



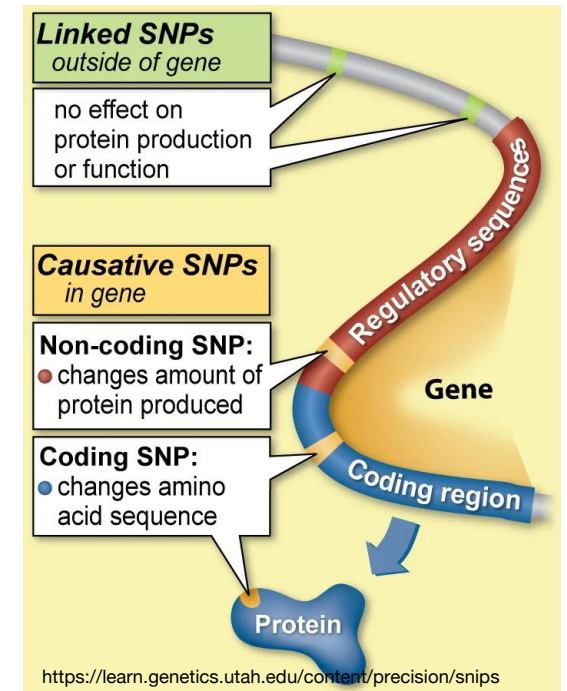
# OmicNet Tutorial: Build network from a SNPs list

# 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

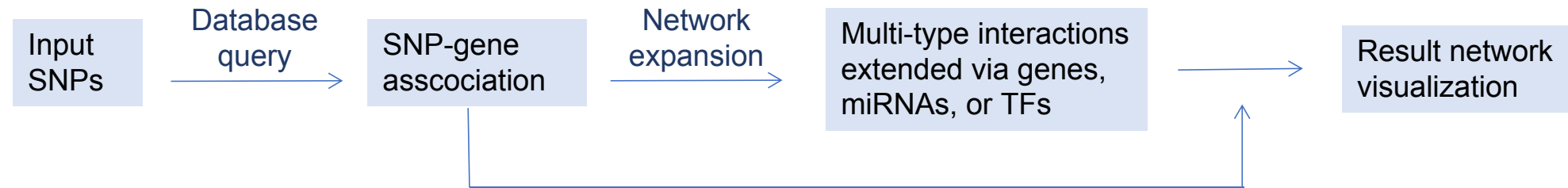
# Motivation

- **Background:** Single nucleotide polymorphism (SNP), the simplest form of DNA variation among individuals, was known to be responsible for interindividual differences in various phenotypes including disease states, cellular processing and drug response. Identify and annotate the numerous variations in genes can serve as a stepping stone for better understanding of their impact on gene functions and for further facilitating treatment options and future drug discovery.
- **Bottleneck:** Despite our accumulating knowledge to the human genome landscape and documentation of sequence variations among individuals due to the advances in genome sequencing during the past two decades, the functional interpretation of the SNPs is still at the starting point.



# Overview

- **Aim:** To facilitate the understanding of the potential function of the user interested SNPs.
- **Procedure:**



- **SNP Annotation Database:** Ensembl Variant Effect Predictor (VEP) toolset and PhenoScanner<sub>v2</sub> are leveraged to query the general SNP-gene association for the input SNPs. User can choose either the positional mapping or to use the expression quantitative trait loci (eQTL) analysis. ADmiRE and SNP2TFBS are dedicated specifically for mapping SNPs to miRNAs and transcription factor binding sites.
- **Network expansion:** The SNP-gene interaction can be extended via genes, miRNAs, or TFs (e.g. by adding PPI)
- **Network analysis and visualization:** Approches such as Steiner forest can be used to pruning the network for better understanding the potential functional pathway in downstream. The final relsult will be present as an interactive multi-layers network.

# 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			
Network analysis of one or more list(s) of molecules	Genes	Proteins	Transcription Factors	miRNAs	Metabolites

[▶ Proceed](#) [↺ Reset](#)

### Upload a list of SNPs

Enter your data below: ?

Specify organism:

Set ID type:

```
rs1428554
rs41290504
rs3197999
rs516246
rs2228058
```

Use our example data

[▲ Upload](#) [Cancel](#)

Users can upload a **SNP list** using **rsID** to start the analysis.  
We support only for **human** study currently.

# Database Selection

Input list(s) ?

SNP (5)

Records of type and number of the input list

## 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

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

**Set Parameters for SNP-Gene interaction**

Expression quantitative trait loci (eQTLs) analysis  
 Positional mapping nearest gene

Submit

**Set Parameters for SNP-Gene interaction**

Genes within  kb  
 Top  nearest gene(s) within 50kb

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
SNP	SNP Annotation	78 - 73 - 5			
Gene	PPI	574 - 642 - 0			
Gene	Metabolite-protein	289 - 296 - 0			

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Proceed >>

Records of the generated network that users can browse, download or deleted accordingly

Users need to select the database and related parameter to perform the SNP-gene association:

- PhenoScanner: positional mapping merely provide the nearest gene associated with the input SNPs; eQTLs analysis provide all the related genes within 500 Kb with P value < 10<sup>-5</sup>.
- VEP: user need to select either the distance (5kb~50kb) or a top rank to perform the positional mapping.

Details for the database please refer to FAQ #8

# Network expansion

In the **database selection page**, users can also expand their SNP-gene network:

The SNP-gene network can be extended to include Protein-protein, miRNA-gene, or TF-gene interactions by querying the related databases.

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- [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

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« < 1 > »

Users can trace the networks built in different types individually:

# Network interaction table

For each individual network, an interaction table is provided for users to dig into the details of their query results in :

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Gene	PPI	574 - 642 - 0			
Gene	Metabolite-protein	289 - 296 - 0			

Note: Query ID list is the input SNPs for the first network and result genes can be used as queries in the following networks, and so forth.

**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 ↑↓	Query ID	Id2 ↑↓	Result ID	Name1 ↑↓	Query Name	Name2 ↑↓	Result Name	Action
rs1428554		134466		rs1428554		ZNF300P1		Delete
rs1428554		345611		rs1428554		IRGM		Delete
rs1428554		91975		rs1428554		ZNF300		Delete
rs1428554		2878		rs1428554		GPX3		Delete
rs1428554		55696		rs1428554		RBM22		Delete
rs1428554		10318		rs1428554		TNIP1		Delete
rs41290504		RP11-129J12.2		rs41290504		RP11-129J12.2		Delete
rs41290504		159296		rs41290504		NKX2-3		Delete
rs41290504		7484		rs41290504		WNT9B		Delete
rs41290504		55280		rs41290504		CWF19L1		Delete
rs3197999		327		rs3197999		APEH		Delete
rs3197999		7318		rs3197999		UBA7		Delete
rs3197999		100847079		rs3197999		MIR5193		Delete
rs3197999		4485		rs3197999		MST1		Delete
rs3197999		8927		rs3197999		BSN		Delete

Navigation: << Previous (1 of 5) 1 2 3 4 5 >> 15 Proceed >>

Users can tailor their network by deleting the results they are not interested in



# Network Building

After generating the network individually, users will be lead to the summary of the integrated network:

## Network Tools ?

Degree Filter

Betweenness Filter

Minimum Network

Steiner Forest (PCSF)

Tissue Filter

P-value Filter

Zero-order Network

Reset to First-order

Methods for pruning and tailoring the network for better visualization and enhanced functional interpretation

## Multi-omics Network Building

If more than one network was generated in the previous page, they are merged together to form multi-omics network through shared nodes. In some cases, the result will contain a larger subnetwork containing most of queries, and several smaller subnetworks containing one or a few queries. These subnetworks will be available for visual analysis in the next page.

If the network is too large, it is recommended to trim the network to a smaller size that is suitable for visual analytics (less than 2000 nodes), you can use network tools located on the left hand side for trimming and filtering.

Networks	Sizes (node# - edge# - seed#)	Topology	Download (edge list)
subnetwork1	168 - 230 - 3	<a href="#">Details</a>	<a href="#">Download</a>
subnetwork2	5 - 4 - 1	<a href="#">Details</a>	<a href="#">Download</a>
subnetwork3	4 - 3 - 1	<a href="#">Details</a>	<a href="#">Download</a>

<< < 1 > >>

Detail topology information of the final integrated network.

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Proceed for visualization

# Network Visualization

Network: subnetwork1 Background: Black Layout: Circular Bipartite/Tripartite Styling: -- Specify -- Scope: -- Specify -- Download: -- Specify -- More Options ?

**Global Node Styles**

Type	Size	Color
SNP	<input type="range"/>	<input type="checkbox"/> Orange
Metabolite	<input type="range"/>	<input type="checkbox"/> Yellow
Gene/Protein	<input type="range"/>	<input type="checkbox"/> Red

**Node Explorer**

ID	Name	Degree	Betweenness	Expri
<input type="checkbox"/>	8605 PLA2G4C	8	977.7284	
<input type="checkbox"/>	C00002 Adenosine	7	446.0403	
<input type="checkbox"/>	7318 UBA7	7	352.0435	
<input type="checkbox"/>	63891 RNF123	7	352.0435	
<input type="checkbox"/>	55907 CMAS	7	839.7194	
<input type="checkbox"/>	7867 MAPKAP	7	394.9176	
<input type="checkbox"/>	5576 PRKAR2	7	394.9176	
<input type="checkbox"/>	rs142855 rs1428554	6	820	
<input type="checkbox"/>	51171 HSD17B1	6	498.3092	
<input type="checkbox"/>	C00008 ADP	5	233.4984	
<input type="checkbox"/>	4486 MST1R	5	398.9176	
<input type="checkbox"/>	7375 USP4	5	439.3987	
<input type="checkbox"/>	339221 ENPP7	5	609.6239	
<input type="checkbox"/>	8372 HYAL3	5	550.8836	
<input type="checkbox"/>	64180 DPEP3	5	415.3523	
<input type="checkbox"/>	C00013 Pyrophosphate	4	107.0014	

**Current Selections**

- Name: S-aminomethylidihydroipoamide
- KEGG:

**Function Explorer**

Query: All nodes Database: KEGG (Metabolite) Submit Save

Name	Hits	P-val	P-val(adj.)	Color
AMPK signaling pathway	4	0.00115	0.0159	
Glutathione metabolism	5	0.00123	0.0159	
Glycosaminoglycan biosynthe	2	0.00139	0.0159	
RNA transport	2	0.00139	0.0159	
Influenza A	2	0.00139	0.0159	
Ovarian steroidogenesis	4	0.00159	0.0174	
Sphingolipid metabolism	4	0.00186	0.019	
Synaptic vesicle cycle	3	0.0019	0.019	
Lysosome	2	0.00274	0.0253	
Apoptosis	2	0.00274	0.0253	
Gastric acid secretion	3	0.00305	0.0271	

**Module Explorer**

Algorithm: InfoMap Submit Save

Module	Size	Qu	P-value	Color
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**Network Visualization**

Result list of the SNPs and their associated genes or other features queried

Result panel provides the detail information of the highlight nodes

Functional pathway enrichment

**The End**

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