

MiMI Plugin User Guide

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OVERVIEW

About data sources

The MiMI Plugin provides access to data in the MiMI database from within the Cytoscape bioinformatics network visualization tool. The MiMI database integrates molecular data from numerous protein-interaction databases, including:

- BIND (Biomolecular Interaction Network Database)
 (<u>http://bond.unleashedinformatics.com/</u>)
- CCSB (Center for Cancer Systems Biology) (<u>http://ccsb.dfci.harvard.edu/web/www/ccsb</u>)
- DIP (Database of Interacting Proteins) (<u>http://dip.doe-mbi.ucla.edu/dip/Main.cgi</u>)
- GRID (General Repository for Interaction Datasets) (<u>http://www.thebiogrid.org/</u>)
- HPRD (Human Protein Reference Database) (<u>http://www.hprd.org/</u>)
- IntAct (<u>http://www.ebi.ac.uk/intact/main.xhtml</u>)
- KEGG (Kyoto Encyclopedia of Genes and Genomes) (<u>http://www.genome.jp/kegg/</u>)
- MDC (Max Delbrück Center) (<u>http://www.mdc-berlin.de/en/index.html</u>)
- MINT (Molecular INTeraction database) (<u>http://mint.bio.uniroma2.it/mint/Welcome.do</u>)
- PubMed (<u>http://www.ncbi.nlm.nih.gov/pubmed/</u>)
- Reactome
 (<u>http://www.reactome.org/</u>)

Each of these data sources is updated on its own schedule. The MiMI Plugin reflects updates as they become available.

For information on additional data sources available through the MiMI Plugin, see the <u>About MiMI</u> page.

Workflow overview

With the MiMI Plugin for Cytoscape, you can visualize interactions between genes or proteins, and interactively explore the network of relationships among them. The basic steps in the workflow include:

- 1. <u>Enter a set of genes</u>. You can type in a list of genes or upload a file of gene symbols.
- 2. <u>Select gene and gene interaction attributes</u>. Choose which attributes to display in a table as you work with a visual network graph, including any attributes you import into Cytoscape.
- 3. Explore the visual network and table of attributes:
 - Expand and collapse the network.
 - Sort and filter data.
 - Visualize your data in a wide variety of network layouts provided by Cytoscape.
 - Use color, size, and other effects to visually reflect a set of attribute values.
- 4. Select genes or gene interactions to access more detailed information about them:
 - Link out to additional information about selected objects.
 - <u>Access summaries of abstracts</u> mined from the research literature through natural language processing (BioNLP) related to a selected gene interaction.
 - Compare a part of your network to a database of known biological pathways.
- 5. <u>Save your session and reopen it later</u>.

INSTALLING CYTOSCAPE AND THE MIMI PLUGIN

You can use the MiMI Plugin for Cytoscape in one of two ways:

- **By launching Cytoscape and the MiMI Plugin from MiMI Web**. With this method, you launch a temporary copy of Cytoscape and the MiMI Plugin from a Gene Details page after performing a search on MiMI Web. Use this method when you don't have the administrative privileges to install software on your computer. You will not have access to other plugins when you use this method.
- **By installing Cytoscape and the MiMI Plugin on your local computer**. With this method, you can use other plugins that work with MiMI data, such as Shortest Path and MCODE.

Launching Cytoscape and the MiMI Plugin from the Web

To launch Cytoscape and the MiMI Plugin from MiMI Web:

- 1. Go to http://mimi.ncibi.org/MimiWeb/main-page.jsp.
- 2. On the **Free Text Search** or **List Search** tab, search for one or more genes. (For more information on searching in MiMI Web, click the **Help** tab.)
- 3. On a **Search Results** page, click a gene link.
- 4. On the **Gene Details** page, click the **Cytoscape** button near the bottom of the page.

After launching the Web version of Cytoscape, you can do anything described in this User Guide.

You can save your Cytoscape session on your local computer and reopen it at a later time after launching the application from MiMI Web again.

Installing Cytoscape and the MiMI Plugin on your local computer

- 1. Install Cytoscape on your computer. For more information, go to:
 - The Cytoscape website at <u>http://cytoscape.org/</u>.

or

- The NCIBI Virtual Workshop page at http://portal.ncibi.org/gateway/virtual-workshop.html.
- 2. After Cytoscape is installed, start the application.
- To install the MiMI Plugin, select Plugins → Manage Plugins from the Cytoscape menu.

4. Under **Available for Install**, click the **+** box to expand the **Network and Attribute I/O** group.



5. Find and click the most recent version of the MiMI Plugin.



- 6. Click Install.
- 7. When installation is complete, click **Close**.
- A **MiMI Plugin** option is added to the Cytoscape **Plugins** menu.

ENTERING GENE INFORMATION

- 1. To begin a Cytoscape session with the MiMI Plugin, start Cytoscape.
- 2. Select **Plugins** \rightarrow **MiMI Plugin** \rightarrow **Query** from the Cytoscape menu.
- 3. Choose one of these methods to specify genes.

Option 1: Load a file containing gene symbols

Use when you have a large number of gene symbols. The file:

- Must be a text file.
- Must include a list of official gene symbols, one per line.

Example:

CP
HFE
SLC39A14
FTL
LCN2
TF
UGT1A1
NPC2
B4GALT1
PLD4
SGP11
EDG3
SOAT1
ABCA1

1. Click the **From File** tab.

🐇 Welcome to MiMI Plugin 3.0.1		
Enter Gene Symbol(s) From File		
Query MiMI		
	A Sample File	

- 2. Click Load Gene File...
- 3. Browse to the gene file and click **Open**.
- 4. Continue with <u>Additional options</u>.

Option 2: Enter a list of gene symbols

Use to do a query with a small number of gene symbols.

1. On the **Enter Gene Symbol(s)** tab, enter one or more gene symbols, separated by commas.

الله Welcome to MiMI Plugin 3.0.1	
Enter Gene Symbol(s) From File	
Query MiMI	
CP,HFE,SLC39A14,FTL	(Official Gene Symbols: e.g. csf1r,ccnt2)
Homo sapiens 🔹 🖌 All Molecule Types 👻 All Data Sources 👻	
What to retrieve 1. Query genes + nearest neighbors	▼
Search	

Additional options

1. Select an organism, molecule type, and/or data source, or use the defaults.

Note: Selecting **All Data Sources** includes all of the other data sources listed in the dropdown, as well as additional data sources. For a complete list of data sources, see the <u>About MiMI</u> page.

Dialog box after loading a file containing gene symbols:

🕌 MiMI Plugin	
Use default parameters or change them	
Homo sapiens All Molecule Types All Data Sources	
What to retrieve 1. Query genes + nearest neighbors	•
Search	

Dialog box after entering a list of gene symbols:

الله Welcome to MiMI Plugin 3.0.1	
Enter Gene Symbol(s) From File	
Query MiMI	
CP,HFE,SLC39A14,FTL	(Official Gene Symbols: e.g. csf1r,ccnt2)
Homo sapiens 🔹 🖌 All Molecule Types 👻 All Data Sources 👻	
What to retrieve 1. Query genes + nearest neighbors	•
Search	

 For What to retrieve, select one of the following options (examples show resulting networks for entering a list of the gene symbols CP, HFE, SLC39A14, and FTL):

Query genes + nearest neighbors



26 nodes, 32 edges

Interactions among query genes (include at least 2 genes)







4,607 nodes, 28,221 edges

Nearest neighbors shared by more than one query genes (include at least 2 genes)



2 nodes, 1 edge

3. Click Search.

CHOOSING ATTRIBUTES FOR DISPLAY IN THE DATA PANEL

Attributes of genes (nodes) and gene interactions (edges) you have selected in the network appear in the Cytoscape Data Panel.

Choosing attributes provided through MiMI

To choose which attributes to view:

- To choose attributes for gene nodes, click the Node Attribute Browser tab in the Data Panel; for gene interaction edges, click the Edge Attribute Browser tab.
- 2. Click the **Select Attributes** icon in the Data Panel toolbar.



3. Select the attributes you want displayed in the Data Panel.



Note: Other plugins used earlier in your Cytoscape session may leave behind attributes that don't apply to MiMI Plugin data.

4. When you are done, click anywhere outside the list.

NCIBI

5. Select genes or gene interactions to view their attributes in the Data Panel (see "<u>Selecting Genes and Gene Interactions</u>").



Importing your own attributes

To add your own attributes to the Data Panel, you can import an attribute file. The file:

- Must be a text file or a Microsoft Excel 97-2003 workbook file (.xls).
- If a text file:
 - Attributes (columns) must be tab-separated.
 - Records (rows) must be on their own line.
- Attribute names (column headings) are optional.
- One column must be a key column (for example, Gene Symbol) to map to a key attribute in the existing network.

Excel example:

	Ke	y column	\mathbf{D}	Optional column	headings
1	A P	В	С		E
1	Gene Name	p-Value A	p-Value B	GO term	
2	CP	0.038	0.007	iron homeostatis	Heme metabolism
3	HFE	0.011	0.001	iron homeostatis	Heme metabolism
4	SLC39A14	0.17	0.06	iron homeostatis	Heme metabolism
5	FTL	0.302	0.007	iron homeostatis	Heme metabolism
6	LCN2	0.55	0.08	iron homeostatis	Heme metabolism
7	TF	0.6	0.06	iron homeostatis	Heme metabolism
8	UGT1A1	0.001	0.0004	iron homeostatis	Heme metabolism
9	NPC2	0.34	0.008	Cholesterol Homeostatis	
10	B4GALT1	0.28	0.003	Sphingolipid Metabolism	
11	PLD4	0.38	0.0001	Sphingolipid Metabolism	
12	SGP11	0.044	0.009	Sphingolipid Metabolism	
13	EDG3	0.016	0.0005	Sphingolipid Metabolism	
14	SOAT1	0.37	0.0006	Cholesterol Homeostatis	
15	ABCA1	0.008	0.004	Cholesterol Homeostatis	
16	APOD	0.002	0.001	Cholesterol Homeostatis	

For information on other importing options, see "Import Attribute Table Files" in the *Cytoscape User Manual*.

To import attributes:

 From the Cytoscape menu, select File → Import → Attribute from Table (Text/MS Excel)...

2. For **Attributes**, select **Node**, **Edge**, or **Network**, depending on the attributes you're adding, and click **Select File(s)**.

•	0	Select the attribute typ			
)ata Sources Attributes Input File	Node	© Edge © Network	lick Se	Sele	ct File(s)
dvanced					
Show Map	ping Options	Show Text File Import Options I Import everything (Key is always ID)	Case	Sensitive	
review Le	eft Click:	Enable/Disable Column, Right Click: Edit Column	L	egend: Key	Alias
review	eft Click: ew Window	Enable/Disable Column, Right Click: Edit Column	L	egend: Key Key Attributes 10117	Alias
review	eft Click: ew Window	Enable/Disable Column, Right Click: Edit Column	L	egend: Key Key Attributes 10117 10200	Alias
review	eft Click:	Enable/Disable Column, Right Click: Edit Column		egend: Key Key Attributes 10117 10200 10381	Alias
review	eft Click: ew Window	Enable/Disable Column, Right Click: Edit Column	U \$	egend: Key Key Attributes 10117 10200 10381 10382 10577	Alias
review	eft Click:	Enable/Disable Column, Right Click: Edit Column	L 	egend: Key Key Attributes 10117 10200 10381 10382 10577 10672	Alias
r review	eft Click:	Enable/Disable Column, Right Click: Edit Column	¢	egend: Key Key Attributes 10117 10200 10381 10382 10577 10672 10720	Alias
r review L€ Data File Previ	eft Click: ew Window	Enable/Disable Column, Right Click: Edit Column	L ¢	egend: Key 10117 10200 10381 10382 10577 10672 10720 1356	Alias

3. Browse to your attribute file, and click **Open**. Attribute data is imported:

	Import A	ttribute from	Table				
ata Sources Attributes (@) Input File (File:	Node () Edge () Ne C: Users /Deskto	twork pp/CytoiHemeAndSphin	gNoHdgReadInList.xls			Sele	ct File(s)
Show Mapping O	ptions 📄 Show Text I	File Import Options	Import everything (Key is always ID)	V Case Se	ensitiv	/e	
ibeet1	orkbook <mark>Left Cli</mark>	ick: Enable/Disal	ble Column, Right Click: Ec	lit Colum	IN L	egend: Key	Alias
Excel™ W Sheet1 ✓ Column 1 Gene Name	orkbook Left Cli	ick: Enable/Disal	ble Column, Right Click: Ed	lit Colum	in L	egend: Key Key Attributes 10117 10200 10381	Alias
Excel™ W iheet1 ✓ Column 1 <u>Gene Name</u> CP	orkbook Left Cli Column 2 p-Value A 0.038	ick: Enable/Disal	ble Column, Right Click: Ed	lit Colum	In L	egend: Key Key Attributes 10117 10200 10381 10382	Alias
Excel™ W Sheet1 ✓ Column 1 Gene Name CP HFE	vrkbook Left Cli ✓ Column 2 p-Value A 0.038 0.011	ick: Enable/Disal	ble Column, Right Click: Eo ✓ Column 4 GO term iron homeostatis iron homeostatis	lit Colum ⊗ → ↓ ▲	in L	egend: Key Key Attributes 10117 10200 10381 10382 10572	Alias
Excel TM W Sheet1 Column 1 Gene Name CP HFE SLC39A14	 ✓ Column 2 p-Value A 0.038 0.011 0.17 	ick: Enable/Disal	ble Column, Right Click: Eo ✓ Column 4 GO term iron homeostatis iron homeostatis	lit Colum	in L	egend: Key Key Attributes 10117 10200 10381 10382 10577	Alias
Excel™ Wi Sheet1 ✓ Column 1 Gene Name CP HFE SLC39A14 FTL	 ✓ Column 2 p-Value A 0.038 0.011 0.17 0.302 	ick: Enable/Disal ✓ Column 3 p-Value B 0.0070 0.0010 0.06 0.0070	ble Column, Right Click: Eo ✓ Column 4 GO term iron homeostatis iron homeostatis iron homeostatis iron homeostatis	lit Colum	in L	key Attributes 10117 10200 10381 10382 10577 10672	Alias
Excel™ W Sheet1 ✓ Column 1 Gene Name CP HFE SLC39A14 FTL LCN2	 ✓ Column 2 P-Value A 0.038 0.011 0.17 0.302 0.55 0.55 	ick: Enable/Disal ✓ Column 3 p-Value B 0.0070 0.0010 0.06 0.0070 0.08	ble Column, Right Click: Ed ✓ Column 4 GO term iron homeostatis iron homeostatis iron homeostatis iron homeostatis iron homeostatis	lit Colum	in L	Legend: Key Key Attributes 10117 10200 10381 10382 10577 10672 10720	Alias
Excel™ Wo Sheet1 Column 1 Gene Name CP HFE SLC39A14 FTL LCN2 TF	 ✓ Column 2 p-Value A 0.038 0.011 0.17 0.302 0.55 0.6 	 ick: Enable/Disal ✓ Column 3 p-Value B 0.0070 0.06 0.0070 0.08 0.06 	ble Column, Right Click: Eo ✓ Column 4 GO term iron homeostatis iron homeostatis iron homeostatis iron homeostatis iron homeostatis iron homeostatis	lit Colum	n L	key Attributes 10117 10200 10381 10382 10577 10672 10720 1356	Alias
Excel™ Wi Sheet1 Column 1 Gene Name CP HFE SLC39A14 FTL LCN2 TF ✓	 ✓ Column 2 p-Value A 0.038 0.011 0.17 0.302 0.55 0.6 	ick: Enable/Disal ✓ Column 3 p-Value B 0.0070 0.006 0.0070 0.08 0.06 0.06	ble Column, Right Click: Eo ✓ Column 4 GO term iron homeostatis iron homeostatis iron homeostatis iron homeostatis iron homeostatis iron homeostatis	lit Colum	in L	egend: Key Key Attributes 10117 10200 10381 10382 10577 10672 10720 1356	c Alia:

4. If your attribute file includes attribute names as column headings, select **Show Text File Import Options**, and then select **Transfer first line as attribute names**.

	Select	Import Options	•
Advanced			
Show Mapping Option	s 🔽 Show Text File Ir	mport Options 📄 Imp	ort everything (Key is always ID)
Text File Import Optio	ns		
Delimiter			Preview Options
Tab Comma	Semicolon 🔲 Space [Other	Show all entries in the fill
Attribute Names			Net
Transfer first line as	attribute names Start I	Import Row: 1	Comment Line: De
Excel™ Work	book Left Click	: Enable/Disable	Column, Right Click: E
✓ Gene Name	🖉 p-Value A	🖉 p-Value B	✓ GO term
CP	0.038	0.0070	iron homeostatis
HFE	0.011	0.0010	iron homeostatis
SLC39A14	0.17	0.06	iron homeostatis
	First-row val	ues become at	tribute names

If your attribute file does not include column headings for attribute names, name them by right-clicking the default column headings and entering a new attribute name.

Excel Work	book Left Click: Enable/Disable Column, Right Click: Edit Column
neet1	Set Attribute Name and Type
° Column 1 🔗	, Attribute Name and Type Then enter a new attribute n
CP	Attribute name for Column 1 entry
HFE	Column 1
SLC39A14 FTL	Attribute Data Type
LCN2	String Integer Floating Point Boolean
TF	List: List of Strings
UGTIAI	List Delimiter is: 0

5. To map your key column to the key attribute, first click **Show Mapping Options**, and then select the column from the **Primary Key** dropdown.

vanced	Manning Onling Show Text File Impo	ort Ontions		vave ID) IZ Case Sensitive	
nnotati	on File to Attribute Mapping	Select a key co	lu	imn i cue service	
Key Co	lumn in Annotation File			Key Attribute for Network	
Primary	Key: ab Gene Name				
		Data Tura	1	ID	
Alias?	Column (Attribute Name)	Data Type	1		
Alias?	Column (Attribute Name)	ata Type			
Alias?	Column (Attribute Name) Gene Name	at Type			
Alias?	Column (Attribute Name) Gene Name p-Value A D-Value B	alt String A			

6. Select the corresponding key attribute in the existing network.



- 7. Click **Import** at the bottom of the dialog box.
- 8. To view your attributes in the Data Panel, click the **Select Attributes** icon in the Data Panel toolbar and select the attributes, which will appear in the panel when you select nodes and edges that have imported attributes associated with them.

Data Pane		Imported are displ matching sel	attributes ayed when nodes are ected		
ID	Gene Name	p-Value A	p-Value B	GO term /	Component
54658	UGT1A1	0.0010	4.0E-4	iron homeostatis	endoplasmic reticulum [GO:000
10577	NPC2	0.34	0.0080	Cholesterol Homeostatis	extracellular region [GO:000557
3984	LIMK1	1.5 Porting			cytoplasm [GO:0005737]; focal :
3077	HFE	0.011	0.0010	iron homeostatis	cytoplasm [GO:0005737]; integr
79947	DHDDS				
2512	FTL	0.302	0.0070	iron homeostatis	ferritin complex [GO:0008043]
6927	HNF1A				nucleus [GO:0005634]; protein
7037	TFRC				cytoplasmic membrane-bound

Rearranging attributes in the Data Panel

To reorder attributes in the Data Panel, click an attribute column heading and drag it to a new location.

Data Panel	U.,						
	8	Click the co	lumn				
ID		Component		Gene Name			
9543	integral to memb	rane [GO:0016021]; mem	brane [G	PUNC			
8029	brush border me	mbrane [GO:0031526]; en	dosome	CUBN			
7786	cytoplasm [GO:0	005737]; cytosol [GO:0005	i829]; m	MAP3K12			
7036	cytoplasm [GO:0	005737]; integral to plasm	a memb	TFR2			
7018	endocytic vesicle	[GO:0030139]; endosome	e [GO:00	TF			
6872	nucleus [GO:000	5634]; transcription factor	TFIID co	TAF1			
5764	endoplasmic reti	culum [GO:0005783]; extra	acellular	PTN			
567	extracellular regi	on IGO:0005576]; MHC cla	ass I prot	B2M			
Data Panel	Drag the	column					
	8	\prec					
ID		Componer Gene Name					
9543	integral to memb	rane [GO:00] PUNC	Line (G				
8029	brush border me	mbrane IGO CUBN	ome				
7786	cytoplasm [GO:0	005737]; cyto MAP3K12]; m				
7036	cytoplasm [GO:0						
7018	endocytic vesicle	endocytic vesicle [GO:003013 TF D:00					
6872	nucleus [GO:000	5634]; trans(TAF1	D co				
5764	endoplasmic reti	culum (GO:0 PTN	lular				
567	extracellular	on the column inte	nositio	n			
Data Panel			positio	9			
	8						
ID	Gene Name	- Comp					
9543	PUNC N	htegral to membrane (GO:0016021); membrane (G.					
8029	CUBN 13	rush border membrane	GO:003152	26]; endosome			
7786	MAP3K12	ytoplasm [GO:0005737];	cytosol [GO	:0005829]; m			
7036	TFR2	ytoplasm [GO:0005737];	integral to p	olasma memb			
7018	TF	ndocytic vesicle [GO:003	0139]; end	osome [GO:00			
6872	TAF1	ucleus [GO:0005634]; tra	anscription	factor TFIID co			
5764	PTN	ndoplasmic reticulum [G	0:0005783]; extracellular			
567	B2M	xtracellular region [GO:0	005576]; MI	HC class I prot			

To sort by an attribute, click the attribute column heading; to sort in the reverse direction, click again.

Data Panel					
🖽 🗋 🕻	3				
ID	Gene N	ame 🗸		Component	
19	ABCA1	5	integral to pla	asma membrane (GO:0005	
335	APOA1		cytoplasmic v	esicle [GO:0031410]; endo	
336	APOA2		chylomicron [GO:0042627]; extracellular	
347	APOD		extracellular r	region [GO:0005576]; extra	
9826	ARHGEF	11	cytoplasm [G	O:0005737]; intracellular [G	
23365	ARHGEF	12	cytoplasm [G	O:0005737]; intracellular [G	
538	ATP7A		basolateral plasma membrane [GO:0/		
567	B2M		extracellular r	region [GO:0005576]; MHC	
Node Attribute Browser Edge Att			tribute Browser	Network Attribute Browser	

NAVIGATING A NETWORK

Navigating among networks

To navigate among multiple open networks, use the **Network** tab in the Cytoscape Control Panel.



To view a network, click on its entry on the **Network** tab.

Note: The default network title is a list of the queried genes followed by the options you selected for the query. To edit a title, right-click the network entry and select **Edit Network Title**.

For more information about working with networks and the **Network** tab, see the *Cytoscape User Manual.*

Navigating within a network

To navigate within a network, use the network overview pane at the bottom of the **Network** tab in the Cytoscape Control Panel.



To view another part of the network, click on the shaded area in the network overview pane and drag it into place.

To adjust the view magnification, use the Zoom tools in the Cytoscape toolbar:

- Zoom Out and Zoom In 🗘 .
- **Zoom Selected Region** . Make one or more selections using any Cytoscape methods, then click this tool to display the region that encompasses all of them.
- Zoom Entire Network

U,

For more information about zooming and using the network overview pane, see the *Cytoscape User Manual.*

Locating genes or gene interactions within a network by searching

You can locate and select a specific gene or gene interaction within a network by using the Search feature of Cytoscape. You can also use search to find a group of genes or interactions with common attribute values. Search is especially useful with large, complex networks.

Limitations of the Search feature in Cytoscape:

- For a successful match, the search term must match the entire attribute value. For example, the following Gene Description attributes do not match:
 - NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 8, 19kDa
 - NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 2, 8kDa
- For a successful match, the search term must match the attribute value from the start of the string—you cannot match a substring within an attribute value. For example, the search term Lysine biosynthesis does not match the following attribute value:
 - Citrate cycle (TCA cycle) [path:hsa00020]; Lysine biosynthesis [path:hsa00300]; D-Glutamine and D-glutamate metabolism [path:hsa00471]
- Search does not support logical operators, wildcards, or other advanced search features.

Note: For more flexible and powerful searching, including logical operators and wildcards, you can use the Enhanced Search plugin for Cytoscape. For more information, see the Analysis group of plugins on the <u>Cytoscape Plugins page</u>.

To search for genes or interactions:



2. Set search options.

Nodes C Edges		Select w	hich a	ttribu	tes to li
Select Attribute:					
Gene Name		-	Cala	o 4 4 lo o	
Chromosome			Sele	ct the	attribu
Component			t	o sea	rch by
Description		E	\succ		
Function					
GO term					
Gene Name	N				
Gene type	13				
Kegg gene		-			
Sample Attribute Values:	(1			
PREP				- 1	
EXEP4	Clic	k Annly			
SERPING1			<u>ノ</u>		
/TN					
rK2					

3. Enter a search term in the **Search** box. As you type, matching attribute values appear in a dropdown list.



4. Select an item in the list to locate the node or edge. Cytoscape zooms to the item and selects it.

Search: masp1

FZP1 AFAM1 CF M...|Homo sapiens|All Molecule Types|All Data Sources|1. Query genes + nearest neighbors|

PLG

IMASP

Note: Using Search to select a gene interaction also selects the connected genes.

Example: Locating genes on the same chromosome (chromosome 13)

1. In the **Configure Search Options** dialog, select the **Chromosome** attribute for genes (nodes).

Cor	nfigure Search Options for: FZP1 AFAM1 CF M H	Х
Sear	rch:	
0	Nodes 🔘 Edges	
Sele	ct Attribute:	
Chro	omosome 👻	
Attri	ibute Description:	
Sam	ple Attribute Values:	
1		_
6		_
1/		_
11		_
	Cancel Apply	y

2. Type in the **Search** box and select **13** (with 6 matching genes).



3. The 6 genes are selected.



4. The Data Panel displays attributes for the selected genes.

Data Panel						
ID	Chromosome	Gene Name	Component			
8428	13	STK24	cytoplasm [GO:0005737]			
8803	13	SUCLA2	mitochondrion [GO:0005739]			
1045	13	CDX2	condensed nuclear chromosome			
1282	13	COL4A1	basement membrane [GO:00056			
10562	13	OLFM4	extracellular region [GO:0005576			
1284	13	COL4A2	collagen [GO:0005581]; collagen			

Locating genes or interactions using the Data Panel

You can locate specific gene nodes and interaction edges in the network view by selecting their attributes in the Data Panel.

- 1. Click the **Node Attribute Browser** or **Edge Attribute Browser** tab in the Data Panel.
- 2. Select attribute rows for the nodes or edges you want to locate.
 - Click on a single row to highlight a single gene or interaction.
 - Use Ctrl-click to select multiple discontiguous rows.
 - Use Shift-click to select a range of contiguous rows.
- 3. The corresponding genes or interactions are highlighted in green in the network view.



Note: This procedure helps you visually identify individual nodes or edges from among those already selected in the network view, but does not create an actionable subset. Cytoscape functions will continue to operate on all selected nodes or edges, not just those you have located using this procedure.

SELECTING GENES AND GENE INTERACTIONS

Use Cytoscape methods to select nodes (representing genes) and edges (representing interactions between genes).

Selecting a single gene Click the gene node.	UTRN ENTA
A selected node appears in yellow.	CSNK2B CSNK2A2
Selecting a single gene interaction	
Click and drag a rectangle around any segment of the gene interaction edge, then release the left mouse button.	SNTA SNTA
A selected edge appears in red.	CSNK2B CSNK2A2



For more information

For detailed information on selecting nodes and edges in a network, see the *Cytoscape User Manual.*

ACCESSING GENE AND GENE INTERACTION INFORMATION

In addition to viewing gene and gene interaction attribute values in the Cytoscape Data Panel, you can link to related information in additional data sources.

Linking to gene literature through Gene2MeSH

To access PubMed articles related to a gene through matching MeSH subject headings:

- Right-click a gene node, and select MiMI Plugin → LinkOut NCIBI → Gene2Mesh.
- The Gene2MeSH page for the selected gene appears in a new browser window or tab.

	🖗 Gene2MeS	H – G	ene Annotation	with MeS	H Terms	NCIBI
Search Ge	ne2MeSH About Gene2Me	5H				
HFE	e2MeSH Search e	rch by: O G xamples: b	iene 🔍 MeSH Term 🔍 Both rca2, "Prostatic Neoplasms"	Limit Search by Or Substances only	ganism: Homo sapiens /	-
story : HFE	(109)					
🤤 = lookup g	ene or MeSH heading at NCBI; M	= view intera	actions in MiMI		Show All Columns 🔲 dov	vnload tab-delimited results
iene Symbol	MeSH Heading	TaxID	P-Value	MeSH Qualifier	Gene Description	PubMed Articles*
fe 🖗 M	Hemochromatosis 👂	9606	0	genetics	hemochromatosis	<u>392</u>
FE 🖗 M	Histocompatibility Antigens Class	9606	0	genetics	hemochromatosis	<u>456</u>
EE 👂 M	Membrane Proteins 🖻	9606	0	genetics	hemochromatosis	<u>457</u>
FE 📚 M	Iron 🖻	9606	3.8973051127583E-281	metabolism	hemochromatosis	<u>168</u>

For more information about using Gene2MeSH, see the Gene2MeSH About page.

Linking to detailed information on MiMI Web

To access more detailed information about a gene or gene interaction:

- 1. Right-click a gene node or gene interaction edge, and select MiMI Plugin → LinkOut NCIBI → MiMIWeb.
- 2. The Details page in MiMI Web for the selected gene or interaction appears in a new browser window or tab.

For a gene:

Free Text Search List Search Query	INTERCOLAR IN	Help
Gene Details	eneId: 3077) - <u>show/hide</u>	
emochromatosis	Gene Attributes	
FE(Homo sapiens) Gene Type: protein-coding Chromosome: 6 Map Locus: 6p21.3 Locus Tag: null ther Names HFE dJ221C16.10.1 HFE1 HH HLA-H MGC103790 escriptions Authorized Gene Description: hemochromatosis Other descriptions MHC class I-like protein HFE hemochromatosis protein HLA-H	Cellular Components MHC class I protein complex cytoplasm integral to plasma membrane membrane plasma membrane	Biological Processes antigen processing and presentatio of peotide antigen via MHC class I cellular iron ion homeostasis immune response ion transport iron ion transport protein complex assembly receptor-mediated endocytosis
V Protein Interactions (3 gene interaction	s found) - <u>show/hide</u>	
Literature Mined Interactions (6 Interac	tions found) - <u>show/hide</u>	

For an interaction:

Free Text Search List Search Query Interactions About MiMI Help B Interaction Details Genes B2M Pathways - show/hide
Genes - B2M Pathways - show/hide
Genes
E B2M
Pathways - show/hide
GO GO Terms - <u>show/hide</u>
Protein Interaction Types And Annotations - <u>show/hide</u>
Provenance Sources - <u>show/hide</u>
Literature associating interactions - <u>show/hide</u>
NCTBI CONTRACTOR National Institutes of Health grant #U54DA021519. Copyright 2008 by The University of Michigan

For more information on using MiMI Web, see the <u>MiMI Help and Support page</u>.

Linking to gene interaction literature through BioNLP

To access summaries of abstracts related to a gene interaction through BioNLP (Natural Language Processing of Biology text):

1. Right-click a gene interaction edge, and select **MiMI Plugin** \rightarrow **BioNLP**.

2. A list of matching sentences appears.



Linking to other data sources

You can access gene and gene interaction information from numerous external data sources using LinkOut menus in Cytoscape.

Linking to external sources from the network view

- 1. In the Cytoscape network view, right-click a gene node or interaction edge.
- 2. Move to the **LinkOut** menu.
- 3. Choose a data source from the LinkOut submenus.

For exa	mple, selecting) Li	$nkOut \rightarrow Entre$	ez	→ Gene:
HF	3077 Visual Mapping Bypa Use Web Services		RC HNF1A		
	LinkOut	•	Database		
	MiMI Plugin MetScape	•	Reactome Model Organism DB Array Express Ensembl Gene View KEGG		ONECUTI UGT2B1
			Entrez	Þ	All Databases (Global search by free keyword)
			Interaction Databases	•	Structure
			iHOP	•	Pubmed
			Other Biological DB	1	Gene
			Ontology	•	Protein 14
			EBI Tools	•	OMIM
			UniProt	ł	Nucleotide
			Search Engines	•	

results in the following Entrez Gene page for the selected gene:

S NCBI	Intrez Gene			
All Databases Pu	ıbMed Nucleotide Protein Genome Structure C	MIM		
Search Gene	 ✓ for 3077[uid] Go 	Clear		
Limits Preview/Index	History Clipboard Details			
Display Full Report	✓ Send to ✓			
1: HFE hemochroma GeneID: 3077 Summary	tosis [Homo sapiens]			
Official Symbol	HFE			
Official Full Name	hemochromatosis			
Primary source	HGNC:4886			
See related	Ensembl:ENSG00000010704; HPRD:01993; MIM:235200			
Gene type	protein coding			
RefSeq status	REVIEWED			
Organism	n <u>Homo sapiens</u>			
Lath Carlos Alistenan	Fukari ************************************	stam		

NCIBI

Note: The external data sources available for genes differ from those available for gene interactions.

Linking to external sources from the Data Panel

When linking to external data sources from the Cytoscape Data Panel, you can link to the external source using a specific attribute value. However, not all attribute values are appropriate for all data sources.

1. In the Cytoscape Data Panel, right-click on the value in the attribute column in the row for the gene or interaction of interest.

Data Panel					
ID	Gene Name	Kegg gene		Component	
3984	LIMK1	hsa:3984		cytoplasm [GO:0005737]; focal	
3175	ONECUT1	hsa:3175		nucleus [GO:0005634]	
6927	HNF1A	hsa:6927		nucleus [GO:0005634]; protein	
10720	UGT2B11	hsa:10720		endoplasmic reticulum [GO:000	
3077	HFE	hsa:3077			
7037	TFRC	hsa:7037	2	Select from table	
				Сору	
				Select All	
				Export 🕨	
				Search hsa:3077 on the web 🕨	

2. Move to the **Search...on the web** menu, and choose an appropriate data source from the submenus.

				Ensembl Gene View	•	
Data Pane	l,			EBI Tools		
				UniProt	٠	
ID	Gene Name	Kegg gene	Componen	Model Organism DB	۲	Function
3984	LIMK1	hsa:3984	cytoplasm [GO:0005737]; foca	Entrez	•	P binding [GO:0005524]; metal
3175	ONECUT1	hsa:3175	nucleus [GO:0005634]	Array Express		equence-specific DNA binding [C
6927	HNF1A	hsa:6927	nucleus [GO:0005634]; protei			otein binding [GO:0005515]; sec
10720	UGT2B11	hsa:10720	endoplasmic reticulum [GO:0]	Other Biological DB	•	ucuronosyltransferase activity [G
3077	HFE	hsa:3077	Salast frages table	iHOP	۰.	n ion binding [GO:0005506]
7037	TFRC	hsa:7037	Select from table	KEGG	►	yeast (use ORF name)
			Сору	Interaction Databases	•	All Species (use KEGG ID)
			Select All	Reactome	•	mouse (use NCBI GeneID)
		_	Export	Ontology	•	human (use NCBI GeneID)
			Search hsa:3077 on the web >	Search Engines	•	

For example, right-clicking the value **hsa:3077** in the **Kegg gene** attribute column and selecting **KEGG** → **All Species (use KEGG ID)** results in the following KEGG page for the corresponding gene:

KEGG	Homo sapiens (human): 3077
Entry	3077 CDS H.sapiens
Gene name	HFE
Definition	hemochromatosis
Disease	H00211 Hemochromatosis (HFE)
Class	BRITE hierarchy
SSDB	Ortholog Paralog Gene cluster GFIT
Motif	Pfam: MHC_I C1-set DUF912 Peptidase_C5 PROSITE: IG_MHC IG_LIKE Motif
Other DBs	NCBI-GI: 4504377 NCBI-GeneID: 3077 OMIM: 235200 HGNC: 4886 HPRD: 01993 Ensembl: ENSG0000010704 UniProt: B2CKL0 Q30201
LinkDB	All DBs
Structure	PDB: 1A62 1DE4 Thumbnails
	Jmol
Position	6p21.3
AA seq	348 aa AA seq DB search MGPRARPALLLLMLLQTAVLQGRLLRSHSLHYLFMGASEQDLGLSLFEALGYVDD YDHESRRVEPRTPWVSSRISSQMWLQLSQSLKGWDHMFTVDFWTIMENHNHSKE ILGCEMQEDNSTEGYWKYGYDGODHLEFCPDTLDWRAAEPRAWPTKLEWERHKI

MATCHING PATHWAY GRAPHS USING SAGA

Use SAGA (Substructure Index-based Approximate Graph Alignment) with the MiMI Plugin to compare and match selected nodes and edges to a database of known biological pathways.

- 1. Select a subset of a MiMI network in Cytoscape, with the following requirements:
 - Select at least 2, but no more than 50, gene nodes.
 - Select at least 1, but no more than 80, gene interaction edges.



 Right-click any selected node and select MiMI Plugin → SAGA → Do SAGA (Choose multiple nodes & edges).

🕌 MiMI Plugin	
Query SAGA KEGG Human Pathways Percentage of Matched Nodes: 10.0	% Query Cancel

- 3. Select either **KEGG Human Pathways** or **All KEGG Pathways**.
- 4. For **Percentage of Matched Nodes**, specify the percentage of selected nodes that must match a known biological pathway for the subset of nodes to be considered a successful match with the pathway. The default is 10%.

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5. Click **Query**. The results appear in a new browser window or tab.

The Query Result:						
Result for the Query	: MiMIPlugin2SAGA					
Total Execution Time (s): 0.030983					
Number of Matches: 4	Number of Matches: 4 (excluding self matches)					
Matches Overview:						
Match No.	Match Graph Name (#Nodes, #Edges)	Graph Distance	Matching Nodes			
Match #1	path:hsa04610 (50,67) [Complement and coagulation cascades]	21.00	3 out of 8			
Match #2	path:hsa04620 (62,79) [Toll-like receptor signaling pathway]	24.00	2 out of 8			
Match #3	path:hsa04012 (53,85) [ErbB signaling pathway]	25.00	2 out of 8			
Match #4	path:hsa04630 (22,27) [Jak-STAT signaling pathway]	25.00	2 out of 8			

6. Click a link in the **Match No.** column to view a visual representation of the match between selected network nodes in your query and the matching graph.



7. To view the complete KEGG pathway that was matched, click the **[Link to KEGG Picture]** link.

WORKING WITH NETWORKS

Expanding a network on a gene node

You can expand the current network to the nearest neighbors of a gene node.

Original network:



- 1. Double-click a gene node (the *expansion seed*).
- 2. If the number of additional gene nodes exceeds 30, Cytoscape displays the number and asks if you want to continue. Click **Yes** or **No**.
- 3. If expansion continues:
 - The network expands, adding the nearest neighbors of the expansion seed.
 - The network view may be redrawn, and the expansion seed may appear in a different location.
 - On the **Network** tab in the Control Panel, the number of nodes and edges is updated.

Expanded network:



Symbols appearing in a network expansion:



Collapsing an expanded gene node

To collapse an expanded gene node, double-click the expansion seed. The network returns to its original state.

Note: For best results, if you have further expanded a network by expanding on an expansion neighbor, collapse the nodes in the reverse order in which you expanded them.

Destroying a network

To destroy a network you no longer need:

- 1. Make sure you want to destroy the network:
 - Cytoscape will not ask you to confirm the deletion.
 - Destroying the network is irreversible.
 - Note: If you want to destroy a network view without destroying the network itself, use **Destroy View** instead of **Destroy Network**. See the *Cytoscape User Manual* for more information.
- On the Network tab in the Control Panel, right-click on the network you want to destroy (the network does not need to be selected), and select Destroy Network.

SAVING AND REOPENING A SESSION

Saving a session

To save a Cytoscape session containing one or more MiMI Plugin networks:

- 1. From the Cytoscape menu, select **File → Save** (or **Save As...**).
- 2. Browse to a location for the session file.
- 3. Name the file.
- 4. Click Save.

Reopening a session

To reopen a saved session containing MiMI Plugin data:

- 1. From the Cytoscape menu, select **File** \rightarrow **Open**.
- 2. Navigate to the file location.
- 3. Select the file.

- 4. Click **Open**.
- 5. After Cytoscape reports that the session file was successfully loaded, click **Close**.

USING MIMI PLUGIN-SPECIFIC FEATURES IN CYTOSCAPE

Restoring the MiMI visual style

You may need to restore the MiMI visual style after using a different plugin that uses its own style.

Network after using the MCODE plugin with MCODE visual style



- 1. In the Cytoscape Control Panel, click the **VizMapper**[™] tab. You may need to use the scroll arrows **I** → at the top of the Control Panel to see the tab.
- 2. For Current Visual Style, select MiMI:

Cont	trol Panel			
twork	VizMapper™	Editor	Filters	Mil
Cur	rent Visual S	tyle		
Mi	MI			•

3. The MiMI visual style is restored:

Network after resetting the MiMI visual style



Annotations

You can add public or private annotations to a gene node or gene interaction edge. For more information:

- See <u>Adding your own node/edge annotation</u> in the MiMI Plugin tutorial on the NCIBI website.
- Explore on your own by right-clicking a node or edge and selecting MiMI Plugin
 → User Annotation → Add Your Annotation. (You will need to sign up and
 then sign in to create your own annotations.)

Accessing the MiMI Plugin legend

In the Cytoscape Control Panel, click the **MiMI Legend** tab. You may need to use the scroll arrows at the top of the Control Panel to see the tab.

VizMappe	er™ Editor	Filters MiMI Legend
	\diamond	Initial seed node
	\bigcirc	Neighboring node
		Expansion seed
	\bigcirc	Expansion neighbor
	0	User annotation
		Normal Interaction
	·	User annotation

Note: If you open a saved Cytoscape session, the **MiMI Legend** tab does not appear in the Control Panel until you use the MiMI Plugin to <u>enter gene information</u> in a new query.

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MiMI Plugin selection behavior

When you select nodes and edges, they are highlighted in the network view, and the attributes of the selected nodes or edges are displayed on the **Node Attribute Browser** or **Edge Attribute Browser** tab in the Cytoscape Data Panel:

