

BCB420 - Computational Systems Biology

Lecture 10 - Enrichment Map and other Cytoscape Apps

Ruth Isserlin

2020-03-22

Assignment #3

- Data set Pathway and Network Analysis
- Due April 3, 2020! @ 13:00

What to hand in?

- **html rendered RNotebook** - you should submit this through quercus
- Make sure the notebook and all associated code is checked into your github repo as I will be pulling all the repos at the deadline and using them to compile your code. - Your checked in code must replicate the handed in notebook.
- Document your work and your code directly in the notebook.
- **Reference the paper associated with your data!**
- **Introduce your paper and your data again**
- You are allowed to use helper functions or methods but make sure when you source those files the paths to them are relative and that they are checked into your repo as well.

Outline for Today's lecture

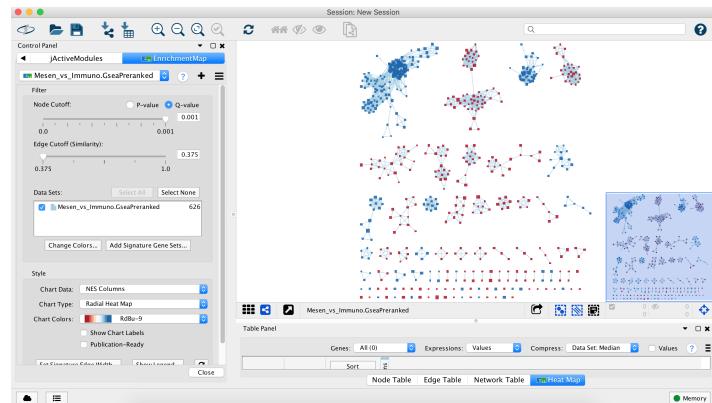
- review of Enrichment map
- looking at Pathways in depth - Reactome app, Pathway commons, String and GeneMania
- Post analysis
- Enrichment Map Dark Matter

Enrichment Map

Enrichment Map is a Cytoscape App that translates enrichment results from:

- GSEA,
- g:Profiler,
- DAVID,
- GREAT or
- generic results

into a network where nodes are gene sets and the connection between them are the genes that the sets have in common.



Enrichment Map

Enrichment Map is a Cytoscape App that translates enrichment results from:

- GSEA,
- g:Profiler,
- DAVID,
- GREAT or
- generic results

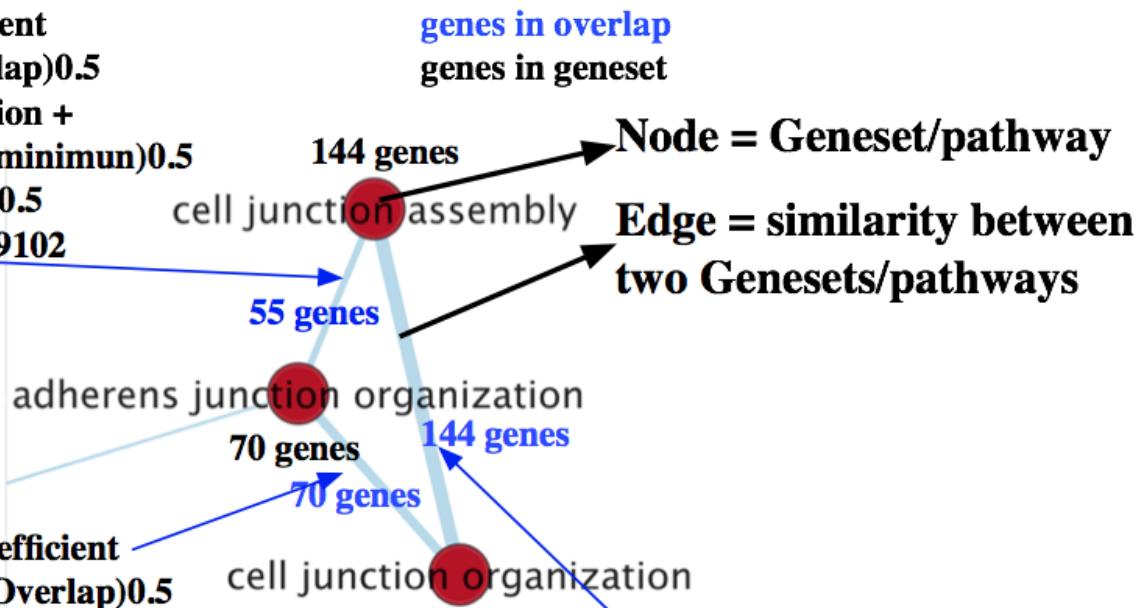
into a network where nodes are gene sets and the connection between them are the genes that the sets have in common.

The Enrichment Map takes a lot of different types of input but in the most basic sense it requires:

- An enrichment file - a table containing the genesets/pathways with associated statistics.
- (optional) Definition of the genesets - the set of genes that are associated with each geneset. (The make up of the genesets is **required** but is optional because some enrichment file formats include a column with the list of genes associated with the given geneset.)

Enrichment Map Basics

$$\begin{aligned}\text{similarity Coefficient} &= (\text{Jaccard} + \text{Overlap})0.5 \\ &= (\text{intersection}/\text{union} + \text{intersection}/\text{minimum})0.5 \\ &= (55/159 + 55/70)0.5 \\ &= 0.5658131176999102\end{aligned}$$



$$\begin{aligned}\text{similarity Coefficient} &= (\text{Jaccard} + \text{Overlap})0.5 \\ &= (\text{intersection}/\text{union} + \text{intersection}/\text{minimum})0.5 \\ &= (70/178 + 70/70)0.5 \\ &= 0.6966292134831461\end{aligned}$$

$$\begin{aligned}\text{similarity Coefficient} &= (\text{Jaccard} + \text{Overlap})0.5 \\ &= (\text{intersection}/\text{union} + \text{intersection}/\text{minimum})0.5 \\ &= (144/178 + 144/144)0.5 \\ &= 0.9044943820224719\end{aligned}$$

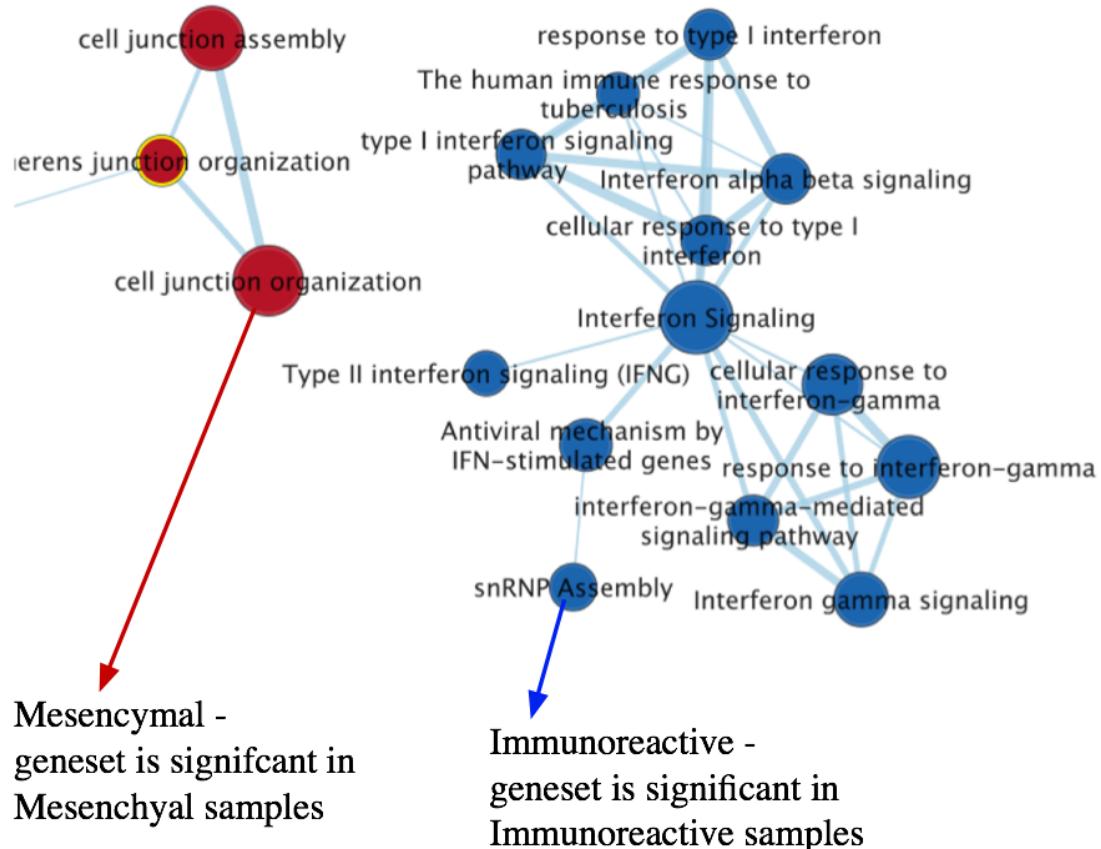
Similarity coefficient can be defined using:

Jaccard coefficient - Intersection/Union

Overlap - Intersection/Minimum

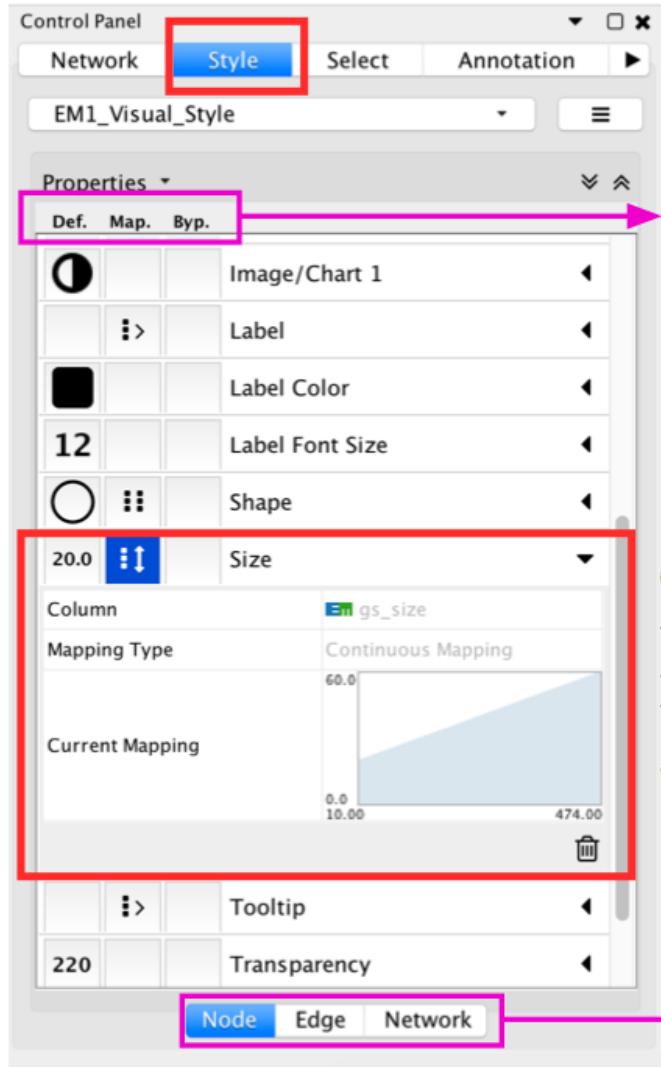
Combination of the two

Enrichment Map Details



- Example subset of an Enrichment map

Enrichment Map Details



There are three different types of mappings:

Default - by default what is the value of this property

Mapping - define a rule to map these values

Bypass - ignore the default and the rule and set this specific value

There are three separate columns associated with each attribute. Click on the corresponding square you want to set.

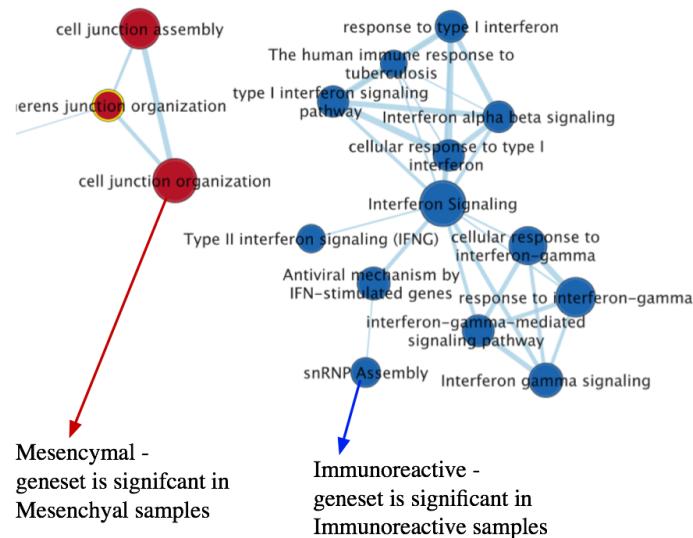
Continuous Mapper- maps a continuous value to the given attribute

Maps gs_size (geneset size i.e. Number of genes) to node size

You can set attributes for a:
node
edge
network

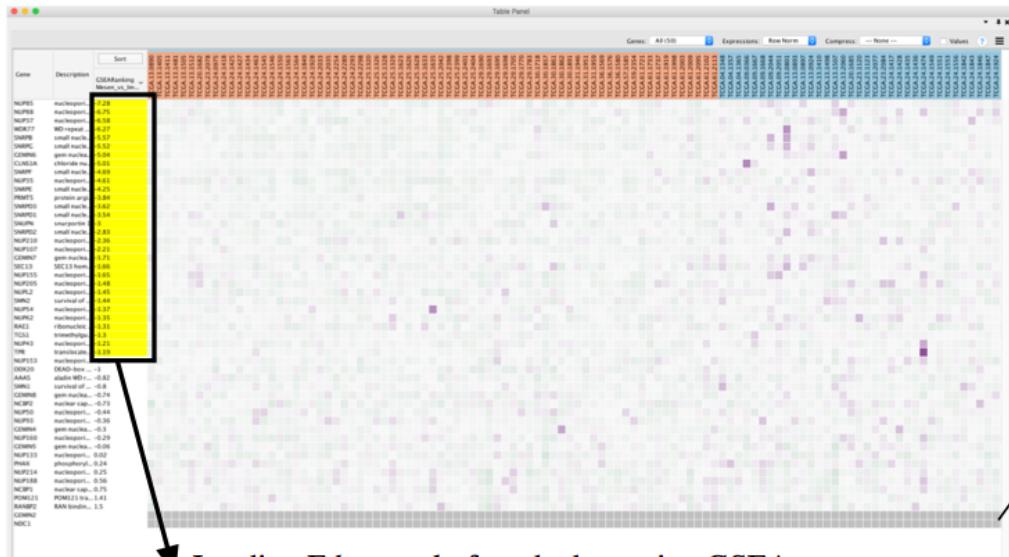
Enrichment Map Details

- Default Enrichment Map Style:
 - size of node corresponds to the size of the geneset
 - colour of node corresponds to the phenotype and the p-value
 - label of the node corresponds to the geneset description
 - thickness of the edge corresponds to overlap statistic. The more genes two nodes have in common the thicker the edge.



Enrichment Map Details - cont'd

click on an individual node or a set of nodes to see the expression of the genes associated with it

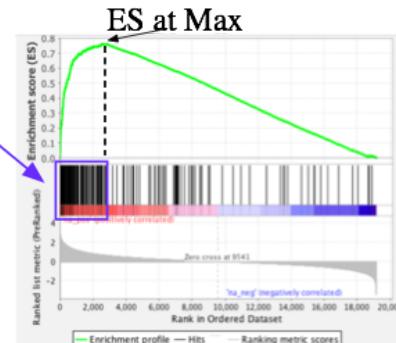


Leading Edge - only found when using GSEA
Will only appear when an **individual** GSEA
node is selected. Leading edge is specific
to an **individual** pathway/geneset.

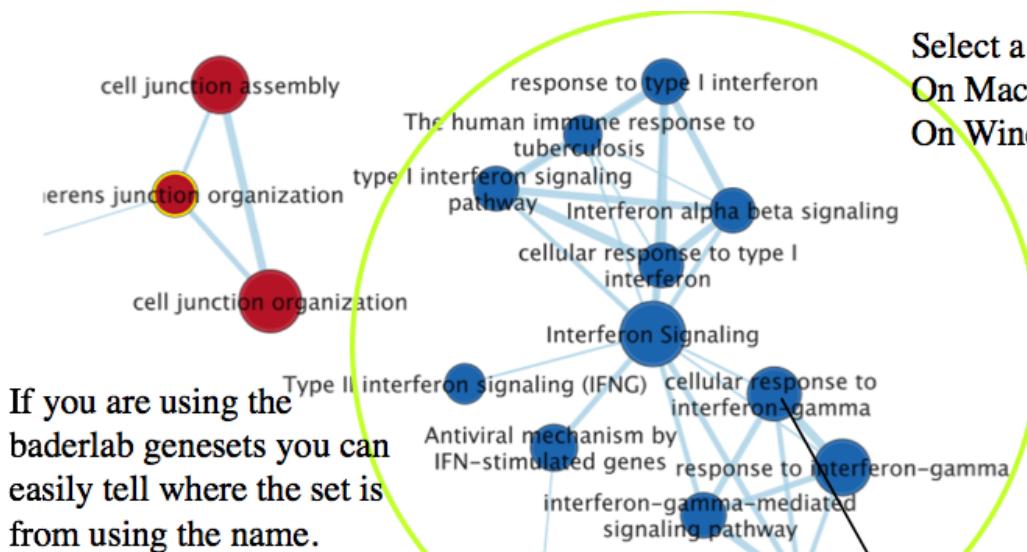
Red Samples - mesenchymal
Blue Samples - immunoreactive
(in order to get this feature
you must import a class file
to Enrichment map)

Values are Row normalized

Genes found in the gene set
but are not found in the expression set



Pathway Details



Select a cluster:

On Mac - command, click and drag

On Windows - ctrl, click and drag

Node name is mapped to GS_descr

EnrichmentMap

Name
INTERFERON SIGNALING%REACTOME DATABASE ID RELEASE 70%913531
RESPONSE TO INTERFERON-GAMMA%GOBP%GO:0034341
CELLULAR RESPONSE TO INTERFERON-GAMMA%GOBP%GO:0071346
INTERFERON GAMMA SIGNALING%REACTOME%R-HSA-877300.1
ANTIVIRAL MECHANISM BY IFN-STIMULATED GENES%REACTOME DATABASE ID RELEASE 70%1169410
INTERFERON-GAMMA-MEDIATED SIGNALING PATHWAY%GOBP%GO:0060333
RESPONSE TO TYPE I INTERFERON%GOBP%GO:0034340
INTERFERON ALPHA BETA SIGNALING%REACTOME%R-HSA-909733.2
CELLULAR RESPONSE TO TYPE I INTERFERON%GOBP%GO:0071357
TYPE I INTERFERON SIGNALING PATHWAY%GOBP%GO:0060337
SNRNP ASSEMBLY%REACTOME DATABASE ID RELEASE 70%191859
TYPE II INTERFERON SIGNALING (IFNG)%WIKIPATHWAYS_20191010%WP619%HOMO SAPIENS
THE HUMAN IMMUNE RESPONSE TO TUBERCULOSIS%WIKIPATHWAYS_20191010%WP4197%HOMO SAPI...

EnrichmentMap

GS_DESCR	gs_size
Interferon Signaling	194
response to interferon-gamma	139
cellular response to interferon-gamma	123
Interferon gamma signaling	90
Antiviral mechanism by IFN-stimulated genes	78
interferon-gamma-mediated signaling pathway	69
response to type I interferon	68
Interferon alpha beta signaling	66
cellular response to type I interferon	64
type I interferon signaling pathway	64
snRNP Assembly	50
Type II interferon signaling (IFNG)	37
The human immune response to tuberculosis	23

Node Table Edge Table Network Table Heat Map

**Click on any column to sort table by that column

Pathway Details - Reactome

The screenshot shows the Reactome website interface. At the top, there's a navigation bar with links for About, Content, Docs, Tools, Community, and Download. Below the navigation is a search bar containing the identifier "913531" and a "Go!" button. The main content area displays the search results for "913531", which is identified as a Pathway. It shows one result from a total of 1, specifically "Interferon Signaling". The result includes the identifier R-HSA-913531, the species Homo sapiens, and a brief description stating that Interferons (IFNs) play a central role in initiating immune responses, especially antiviral and antitumor effects. There are three types of IFNs: Type I (IFN-alpha, -beta and others). A "Read more" link is provided. On the left side, there are filters for Species (Homo sapiens selected), Types (Pathway selected), and Search properties (clustered Search selected). A "Reset filters" button is located at the bottom of the filter sidebar.

Reactome | Search results for 913531

reactome.org/content/query?q=913531&species=Homo+sapiens&species=Entries+without+species&cluster=true

reactome

913531 Go!

Search results for 913531

Showing 1 results out of 1

Species

Homo sapiens (1)

Types

Pathway (1)

Search properties

clustered Search

Reset filters

Pathway (1 results from a total of 1)

Interferon Signaling

Identifier: R-HSA-913531

Species: Homo sapiens

Interferons (IFNs) are cytokines that play a central role in initiating immune responses, especially antiviral and antitumor effects. There are three types of IFNs: Type I (IFN-alpha, -beta and others,... [Read more](#)

About

What is Reactome ?

News

Content

Table of Contents

DOIs

Docs

Userguide

Developer's Zone

Tools

Pathway Browser

Analyze Data

Community

Icon Library

Outreach

Download

Pathway Details - Reactome

← → ⌂ 🔒 reactome.org/content/detail/R-HSA-913531 ⌂ ☆ Pinterest Cloud Export

Interferon Signaling

Stable Identifier	R-HSA-913531
Type	Pathway
Species	Homo sapiens

Locations in the PathwayBrowser

Expand All

immune system (Homo sapiens)

General

SBML | BioPAX | PDF

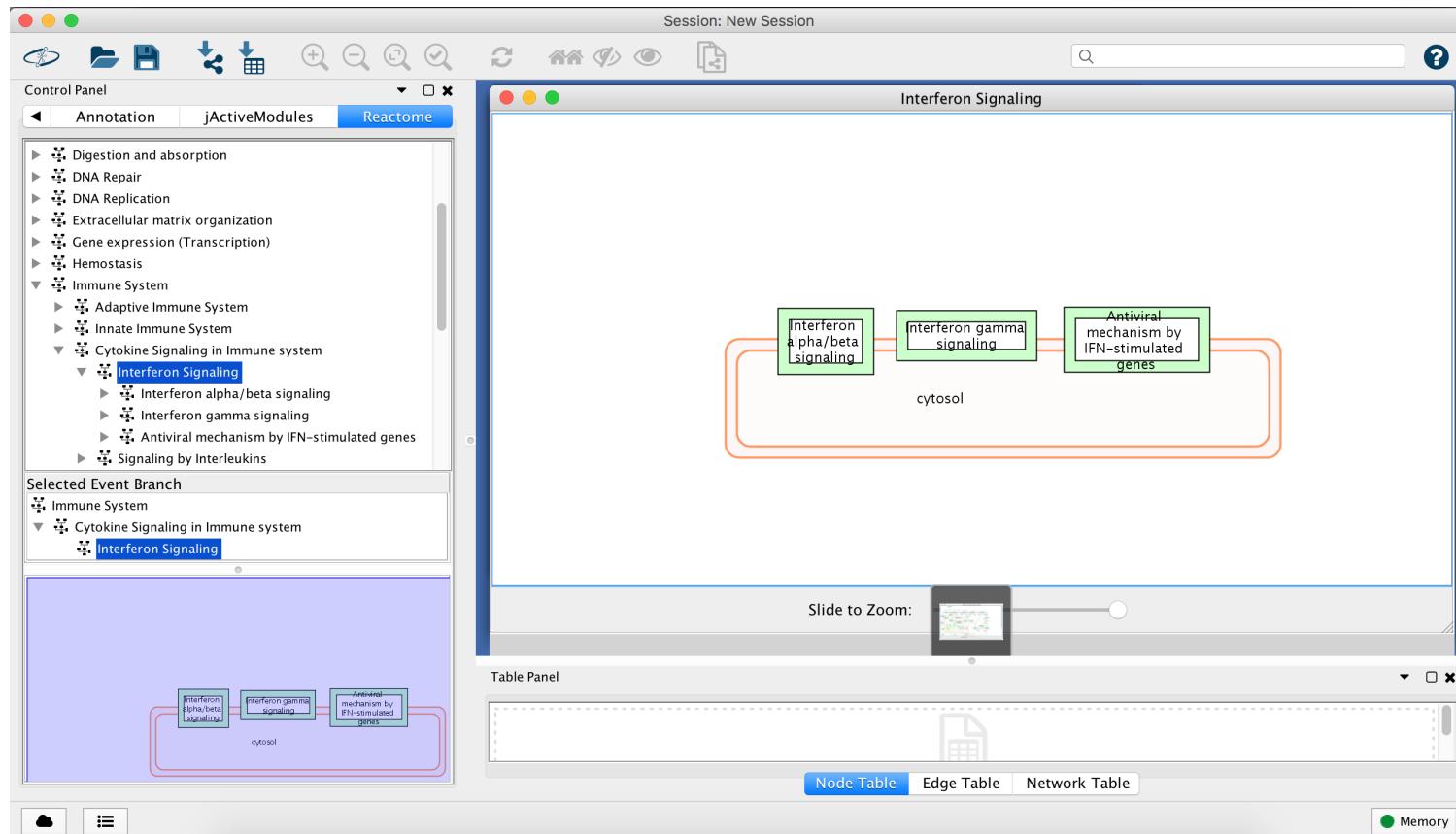
SVG | PNG

The diagram illustrates the Interferon Signaling pathway. It shows three main signaling pathways: INTERFERON ALPHABETA SIGNALING, INTERFERON GAMMA SIGNALING, and ANTI VIRAL MECHANISM BY IFN-STIMULATED GENES.

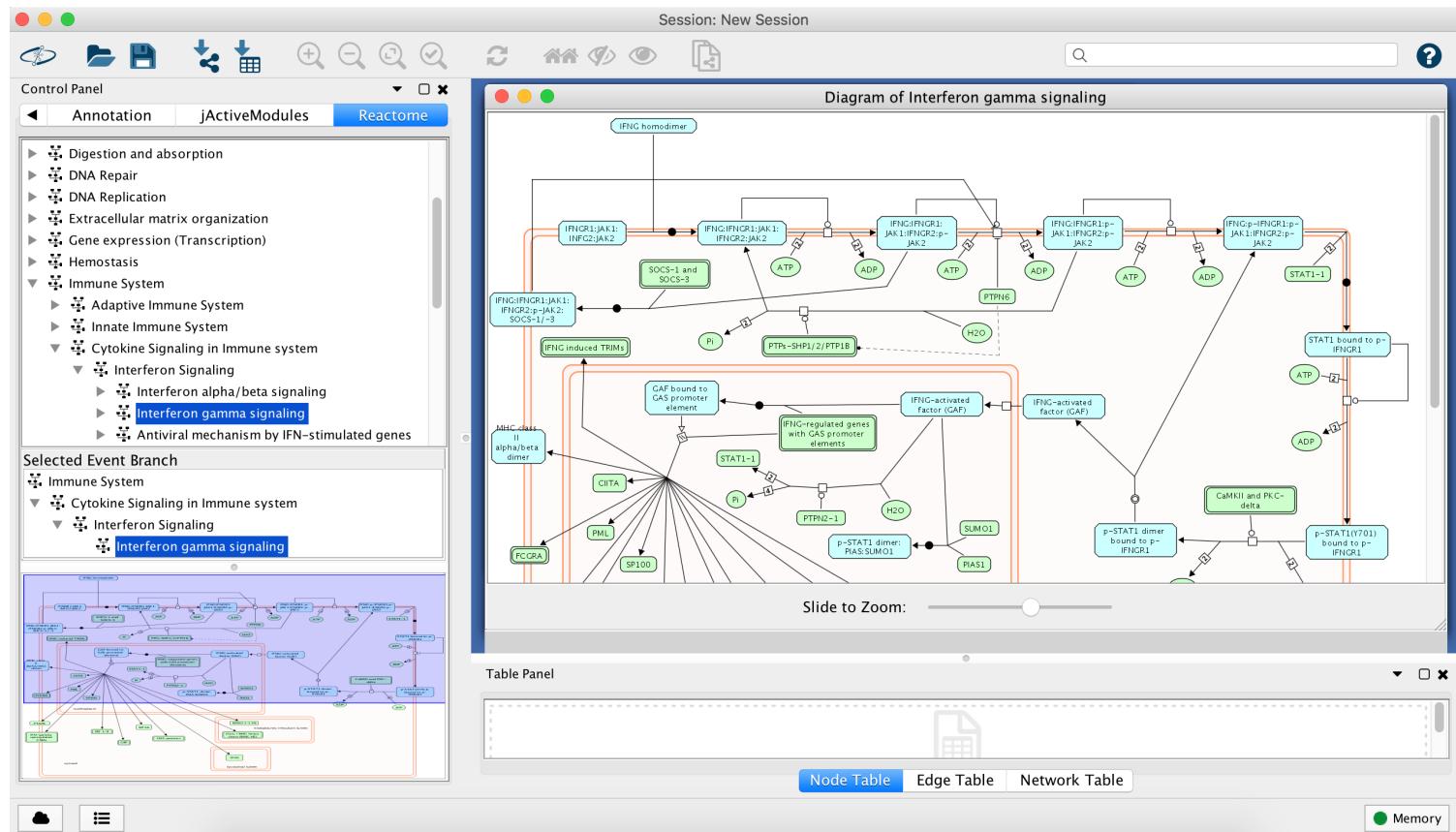
- INTERFERON ALPHABETA SIGNALING:** This pathway is triggered by the binding of IFN alpha or IFN beta to their respective receptors (IFNAR1 and IFNAR2). The receptor complex activates TYK2 and JAK1 kinases. These kinases phosphorylate STAT1 and STAT2 proteins. The phosphorylated STAT1 and STAT2 proteins dimerize and bind to the ISRE (Interferon Stimulated Response Element) in the DNA. This leads to the recruitment of MsGTPases, IFIT, OAS, and ISG15 proteins, which inhibit viral RNA synthesis.
- INTERFERON GAMMA SIGNALING:** This pathway is triggered by the binding of IFN gamma to its receptor (IFNGR1 and IFNGR2). The receptor complex activates JAK1 and JAK2 kinases. These kinases phosphorylate STAT1 and STAT3 proteins. The phosphorylated STAT1 and STAT3 proteins dimerize and bind to the GAS (Gamma Activated Site) in the DNA. This leads to the recruitment of MsGTPases, IFIT, OAS, and ISG15 proteins, which inhibit viral RNA synthesis.
- ANTI VIRAL MECHANISM BY IFN-STIMULATED GENES:** This pathway involves the expression of IFN-stimulated genes (ISGs). The ISGs encode various proteins such as OAS, ISG15, and T2M, which have antiviral activities. These proteins target viral RNA and inhibit viral replication.

Click the image above or [here](#) to open this pathway in the Pathway Browser

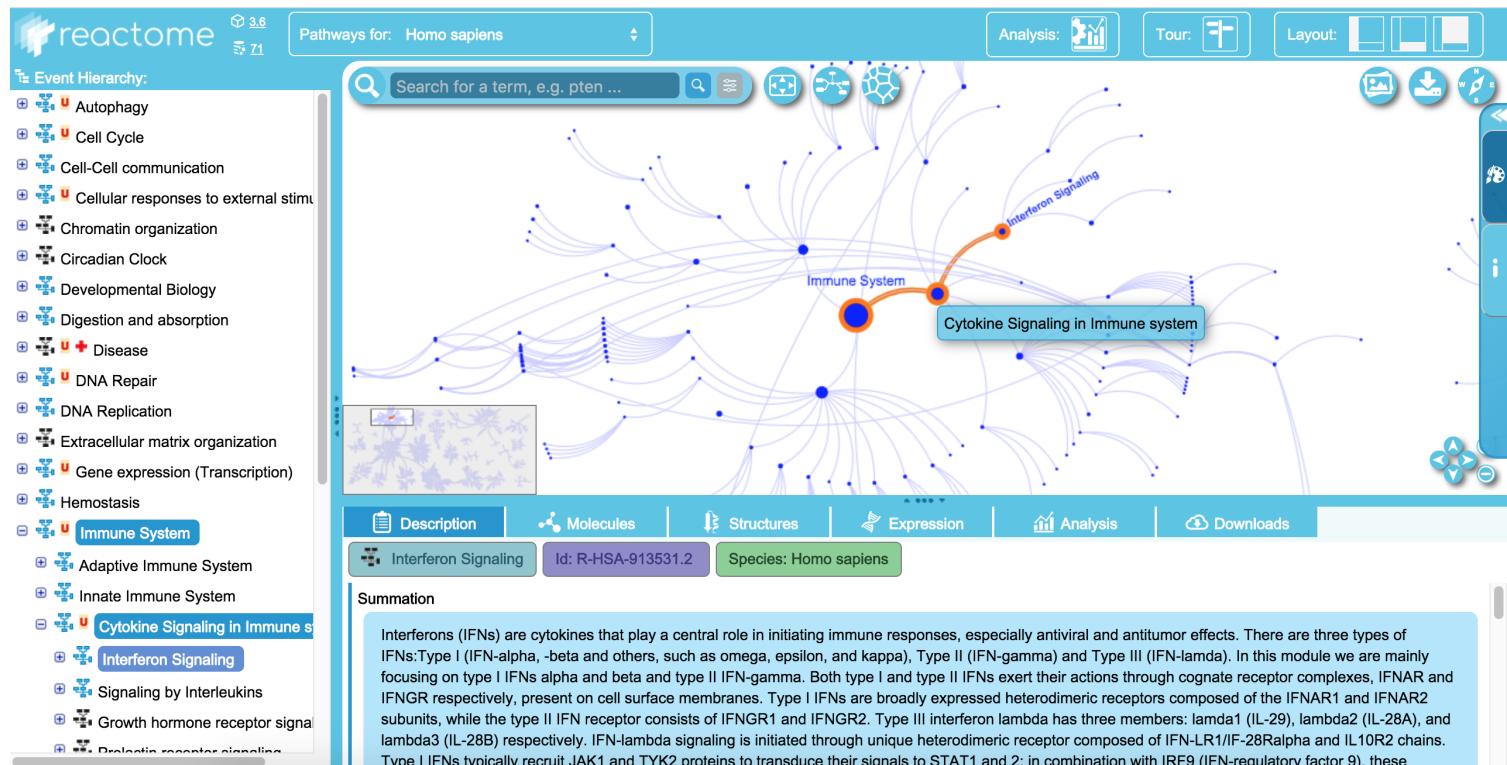
Pathway Details - Reactome



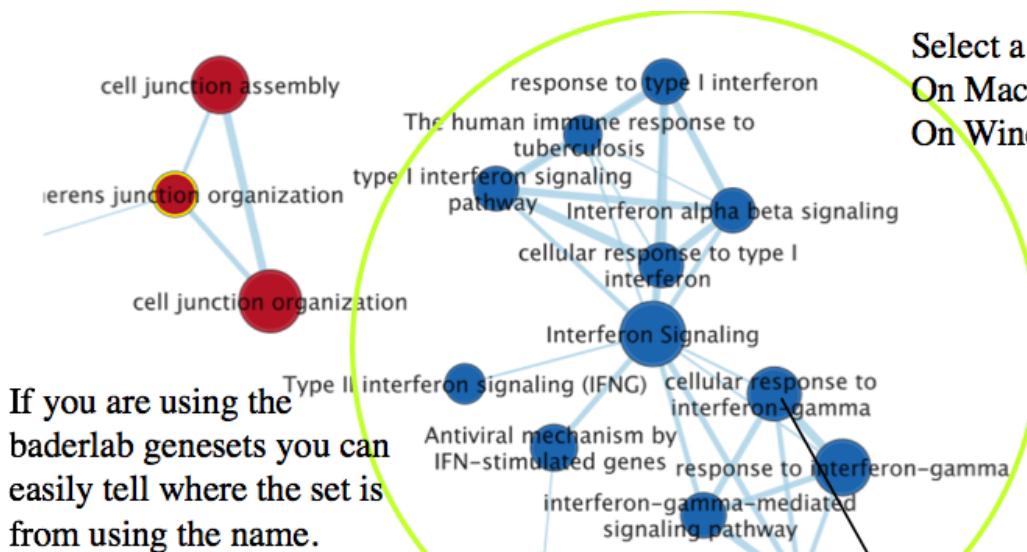
Pathway Details - Reactome



Pathway Details - Reactome



Pathway Details



Select a cluster:

On Mac - command, click and drag

On Windows - ctrl, click and drag

Node name is mapped to GS_descr

EnrichmentMap

Name
INTERFERON SIGNALING%REACTOME DATABASE ID RELEASE 70%913531
RESPONSE TO INTERFERON-GAMMA%GOBP%GO:0034341
CELLULAR RESPONSE TO INTERFERON-GAMMA%GOBP%GO:0071346
INTERFERON GAMMA SIGNALING%REACTOME%R-HSA-877300.1
ANTIVIRAL MECHANISM BY IFN-STIMULATED GENES%REACTOME DATABASE ID RELEASE 70%1169410
INTERFERON-GAMMA-MEDIATED SIGNALING PATHWAY%GOBP%GO:0060333
RESPONSE TO TYPE I INTERFERON%GOBP%GO:0034340
INTERFERON ALPHA BETA SIGNALING%REACTOME%R-HSA-909733.2
CELLULAR RESPONSE TO TYPE I INTERFERON%GOBP%GO:0071357
TYPE I INTERFERON SIGNALING PATHWAY%GOBP%GO:0060337
SNRNP ASSEMBLY%REACTOME DATABASE ID RELEASE 70%191859
TYPE II INTERFERON SIGNALING (IFNG)%WIKIPATHWAYS_20191010%WP619%HOMO SAPIENS
THE HUMAN IMMUNE RESPONSE TO TUBERCULOSIS%WIKIPATHWAYS_20191010%WP4197%HOMO SAPI...

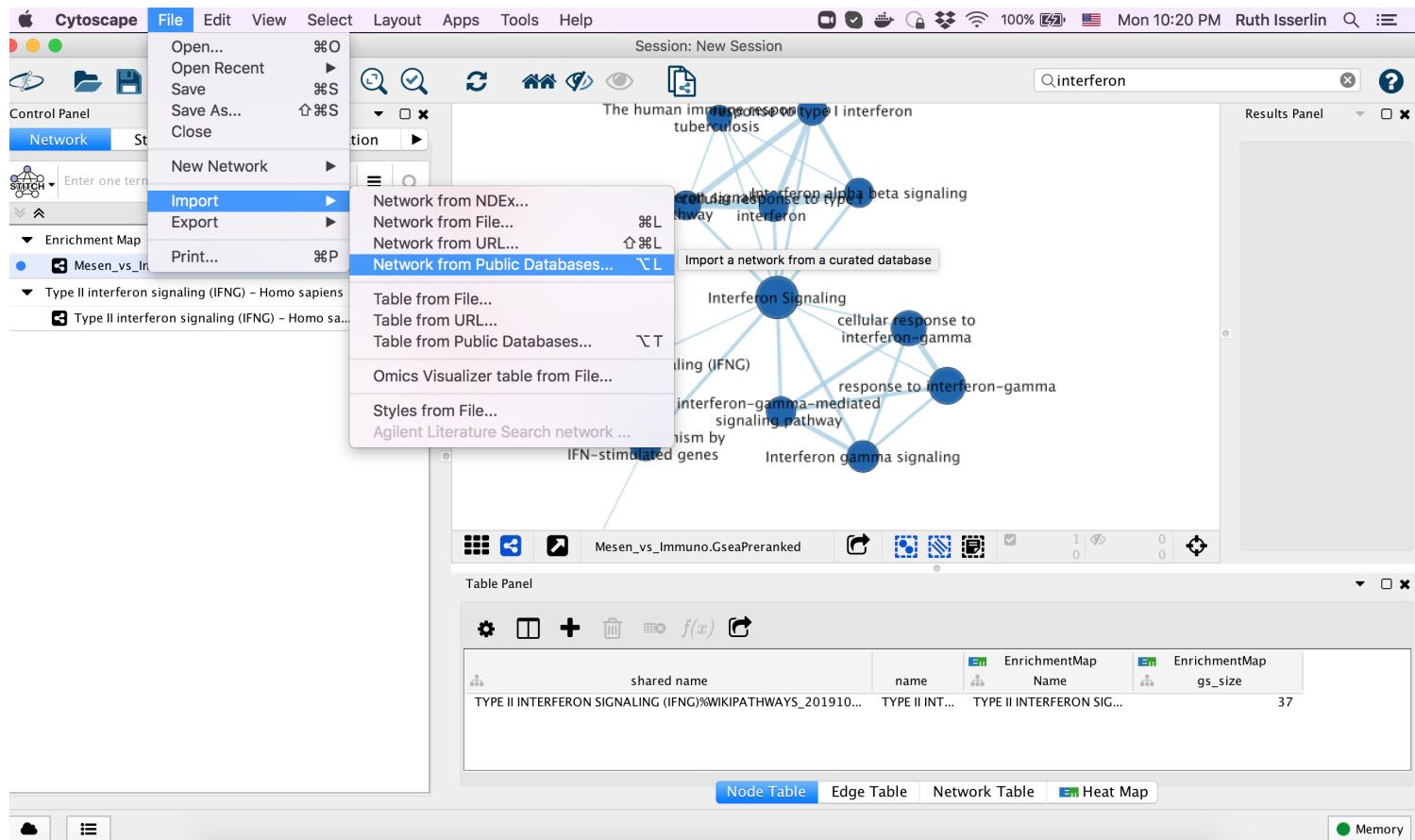
EnrichmentMap

GS_DESCR	gs_size
Interferon Signaling	194
response to interferon-gamma	139
cellular response to interferon-gamma	123
Interferon gamma signaling	90
Antiviral mechanism by IFN-stimulated genes	78
interferon-gamma-mediated signaling pathway	69
response to type I interferon	68
Interferon alpha beta signaling	66
cellular response to type I interferon	64
type I interferon signaling pathway	64
snRNP Assembly	50
Type II interferon signaling (IFNG)	37
The human immune response to tuberculosis	23

Node Table Edge Table Network Table Heat Map

**Click on any column to sort table by that column

Pathway Details - Wiki Pathways



Pathway Details - Wiki Pathways

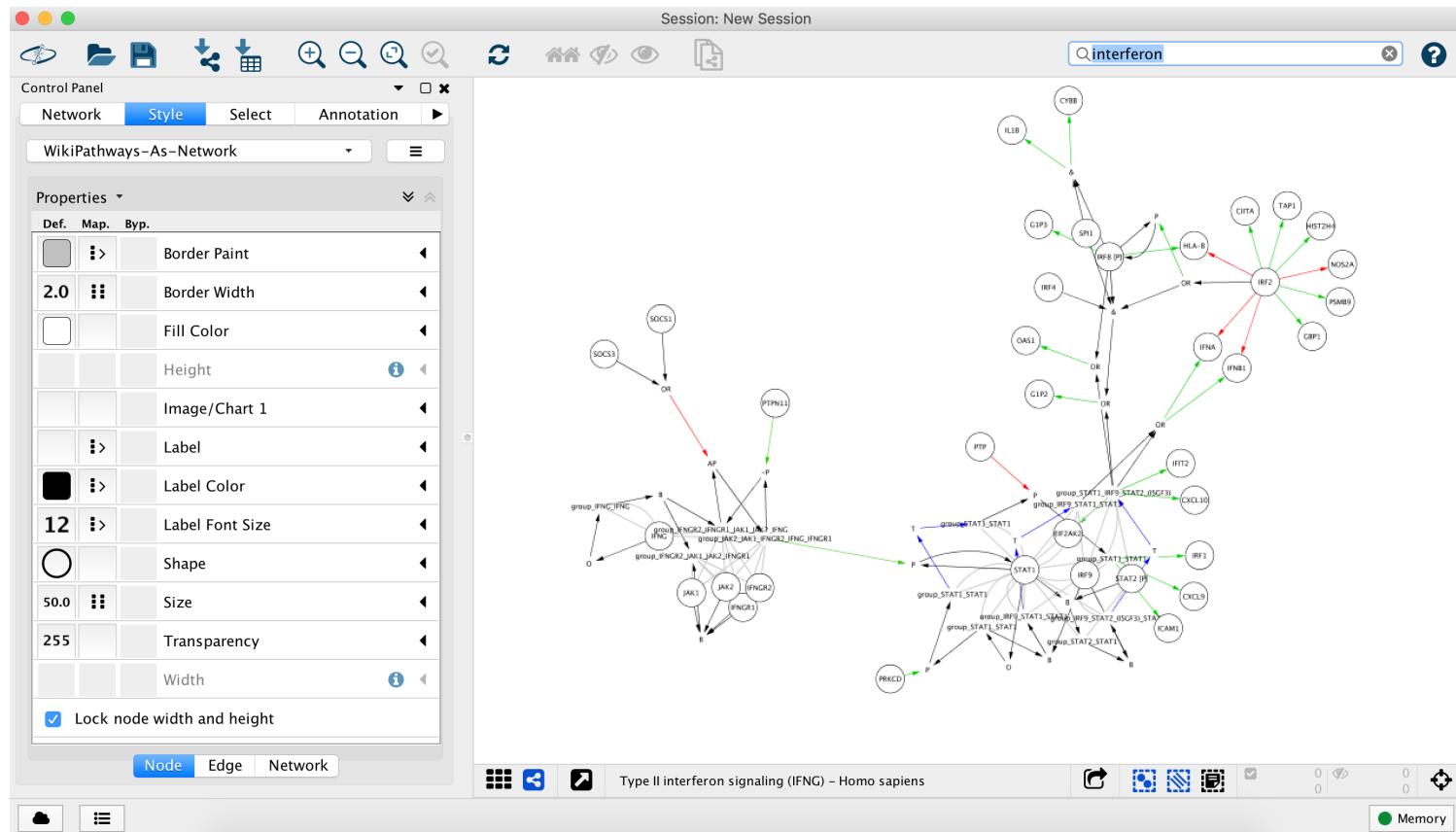
Import Network from Public Databases

Data Source: **WikiPathways**

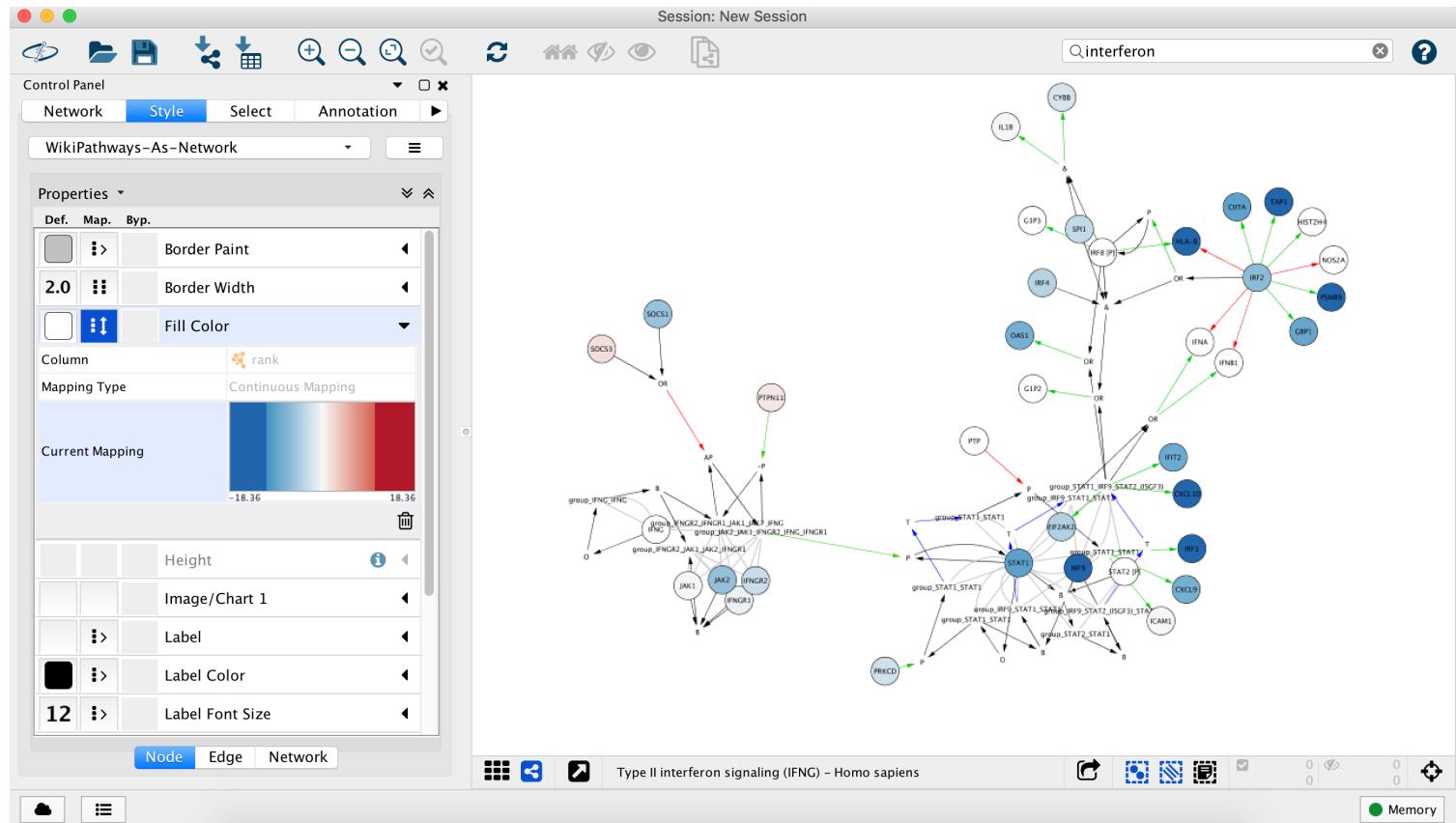
interferon Only: **Anopheles gambiae**

Pathway	Species	ID
Apoptosis	Danio rerio	WP1351
Apoptosis	Homo sapiens	WP254
Apoptosis	Gallus gallus	WP787
Apoptosis	Pan troglodytes	WP901
Cytosolic sensors of pathogen-associated DNA	Homo sapiens	WP2794
DDX58/IFIH1-mediated induction of interferon...	Homo sapiens	WP1904
Ebola Virus Pathway on Host	Homo sapiens	WP4217
Hair Follicle Development: Cytodifferentiation (...)	Homo sapiens	WP2840
Interferon alpha/beta signaling	Homo sapiens	WP1835
Interferon gamma signaling	Homo sapiens	WP1836
Interferon type I signaling pathways	Bos taurus	WP3213
Interferon type I signaling pathways	Homo sapiens	WP585
Osteoclast	Danio rerio	WP1342
Osteoclast	Mus musculus	WP454
Osteoclast	Rattus norvegicus	WP489
Osteoclast Signaling	Homo sapiens	WP12
Overview of interferons-mediated signaling pa...	Homo sapiens	WP4558
Type III interferon signaling	Homo sapiens	WP2113
Type III interferon signaling	Bos taurus	WP3173
Type II interferon signaling (IFNG)	Bos taurus	WP1017
Type II interferon signaling (IFNG)	Canis familiaris	WP1136
Type II interferon signaling (IFNG)	Mus musculus	WP1253
Type II interferon signaling (IFNG)	Rattus norvegicus	WP1289
Type II interferon signaling (IFNG)	Homo sapiens	WP619
Type II interferon signaling (IFNG)	Gallus gallus	WP786

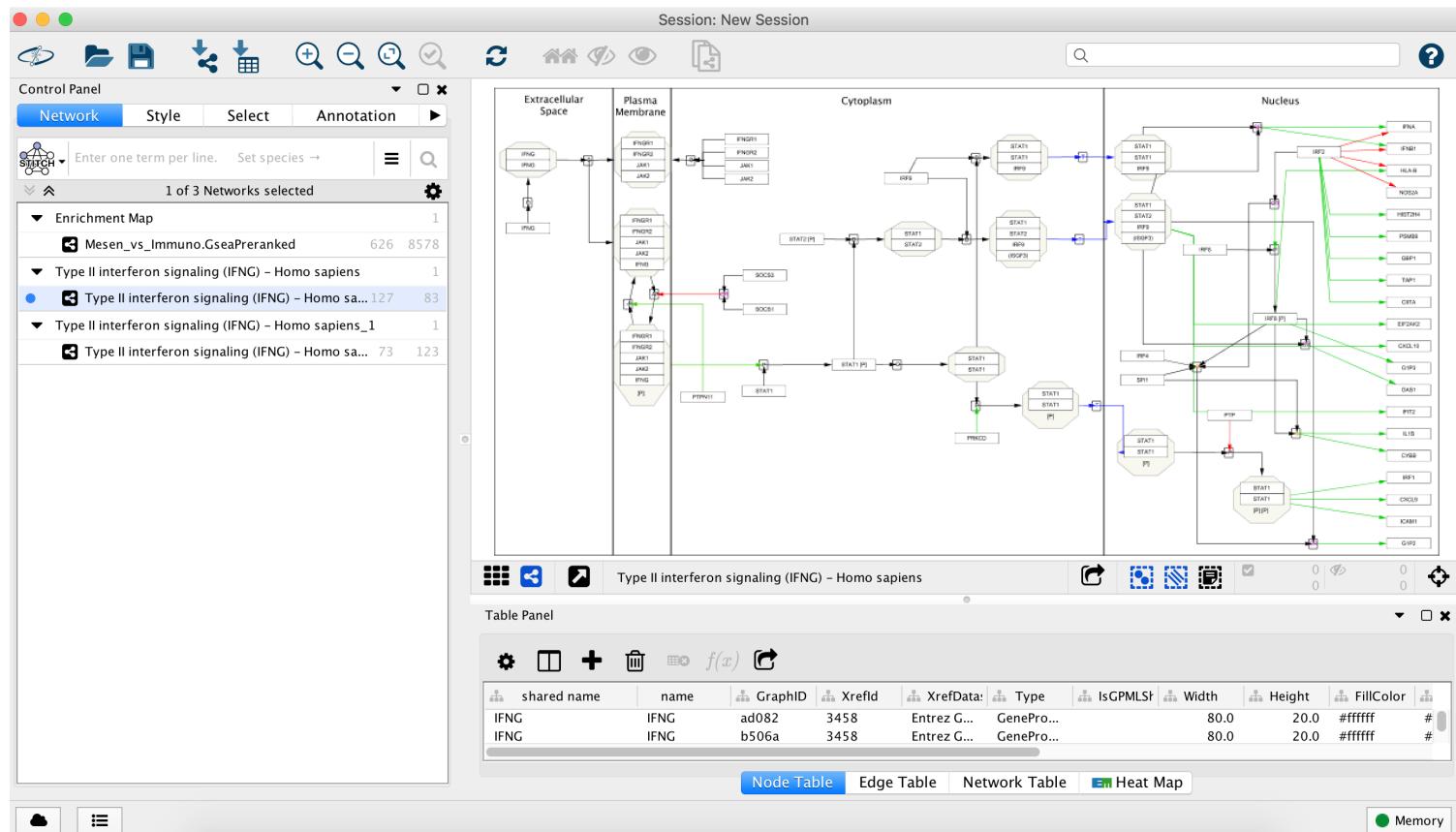
Pathway Details - Wiki Pathways



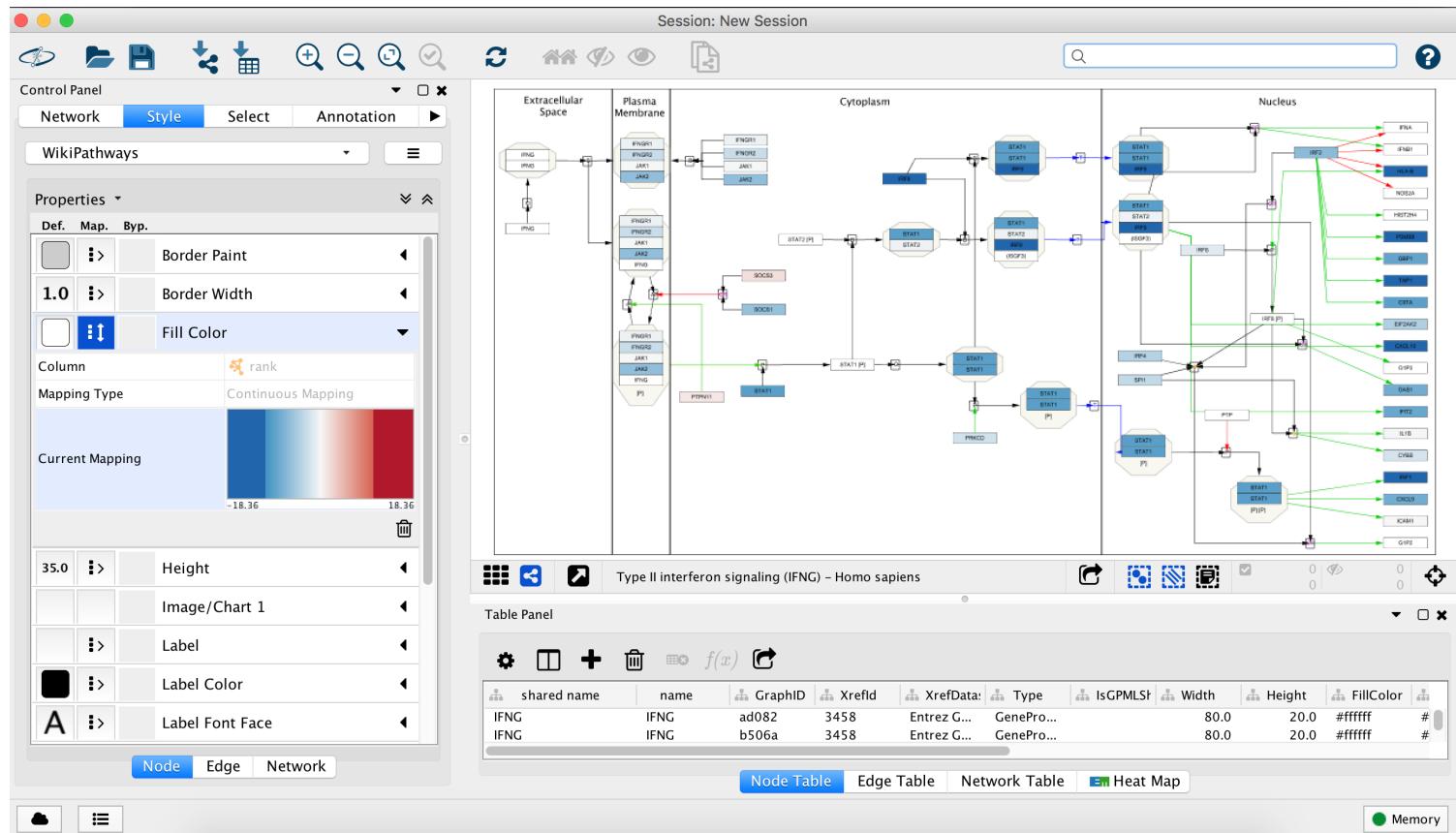
Pathway Details - Wiki Pathways



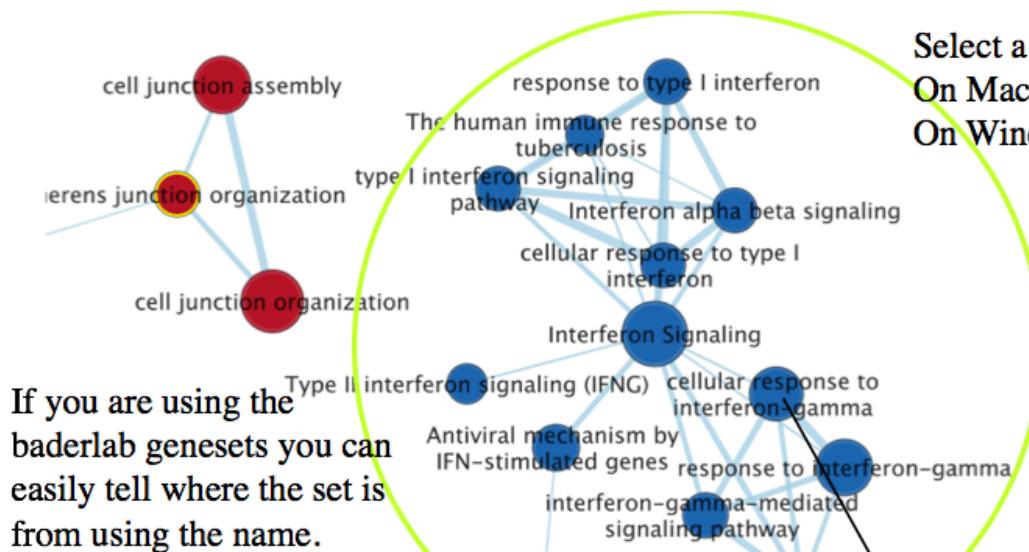
Pathway Details - Wiki Pathways



Pathway Details - Wiki Pathways



Pathway Details



Select a cluster:

On Mac - command, click and drag

On Windows - ctrl, click and drag

Node name is mapped to GS_descr

EnrichmentMap

Name
INTERFERON SIGNALING%REACTOME DATABASE ID RELEASE 70%913531
RESPONSE TO INTERFERON-GAMMA%GOBP%GO:0034341
CELLULAR RESPONSE TO INTERFERON-GAMMA%GOBP%GO:0071346
INTERFERON GAMMA SIGNALING%REACTOME%R-HSA-877300.1
ANTIVIRAL MECHANISM BY IFN-STIMULATED GENES%REACTOME DATABASE ID RELEASE 70%1169410
INTERFERON-GAMMA-MEDIATED SIGNALING PATHWAY%GOBP%GO:0060333
RESPONSE TO TYPE I INTERFERON%GOBP%GO:0034340
INTERFERON ALPHA BETA SIGNALING%REACTOME%R-HSA-909733.2
CELLULAR RESPONSE TO TYPE I INTERFERON%GOBP%GO:0071357
TYPE I INTERFERON SIGNALING PATHWAY%GOBP%GO:0060337
SNRNP ASSEMBLY%REACTOME DATABASE ID RELEASE 70%191859
TYPE II INTERFERON SIGNALING (IFNG)%WIKIPATHWAYS_20191010%WP619%HOMO SAPIENS
THE HUMAN IMMUNE RESPONSE TO TUBERCULOSIS%WIKIPATHWAYS_20191010%WP4197%HOMO SAPIENS

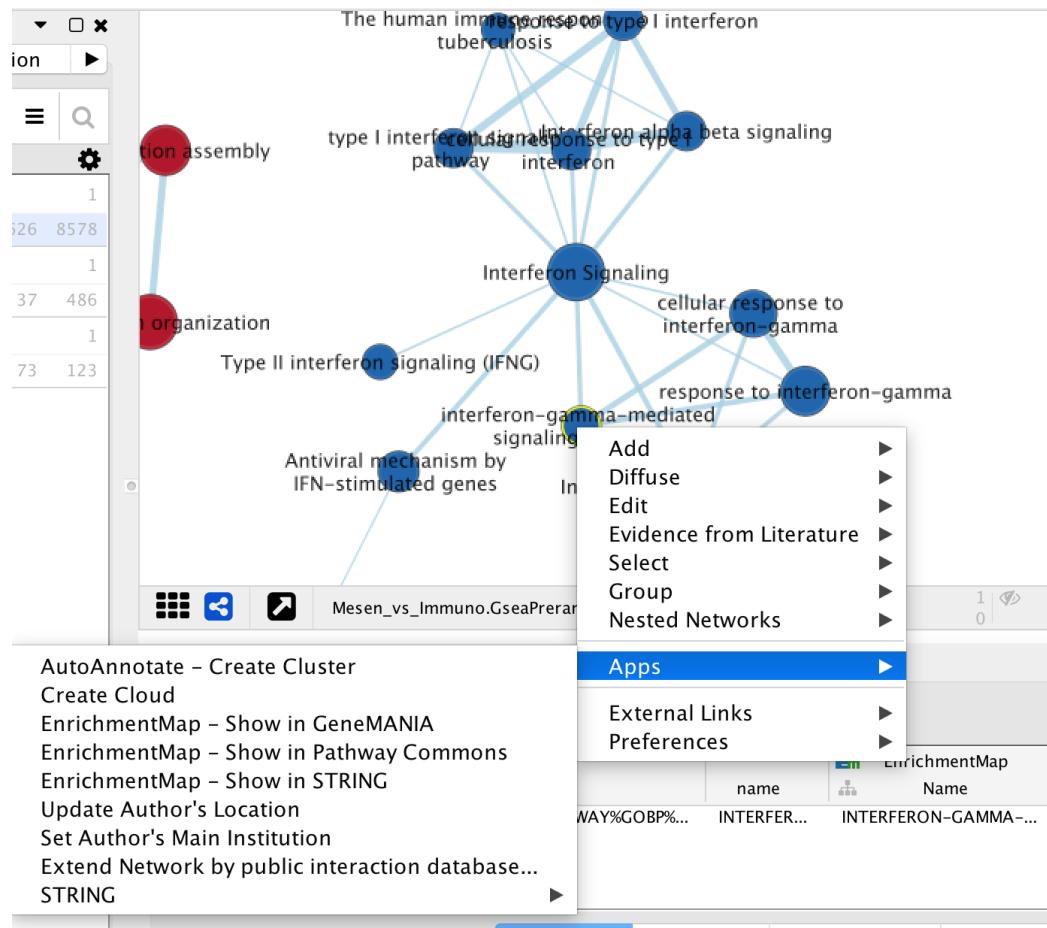
EnrichmentMap

GS_DESCR	gs_size
Interferon Signaling	194
response to interferon-gamma	139
cellular response to interferon-gamma	123
Interferon gamma signaling	90
Antiviral mechanism by IFN-stimulated genes	78
interferon-gamma-mediated signaling pathway	69
response to type I interferon	68
Interferon alpha beta signaling	66
cellular response to type I interferon	64
type I interferon signaling pathway	64
snRNP Assembly	50
Type II interferon signaling (IFNG)	37
The human immune response to tuberculosis	23

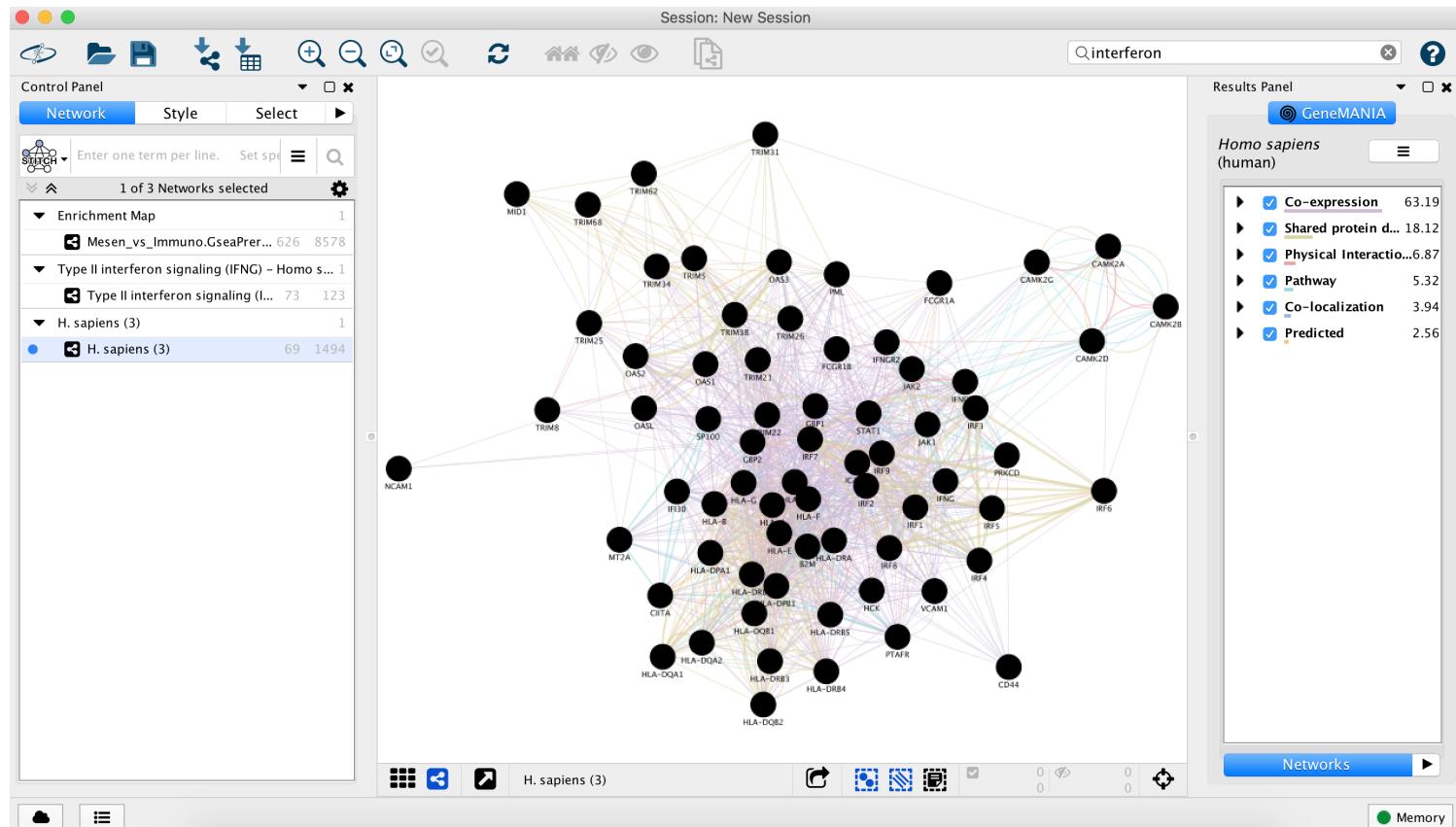
**Click on any column to sort table by that column

Node Table Edge Table Network Table Heat Map

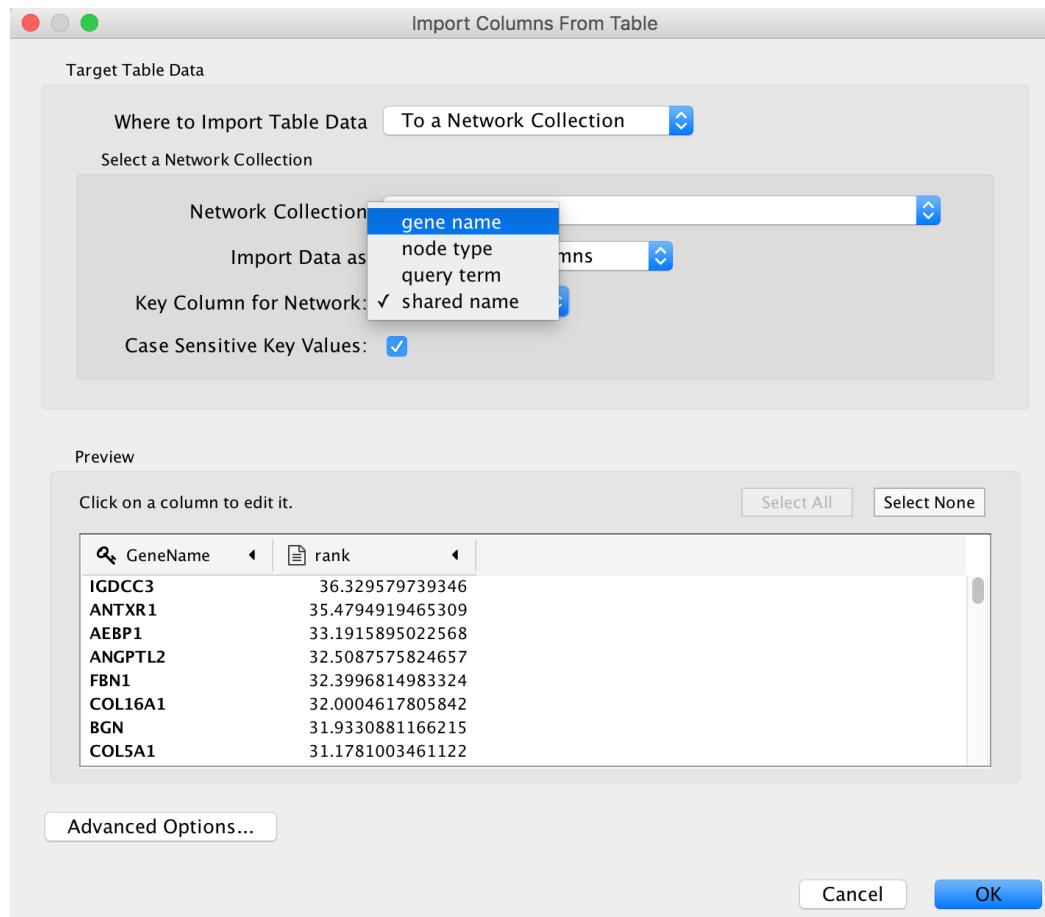
Pathway Details - GO and Other Pathways



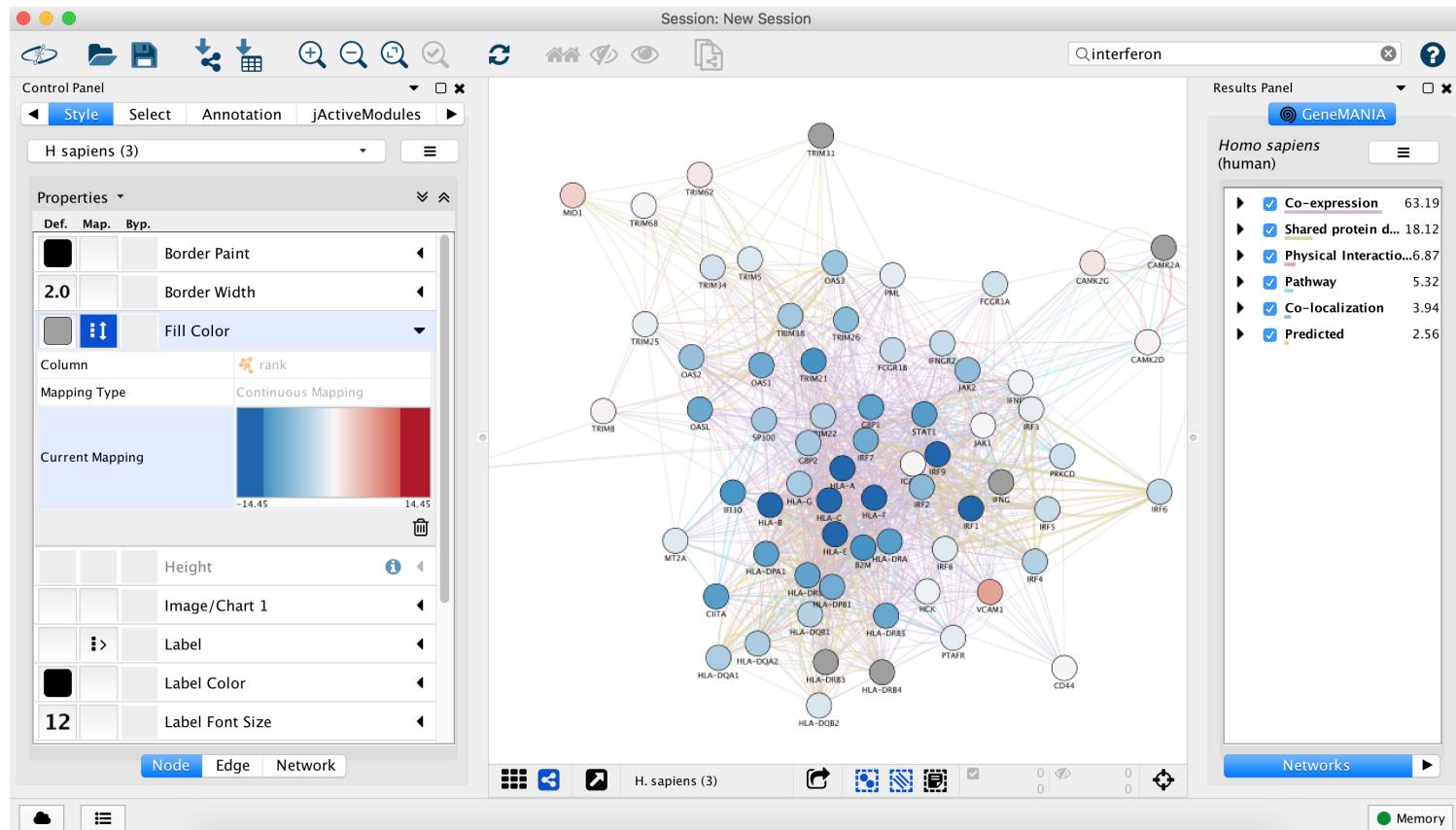
Pathway Details - GO and Other Pathways



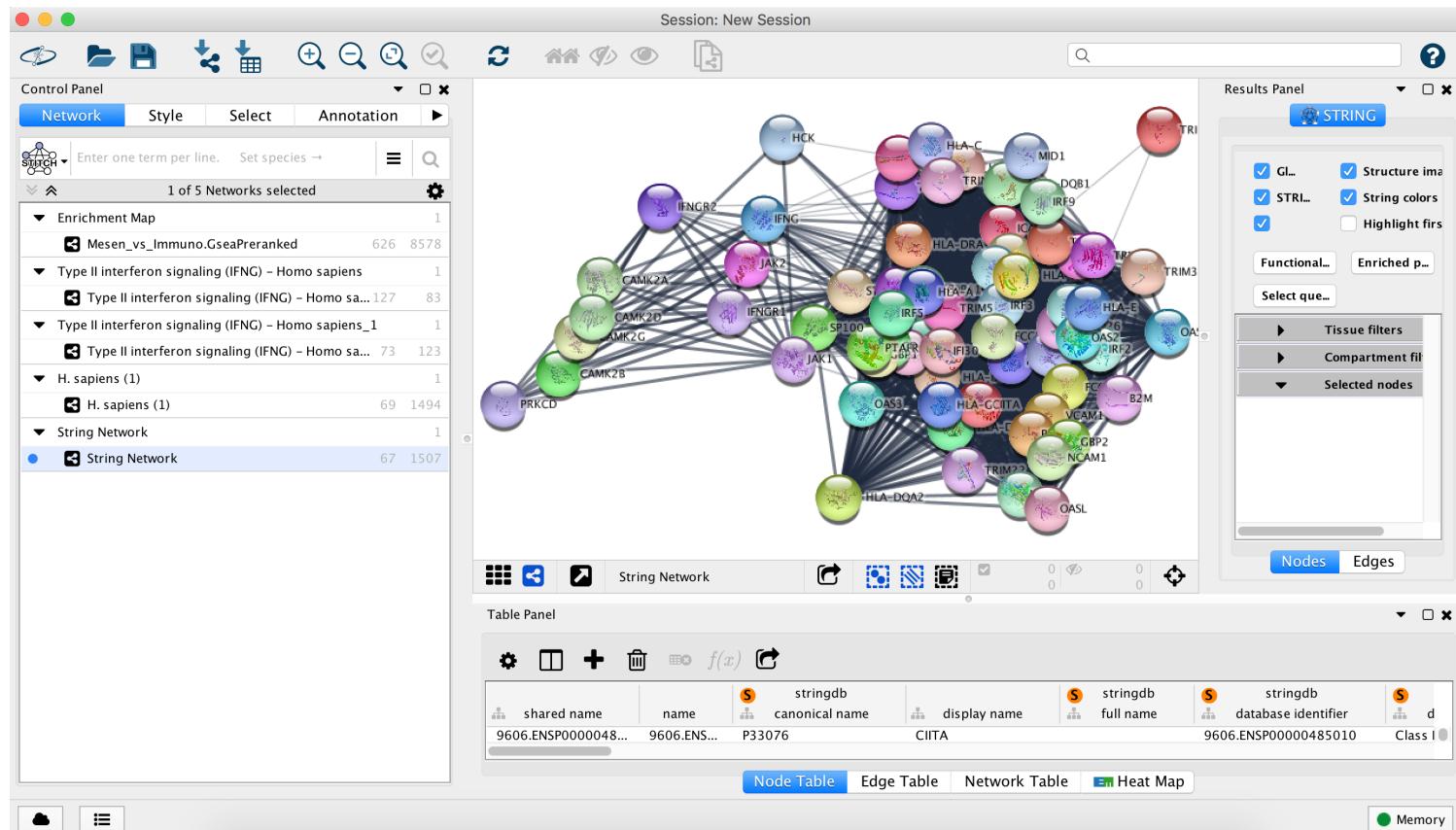
Pathway Details - GO and Other Pathways



Pathway Details - GO and Other Pathways



Pathway Details - GO and Other Pathways



Pathway Details - GO and Other Pathways

