

A Quick Guide to Using Cerebral in InnateDB



- Cerebral can be used to visualize interaction networks from a set of interactions from InnateDB.
- Cerebral uses subcellular localization annotations to provide more biologically intuitive pathway-like lay-outs of interaction networks.
- Note: the subcellular localizations in Cerebral should only be used as a guide. There are many proteins with no annotated subcellular localizations and many others that have multiple possible localizations (only 1 will be shown, nuclear, extracellular and membrane localizations will take precedence over cytoplasm if there are multiple).
- InnateDB batch searching allows users to upload a list of genes along with associated gene expression data from up to 10 different conditions.
- Gene expression data can be overlaid on network data and you can visualize this in Cerebral.

Visualize Interactions in a subcellular localization-based layout using the Cerebral plugin for Cytoscape.



Click here to visualize interactions in Cerebral
You must have a recent version of Java installed.

InnateDB
A Knowledge Resource For Innate Immunity Interactions & Pathways

Home About Search Browse Download Resources

Display Options (Show/Hide)

Sorted by: Interaction Level ascending then by Group ID ascending Sort

Click here to show redundant interactions

Download XML TAB MS Excel CSV SIF Visualize Cerebral (?)

Viewing interactions 1 to 20 of 66 hits matching query (Participant idphysical_molecule: 90782)

Page(s): 1 2 3 4 [Next]

Group ID	Interaction	Interactors	Species	Interaction level	Interaction type	Supporting Publications	
14062	Coimmunoprecipitation reveals interaction between the pellino protein homolog 1(Pellino) and Interleukin-1 receptor-associated kinase 1 (IRAK) and the Interleukin-1 receptor-associated kinase-4 (IRAK4) proteins	IRAK1 :: IRAK4 :: PELI1	<i>Homo sapiens</i>	direct interaction	physical interaction	1	Interaction Details
14064	IRAK4 phosphorylates IRAK1	IRAK1 :: IRAK4	<i>Homo sapiens</i>	direct interaction	phosphorylation	1	Interaction Details
14224	IRAK1 phosphorylates TOLLIP	IRAK1 :: TOLLIP	<i>Homo sapiens</i>	direct interaction	phosphorylation	1	Interaction Details
14237	IRAK1 phosphorylates IRAK3	IRAK1 :: IRAK3	<i>Homo sapiens</i>	direct interaction	phosphorylation	1	Interaction Details
16078	IRAK1 phosphorylates IRAK2	IRAK1 :: IRAK2	<i>Homo sapiens</i>	direct interaction	phosphorylation	1	Interaction Details



Opening Interaction Data in Cerebral from an Interaction Results page in InnateDB.

- You will be prompted to open a .jnlp file.
- You are recommended to save this file to your computer and then open it – this will allow you save a copy of this dataset.
- Opening the .jnlp file directly without saving sometimes causes Cerebral to hang when loading large datasets.
- Note: to use Cerebral you need to install Java version 6 or greater.
- You can get this from <http://java.com/en/download/index.jsp>

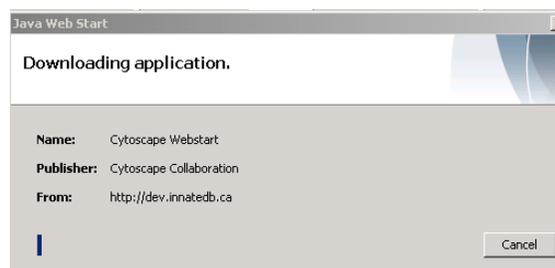
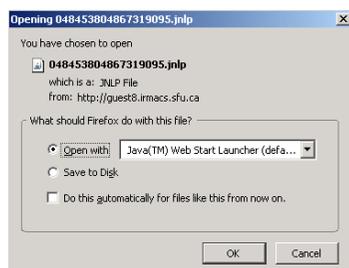
The screenshot shows the InnateDB website interface. At the top, there is a navigation bar with links: Home, About, Search, Browse, Download, Resources, Statistics, Contact, Help. Below the navigation bar, there are sorting options: "Sorted by: Interaction Level ascending then by Group ID ascending Sort". A "File Download" dialog box is open in the foreground, displaying the file name "temp_05658339911273171.jnlp", type "JNLP File", and source "dev.innatedb.ca". The dialog box has "Open", "Save", and "Cancel" buttons. Below the dialog box, a table of interaction data is visible. The table has columns: Group ID, Interaction, and several other columns. The table contains three rows of data.

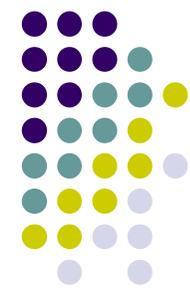
Group ID	Interaction	Interaction Level	Interaction type	Supporting Publications	Interaction Details
14062	Coimmunoprecipitation reveals interaction between pellino protein homolog 1(Pellino) and Interleukin-1 receptor associated kinase 1 (IRAK) and the Interleukin-1 receptor associated kinase-4 (IRAK4) proteins	direct interaction	physical interaction	1	Interaction Details
14064	IRAK4 phosphorylates IRAK1	direct interaction	phosphorylation	1	Interaction Details
14224	IRAK1 phosphorylates TOLLIP	direct interaction	phosphorylation	1	Interaction Details
14237	IRAK1 phosphorylates IRAK3	direct interaction	phosphorylation	1	Interaction Details



Opening Cerebral

- Cerebral is a Java plugin for the Cytoscape Visualization software.
- When you open the .jnlp file Cytoscape will begin downloading.
- You will then be prompted – “Do you want to run the application” – click Run.





Cerebral is now open and displays interactions based on protein subcellular localizations.

The screenshot displays the Cytoscape Desktop interface with a network diagram titled "temp_05658339911273171_sif.sif". The network is organized into horizontal layers representing subcellular localizations: Extracellular, Cell surface, Plasma membrane, Cytoplasm, and Nucleus. Nodes are represented by colored circles, and edges represent interactions between them. Key nodes include IL10, TRIP6, IRAK2, IL1R1, NTRK3, IRAK1, STIP1, IKKB, SQSTM1, TRAF6, TRAF3, SUMO1P3/SUMO1, ITGAM, TRAF4, IRAK1, PRKCI, MAP3K7IP1, IRAK4, PELI1, and NGFR. The interface includes a menu bar (File, Edit, View, Select, Layout, Plugins, Help), a toolbar with icons for file operations and search, and a CytoPanel 1 on the left with various settings like "Edge curviness", "Label density", and "Group label size". At the bottom, there are tabs for "Node Attribute Browser", "Edge Attribute Browser", "Network Attribute Browser", and "Parallel Coordinates".

Re-size the Network



Click here to re-size the network display to full-screen.

The screenshot shows the Cytoscape Desktop interface with a network diagram. A callout box points to the full-screen icon in the top toolbar. The network diagram is organized into layers: Extracellular, Cell surface, Plasma membrane, Cytoplasm, Nucleus, and Unknown. Nodes are represented by colored circles, and edges are lines connecting them. The interface includes a menu bar, a toolbar, a toolbar with icons for file operations, a search bar, and a toolbar with icons for network manipulation. The bottom panel shows the 'Parallel Coordinates' view.

File Edit View Select Layout Plugins Help

Cerebral Search:

temp_05658339911273171_sif

Extracellular
Cell surface
Plasma membrane
Cytoplasm
Nucleus
Unknown

IL10
TRIP6
IL1RAP ::
IRAK1
IL1R1
TLR4
NTRK3
IRAK2
IRAK1
HRAS
STIP1
IKBKB
SQSTM1
TRAF6
TRAF3
SUMO1P3/SUMO1
ITGAM
TRAF4
IRAK1
PRKCI
MAP3K7IP1
IRAK4 ::
NGFR ::
IRAK2
SIGIRR

Off Small Large
 Show function clusters
 Show layer separators
 High quality rendering
Relayout

Supporting publications
1 2 or 3 4 or more
Expression color scale
-16 0 16
Comparison color scale
-16 0 16
Significance cut-off
1 0.1 0.01 0.001 0.05
Expression cutoff
±0 ±1 ±2 ±3 ±4 1.5
 Expression data are ratios
Add group Delete group

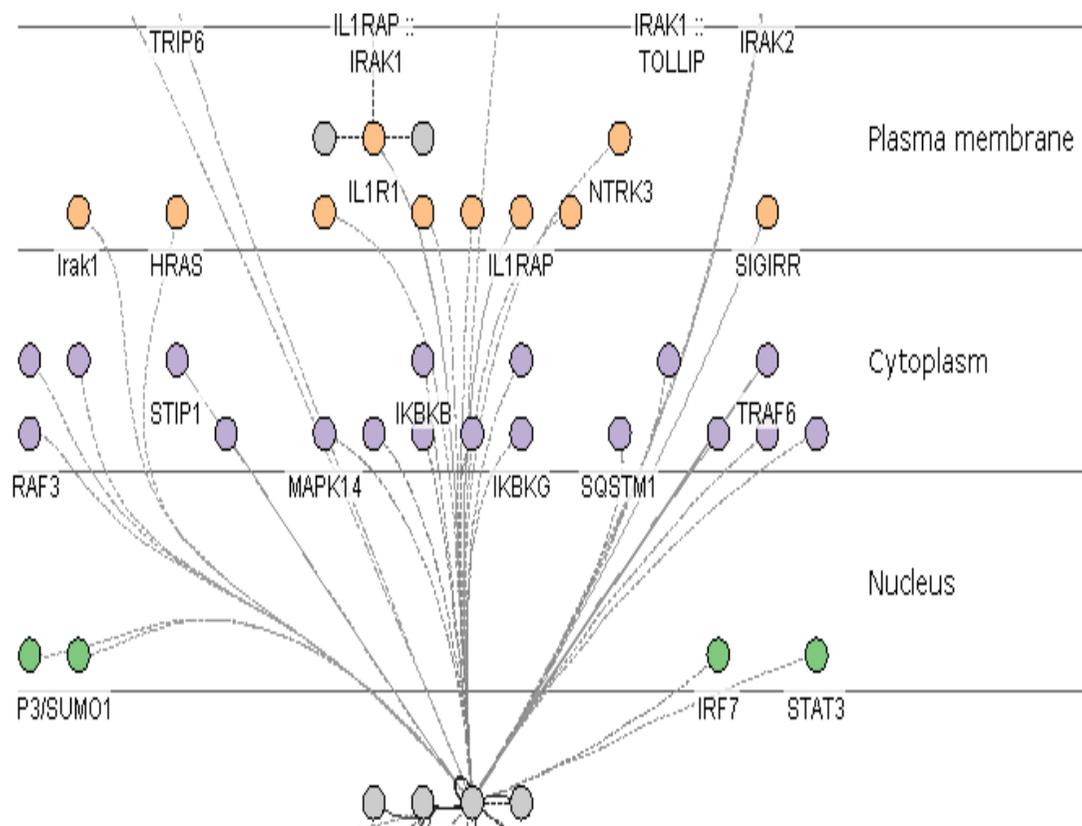
Node Attribute Browser Edge Attribute Browser Network Attribute Browser Parallel Coordinates

Welcome to Cytoscape 2.4.1 Right-click + drag to ZOOM Middle-click + drag to PAN



Navigating in Cerebral

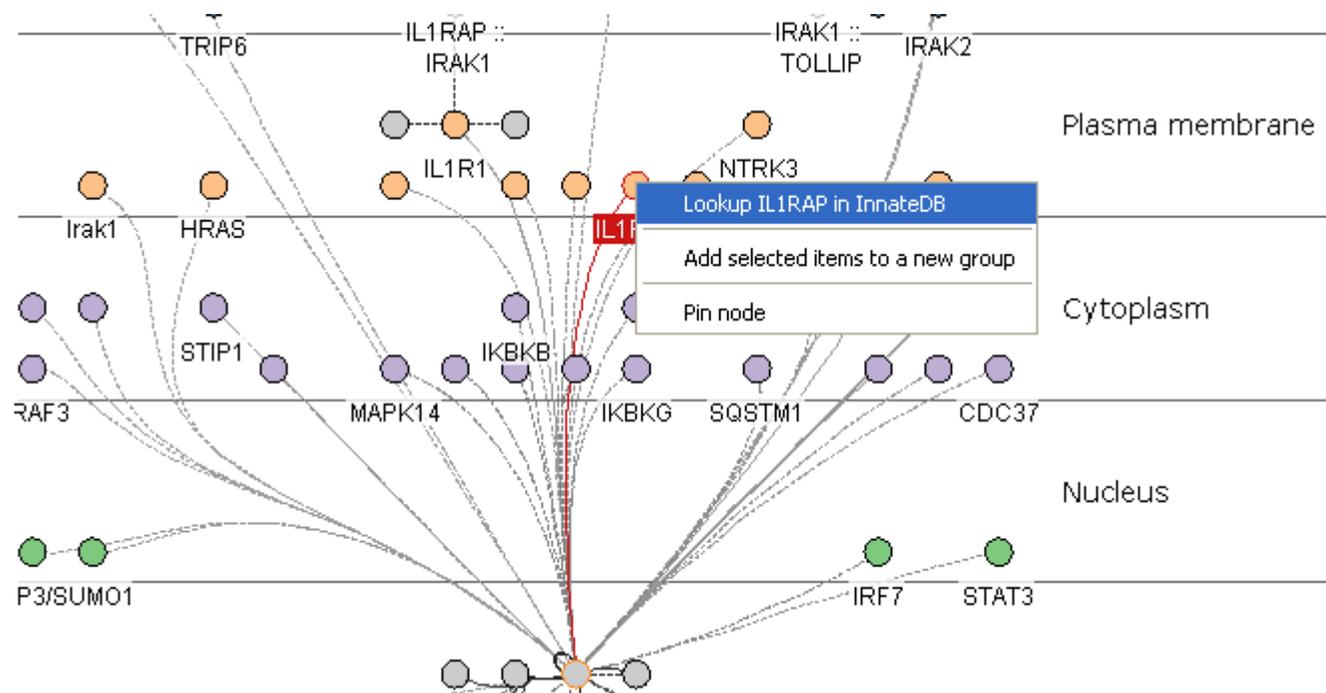
- Right click and push your mouse forward or back to zoom.
- Hold middle button of your mouse and drag to navigate around the network.
- Grey nodes do not have an annotated subcellular localization (from Gene Ontology data in InnateDB).
- Lines connecting nodes represent interactions. Dashed lines have only 1 supporting publication in InnateDB. The thicker the line the more publications support the interaction.

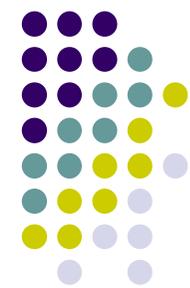




Interactively Link back to InnateDB to Look up Information on Particular Genes/Interactions of Interest.

- Right-click on a node (protein/gene) or edge (interaction line) to link to the relevant gene or interaction details page in InnateDB.





Nodes can be dragged to other layers as desired.

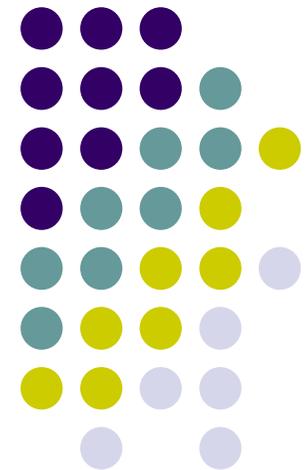
Click on & drag nodes to other layers.

Click "Node Attribute Browser" and select from list to see node attributes.

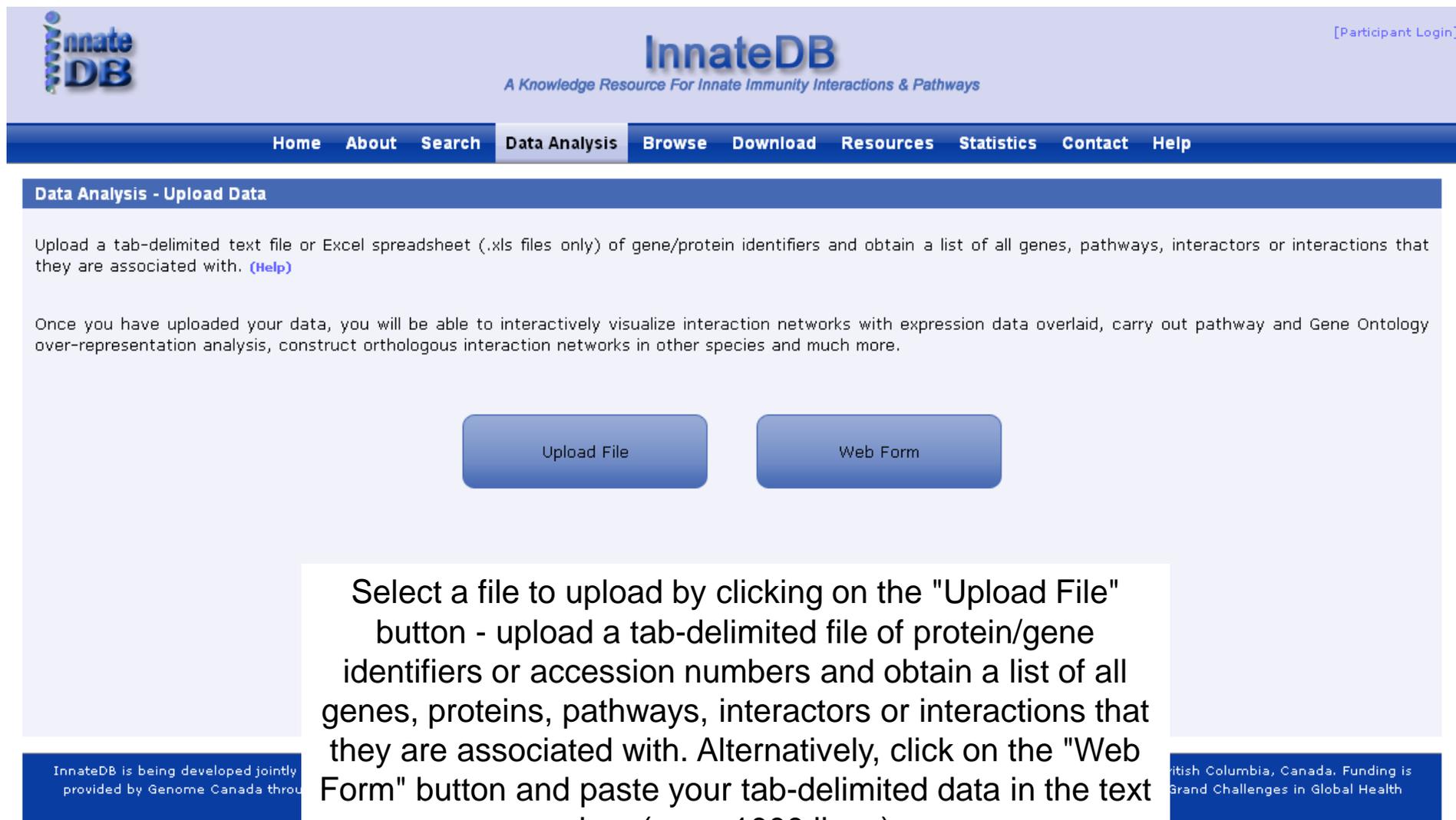
The screenshot shows the Cytoscape Desktop interface with a network diagram. The diagram is organized into layers: Extracellular, Cell surface, Plasma membrane, Cytoplasm, Nucleus, and Unknown. Nodes are represented by colored circles, and edges are lines connecting them. A callout box points to a node in the Cytoplasm layer, and another callout box points to the Node Attribute Browser table at the bottom.

ID	Function	InnateDB...	Localization	canonical...
MAP3K...	Signaling	http://dev.i...	Cytoplasm	MAP3K7IP2
IRAK4	Interleukin	http://dev.i...	Unknown	IRAK4
SQSTM...				SQSTM1 ...
NLRP12	Hydrolase	http://dev.i...	Cytoplasm	NLRP12
IRF7	Nucleic A...	http://dev.i...	Nucleus	IRF7
MAP3K7	Kinase	http://dev.i...	Unknown	MAP3K7
CAV1	Membran...	http://dev.i...	Cell surfa...	CAV1
AKT1	Kinase	http://dev.i...	Cytoplasm	AKT1

Overlay Gene Expression Data on Interaction Networks



Upload Gene/Protein List to InnateDB Along with Any Associated Quantitative Data



InnateDB
A Knowledge Resource For Innate Immunity Interactions & Pathways

[Participant Login]

Home About Search **Data Analysis** Browse Download Resources Statistics Contact Help

Data Analysis - Upload Data

Upload a tab-delimited text file or Excel spreadsheet (.xls files only) of gene/protein identifiers and obtain a list of all genes, pathways, interactors or interactions that they are associated with. ([Help](#))

Once you have uploaded your data, you will be able to interactively visualize interaction networks with expression data overlaid, carry out pathway and Gene Ontology over-representation analysis, construct orthologous interaction networks in other species and much more.

[Upload File](#) [Web Form](#)

Select a file to upload by clicking on the "Upload File" button - upload a tab-delimited file of protein/gene identifiers or accession numbers and obtain a list of all genes, proteins, pathways, interactors or interactions that they are associated with. Alternatively, click on the "Web Form" button and paste your tab-delimited data in the text box (max. 1000 lines)

InnateDB is being developed jointly provided by Genome Canada through the Strategic Alliances Program and the British Columbia, Canada. Funding is provided by the Grand Challenges in Global Health.

Preview of Uploaded Data



InnateDB

A Knowledge Resource For Innate Immunity Interactions & Pathways

Home About Search **Data Analysis** Browse Download Resources Statistics Contact Help

Data Analysis - Specify which data is in each column

Click on the column headers to specify which column in your data file contains the identifiers/accession numbers for each gene (and which database they come from). This is called the "Cross-reference ID". Please note that when using InnateDB identifiers, only gene IDs are valid, not interaction IDs!

If you have included gene expression data - identify which columns contain the gene expression values and their associated p-values.

You may also identify the column containing the probe IDs if you have included them in your file. [\(Help\)](#)

Dataset Preview

Column 1	Column 2	Column 3	Column 4	Column 5
Ensembl Gene	Day 3 fold change	Day 3 p-value	Day 4 fold change	Day 4 p-value
ENSG00000002586	-0.9	0.0080	-1.9	0.041
ENSG00000002834	1.2	0.046	1.6	0.01
ENSG00000004799	2.3	0.045	1.6	0.03
ENSG00000005249	-1.8	0.046	-2.3	0.017
ENSG00000005339	-0.2	0.03	-2.2	0.04
ENSG00000005381	2.3	0.042	2.4	0.043
ENSG00000005961	-0.8	0.02	-1.7	0.036
ENSG00000006075	1.4	0.021	1.8	0.014
ENSG00000006327	-1.6	0.0030	-1.1	0.048
ENSG00000006652	3.0	0.047	3.1	0.0020
ENSG00000008130	1.6	0.043	0.8	0.0060
ENSG00000011009	1.5	0.0020	2.0	0.02

20 Page 1 of 25 Displaying 1 to 20 of 491 items

Click on the column headers to specify which column in your data file contains the identifiers/accession numbers for each gene.



If you have included gene expression data - identify which columns contain the gene expression values and their associated p-values.

InnateDB
A Knowledge Resource For Innate Immunity Interactions & Pathways

Home About Search **Data Analysis** Browse Download Resources Statistics Contact Help

Data Analysis - Specify which data is in each column

Click on the column headers to specify which column in your data file contains the identifier. Please note that when using InnateDB identifiers, only gene IDs are valid, not interaction IDs. This column is called the "Cross-reference ID".

If you have included gene expression data - identify which columns contain the gene expression values and their associated p-values.

You may also identify the column containing the probe IDs if you have included them in your data file.

This column is:

- (undefined)
- Cross-reference ID**
- Expression value
- P-Value
- Probe ID
- (undefined)

Dataset Preview

Column 1	Column 2	Column 3	Column 4	Column 5
Ensembl Gene	Day 3 fold change	Day 3 p-value	Day 4 fold change	Day 4 p-value
ENSG00000002586	-0.9	0.0080	-1.9	0.041
ENSG00000002834	1.2	0.046	1.6	0.01
ENSG00000004799	2.3	0.045	1.6	0.03
ENSG00000005249	-1.8	0.046	-2.3	0.017
ENSG00000005339	-0.2	0.03	-2.2	0.04
ENSG00000005381	2.3	0.042	2.4	0.043
ENSG00000005961	-0.8	0.02	-1.7	0.036
ENSG00000006075	1.4	0.021	1.8	0.014
ENSG00000006327	-1.6	0.0030	-1.1	0.048
ENSG00000006652	3.0	0.047	3.1	0.0020
ENSG00000008130	1.6	0.043	0.8	0.0060
ENSG00000011009	1.5	0.0020	2.0	0.02

20 Page 1 of 25 Displaying 1 to 20 of 491 items

If you have included gene expression data - identify which columns contain the gene expression values and their associated p-values.

Click Next.

Data Analysis - Specify which data is in each column

Click on the column headers to specify which column in your data file contains the identifiers/accession numbers for each gene (and which database they come from). This is called the "Cross-reference ID". Please note that when using InnateDB identifiers, only gene IDs are valid, not interaction IDs!

If you have included gene expression data - identify which columns contain the gene expression values and their associated p-values.

You may also identify the column containing the probe IDs if you have included them in your file. [\(Help\)](#)

Dataset Preview

Cross-reference ID	Exp.Value (Day3)	P-value (Day3)	Exp.Value (Day4)	P-value (Day4)
Ensembl Gene	Day 3 fold change	Day 3 p-value	Day 4 fold change	Day 4 p-value
ENSG00000002586	-0.9	0.0080	-1.9	0.041
ENSG00000002834	1.2	0.046	1.6	0.01
ENSG00000004799	2.3	0.045	1.6	0.03
ENSG00000005249	-1.8	0.046	-2.3	0.017
ENSG00000005339	-0.2	0.03	-2.2	0.04
ENSG00000005381	2.3	0.042	2.4	0.043
ENSG00000005961	-0.8	0.02	-1.7	0.036
ENSG00000006075	1.4	0.021	1.8	0.014
ENSG00000006327	-1.6	0.0030	-1.1	0.048
ENSG00000006652	3.0	0.047	3.1	0.0020
ENSG00000008130	1.6	0.043	0.8	0.0060
ENSG00000011009	1.5	0.0020	2.0	0.02

20 Page 1 of 25 Displaying 1 to 20 of 491 items

« Previous

Next »

Data Analysis Options



InnateDB

A Knowledge Resource For Innate Immunity Interactions & Pathways

[Home](#) [About](#) [Search](#) [Data Analysis](#) [Browse](#) [Download](#) [Resources](#) [Statistics](#) [Contact](#) [Help](#)

Data Analysis - Output

- Returning a list of **genes** provides detailed annotation for each gene in the uploaded list and is a prerequisite to performing a Gene Ontology over-representation analysis.
- Returning a list of **pathways** provides pathway annotation for each gene in the uploaded list and is a prerequisite to performing a pathway over-representation analysis.
- Returning a list of **interactors** allows one to identify all molecules in InnateDB which interact with the genes (or their encoded products) in the uploaded list.
- Returning a list of **interactions** allows one to identify all interactions in InnateDB in which the genes (or their encoded products) in the uploaded list are a participant and to construct a network of these interactions for visualization and further analysis.
- Returning a list of **Predicted TF Interactions** allows one to identify transcription factors which are predicted by the CisRED database to bind genes in the uploaded list and to construct a network of these interactions for visualization and further analysis.

Return a list of:

- Interactions ←
- Interactors
- Genes
- Pathways
- Predicted TF Interactions

Filter Interactions: [\(Help\)](#)

- Do not filter the results
- Only show interactions *between* uploaded molecules ←
- Filter for interactions in pathway

« Previous

Next »

InnateDB is being developed jointly by the Brinkman Laboratory, Simon Fraser University and the Hancock Laboratory, University of British Columbia, Vancouver, British Columbia, Canada and the Lynn Laboratory, Teagasc Animal Bioscience Department, Ireland. Funding is provided by Genome Canada through the Pathogenomics of Innate Immunity (PI2) project, and the Foundation for the National Institutes of Health through the Grand Challenges in Global Health initiative.

*This will only return molecular interactions **between** the genes and their encoded products in the uploaded list*

i.e. will not return interactions with other genes/proteins not in the uploaded list.

Results: Visualize Gene Expression Data in an Interaction Network Context

Click here to visualize interactions in Cerebral with overlaid gene expression data.
Open Cerebral as previously shown.

Home About Search Data Analysis Browse Download Resources Statistics

Display Options (Show/Hide)

Sorted by: Name (query) ascending then by Interaction Type ascending Sort

Download XML TAB MS Excel CSV SIF Show Orthologous Interactions Visualize **Cerebral** (Help)

Viewing interactions 1 to 20 of 1053 hits matching query

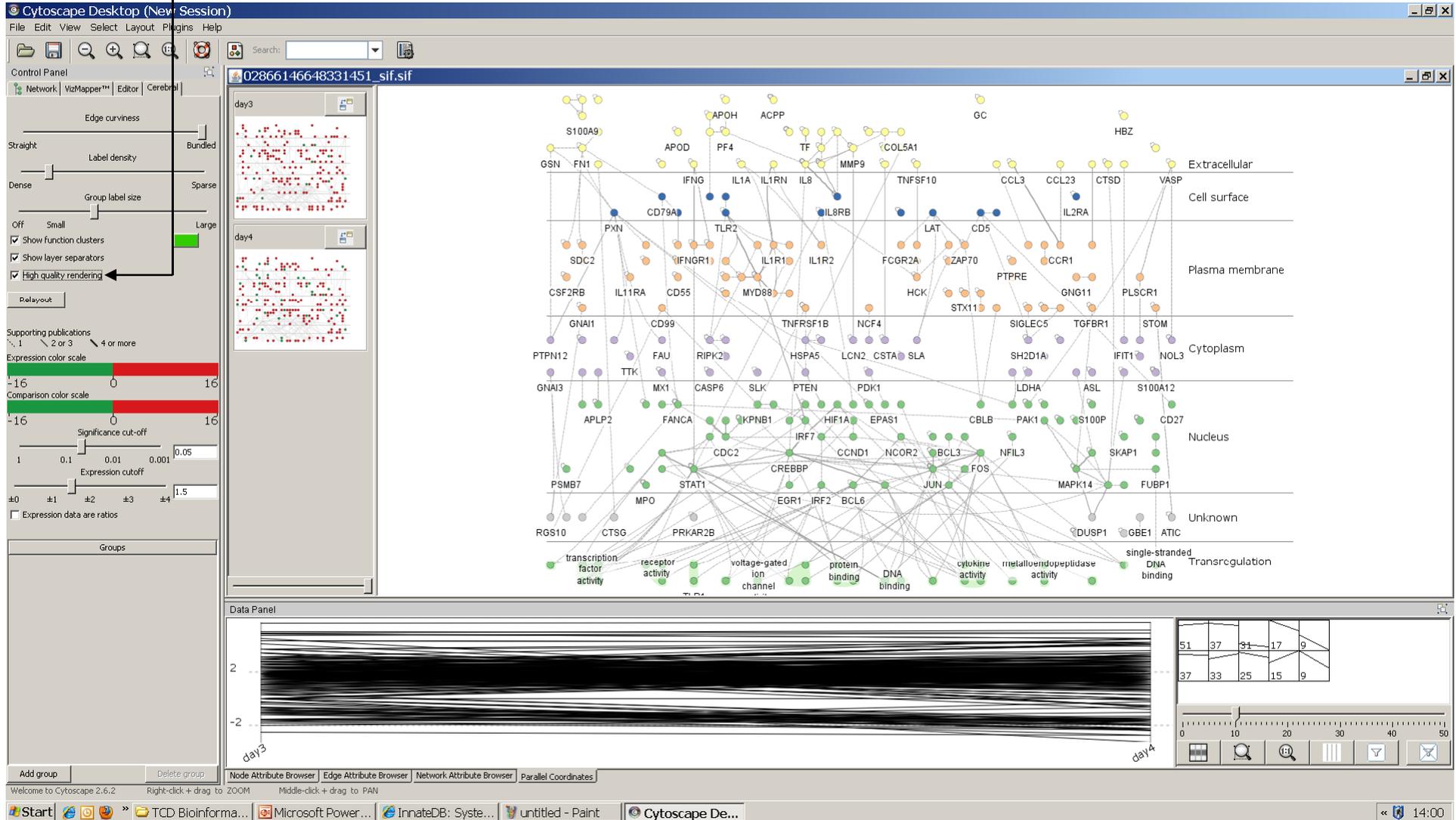
Page(s): 1 2 3 4 5 6 7 8 9 10 [Next]

Query Xref	Query Name	day3 (fold change)	P-Value	day4 (fold change)	P-Value	Group ID	Interaction Level	Interaction	Interactors	Interactor Species	Interaction Type	Supporting Publications	
ENSG00000128274	A4GALT	1.5	0.015	1.7	0.014			No interactions					
ENSG00000140526	ABHD2	1.6	0.006	2.1	0.013			No interactions					
ENSG00000014257	ACPP	2.0	0.049	1.7	0.011	6475	direct interaction	ACPP (complex)	ACPP	<i>Homo sapiens</i>	physical association	1	Interaction Details
ENSG00000014257	ACPP	2.0	0.049	1.7	0.011	6476	direct interaction	ACPP interacts with ACPP	ACPP :: ACPP	<i>Homo sapiens</i>	unspecified	5	Interaction Details
ENSG00000151726	ACSL1	3.7	0.014	4.7	0.013			No interactions					
ENSG00000135074	ADAM19	1.0	0.007	1.6	0.049			No interactions					
ENSG00000147872	ADFP	1.0	0.006	2.9	0.049			No interactions					
ENSG00000148926	ADM	3.1	0.036	3.0	0.012			No interactions					
ENSG00000100077	ADRBK2	2.2	0.032	3.0	0.026			No interactions					
ENSG00000177674	AGTRAP	1.8	0.043	1.2	0.048	25636	direct interaction	AGTRAP interacts with AGTRAP	AGTRAP :: AGTRAP	<i>Homo sapiens</i>	physical association	1	Interaction Details
ENSG00000177674	AGTRAP	1.8	0.043	1.2	0.048	25635	direct interaction	AGTRAP interacts with AGTRAP	AGTRAP :: AGTRAP	<i>Homo sapiens</i>	unspecified	1	Interaction Details
ENSG00000106992	AK1		0.026	1.6	0.014			No interactions					
ENSG00000131016	AKAP12	0.0	0.023	1.7	0.004			No interactions					
ENSG00000111275	ALDH2	2.0	0.047	1.0	0.039	27028	direct interaction	ALDH2 interacts with ALDH2	ALDH2 :: ALDH2	<i>Homo sapiens</i>	unspecified	3	Interaction Details
ENSG00000132746	ALDH3B2	-1.3	0.018	-2.0	0.032			No interactions					

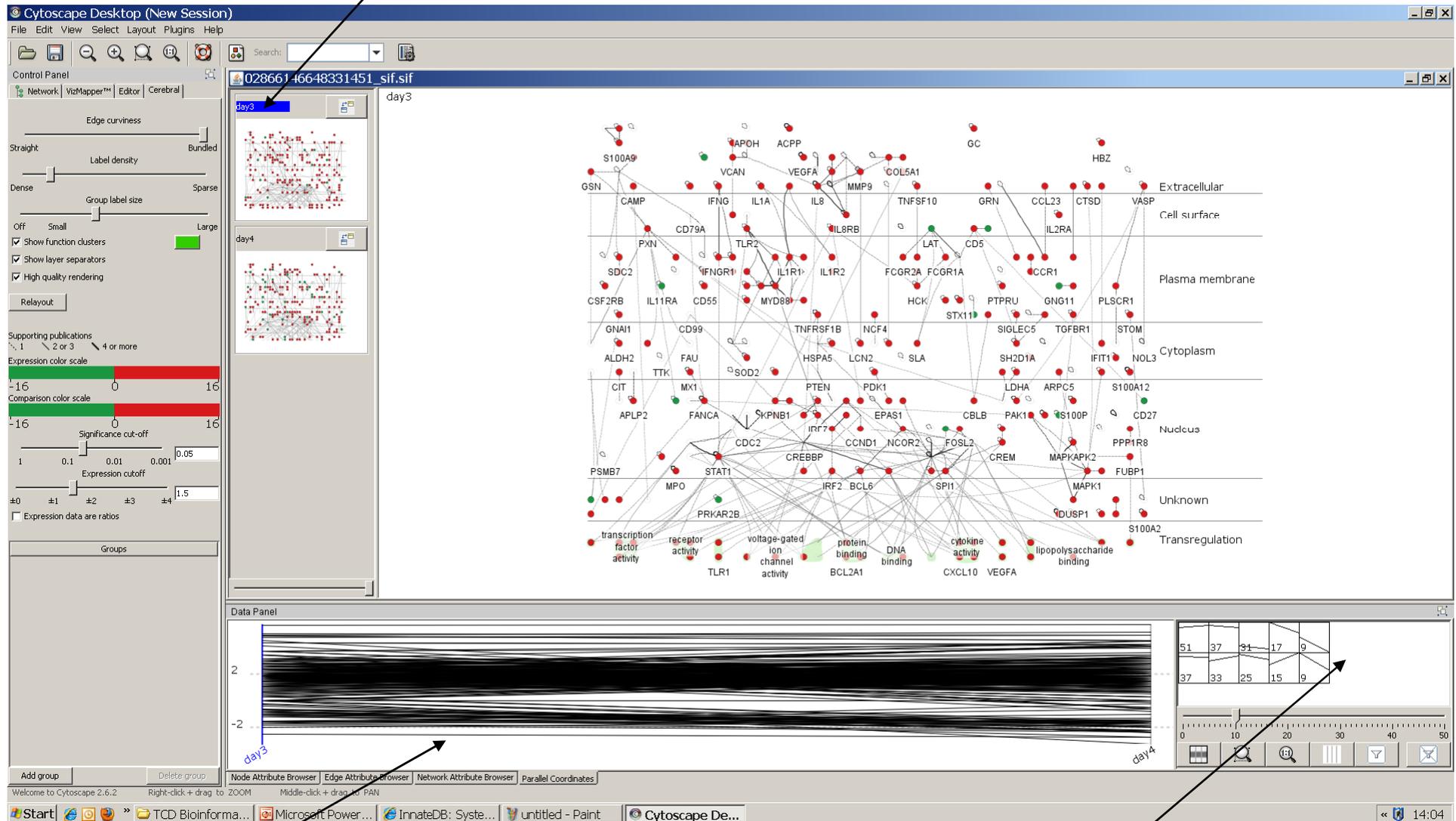
Multi-experiment View in Cerebral

Check this box
To sharpen image

Mini-windows show overlaid gene expression data for each condition.
Red = upreg. Green = downreg.



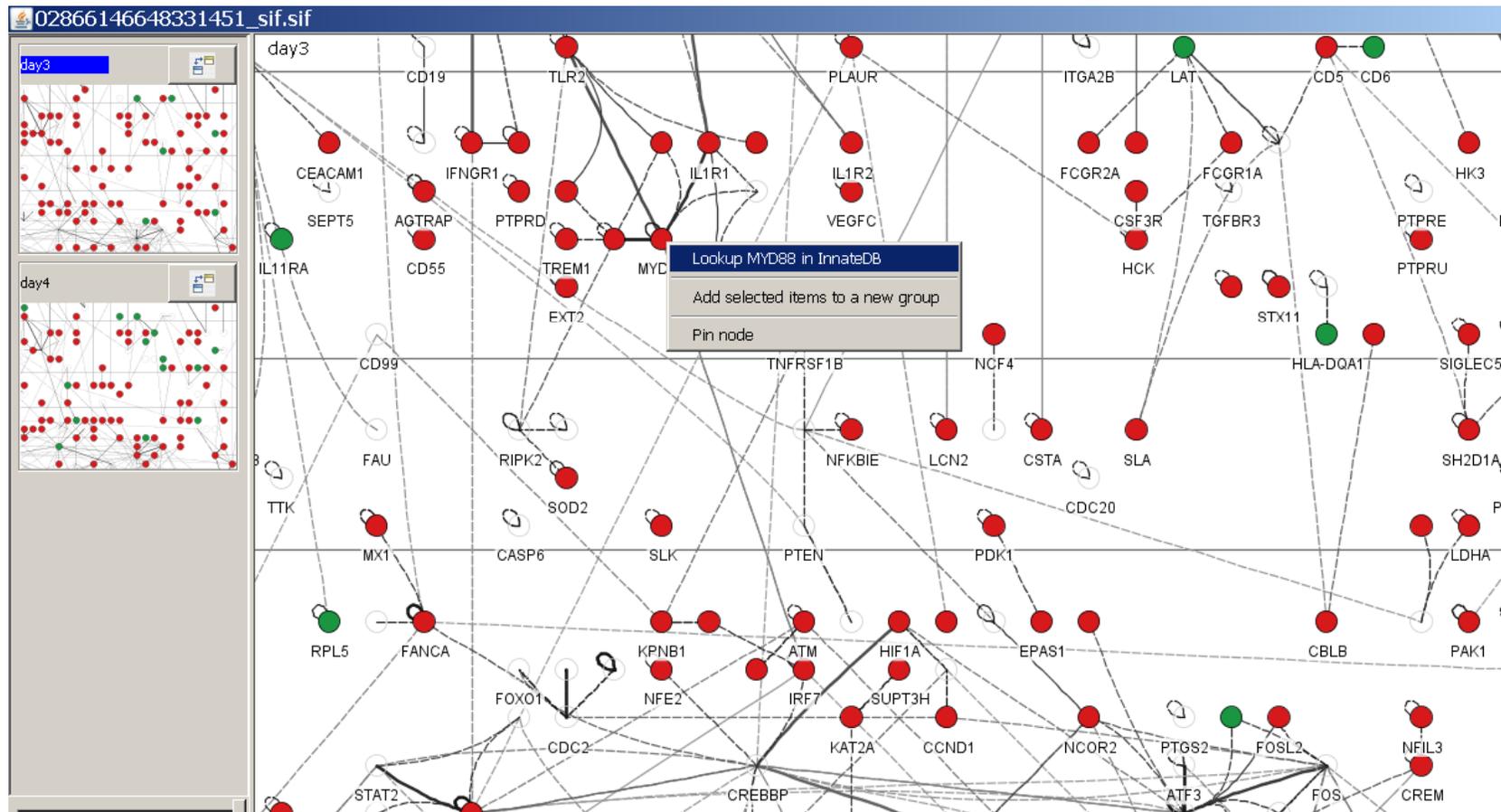
Click on one of the mini-windows to view data for condition in large window.



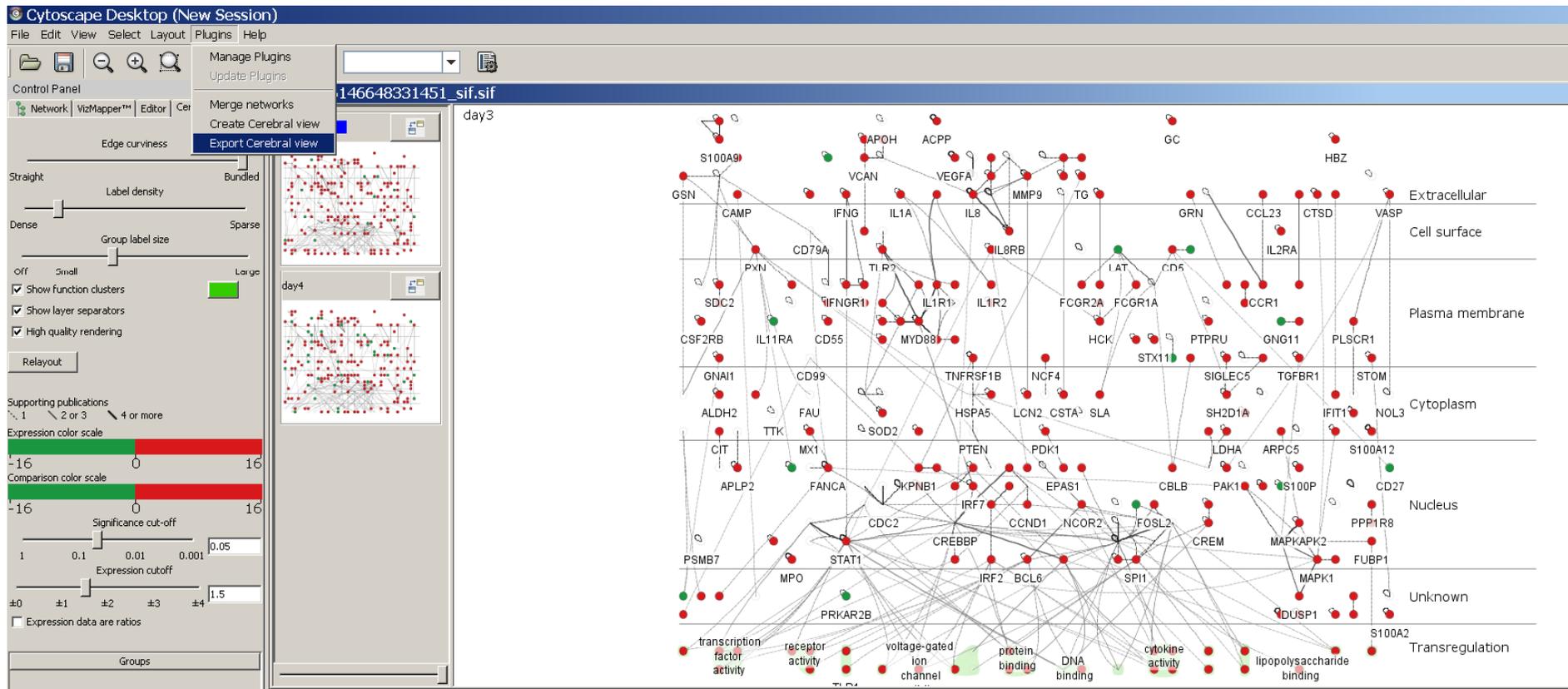
Graph of changes in gene expression across time-points

K-means clustering – clusters genes with similar patterns of gene expression

Interactively Link back to InnateDB to Look up Information on Particular Genes/Interactions of Interest – Right Click on a Node or an Edge.



Export an Image of the Network



The screenshot displays the Cytoscape Desktop interface for a network visualization. The window title is "Cytoscape Desktop (New Session)". The menu bar includes File, Edit, View, Select, Layout, Plugins, and Help. The Control Panel on the left contains several sections:

- Manage Plugins:** Includes "Update Plugins" and a search field.
- Network:** Shows the file name "146648331451_sif.sif" and a "day3" label.
- Edge curviness:** Options for "Straight" and "Bundled".
- Label density:** A slider between "Dense" and "Sparse".
- Group label size:** A slider between "Small" and "Large".
- Rendering options:**
 - Show function clusters
 - Show layer separators
 - High quality rendering
- Supporting publications:** A dropdown menu with options "1", "2 or 3", and "4 or more".
- Expression color scale:** A horizontal bar from -16 to 16.
- Comparison color scale:** A horizontal bar from -16 to 16.
- Significance cut-off:** A slider with values 1, 0.1, 0.01, 0.001, and 0.05.
- Expression cutoff:** A slider with values ±0, ±1, ±2, ±3, and ±4.
- Expression data are ratios

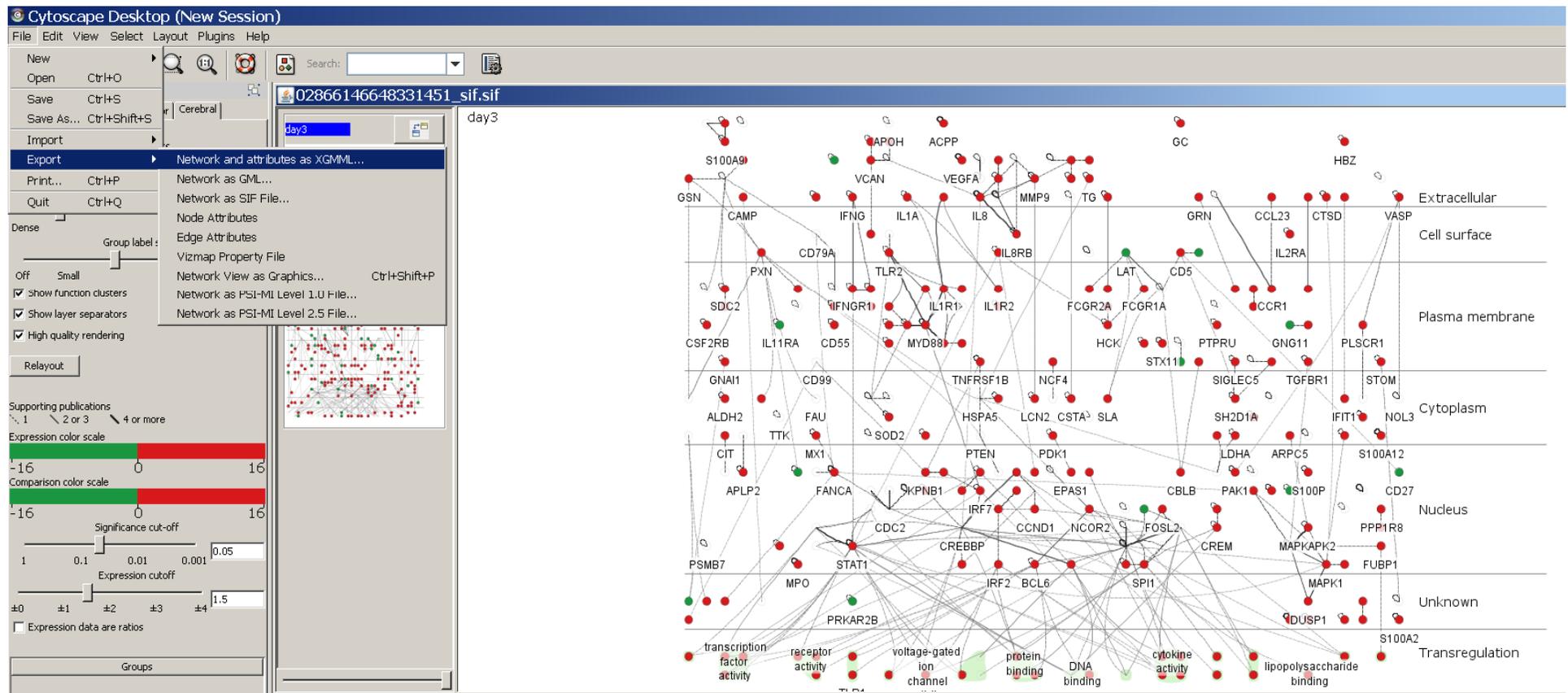
The main network graph shows a complex web of interactions between nodes. The nodes are color-coded based on expression levels and are grouped into layers on the right side of the graph:

- Extracellular
- Cell surface
- Plasma membrane
- Cytoplasm
- Nucleus
- Unknown
- Transregulation

At the bottom of the graph, several functional categories are listed with corresponding icons:

- transcription factor activity
- receptor activity
- voltage-gated ion channel
- protein binding
- DNA binding
- cytokine activity
- lipopolysaccharide binding

Export the Graph as XGMML File to Use Later in Local Version of Cytoscape



The screenshot displays the Cytoscape Desktop interface with a network graph loaded. The graph is organized into layers representing cellular compartments: Extracellular, Cell surface, Plasma membrane, Cytoplasm, Nucleus, and Transregulation. Nodes are represented by red circles, and edges are grey lines. The left sidebar shows the 'Export' menu with 'Network and attributes as XGMML...' selected. The main window shows a dense network of nodes and edges, with various gene symbols labeled.

Cytoscape Desktop (New Session)
 File Edit View Select Layout Plugins Help

Search:

02866146648331451_sif.sif

day3

Export

- Network and attributes as XGMML...
- Network as GML...
- Network as SIF File...
- Node Attributes
- Edge Attributes
- Vizmap Property File
- Network View as Graphics... **Ctrl+Shift+P**
- Network as PSI-MI Level 1.0 File...
- Network as PSI-MI Level 2.5 File...

Relayout

Supporting publications: 1, 2 or 3, 4 or more

Expression color scale: -16 to 16

Comparison color scale: -16 to 16

Significance cut-off: 1, 0.1, 0.01, 0.001, 0.05

Expression cutoff: ±0, ±1, ±2, ±3, ±4, 1.5

Expression data are ratios

Groups

Extracellular

Cell surface

Plasma membrane

Cytoplasm

Nucleus

Unknown

Transregulation

transcription factor activity

receptor activity

voltage-gated ion channel

protein binding

DNA binding

cytokine activity

lipopolysaccharide binding