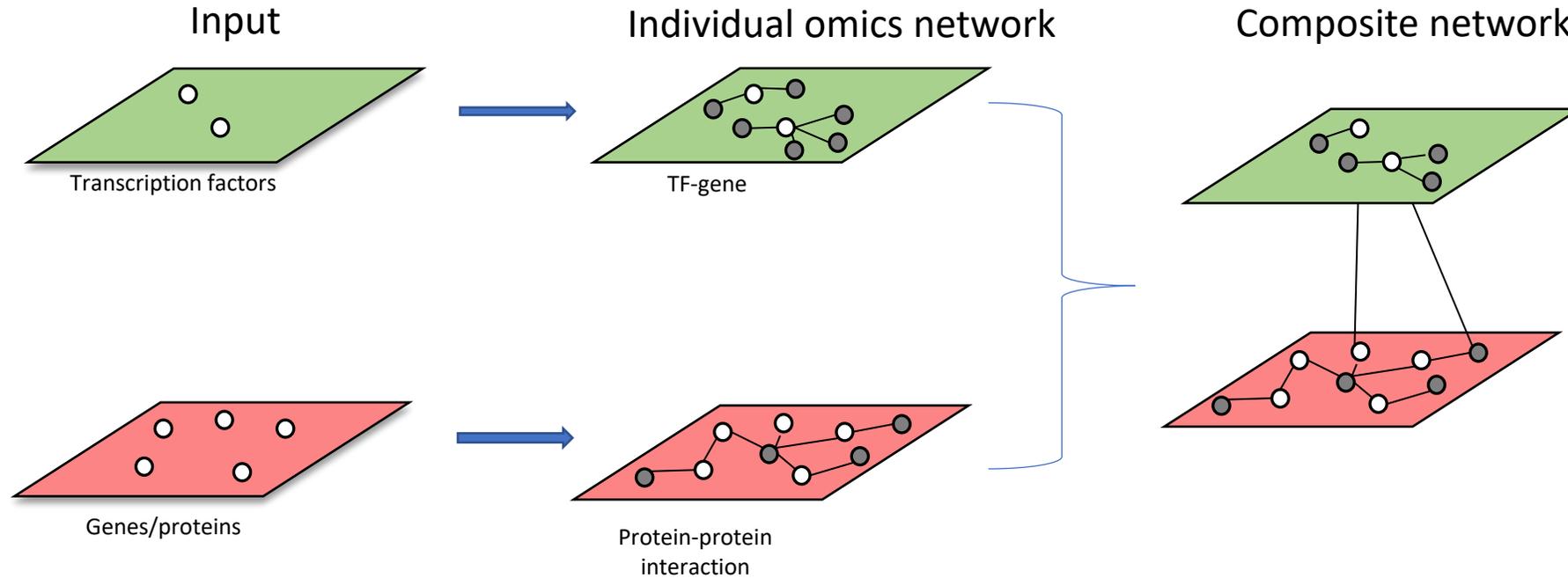
**Input nodes**

- rs1000778
- rs10069036
- rs10821582
- rs10942887
- rs10944

Page 1 of 10

Navigation: << Previous [ -> Logout

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



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

# Network Building

Database Selection

Navigate to:

Input list(s) ?

Gene (51)

Transcription factor (6)

## Database Selection

Databases are organized under different tabs. Please choose proper database(s) for network creation based on your analysis objectives. Multiple types of networks will be merged (based on shared nodes) and customized in the next page

### TF-gene

- TRRUST** TF-gene interactions constructed using text mining, followed by manual curation (updated on 01/04/2022)
- ENCODE** TF-gene interactions derived from ENCODE CHIP-seq data (updated on 01/04/2022)
- JASPAR** TF-gene interactions derived from transcription factor binding profiles (updated on 01/04/2022)

Submit

## Individual Omics Networks

Each network is created independently by searching input list against a selected database. The network usually contains several disconnected subnetworks.

Input Type	Network Type	Sizes (node# - edge# - seed#)	Browse	Download	Delete
Gene	PPI	449 - 489 - 46			
Transcription factor	TF-gene	487 - 501 - 8			

<< < 1 > >>

## R Command History

Save

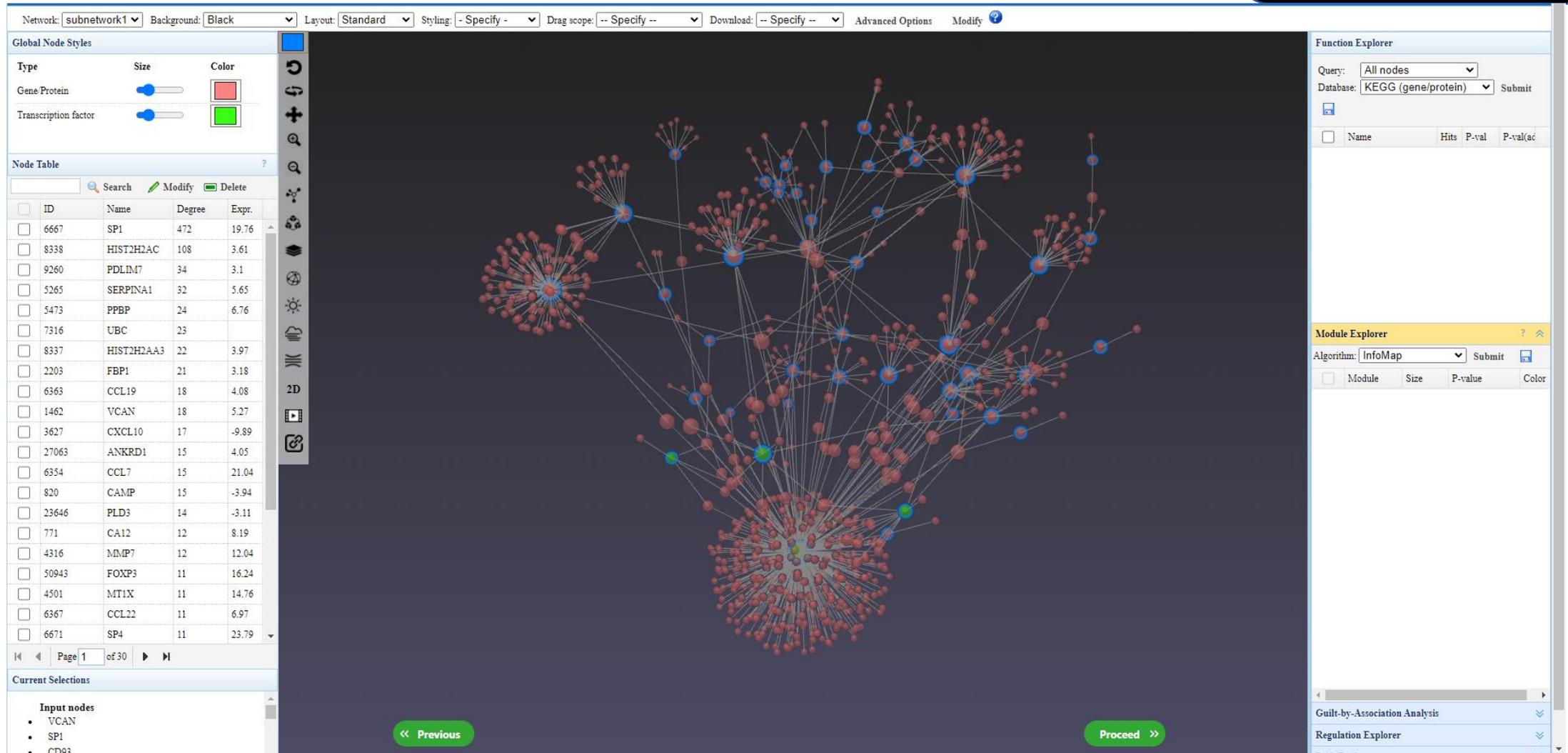
```
1. dataSet<-Init.Data()
2. dataSet<-PrepareInputList(dataSet,"Your input list", "hsa", "gene", "entre");
3. dataSet<-PrepareInputList(dataSet,"Your input list", "hsa", "tf", "symbol");
4. dataSet<-QueryNetMulti(dataSet, "gene", "innate", "gene")
5. CreateGraph()
6. dataSet<-QueryNetMulti(dataSet, "tf", "trrust", "tf")
7. CreateGraph()
```

<< Previous

Proceed >>

# Network Visualization

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



# Color nodes by expression values

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

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

The screenshot displays a network visualization software interface. The main window shows a network graph with nodes colored by expression values. The 'Global Node Styles' panel on the left shows 'Gene Protein' and 'Transcription factor' with size and color sliders. The 'Node Table' lists nodes with their IDs, names, degrees, and expression values. The 'Function Explorer' panel on the right shows a query for 'All nodes' in the 'KEGG (gene/protein)' database. The 'Module Explorer' panel shows the 'InfoMap' algorithm. The 'Current Selections' panel lists 'Input nodes' including VCAN, SP1, and CD93. The interface also includes a navigation bar at the top and a 'Navigate to:' dropdown.

ID	Name	Degree	Expr.
6667	SP1	472	19.76
8338	HIST2H2AC	108	3.61
9260	PDLIM7	34	3.1
5265	SERPINA1	32	5.65
5473	PPBP	24	6.76
7316	UBC	23	
8337	HIST2H2AA3	22	3.97
2203	FBP1	21	3.18
6363	CCL19	18	4.08
1462	VCAN	18	5.27
3627	CXCL10	17	-9.89
27063	ANKRD1	15	4.05
6354	CCL7	15	21.04
820	CAMP	15	-3.94
23646	PLD3	14	-3.11
771	CA12	12	8.19
4316	MMP7	12	12.04
50943	FOXP3	11	16.24
4501	MT1X	11	14.76
6367	CCL22	11	6.97
6671	SP4	11	23.79

<< Previous

Proceed >>

# Trimming network

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

🏠 > Database Selection > Network Builder > Network Viewer > Result Download ⌵ Navigate to:

### Network Tools ?

- Degree Filter
- Betweenness Filter
- Minimum Network**
- Steiner Forest (PCSF)
- Tissue Filter
- P-value Filter
- Zero-order Network
- Reset to First-order

### Multi-omics Network Building

If more than one network was generated in the previous page, they will be merged together to form multi-omics network through shared nodes. The network is then decomposed into connected subnetworks available for visual analysis in the next page. If the resulting subnetwork1 is too large, you can trim the network to be suitable for visual analytics (< 2000 nodes) using the **Network Tools** on the left.

Subnetworks	Sizes (node# - edge# - seed#)	Topology	Download
subnetwork1	75 - 110 - 45	<a href="#">View</a>	<a href="#">Download</a>

<< < 1 > >>

### R Command History Save

- dataSet<-Init.Data()
- dataSet<-PrepareInputList(dataSet,"your input list", "hsa", "gene", "entrez");
- dataSet<-PrepareInputList(dataSet,"your input list", "hsa", "tf", "symbol");
- dataSet<-QueryNetMulti(dataSet, "gene", "innate", "gene" );
- CreateGraph()
- dataSet<-QueryNetMulti(dataSet, "tf", "trrust", "tf" );
- CreateGraph()
- CreateGraph()
- dataSet<-PrepareNetwork(dataSet, "subnetwork1", "omicsnet\_0.json")
- dataSet<-BuildMinConnectedGraphs(dataSet)

Minimum network try to identify a minimal network connecting all seed nodes by computing shortest-paths between nodes.

<< Previous Proceed >>

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# 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

Network: subnetwork1 Background: Black Layout: Standard Styling: - Specify - Drag scope: -- Specify -- Download: -- Specify -- Advanced Options Modify

**Global Node Styles**

Type	Size	Color
Gene	<input type="range"/>	<input type="checkbox"/> Red
Transcription factor	<input type="range"/>	<input type="checkbox"/> Green

**Node Table**

ID	Name	Degree	Expr.	
<input type="checkbox"/>	7316	UBC	23	
<input type="checkbox"/>	6667	SP1	17	19.76
<input type="checkbox"/>	6363	CCL19	7	4.08
<input type="checkbox"/>	6354	CCL7	7	21.04
<input type="checkbox"/>	3172	HNF4A	7	
<input type="checkbox"/>	5970	RELA	6	
<input type="checkbox"/>	3627	CXCL10	6	-9.89
<input type="checkbox"/>	4790	NFKB1	6	
<input type="checkbox"/>	6367	CCL22	5	6.97
<input type="checkbox"/>	1462	VCAN	4	
<input type="checkbox"/>	3659	IRF1	4	
<input type="checkbox"/>	1252	CCR3	3	
<input type="checkbox"/>	5265	SERPINA1	3	5.65
<input type="checkbox"/>	672	BRCA1	3	
<input type="checkbox"/>	5971	RELB	3	
<input type="checkbox"/>	5473	PPBP	3	6.76
<input type="checkbox"/>	4501	MT1X	3	14.76
<input type="checkbox"/>	1994	ELAVL1	3	

2D

**Current Selections**

**Input nodes**

- VCAN
- SP1
- CD93
- PLD3
- FPR1

**Function Explorer**

Query: All nodes Database: KEGG (gene) Submit

Name	Hits	P-val	P-val(ac)
------	------	-------	-----------

**Module Explorer**

Algorithm: InfoMap Submit

Module	Size	P-value	Color
--------	------	---------	-------

Guilt-by-Association Analysis  
Regulation Explorer  
Path Explorer  
Batch Selection

Previous Logout

# Enrichment analysis uncovers involved pathways

Selecting enriched pathways will highlight corresponding genes in the network.

The screenshot displays a network analysis software interface. The central part of the interface shows a network graph with nodes of various sizes and colors (red, blue, green) connected by edges. A callout box points to a 'Submit' button in the Function Explorer table, with the text 'Perform enrichment analysis by click on submit here.'

**Global Node Styles**

Type	Size	Color
Gene	<input type="range"/>	<input type="color" value="#ff0000"/>
Tf	<input type="range"/>	<input type="color" value="#00ff00"/>

**Node Explorer**

ID	Name	Degree	Betweenness	Exp	
<input type="checkbox"/>	7316	UBC	23	1165.163	
<input type="checkbox"/>	6667	SP1	17	1358.68	-4.5
<input type="checkbox"/>	6354	CCL7	7	188.9769	
<input type="checkbox"/>	3172	HNF4A	7	159.4487	
<input type="checkbox"/>	6363	CCL19	7	428.2274	6.97
<input type="checkbox"/>	4790	NFKB1	6	188.8004	
<input type="checkbox"/>	3627	CXCL10	6	201.5519	3.04
<input type="checkbox"/>	5970	RELA	6	230.181	
<input type="checkbox"/>	6367	CCL22	5	97.91905	61.1
<input type="checkbox"/>	1462	VCAN	4	136.9729	19.7
<input type="checkbox"/>	4501	MT1X	3	49.67017	
<input type="checkbox"/>	5597	MAPK6	3	30.66667	
<input type="checkbox"/>	5265	SERPINA	3	79.86675	21.0
<input type="checkbox"/>	3659	IRF1	3	209.5857	
<input type="checkbox"/>	5473	PPBP	3	53.67333	51.0
<input type="checkbox"/>	960	CD44	3	85.21872	
<input type="checkbox"/>	196	AHR	3	143.8577	
<input type="checkbox"/>	1994	ELAVL1	3	38.38986	

**Function Explorer**

Name	Pval	AdjP	Col		
<input type="checkbox"/>	phosphatidylinositol	12	8.68e-12	2.92e-9	
<input type="checkbox"/>	Sphingolipid signal	14	1e-10	1.69e-8	
<input checked="" type="checkbox"/>	FoxO signaling path	14	3.21e-8	0.0000276	
<input type="checkbox"/>	Fc epsilon RI signal	9	3.29e-8	0.0000276	
<input type="checkbox"/>	Thermogenesis	7	0.000217	0.00146	
<input type="checkbox"/>	Insulin resistance	7	0.000054	0.00303	
<input type="checkbox"/>	Huntington disease	5	0.0000766	0.00338	
<input type="checkbox"/>	Colorectal cancer	8	0.0000805	0.00338	
<input type="checkbox"/>	TNF signaling path	6	0.00016	0.00597	
<input type="checkbox"/>	Necroptosis	6	0.000585	0.0197	

**Module Explorer**

Module	Size	Query	P-value	Color
--------	------	-------	---------	-------

**Current Selections**

**FoxO signaling pathway**

- CCR4
- CCL22 61.12
- PPBP 51.06
- CCL7
- IL3RA 12.04
- CXCL10 3.04
- CCR1
- CCL19 6.97
- CCL1
- CCL24

# 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

Network: subnetwork1 Background: Purple-gradient Layout: Concentric circle Styling: Label Scope: -- Specify -- Download: -- Specify -- More Options

**Global Node Styles**

Type	Size	Color
Gene	<input type="range"/>	<input type="checkbox"/>
Tf	<input type="range"/>	<input type="checkbox"/>

**Node Explorer**

Gene	Size	Color	Exp
6667	SP1	17	1358.68
6354	CCL1	188.9769	21.0
4087	SMAD2	1	21.0
6369	CCL24	1	0
50943	FOXP3	2	11.45238
4494	MTIF	1	0
4501	MT1X	3	49.67017
4316	MMP7	1	0
771	CA12	2	41.21334
6346	CCL1	2	21.40772
6367	CCL22	5	97.91905
5473	PPBP	3	53.67333
2357	FPR1	1	0
5265	SERPINA3	3	79.86675

**Current Selections**

**FoxO signaling pathway**

CCR4	
CCL22	6.97
PPBP	6.76
CCL7	21.04
IL3RA	4.21
CXCL10	-9.89
CCR1	
CCL19	4.08
CCL1	7.07
CCL24	19.76

**Fuction Explorer**

Query: All nodes Database: KEGG (gene)

Name	Hits	Pval	AdjP	Col
Phosphatidylinositol	12	8.68e-12	2.92e-9	
Sphingolipid signal	14	1e-10	1.69e-8	
<input checked="" type="checkbox"/> FoxO signaling path	14	3.21e-8	0.0000276	
Fc epsilon RI signal	9	3.29e-8	0.0000276	
Thermogenesis	7	0.0000217	0.00146	
Insulin resistance	7	0.000054	0.00303	
Huntington disease	5	0.0000766	0.00338	
Colorectal cancer	8	0.0000805	0.00338	
TNF signaling path	6	0.00016	0.00597	
Necroptosis	6	0.000585	0.0197	

**Module Explorer**

Algorithm: InfoMap

Module	Size	Query	P-value	Color
<input type="checkbox"/> 0	18	183	1.25e-05	

<< Previous

Logout >>

The End

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