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An introduction to Cytoscape

18 February 2020

Joan Gibert
 @joangibert4

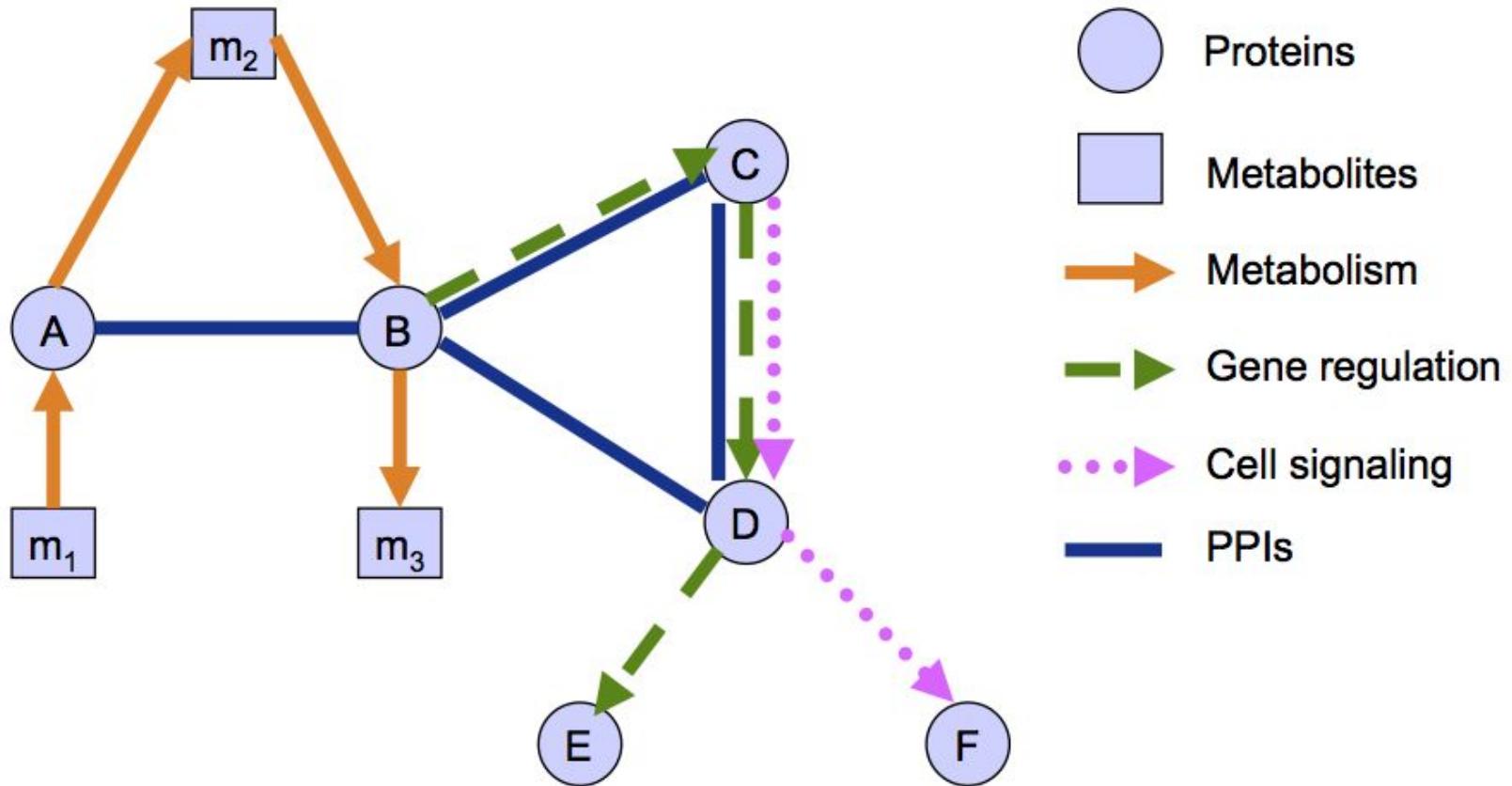
MARGenomics



Outline

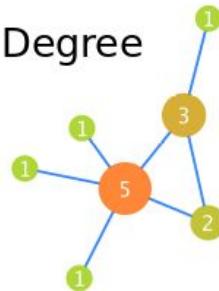
- Introduction to Networks: Main concepts
- Databases
- Introduction to Cytoscape
- Cytoscape hands-on:
 - Basics
 - Network analysis
 - Gene Ontology Networks
 - Reactome

Introduction - Networks

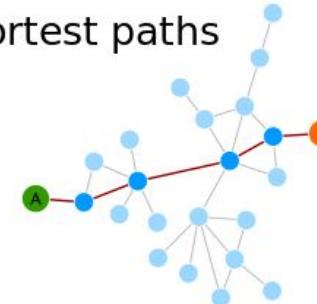


Introduction - Basics

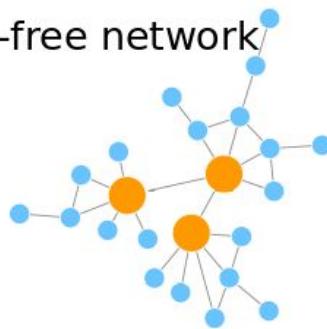
Degree



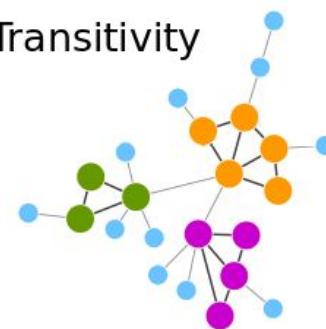
Shortest paths



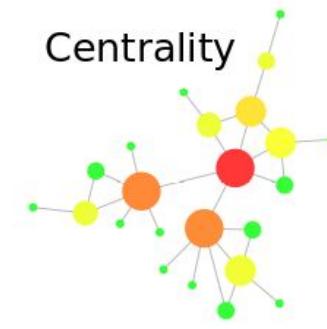
Scale-free network



Transitivity

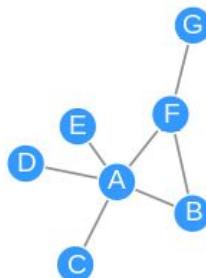


Centrality

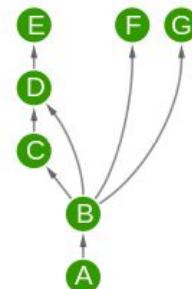


Introduction - Graph Types

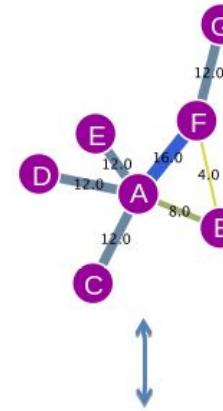
Undirected



Directed



Weighted



| | A | B | C | D | E | F | G | Degree |
|---|---|---|---|---|---|---|---|--------|
| A | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 5 |
| B | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 2 |
| C | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| D | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| E | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| F | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 3 |
| G | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 1 |

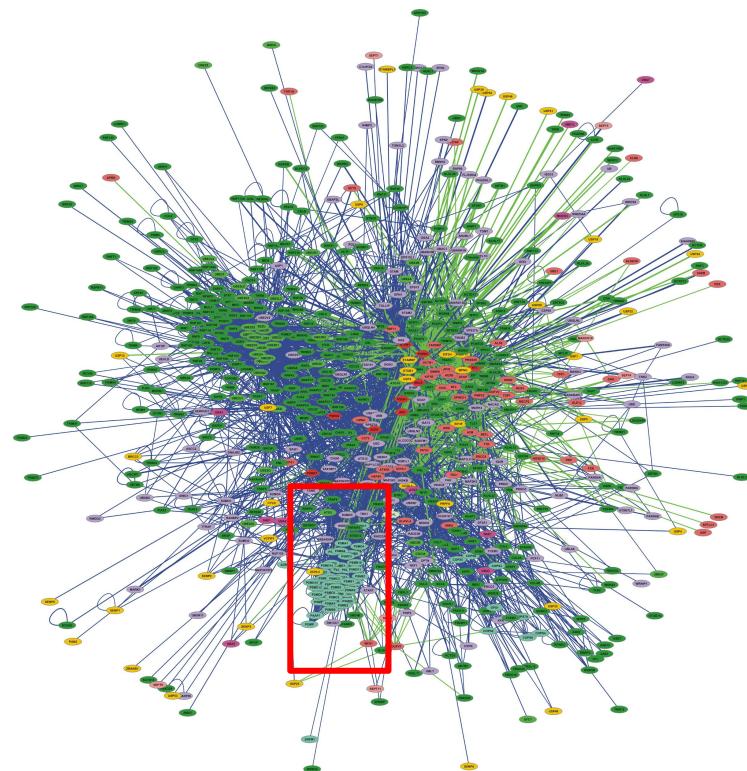
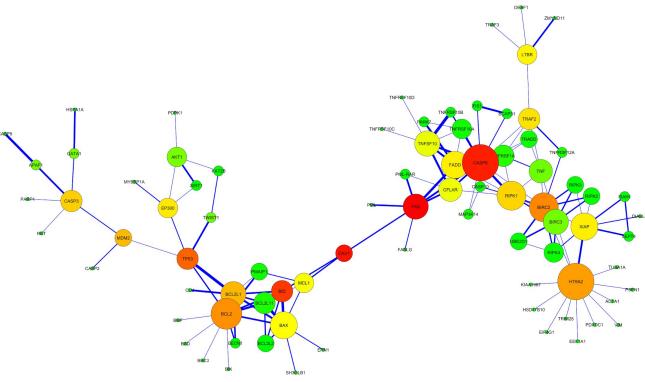
| | A | B | C | D | E | F | G | Out-Degree |
|---|---|---|---|---|---|---|---|------------|
| A | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| B | 0 | 0 | 1 | 1 | 0 | 1 | 1 | 4 |
| C | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 |
| D | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| E | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| F | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| G | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

Adjacency matrices

| | A | B | C | D | E | F | G | Degree |
|---|----|---|----|----|----|----|----|--------|
| A | 0 | 8 | 12 | 12 | 12 | 16 | 12 | 72 |
| B | 8 | 0 | 0 | 0 | 0 | 0 | 4 | 12 |
| C | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 12 |
| D | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 12 |
| E | 12 | 0 | 0 | 0 | 0 | 0 | 0 | 12 |
| F | 16 | 4 | 0 | 0 | 0 | 0 | 12 | 32 |
| G | 12 | 0 | 0 | 0 | 0 | 12 | 0 | 24 |

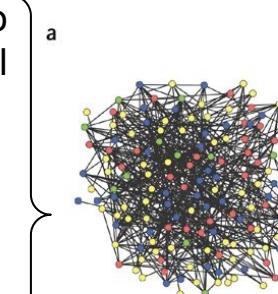
Introduction - Graph causality?

- Represent relationships
 - Physical, regulatory, genetic, functional interactions
- Useful for discovering relationships in large data sets
 - Better than tables
- Visualize multiple data types together
 - See interesting patterns
- Network analysis

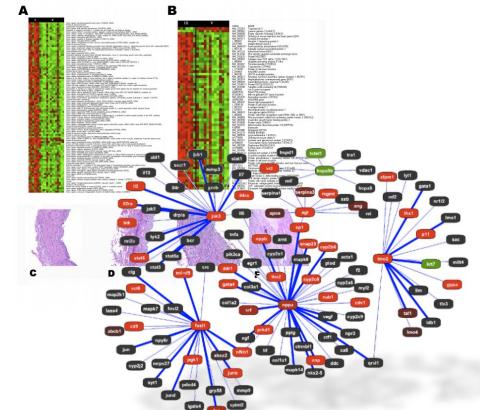
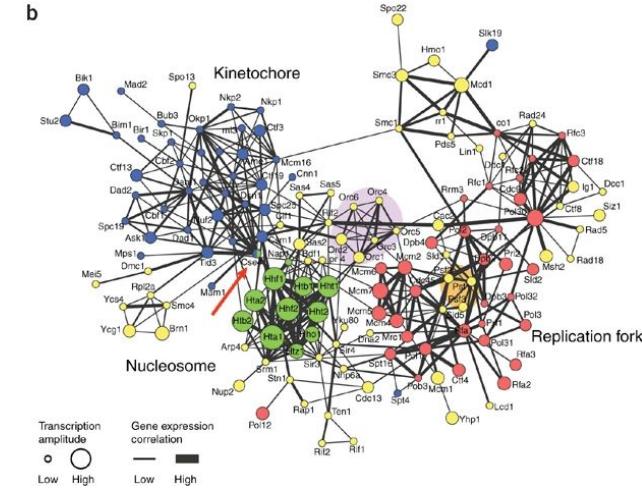


Introduction - Graph Types

- Gene Function Prediction – shows connections to sets of genes/proteins involved in same biological process
- Detection of protein complexes/other modular structures
- Prediction of new interactions and functional associations



- Identification of disease subnetworks – identification of disease network subnetworks that are transcriptionally active in disease.
- Subnetwork-based diagnosis – source of biomarkers for disease classification, identify interconnected genes whose aggregate expression levels are predictive of disease state



Databases: IntAct

The screenshot shows the IntAct Molecular Interaction Database homepage. At the top, there's a navigation bar with links for Services, Research, Training, and About us. Below the header, there's a search bar with placeholder text "Enter search term(s)...". To the right of the search bar is a "Feedback" link. The main content area has several sections: "Examples" (listing Gene, Protein, RNA or Chemical name: BRCA2, Stauroporine, UniProtKB or ChEBI AC: Q06609, CHEBI:15996, UniProtKB ID: LCK_HUMAN, RNACentral ID: URSG00004C95F4_559292, PMID: 25416956, IMEx ID: IM-23318), "Data Content" (Publications: 20042, Interactions: 794922, Interactors: 104510), "Submission" (Submit your data to IntAct to increase its visibility and usability!), "Contributors" (Manually curated content is added to IntAct by curators at the EMBL-EBI and the following organisations: MINT, UniProt, SIB, i2D, InnateDB, Molecular Connections, MatrixDB, MBInfo, AgBase, G2, and IMEx), "Training" (Online & upcoming courses), and "Citing IntAct" (The MIIntAct project—IntAct as a common curation platform for 11 molecular interaction databases. Orchard S et al [PMID:24234451] [Full Text]). On the right side, there are "Featured Dataset" (Widespread Expansion of Protein Interaction Capabilities by Alternative Splicing) and "News" (IntAct at EBI Retweeted, PSICQUIC @PSICQUIC HUPO-PSI April 18-20 2018 EMBL-Heidelberg Germany now open for registration psidev.info/content/hupo-p... Free meeting (inc. lunches, refreshments and workshop dinner) to work on standards & formats for #proteomics, molecular interactions @embl @embl_ebi @huopo.org #psi2018), and "Embed" and "View on Twitter" buttons.

- Curation platform for all members of the IMEx Consortium.
- Double curator process for quality control.

- Holds molecular interaction data curated to IMEx standards (high detail).
- ~ 800,000 protein interactions and ~100,000 interactors from ~14K publications.
- No specific organism focus.



Databases: BioGRID

BioGRID 3.4

home help wiki tools contribute stats downloads partners about us | [B](#)

Result Summary

GLRX2 *Homo sapiens*

CGI-133, GRX2, RP11-101E13.4

glutaredoxin 2

GO Process (12) GO Function (4) GO Component (4)

EXTERNAL DATABASE LINKOUTS
VEGA | HGNC | OMIM | Entrez Gene | RefSeq | UniprotKB | Ensembl | HPRD

Download 6 Published Interactions For This Protein

Stats & Options

Current Statistics Publications: 3
High Throughput Low Throughput
5 (83%) 6 Physical Interactions 1 (17%)
0 (0%) 0 Genetic Interactions 0 (100%)

Search Filters Customize how your results are displayed...
No Filter: Show All Associations

Switch View: Interactors (6) Interactions (6) Network Chemicals (1)

Displaying 6 total unique interactions

| Interactor | Role | Organism | Experimental Evidence Code | Dataset | Throughput | Score | Curated By | Notes |
|---------------|------|------------|-------------------------------|--------------------|------------|--------|------------|-------|
| BAG3 | BAIT | H. sapiens | Affinity Capture-Luminescence | Chen Y (2013) | High | - | BioGRID | - |
| CYCS | BAIT | H. sapiens | Co-fractionation | Cuihong W (2015) | High | 0.2141 | BioGRID | |
| GPX4 | BAIT | H. sapiens | Co-fractionation | Cuihong W (2015) | High | 0.3946 | BioGRID | |
| MDH2 | HIT | H. sapiens | Co-fractionation | Cuihong W (2015) | High | 0.074 | BioGRID | |
| PITPNB | HIT | H. sapiens | Co-fractionation | Cuihong W (2015) | High | 0.083 | BioGRID | |
| TXNRD1 | BAIT | H. sapiens | Biochemical Activity | Johansson C (2004) | Low | - | BioGRID | |

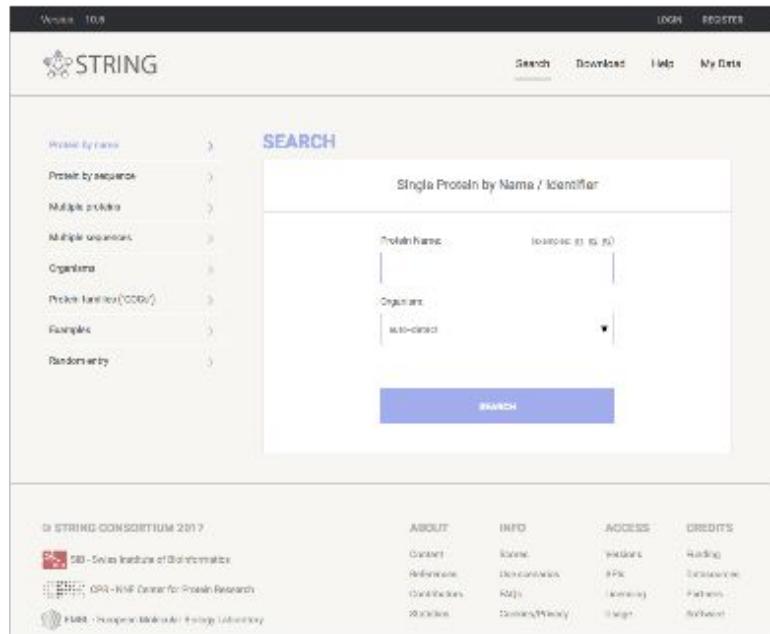
Copyright © 2016 TyersLab.com, All Rights Reserved.

Terms and Conditions | Privacy Policy | Osprey Network Visualization System | TyersLab.com | SGD | GitHub | YouTube | Twitter



Databases: STRING

<http://string-db.org/>



- Holds physical and functional interactions.
- Covers over 9.6 M proteins from over 2000 organisms.
- Results show a pre-filtered summary of multiple evidence types: experimental, gene fusion, co-occurrence, co-expression, text mining...

- Website allows individual and multiple gene/protein/sequence searches.
- Data available also via download from their website and a Cytoscape app.



Databases: Reactome



The screenshot shows the Reactome website homepage. At the top is a navigation bar with links for About, Content, Docs, Tools, Community, and Download. Below the navigation is a search bar with placeholder text "e.g. O95631, NTN1, signaling by EGFR, glucose" and a "Go!" button. Underneath the search bar are four large blue icons with corresponding labels: "Pathway Browser" (with a tree icon), "Analyze Data" (with a bar chart icon), "ReactomeFIViz" (with a network icon), and "Documentation" (with a document icon). Each tool has a brief description below its label.

Find Reactions, Proteins and Pathways

e.g. O95631, NTN1, signaling by EGFR, glucose **Go!**

Pathway Browser
Visualize and interact with Reactome biological pathways

Analyze Data
Merges pathway identifier mapping, over-representation, and expression analysis

ReactomeFIViz
Designed to find pathways and network patterns related to cancer and other types of diseases

Documentation
Information to browse the database and use its principal tools for data analysis

USE REACTOME GRAPH DATABASE IN YOUR PROJECT **LEARN MORE**

Why Reactome
Reactome is a free, open-source, curated and peer-reviewed pathway database. Our goal is to provide intuitive bioinformatics tools for the visualization, interpretation and analysis of pathway knowledge to support basic research, genome analysis, modeling, systems biology and education.
If you use Reactome in Asia, we suggest using our Chinese mirror site at reactome.ncpsb.org.

Tweets
reactome Retweeted
eLife Innovation @eLifeInnovation
FAIR-blomed allows you to search #opendata on 21 distinct resources, including @EuropePMC_news @uniprot @ClinGenResource @reactome @jaspar_db and more! Find out more and try out the browser extension [elife.org/labs/8c7cc651/...](https://elifesciences.org/labs/8c7cc651/)

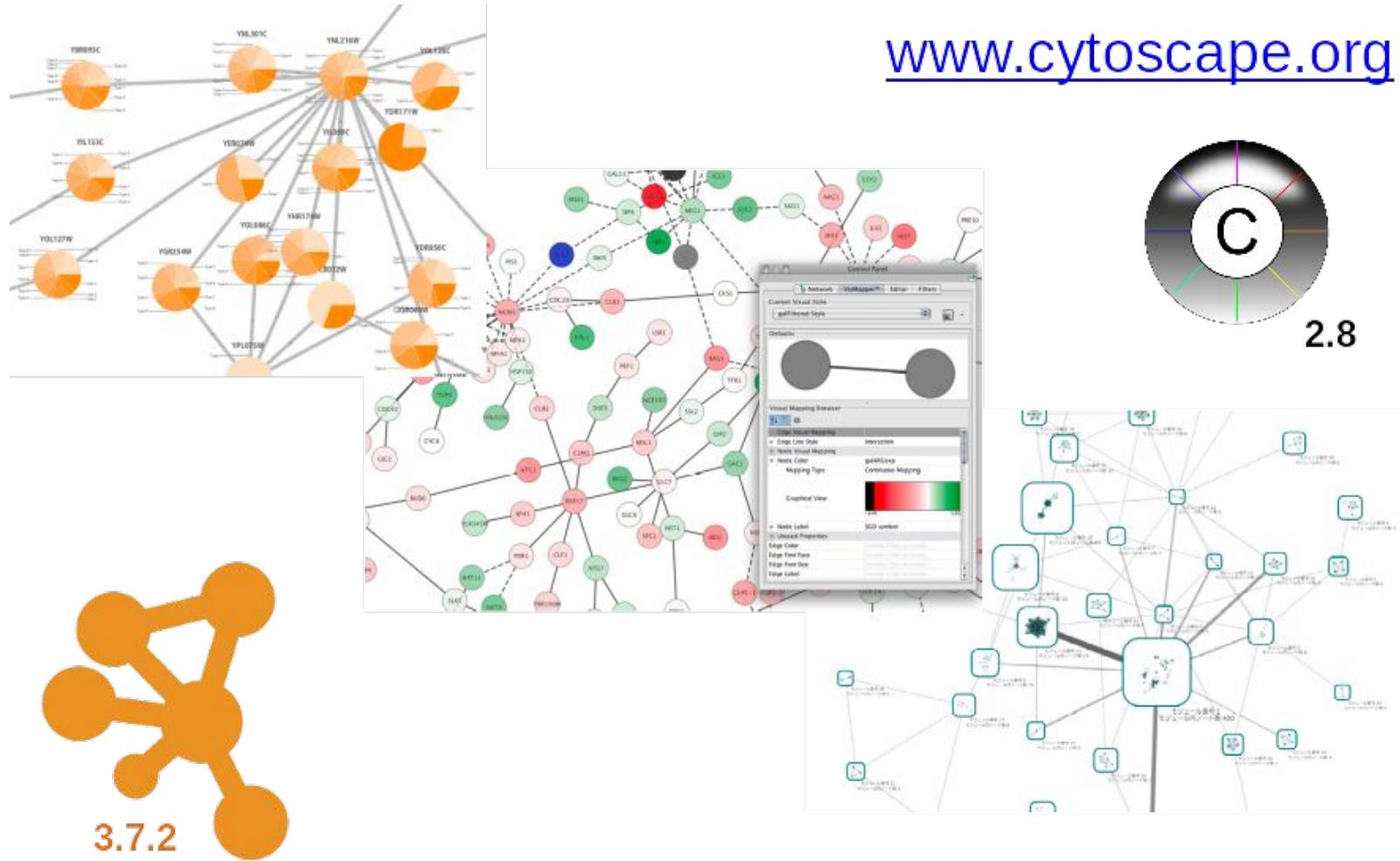
The development of Reactome is supported by grants from the US National Institutes of Health (P41)

REACTOME is an open-source, open access, manually curated and peer-reviewed pathway database. Our goal is to provide intuitive bioinformatics tools for the visualization, interpretation and analysis of pathway knowledge.



Cytoscape

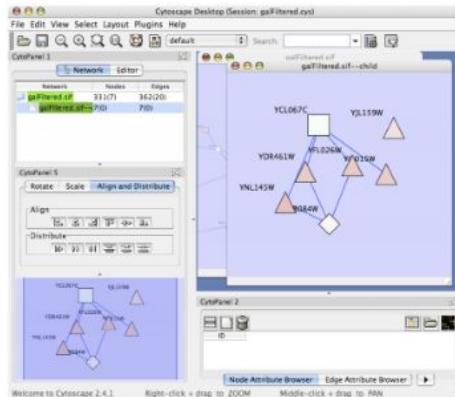
Open-source network representation and analysis tool



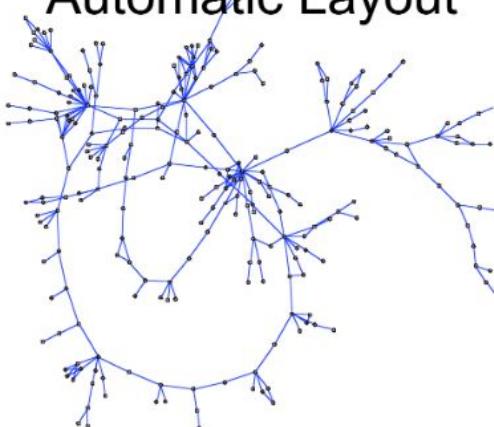
Cytoscape

Open-source network representation and analysis tool

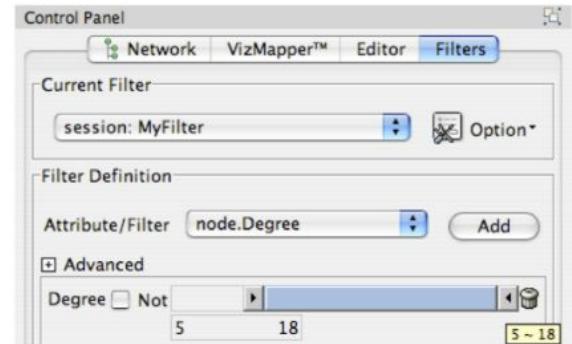
Manipulate Networks



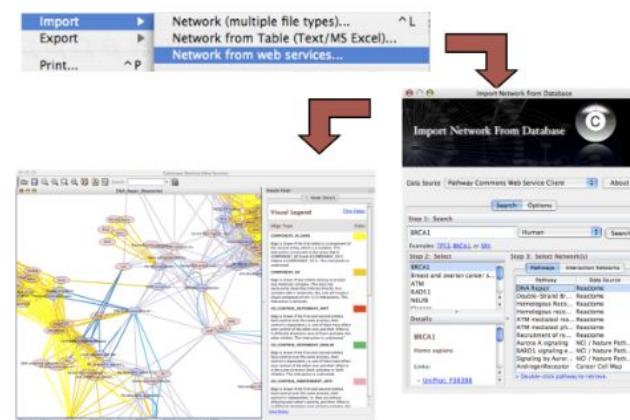
Automatic Layout



Filter/Query



Interaction Database Search



Cytoscape apps

 Cytoscape App Store

Submit an App ▾ Search the App Store Sign In

All Apps

Categories

- collections
- data visualization
- network generation
- graph analysis
- network analysis
- online data import
- automation
- integrated analysis
- clustering
- systems biology
- utility
- enrichment analysis
- visualization
- data integration
- layout
- core app
- annotation
- ontology analysis
- pathway database
- network comparison

[more »](#)

Newest Releases

[Get Started with the App Store »](#)

**enhancedGraphics** 3.0+
A passthrough mapper for charts and gradients

**ReactomeFIPlugin** 3.0+
Explore Reactome pathways and search for diseases related

**Omics Visualizer** 3.0+
Import & Visualize several data for the same node

**Analyzer** 3.0+
Calculate network, node, and edge statistics for any connected

**MCODE** 3.0+
Clusters a given network based on topology to find densely

**Assembly** 3.0+
Import sequence graphs in Graphical Fragment Assembly

[more newest releases »](#)

Top Downloaded Apps

**ClueGO** 3.0+
Creates and visualizes a functionally grouped network of

**BiNGO** 3.0+
Calculates overrepresented GO terms in the network and display

**CluePedia** 3.0+
CluePedia: A ClueGO plugin for pathway insights using integrated

**GeneMANIA** 3.0+
Imports interaction networks from public databases from a list of

**MCODE** 3.0+
Clusters a given network based on topology to find densely

**clusterMaker2** 3.0+
Multi-algorithm clustering app for Cytoscape

[more top downloads »](#)

- Large variety of apps/plugins (~330)
 - Great flexibility, adaptable to multiple types of analysis, in various domains of knowledge:
bioinformatics, social network analysis, semantic web...
 - Possibility to create your own.
 - Some deprecated or obsolete
 - Different functionality depending on the Cytoscape version



Cytoscape Hands-on

The landing page features a large network graph at the top, with a prominent orange Cytoscape logo and the text "Network Data Integration, Analysis, and Visualization in a Box". Below the logo is a yellow box containing the word "Introduction". To the right of the graph is a yellow box with the text "Download 3.7.2". The network graph itself contains numerous gene names as nodes, such as PTN, ESR1, MDM2, BRAP, and many others.

Introduction

Download 3.7.2

Cytoscape is an open source software platform for visualizing complex networks and integrating these with any type of attribute data. A lot of [Apps](#) are available for various kinds of problem domains, including bioinformatics, social network analysis, and semantic web. [Learn more...](#)

Welcome Letter

Release Notes

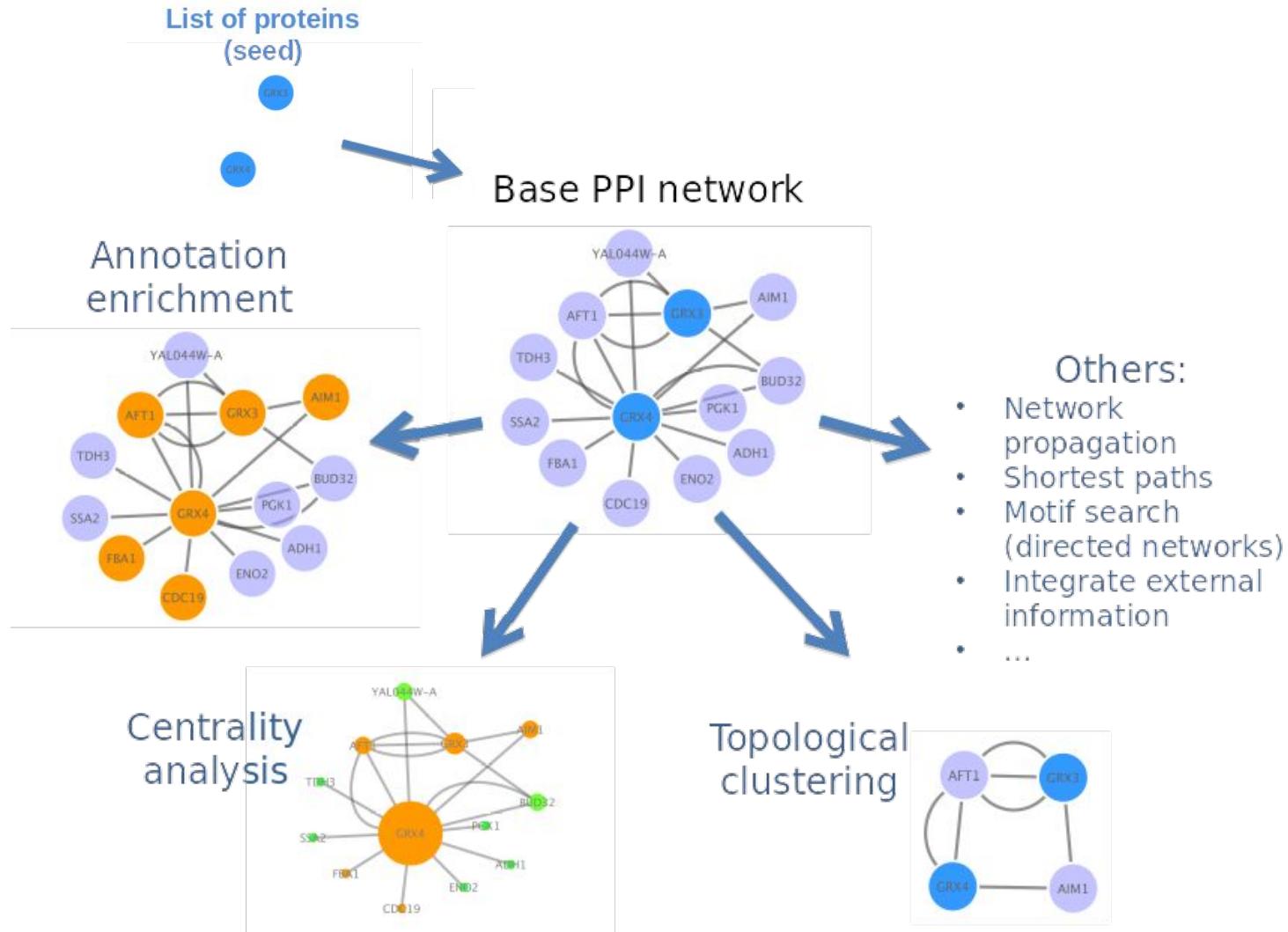
Sample Visualizations

Cytoscape Tutorials

App Developers Docs



Cytoscape Hands-on



Cytoscape Hands-on

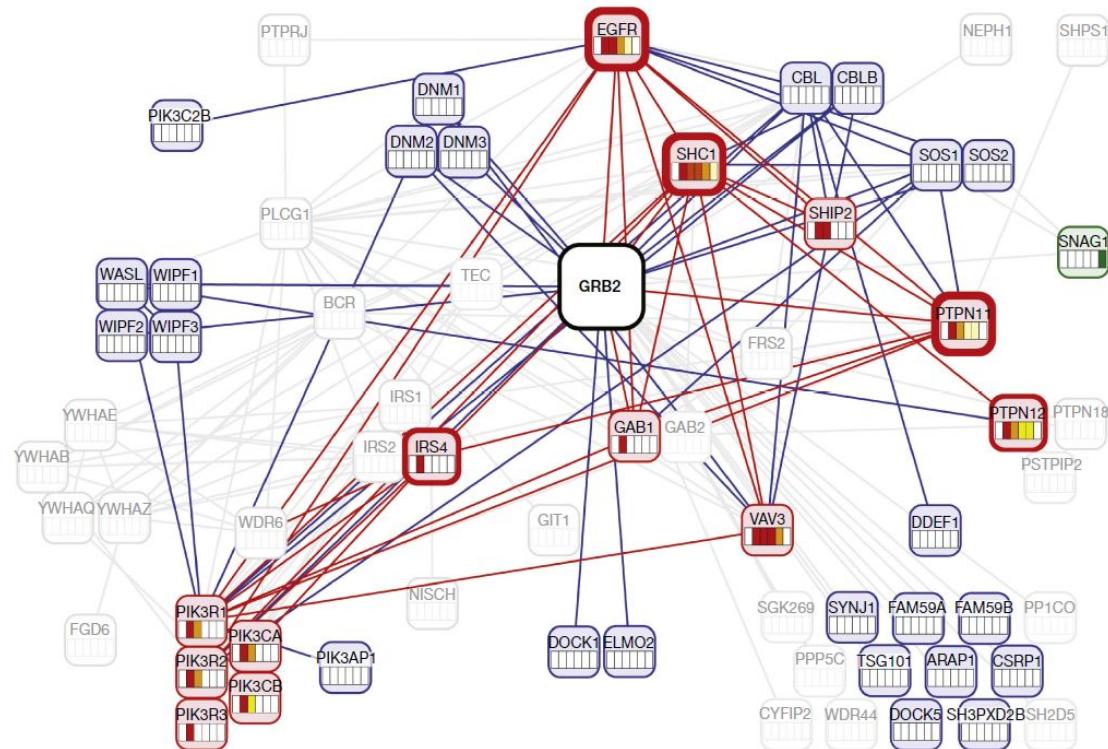
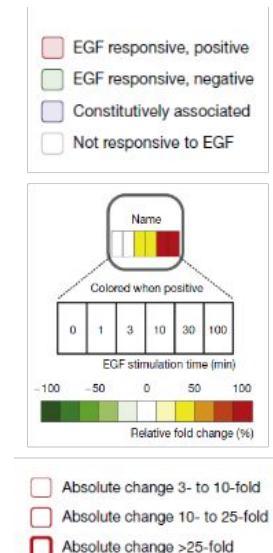
nature
biotechnology

Letter | Published: 26 June 2011

Selected reaction monitoring mass spectrometry reveals the dynamics of signaling through the GRB2 adaptor

Nicolas Bisson, D Andrew James, Gordana Ivosev, Stephen A Tate, Ron Bonner, Lorne Taylor & Tony Pawson

Nature Biotechnology 29, 653–658(2011) | Cite this article



Cytoscape Hands-on

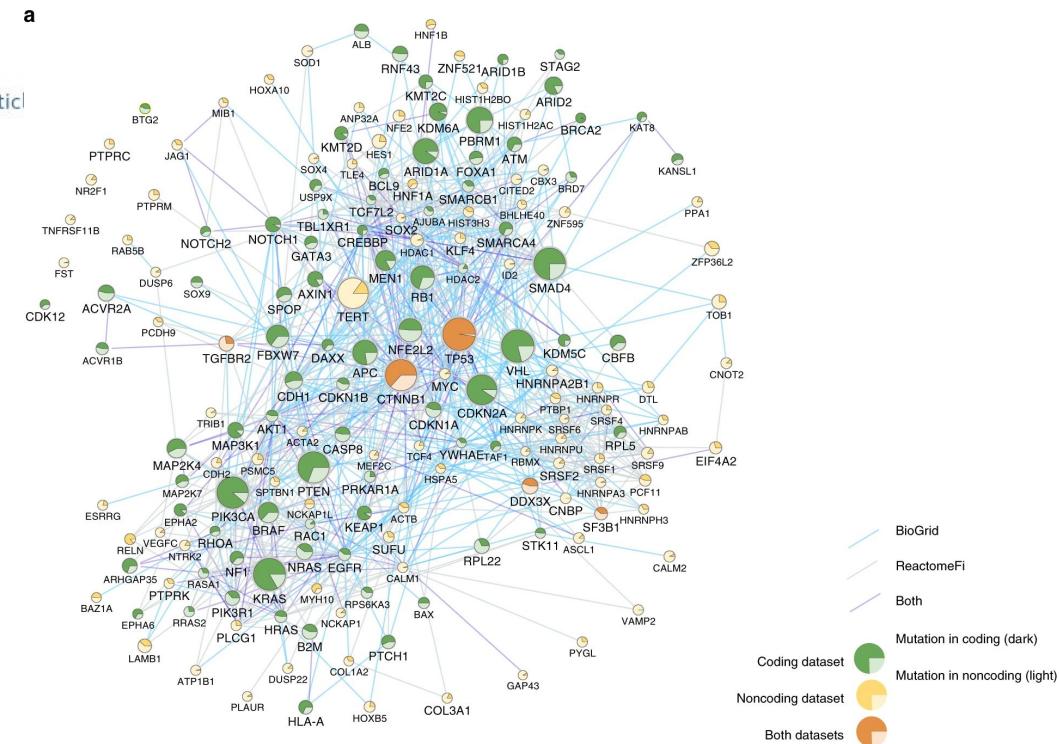
nature
communications

Article | Open Access | Published: 05 February 2020

Pathway and network analysis of more than 2500 whole cancer genomes

Matthew A. Reyna, David Haan, [...] PCAWG Consortium

Nature Communications 11, Article number: 729 (2020) | Cite this article



Disclaimers

Memory

- Cytoscape uses lots of it
- Doesn't like to let go of it
- An occasional SAVE and restart when working with large networks is a good thing
- Destroy views when you don't need them
- Cytoscape tries to “guess” good default memory based on how much memory you have, but it can fail
- To improve interactive performance, Cytoscape has the concept of “Levels of Detail”

Cytoscape Hands-on: Data

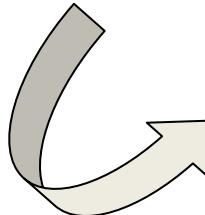
www.nature.com/scientificreports/

SCIENTIFIC REPORTS

OPEN Transcriptomic and functional network features of lung squamous cell carcinoma through integrative analysis of GEO and TCGA data

Received: 31 May 2018
Accepted: 12 October 2018
Published online: 26 October 2018

Yin Li, Jie Gu, Fengkai Xu, Qiaoliang Zhu, Di Ge & Chunlai Lu



Supplementary Table 2.xlsx
or
1_TCGA_LUSC_DEG.csv

TCGA LUSC (500 cases)

NIH ➤ NATIONAL CANCER INSTITUTE

ABOUT CANCER CANCER TYPES RESEARCH GRANTS & TRAINING NEWS & EVENTS ABOUT NCI search Q

Home > About NCI > NCI Organization > CCG > Research > Structural Genomics



TCGA

- Program History +
- TCGA Cancers Selected for Study
- Publications by TCGA
- Using TCGA +
- Contact

The Cancer Genome Atlas Program

The Cancer Genome Atlas (TCGA), a landmark cancer genomics program, molecularly characterized over 20,000 primary cancer and matched normal samples spanning 33 cancer types. This joint effort between the National Cancer Institute and the National Human Genome Research Institute began in 2006, bringing together researchers from diverse disciplines and multiple institutions.

Over the next dozen years, TCGA generated over 2.5 petabytes of genomic, epigenomic, transcriptomic, and proteomic data. The data, which has already led to improvements in our ability to diagnose, treat, and prevent cancer, will remain publicly available for anyone in the research community to use.



TCGA Outcomes & Impact

TCGA has changed our understanding of cancer, how research is conducted, how the disease is treated in the clinic, and more.

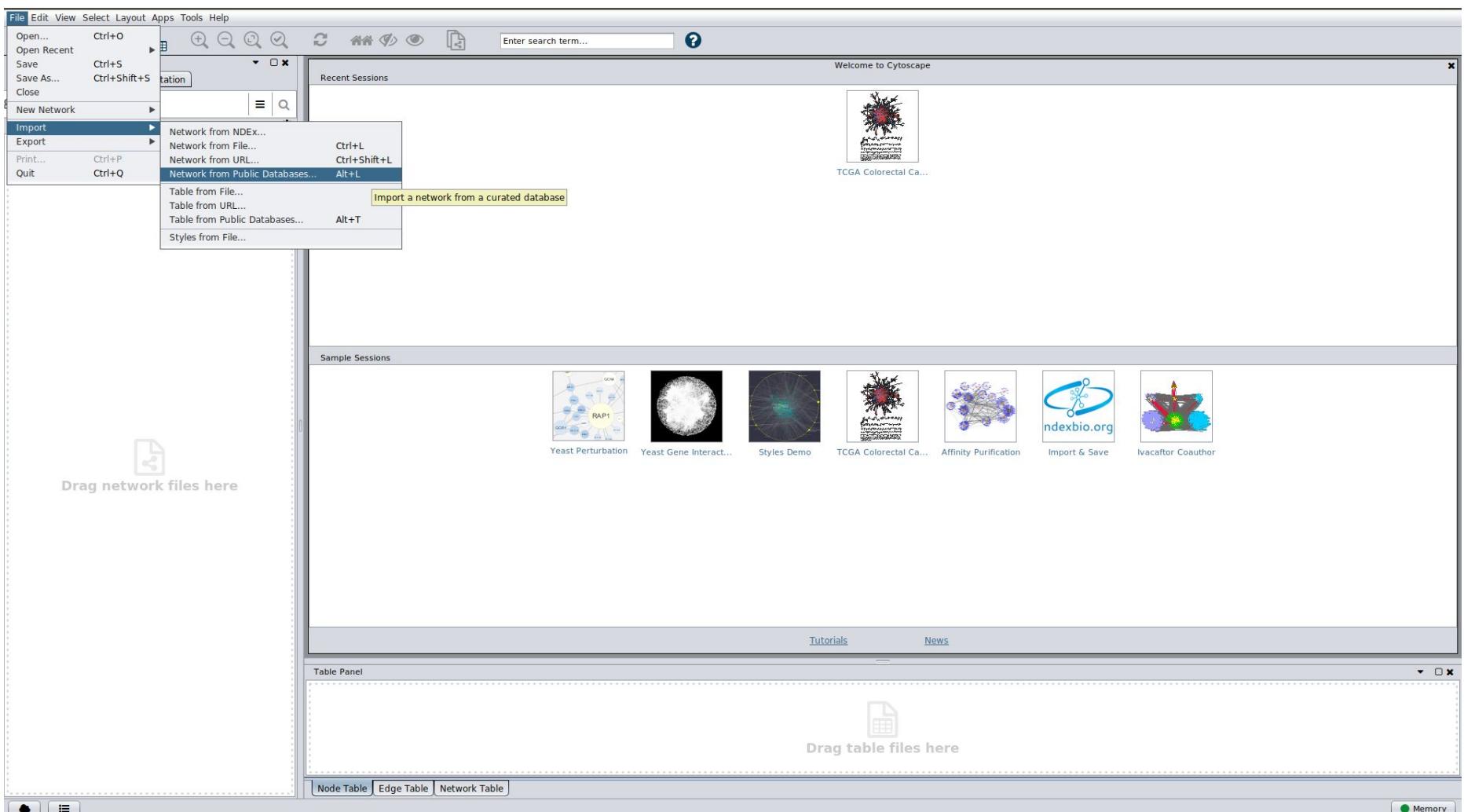


TCGA's PanCancer Atlas

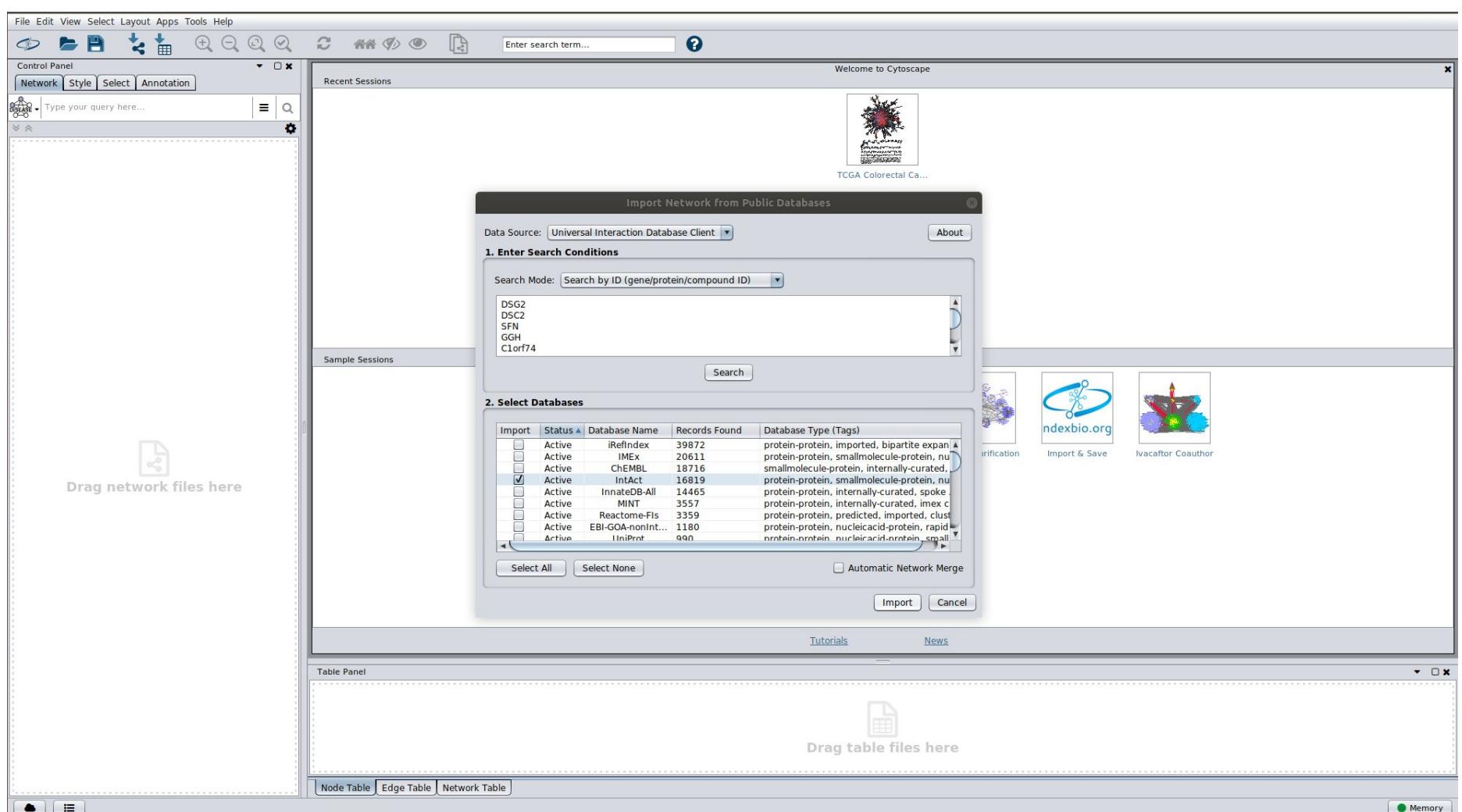
A collection of cross-cancer analyses delving into over arching themes on cancer, including cell-of-origin patterns, oncogenic processes and signaling pathways. Published in 2018 at the program's close.



Cytoscape Hands-on: Data



Cytoscape Hands-on: Data



Cytoscape Hands-on

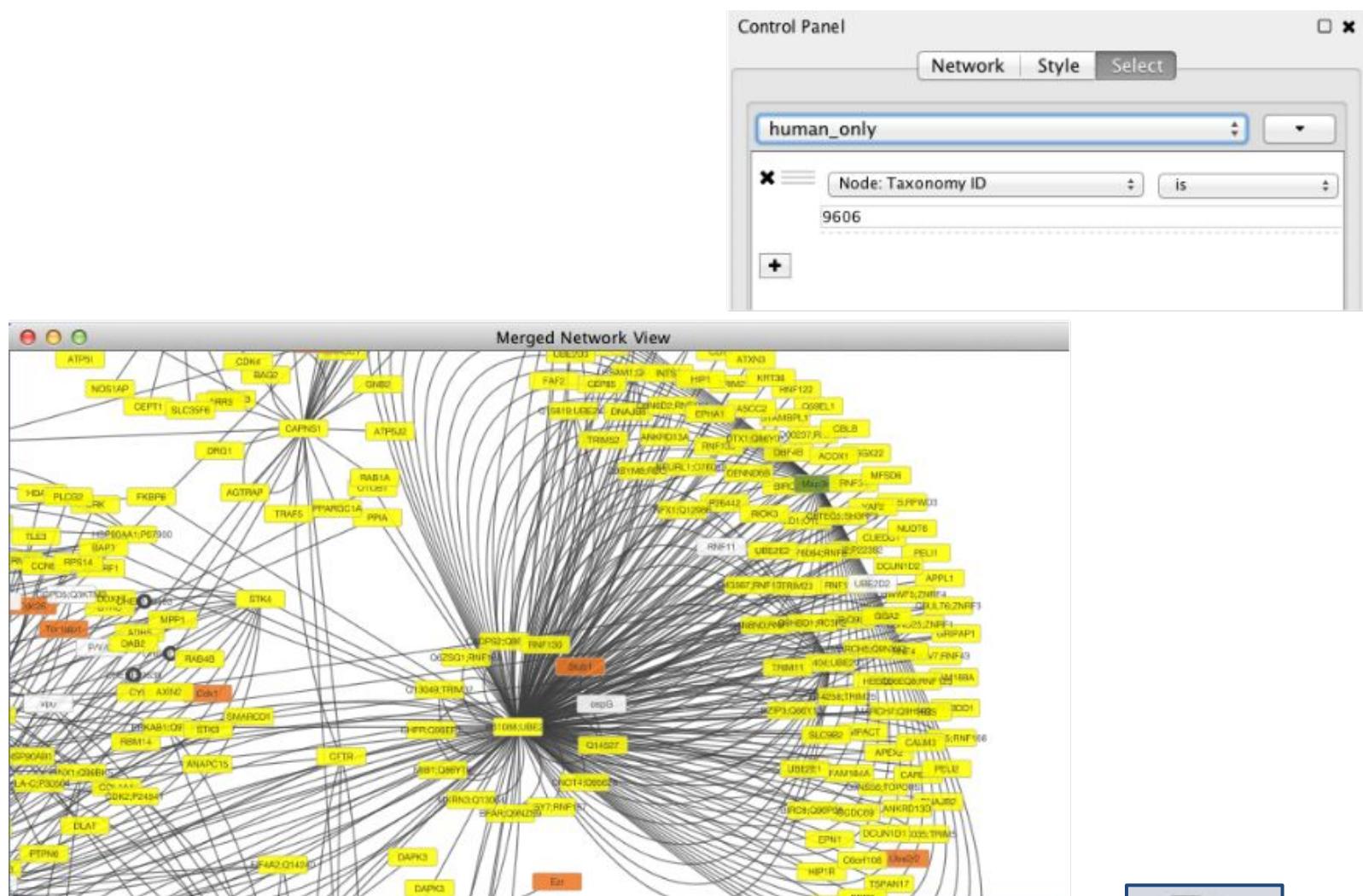
The screenshot shows the Cytoscape software interface. At the top, there is a menu bar with File, Edit, View, Select, Layout, Apps, Tools, Help. Below the menu is a toolbar with various icons, some of which are highlighted with red boxes. To the right of the toolbar is a search bar labeled "Enter search term...". The main workspace displays a complex network graph with many nodes and edges. Some nodes are colored blue or orange. A small inset window in the bottom right corner shows a zoomed-in view of a portion of the network. At the bottom of the screen is a table panel titled "Table Panel" with a red border around it. The table has columns for shared name, name, Taxonomy ID, Taxonomy Name, Human Readable Label, uniprotkb_accession, uniprot, psi-mi, intact, Interactor Type, and Interactor Type ID. The data in the table is as follows:

| shared name | name | Taxonomy ID | Taxonomy Name | Human Readable Label | uniprotkb_accession | uniprot | psi-mi | intact | Interactor Type | Interactor Type ID |
|-------------|----------|-------------|---------------|----------------------|---------------------|----------------------------------|------------------------------|-----------|-----------------|--------------------|
| Q02487 | Q02487 | 9606 | human | DSC2 | Q02487 | [Desmosomal... [desmocadherin-2] | [dscc2_huma... [EPI-3048545] | [protein] | [M:0326] | |
| Q14126 | Q14126 | 9606 | human | DSG2 | Q14126 | [CDH12] | [dsq2_huma... [EPI-2556545] | [protein] | [M:0326] | |
| O60566 | O60566 | 9606 | human | BUB1B | O60566 | [Ssk1] | [BUB1B] | [protein] | [M:0326] | |
| Q02224 | Q02224 | 9606 | human | CENPE | Q02224 | [Kinesin-relat... [CENPE] | [centromeric protein E] | [protein] | [M:0326] | |
| P15924 | P15924 | 9606 | human | DSP | P15924 | [DSP] | [desmosomal protein] | [protein] | [M:0326] | |
| Q02487-1 | Q02487-1 | 9606 | human | DSC2 | Q02487-1 | [Desmosomal... [desmocadherin-2] | [dscc2_huma... [EPI-6900677] | [protein] | [M:0326] | |
| O95229 | O95229 | 9606 | human | ZWINT | O95229 | [O9BWDD0] | [zwint_huma... [EPI-1001132] | [protein] | [M:0326] | |
| O9Z150 | O9Z150 | 10090 | mouse | Bub1b | O9Z150 | [Mad3l] | [Bub1b] | [protein] | [M:0326] | |

At the very bottom of the interface, there are three tabs: Node Table, Edge Table, and Network Table. On the far right, there is a "Memory" button.

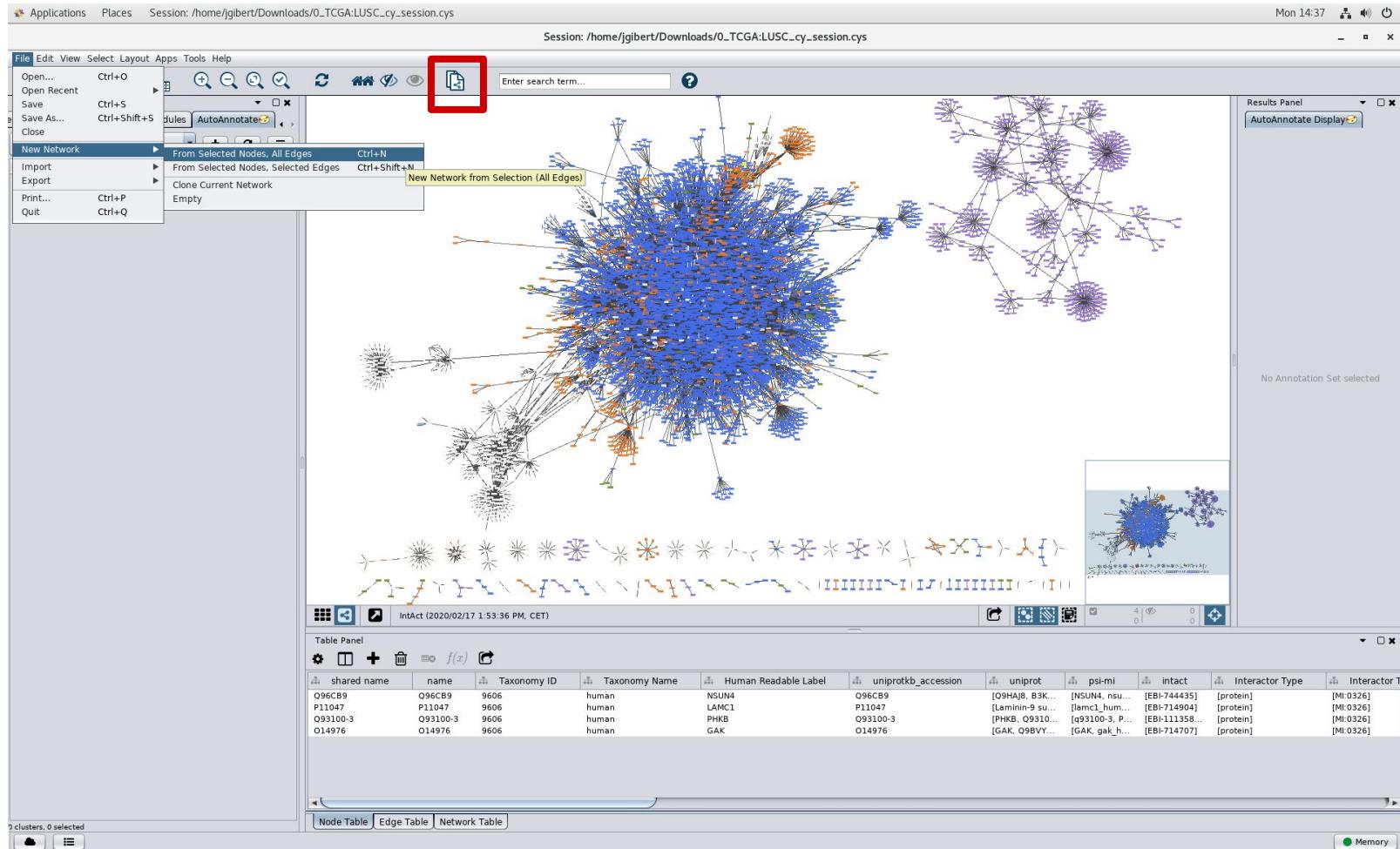


Cytoscape Hands-on

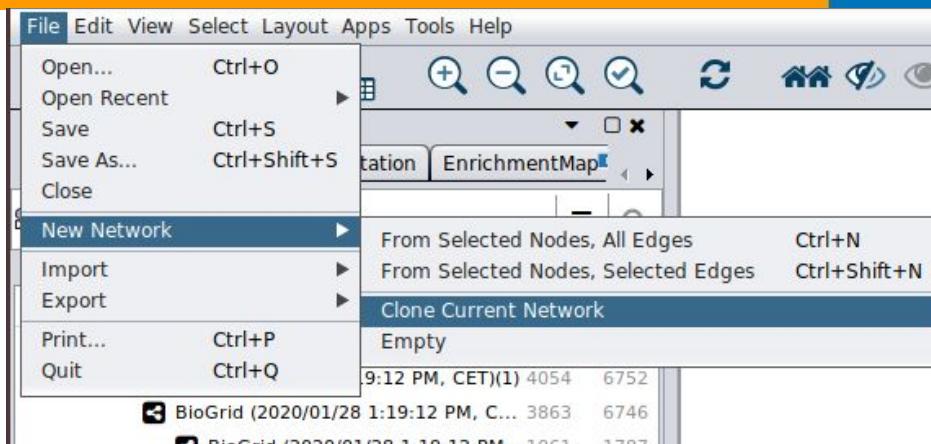


File → New Network → New Network from selected Nodes
www.imim.es

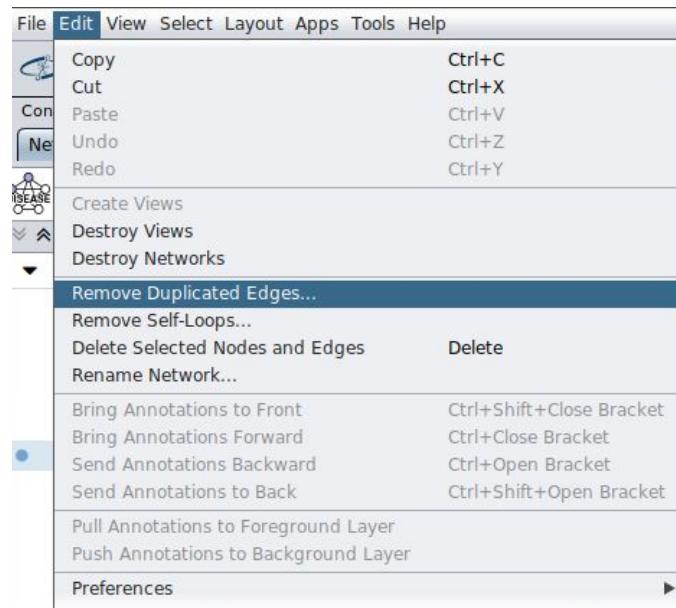
Cytoscape Hands-on



Cytoscape Hands-on



Remember to remove unuseful networks



Cytoscape Hands-on

SAVE BEFORE DOING THE EXERCISE!!!!



Find a layout that sorts your network nodes by the number of interactions that each one of them has.

Cytoscape Hands-on



&



File → Import → Table file

The screenshot shows the Cytoscape interface with the "Import Columns From Table" dialog open. The dialog has sections for "Select a Network Collection" (set to BioGrid) and "Import Data as" (set to Node Table Columns). It also includes fields for "Key Column for Network" (shared name) and "Case Sensitive Key Values" (checked). Below the dialog is a preview table with columns: Gene_name, EnsemblID, Median(Tumor), Median(Normal), log2FC, and FC. The table lists various genes like A2M, A2ML1, ADAACP1, AAS5, ARCK, ABC7-24044400C24.1, ARCA10, ARCA12, ARCA13, ARCA3, and ARCA6, along with their corresponding values. At the bottom of the dialog, there are "Advanced Options..." and "OK" and "Cancel" buttons. The background shows a network graph with nodes and edges. To the right, a red box highlights a portion of the Cytoscape interface showing a table with columns Freq, Gen, and others, and a context menu with options like "Delete Column", "Map column...", and "Rename Column...".



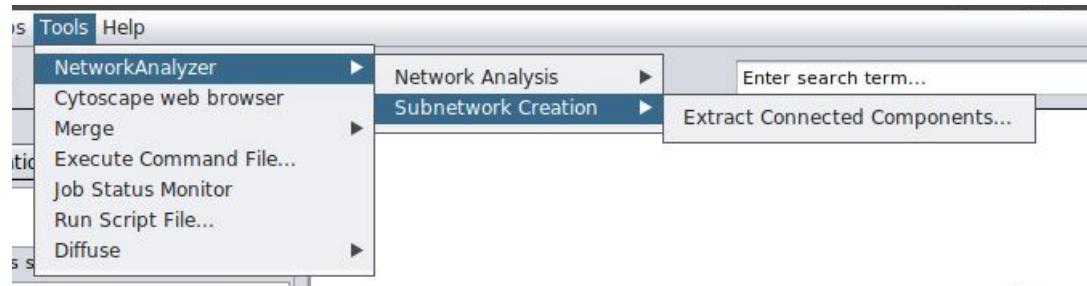
Cytoscape Hands-on



Use node columns to create a network in which all the genes have >2% patient mutation

Use edge columns to create a network in which all the interactions have been found using the 'two hybrid' interaction detection method.

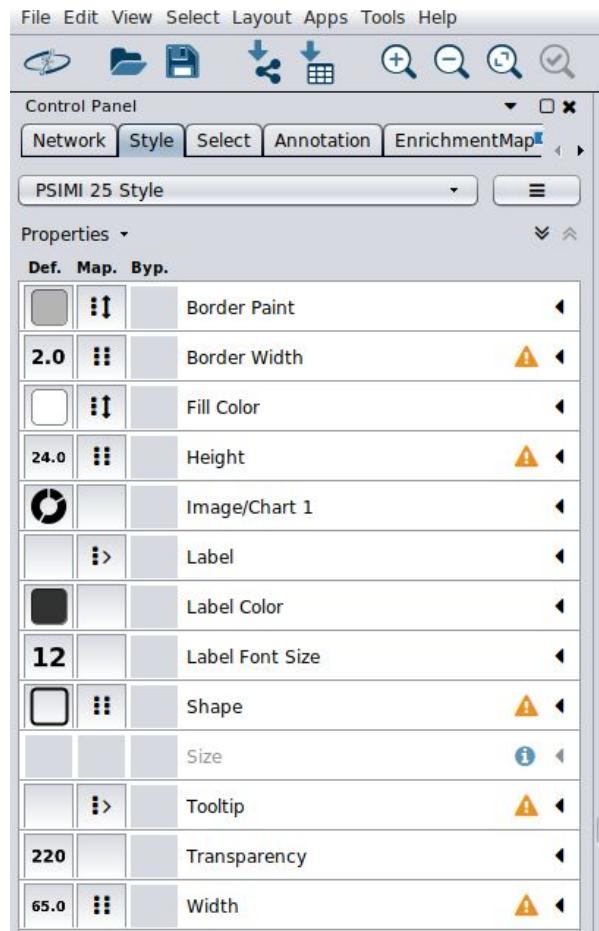
Cytoscape Hands-on



Depending on how fast your laptop performed until here:

Select **bigest** or **part** of the network

Cytoscape Hands-on



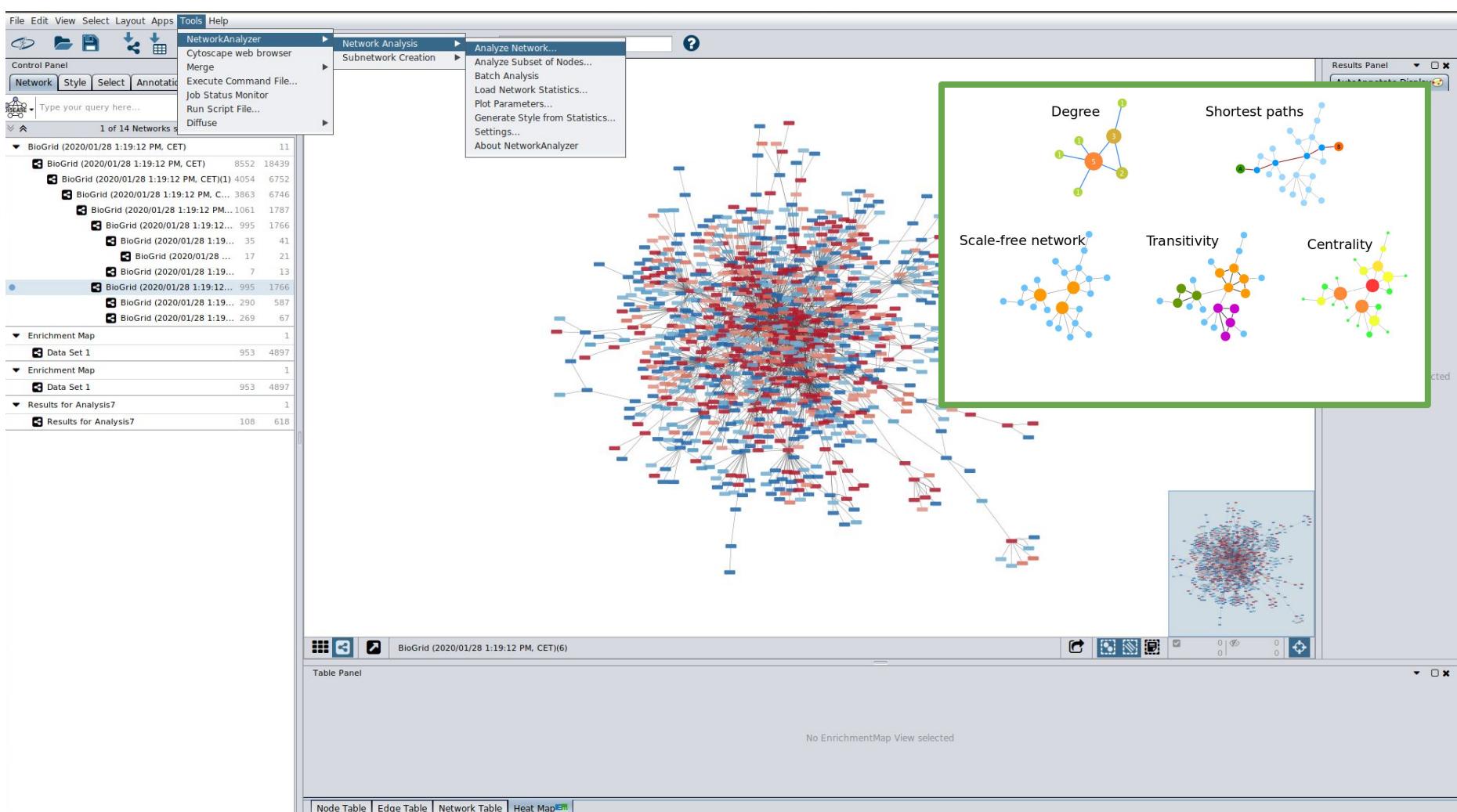
- Predefined styles
- Can change Nodes, Edges and Network features
- Properties can be related to a node/edge variable

Cytoscape Hands-on

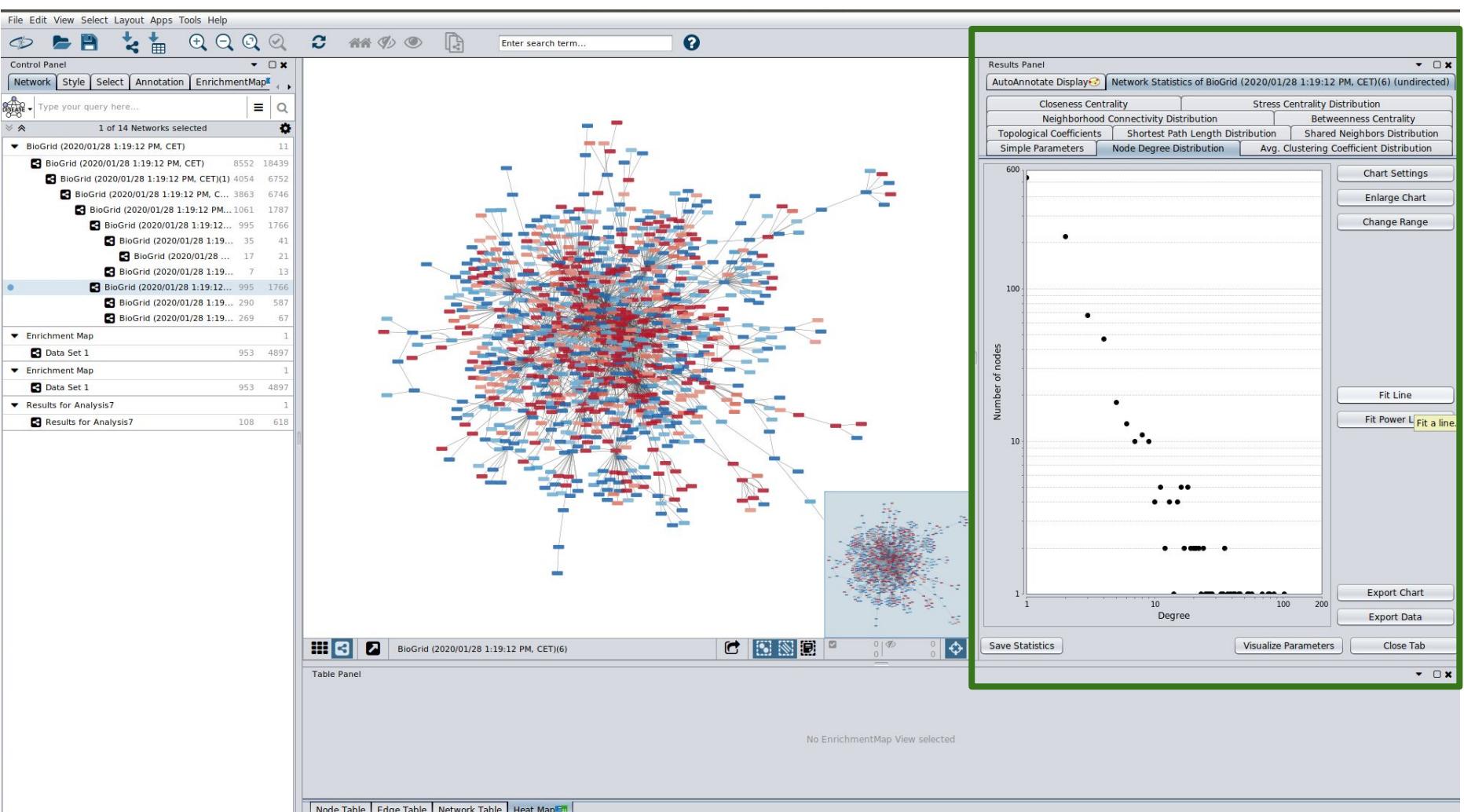
The screenshot shows the Cytoscape application interface. The main window displays a network graph with various nodes represented by circles with different colors (blue, red, grey) and sizes. Nodes are labeled with gene symbols such as STAT1, GAS41, MAPK7, DDX17, NMOR1, AHCY, DBP, SET, TRPM-2, BCL4, CYTH4, HU-2, NFAT5, NEFLX, SP1, JUND, bHLH632, GAMT, and others. A large orange circle with a white question mark is positioned in the center-left area of the graph. The left side of the interface features the 'Control Panel' with settings for 'Network Style' (selected), 'Select', 'Annotation', and 'EnrichmentMap'. The 'Properties' panel is open, showing options for 'Def. Map. Byp.', 'Border Paint', 'Border Width', 'Fill Color', 'Height', 'Image/Chart 1', 'Label', 'Label Color', 'Label Font Size', 'Shape', 'Size', 'Tooltip', 'Transparency', and 'Width'. The right side includes the 'Results Panel' with a 'Node Selector' section for 'Heat Threshold' (Hot (0.03), Cold (0.00), Current Heat: 0.0276832369706, Set), 'Create subnetwork from...', and 'Visual Style' (Create). Below the main graph is a smaller inset showing a zoomed-in view of the network. The bottom of the interface has a 'Table Panel' showing a table of node properties, a 'Network Table' tab selected, and a 'Memory' indicator.

| shared name | name | AverageShortestPathLength | BetweennessCentrality | ClosenessCentrality | ClusteringCoefficient | Degree | diffusion_input | diffusion_output_heat | diffusion_output_rain |
|-------------|-------|---------------------------|-----------------------|---------------------|-----------------------|--------|-----------------|-----------------------|-----------------------|
| 3726 | 3726 | 4.15950285 | 0.0 | 0.24041335 | 1.0 | 3 | | 0.0276832369706 | |
| 10521 | 10521 | 3.62221647 | 0.00149178 | 0.27607406 | 0.0 | 4 | | 0.0225942882434 | |
| 602 | 602 | 4.16468151 | 0.0 | 0.2401144 | 0.0 | 2 | | 0.0276832369706 | |
| 3295 | 3295 | 4.16468151 | 0.0 | 0.2401144 | 0.0 | 1 | | 0.0276832369706 | |
| 7025 | 7025 | 4.16468151 | 0.0 | 0.2401144 | 0.0 | 1 | | 0.0276832369706 | |
| 3725 | 3725 | 4.15950285 | 0.0 | 0.24041335 | 1.0 | 3 | | 0.0276832369706 | |
| 4784 | 4784 | 4.16468151 | 0.0 | 0.2401144 | 0.0 | 1 | | 0.0276832369706 | |
| 4286 | 4286 | 4.16468151 | 0.0 | 0.2401144 | 0.0 | 1 | | 0.0276832369706 | |
| 6418 | 6418 | 3.84179382 | 5.6605E-4 | 0.26039521 | 0.0 | 2 | | 0.0258200071144 | |

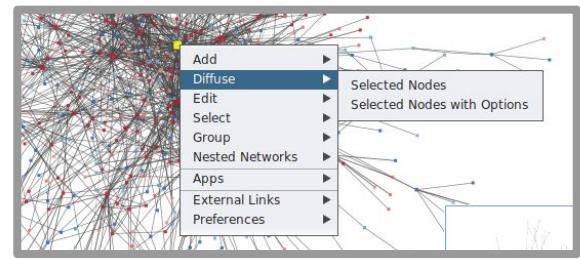
Cytoscape Hands-on



Cytoscape Hands-on



Cytoscape Hands-on



Use Network Analysis to find nodes with maximum degree in Node Table. Run heat diffusion to explore the new cluster

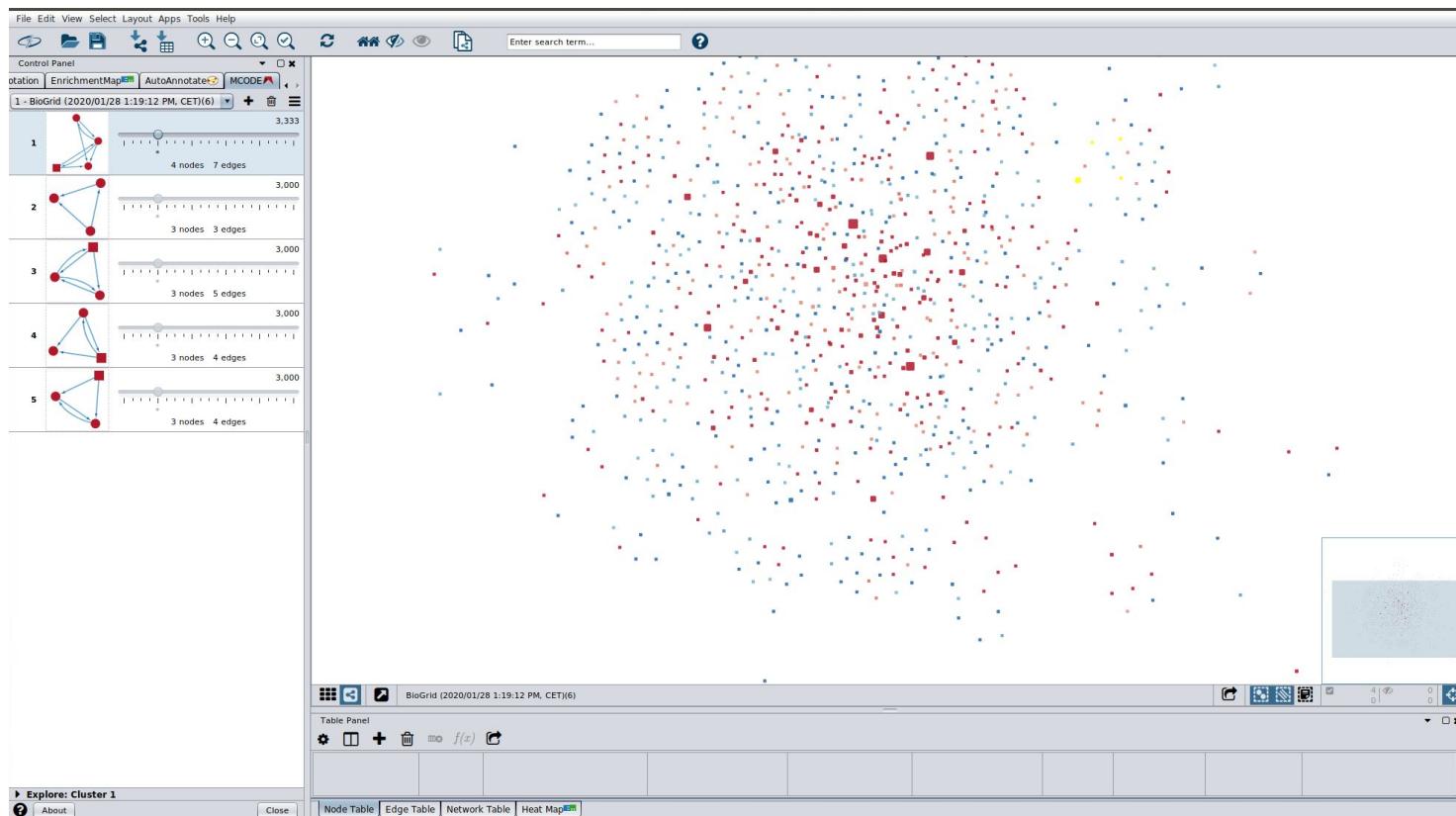
Edit the style node size (height/width) using centrality coefficient

Cytoscape Hands-on



MCODE app

Clusters a given network based on topology to find densely connected regions.



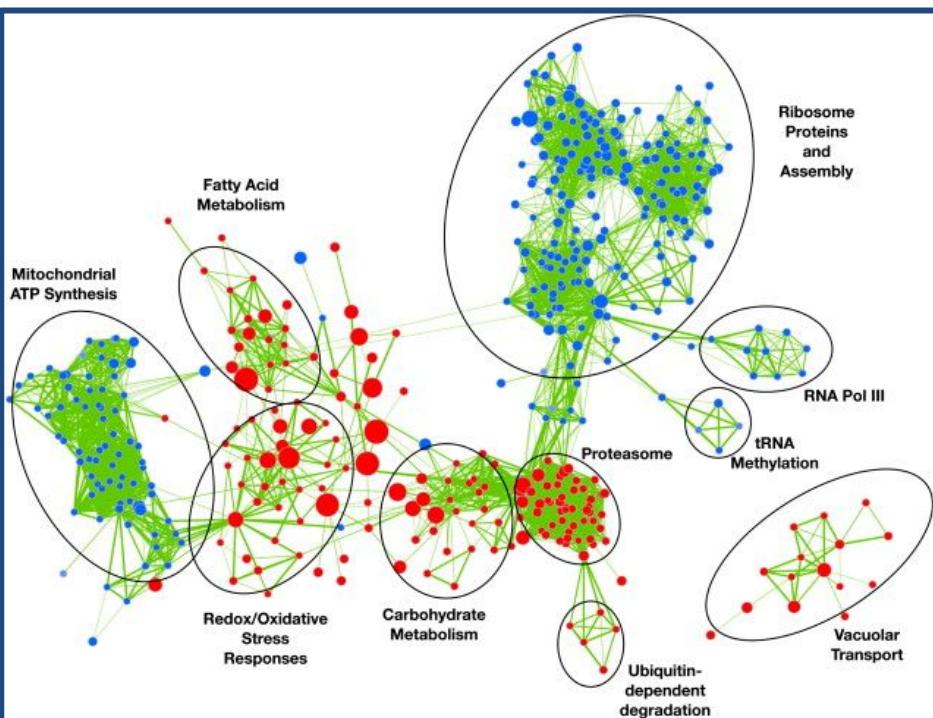
http://www.baderlab.org/Software/MCODE/UsersManual#Cytoscape_Tutorial



Cytoscape Hands-on

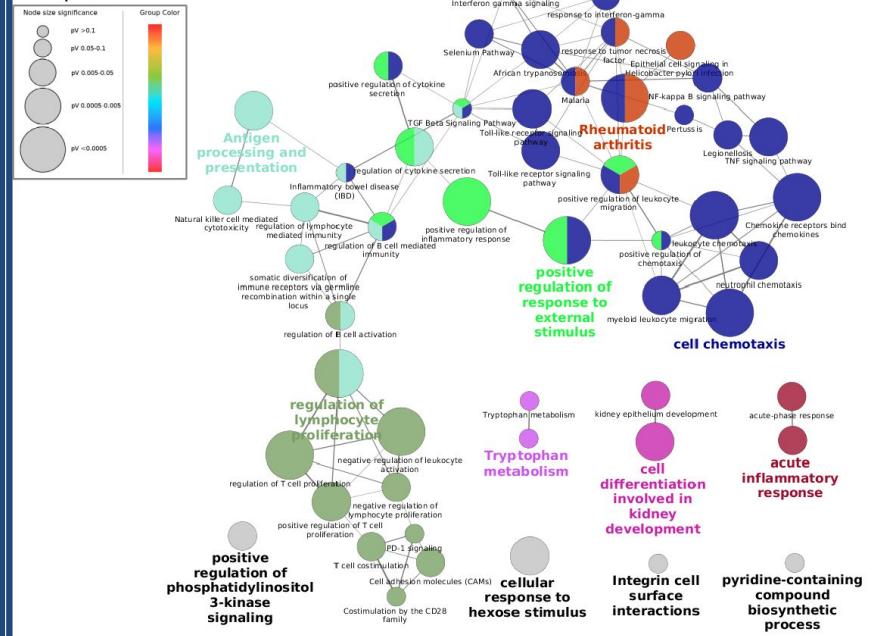


EnrichmentMap



ClueGO

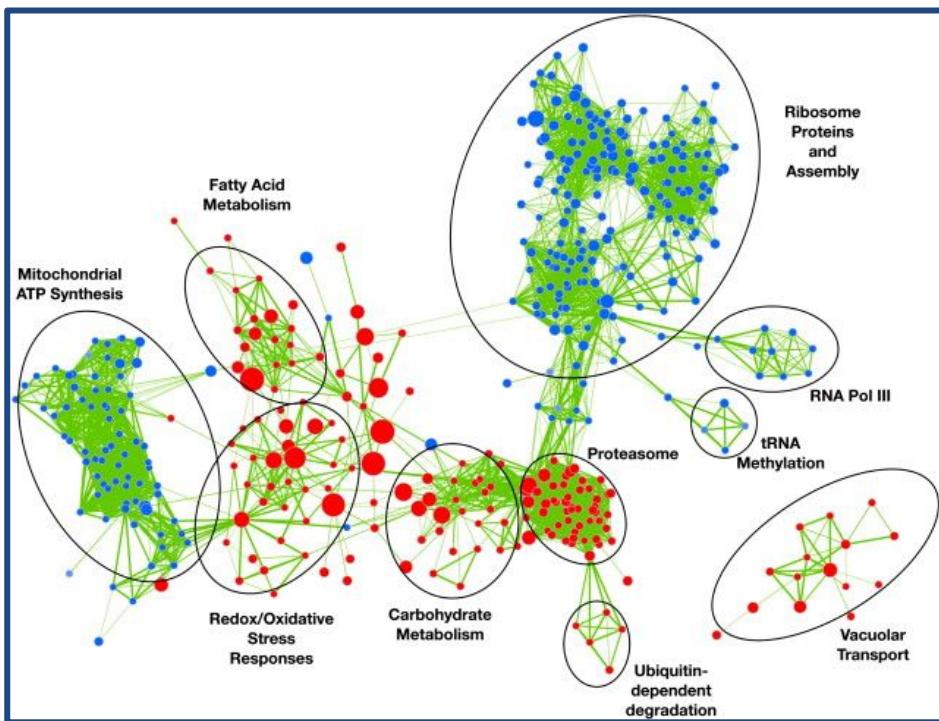
ClueGO network of terms/pathways
Group view



Cytoscape Hands-on

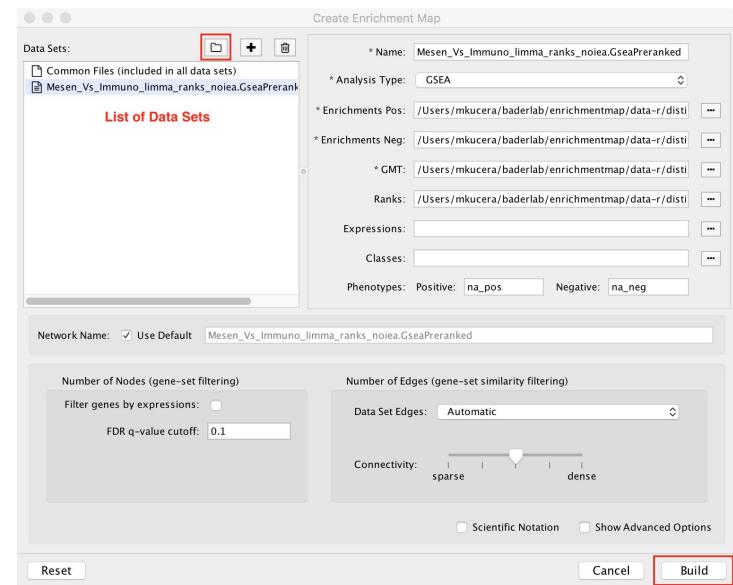


EnrichmentMap



<https://enrichmentmap.readthedocs.io/en/latest/QuickTour.html#>

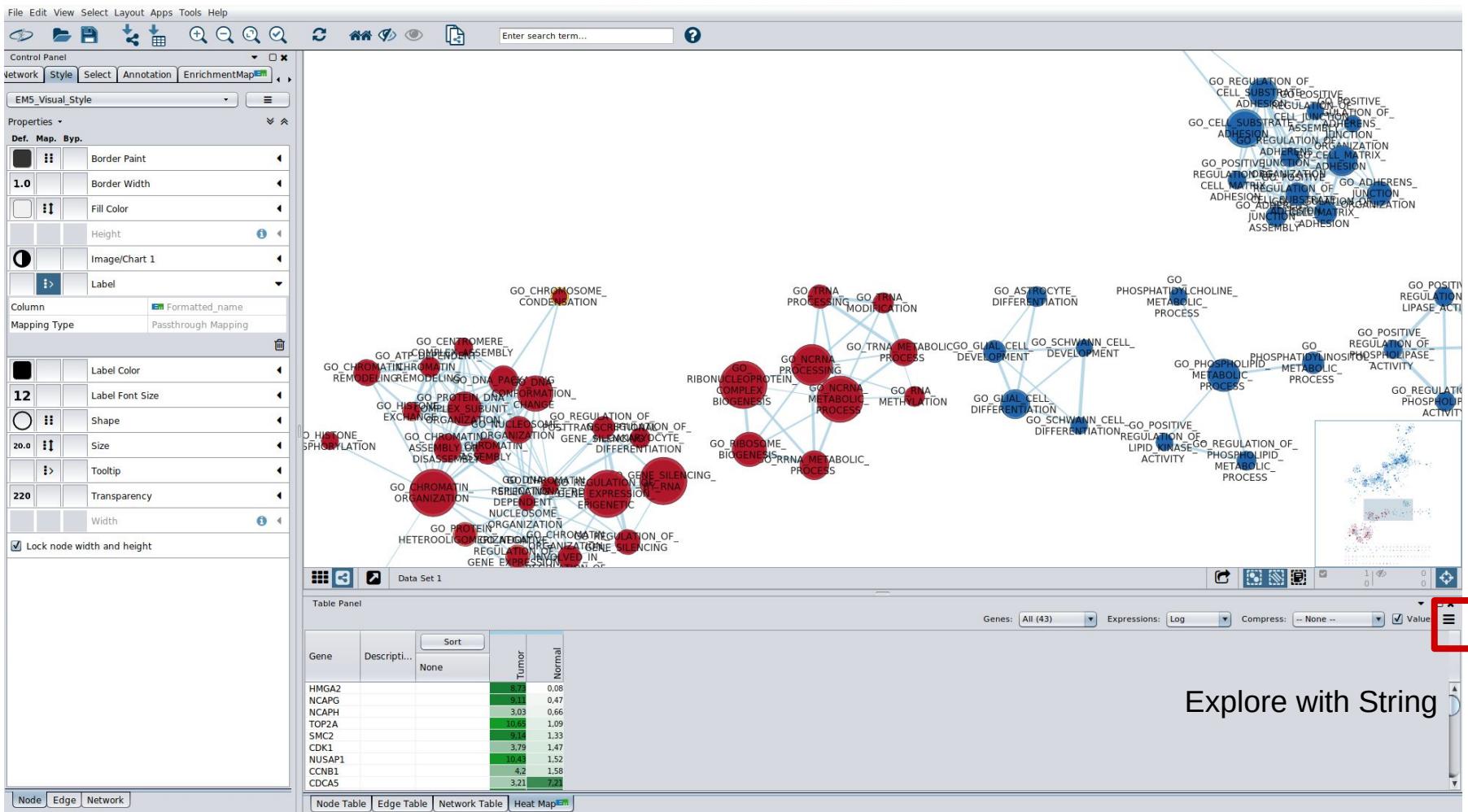
www.imim.es



3_c5.bp.v7.0.symbols.gmt
3_*.xls
3_TCGA_LUSC_ALL_medians.txt



Cytoscape Hands-on



Cytoscape Hands-on

AutoAnnotate
Finds clusters and visually annotates them with labels and groups.

Control Panel
Annotation EnrichmentMap AutoAnnotate MCODE

MCL Cluster Annotation Set

| Cluster | Nodes | Collapsed |
|--------------------------------------|-------|-----------|
| systemic blood contraction | 55 | |
| calcium ion import | 49 | |
| projection muscle growth | 39 | |
| repair dna telomere | 32 | |
| organization chromosome segregati... | 30 | |
| endothelial migration vasculature | 27 | |
| heart morphogenesis septum | 24 | |
| filament actin bundle | 16 | |
| receptor endocytosis import | 14 | |
| atp dependent chromatin | 13 | |
| mitotic dna checkpoint | 13 | |
| wound healing wounding | 13 | |
| adenylyl cyclase cyclic | 12 | |
| gene expression circadian | 12 | |
| matrix adhesion junction | 12 | |
| transforming growth factor | 12 | |
| reactive oxygen species | 9 | |
| tRNA modification biogenesis | 9 | |
| renal homeostasis excretion | 7 | |
| hydroxy amine monoamine | 6 | |
| replication fidelity dna | 6 | |
| smooth muscle locomotion | 6 | |
| synaptic long term | 6 | |
| phospholipid metabolic phosphatid... | 5 | |
| schwann glial astrocyte | 5 | |
| sodium ion transmembrane | 5 | |
| anabolic carbohydrate catabolism | 4 | |
| branching lung morphogenesis | 4 | |
| lung epithelium alveoli | 4 | |
| phosphatidylinositol 3 kinase | 4 | |
| phospholipase activity lipase | 4 | |
| positive cold thermogenesis | 4 | |
| regulation chemotaxis taxis | 4 | |
| rho signal gtpase | 4 | |
| translational elongation termination | 4 | |
| urogenital system glomerulus | 4 | |
| cell division mitotic | 3 | |
| drug metabolism antibiotic | 3 | |
| endothelium endothelial cell | 3 | |
| fatty acid derivative | 3 | |
| gaseous exchange respiratory | 3 | |
| left asymmetry symmetry | 3 | |
| membrane depolarization potential | 3 | |
| mesoderm mesodermal differentiation | 3 | |
| ribonucleoside monophosphate nuc... | 3 | |
| term memory cognition | 3 | |
| bone mineralization biomimetic | 2 | |
| camp response purine | 2 | |
| cell morphogenesis involved | 2 | |
| cellular ovule development | 2 | |
| digestive tract development | 2 | |
| erk1 erk2 cascade | 2 | |
| glycolytic fructose phosphate | 2 | |
| insulin secretion glucose | 2 | |
| interleukin 7 pathway | 2 | |
| localization cell surface | 2 | |
| ovulation cycle process | 2 | |
| 01 clusters. 0 selected | 2 | |

Enter search term... ?

Results Panel

AutoAnnotate Display Network Statistics of BioGrid (2020/01/28 11:11:11)

Shape: Border Width: 3
Opacity: 20%

Fill: Border: Hide Shapes

Font Scale: 34% Scale font by cluster size
Font Color: Word Wrap
Wrap Length: 20 Hide Labels

Data Set 1

Table Panel

| Gene | Description | Sort | Tumor | Normal |
|------|-------------|------|-------|--------|
| | | None | | |

Genes: All (0) Expressions: Log Compress: -- None -- Values

Node Table Edge Table Network Table Heat Map



Cytoscape Hands-on



SAVE BEFORE STARTING !!!

The screenshot shows the Cytoscape application window. The menu bar includes File, Edit, View, Select, Layout, Apps, Tools, and Help. The Apps menu is open, showing various analysis tools like AutoAnnotate, clusterMaker, and Reactome Fiz. The Reactome Fiz option is highlighted. The main workspace displays a "Welcome to Cytoscape" message and several network visualization thumbnails. A sidebar on the left contains a "Control Panel" with style and annotation options, and a large tree view of biological pathways. At the bottom, there's a "Table Panel" with a "Drag table files here" area and tabs for Node Table, Edge Table, and Network Table. A status bar at the bottom right shows memory usage.



Cytoscape Hands-on

The screenshot shows the Cytoscape application interface with the Reactome FI app open. The main window displays a network graph. The top menu bar includes Applications, Places, Session: New Session, File, Edit, View, Select, Layout, Apps, Tools, and Help. The Apps menu is expanded, showing various options like AutoAnnotate, clusterMaker, and Reactome FI. A context menu is also open over the network graph, listing options such as View Reactome Source, View in Reactome, Show Diagram, Search, Analyze Pathway Enrichment (which is highlighted in blue), Perform GSEA Analysis, Run Graphical Model Analysis, Load Graphical Model Results, View Cancer Drugs, View DrugCentral Drugs, Expand Pathway, and Collapse Pathway.

Reactome Pathway Enrichment Analysis

Gene Set Loading

Choose a gene set file:

Or enter gene set:

Specify file format: One gene per line
 Comma delimited (e.g. TP53, EGFR)
 Tab delimited (e.g. TP53 EGFR)

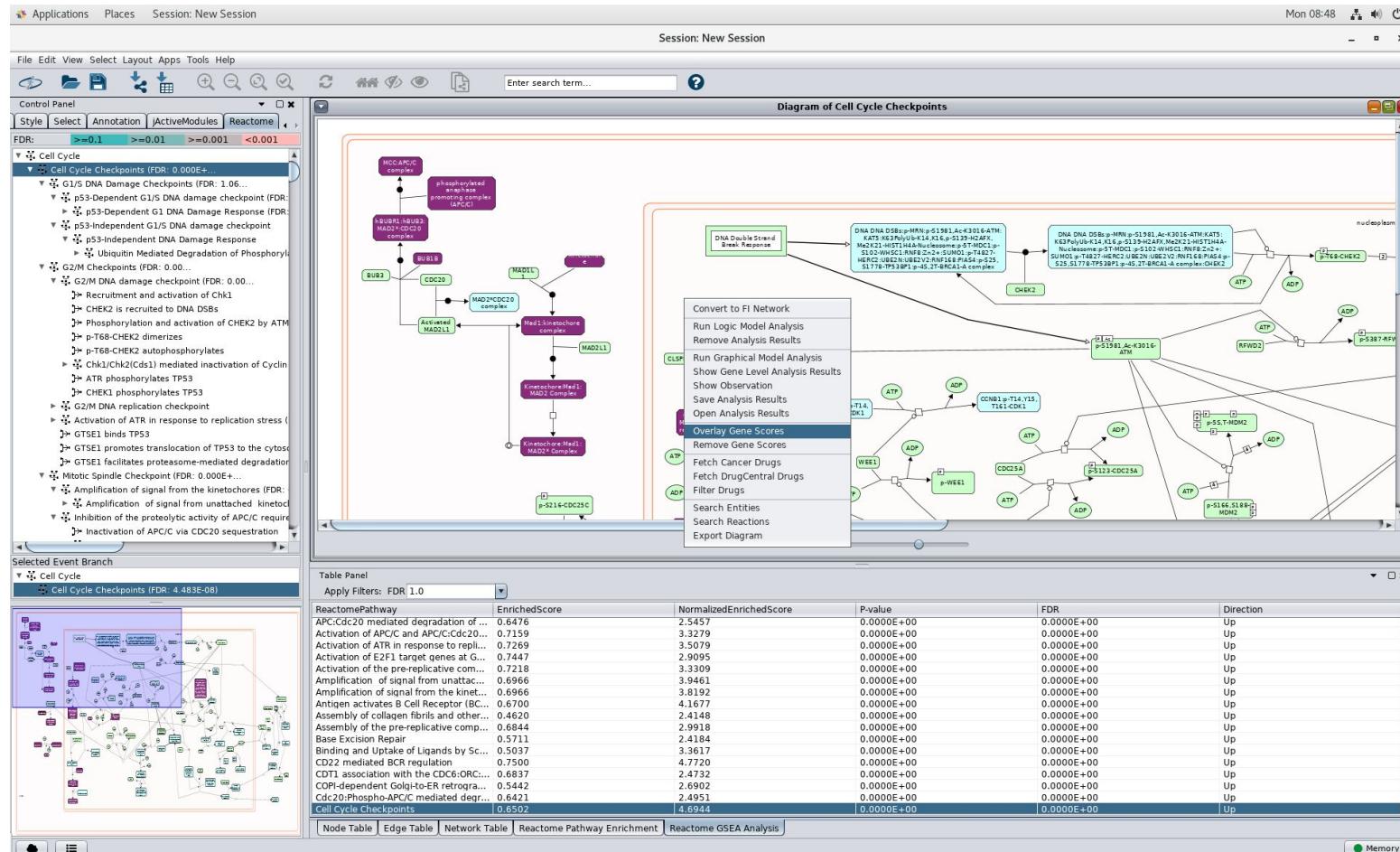
Gene names
4.1_GSEA_Cytoscape.txt

Cytoscape Hands-on

The screenshot shows the Cytoscape application window titled "Session: New Session". The main panel displays a network diagram with various nodes and edges. On the left, a "Control Panel" shows a tree view of pathway categories under "Cell Cycle" and "Mitotic Spindle Checkpoint". A "Selected Event Branch" panel highlights the "Mitotic Spindle Checkpoint (FDR: 1.786E-06)". Below the main panel, there are several small thumbnail previews of other network sessions. At the bottom, a "Table Panel" is open, showing a table of ReactomePathway data with columns for RatioOfProteinInPathway, NumberOfProteinInPathway, ProteinFromGeneSet, P-value, FDR, and HitGenes. The table includes rows for Cell Cycle, Mitotic Spindle Checkpoint, and various M Phase processes. The "Table Panel" has a dropdown menu with options like "Export Table" and "View in Diagram". The status bar at the bottom right indicates "Memory" usage.

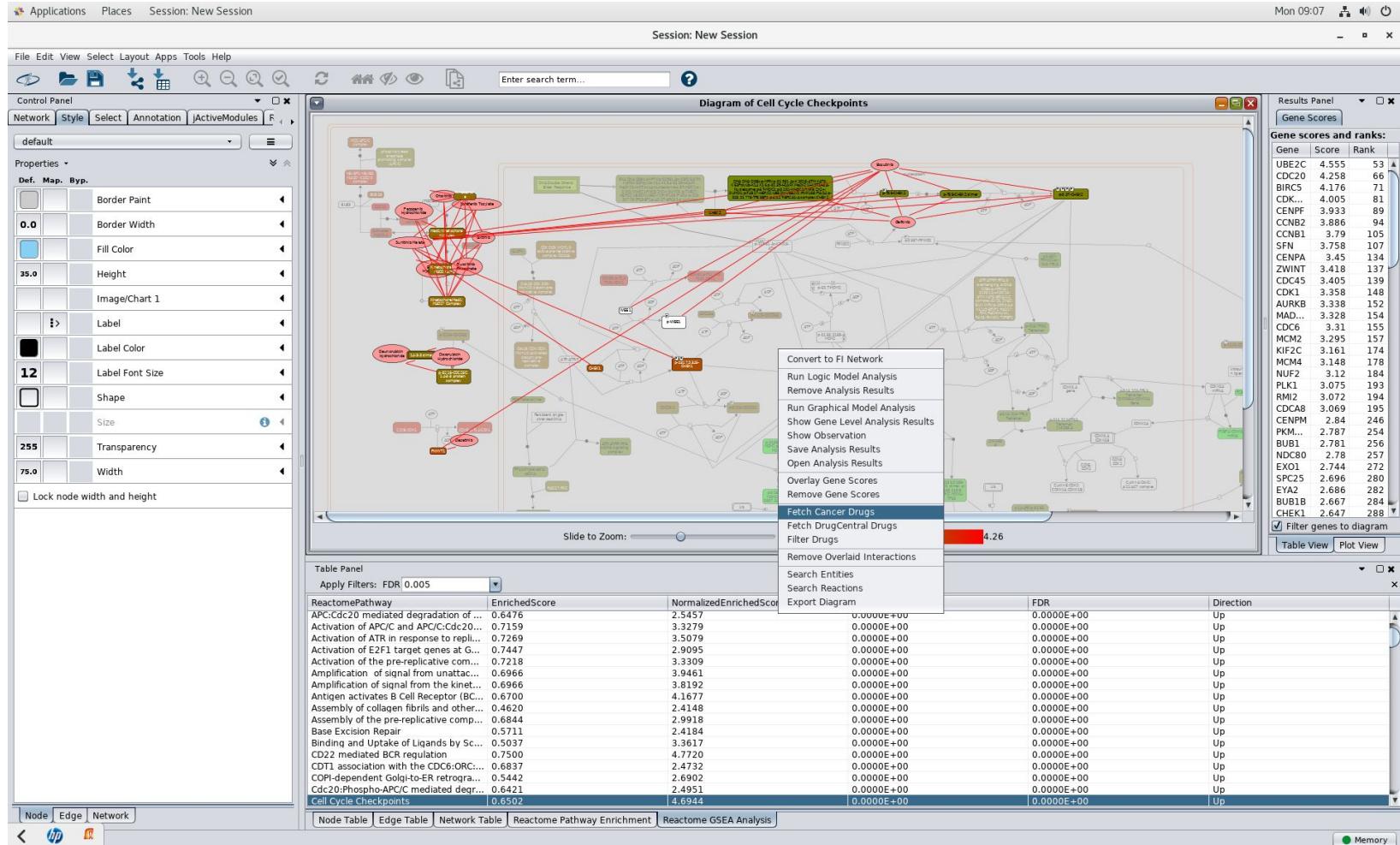
| ReactomePathway | RatioOfProteinInPathway | NumberOfProteinInPathway | ProteinFromGeneSet | P-value | FDR | HitGenes |
|---|-------------------------|--------------------------|--------------------|-------------------|-------------------|--------------------------------------|
| Cell Cycle, Mitotic | 0.0497 | 430 | 27 | 1.1724E-13 | 4.3027E-11 | BUB1B,KIF20A,HMMR,PK... |
| Cell Cycle Checkpoints | 0.0285 | 246 | 18 | 2.4497E-10 | 4.4829E-08 | BUB1B,CHEK1,PKMYT1,CCNB... |
| Resolution of Sister Chromatid ... | 0.0112 | 97 | 11 | 1.3049E-08 | 1.5919E-06 | BUB1B,CCNB2,PLK1,ZWINT,BIR... |
| Mitotic Spindle Checkp... | | 101 | 11 | 1.9629E-08 | 1.7862E-06 | BUB1B,UBE2C,PLK1,ZWINT,BIR... |
| Polo-like kinase mediates | 0.0125 | 16 | 6 | 3.2327E-08 | 2.2966E-06 | PKMYT1,CCNB2,PLK1,FOXM1,M... |
| Amplification of signal from un... Amplification of signal from unattached kinetochore | 0.0125 | 85 | 10 | 4.4165E-08 | 2.2966E-06 | BUB1B,PLK1,ZWINT,BIRC5,JIP2... |
| RHO GTPases Activate Formins | 0.0125 | 85 | 10 | 4.4165E-08 | 2.2966E-06 | BUB1B,PLK1,ZWINT,BIRC5,KIF2... |
| Mitotic Prometaphase | 0.0202 | 108 | 12 | 3.9316E-07 | 1.7692E-05 | BUB1B,NEK2,CCNB2,PLK1,ZWINT... |
| M Phase | 0.0348 | 175 | 15 | 6.1209E-07 | 2.4484E-05 | BUB1B,NEK2,KIF20A,CCNB2,U... |
| Separation of Sister Chromatids | 0.0386 | 161 | 11 | 1.9249E-06 | 6.3522E-05 | BUB1B,UBE2C,PLK1,ZWINT,BIR... |
| Formation of the constricted envelope | 0.0063 | 54 | 7 | 2.7226E-06 | 8.1677E-05 | PKP1,DSC3,DSG3,SRRB1,BSP... |
| Mitotic Anaphase | 0.0196 | 169 | 11 | 3.0520E-06 | 8.3907E-05 | BUB1B,UBE2C,PLK1,ZWINT,BIR... |
| Mitotic Metaphase and Anaphase | 0.0197 | 170 | 11 | 3.2272E-06 | 8.3907E-05 | BUB1B,UBE2C,PLK1,ZWINT,BIR... |
| RHO GTPase Effectors | 0.0263 | 227 | 12 | 8.6740E-06 | 2.0818E-04 | BUB1B,SFN,PLK1,ZWINT,BIRC5... |
| G2/M Transition | 0.0202 | 175 | 10 | 2.6714E-05 | 5.8771E-04 | NEK2,HMMR,PKMYT1,CCNB2,PL... |
| Mitotic G2-G2/M phases | 0.0205 | 177 | 10 | 2.9391E-05 | 6.0483E-04 | NEK2,HMMR,PKMYT1,CCNB2,PL... |

Cytoscape Hands-on



4.2_TCGA_LUSC_ALL_reactome.txt

Cytoscape Hands-on



Cytoscape Hands-on

Run Logic Model Analysis

The screenshot shows the CellDesigner interface with several open windows:

- Control Panel**: Shows network, style, select, annotation, active modules, and Reactome buttons. A sidebar displays Cell Cycle Checkpoints with FDR values.
- Diagram of the Cell Cycle Pathway**: A complex biological network diagram showing interactions between various proteins like Cyclin B1, CDK1, and APC/C.
- New Logic Model Simulation**: A dialog box for setting up a simulation. It includes tabs for General, Transfer Function, and Drug Application. It allows selecting a targetome, drugs, targets, and filtering by drug targets only. Buttons for OK and Cancel are present.
- Drug Selection**: A dialog box listing drugs for Doxorubicin Hydrochloride. It includes columns for ID, Drug, Target, Interaction, IC50 (nM), Ki (nM), Modification, and Strength. Drugs listed include Carfilzomib, Crizotinib, Dasatinib, Daunorubicin Hydrochloride, Erlotinib, Ixazomib, Lapatinib, Nitrofen, Pazopanib, Raloxifene, Roxulostinil, and YWHAG. The last row is for Doxorubicin Hydrochloride, with a note about its interaction with YWHAG.
- Table Panel**: A table showing the ratio of protein in different pathways across various stages of the cell cycle.
- Network Table**: A table showing the number of proteins in different pathways.
- Results Panel**: A sidebar showing the Boolean Network Model, with buttons for Simulate and New.

Cytoscape Hands-on

Session: New Session

File Edit View Select Layout Apps Tools Help

Enter search term...

Control Panel

Network Style Select Annotation ActiveModules Reactome

FDR: >=0.1 >=0.01 >=0.001 <0.001

Cell Cycle Checkpoints (FDR: 4.48E-08)

- G1/S DNA Damage Checkpoints (FDR: 0.505)
 - p53-Dependent G1/S DNA damage checkpoint
 - p53-Independent G1/S DNA damage checkpoint (FDR: 0.446)
 - p53-Independent DNA Damage checkpoint (FDR: 0.446)
 - Ubiquitin Mediated Degradation of Phosphorylated Cdc25A (FDR: 0.011)
 - G2/M DNA damage checkpoint (FDR: 0.041)
 - Recruitment and activation of Chk1
 - CHEK2 is recruited to DNA DSBs
 - Phosphorylation and activation of CHEK2 by ATM
 - p-T68-CHEK2 dimerizes
 - p-T68-CHEK2 autophosphorylates
 - Chk1/Chk2(Cds1) mediated inactivation of Cyclin B:Cdk1 complex (FDR: 0.011)
 - ATR phosphorylates TP53
 - CHEK1 phosphorylates TP53
 - G2/M DNA replication checkpoint (FDR: 0.015)
 - Activation of ATR in response to replication stress (FDR: 0.054)
 - GTSE1 binds TP53
 - GTSE1 promotes translocation of TP53 to the cytosol
 - GTSE1 facilitates proteasome-mediated degradation of TP53
 - Mitotic Spindle Checkpoint (FDR: 1.786E-06)
 - Amplification of signal from the kinetochores (FDR: 2.297E-06)
 - Amplification of signal from unattached kinetochores via a MAD2
 - Inhibition of the proteolytic activity of APC/C required for the onset of inactivation of APC/C via CDC20 sequestration
 - Inactivation of APC/C via direct inhibition of the APC/C complex (FDR: 0.001)
 - Cell Cycle, Mitotic (FDR: 4.303E-11)

Selected Event Branch

Cell Cycle

Cell Cycle Checkpoints (FDR: 4.48E-08)

Diagram of Cell Cycle Checkpoints

Results Panel

Gene Scores Boolean Network Modelling

Simulate New Delete Compare

Entity Type Initial Modification Strength

ATR(ATRIP...) Respondent 0.0 None 0.0

ATR(ATRIP...) Respondent 0.0 None 0.0

Activated... Respondent 0.0 None 0.0

BUB1B([c... Respondent 1.0 None 0.0

BUB3([cyt... Respondent 1.0 None 0.0

CCNA(CDK... Respondent 0.0 None 0.0

CCNB1(p... Respondent 0.0 None 0.0

CCNB(CDK... Respondent 0.0 None 0.0

CCNE(CDK... Respondent 0.0 None 0.0

CDC20([c... Respondent 1.0 None 0.0

CDC25A([... Respondent 1.0 None 0.0

CDK(DDK... Respondent 0.0 None 0.0

CDKN1A(g... Respondent 1.0 None 0.0

CDKN1A(c... Respondent 0.0 None 0.0

CHEK1(n... Respondent 1.0 None 0.0

CHEK2(n... Respondent 1.0 None 0.0

CLSPN(n... Respondent 1.0 None 0.0

Cdc45(CD... Respondent 0.0 None 0.0

Cdc45(A... Respondent 0.0 None 0.0

Cyclin E(C... Respondent 0.0 None 0.0

DNA(DNA... Respondent 1.0 None 1.0

Use larger values for stimulation variables

*: Simulation for Cell Cycle Checkpoints using identity function (Doxorubicin Hydrochloride).

Slide to Zoom: 0.0 1.0

Table Panel

Choose time to highlight pathway: Step 24

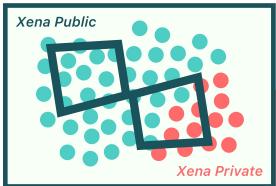
Time Step

Note: The plot shows all results. But the table may show partial results. Use "Configure Columns" popup menu to set columns for display.

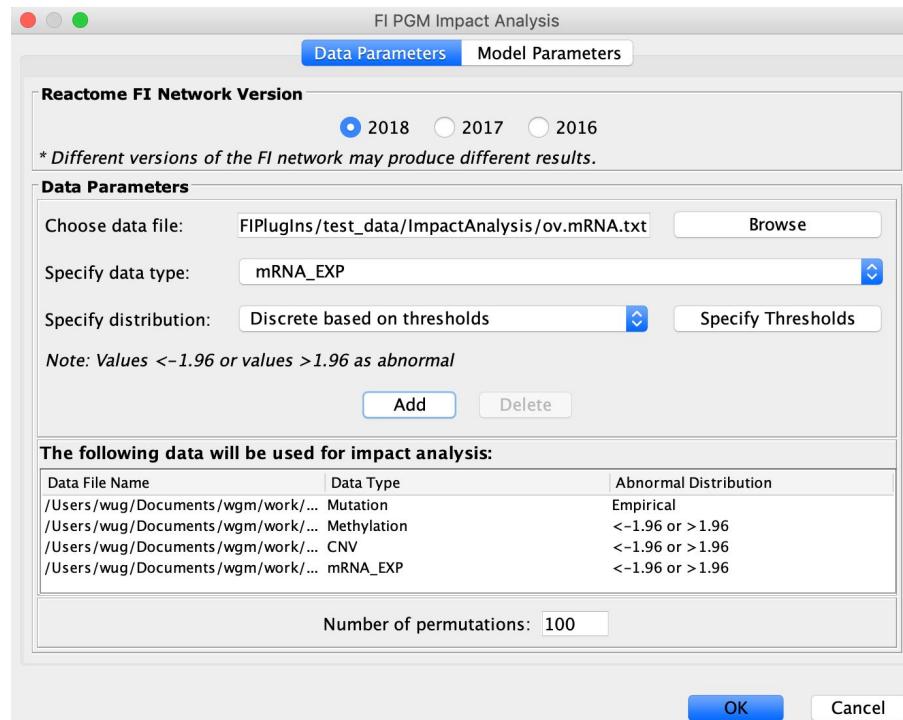
Node Table Edge Table Network Table Reactome Pathway Enrichment BN: Doxo BN: Untitled

Memory

Cytoscape Hands-on



<https://xenabrowser.net/hub/>



The dialog box is titled "FI PGM Impact Analysis". It has tabs for "Data Parameters" (selected) and "Model Parameters".

Data Parameters

- Reactome FI Network Version: 2018 (radio button selected)
- * Different versions of the FI network may produce different results.
- Choose data file: FIPlugins/test_data/ImpactAnalysis/ov.mRNA.txt
- Specify data type: mRNA_EXP
- Specify distribution: Discrete based on thresholds
- Note: Values <-1.96 or values >1.96 as abnormal
- Add Delete

The following data will be used for impact analysis:

| Data File Name | Data Type | Abnormal Distribution |
|-----------------------------------|-------------|-----------------------|
| /Users/wug/Documents/wgm/work/... | Mutation | Empirical |
| /Users/wug/Documents/wgm/work/... | Methylation | <-1.96 or >1.96 |
| /Users/wug/Documents/wgm/work/... | CNV | <-1.96 or >1.96 |
| /Users/wug/Documents/wgm/work/... | mRNA_EXP | <-1.96 or >1.96 |

Number of permutations: 100

OK Cancel

XENA + Change ID to Symbol + Z-score RNAseq

4.3_TCGA_LUSC_gistic_small.txt
4.3_TCGA_LUSC_htseq_fpkm_uq_small.txt



Cytoscape Hands-on

Conclusions

- Network analysis give an extra layer for causal inference
- Cytoscape could visualize interaction easily using different databases as a source of PPI
- Network analysis could show important actors in our DEG lists
- Cytoscape Apps are powerful tools to perform specific analysis





Cytoscape Hands-on

a) Open, b) Save ClueGO project

b) Results for Analysis4 (Kappa=0.4)

Network of terms

c) Restore analysis settings, d) Save result table, e) Close project

Result table: overrepresentation of terms/pathways

ClueGO network of terms/pathways

Gene distribution view

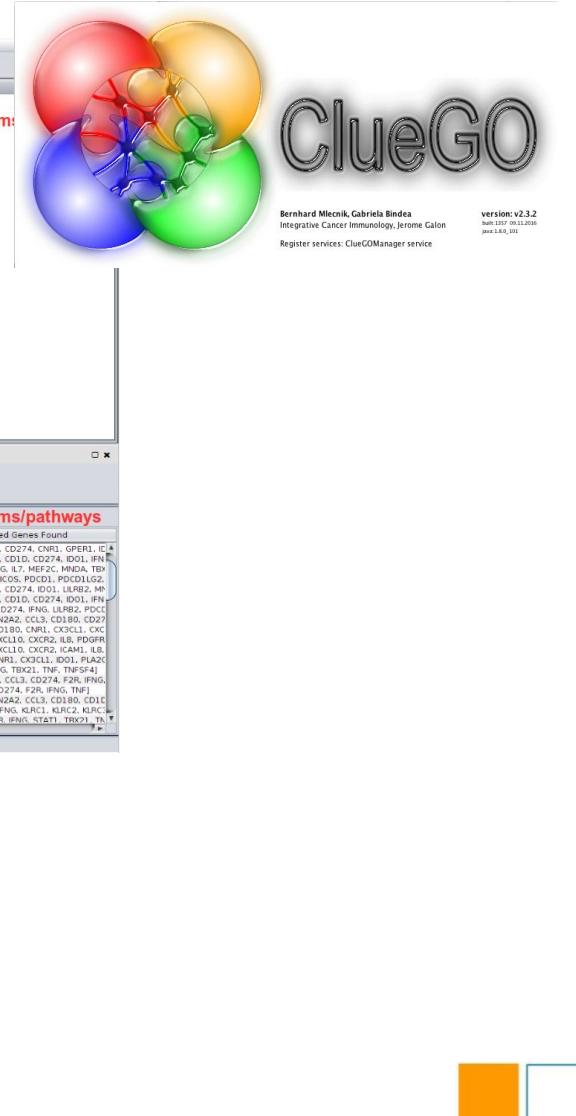
Control Panel

1. Select the organism & upload lists with markers
2. Select a visual style
3. Select Ontologies
4. Use predefined/custom pathway selection
5. Start the analysis

Remaining Free Cytoscape Memory: 98%

Node Table | **Edge Table** | **Network Summary**

www.imim.es



Cytoscape Hands-on

The screenshot shows the Cytoscape application interface. The main window displays a network graph with nodes colored by category (yellow, orange, green) and edges representing connections. A control panel on the left shows a filter for 'brain_exp' with the condition 'Node: brain between 1 and 14,699 inclusive'. An 'Apps' menu is open, highlighting 'ClueGO'. Below the graph is a table panel titled 'f(x)' containing a list of shared names and their corresponding details.

| shared name | name | isExcludedFromPaths | Matching.Attribute | Annotations |
|-------------|--------|--------------------------|--------------------|------------------------|
| P03886 | P03886 | <input type="checkbox"/> | [P03886] | [] |
| O75306 | O75306 | <input type="checkbox"/> | [O75306] | [author-confidence...] |
| Q9Y311 | Q9Y311 | <input type="checkbox"/> | [Q9Y311] | [comment:\Stoichi...] |
| P49821 | P49821 | <input type="checkbox"/> | [P49821] | [author-confidence...] |
| Q9BU61 | Q9BU61 | <input type="checkbox"/> | [Q9BU61] | [] |
| Q8N183 | Q8N183 | <input type="checkbox"/> | [Q8N183] | [comment:Missing ...] |
| P00414 | P00414 | <input type="checkbox"/> | [P00414] | [author-confidence...] |
| Q9P032 | Q9P032 | <input type="checkbox"/> | [Q9P032] | [] |
| P03905 | P03905 | <input type="checkbox"/> | [P03905] | [] |
| P55072 | P55072 | <input type="checkbox"/> | [P55072] | [comment:\Stoichi...] |
| Q13501 | Q13501 | <input type="checkbox"/> | [Q13501] | [author-confidence...] |

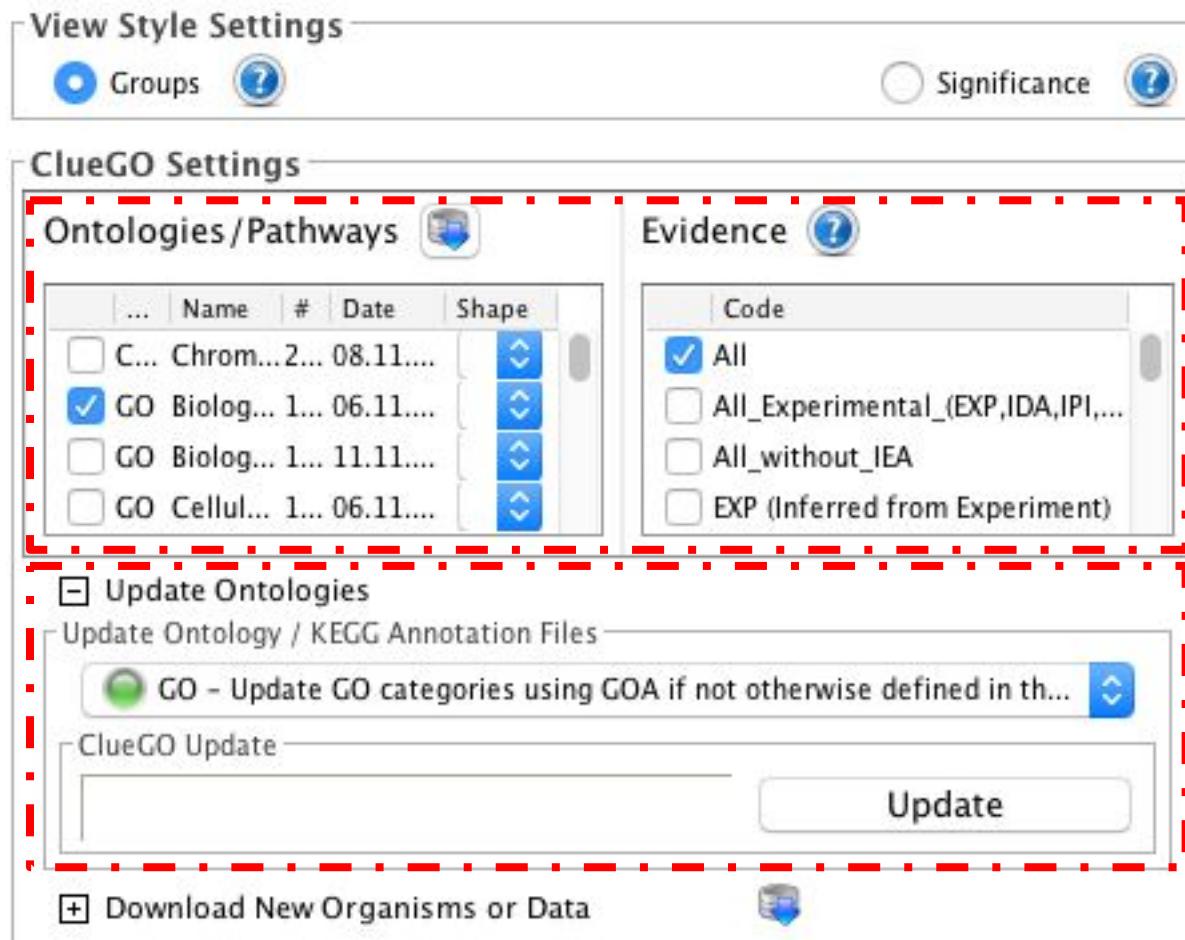
www.jmimes.org
Apps □ ClueGO



Cytoscape Hands-on

The screenshot shows the ClueGO v2.3.2 interface. The main window displays a complex network graph of protein interactions, with nodes represented by yellow circles and edges by blue lines. A legend on the right side indicates node types: orange (Protein), green (Protein), blue (Protein), red (Protein), and purple (Protein). The Control Panel at the top has tabs for Network, Style, Select, and ClueGO. The ClueGO tab is active. Below the tabs, there are sections for "Get CluePedia!" and "Get CluePedia Extension!". The "Load Marker List(s)" section contains a dropdown menu set to "Homo Sapiens [9606]", a "UniProtKB_AC" button, and a "Load Attribut..." button. To the left of this section is a list of UniProtKB accession numbers: 043181, 043464, 060260, and 075251. A "File" button is located below the accession list. Red numbers 1 through 4 are overlaid on the interface: 1 is on the "Network" tab, 2 is on the "UniProtKB_AC" button, 3 is on the "File" button, and 4 is on the "Load Attribut..." button.

Cytoscape Hands-on



Cytoscape Hands-on

Network Specificity



Global Medium Detailed

Use GO Term Fusion 

Show only Pathways with p... 

Advanced Term/Pathway Selection Options

GO Tree Interval

3  Min Level 8  Max Level 

GO Term/Pathway Selection (#/% Genes)

Cluster #1

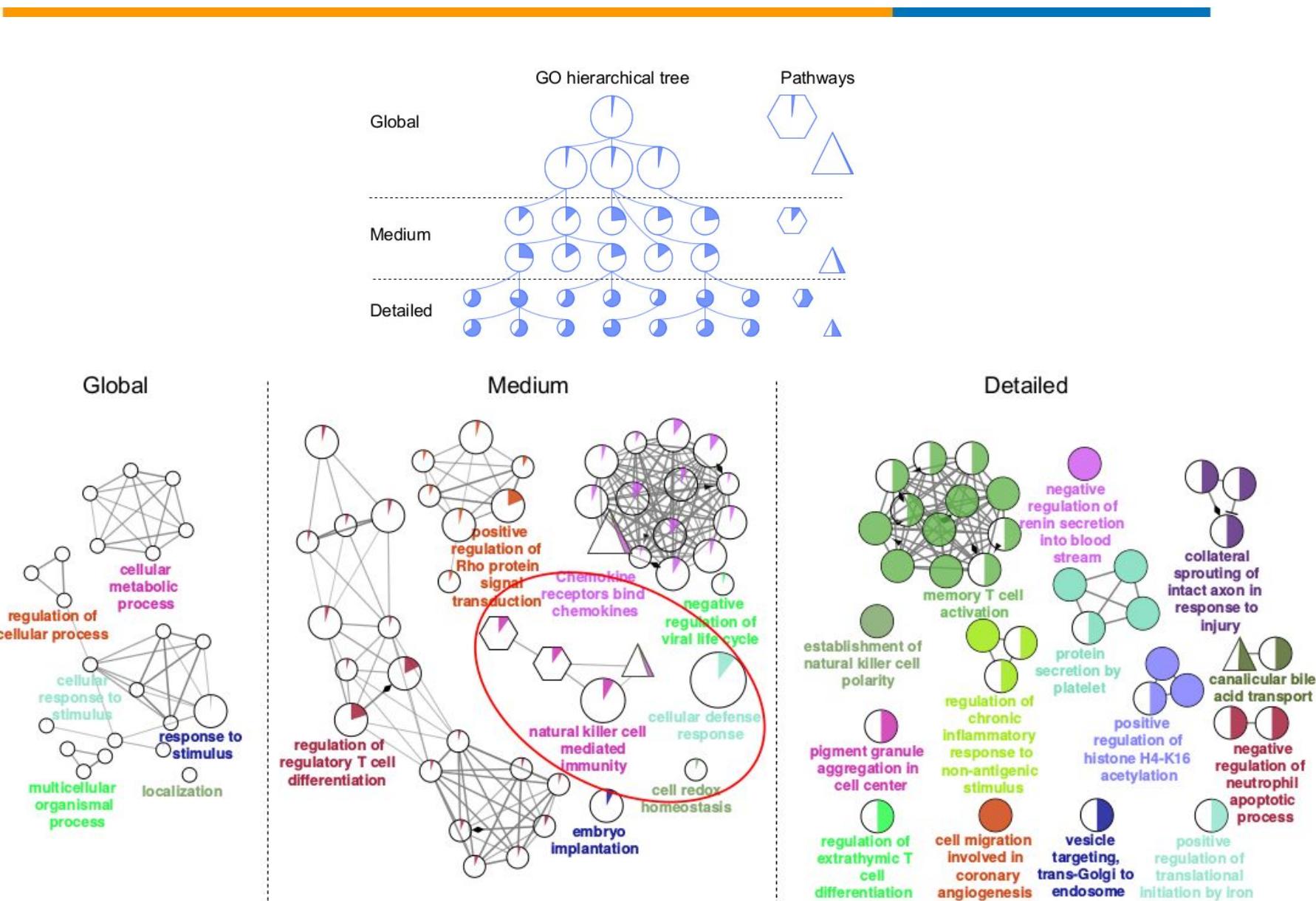
3  Min #Genes 4.000  %Genes 

GO Term/Pathway Network Connectivity (Kappa Score)



Low Medium High Score: 0.4 

Cytoscape Hands-on



Cytoscape Hands-on

Network Specificity

Global Medium Detailed

Use GO Term Fusion

Show only Pathways with p... 0.05000

Advanced Term/Pathway Selection Options

GO Tree Interval

Min Level: 3 Max Level: 8

GO Term/Pathway Selection (#/% Genes)

Cluster #1

Min #Genes: 3 %Genes: 4.000

GO Term/Pathway Network Connectivity (Kappa Score)

Score: 0.4

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Statistical Options

Advanced Statistical Options

Enrichment (Right-sided hypergeometric test)

Bonferroni step down pV Correcti...

mid-P-values Doubling

Reference Set Options

Selected Ontologies Reference Set

Predefined IDs Reference Set

Custom Reference Set

16/tutorial_files/brain_uniprot_ac.txt

Grouping Options

GO Term Grouping (Functional Grouping)

Use GO Term Grouping 

Group coloring

Fix Random

Leading Group Term based on

Highest Significance

Tree Kappa Score

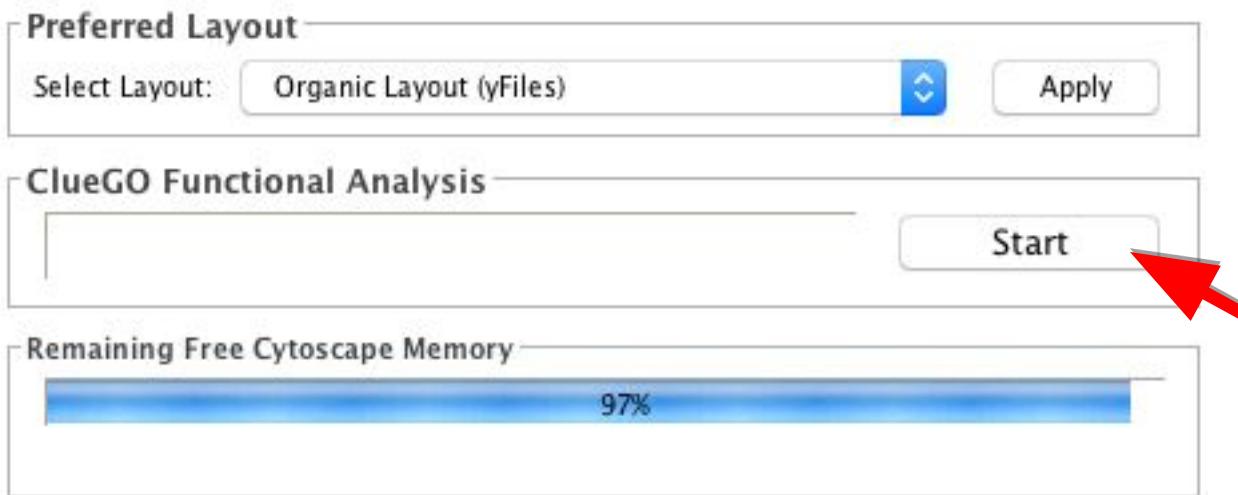
1 Initial Group Size

60 % Genes for Group Merge

60 % Terms for Group Merge



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ClueGO Result Information



```
### All results were created with ClueGO v2.3.2 ###

Organism analyzed: Homo Sapiens [9606]
Identifier types used: [AccessionID, UniProtKB_AC]
Evidence codes used: [All]
#Genes in custom reference set (/Users/ppm/Documents/Teaching/ProteomicsWT course/2016/tutorial_files/brain_uniprot_ac.txt) : 11996
#All unique genes in selected ontologies: 11996 (reference set for hypergeometric test)
#Genes from Cluster#1: uploaded ids 53 -> unique genes 53, with 0 (0.0%) missing -> All genes were recognized by ClueGO.
#Genes with functional annotations in all selected Ontologies from Cluster#1: 53 (100.0%)

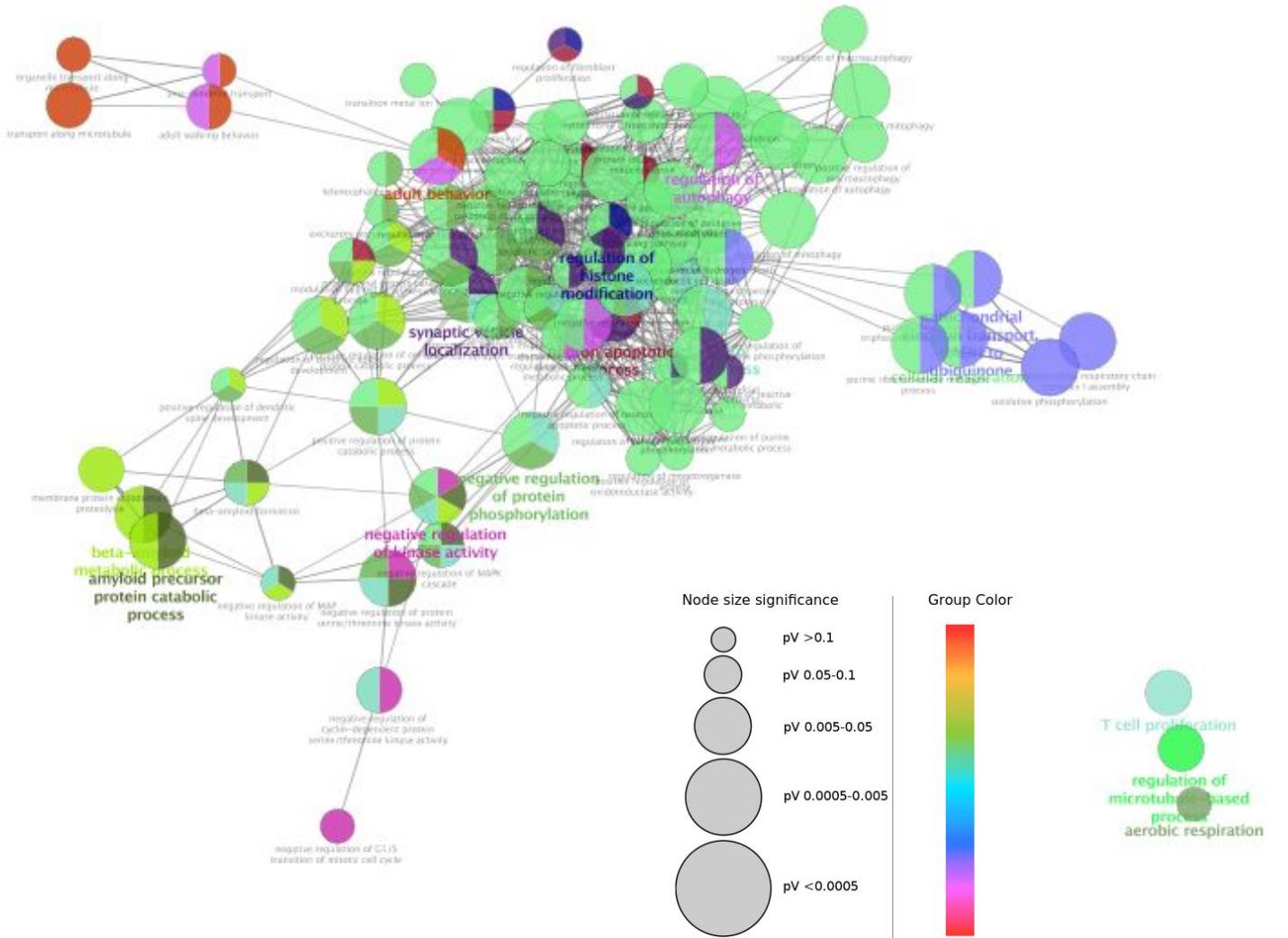
#Genes from all Clusters associated to representative Terms and Pathways (after applying selection criteria): 49 (92.45%)

KappaScore Grouping:
Iteration: 0 with 60 groups
Iteration: 1 with 81 groups
Iteration: 2 with 180 groups
Iteration: 3 with 113 groups
Iteration: 4 with 21 groups
Iteration: 5 with 15 groups
Final KappaScore groups = 15
# Terms not grouped = 0

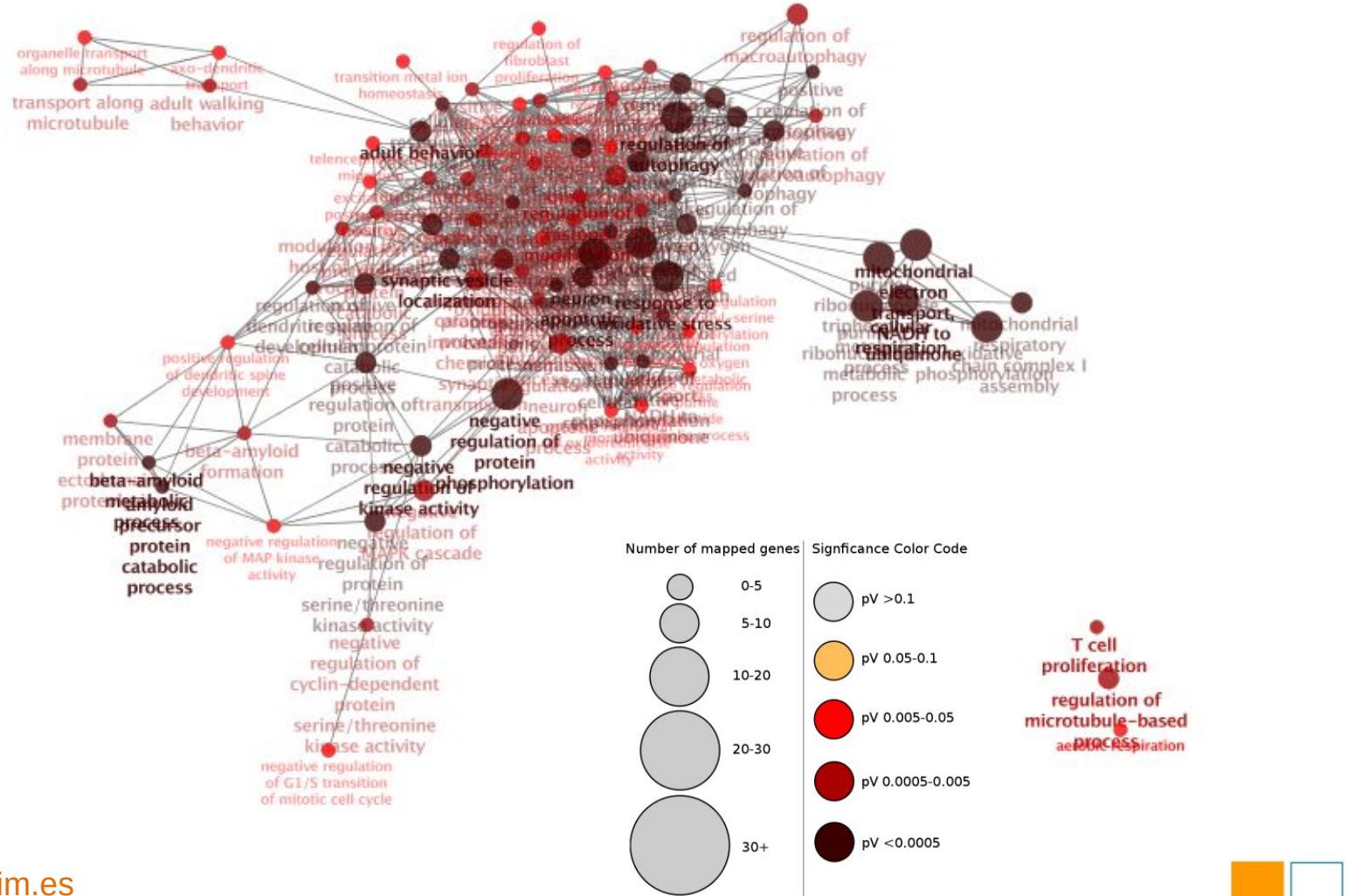
# Merge redundant groups with >60.0% overlap
Final group size after merging: 15
#GO All Terms Specific for Cluster #1: 91
#GO Terms: 91
#GO Term Connections: 369
```

OK

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Results for Analysis0

ClueGO Results (Cluster #1) Cluster #1 ClueGO Log

Hide Labels Label

| GOID | GOTerm | Ontology Source | Term PValue | Term PValue Corrected ... | Group PValue | Group PValue Corrected ... | GOLevels | GOGroups | % Associat |
|----------|--|---------------------------|-------------|---------------------------|--------------|----------------------------|----------|----------|------------|
| 9060 | aerobic respiration | GO_BiologicalProcess-G... | 3.6 E-3 | 1.0 E-2 | 3.6 E-3 | 3.6 E-3 | [5, 6] | Group00 | 4 |
| 32886 | regulation of microtubule-based process | GO_BiologicalProcess-G... | 2.4 E-5 | 1.0 E-3 | 2.4 E-5 | 7.4 E-5 | [3, 4] | Group01 | 4 |
| 42098 | T cell proliferation | GO_BiologicalProcess-G... | 1.4 E-4 | 3.8 E-3 | | | | | 4 |
| 48145 | regulation of histone methylation | GO_BiologicalProcess-G... | 3.9 E-3 | 7.8 E-3 | | | | | 4 |
| 19012... | positive regulation of neuron death | GO_BiologicalProcess-G... | 1.6 E-4 | 4.1 E-3 | | | | | 4 |
| 31056 | positive regulation of cell migration | GO_BiologicalProcess-G... | 1.4 E-4 | 3.8 E-3 | | | | | 4 |
| 33673 | negative regulation of kinase activity | GO_BiologicalProcess-G... | 3.7 E-8 | 2.6 E-6 | | | | | 4 |
| 20001... | negative regulation of G1/S transition of mitotic cell cycle | GO_BiologicalProcess-G... | 6.0 E-4 | 1.0 E-2 | | | | | 4 |
| 45736 | negative regulation of cyclin-dependent protein serine/threonine kinase activity | GO_BiologicalProcess-G... | 8.8 E-5 | 2.6 E-3 | | | | | 4 |
| 71901 | negative regulation of protein serine/threonine kinase activity | GO_BiologicalProcess-G... | 9.2 E-6 | 4.5 E-4 | | | | | 4 |
| 30534 | adult behavior | GO_BiologicalProcess-G... | 1.2 E-9 | 9.0 E-8 | | | | | 4 |
| 7628 | adult walking behavior | GO_BiologicalProcess-G... | 1.7 E-4 | 4.1 E-3 | | | | | 4 |
| 10970 | transport along microtubule | GO_BiologicalProcess-G... | 7.6 E-5 | 2.4 E-3 | | | | | 4 |
| 72384 | organelle transport along microtubule | GO_BiologicalProcess-G... | 2.8 E-3 | 1.6 E-2 | | | | | 4 |
| 8088 | axo-dendritic transport | GO_BiologicalProcess-G... | 6.1 E-4 | 9.8 E-3 | | | | | 4 |
| 30534 | adult behavior | GO_BiologicalProcess-G... | 1.2 E-9 | 9.0 E-8 | | | | | 4 |
| 10506 | regulation of autophagy | GO_BiologicalProcess-G... | 9.6 E-10 | 7.2 E-8 | | | | | 4 |
| 7628 | adult walking behavior | GO_BiologicalProcess-G... | 1.7 E-4 | 4.1 E-3 | | | | | 4 |
| 8088 | axo-dendritic transport | GO_BiologicalProcess-G... | 6.1 E-4 | 9.8 E-3 | | | | | 4 |
| 42053 | regulation of dopamine metabolic process | GO_BiologicalProcess-G... | 3.5 E-5 | 1.2 E-3 | | | | | 4 |
| 51583 | dopamine uptake involved in synaptic transmission | GO_BiologicalProcess-G... | 4.4 E-6 | 2.3 E-4 | | | | | 4 |
| 48145 | regulation of fibroblast proliferation | GO_BiologicalProcess-G... | 3.9 E-3 | 7.8 E-3 | | | | | 4 |
| 43388 | positive regulation of DNA binding | GO_BiologicalProcess-G... | 3.3 E-4 | 6.7 E-3 | | | | | 4 |
| 19012... | positive regulation of neuron death | GO_BiologicalProcess-G... | 1.6 E-4 | 4.1 E-3 | | | | | 4 |

Hide Labels Label

Network of pathways Export results

Show/Hide pathway names except group name

Change group colors

Update pathway names

Restore project settings

Save result tables and figures

Save result tables as xls

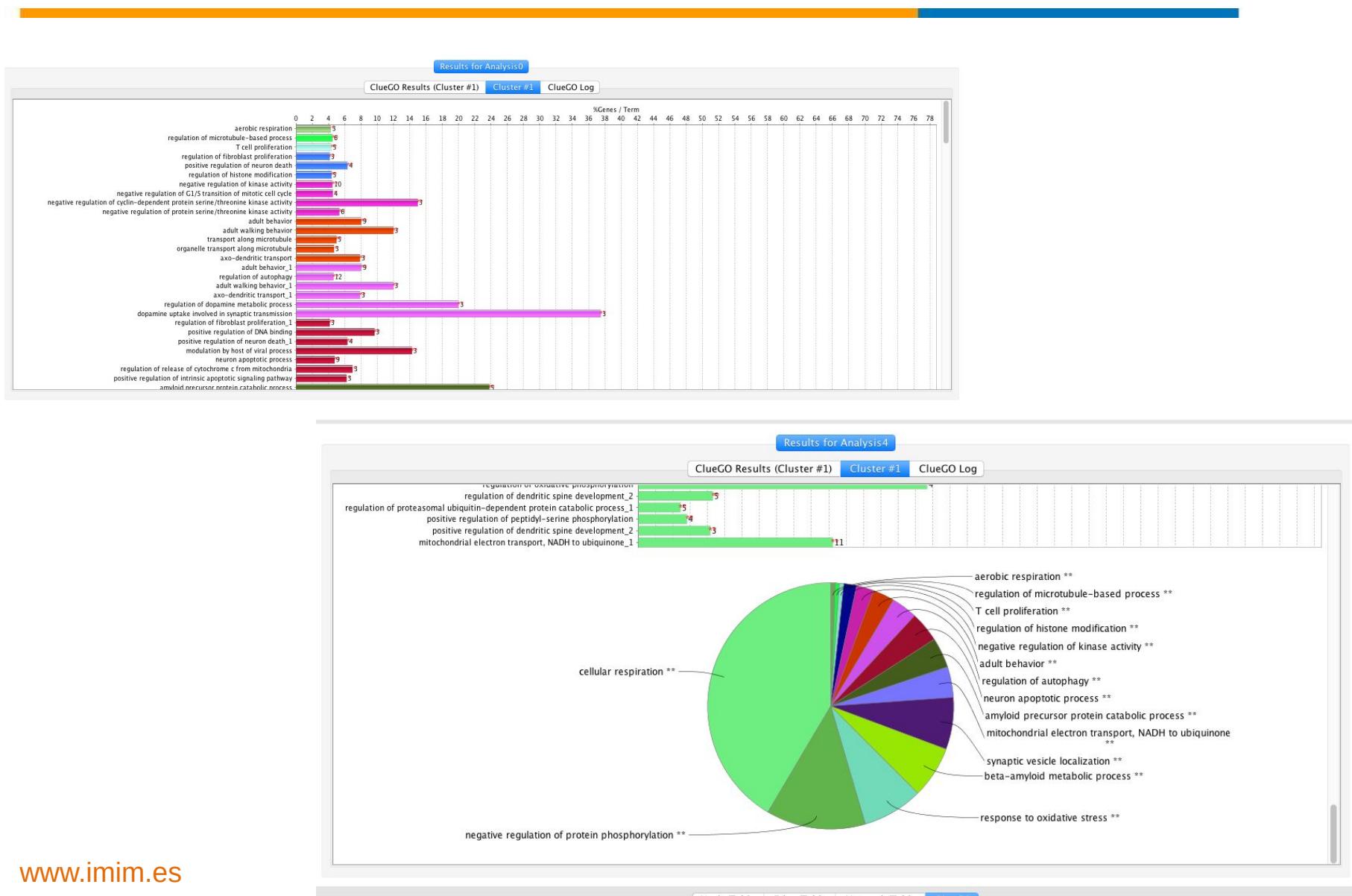
Close project

Actions

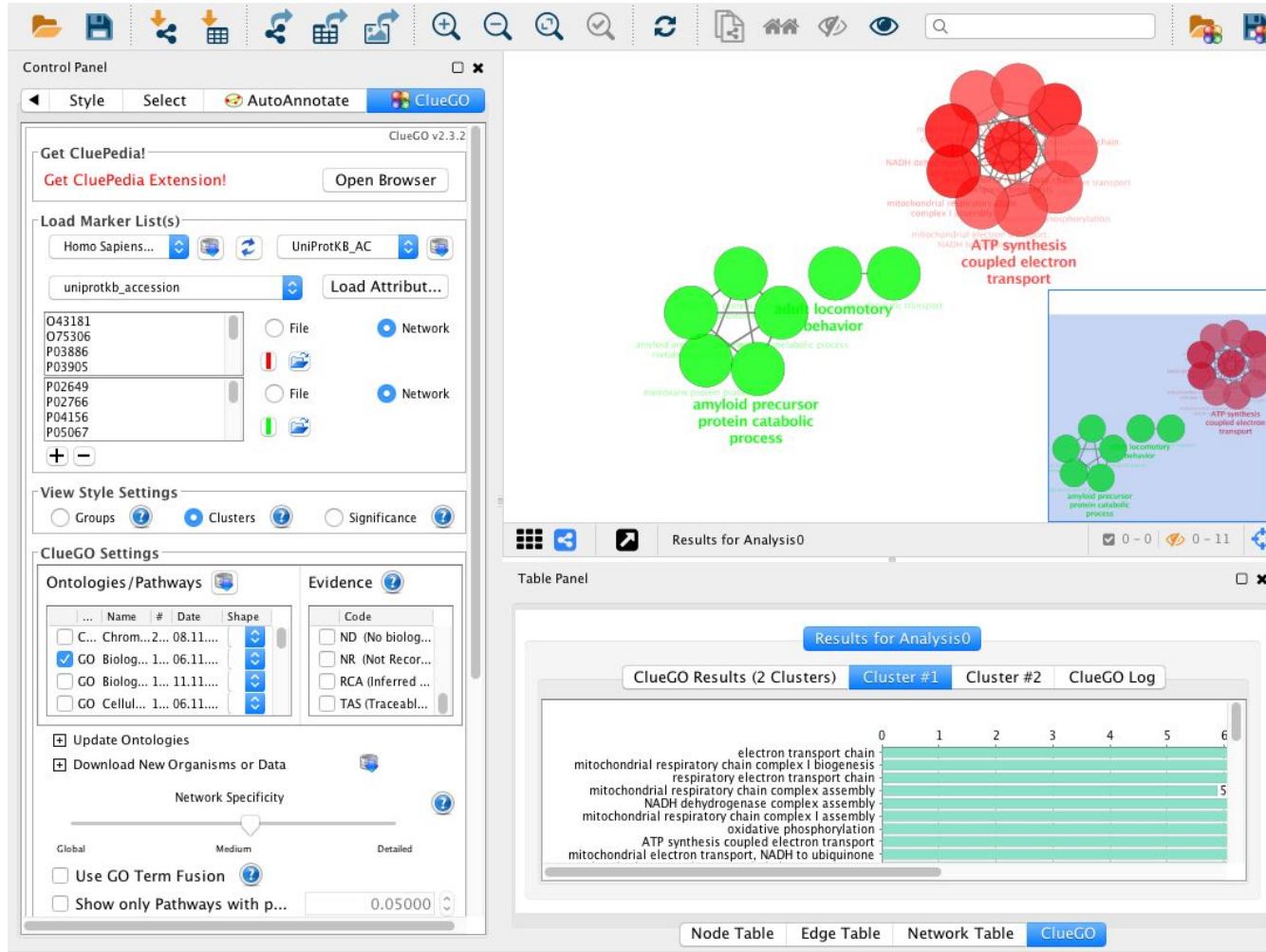
Update Cancel

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Apply the analysis to different sections of the network
and try to establish differences between them.