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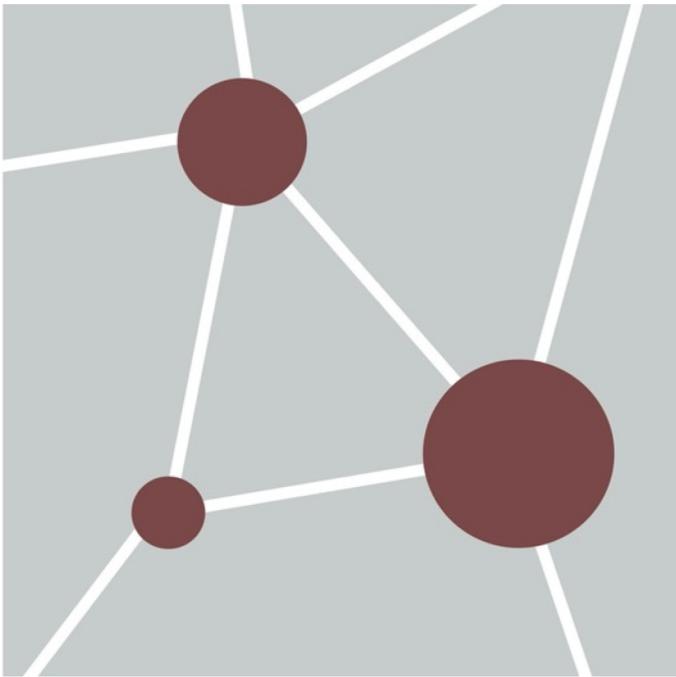
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More Depth on Pathway & Network Analysis Lab

Robin Haw

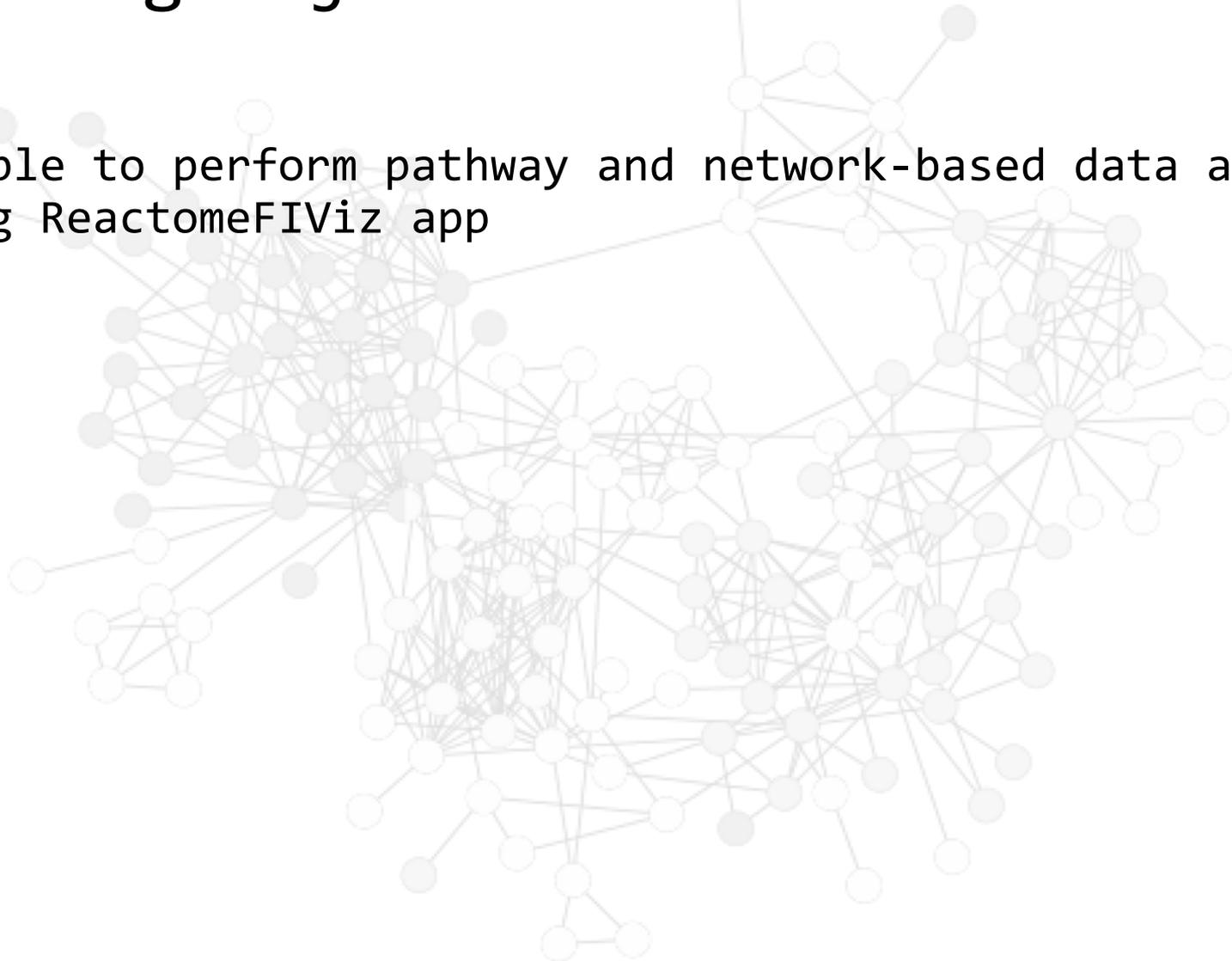
Pathway and Network Analysis of -Omics Data

July 27-29, 2020



Learning Objectives of Module

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



A1) Reactome Pathway Enrichment Analysis

The screenshot displays the Reactome web application interface. The main window, titled "Diagram of Cell Cycle Checkpoints", shows a hierarchical pathway diagram. The nodes are represented as boxes: "MCC:APC/C complex" (top), "phosphorylated anaphase promoting complex (APC/C)" (middle), "hBUBR1:hBUB3:MAD2*:CDC20 complex" (middle), "BUB3" (bottom left), "BUB1B" (bottom left), "CDC20" (bottom left), "MAD1L1" (bottom right), and "Kinetochores" (bottom right). A "Slide to Zoom" slider is located below the diagram.

A context menu is overlaid on the left side of the diagram, listing the following actions:

- View Reactome Source
- View in Reactome
- Show Diagram
- Search
- Analyze Pathway Enrichment
- Perform GSEA Analysis
- Run Graphical Model Analysis
- Load Graphical Model Results
- View Cancer Drugs
- View DrugCentral Drugs
- Expand Pathway
- Collapse Pathway
- Open Reactome Reactoam

The interface also includes a "Control Panel" on the left with tabs for "Network", "Style", "Select", and "Reactome". The "Cell Cycle" category is expanded, showing "Cell Cycle Checkpoint" as the selected event branch. At the bottom, there are tabs for "Node Table", "Edge Table", and "Network Table", along with a "Memory" indicator.

Displaying Reactome Pathways in the FI Network View

The screenshot displays the FI Network View interface for a 'Diagram of Cell Cycle Checkpoints'. The main window shows a network diagram with nodes representing proteins and their interactions. A red line highlights a path from MAD1L1 to a cluster of other proteins.

Control Panel: The left sidebar contains a tree view of biological pathways. The 'Mitotic Spindle Checkpoint' is selected and highlighted in red. Below the tree, a diagram shows the 'hBUBR1:hBUB3:MAD2+:CDC20 complex' interacting with 'BUB1B', 'BUB3', and 'CDC20'. A 'Slide to Zoom' slider is at the bottom of this panel.

Table Panel: A table below the network diagram lists various entities. The table has columns for shared name, name, module, commonName, nodeToolTip, and nodeLabel.

shared name	name	module	commonName	nodeToolTip	nodeLabel
BABAM1	BABAM1		BABAM1	BABAM1	BABAM1
BRCA1	BRCA1		BRCA1	BRCA1	BRCA1
PSMB1	PSMB1		PSMB1	PSMB1	PSMB1
PSME2	PSME2		PSME2	PSME2	PSME2
HERC2	HERC2		HERC2	HERC2	HERC2
HIST3H2BB	HIST3H2BB		HIST3H2BB	HIST3H2BB	HIST3H2BB
PSME1	PSME1		PSME1	PSME1	PSME1
HIST1H2BO	HIST1H2BO		HIST1H2BO	HIST1H2BO	HIST1H2BO
KDM4B	KDM4B		KDM4B	KDM4B	KDM4B

Menu: A vertical menu on the right side of the interface lists various analysis and visualization options:

- Convert to FI Network
- Run Logic Model Analysis
- Remove Analysis Results
- Run Graphical Model Analysis
- Show Gene Level Analysis Results
- Show Observation
- Save Analysis Results
- Open Analysis Results
- Overlay Gene Scores
- Remove Gene Scores
- Fetch Cancer Drugs
- Fetch DrugCentral Drugs
- Filter Drugs
- Load Mechismo Results
- Remove Mechismo Results
- Search Entities
- Search Reactions
- Export Diagram

At the bottom right, there is a 'Memory' indicator with a green dot.

Pathway Enrichment Analysis

Session: New Session

Control Panel

Network Style Select Reactome

FDR: ≥ 0.1 ≥ 0.01 ≥ 0.001 < 0.001

- Interleukin-7 signaling (FDR: 0.091)
 - IL7 binds HGF(495-728)
 - IL7R binds JAK1
 - IL2RG binds JAK3
 - IL7 binds IL7R:JAK1
 - IL7:IL7R:JAK1 binds IL7
 - IL7 is phosphorylated
 - IL7-p-Y449-IL7R:JAK1
 - IL7-p-Y449-IL7R:JAK1
 - IL7-p-Y449-IL7R:JAK1
 - Interleukin-11 receptor a
 - Interleukin-11 receptor a
 - IL27 is a dimer of IL27A a
 - IL27 binds IL27RA:gp130

Selected Event Branch

- Immune System (FDR: 0.291)
 - Cytokine Signaling in Immune system (FDR: 0.089)
 - Signaling by Interleukins (FDR: 0.045)
 - Interleukin-7 signaling (FDR: 0.091)

Diagram of Interleukin-7 signaling and JAK3 deficiency causes SCID (IL7R)

Reactome Pathway Enrichment Analysis

Gene Set Loading

Choose a gene set file: `hs_geneNames.txt`

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

Table Panel

Apply Filters: FDR 1.0

ReactomePathway	RatioOfProteinInPat...	NumberOfProteinIn...	ProteinFromGeneSet	P-value	FDR	HitGenes
Laminin interactions	0.0032	23	5	0.0111	0.0890	ITGA6,LAMC1,LAMB...
Activation of Rac	0.0011	8	3	0.0114	0.0911	ROBO1,SOS1,SLIT2
Interleukin-7 signali...	0.0011	8	3	0.0114	0.0911	IL7R,HGF,JAK1
CREB phosphorylati...	0.0021	15	4	0.0115	0.0917	GRIN2B,GRIN2A,AKA...
Mismatch Repair	0.0021	15	4	0.0115	0.0917	RPA1,POLD3,MLH1,...
M Phase	0.0315	225	22	0.0117	0.0937	KNTC1,NDE1,UBC,A...
GABA receptor activ...	0.0074	53	8	0.0124	0.0993	GABBR2,GNAT3,GAB...
Mitotic Prometaphase	0.0139	99	12	0.0131	0.1016	KNTC1,NDE1,PD55B,...
Digestion of dietary ...	0.0004	3	2	0.0132	0.1016	MGAM,LT
Mitotic Anaphase	0.0227	162	17	0.0136	0.1016	KNTC1,NDE1,UBC,A...
TGF-beta receptor s...	0.0022	16	4	0.0142	0.1016	UBC.PARD3,TCFBR2...

Node Table Edge Table Network Table Reactome Pathway Enrichment

Memory

Gene Set Enrichment Analysis (GSEA)

Diagram of Cell Cycle Checkpoints

Results Panel

Diffusion Output **Gene Scores**

Gene scores and ranks:

Gene	Score	Rank
CDK2	3.358	5
WEE1	2.743	29
CENPT	2.343	103
CCNA2	2.224	130
PCBP4	2.087	204
MCM3	2.032	235
CLASP1	1.969	271
NSD2	1.751	442
RPA1	1.677	540
ANAPC4	1.668	553
YWHAH	1.424	938
CDC20	1.338	1125
CKAP5	1.329	1136
SGO1	1.324	1147
CDC23	1.277	1263
KIF2A	1.265	1295
ATR	1.129	1633
KDM4A	1.123	1657
MCM5	1.092	1744
CDC7	1.061	1824
XPO1	1.008	1961
RAD17	1.003	1976
YWHAE	0.992	2013
EXO1	0.989	2025
CDC16	0.972	2078
CCNA1	0.905	2317
KNTC1	0.903	2323
HERC2	0.897	2347
ANAPC5	0.883	2398
ITGB3BP	0.867	2458
NUP133	0.849	2520
CENPK	0.822	2630
ORC2	0.777	2774
ZNF385A	0.769	2802

Filter genes to diagram

Table View Plot View

Reactome GSEA Analysis

Data

Choose a gene score file: Browse

Note: The gene score file should contain at least two tab-delimited columns, first for human gene symbols and second for scores. The first row should be for column headers.

Configuration

Choose pathways having sizes: Minimum: Maximum:

Set number of permutations:

OK Cancel

Visualize Cancer Targetome in Reactome Pathways

The screenshot displays the Reactome pathway visualization tool interface. The main window shows a detailed network diagram titled "Diagram of Cell Cycle Checkpoints". The diagram features various nodes representing proteins and complexes, such as "CHEK2", "p-168-CHEK2 dimer", "p-53T-CHEK2", "WEE1", "p-WEE1", "CHK1", "p-S317.S348-CHEK1", "ATR-ATRIP", "MCM2", "p-S5.T-MDM2", "p-S387-RFWD2", "p-S166.S188-MDM2", "ATR-ATRIP:PPA:3' overhanging ssDNA-DSSB-p-MRN-p-S1981.Ac-K3016-ATM:KATS:K63PolyUb-K14.K16.p-S139-H2AFX.Mc2K21-HST1H4A.Nucleosome-p-ST-MDC1-p-S102-WHSC1-ENHBP24:SUMO1-p-T4827-HERC2:UBE2N:UBE2A:PNF168:PIASA-S35.S3778-TP53BP1-p-4527-TP53:BRCA1-A complex", "p-MRN-p-S1981.Ac-K3016-ATM:KATS:K63PolyUb-K14.K16.p-S139-H2AFX.H4A-Nucleosome-p-ST-MDC1-p-S102-WHSC1-ENHBP24:SUMO1-p-T4827-HERC2:UBE2N:UBE2A:PNF168:PIASA-S35.S3778-TP53BP1-p-4527-TP53:BRCA1-A complex", "p-S1981.Ac-K3016-ATM:KATS:K63PolyUb-K14.K16.p-S139-H2AFX.H4A-Nucleosome-p-ST-MDC1-p-S102-WHSC1-ENHBP24:SUMO1-p-T4827-HERC2:UBE2N:UBE2A:PNF168:PIASA-S35.S3778-TP53BP1-p-4527-TP53:BRCA1-A complex", and "p-S1981.Ac-K3016-ATM:KATS:K63PolyUb-K14.K16.p-S139-H2AFX.H4A-Nucleosome-p-ST-MDC1-p-S102-WHSC1-ENHBP24:SUMO1-p-T4827-HERC2:UBE2N:UBE2A:PNF168:PIASA-S35.S3778-TP53BP1-p-4527-TP53:BRCA1-A complex". Red lines highlight connections between these nodes and two drug nodes: "Bosutinib" and "Sunitinib Malate".

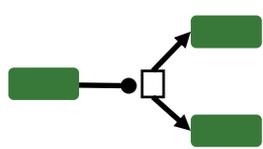
On the left, the "Control Panel" shows a hierarchical tree of pathways, with "Cell Cycle Checkpoints" selected. Below it, the "Selected Event Branch" also shows "Cell Cycle Checkpoints".

On the right, a context menu is open, listing various analysis options:

- Convert to FI Network
- Run Logic Model Analysis
- Remove Analysis Results
- Run Graphical Model Analysis
- Show Gene Level Analysis Results
- Show Observation
- Save Analysis Results
- Open Analysis Results
- Overlay Gene Scores
- Remove Gene Scores
- Fetch Cancer Drugs**
- Fetch DrugCentral Drugs
- Filter Drugs
- Load Mechismo Results
- Remove Mechismo Results
- Search Entities
- Search Reactions
- Export Diagram

At the bottom, there is a "Table Panel" with a "Drag table files here" instruction and buttons for "Node Table" and "Edge Table".

A2) De Novo Subnetwork Construction & Clustering



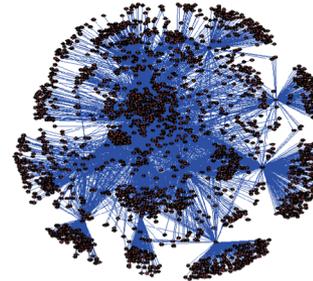
Curated Pathway DBs

+



Uncurated Interaction Evidence

Machine Learning



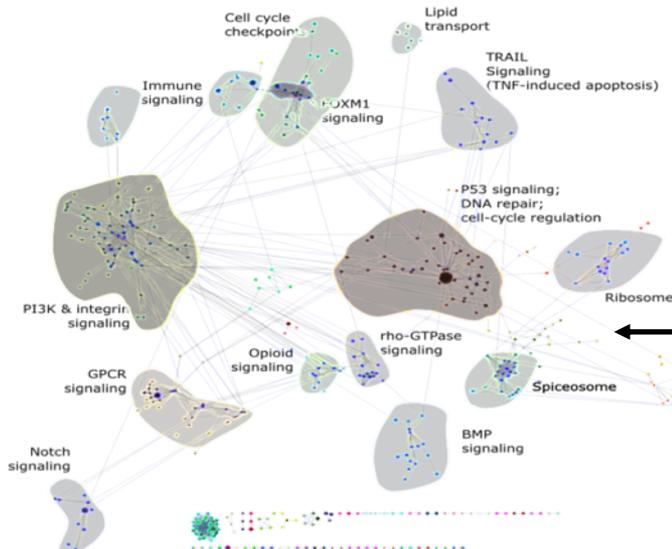
Reactome Functional Interaction Network
(~13K proteins; ~436K interactions)

+



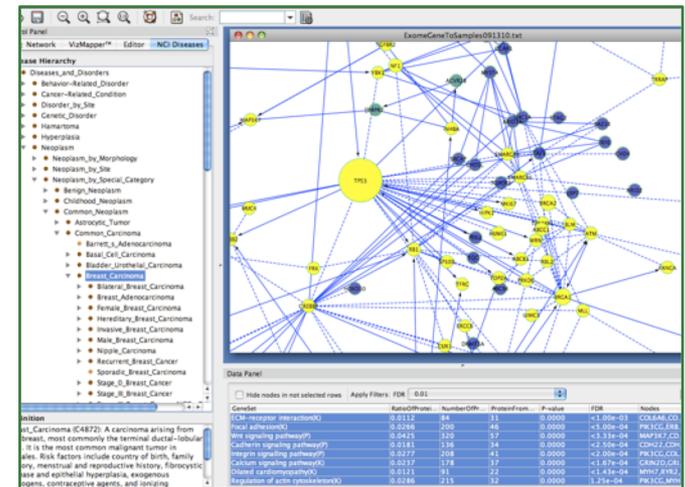
DATA

Project your data into Reactome FI Network



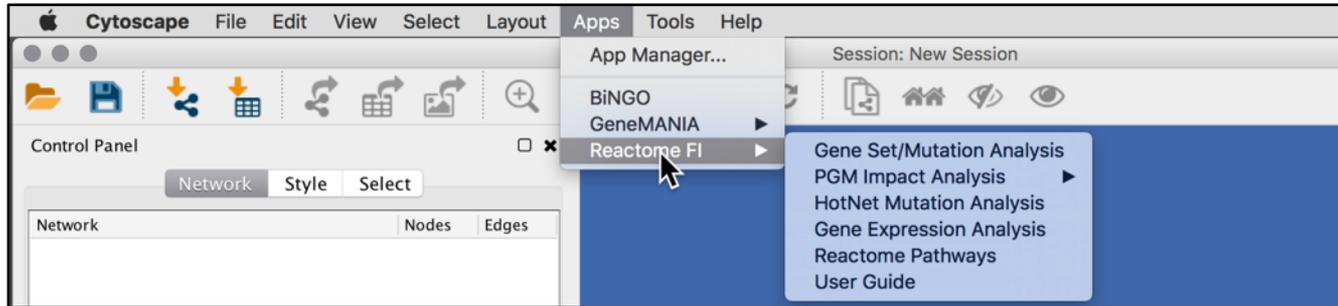
Disease "modules" (10-30)

Extract and Cluster, and Annotate Altered Genes



Cytoscape using ReactomeFIViz app

Upload your data



- FI plug-in supports four file formats:
 - Simple gene set: one line per gene
 - Gene/sample number pair. Contains two required columns, gene and number of samples having gene mutated, and an optional third column listing sample names (delimited by semi-colon ;)
 - NCI MAF (mutation annotation file)
 - Sample Gene Expression data file

File Formats

- Choose Plugins, Reactome FIs.

Simple Gene List

MSI2
 PTPRT
 PELO
 SLC18A1
 TACC2
 FAM148B
 PRC1
 MSTN
 ATP6V1G2
 APOE
 IMPA2
 AGER
 XPO5
 MEST
 RREB1
 BAT1
 WIPI1

NCI MAF (mutation annotation file)

Hugo_Symbol	Entrez_Gene_Center	NCBI_Build	Chromosome	Start_position	End_position	Strand
BAI2	576 broad.mit.edu	36	1	31974808	31974808	+
LRRRC41	10489 broad.mit.edu	36	1	46524584	46524584	+
C1orf173	127254 broad.mit.edu	36	1	74828082	74828082	+
SSX2IP	117178 broad.mit.edu	36	1	84900740	84900740	+
NTNG1	22854 broad.mit.edu	36	1	107668441	107668441	+
PGLYRP3	114771 broad.mit.edu	36	1	151541551	151541551	+
FCRL5	83416 broad.mit.edu	36	1	155783467	155783467	+
FBXO28	23219 broad.mit.edu	36	1	222388418	222388418	+
OR2M2	391194 broad.mit.edu	36	1	246410342	246410342	+
MKK	283078 broad.mit.edu	36	10	28063690	28063690	+

Variant_Classification	Variant_Type	Reference_Allele	Tumor_Seq_Allele1	Tumor_Seq_dbSNP_RS	dbSNP_Val_1	Tumor_Samp
Missense_Mutation	SNP	C	G	novel	none	TCGA-04-1331
Missense_Mutation	SNP	C	novel	novel	none	TCGA-04-1331
Missense_Mutation	SNP	T	T	novel	none	TCGA-04-1331
Silent	SNP	A	A	G	novel	TCGA-04-1331
Missense_Mutation	SNP	G	G	A	novel	TCGA-04-1331
Missense_Mutation	SNP	G	G	T	novel	TCGA-04-1331
Missense_Mutation	SNP	A	A	C	novel	TCGA-04-1331
Missense_Mutation	SNP	A	A	T	novel	TCGA-04-1331
Missense_Mutation	SNP	G	G	A	novel	TCGA-04-1331
Missense_Mutation	SNP	C	C	A	novel	TCGA-04-1331

Matched_No	Match_Norm	Match_Norm	Tumor_Valid	Tumor_Valid	Match_Norm	Match_Norm	Verification	Validation_S	Mutation_Si	Sequencing	Sequence_Si	Validation_M	Score	BAM_File	Sequencer
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x
TCGA-04-1331-10A-01W	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	x	x	x

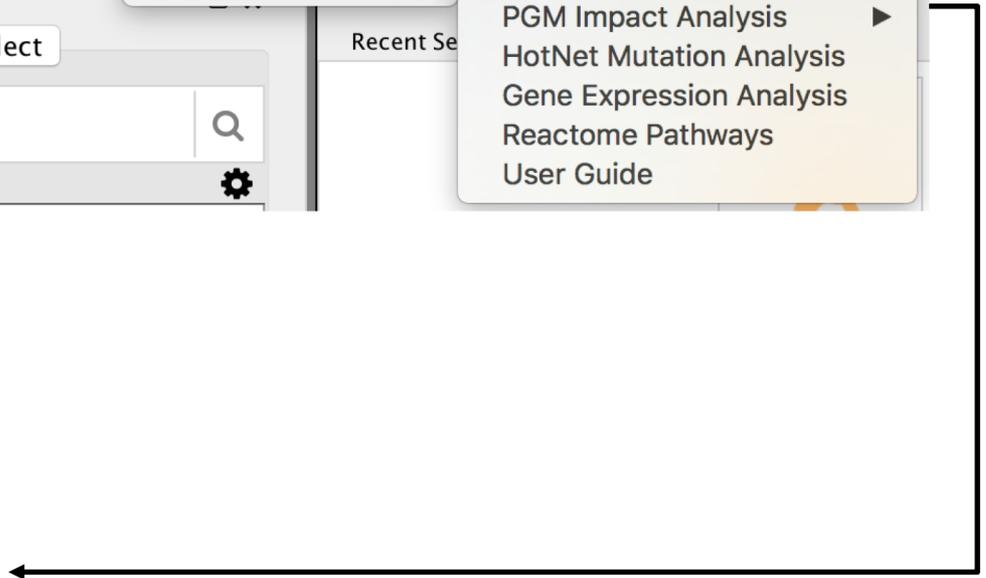
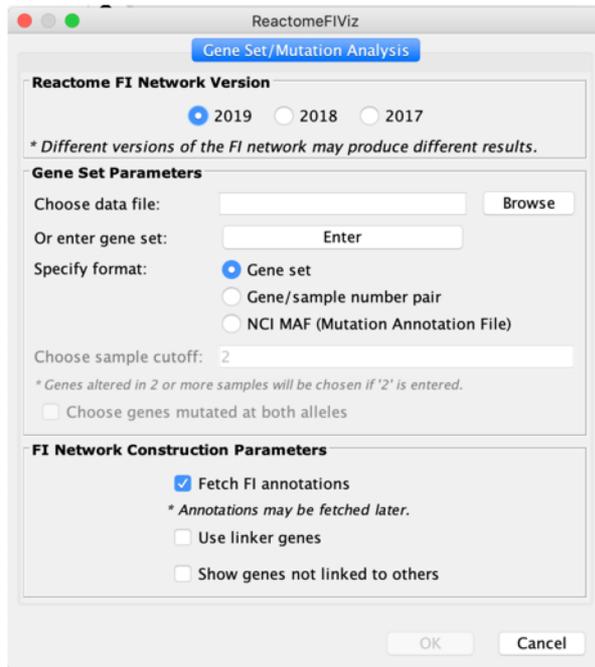
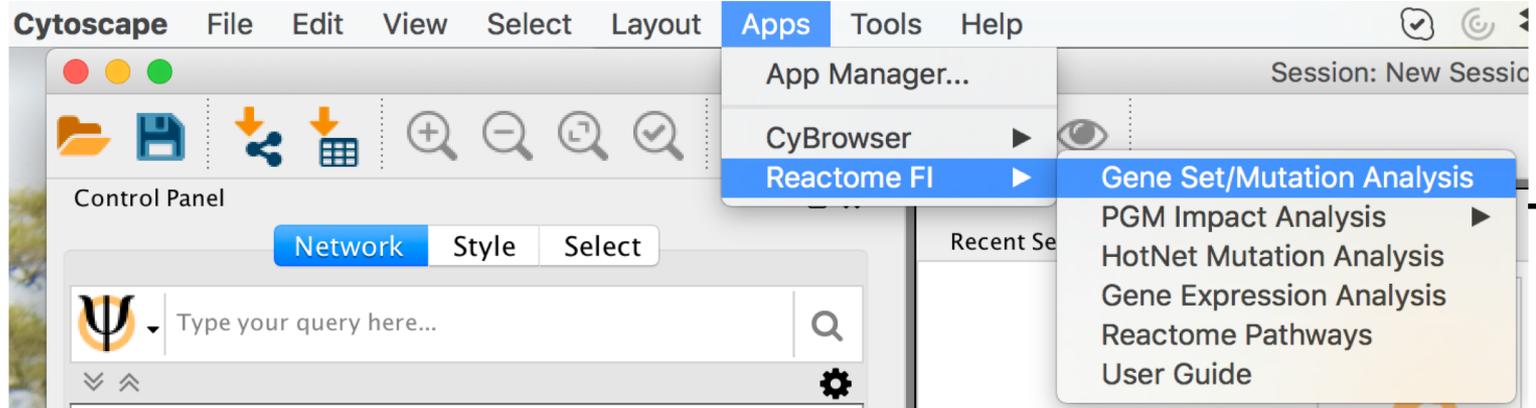
Gene/Sample Number Pairs

Gene	Sample_Number	Samples
IFT88	1	TCGA-10-0937
TACC2	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	1	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
FERM1T3	1	TCGA-24-1464
ZCCHC2	1	TCGA-61-1998
DDX18	1	TCGA-13-1509
TGM1	2	TCGA-24-0975;TCGA-25-1321
SAMD7	1	TCGA-09-2051
OR2F2	3	TCGA-13-0723;TCGA-24-2267;TCGA-25-2392
ZSWIM3	2	TCGA-24-1466;TCGA-23-1118
EIF2AK2	1	TCGA-59-2355;TCGA-24-1463
KIAA2018	4	TCGA-23-1024;TCGA-04-1367;TCGA-24-2288;TCGA-24-2289
.....		

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	0.106486375	0.40767808
KIF9	0.349692236	-0.093947168	-0.568902295	0.177455762	-0.307937394	-0.574121582	-0.772454492	0.850743799	0.13983291
CFP3	0.628848678	-0.519774777	0.200101088	-0.388882856	-0.094393584	0.549118111	0.44005971	-0.247094525	1.421708617
TACC2	0.985299156	-0.732555355	1.013646591	-0.057886422	0.730172249	0.554418157	1.280112472	0.463706367	0.956951722
C14orf132	1.249528811	0.104876045	0.524096007	-0.43464182	-1.528259113	-0.467450338	-0.715336925	-0.525776594	-1.06893985
RTN3	0.10643433	-0.286920286	-0.329065423	0.548958273	1.054699921	-0.827782882	-0.462525025	1.398885214	-0.588960437
PODXL2	-0.031430138	-0.390413822	-0.075387324	-0.412392415	0.085789024	-0.097365917	-0.053408711	-0.104692114	1.43380939
CORO1A	-0.247037235	0.664838693	-0.423713196	-0.001970579	0.488162732	-0.435111645	0.596447999	-0.463607768	0.055021666
RBM17	-0.360070659	-0.142165087	-0.233914802	0.018396914	-0.130696373	-0.394476802	-0.818819233	-0.692663375	0.993237633
WTF1	-0.768498156	-0.669419285	-0.763866504	-0.674252401	-0.618671571	-0.393931693	-0.906241952	-0.35285021	-0.538925163
SULF1	-0.863622291	1.588947769	0.272263522	-0.419487008	0.401966747	-0.081472544	-1.17805435	0.372891933	-0.21903657
SYCP2	-0.365259803	1.246319117	-0.107066702	0.891658263	0.914356558	0.091543376	-1.037696782	0.727095627	0.009262058
PHYH	-0.252934465	-0.340129465	0.084219531	-0.61340462	-1.85732245	0.479503528	0.22954453	-1.130697457	0.103755123
RCBTB2	-1.216044791	1.137367735	-0.741461062	0.636779988	-0.695953625	-0.46841374	-0.344892088	-1.130354482	-0.572431973
TOP2B	1.329376011	1.272684609	0.636481097	0.611284918	0.466406891	0.982928554	-0.749308731	0.397117399	0.050669942
SEC22B	-0.712050988	0.661526326	-0.33943161	0.917245507	0.427725933	0.413113408	-0.638988365	0.632301277	0.486176031
ATP9A	1.547427859	0.44411328	1.415509578	-0.14352465	0.540051896	0.510070468	-0.23468993	-0.149520936	-0.047584083
GFBR1	-0.782212802	-0.264862477	-0.123008356	0.027190136	-0.239829397	0.427719409	-0.773868442	0.110633726	1.270499777
NUDT5	-0.616643202	-0.117594702	0.072831699	-0.025664715	-0.37488737	0.433985219	-0.89899559	0.020300278	0.112230265
VT118	1.252187159	0.515526231	0.073529674	0.770902019	-0.368466883	-1.684634408	0.191395423	0.967344934	0.116535981
RP6KB1	-0.387163384	0.639591396	-0.597648114	-0.392297158	0.932216509	1.563670699	-0.782463975	0.465043084	-0.674654723
RAPGF4	0.202545341	0.240920292	0.106607966	1.564856103	0.557513638	-0.061297345	-0.651297319	-0.612922368	-1.178952896
PRO1596	-0.010044297	0.228155239	0.228155239	0.445509484	0.148635994	0.079718194	-0.376195587	1.138032748	0.03730761
KCNB1	0.093447081	-0.061401218	1.139678435	0.628377569	0.656531805	1.458927537	1.318159636	-0.469637643	0.346833207
LDH9A1	0.702468807	-0.111692273	0.963720452	-1.181038168	-1.08384907	1.698904754	1.844724649	-0.038782325	-1.545587905
ZCCHC2	0.53864339	0.120590563	0.845270548	-0.479704052	0.477522496	-1.144895382	-0.39831358	0.53235333	-0.095731821
KIIS1274	-0.291416641	-0.264217345	0.134705668	-0.527143876	-0.073822271	-0.699406086	-0.971399049	-0.218885185	-0.146353728
DDX18	0.34967191	0.294984327	-1.00840307	1.015037505	0.140036175	0.076233995	-0.160745532	0.51373466	1.069725088

Gene Set-based Analysis



FI Results Display

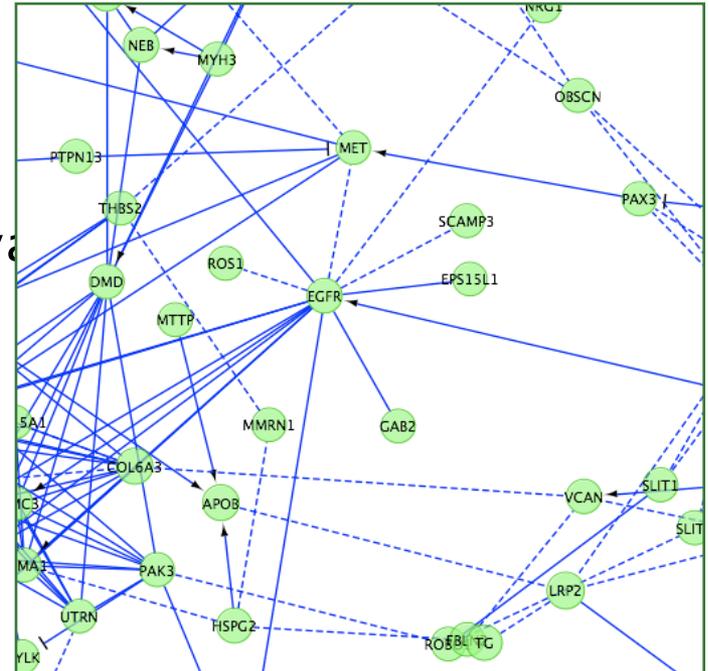
The screenshot displays a software interface for network visualization. The main window, titled 'LAC_genelist.txt', shows a dense network graph with numerous green circular nodes and black edges. A context menu is open over a node, listing options: Add, Delete, Edit, Select, Group, Apps, and Preferences. The 'Apps' option is selected, showing a sub-menu with 'Reactome FI' highlighted. Other options in the sub-menu include 'Fetch FI Annotations', 'Analyze Network Functions', 'Cluster FI Network', 'Analyze Module Functions', and 'Load Cancer Gene Index'. The interface also includes a 'Control Panel' on the left with 'Network', 'Style', and 'Select' tabs, and a 'Table Panel' at the bottom with a table of node data.

shared name	name	module	commonName	nodeToolTip	nodeLabel	nodeType
ACTB	ACTB		ACTB	ACTB	ACTB	Gene
ITGAV	ITGAV		ITGAV	ITGAV	ITGAV	Gene
RAD21	RAD21		RAD21	RAD21	RAD21	Gene
YAP1	YAP1		YAP1	YAP1	YAP1	Gene
JUN	JUN		JUN	JUN	JUN	Gene
MAP2K7	MAP2K7		MAP2K7	MAP2K7	MAP2K7	Gene
FOS	FOS		FOS	FOS	FOS	Gene
UBC	UBC		UBC	UBC	UBC	Gene
USF1	USF1		USF1	USF1	USF1	Gene

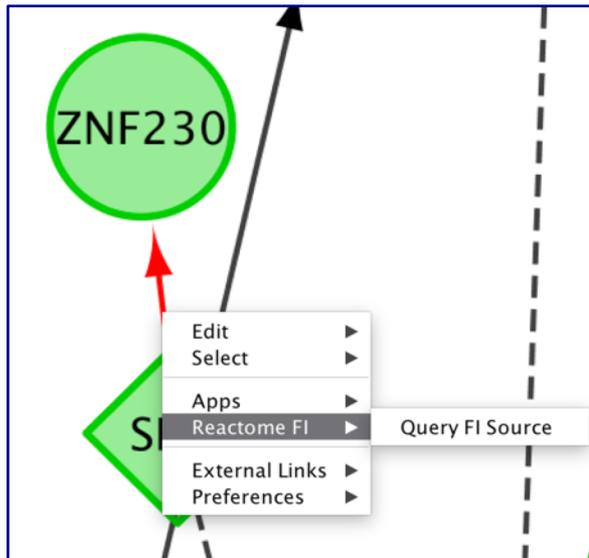
- Constructed network is displayed in the Network View panel using an FI specific visual style

FI Annotations

- Provides detailed information on selected FIs.
- Three edge attributes are created:
 - FI Annotation.
 - FI Direction.
 - FI Score (for predicted FI).
- Edges display direction attribute via
 - --> for activating/catalyzing.
 - --| for inhibition.
 - solid line for complexes or inputs.
 - --- for predicted FIs.



Query FI Source



Annotated FIs

Interaction Info
Interaction: SIX5 - ZNF230

Reactome Sources

Reactome ID	Type	Data Source
6951674	TARGETED_INTERAC	ENCODE

View Reactome Source

Reactome Instance View

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

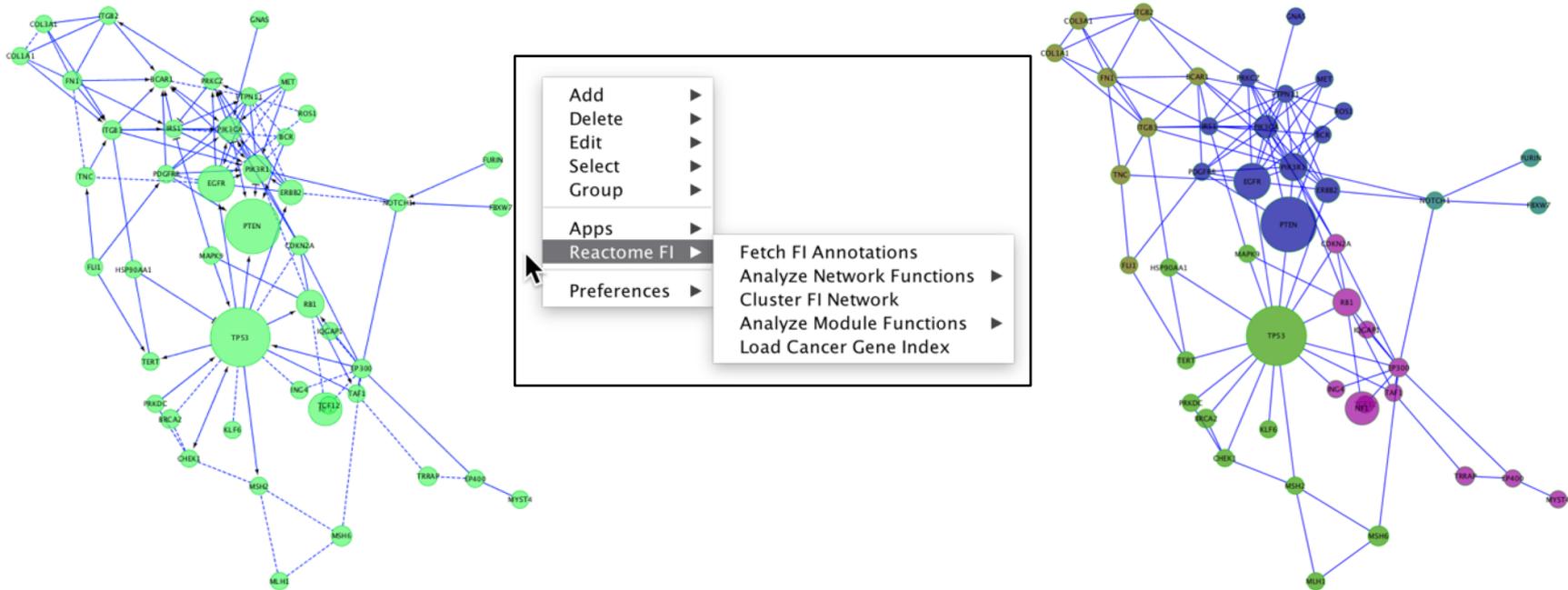
Interaction Info
Interaction: SNX4 - SNX6

Support Evidence

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

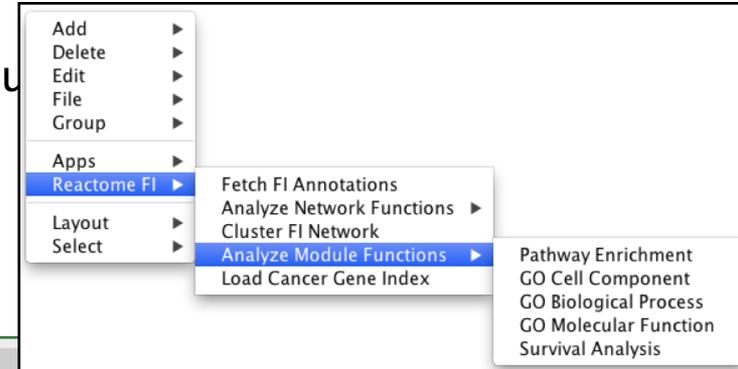
Cluster FI Network

- Runs spectral partition based network clustering ([Newman, 2006](#)) on the displayed FI network.
- Nodes in different network modules will be shown in different colours (max 15 colours).
- Analyze cancer mutation data with HotNet algorithm ([Vandin, 2012](#))



Analyze Module Functions

- Pathway or GO term enrichment analysis on individual network modules.
 - Use filter to remove small network modules
 - Filter by FDR



Data Panel

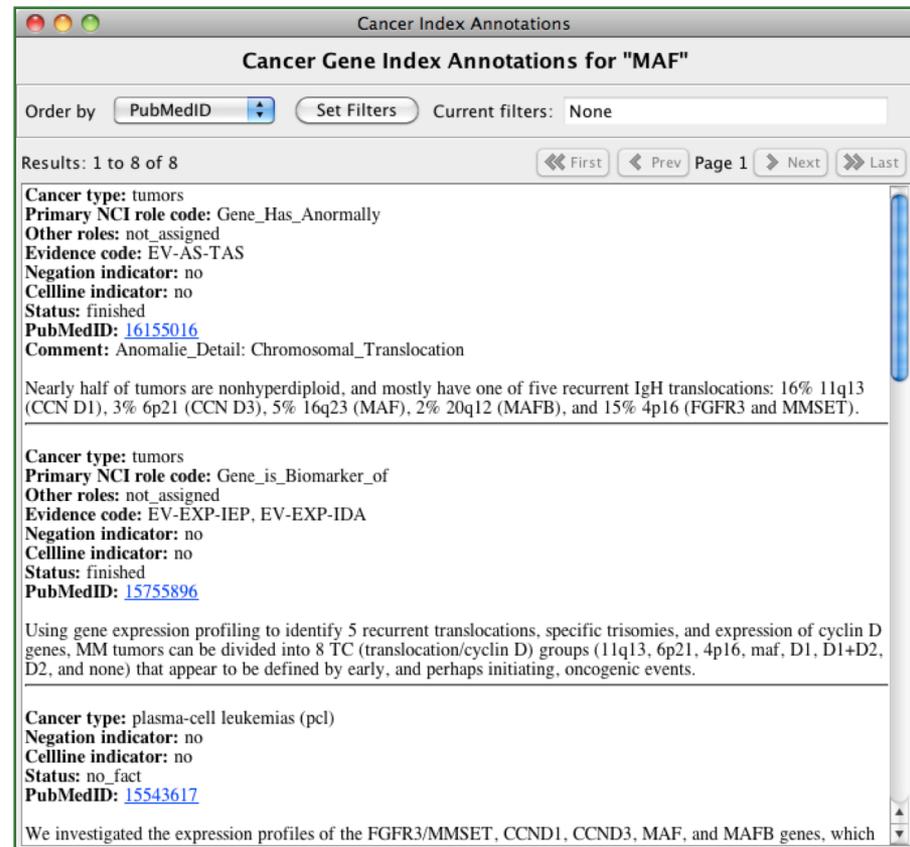
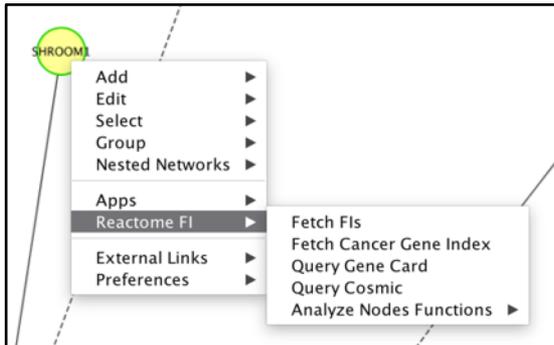
Hide nodes in not selected rows Apply Filters: FDR 0.01 Module Size 10

Module	GeneSet	RatioOfProteinIn	NumberOfProteinCe	Protein	mModule	P	FDR	Nodes
0	Translation(R)	0.0158	0.0010					
0	Influenza Life Cycle(R)	0.0249	0.0050					RPL18,RPL17,RPL36...
0	Ribosome(K)	0.0117	✓ 0.01					RPL18,RPL17,RPL36...
0	Metabolism of protei...	0.0267	0.05					RPL18,RPL17,RPL36...
1	M Phase(R)	0.0128	0.25	119	64	0.0000	<2.50e-04	ITGB3BP,MAD1L1,CC...
1	Aurora B signaling(N)	0.0052	0.5	187	60	0.0000	<5.00e-04	AURKC,AURKB,CDCA...
1	Signaling by Aurora k...	0.0125	1.0	88	38	0.0000	<3.33e-04	AURKC,AURKB,CDCA...
2	Glucose Regulation of...	0.0197	148	16	0.0000	<1.67e-04	<1.67e-04	NDUFB4,NDUFA2,ND...
2	Parkinson's disease(K)	0.0176	132	15	0.0000	<1.67e-04	<1.67e-04	NDUFB4,NDUFA2,ND...
2	Alzheimer's disease(K)	0.0223	168	15	0.0000	<1.67e-04	<1.67e-04	NDUFB4,NDUFA2,ND...
2	Huntington's disease(K)	0.0246	185	15	0.0000	<1.67e-04	<1.67e-04	NDUFB4,NDUFA2,ND...
2	Oxidative phosphoryl...	0.0178	134	15	0.0000	<1.67e-04	<1.67e-04	NDUFB4,NDUFA2,ND...
2	Electron Transport C...	0.0101	76	16	0.0000	<1.67e-04	<1.67e-04	NDUFB4,NDUFA2,ND...
2	Metabolic pathways(K)	0.1489	1120	16	0.0000	<1.43e-04	<1.43e-04	NDUFB4,NDUFA2,ND...
3	Antigen processing a...	0.0104	78	9	0.0000	<1.00e-03	<1.00e-03	KLRC2,KIR2DS1,HLA...
3	Immunoregulatory int...	0.0153	115	8	0.0000	<5.00e-04	<5.00e-04	KIR2DS1,HLA-B,HLA...
3	Natural killer cell me...	0.0182	137	7	0.0000	<3.33e-04	<3.33e-04	KLRC2,KIR2DS1,HLA...

Node Attribute Browser Edge Attribute Browser Network Attribute Browser MCL Module Browser Pathways in Modules

NCI Cancer Gene Index

- View detailed annotations for the selected gene or protein.
- Annotations are sortable by PubMed ID, Cancer type, status, and other criteria.



Cancer Index Annotations

Cancer Gene Index Annotations for "MAF"

Order by PubMedID Set Filters Current filters: None

Results: 1 to 8 of 8

« First < Prev Page 1 > Next » Last

Cancer type: tumors
Primary NCI role code: Gene_Has_Anormally
Other roles: not_assigned
Evidence code: EV-AS-TAS
Negation indicator: no
Cellline indicator: no
Status: finished
PubMedID: [16155016](#)
Comment: Anomalie_Detail: Chromosomal_Translocation

Nearly half of tumors are nonhyperdiploid, and mostly have one of five recurrent IgH translocations: 16% 11q13 (CCN D1), 3% 6p21 (CCN D3), 5% 16q23 (MAF), 2% 20q12 (MAFB), and 15% 4p16 (FGFR3 and MMSET).

Cancer type: tumors
Primary NCI role code: Gene_is_Biomarker_of
Other roles: not_assigned
Evidence code: EV-EXP-IEP, EV-EXP-IDA
Negation indicator: no
Cellline indicator: no
Status: finished
PubMedID: [15755896](#)

Using gene expression profiling to identify 5 recurrent translocations, specific trisomies, and expression of cyclin D genes, MM tumors can be divided into 8 TC (translocation/cyclin D) groups (11q13, 6p21, 4p16, maf, D1, D1+D2, D2, and none) that appear to be defined by early, and perhaps initiating, oncogenic events.

Cancer type: plasma-cell leukemias (pcl)
Negation indicator: no
Cellline indicator: no
Status: no_fact
PubMedID: [15543617](#)

We investigated the expression profiles of the FGFR3/MMSET, CCND1, CCND3, MAF, and MAFB genes, which

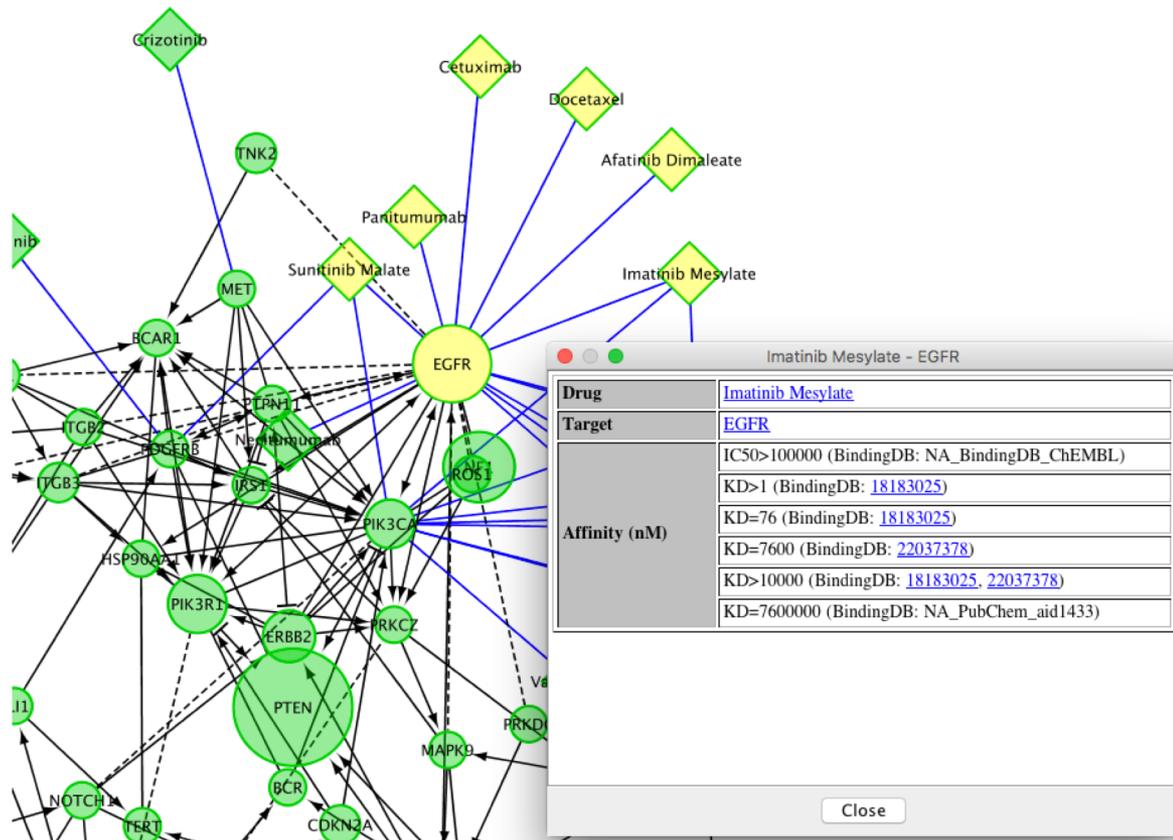
Overlay Cancer Gene Index

- 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.

The screenshot displays the VizMapper software interface. On the left is the 'Control Panel' with a 'Disease Hierarchy' tree. The tree is expanded to 'Papillary_Breast_Neoplasm'. The main window shows a network diagram with nodes representing genes and edges representing interactions. A context menu is open over a node, showing options like 'Add', 'Edit', 'Select', 'Group', 'Nested Networks', 'Apps', 'Reactome FI', 'External Links', and 'Preferences'. The 'Reactome FI' option is highlighted, and a sub-menu is visible with options: 'Fetch Fis', 'Fetch Cancer Gene Index', 'Query Gene Card', 'Query Cosmic', and 'Analyze Nodes Functions'. At the bottom is the 'Table Panel' with a table of gene sets.

Module	GeneSet	RatioOfProteinIn...	NumberOfProtei...	ProteinFromMod...	P-value	FDR	Nodes
0	Bladder cancer(K)	0.0038	38	2	0.0063	2.026e-01	E2F3,CDKN2A
0	Lysosome(K)	0.0123	122	3	0.0065	1.906e-01	ARSG,NEU1,SCA...
0	HTLV-1 infection...	0.0262	260	4	0.0084	2.256e-01	E2F3,CDKN2A,...
0	Validated trans...	0.0049	49	2	0.0103	2.498e-01	PMAIP1,CDKN2A
1	Focal adhesion(K)	0.0208	206	8	0.0000	<1.000e-03	TLN2,TNC,BCA...
1	Integrins in angi...	0.0047	47	4	0.0000	4.000e-03	BCAR1,PTK2B,I...
1	Type II diabetes...	0.0048	48	4	0.0000	2.667e-03	KCNJ11,PRKCE,...
1	Signaling by EG...	0.0172	171	6	0.0000	3.000e-03	FGF9,LRIG1,SPR...
1	Endothelins(NI)	0.0063	62	4	0.0001	4.400e-03	BCAR1,PTK2B,P...

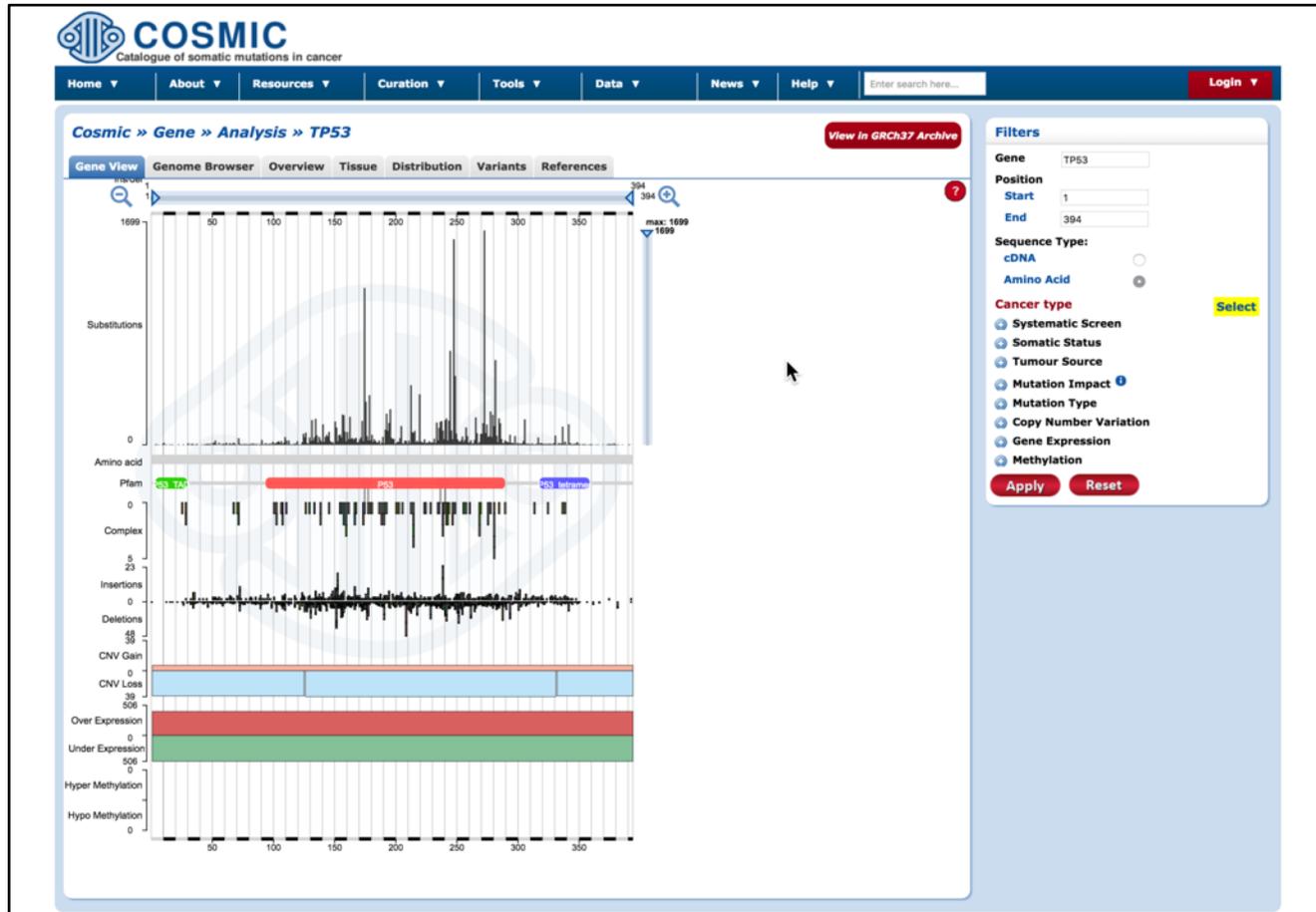
Visualize Cancer Targetome in the Reactome FI Network



TCGA GBM Mutation Profile

COSMIC

- View detailed variant annotations for the selected gene or protein from COSMIC database.



Module Based Survival Analysis

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

Results Panel

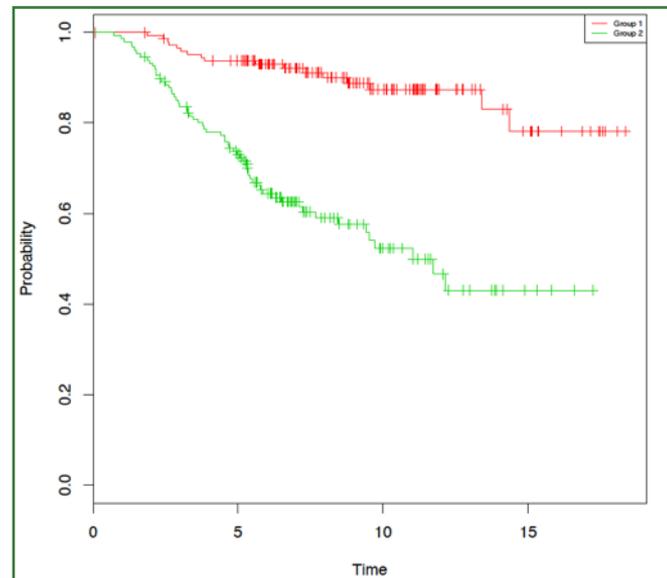
Survival Analysis

Analysis: Coxph (all modules)

----Output----

Note: Click underlined modules in blue for single module-based analysis. You may not see any underlined module if all p-values > 0.05.

Module	Coefficient	P-value
<u>0</u>	<u>-0.6142421</u>	<u>0.0015</u>
<u>1</u>	<u>1.308675</u>	<u>2.7e-10</u>
<u>2</u>	<u>0.4908374</u>	<u>0.015</u>
3	0.3854999	0.071
4	0.1916897	0.38
<u>5</u>	<u>1.015691</u>	<u>4.4e-07</u>
6	-0.06630745	0.71
7	-0.01376751	0.94
8	0.4978022	0.053
<u>9</u>	<u>0.948809</u>	<u>3.8e-06</u>
<u>10</u>	<u>0.6773846</u>	<u>0.024</u>
11	0.09736692	0.61
<u>12</u>	<u>-0.6155788</u>	<u>0.00033</u>



REACTOMEFIVIZ APP DEMO

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