



Canadian Bioinformatics Workshops

www.bioinformatics.ca

bioinformaticsdotca.github.io



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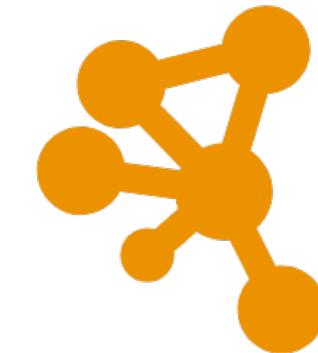
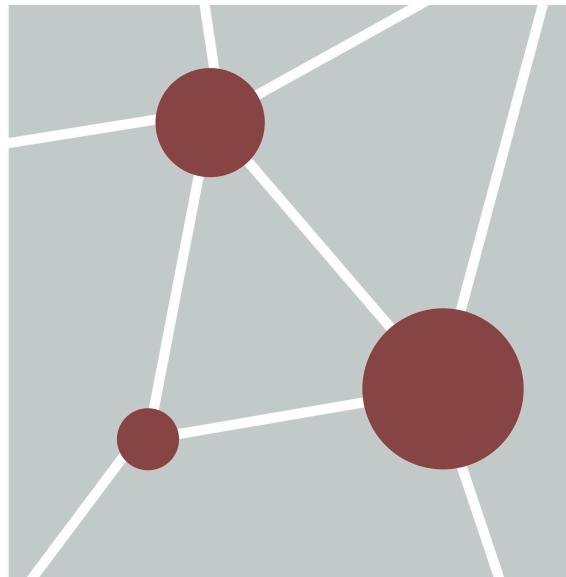
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More Depth on Pathway & Network Analysis

Reactome FI practical lab



Veronique Voisin
Pathway and Network Analysis
June 26-28, 2024



Cytoscape

Learning Objectives of Module

- Be able to perform pathway and network-based data analysis using the ReactomeFIViz app.

Major Features in ReactomeFIViz

The ReactomeFIViz app is designed to find pathways and network patterns related to cancer and other types of diseases.

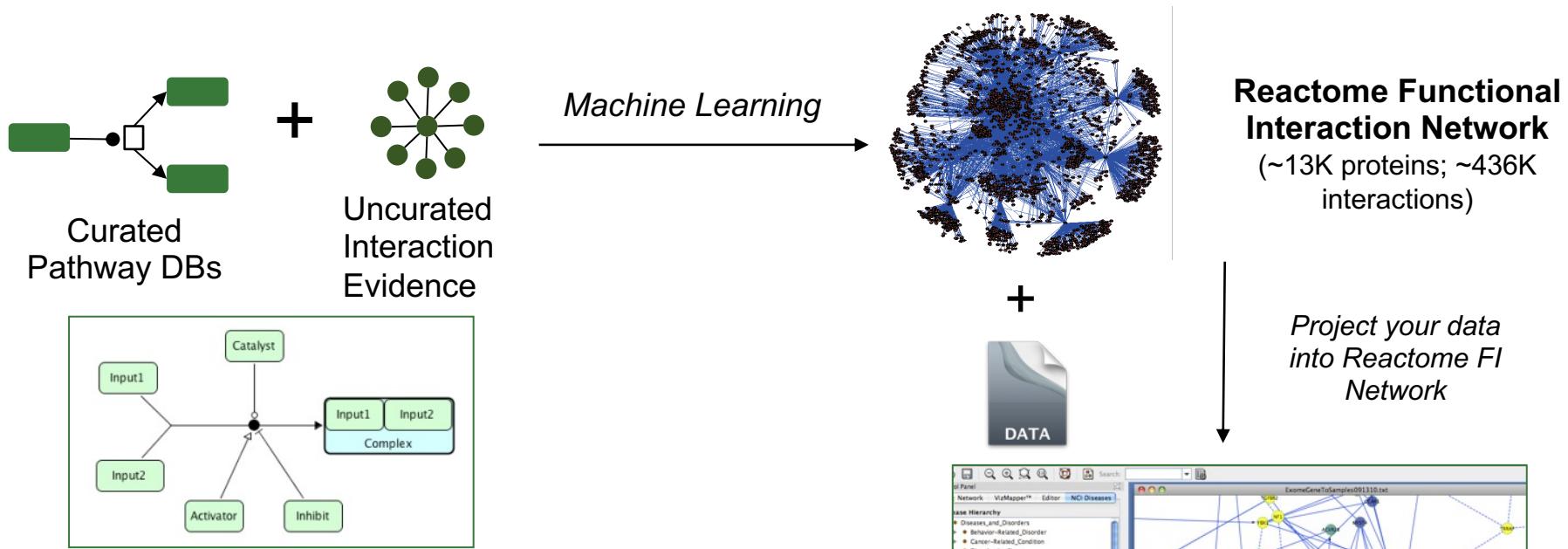
This app accesses the Reactome pathways stored in the database:

- help you to do pathway enrichment analysis for a set of genes
- visualize hit pathways using manually laid-out pathway diagrams directly in Cytoscape
- investigate functional relationships among genes in hit pathways.

The app can also access the Reactome Functional Interaction (FI) network:

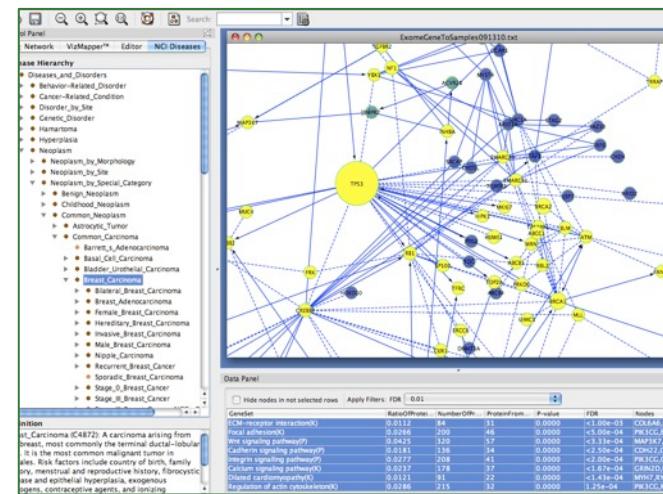
- allows you to construct a FI network based on a set of genes, query the FI data source for the underlying evidence for the interaction
- build and analyze network modules of highly-interacting groups of genes
- perform functional enrichment analysis to annotate the modules
- expand the network by finding genes related to the experimental data set, and overlay with a variety of information sources such as cancer gene index annotations or FDA-approved cancer drugs.

Reactome Functional Interaction Network



What is a Functional Interaction?

- Convert reactions in pathways into pair-wise relationships
- **Functional Interaction:** an interaction in which two proteins are involved in the same reaction as input, catalyst, activator and/or inhibitor, or as components in a complex

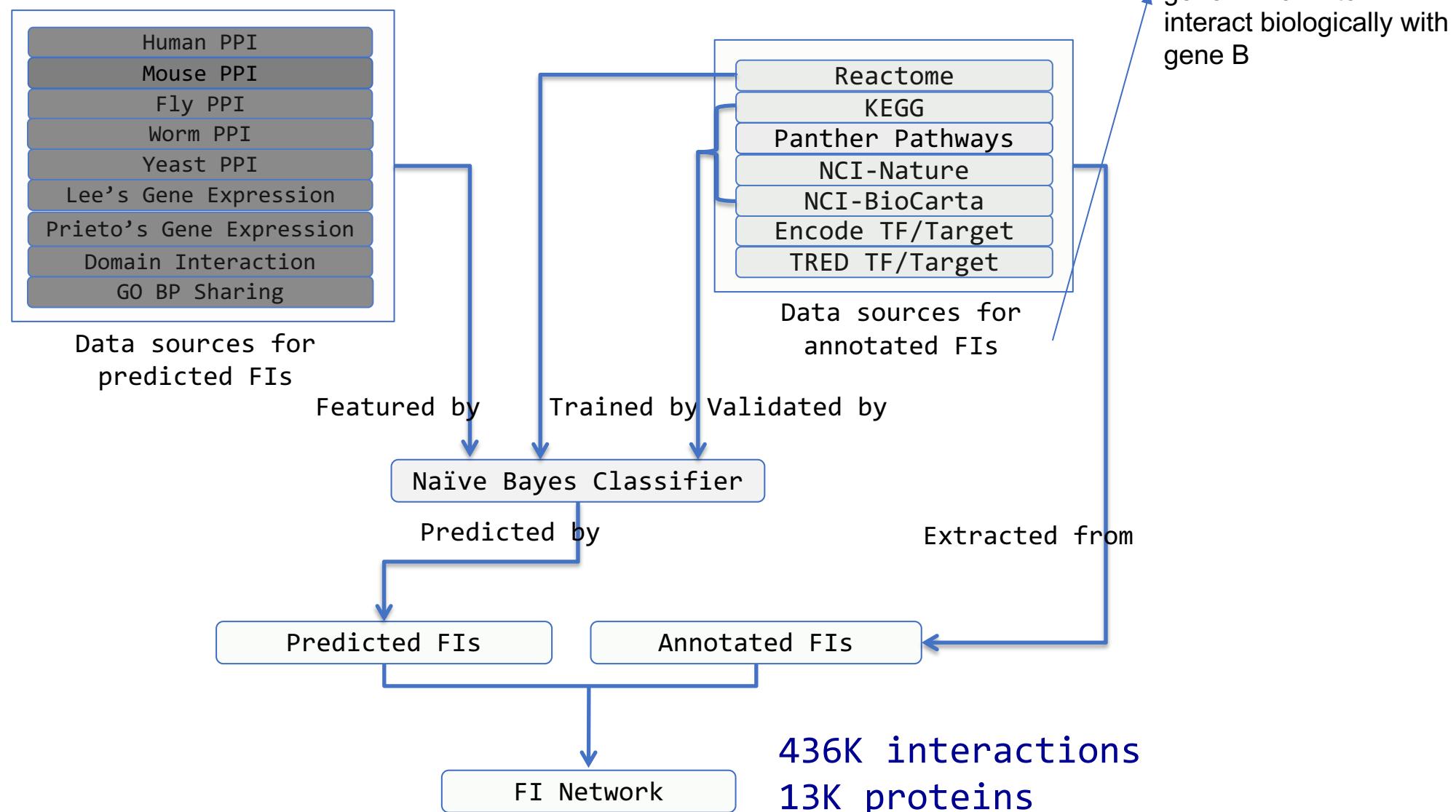


Cytoscape using ReactomeFIViz app

Reactome Functional Interaction Network
(~13K proteins; ~436K interactions)

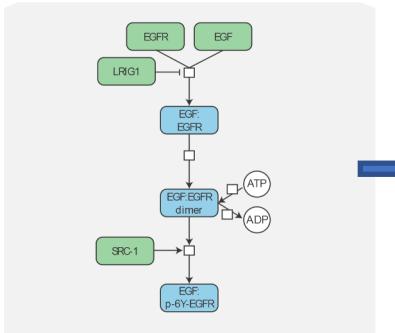
Project your data
into Reactome FI Network

Construction of the FI Network

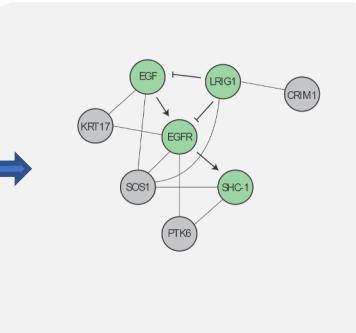


ReactomeFIViz (ReactomeFIPlugin): pathway AND network analysis

Pathway diagram

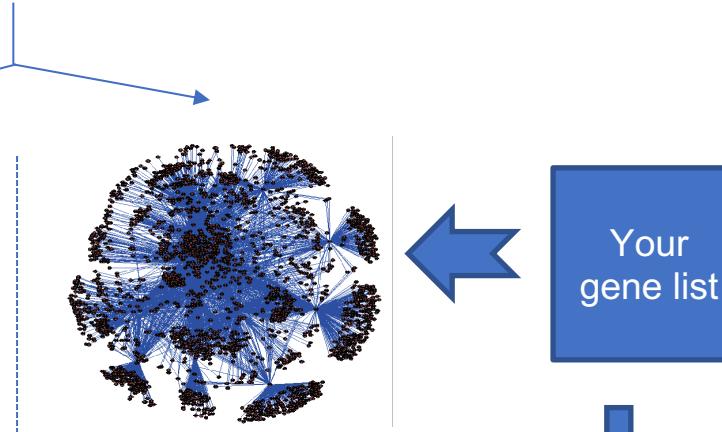


Network



Your gene list

- Browse the collections of the Reactome pathways
- Convert these pathways into a Cytoscape network
- Import your gene list.
- Reactome pathways enriched in your gene list will be returned.
- Genes that in your gene list will be highlighted in the pathway diagrams and network

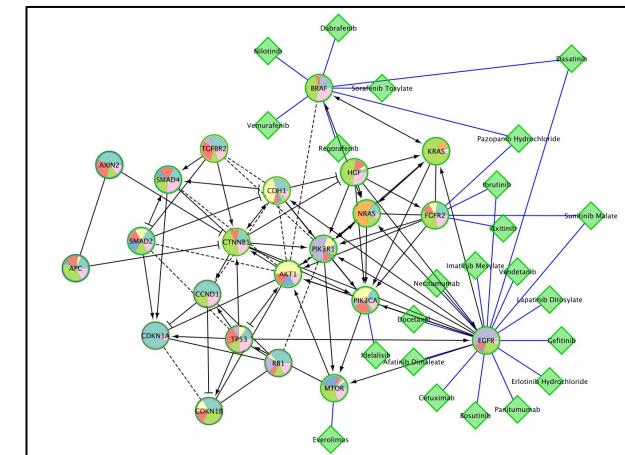


Reactome Functional Interaction Network

(~13K proteins; ~436K interactions)

Your gene list

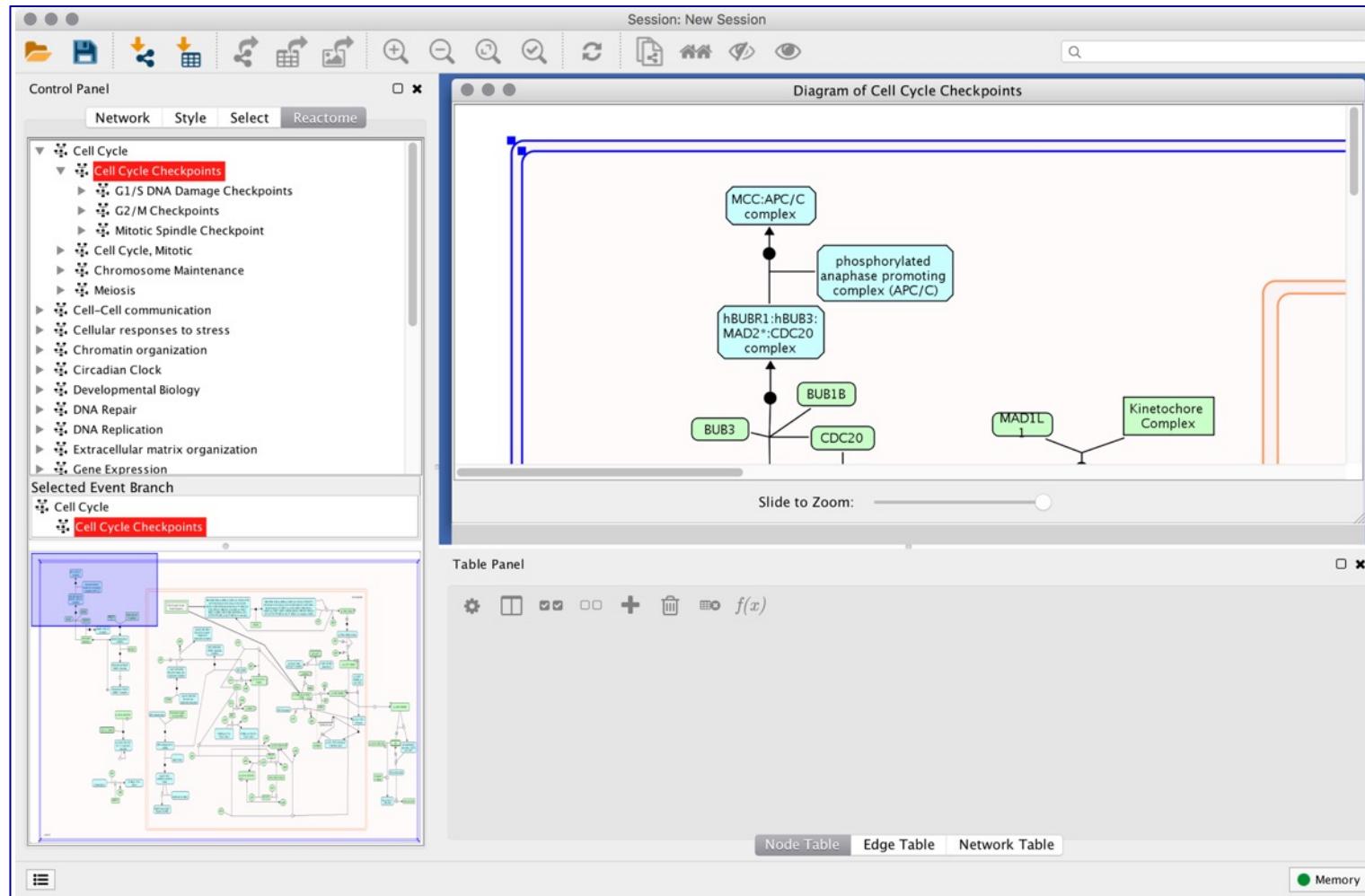
Create a FI network



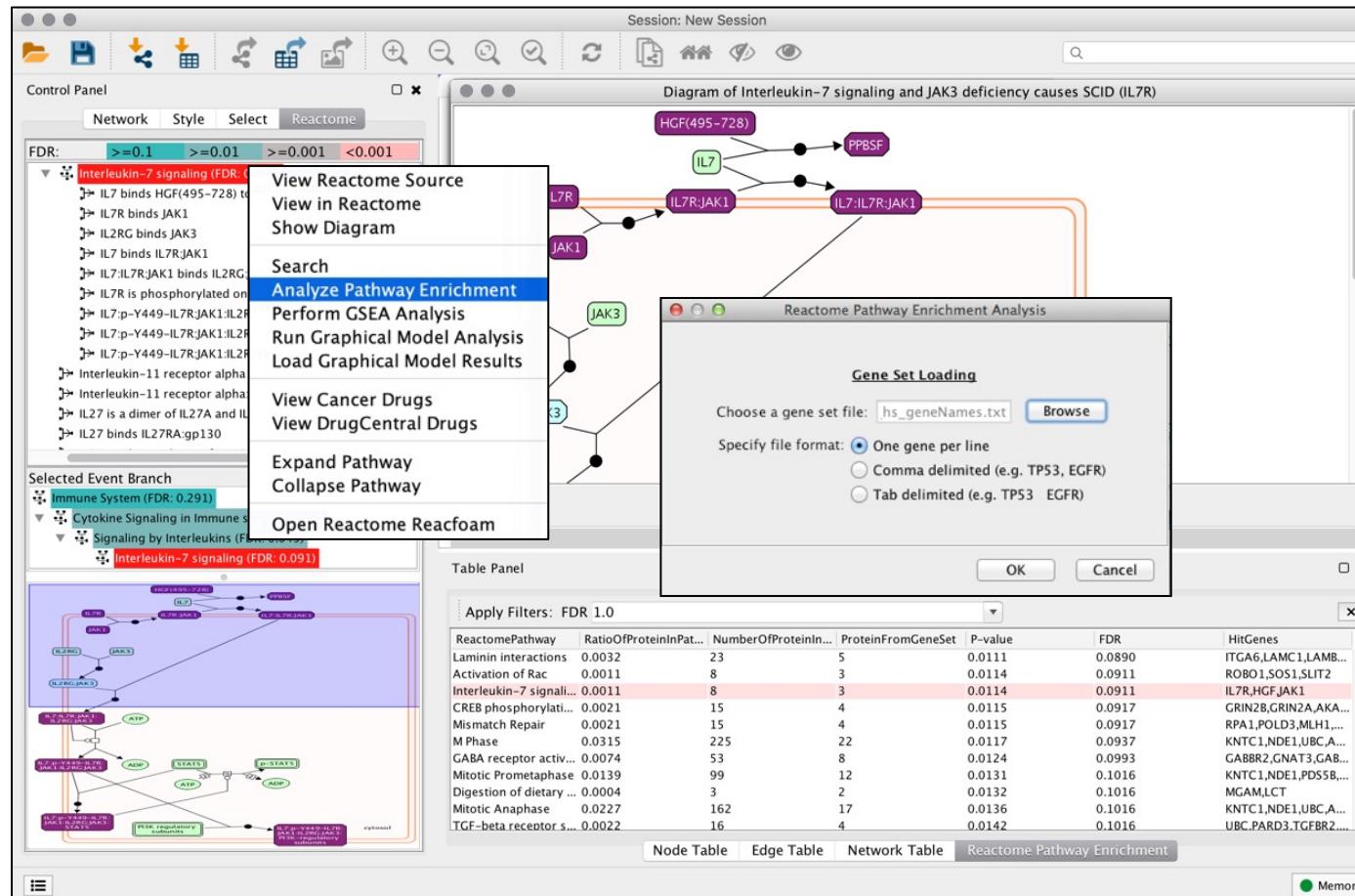
And more...

- Create a FI network using your gene list :
- Genes in your list will be connected by functional interactions.
- You can: further cluster your FI network to find protein complexes
- You can perform pathway analysis on the whole network.
- You can perform pathway analysis on the individual modules and it helps to add a biological label.
- You can add drug targets to the network.

Reactome: Collection of Pathways

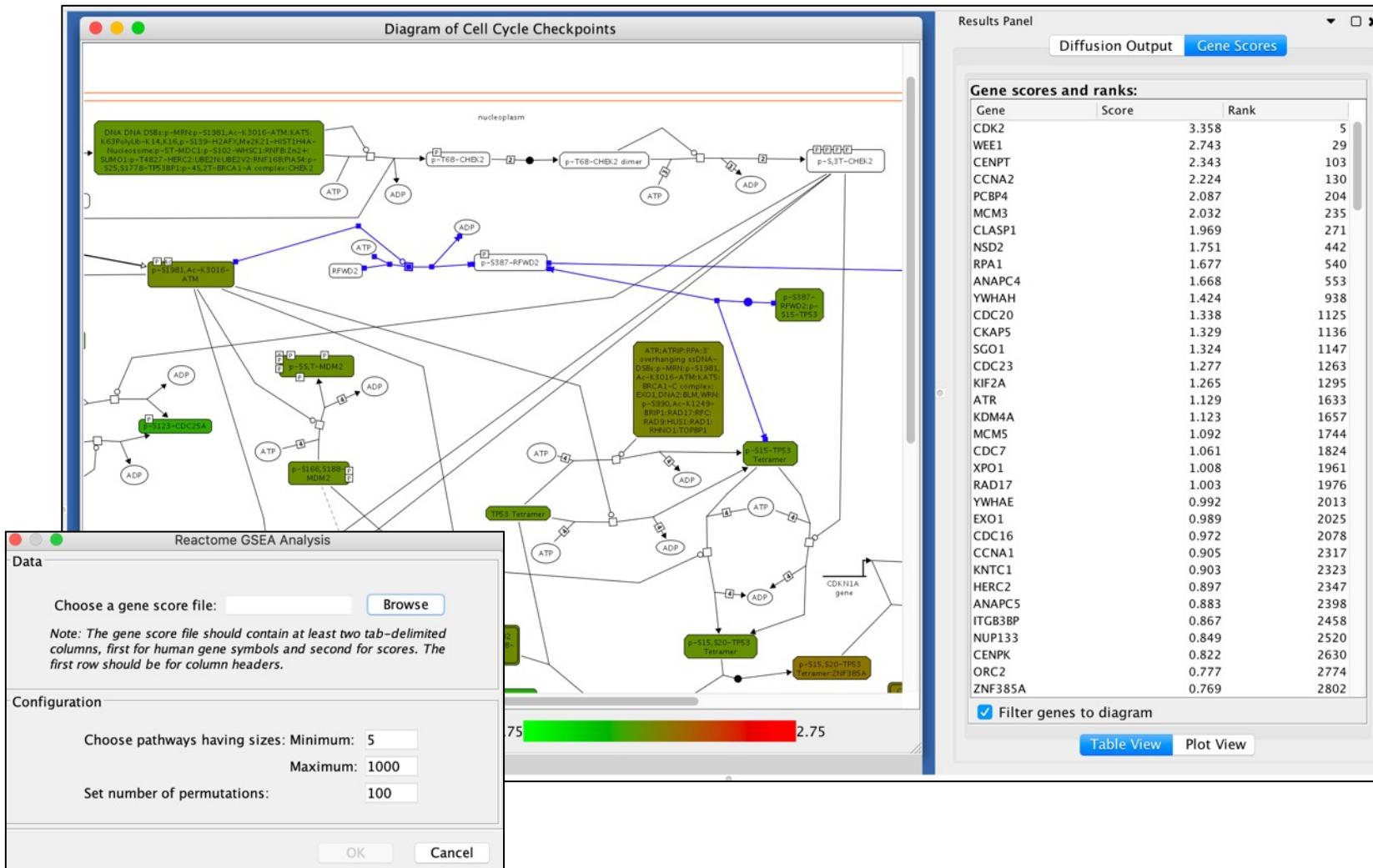


Pathway Enrichment Analysis (gene list) binomial test

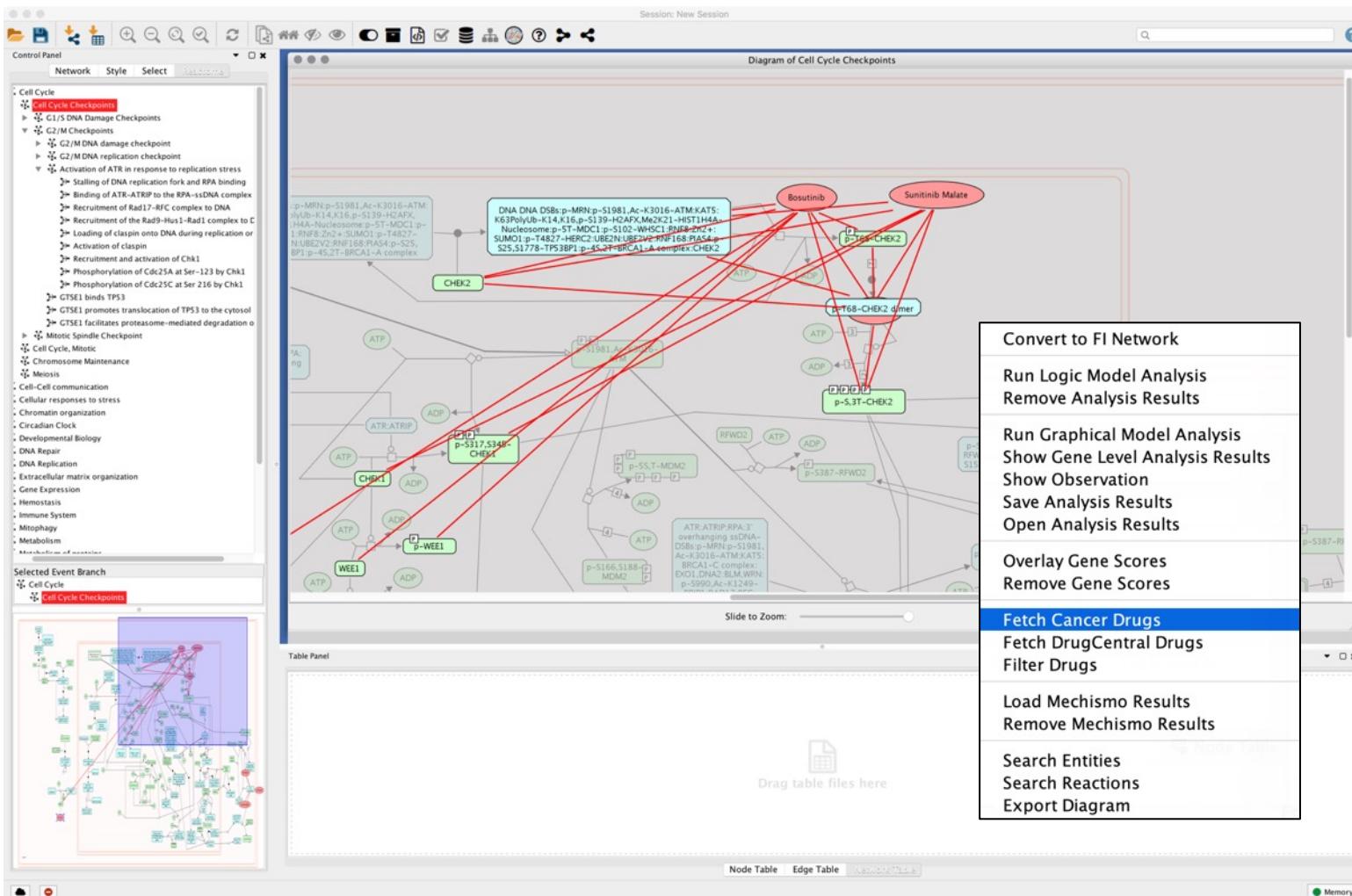


A binomial test uses sample data to determine if the population proportion of one level in a binary (or dichotomous) variable equals a specific claimed value.

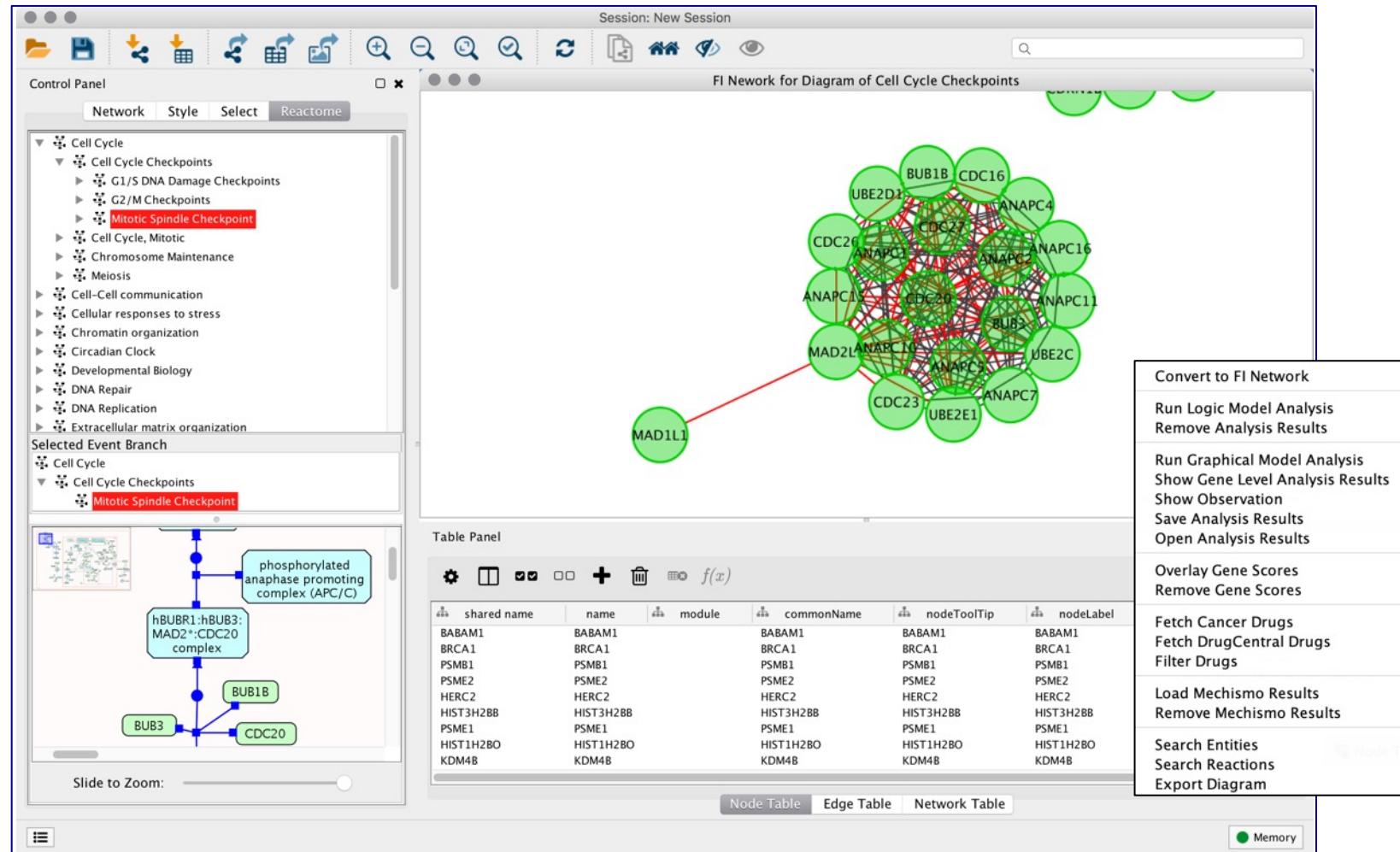
Pathway Enrichment Analysis (ranked list) GSEA



Visualize Cancer Targetome in Reactome Pathways

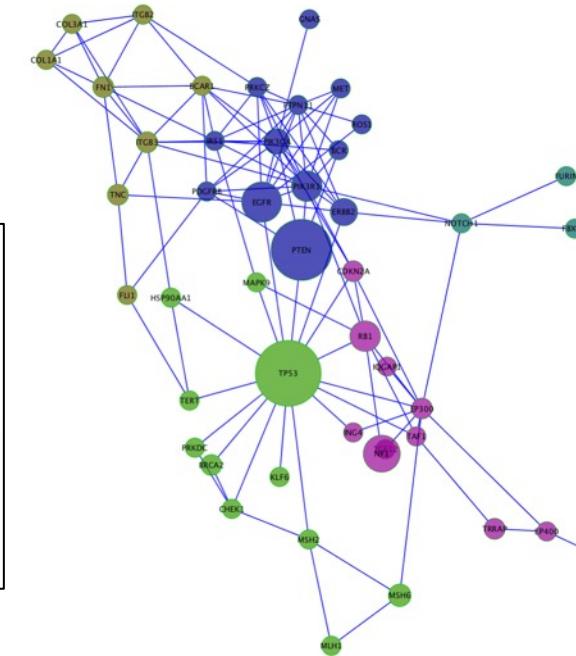
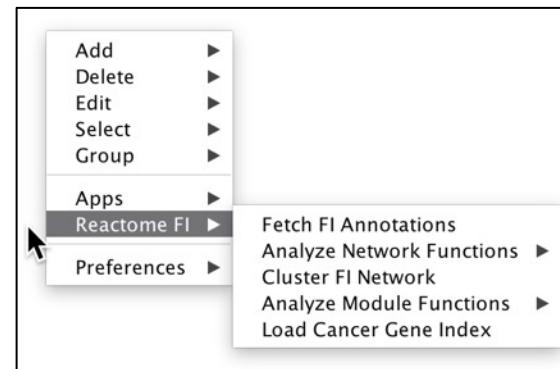
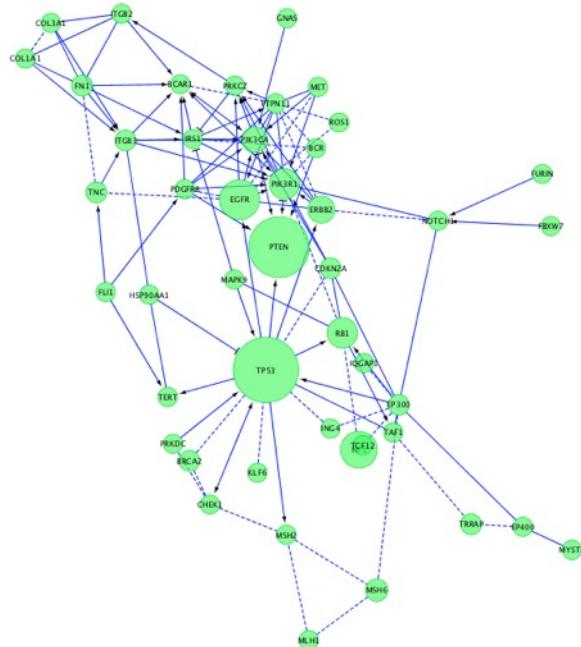


Displaying Reactome Pathways in the FI Network View



Create and Cluster FI Network using a gene list

- Create the network
- Cluster the network
- Perform pathway analysis



File Formats to Create the FI Network

- Choose Plugins, Reactome FIs.

Simple Gene List

MSI2
PTPRT
PELO
SLC18A1
TACC2
FAM148B
PRC1
MSTN
ATP6V1G2
APOE
IMPA2
AGER
XPO5
MEST
RREB1
BAT1
WIP1

Gene/Sample Number Pairs

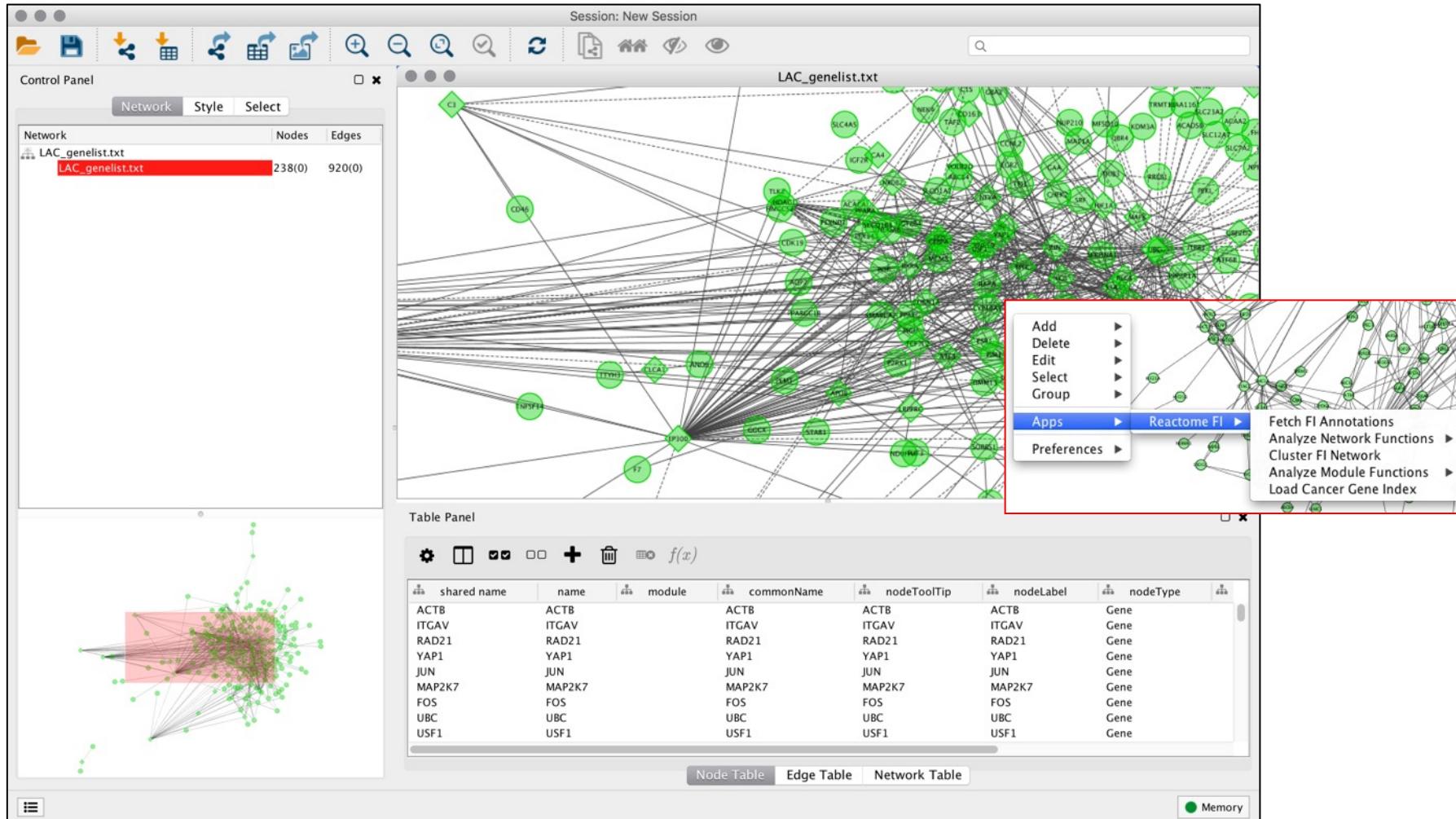
Gene	Sample_Number	Samples
IFT88	1	TCGA-10-0937
TACCC	5	TCGA-24-2288;TCGA-09-1662;TCGA-13-0755;TCGA-13-0920;TCGA-24-2035
ADAD2	1	TCGA-24-1419
PODXL2	1	TCGA-24-2290
RTN3	1	TCGA-13-0726
TADA2B	1	TCGA-25-1313
CD274	1	TCGA-25-1627
SULF1	2	TCGA-24-2262;TCGA-09-2056
SYCP2	3	TCGA-24-1563;TCGA-61-2008;TCGA-24-1427
CD200R1L	1	TCGA-13-1488
RCBTB2	1	TCGA-61-2113
TOP2B	1	TCGA-13-0923
C1orf50	1	TCGA-25-2392
ATP9A	5	TCGA-25-1329;TCGA-04-1530;TCGA-24-2262;TCGA-10-0933;TCGA-13-0795
NUDT5	1	TCGA-61-2003
ZNF189	1	TCGA-24-2254
KCNB1	1	TCGA-23-1028
FERMT3	1	TCGA-24-1464
ZCHC2	1	TCGA-61-1998
DDX18	1	TCGA-13-1509
TGM1	2	TCGA-24-0975;TCGA-25-1321
SAMD7	1	TCGA-09-2051
DR2E2	3	TCGA-13-0723;TCGA-24-2267;TCGA-25-2392
ZSWIM3	2	TCGA-24-1466;TCGA-23-1118
EIF2AK2	2	TCGA-59-2355;TCGA-24-1463
KIAA2018	4	TCGA-23-1024;TCGA-04-1367;TCGA-24-2288;TCGA-24-2289

NCI MAF (mutation annotation file)

Microarray (array) data file

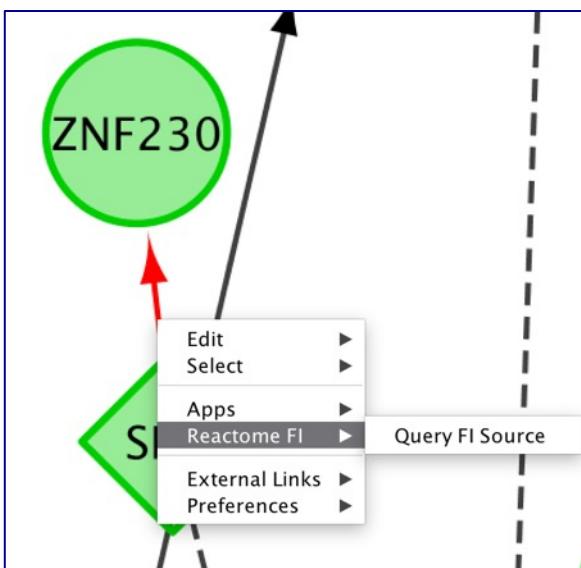
gene	Sample 122	Sample 123	Sample 124	Sample 125	Sample 126	Sample 127	Sample 128	Sample 129	Sample 130
IFT88	1.433357937	0.749571365	0.204170171	1.376375723	0.049504161	0.912377692	0.464660294	0.094684637	0.40767808
KIF9	0.349692236	-0.039741678	-0.568902920	0.174957562	-0.307397394	-0.471521852	-0.772544592	0.850743799	0.188332979
CPSF3	-0.628846878	-0.519774779	0.200101088	-0.388888265	-0.094393584	0.549131818	0.440059711	-0.247094525	1.421076186
TACC2	0.985299156	-0.735535555	0.1013646591	-0.057886422	0.730172279	0.554418157	0.281011247	0.463706367	0.956951722
C14orf102	1.249528811	0.108467065	0.524096007	-0.434648182	-1.528259113	-0.467450538	-0.715336925	-0.252776594	-0.106893839
RTN3	0.106434388	-0.286920286	-0.329065423	0.548592951	0.105649921	-0.872788228	-0.462525052	0.398851852	-0.589804032
PDXDL2	-0.031430138	-0.390143282	-0.075387324	-0.412394154	0.085789024	-0.037693569	-0.053408371	-0.104692114	1.438309928
CORO1A	-0.247037235	-0.564838693	-0.427311396	-0.001970579	0.488162732	-0.435111645	0.596474999	0.463607766	0.050216666
RBM17	-0.360070659	-0.142165028	-0.233914802	0.183996149	-0.130696373	-0.394476028	-0.818819233	-0.629633374	0.993273615
WT1	-0.768491856	-0.694912856	0.763656041	-0.674524201	-0.168165717	-0.393931693	-0.062419245	-0.352852052	-0.589251635
SULF1	-0.863622291	0.158894776	0.272263522	-0.419874008	0.041667647	-0.081472544	-1.178054353	-0.327289133	-0.219036526
SYCP2	-0.365259803	0.146351197	-0.107066702	0.891658263	0.194135655	0.091543376	0.130769762	0.727095627	0.092620508
PHYH	-0.25934465	-0.340194565	0.084219531	-0.613340446	-1.85732245	-0.479503256	-0.229544553	-1.103697457	0.107513571
RCBTR2	-1.21604791	0.137367735	-0.741641602	0.63679988	-0.695593565	-0.46841374	-0.348890288	-0.130354852	-0.572431973
TOPBP2	1.329376011	0.127684069	0.636481097	0.611284984	0.4664606891	0.298285554	0.490380781	-0.397117399	0.050669492
SEC22B	-0.712050988	-0.615625326	-0.339431613	0.917455077	0.277293593	0.413113408	0.583889365	0.632031077	0.486176033
ATP9A	1.547427859	-0.444111337	1.451550978	-0.13542565	0.540051899	0.510070468	0.233468893	-0.149520936	-0.047584080
TGBFR1	-0.782212802	-0.626846247	-0.123008356	0.072190126	-0.239829397	-0.277490940	-0.773868442	0.110632733	0.172099777
NUDT5	-0.616443202	-0.111579407	0.072813169	-0.025664517	0.37488737	0.433985219	-0.89899959	-0.200300728	-0.112230265
VT11B	0.252187159	0.15526231	0.073529674	0.07902019	-0.366846688	-0.684634408	0.191395423	0.967344934	0.216535989
RP5K68L	-0.387163384	0.369359139	-0.596748114	-0.392291725	0.932216509	0.156370699	0.782463975	0.465640208	-0.674657423
RPGEF4	0.203545341	0.430920928	-0.106679623	0.564856109	0.557513268	0.027074065	0.651579319	0.613292236	0.178952896
PRO1596	-0.010404297	0.281552329	0.228155239	0.445509484	0.146353394	-0.077918194	-0.376159587	0.138302748	0.337037678
KCNB1	0.994470843	-0.706140121	0.136578485	0.628377569	0.656531805	0.458975732	0.181156356	-0.469673746	0.364853025
ALDH9A1	0.702468807	-0.111692273	0.963792452	1.181038168	-0.108328490	0.698904754	0.184472446	-0.038728322	-0.154589780
ZCHC2	0.55864339	0.120509562	0.845270548	0.479074052	0.477256496	-1.44895382	0.398635188	0.55323253	0.057189025
LOC51274	-0.291416641	-0.264217463	0.10745668	-0.527143876	-0.073822271	-0.694906046	0.971399049	-0.218889948	-0.146373265
DQ419	-0.3495343	-0.204984332	-0.100929304	-0.02435056	0.490192725	-0.052030906	-0.367453563	-0.514323465	-0.063032996

FI Results Display



- Constructed network is displayed in the Network View panel using an FI specific visual style

Query FI Source



Annotated FIs

Interaction Info
Interaction: SIX5 - ZNF230

Reactome ID	Type	Data Source
6951674	TARGETED_INTERACTION	ENCODE

View Reactome Source

Interaction Info
Interaction: SIX5 - ZNF230

classType	TargetedInteraction
dbId	6951674
displayName	SIX5 ZNF230
dataSource	ENCODE
definition	ENCODE proximal_filtered TF/target interaction; supported by GO BP sharing
factor	SIX5
species	Homo sapiens
target	ZNF230

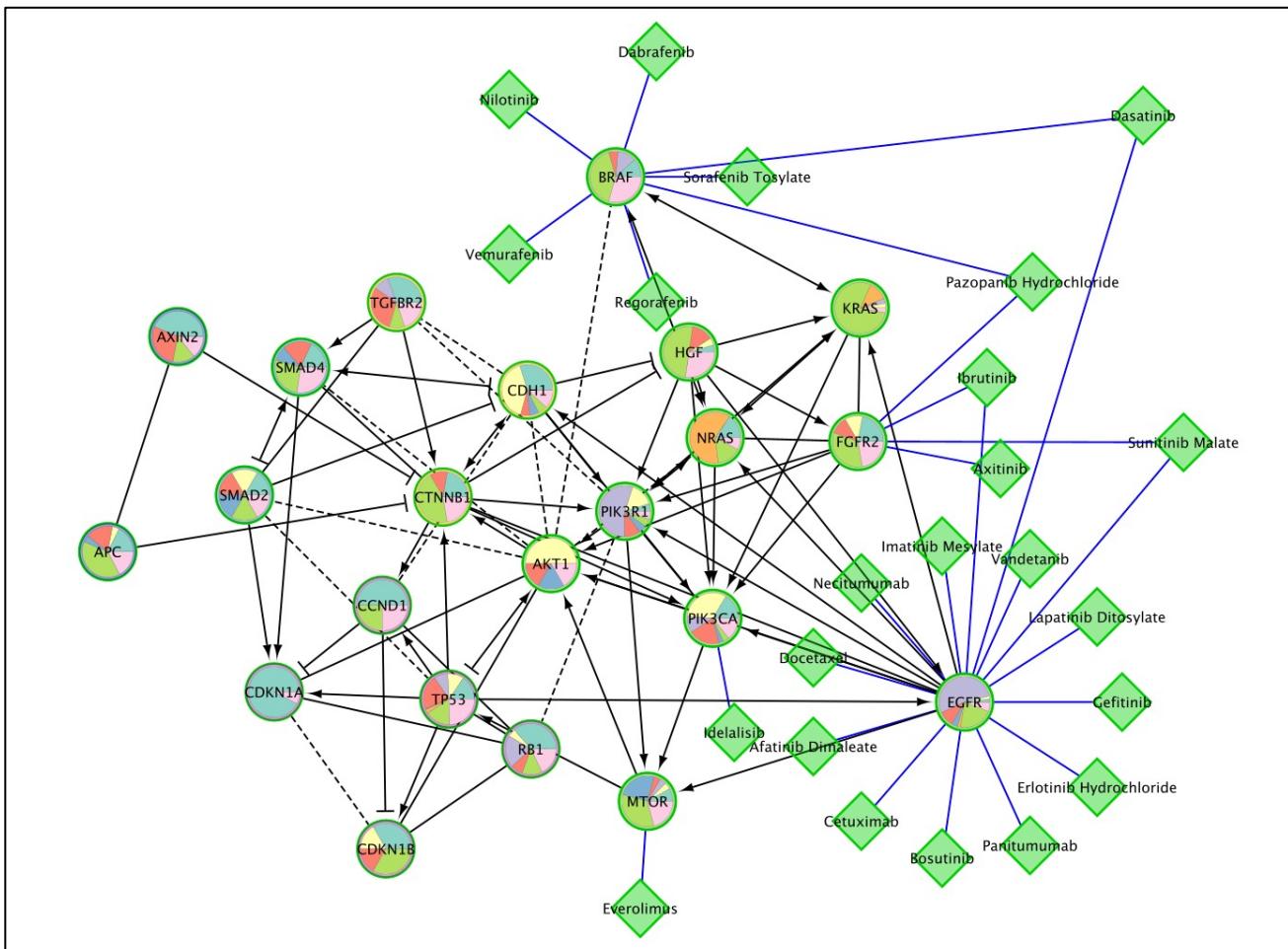
Close

Predicted FIs

Interaction Info
Interaction: SNX4 - SNX6

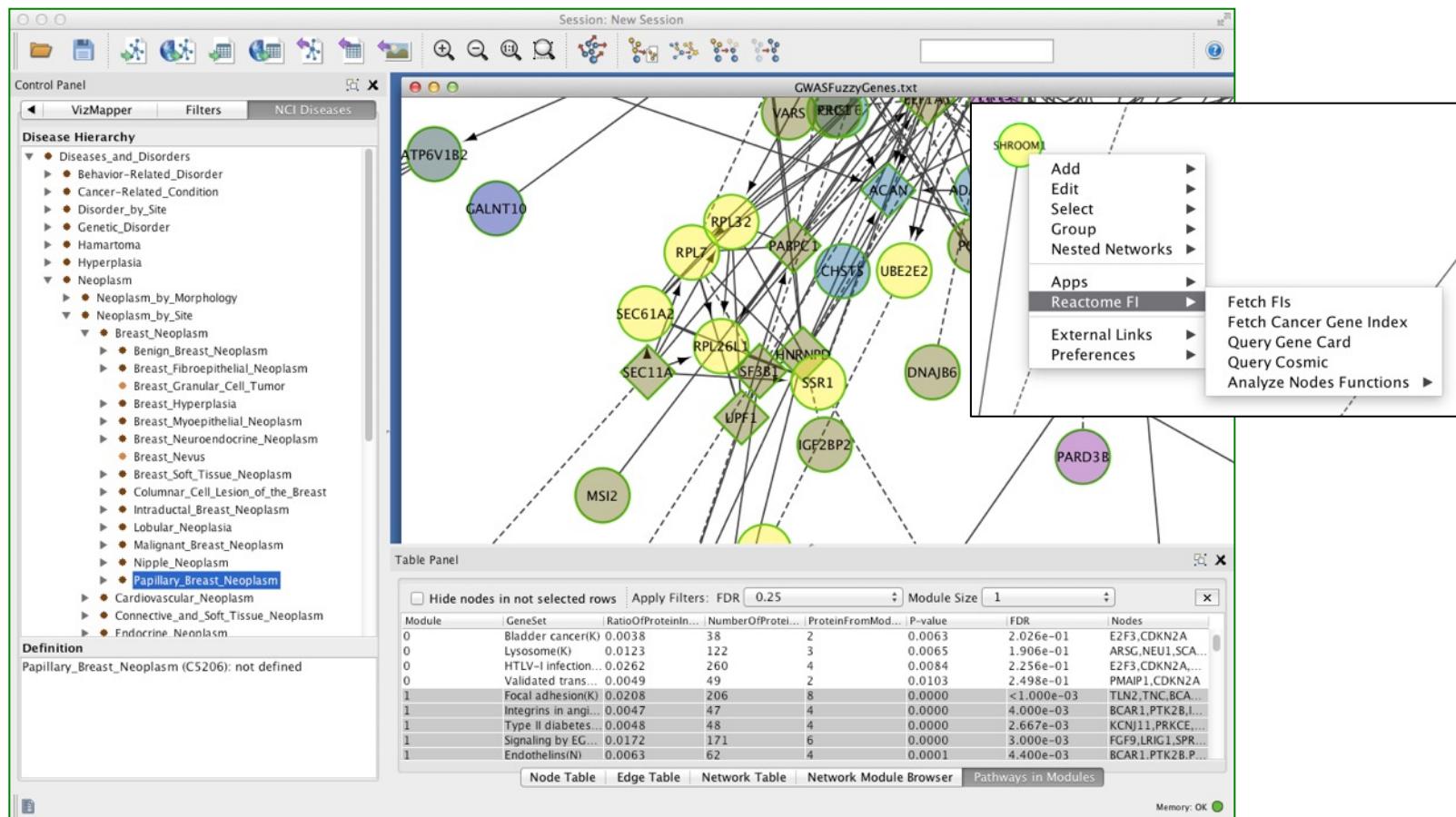
Predictor	Value
Human Interaction	true
Yeast Interaction	false
Fly Interaction	false
Worm Interaction	false
Mouse Interaction	false
Pavlidis Gene Exp	false
Carlos Gene Exp	false
PfamDomain Interaction	true
GO BP Sharing	true
Score	0.9642255584531738

Overlay FDR approved Cancer Drugs



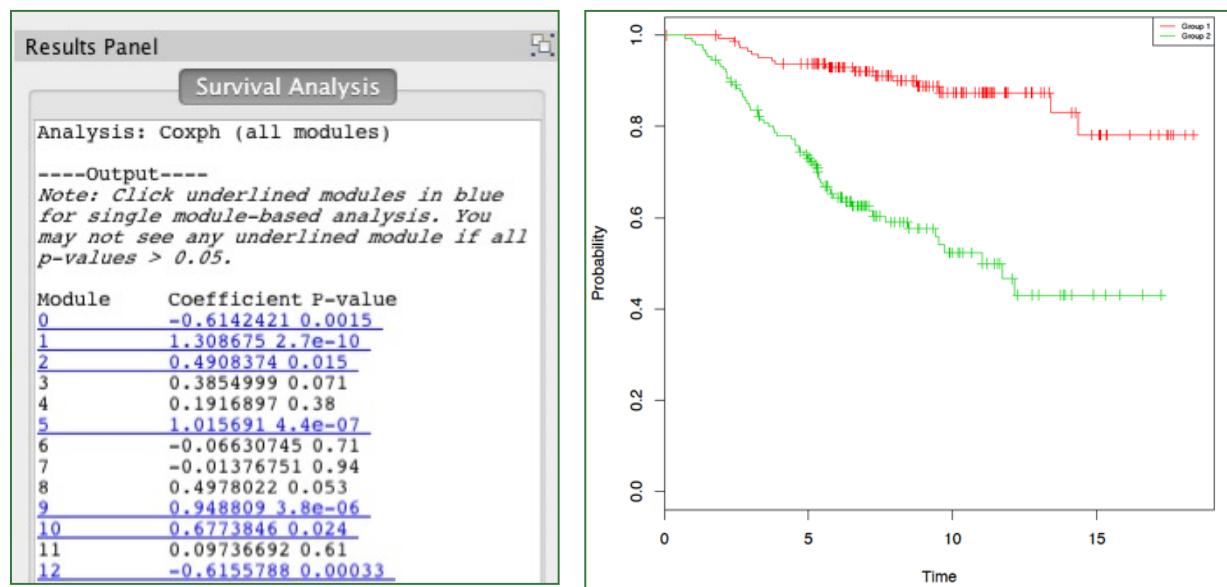
Overlay Cancer Gene Index

- Load the NCI disease terms hierarchy in the left panel.
- Select a disease term in the tree to select all nodes that have this annotation or one of its sub-terms.

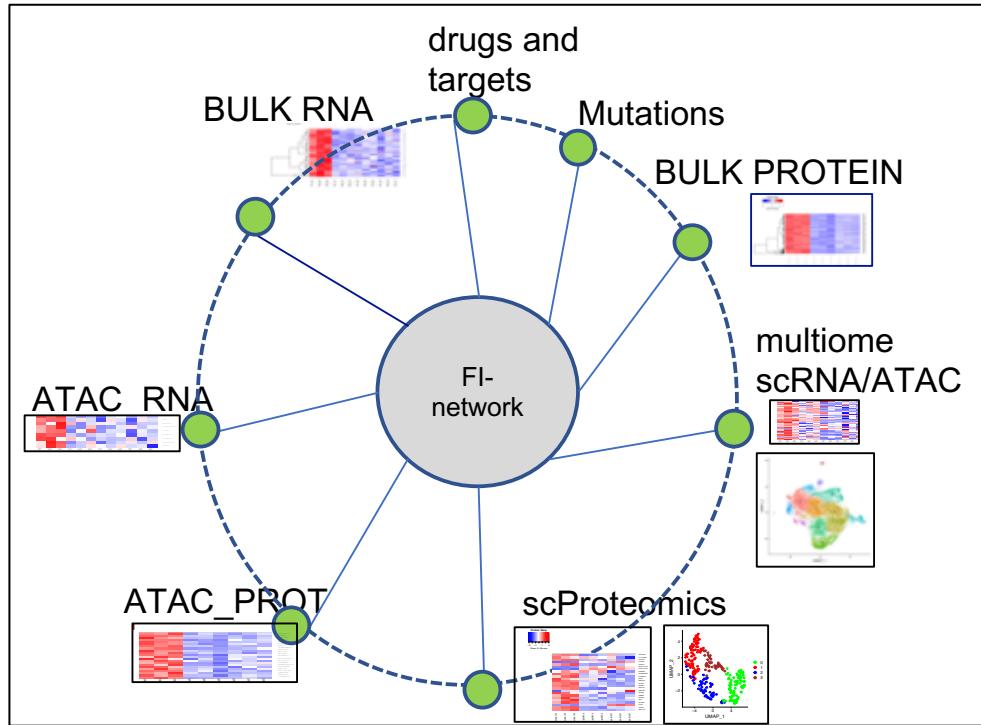


Module Based Survival Analysis

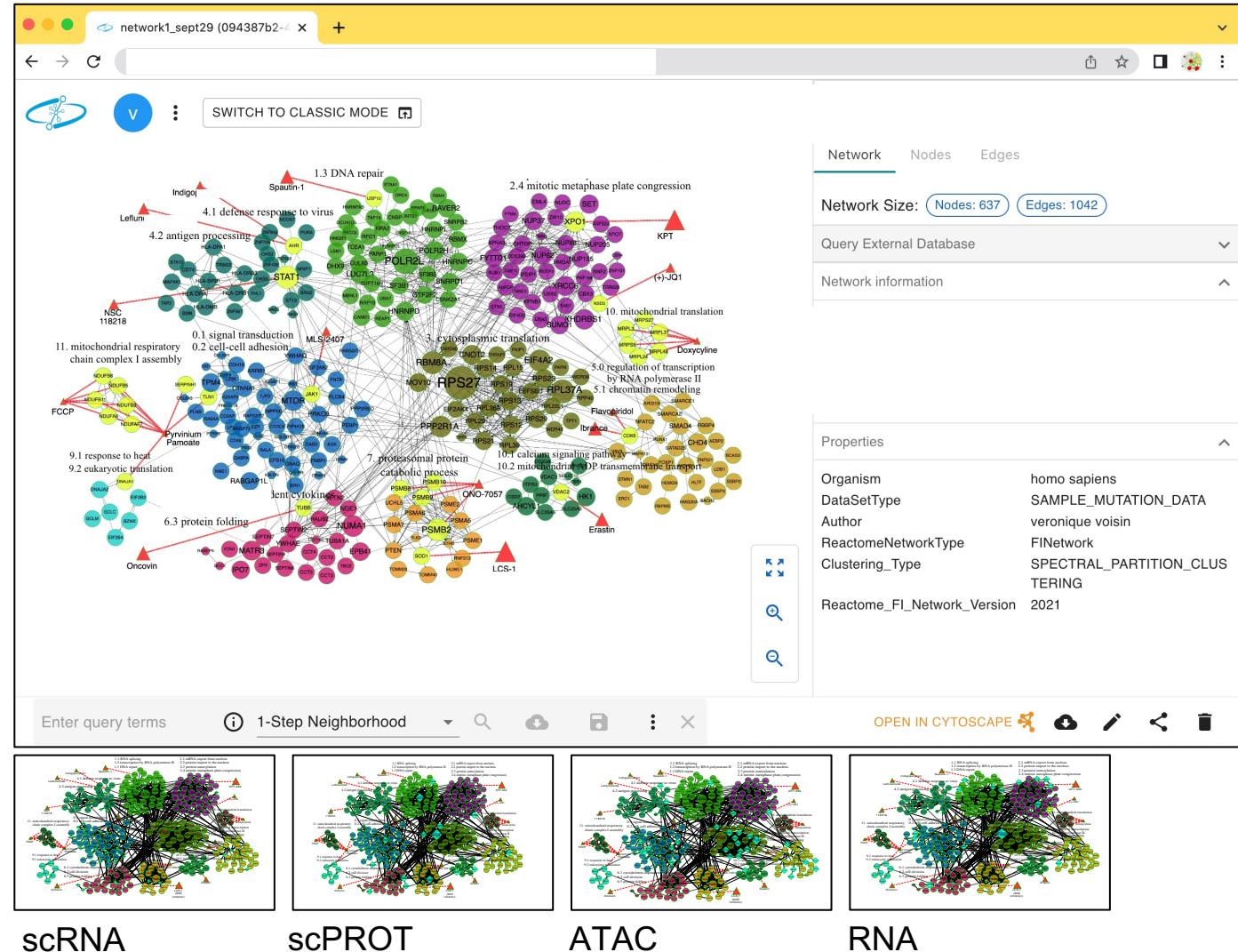
- Discover Prognostic Signatures in Disease Module Datasets.
- Based on a server-side R script that runs either CoxPH or Kaplan-Meyer survival analysis.
- Requires appropriate clinical data file.



One example of use of Reactome FI VIZ



Get gene lists specific to a pure population extracted from the same experiment from different omics data:
• the omics lists have few direct overlaps but the genes might connect with each other if they are put in the same FI network.



We are on a Coffee Break & Networking Session

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