IPA 系統生物學分析軟體暨資料庫

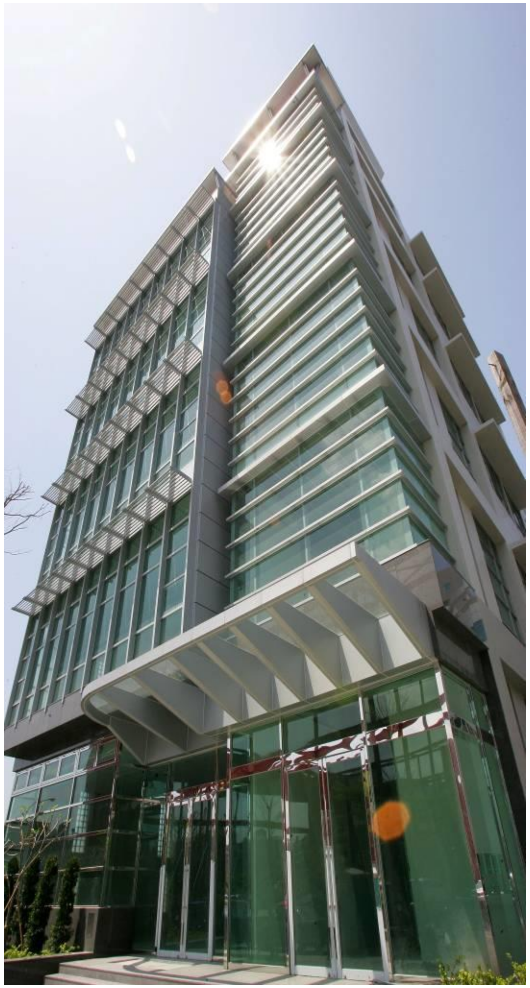
IPA以數據演算及人工閱讀的資料庫文獻，
提供您快速的在數千萬筆的研究分析資料中，
找到最關鍵的生物途徑與分子間調控關係。

Leo Hung 洪慈懋
創源生技 產品專員

Ingenuity **Pathway** Analysis

Office: 02-2795-1777#3014 E-mail: LeoHung@gga.asia

About GGA



GGA is part of the BIONET Group (訊聯生物科技)

CEO: Christopher Tsai, Ph.D. 蔡政憲 博士

Established: Nov. 2008

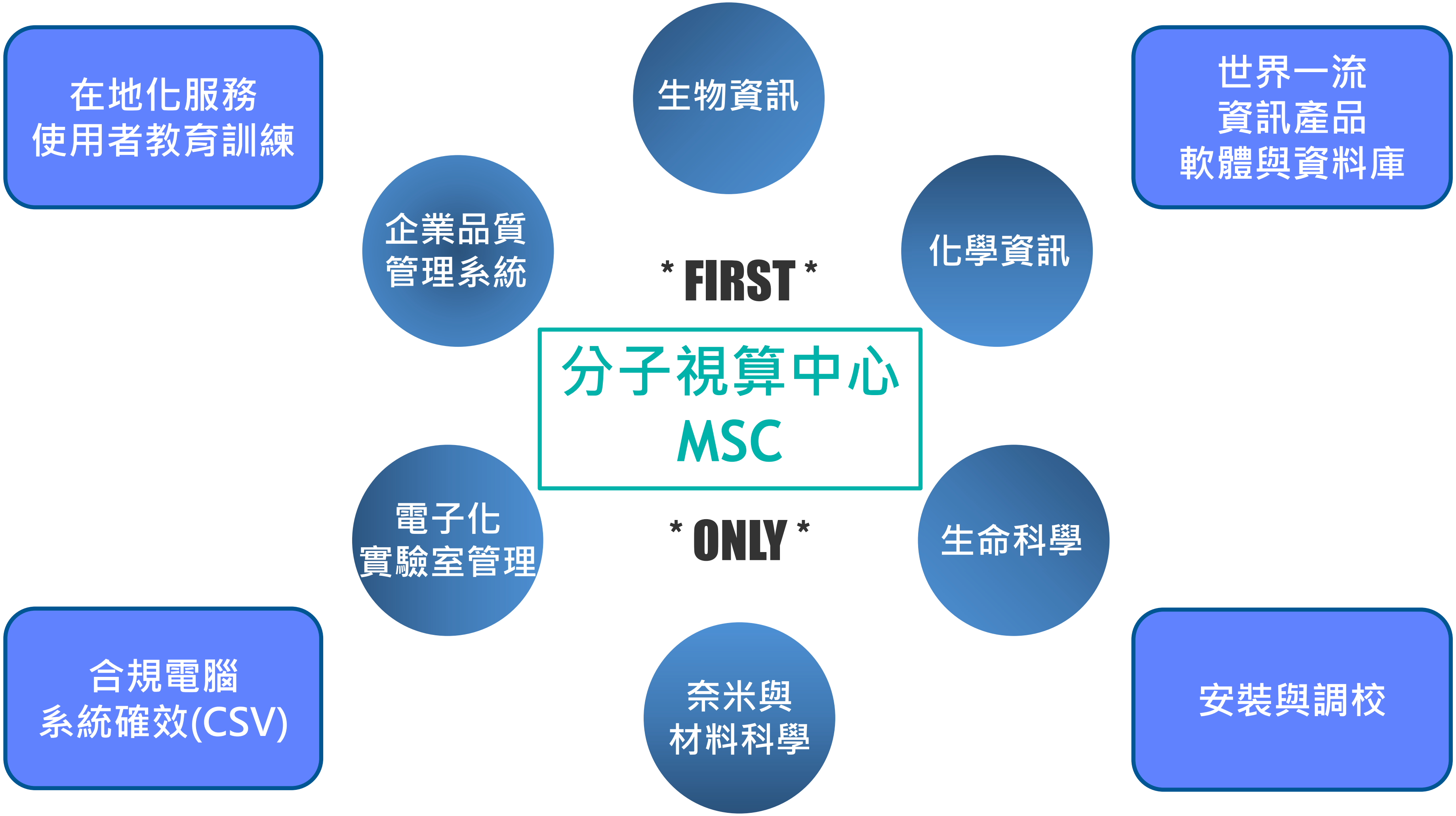
Main Product & Service Areas:

- Genetic Testing & Molecular Diagnosis
- **Scientific Informatics & Bio IT**

IPO Date: September 17, 2012

Stock Ticker: 4160 (Taiwan OTC)

Molecular Science Center in GGA



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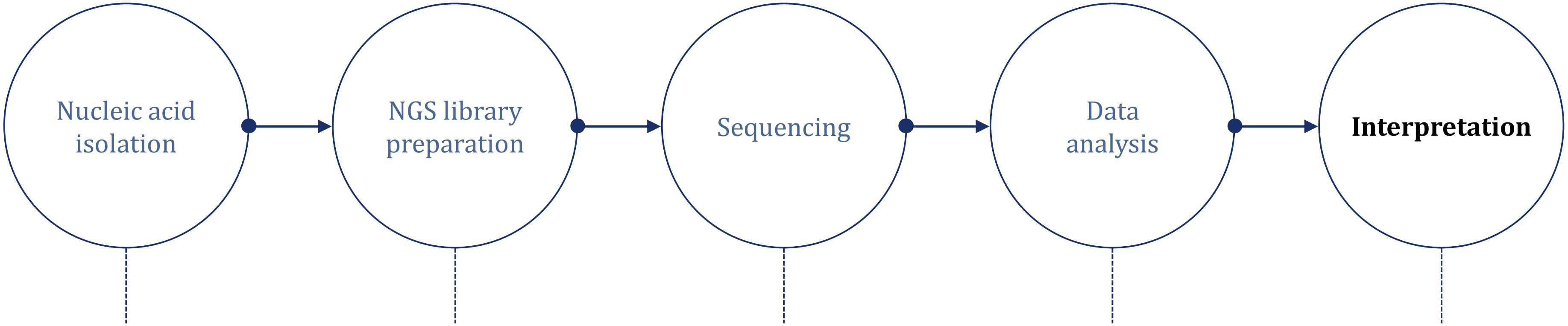
QIAGEN Bioinformatics Solution



Nucleic acid isolation

- QIAcube Connect
- QIAsymphony
- EZ1 Advanced XL

- QIAamp Kits
- RNeasy Kits
- miRNeasy Kits
- exoRNeasy Kits

NGS library preparation

- QIAseq RNA
- QIAseq DNA

Sequencing

- Illumina and Thermo Fisher sequencers

Data analysis

- QIAGEN OmicSoft Array Suite
- QIAGEN CLC Genomics Workbench
- QIAGEN Microbial Genomics Module
- QIAGEN CLC Main Workbench
- QIAGEN CLC Genome Finishing Module

Interpretation

- QIAGEN Ingenuity Pathway Analysis
- QIAGEN Ingenuity Variant Analysis
- HGMD
- QIAGEN OmicSoft Land Explorer
- QIAGEN OmicSoft DiseaseLand
- QIAGEN OmicSoft OncoLand
- QIAGEN OmicSoft GeneticsLand

QIAGEN BioX Product Portfolio

By NGS Data analysis workflow

1st Analysis

From NGS sequencers
Generate NGS reads sequences
*.fastq

2nd Analysis

Reads processing
QC check, Adapter Trimming
Mapping (Resequencing)
Variant call
RNA-seq analysis
Epigenetics analysis
Metagenomics analysis

CLC bio
A QIAGEN Company

3rd Analysis

Annotation interpretation
Variant analysis
Pathway analysis

BIOBASE
BIOLOGICAL DATABASES

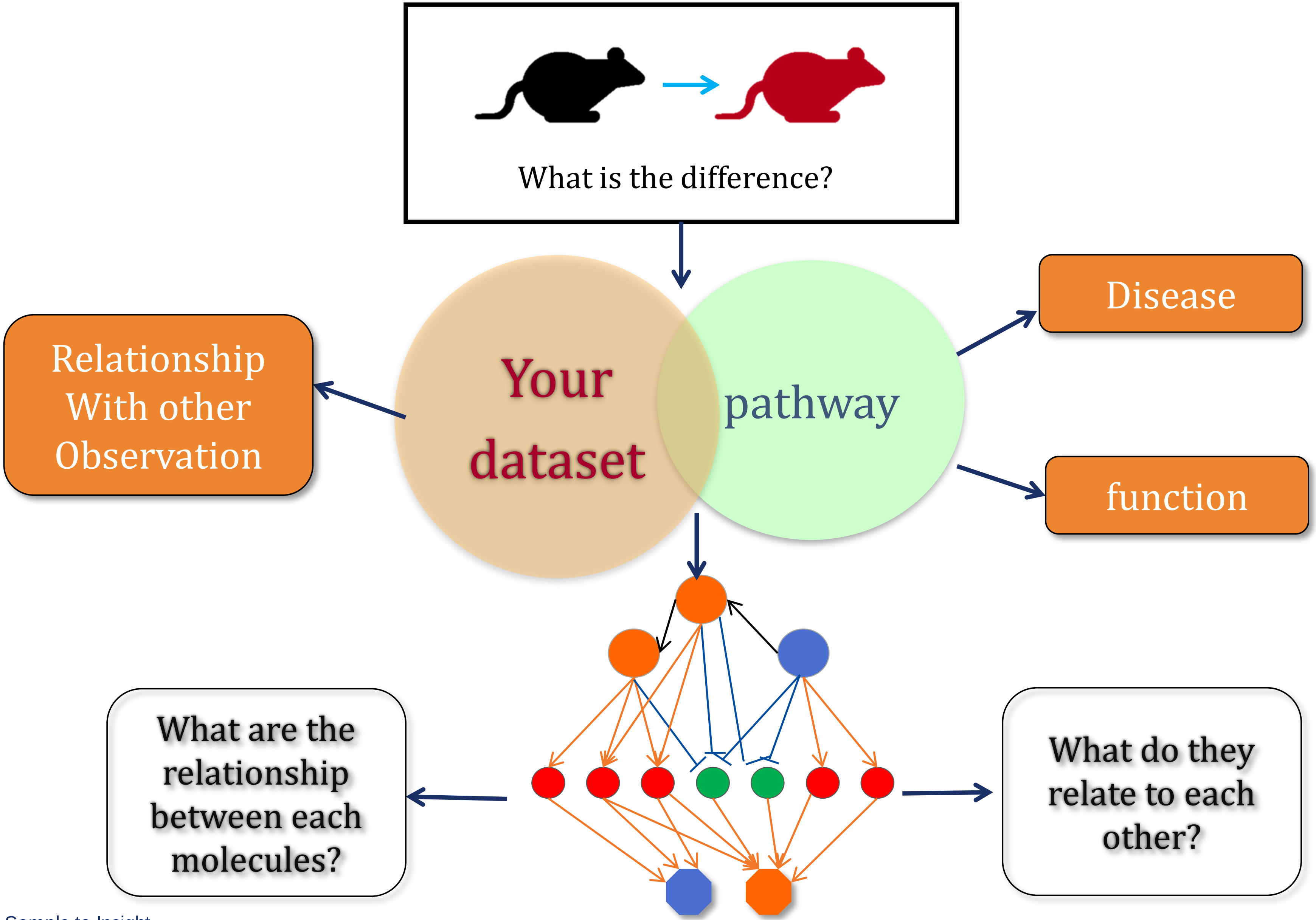
POWERED BY
INGENUITY

← OmicSoft Corporation →

QIAGEN Clinical Insight - Analyze (QCI-A / QCI-AU)

QCI-Interpret (QCI-I)

Why are we using IPA?



What is the difference?

Your dataset

pathway

Relationship With other Observation

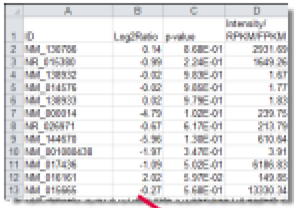
Disease

function

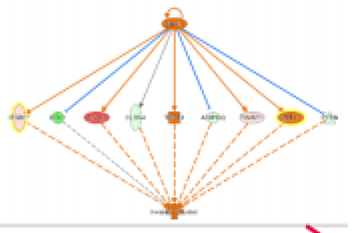
What are the relationship between each molecules?

What do they relate to each other?

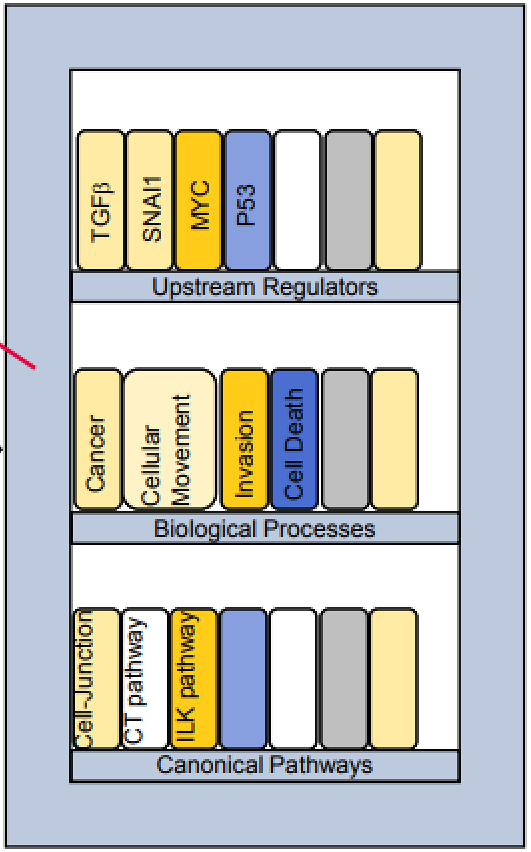
What can Qiagen bioinformatics products do for you?



	A	B	C	D
1	ID	Log2Ratio	p-value	Intensity/ RPKM/FPKM
2	NM_130786	0.14	8.68E-01	2931.69
3	NR_015380	-0.99	2.24E-01	1649.26
4	NM_138932	-0.02	9.83E-01	1.67
5	NM_014576	-0.02	9.88E-01	1.77
6	NM_138933	0.02	9.79E-01	1.83
7	NM_000014	-4.79	1.02E-01	239.75
8	NR_026971	-0.67	6.17E-01	213.79
9	NM_144670	-5.96	1.38E-01	610.84
10	NM_001080438	-1.97	3.47E-01	3.91
11	NM_017436	-1.09	5.02E-01	6186.83
12	NM_016161	2.02	5.97E-02	149.85
13	NM_015665	-0.27	5.68E-01	13330.34



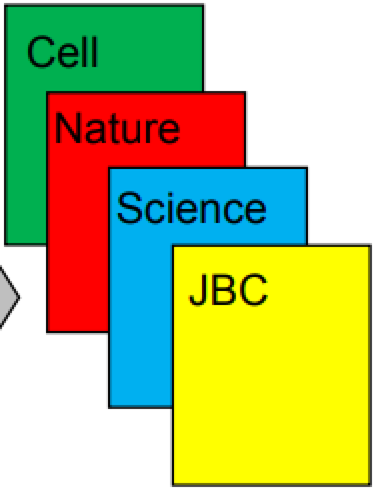
WorkBench
IPA
IVA/HGMD/QCI



TGFβ
SNAI1
MYC
P53
Upstream Regulators

Cancer
Cellular Movement
Invasion
Cell Death
Biological Processes

Cell-Junction
CT pathway
ILK pathway
Canonical Pathways



Cell
Nature
Science
JBC

IPA

IPA orthologous :

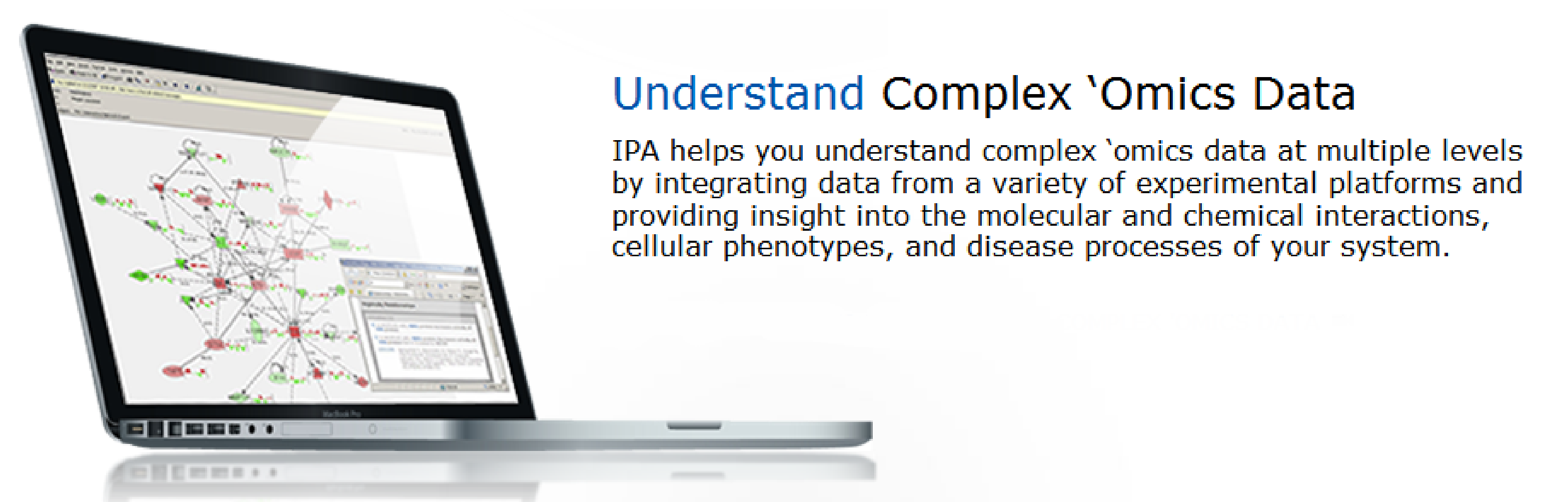
Arabidopsis thaliana
Bos taurus (bovine)
Caenorhabditis elegans
Gallus gallus (chicken)
Pan troglodytes (chimpanzee)
Danio rerio (zebrafish)
Canis lupus familiaris (canine)
Drosophila melanogaster
Macaca mulatta (Rhesus Monkey)
Saccharomyces cerevisiae
Schizosaccharomyces pombe

IPA supported platform :

- **Gene expression:**
  - qPCR analysis
  - Microarray
  - RNA-Seq (NGS)
  - microRNA
  - mRNA
- **Proteomics**
  - PhosphoProteomics New
- metabolomics

IPA application:

- Biomarker finding
- Toxicity Functions
- Diseases regulation



Understand Complex ‘Omics Data

IPA helps you understand complex ‘omics data at multiple levels by integrating data from a variety of experimental platforms and providing insight into the molecular and chemical interactions, cellular phenotypes, and disease processes of your system.

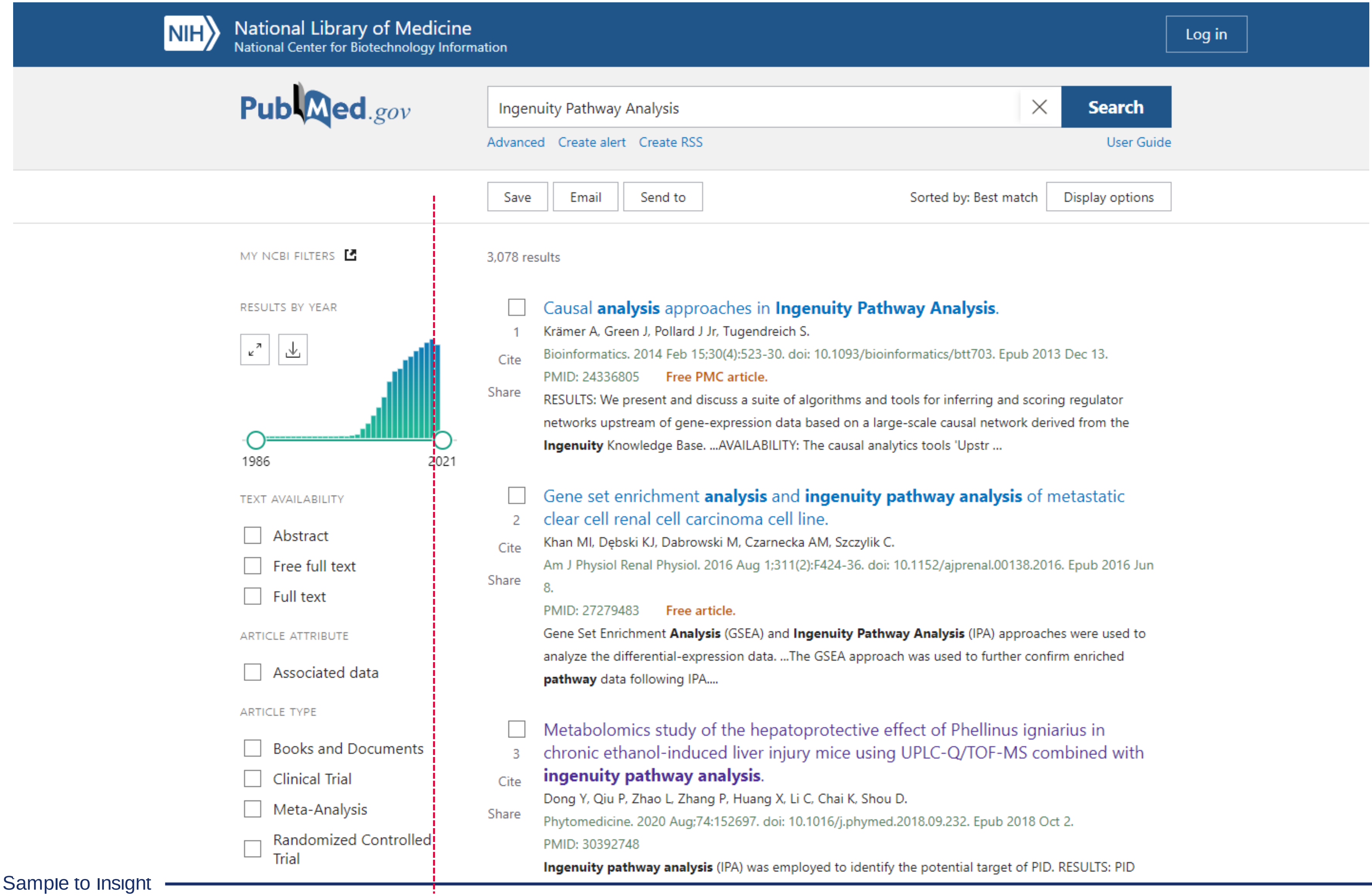
Supported Identifiers for Data Upload

Get more complete mapping during dataset upload!

Vendor IDs	Gene	Protein	Transcript	microRNA	SNP	Chemical
Affymetrix (na36)	Entrez Gene (2020/10)	GenPept	Ensembl (101)	miRBase (mature)	Affy SNP IDs	CAS Registry Number
Agilent	GenBank (239)	International Protein Index (IPI)	RefSeq (human、mouse)	miRBase (stemloop)	dbSNP	HMDB
Life Tech (ABI)	Symbol-human (HUGO/ HGNC, EG)	UniProt/ Swiss-Prot Accession (2020_03)	UCSC (hg18)			KEGG
Codelink	Symbol- mouse (EG)		UCSC (hg19)			PubChem CID
Illumina	Symbol- rat (EG)		UCSC (hg38)			
Ingenuity	GI Number					
	UniGene					

Peer-reviewed publications citing Ingenuity apps

>26,500 publications that used IPA and growing!   (Search Google Scholar for [publications that cite IPA]().)



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Ingenuity Pathway Analysis

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RESULTS BY YEAR

TEXT AVAILABILITY

☐ Abstract
☐ Free full text
☐ Full text

ARTICLE ATTRIBUTE

☐ Associated data

ARTICLE TYPE

☐ Books and Documents
☐ Clinical Trial
☐ Meta-Analysis
☐ Randomized Controlled Trial

3,078 results

☐ 1 Cite Share

Causal **analysis** approaches in **Ingenuity Pathway Analysis**.
Krämer A, Green J, Pollard J Jr, Tugendreich S.
Bioinformatics. 2014 Feb 15;30(4):523-30. doi: 10.1093/bioinformatics/btt703. Epub 2013 Dec 13.
PMID: 24336805   Free PMC article.
RESULTS: We present and discuss a suite of algorithms and tools for inferring and scoring regulator networks upstream of gene-expression data based on a large-scale causal network derived from the **Ingenuity** Knowledge Base. ...AVAILABILITY: The causal analytics tools 'Upstr ...

☐ 2 Cite Share

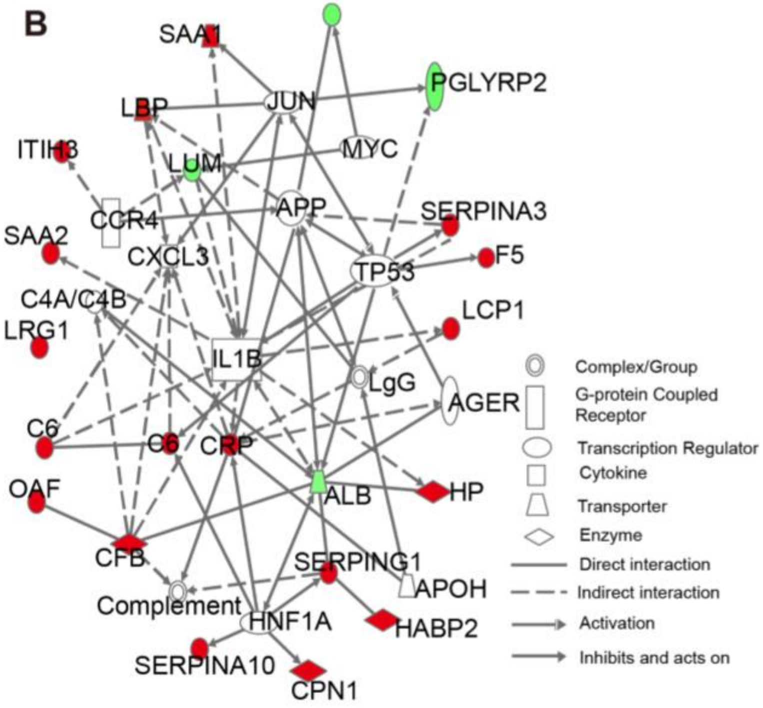
Gene set enrichment **analysis** and **ingenuity pathway analysis** of metastatic clear cell renal cell carcinoma cell line.
Khan MI, Dębski KJ, Dabrowski M, Czarnecka AM, Szczylik C.
Am J Physiol Renal Physiol. 2016 Aug 1;311(2):F424-36. doi: 10.1152/ajprenal.00138.2016. Epub 2016 Jun 8.
PMID: 27279483   Free article.
Gene Set Enrichment **Analysis** (GSEA) and **Ingenuity Pathway Analysis** (IPA) approaches were used to analyze the differential-expression data. ...The GSEA approach was used to further confirm enriched **pathway** data following IPA....

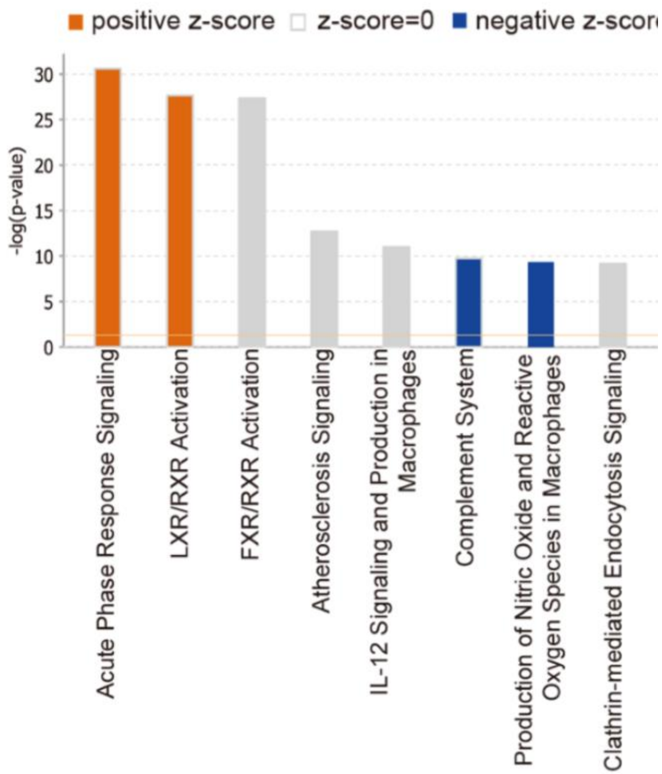
☐ 3 Cite Share

Metabolomics study of the hepatoprotective effect of Phellinus igniarius in chronic ethanol-induced liver injury mice using UPLC-Q/TOF-MS combined with **ingenuity pathway analysis**.
Dong Y, Qiu P, Zhao L, Zhang P, Huang X, Li C, Chai K, Shou D.
Phytomedicine. 2020 Aug;74:152697. doi: 10.1016/j.phymed.2018.09.232. Epub 2018 Oct 2.
PMID: 30392748
Ingenuity pathway analysis (IPA) was employed to identify the potential target of PID. RESULTS: PID

IPA was cited in paper to study severe COVID-19

Here is one latest paper submitted to medRxiv using IPA to identify potential protein and metabolite biomarkers in severe COVID-19 disease. In this study, IPA was used to identify most significantly relevant pathways and build regulation networks. It is welcome to share with your customers or distributor, and please let me know if you need further help.



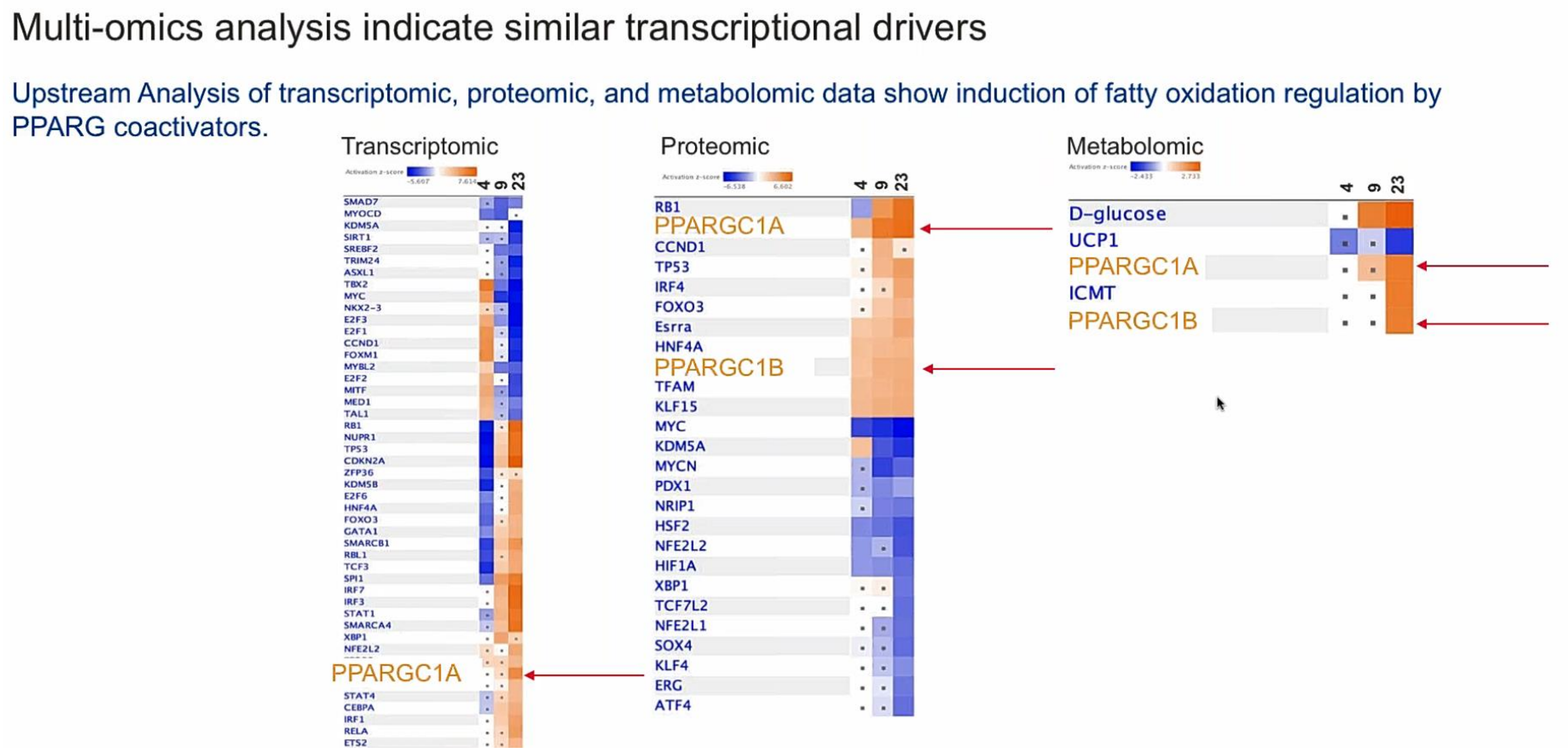


https://www.medrxiv.org/content/10.1101/2020.04.07.20054585v1

Multi-Omics Analysis using IPA

Integrate and compare genomics, transcriptomics, proteomics and metabolomics data to see the big picture on your focus research

Transcriptomics, proteomics and metabolic changes in the postnatal mouse heart identified by QIAGEN IPA and OmicSoft



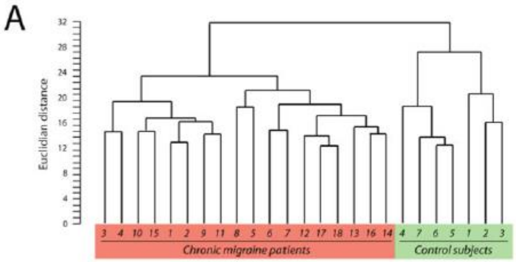
Multi-omics analysis indicate similar transcriptional drivers

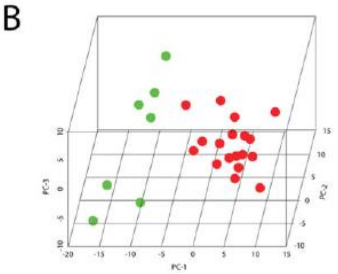
Upstream Analysis of transcriptomic, proteomic, and metabolomic data show induction of fatty oxidation regulation by PPARG coactivators.

https://register.gotowebinar.com/recording/viewRecording/6832529487394361868/7681254608252166657/clairtsai@gga.asia?registrantKey=4064096648078247692&type=ABSENTEEEMAILRECORDINGLINK

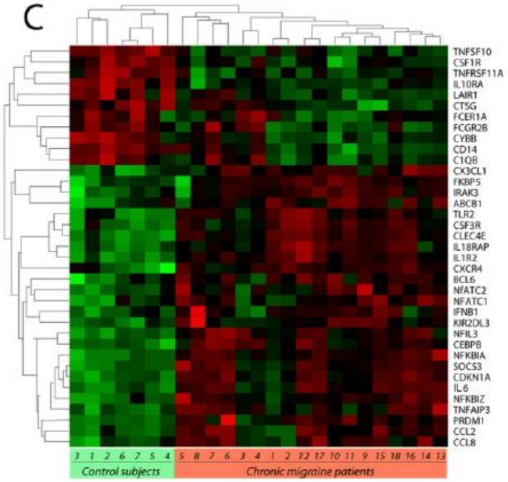
Using QIAGEN CLC & IPA to draw out your significant result.

Clustering patients by their expression profile (mRNA):

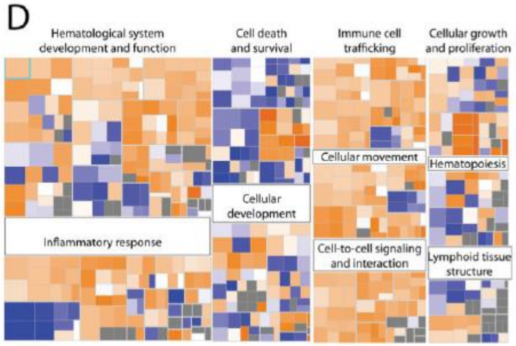




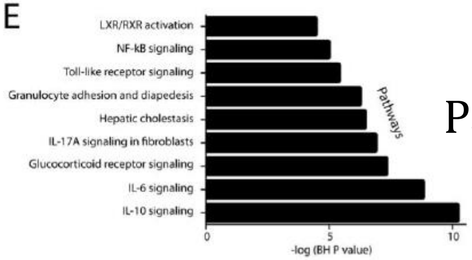
PCA analysis by miRNA profile in two groups



Identify significant mRNA in groups:



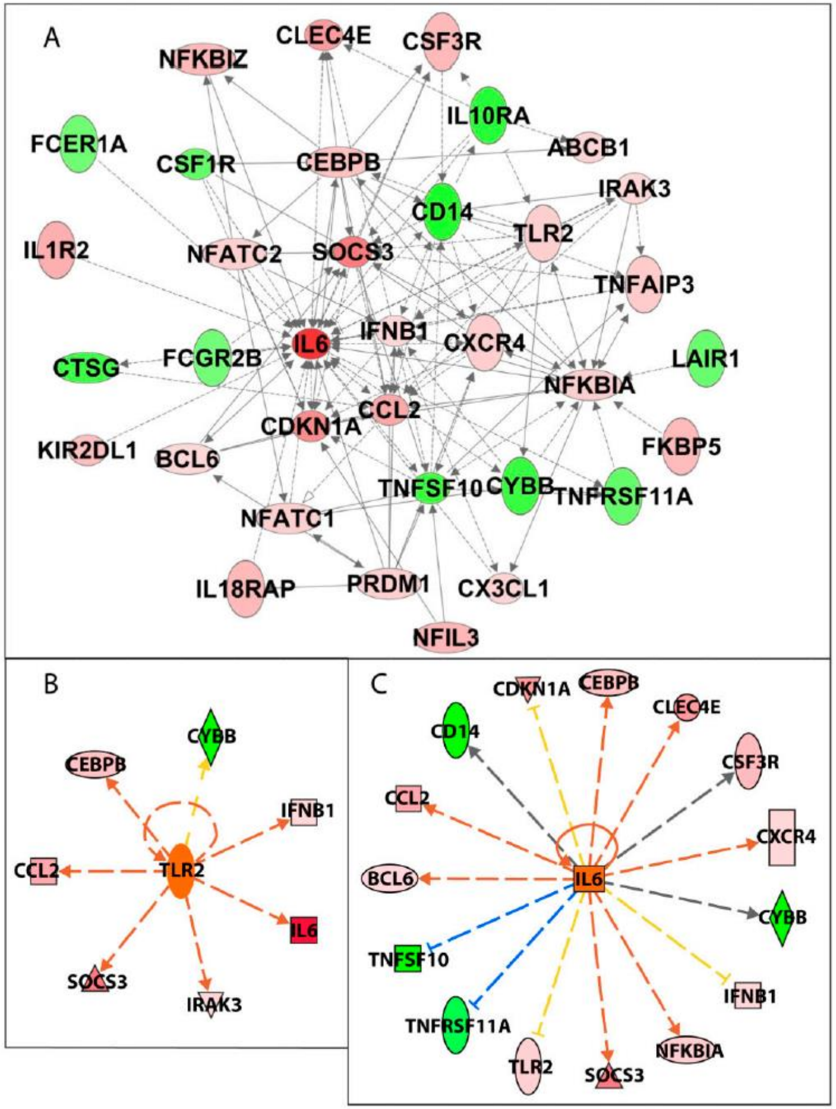
Functional enrichment analysis (IPA) by mRNAs which are regulated by miRNA



Pathway analysis (IPA)

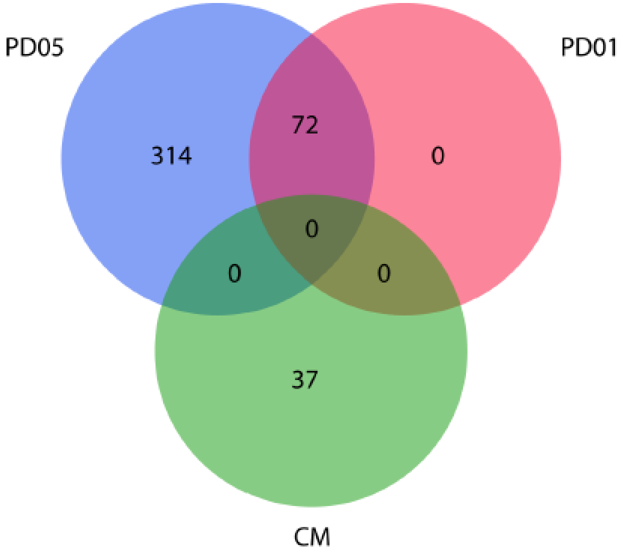
Upregulation of inflammatory gene transcripts in periosteum of chronic migraineurs: Implications for extracranial origin of headache

Using QIAGEN CLC & IPA to draw out your significant result.

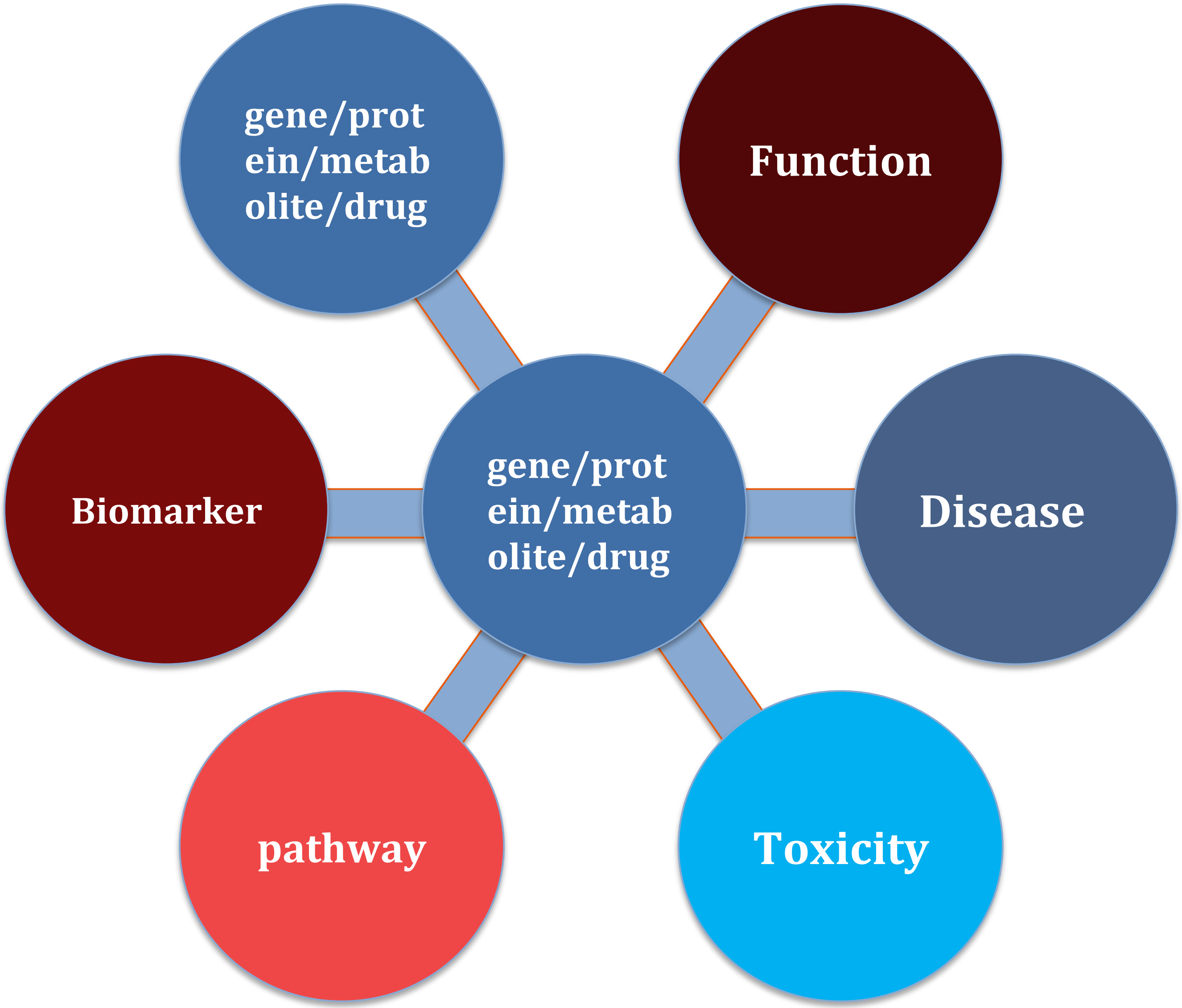


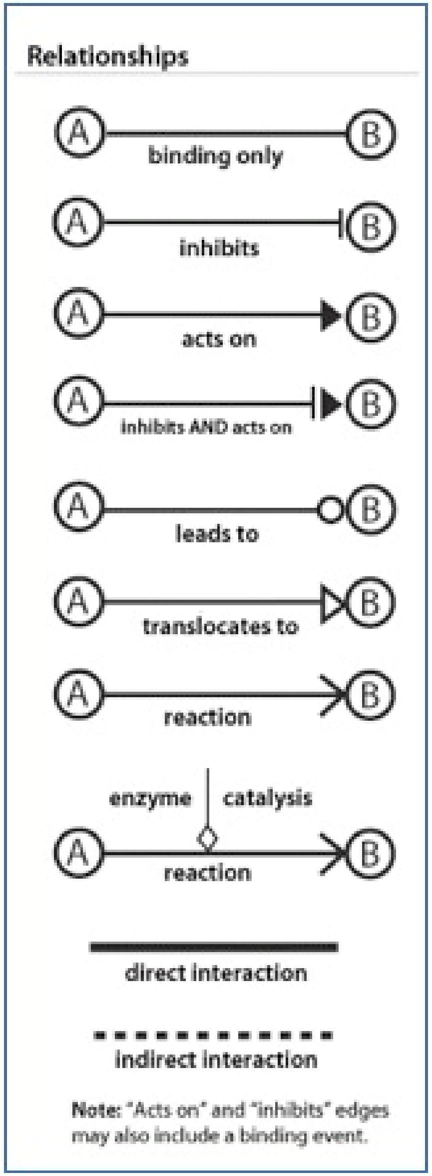
Interactive network (Pathway analysis) (IPA) by mRNAs which are regulated by miRNA

Venn diagram:可依據實驗設計來畫出overlapped 的 miRNA/mRNA/ pathway



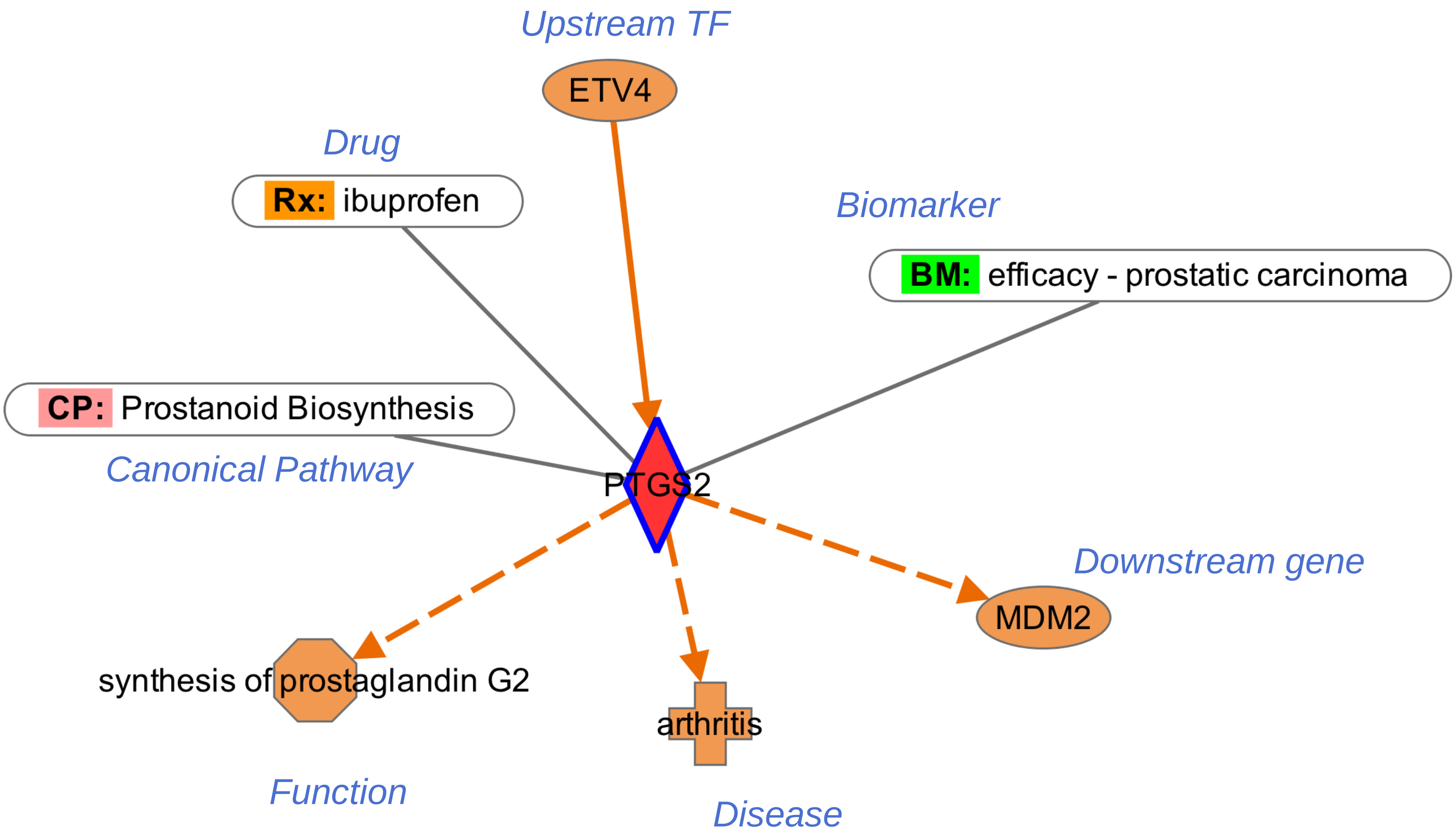
用IPA來發掘實驗資料中各類型關係





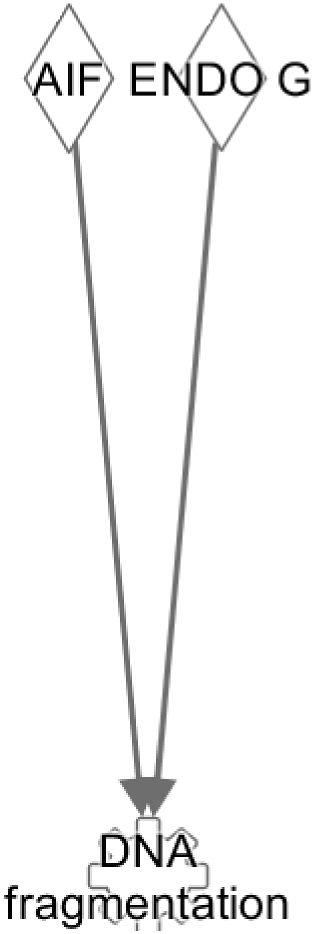
Note: "Acts on" and "inhibits" edges may also include a binding event.

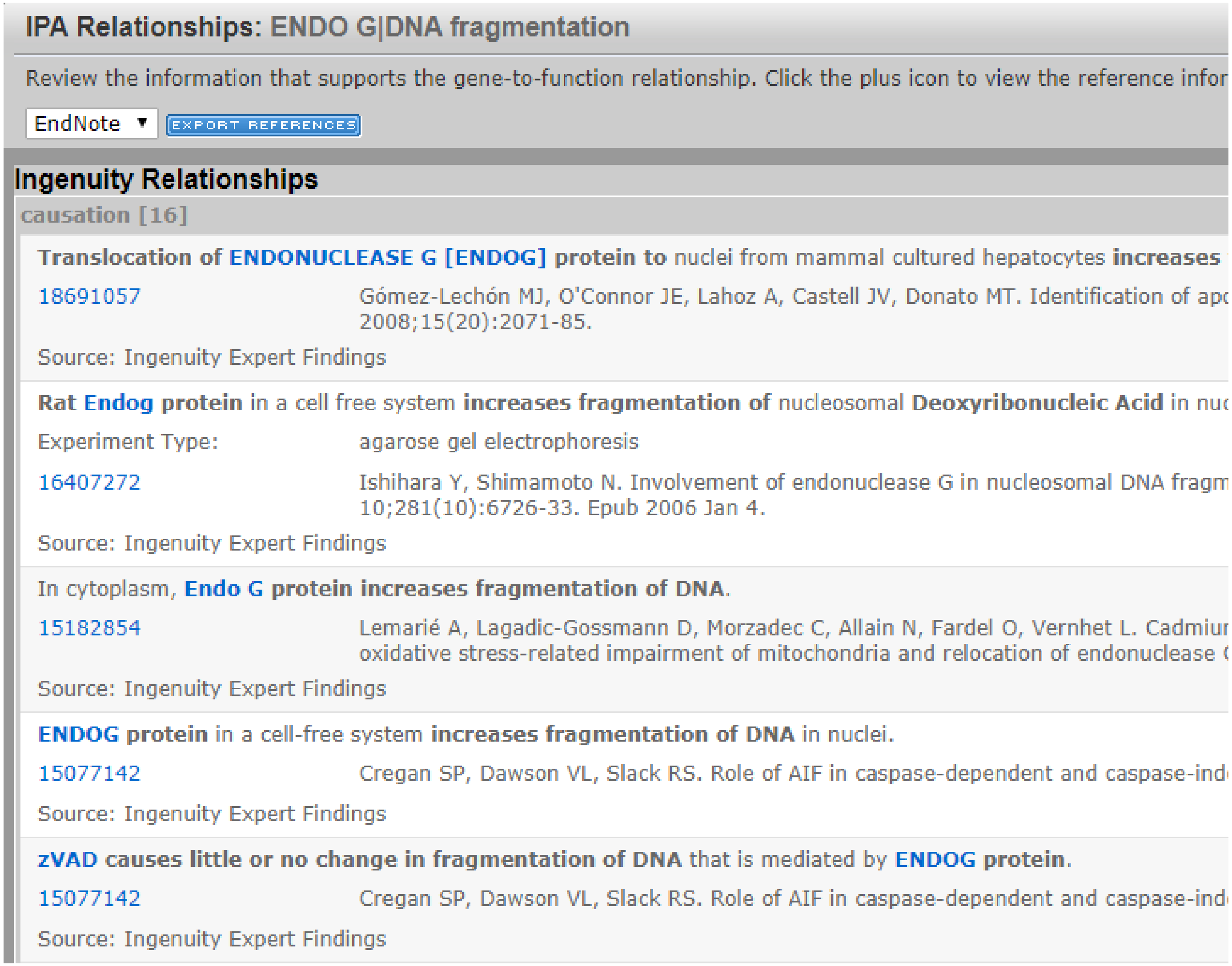
Capturing molecular information from the literature



Gather this type of information for nearly every gene. Inferences can be made from the resulting networks.

How IPA content is different: context and direction of effect





IPA Relationships: ENDO G|DNA fragmentation

Review the information that supports the gene-to-function relationship. Click the plus icon to view the reference infor

Ingenuity Relationships

causation [16]

Translocation of ENDONUCLEASE G [ENDOG] protein to nuclei from mammal cultured hepatocytes **increases**

18691057 Gómez-Lechón MJ, O'Connor JE, Lahoz A, Castell JV, Donato MT. Identification of apc
2008;15(20):2071-85.

Source: Ingenuity Expert Findings

Rat Endog protein in a cell free system **increases fragmentation of** nucleosomal **Deoxyribonucleic Acid** in nuc

Experiment Type: agarose gel electrophoresis

16407272 Ishihara Y, Shimamoto N. Involvement of endonuclease G in nucleosomal DNA fragm
10;281(10):6726-33. Epub 2006 Jan 4.

Source: Ingenuity Expert Findings

In cytoplasm, **Endo G protein increases fragmentation of DNA**.

15182854 Lemarié A, Lagadic-Gossmann D, Morzadec C, Allain N, Fardel O, Vernhet L. Cadmiur
oxidative stress-related impairment of mitochondria and relocation of endonuclease

Source: Ingenuity Expert Findings

ENDOG protein in a cell-free system **increases fragmentation of DNA** in nuclei.

15077142 Cregan SP, Dawson VL, Slack RS. Role of AIF in caspase-dependent and caspase-ind

Source: Ingenuity Expert Findings

zVAD causes little or no change in fragmentation of DNA that is mediated by **ENDOG protein**.

15077142 Cregan SP, Dawson VL, Slack RS. Role of AIF in caspase-dependent and caspase-ind

Source: Ingenuity Expert Findings

Third Party Database

☐ **Synonyms, Protein Family, Domains**
  - GO, Entrez Gene, Pfam

☐ **Tissue and Biofluid Expression & Location**
  - GNF, Plasma Proteome

☐ **Molecular Interactions**
  - BIND, DIP, MIPS, IntAct, Biogrid$^{\text{New}}$, MINT, Cognia, etc.

☐ **miRNA/mRNA target databases**
  - TarBase, TargetScan, miRecords

☐ **Gene to Disease Associations**
  - OMIM, GWAS databases

☐ **Metabolomics**
  - HumanCyc$^{\text{New}}$

☐ **Clinical Trial information**
  - ClinicalTrials.gov

Unique Tools for Biological Analysis and Interpretation

Gene View Summaries

Human & Mouse Isoform Views

BioProfiler

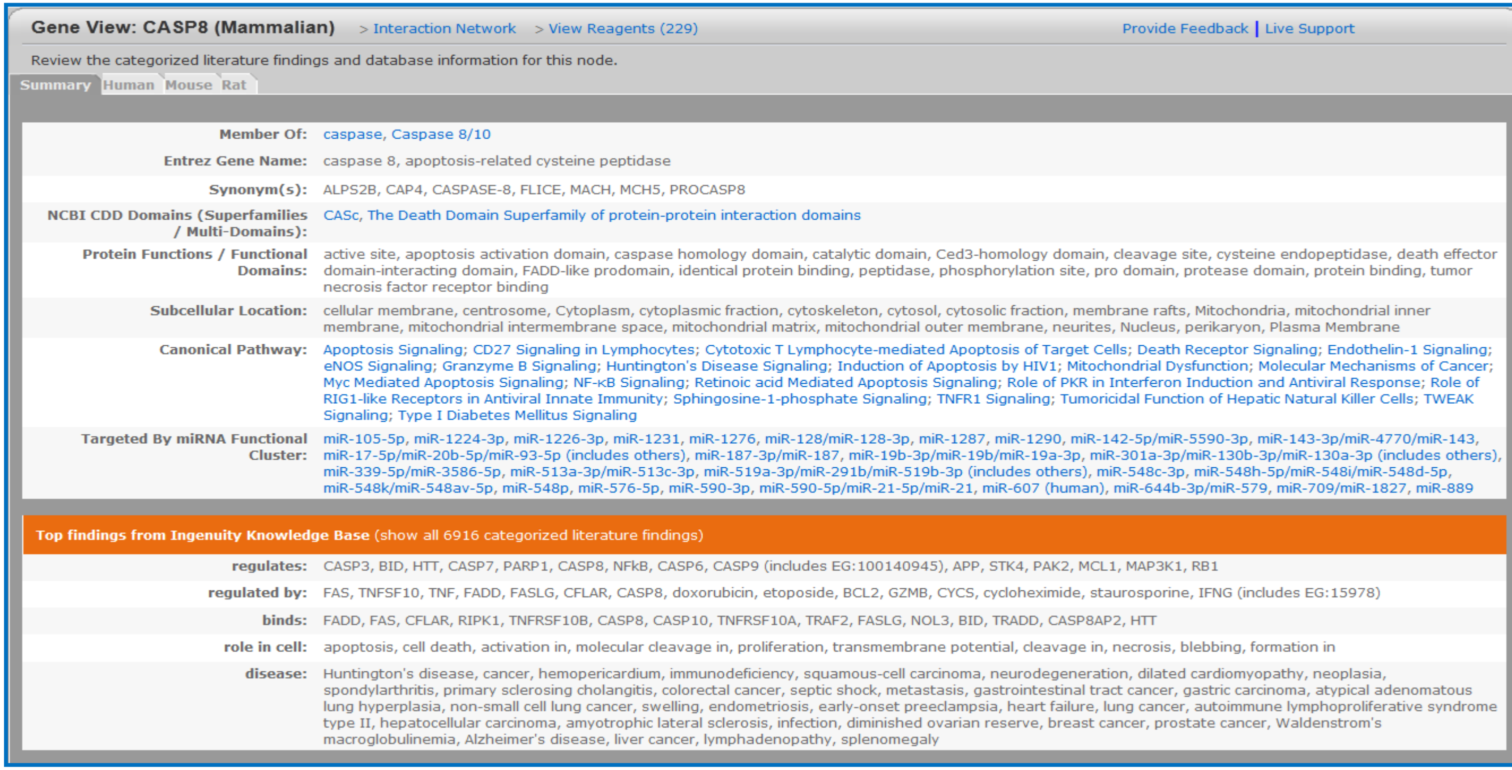
Graphical Summary

Diseases & Bio Functions

Canonical Pathways

Upstream Regulator Analysis

Build & Overlay and Interactions



Review the categorized literature findings and database information for this node.

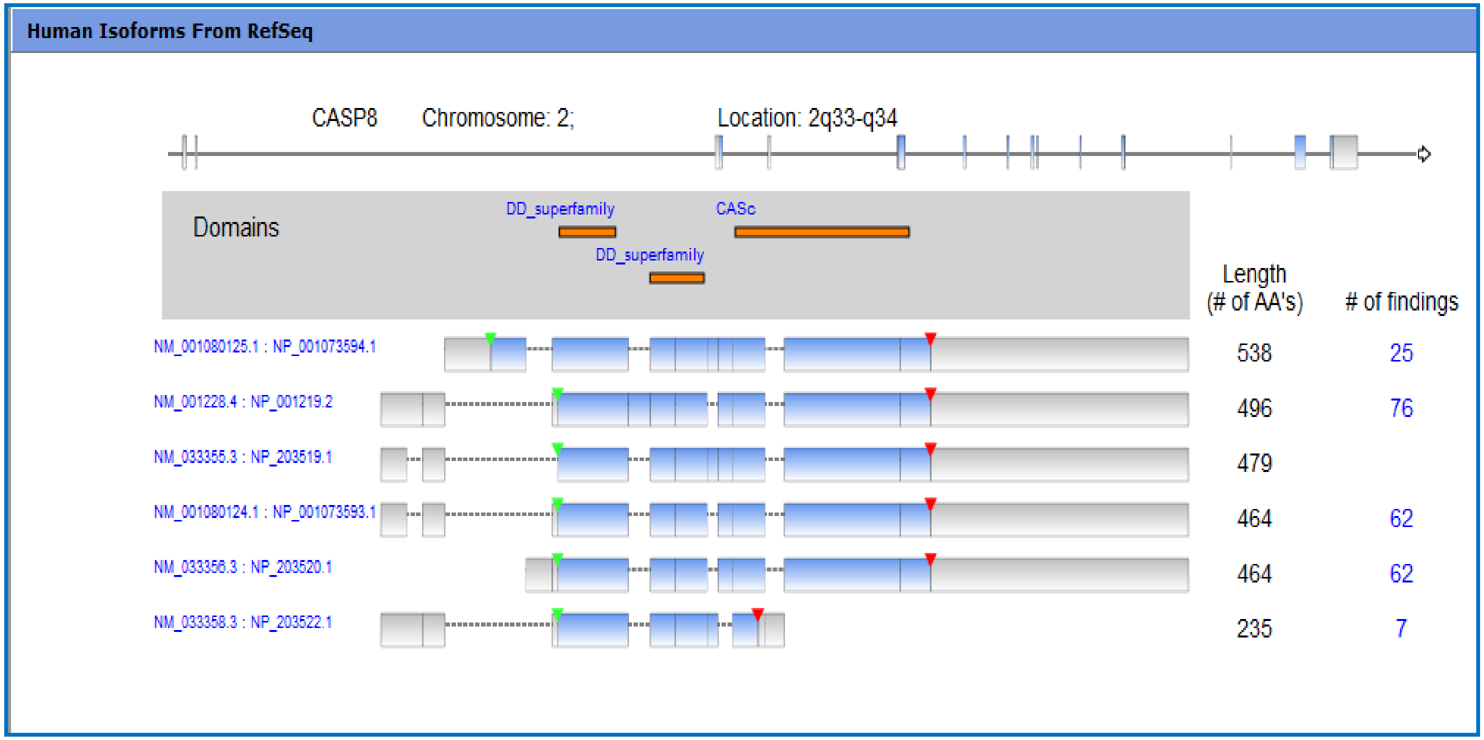
Member Of:	caspase, Caspase 8/10
Entrez Gene Name:	caspase 8, apoptosis-related cysteine peptidase
Synonym(s):	ALPS2B, CAP4, CASPASE-8, FLICE, MACH, MCH5, PROCASP8
NCBI CDD Domains (Superfamilies / Multi-Domains):	CASc, The Death Domain Superfamily of protein-protein interaction domains
Protein Functions / Functional Domains:	active site, apoptosis activation domain, caspase homology domain, catalytic domain, Ced3-homology domain, cleavage site, cysteine endopeptidase, death effector domain-interacting domain, FADD-like prodomain, identical protein binding, peptidase, phosphorylation site, pro domain, protease domain, protein binding, tumor necrosis factor receptor binding
Subcellular Location:	cellular membrane, centrosome, Cytoplasm, cytoplasmic fraction, cytoskeleton, cytosol, cytosolic fraction, membrane rafts, Mitochondria, mitochondrial inner membrane, mitochondrial intermembrane space, mitochondrial matrix, mitochondrial outer membrane, neurites, Nucleus, perikaryon, Plasma Membrane
Canonical Pathway:	Apoptosis Signaling; CD27 Signaling in Lymphocytes; Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells; Death Receptor Signaling; Endothelin-1 Signaling; eNOS Signaling; Granzyme B Signaling; Huntington's Disease Signaling; Induction of Apoptosis by HIV1; Mitochondrial Dysfunction; Molecular Mechanisms of Cancer; Myc Mediated Apoptosis Signaling; NF-κB Signaling; Retinoic acid Mediated Apoptosis Signaling; Role of PKR in Interferon Induction and Antiviral Response; Role of RIG1-like Receptors in Antiviral Innate Immunity; Sphingosine-1-phosphate Signaling; TNFR1 Signaling; Tumoricidal Function of Hepatic Natural Killer Cells; TWEAK Signaling; Type I Diabetes Mellitus Signaling
Targeted By miRNA Functional Cluster:	miR-105-5p, miR-1224-3p, miR-1226-3p, miR-1231, miR-1276, miR-128/miR-128-3p, miR-1287, miR-1290, miR-142-5p/miR-5590-3p, miR-143-3p/miR-4770/miR-143, miR-17-5p/miR-20b-5p/miR-93-5p (includes others), miR-187-3p/miR-187, miR-19b-3p/miR-19b/miR-19a-3p, miR-301a-3p/miR-130b-3p/miR-130a-3p (includes others), miR-339-5p/miR-3586-5p, miR-513a-3p/miR-513c-3p, miR-519a-3p/miR-291b/miR-519b-3p (includes others), miR-548c-3p, miR-548h-5p/miR-548i/miR-548d-5p, miR-548k/miR-548av-5p, miR-548p, miR-576-5p, miR-590-3p, miR-590-5p/miR-21-5p/miR-21, miR-607 (human), miR-644b-3p/miR-579, miR-709/miR-1827, miR-889

Top findings from Ingenuity Knowledge Base (show all 6916 categorized literature findings)

regulates:	CASP3, BID, HTT, CASP7, PARP1, CASP8, NFkB, CASP6, CASP9 (includes EG:100140945), APP, STK4, PAK2, MCL1, MAP3K1, RB1
regulated by:	FAS, TNFSF10, TNF, FADD, FASLG, CFLAR, CASP8, doxorubicin, etoposide, BCL2, GZMB, CYCS, cycloheximide, staurosporine, IFNG (includes EG:15978)
binds:	FADD, FAS, CFLAR, RIPK1, TNFRSF10B, CASP8, CASP10, TNFRSF10A, TRAF2, FASLG, NOL3, BID, TRADD, CASP8AP2, HTT
role in cell:	apoptosis, cell death, activation in, molecular cleavage in, proliferation, transmembrane potential, cleavage in, necrosis, blebbing, formation in
disease:	Huntington's disease, cancer, hemopericardium, immunodeficiency, squamous-cell carcinoma, neurodegeneration, dilated cardiomyopathy, neoplasia, spondylarthritis, primary sclerosing cholangitis, colorectal cancer, septic shock, metastasis, gastrointestinal tract cancer, gastric carcinoma, atypical adenomatous lung hyperplasia, non-small cell lung cancer, swelling, endometriosis, early-onset preeclampsia, heart failure, lung cancer, autoimmune lymphoproliferative syndrome type II, hepatocellular carcinoma, amyotrophic lateral sclerosis, infection, diminished ovarian reserve, breast cancer, prostate cancer, Waldenstrom's macroglobulinemia, Alzheimer's disease, liver cancer, lymphadenopathy, splenomegaly

Unique Tools for Biological Analysis and Interpretation

- Gene View Summaries
- **Human & Mouse Isoform Views**
- BioProfiler
- Graphical Summary
- Diseases & Bio Functions
- Canonical Pathways
- Upstream Regulator Analysis
- Build & Overlay and Interactions



Human Isoforms From RefSeq

CASP8 Chromosome: 2; Location: 2q33-q34

	Length (# of AA's)	# of findings
NM_001080125.1 : NP_001073594.1	538	25
NM_001228.4 : NP_001219.2	496	76
NM_033355.3 : NP_203519.1	479	
NM_001080124.1 : NP_001073593.1	464	62
NM_033356.3 : NP_203520.1	464	62
NM_033358.3 : NP_203522.1	235	7

Unique Tools for Biological Analysis and Interpretation

- Gene View Summaries
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- Graphical Summary
- Diseases & Bio Functions
- Canonical Pathways
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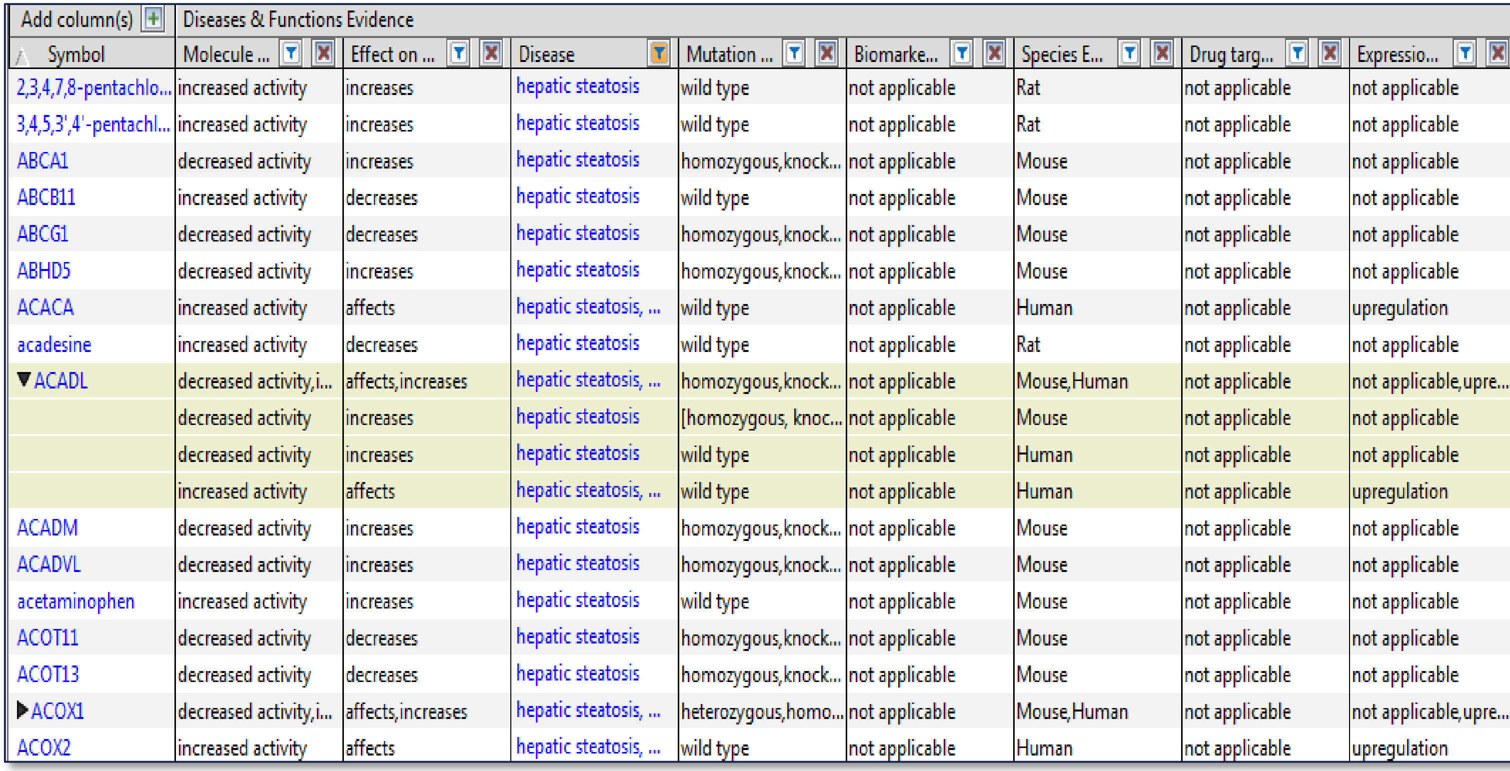

Add column(s) | Diseases & Functions Evidence

Symbol	Molecule ...	Effect on ...	Disease	Mutation ...	Biomarke...	Species E...	Drug targ...	Expressio...
2,3,4,7,8-pentachlo...	increased activity	increases	hepatic steatosis	wild type	not applicable	Rat	not applicable	not applicable
3,4,5,3',4'-pentachl...	increased activity	increases	hepatic steatosis	wild type	not applicable	Rat	not applicable	not applicable
ABCA1	decreased activity	increases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
ABCB11	increased activity	decreases	hepatic steatosis	wild type	not applicable	Mouse	not applicable	not applicable
ABCG1	decreased activity	decreases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
ABHD5	decreased activity	increases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
ACACA	increased activity	affects	hepatic steatosis, ...	wild type	not applicable	Human	not applicable	upregulation
acadesine	increased activity	decreases	hepatic steatosis	wild type	not applicable	Rat	not applicable	not applicable
▼ACADL	decreased activity,i...	affects,increases	hepatic steatosis, ...	homozygous,knock...	not applicable	Mouse,Human	not applicable	not applicable,upre...
	decreased activity	increases	hepatic steatosis	[homozygous, knoc...	not applicable	Mouse	not applicable	not applicable
	decreased activity	increases	hepatic steatosis	wild type	not applicable	Human	not applicable	not applicable
	increased activity	affects	hepatic steatosis, ...	wild type	not applicable	Human	not applicable	upregulation
ACADM	decreased activity	increases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
ACADVL	decreased activity	increases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
acetaminophen	increased activity	increases	hepatic steatosis	wild type	not applicable	Mouse	not applicable	not applicable
ACOT11	decreased activity	decreases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
ACOT13	decreased activity	decreases	hepatic steatosis	homozygous,knock...	not applicable	Mouse	not applicable	not applicable
▶ACOX1	decreased activity,i...	affects,increases	hepatic steatosis, ...	heterozygous,homo...	not applicable	Mouse,Human	not applicable	not applicable,upre...
ACOX2	increased activity	affects	hepatic steatosis, ...	wild type	not applicable	Human	not applicable	upregulation

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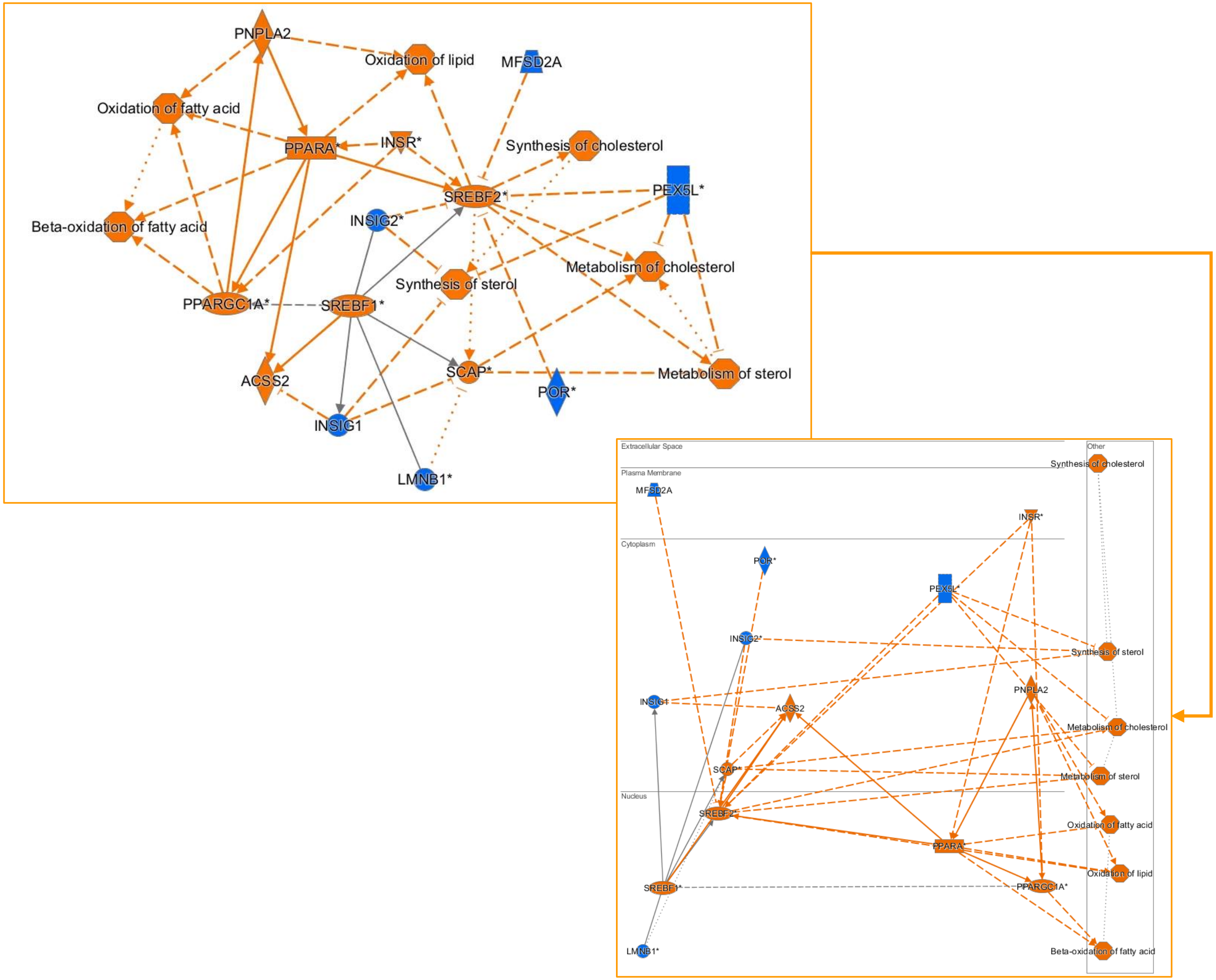

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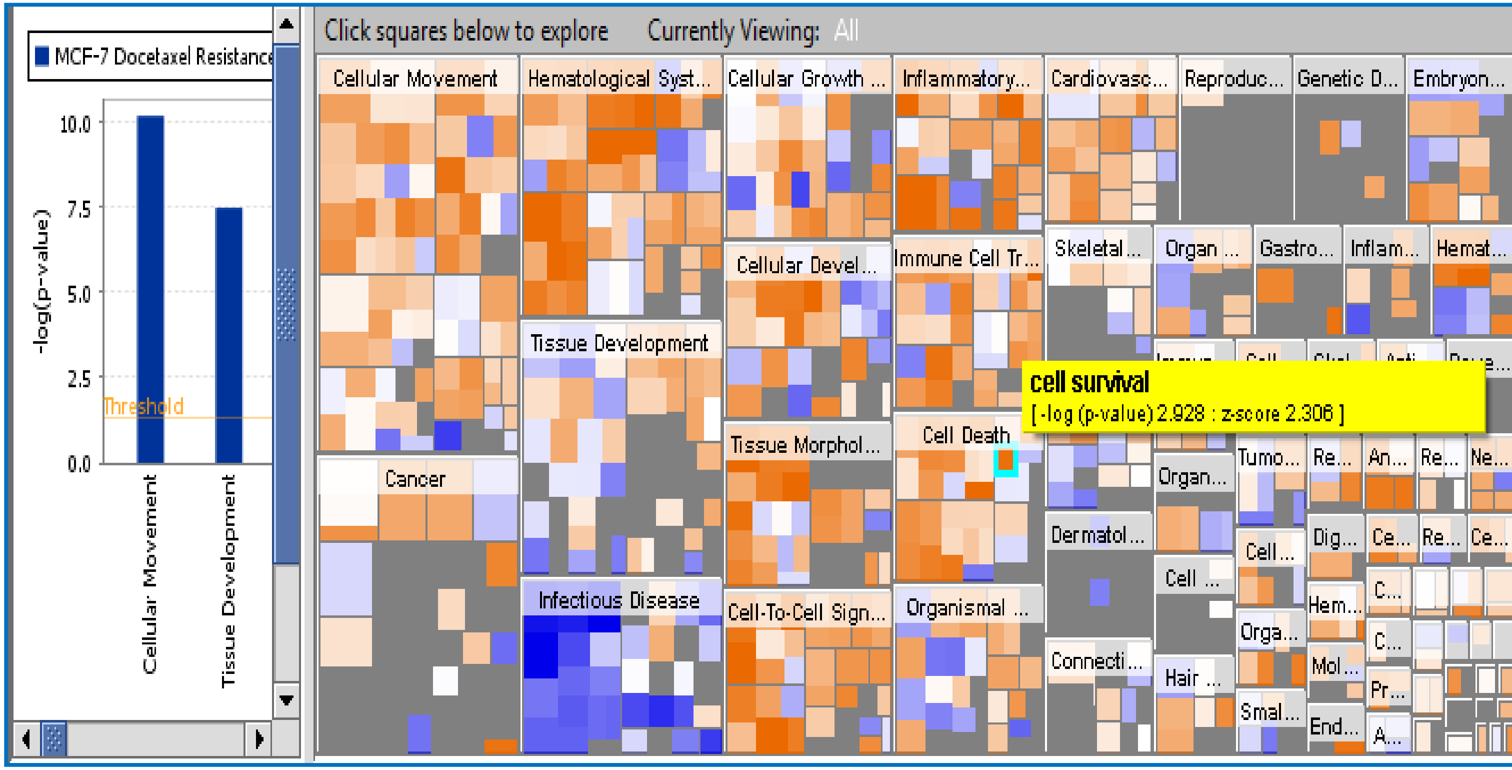

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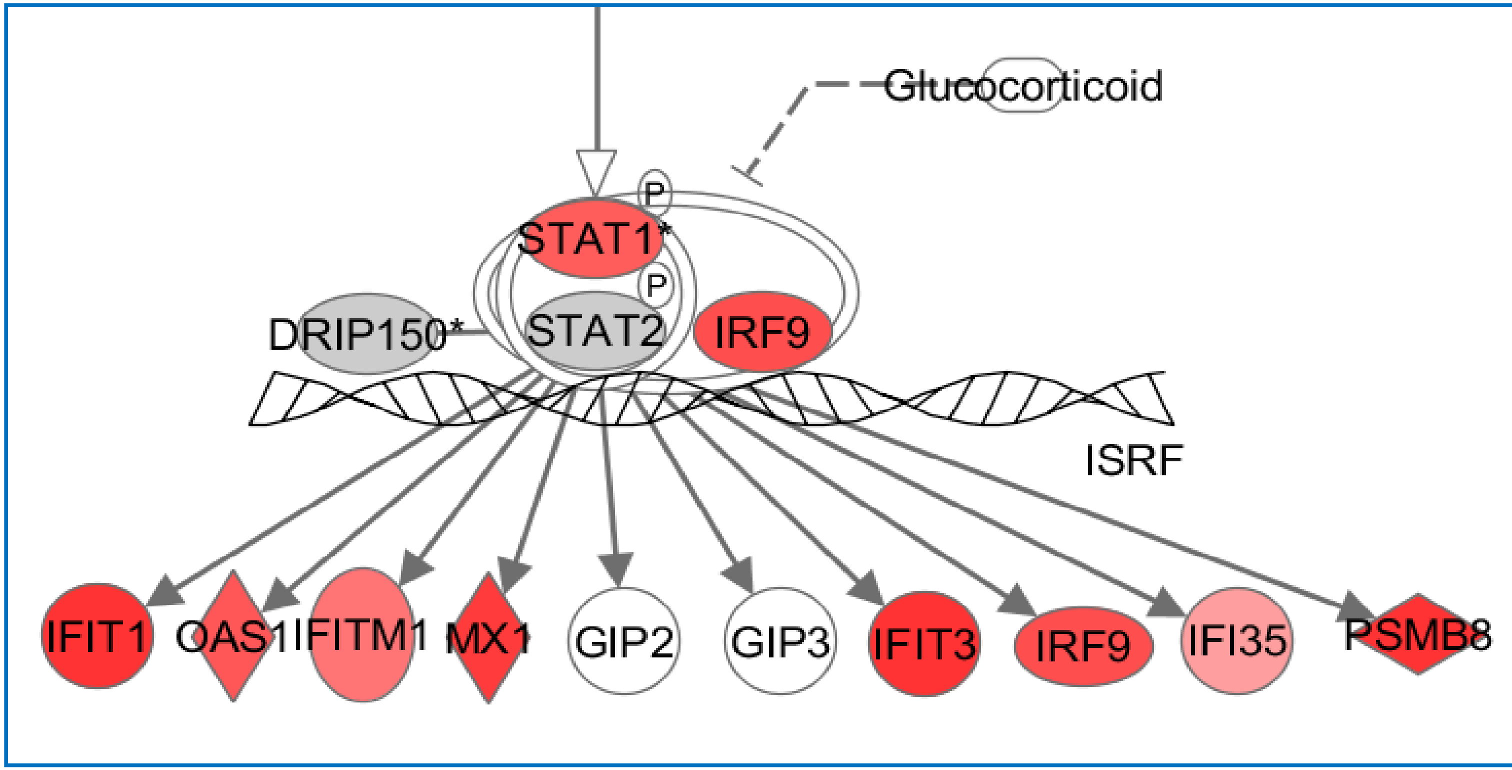

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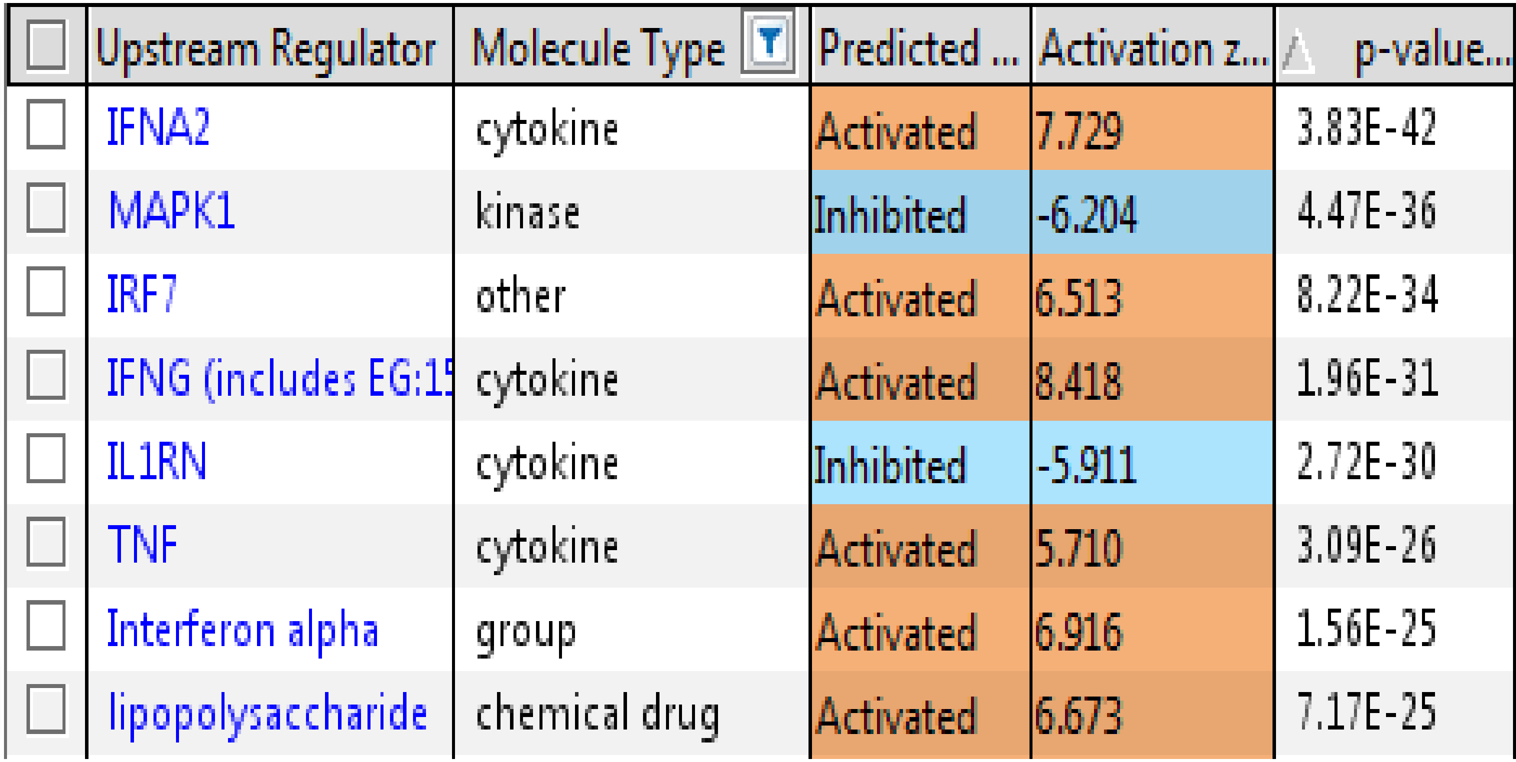

☐	Upstream Regulator	Molecule Type	Predicted ...	Activation z...	p-value...
☐	IFNA2	cytokine	Activated	7.729	3.83E-42
☐	MAPK1	kinase	Inhibited	-6.204	4.47E-36
☐	IRF7	other	Activated	6.513	8.22E-34
☐	IFNG (includes EG:15	cytokine	Activated	8.418	1.96E-31
☐	IL1RN	cytokine	Inhibited	-5.911	2.72E-30
☐	TNF	cytokine	Activated	5.710	3.09E-26
☐	Interferon alpha	group	Activated	6.916	1.56E-25
☐	lipopolysaccharide	chemical drug	Activated	6.673	7.17E-25

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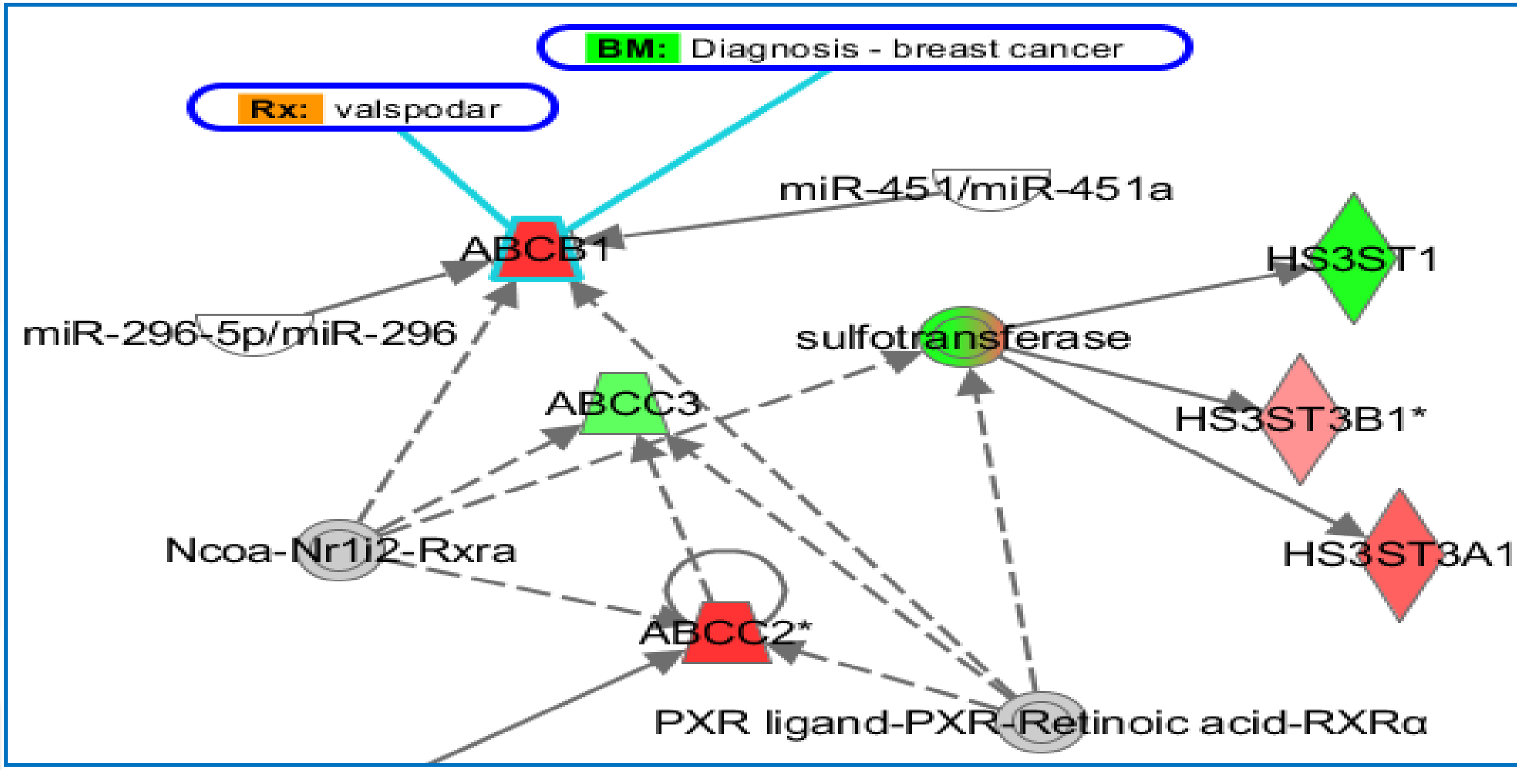

Unique Tools for Biological Analysis and Interpretation (advanced)

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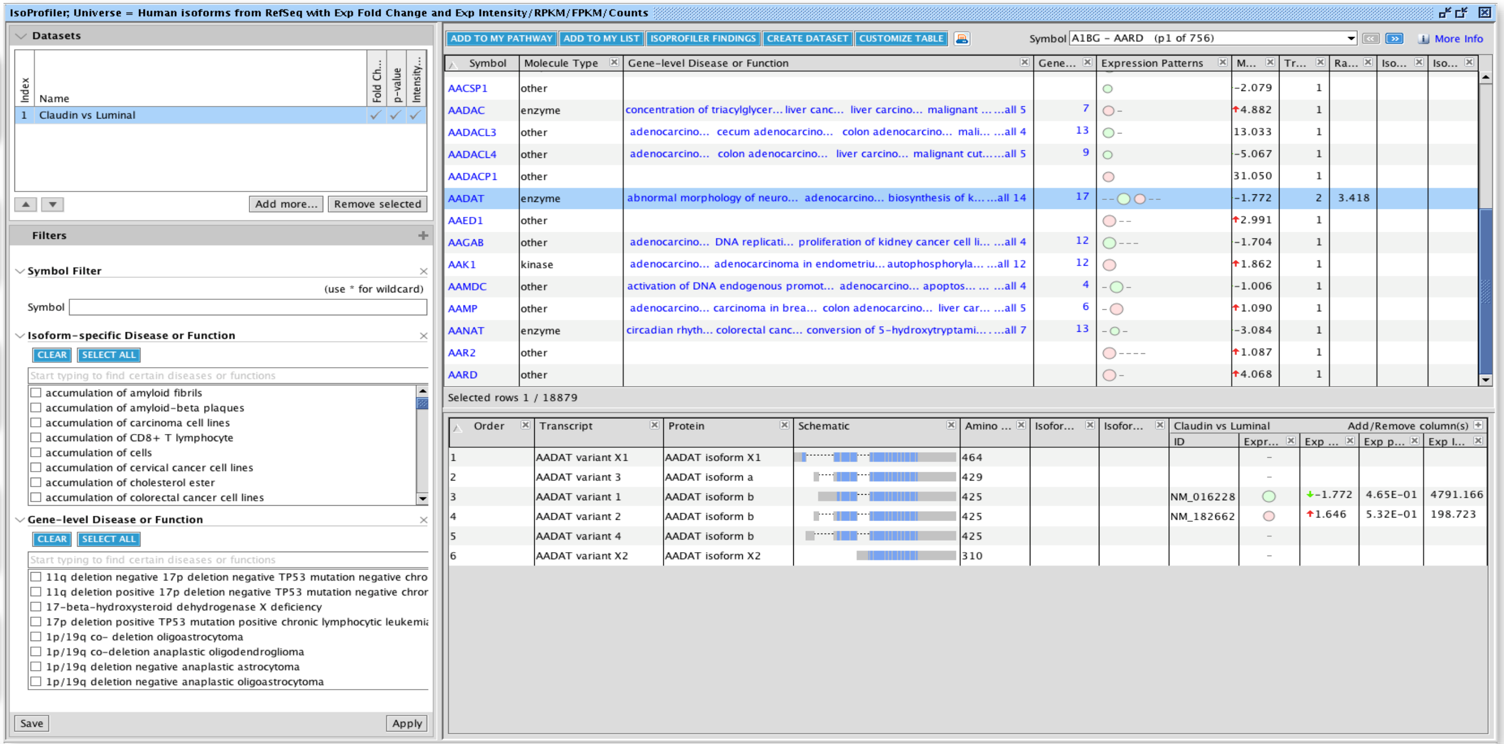
- Phosphorylation Analysis
- Comparison Analysis
- Activity Plot
- Analysis Match w/ OmicSoft Lands



IsoProfiler; Universe = Human isoforms from RefSeq with Exp Fold Change and Exp Intensity/RPKM/FPKM/Counts

Datasets

Index	Name	Fold Ch...	p-value	Intensity...
1	Claudin vs Luminal	✓	✓	✓

Filters

Symbol Filter

(use * for wildcard)

Symbol

Isoform-specific Disease or Function

Start typing to find certain diseases or functions

- ☐ accumulation of amyloid fibrils
- ☐ accumulation of amyloid-beta plaques
- ☐ accumulation of carcinoma cell lines
- ☐ accumulation of CD8+ T lymphocyte
- ☐ accumulation of cells
- ☐ accumulation of cervical cancer cell lines
- ☐ accumulation of cholesterol ester
- ☐ accumulation of colorectal cancer cell lines

Gene-level Disease or Function

Start typing to find certain diseases or functions

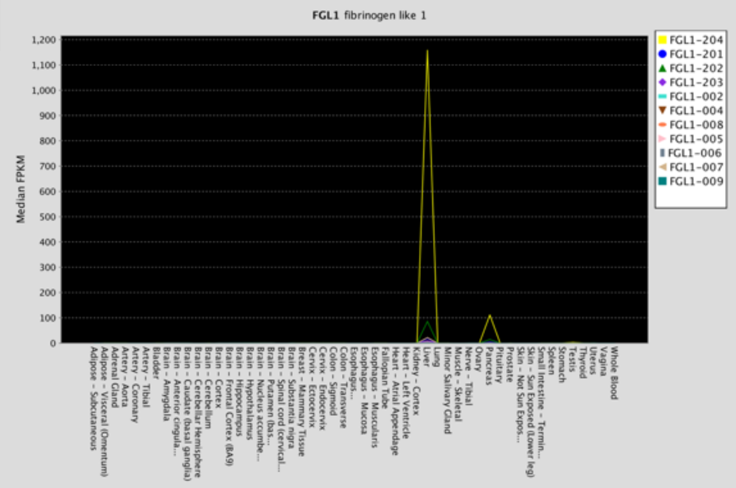
- ☐ 11q deletion negative 17p deletion negative TP53 mutation negative chro
- ☐ 11q deletion positive 17p deletion negative TP53 mutation negative chror
- ☐ 17-beta-hydroxysteroid dehydrogenase X deficiency
- ☐ 17p deletion positive TP53 mutation positive chronic lymphocytic leukemi
- ☐ 1p/19q co- deletion oligoastrocytoma
- ☐ 1p/19q co-deletion anaplastic oligodendroglioma
- ☐ 1p/19q deletion negative anaplastic astrocytoma
- ☐ 1p/19q deletion negative anaplastic oligoastrocytoma

Symbol A1BG – AARD (p1 of 756)

Symbol	Molecule Type	Gene-level Disease or Function	Gene...	Expression Patterns	M...	Tr...	Ra...	Iso...	Iso...
AACSP1	other			○	-2.079	1			
AADAC	enzyme	concentration of triacylglycer... liver canc... liver carcino... malignant ... ...all 5	7	○ -	↑4.882	1			
AADACL3	other	adenocarcino... cecum adenocarcino... colon adenocarcino... mali... ...all 4	13	○ -	13.033	1			
AADACL4	other	adenocarcino... colon adenocarcino... liver carcino... malignant cut... ...all 5	9	○	-5.067	1			
AADACP1	other			○	31.050	1			
AADAT	enzyme	abnormal morphology of neuro... adenocarcino... biosynthesis of k... ...all 14	17	- - ○ ○ - -	-1.772	2	3.418		
AAED1	other			○ - -	↑2.991	1			
AAGAB	other	adenocarcino... DNA replicati... proliferation of kidney cancer cell li... ...all 4	12	○ - - -	-1.704	1			
AAK1	kinase	adenocarcino... adenocarcinoma in endometriu... autophosphoryla... ...all 12	12	○	↑1.862	1			
AAMDC	other	activation of DNA endogenous promot... adenocarcino... apoptos... ... ...all 4	4	- ○ -	-1.006	1			
AAMP	other	adenocarcino... carcinoma in brea... colon adenocarcino... liver car... ...all 5	6	- ○	↑1.090	1			
AANAT	enzyme	circadian rhyth... colorectal canc... conversion of 5-hydroxytryptami... . ...all 7	13	- ○ -	-3.084	1			
AAR2	other			○ - - - -	↑1.087	1			
AARD	other			○ -	↑4.068	1			

Selected rows 1 / 18879

Order	Transcript	Protein	Schematic	Amino ...	Isofor...	Isofor...	Claudin vs Luminal ID	Expr...	Exp ...	Exp p...	Exp I...
1	AADAT variant X1	AADAT isoform X1		464				-			
2	AADAT variant 3	AADAT isoform a		429				-			
3	AADAT variant 1	AADAT isoform b		425			NM_016228	○	↓-1.772	4.65E-01	4791.166
4	AADAT variant 2	AADAT isoform b		425			NM_182662	○	↑1.646	5.32E-01	198.723
5	AADAT variant 4	AADAT isoform b		425				-			
6	AADAT variant X2	AADAT isoform X2		310				-			



Unique Tools for Biological Analysis and Interpretation (advanced)

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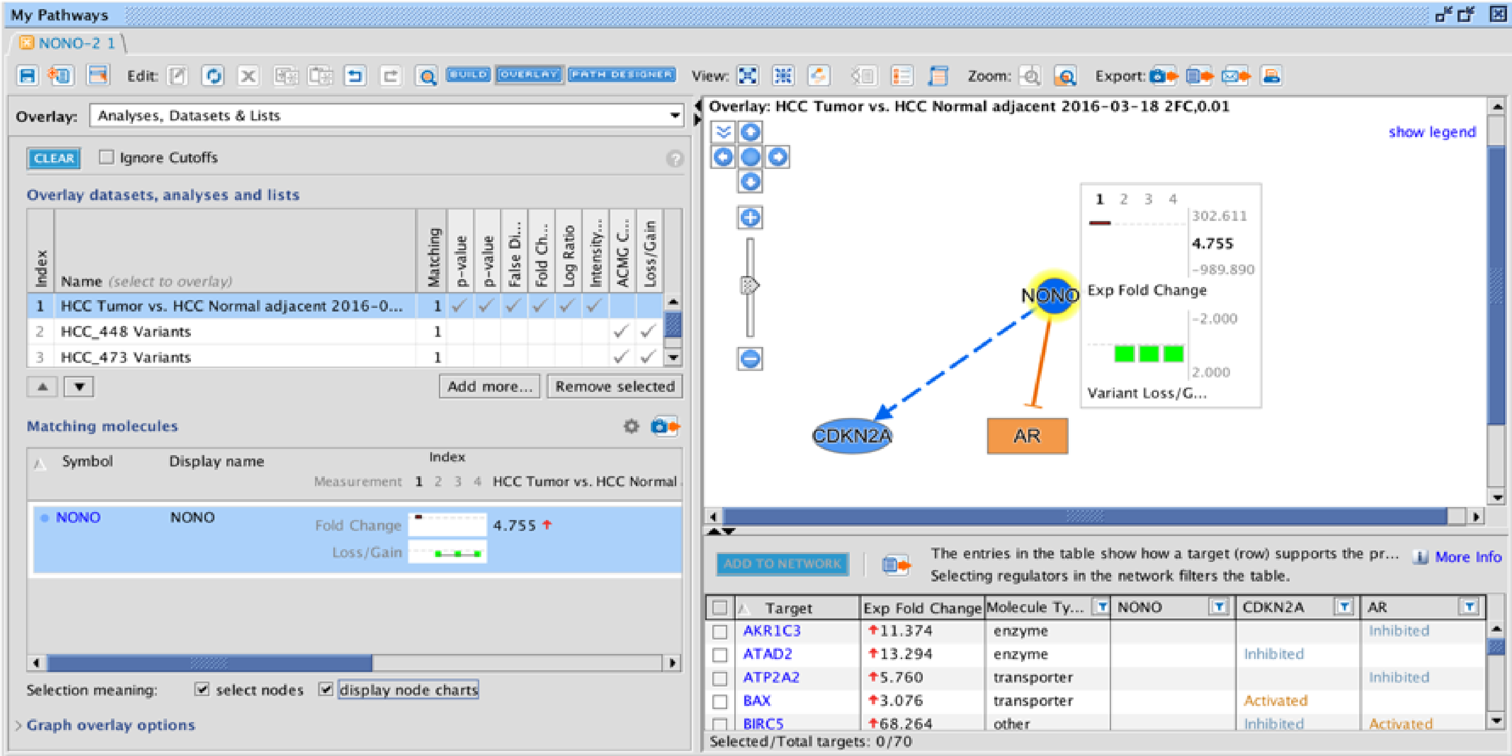

Overlay: Analyses, Datasets & Lists

☐ Ignore Cutoffs

Overlay datasets, analyses and lists

Index	Name *(select to overlay)*	Matching	p-value	p-value	False Di...	Fold Ch...	Log Ratio	Intensity...	ACMG C...	Loss/Gain
1	HCC Tumor vs. HCC Normal adjacent 2016-0...	1	✓	✓	✓	✓	✓	✓		
2	HCC_448 Variants	1							✓	✓
3	HCC_473 Variants	1							✓	✓

Matching molecules

Symbol	Display name	Measurement	Index 1 2 3 4	HCC Tumor vs. HCC Normal
NONO	NONO	Fold Change		4.755 ↑
		Loss/Gain		

Selection meaning: ☑ select nodes ☑ display node charts

Overlay: HCC Tumor vs. HCC Normal adjacent 2016-03-18 2FC,0.01

The entries in the table show how a target (row) supports the pr...
Selecting regulators in the network filters the table.

☐	Target	Exp Fold Change	Molecule Ty...	NONO	CDKN2A	AR
☐	AKR1C3	↑11.374	enzyme			Inhibited
☐	ATAD2	↑13.294	enzyme		Inhibited	
☐	ATP2A2	↑5.760	transporter			Inhibited
☐	BAX	↑3.076	transporter		Activated	
☐	BIRC5	↑68.264	other		Inhibited	Activated

Selected/Total targets: 0/70

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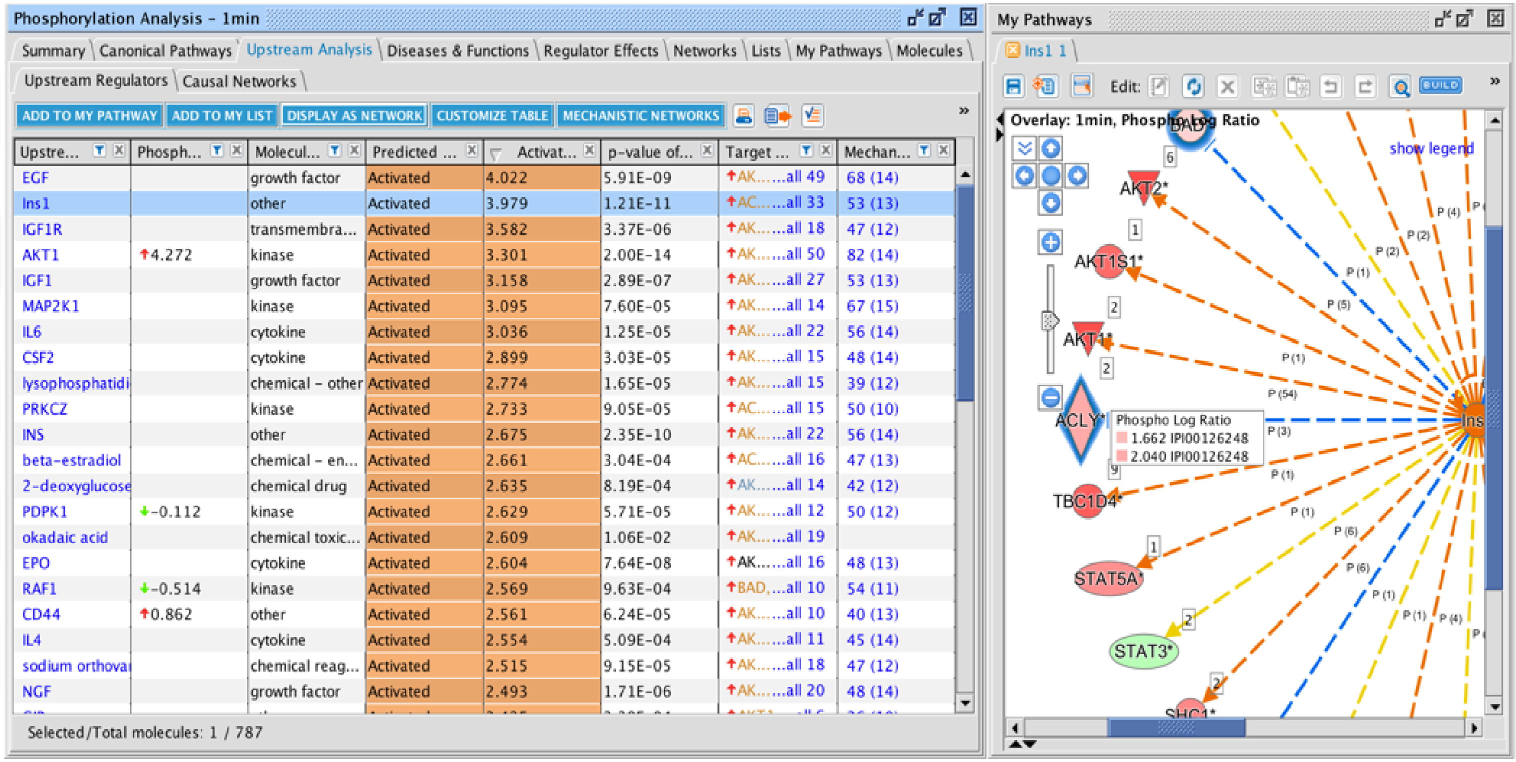

Upstre...	Phosph...	Molecul...	Predicted ...	Activat...	p-value of...	Target ...	Mechan...
EGF		growth factor	Activated	4.022	5.91E-09	↑AK......all 49	68 (14)
Ins1		other	Activated	3.979	1.21E-11	↑AC......all 33	53 (13)
IGF1R		transmembra...	Activated	3.582	3.37E-06	↑AK......all 18	47 (12)
AKT1	↑4.272	kinase	Activated	3.301	2.00E-14	↑AK......all 50	82 (14)
IGF1		growth factor	Activated	3.158	2.89E-07	↑AK......all 27	53 (13)
MAP2K1		kinase	Activated	3.095	7.60E-05	↑AK......all 14	67 (15)
IL6		cytokine	Activated	3.036	1.25E-05	↑AK......all 22	56 (14)
CSF2		cytokine	Activated	2.899	3.03E-05	↑AK......all 15	48 (14)
lysophosphatidi		chemical – other	Activated	2.774	1.65E-05	↑AK......all 15	39 (12)
PRKCZ		kinase	Activated	2.733	9.05E-05	↑AC......all 15	50 (10)
INS		other	Activated	2.675	2.35E-10	↑AK......all 22	56 (14)
beta-estradiol		chemical – en...	Activated	2.661	3.04E-04	↑AC......all 16	47 (13)
2-deoxyglucose		chemical drug	Activated	2.635	8.19E-04	↑AK......all 14	42 (12)
PDPK1	↓-0.112	kinase	Activated	2.629	5.71E-05	↑AK......all 12	50 (12)
okadaic acid		chemical toxic...	Activated	2.609	1.06E-02	↑AK......all 19	
EPO		cytokine	Activated	2.604	7.64E-08	↑AK......all 16	48 (13)
RAF1	↓-0.514	kinase	Activated	2.569	9.63E-04	↑BAD,...all 10	54 (11)
CD44	↑0.862	other	Activated	2.561	6.24E-05	↑AK......all 10	40 (13)
IL4		cytokine	Activated	2.554	5.09E-04	↑AK......all 11	45 (14)
sodium orthovai		chemical reag...	Activated	2.515	9.15E-05	↑AK......all 18	47 (12)
NGF		growth factor	Activated	2.493	1.71E-06	↑AK......all 20	48 (14)

Selected/Total molecules: 1 / 787

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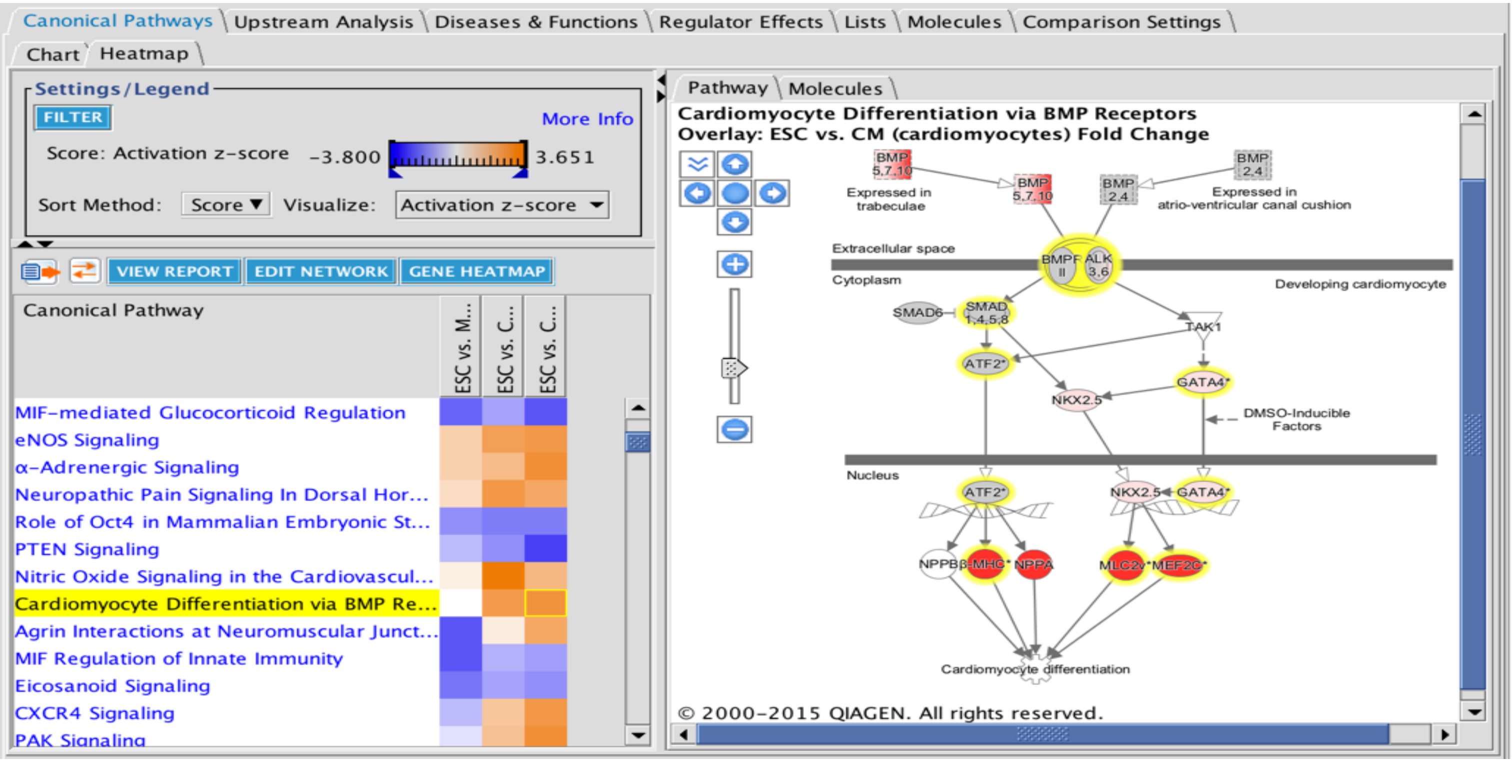

Score: Activation z-score -3.800 3.651

Sort Method: Score ▼ Visualize: Activation z-score ▼

Canonical Pathway	ESC vs. M...	ESC vs. C...	ESC vs. C...
MIF-mediated Glucocorticoid Regulation	🟦	🟦	🟦
eNOS Signaling	🟧	🟧	🟧
α-Adrenergic Signaling	🟧	🟧	🟧
Neuropathic Pain Signaling In Dorsal Hor...	🟧	🟧	🟧
Role of Oct4 in Mammalian Embryonic St...	🟦	🟦	🟦
PTEN Signaling	🟦	🟦	🟦
Nitric Oxide Signaling in the Cardiovascul...	🟧	🟧	🟧
Cardiomyocyte Differentiation via BMP Re...	⬜	🟧	🟧
Agrin Interactions at Neuromuscular Junct...	🟦	🟧	🟧
MIF Regulation of Innate Immunity	🟦	🟦	🟦
Eicosanoid Signaling	🟦	🟦	🟦
CXCR4 Signaling	🟦	🟧	🟧
PAK Signaling	🟦	🟧	🟧

Cardiomyocyte Differentiation via BMP Receptors
Overlay: ESC vs. CM (cardiomyocytes) Fold Change

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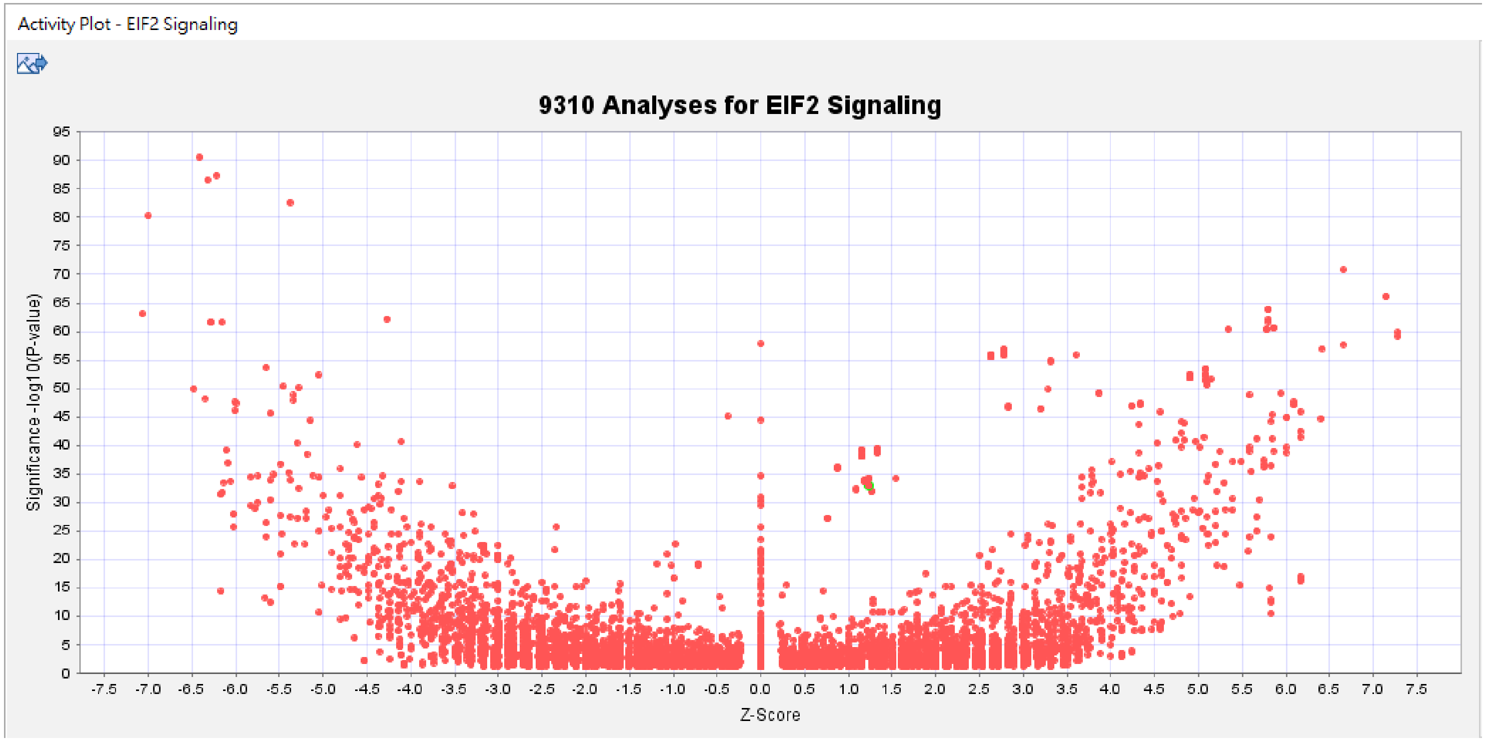

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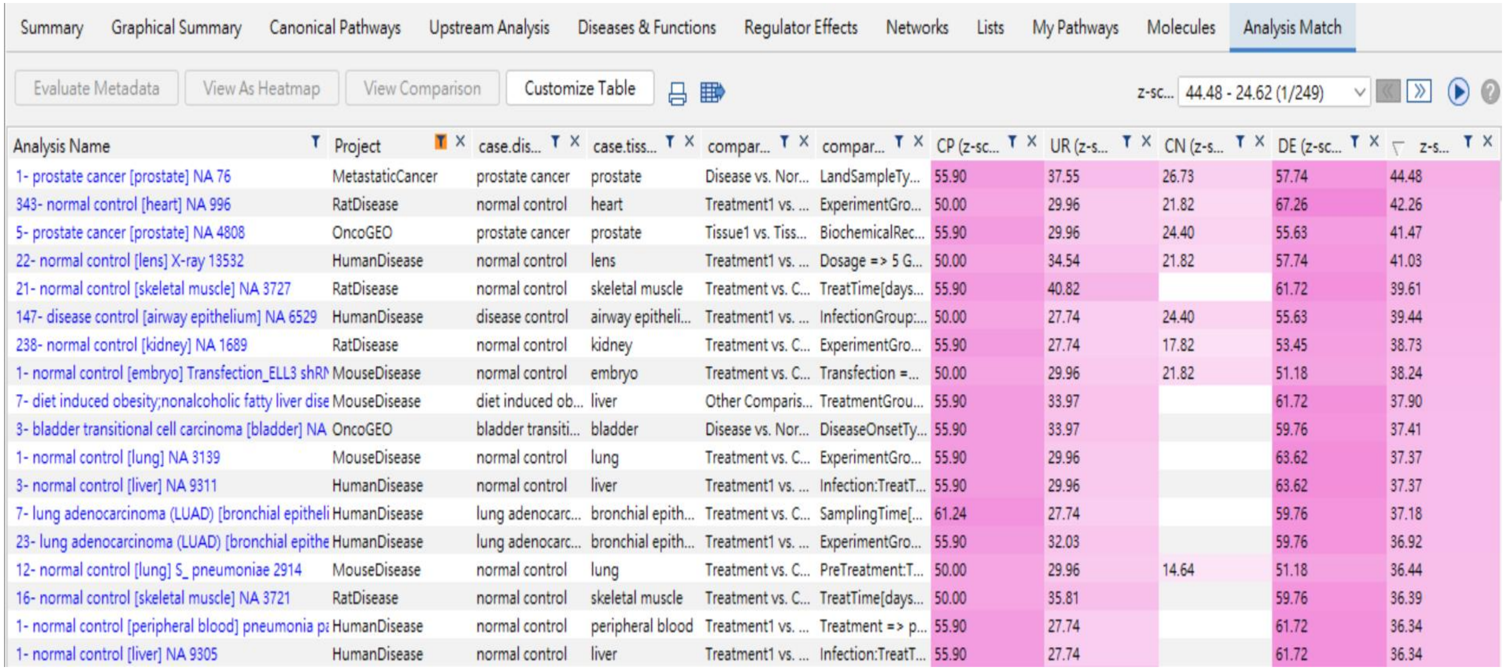


z-sc... 44.48 - 24.62 (1/249)

Analysis Name	Project	case.dis...	case.tiss...	compar...	compar...	CP (z-sc...	UR (z-s...	CN (z-s...	DE (z-sc...	z-s...
1- prostate cancer [prostate] NA 76	MetastaticCancer	prostate cancer	prostate	Disease vs. Nor...	LandSampleTy...	55.90	37.55	26.73	57.74	44.48
343- normal control [heart] NA 996	RatDisease	normal control	heart	Treatment1 vs. ...	ExperimentGro...	50.00	29.96	21.82	67.26	42.26
5- prostate cancer [prostate] NA 4808	OncoGEO	prostate cancer	prostate	Tissue1 vs. Tiss...	BiochemicalRec...	55.90	29.96	24.40	55.63	41.47
22- normal control [lens] X-ray 13532	HumanDisease	normal control	lens	Treatment1 vs. ...	Dosage => 5 G...	50.00	34.54	21.82	57.74	41.03
21- normal control [skeletal muscle] NA 3727	RatDisease	normal control	skeletal muscle	Treatment vs. C...	TreatTime[days...	55.90	40.82		61.72	39.61
147- disease control [airway epithelium] NA 6529	HumanDisease	disease control	airway epitheli...	Treatment1 vs. ...	InfectionGroup:...	50.00	27.74	24.40	55.63	39.44
238- normal control [kidney] NA 1689	RatDisease	normal control	kidney	Treatment vs. C...	ExperimentGro...	55.90	27.74	17.82	53.45	38.73
1- normal control [embryo] Transfection_ELL3 shRI	MouseDisease	normal control	embryo	Treatment vs. C...	Transfection =...	50.00	29.96	21.82	51.18	38.24
7- diet induced obesity;nonalcoholic fatty liver dise	MouseDisease	diet induced ob...	liver	Other Comparis...	TreatmentGrou...	55.90	33.97		61.72	37.90
3- bladder transitional cell carcinoma [bladder] NA	OncoGEO	bladder transiti...	bladder	Disease vs. Nor...	DiseaseOnsetTy...	55.90	33.97		59.76	37.41
1- normal control [lung] NA 3139	MouseDisease	normal control	lung	Treatment vs. C...	ExperimentGro...	55.90	29.96		63.62	37.37
3- normal control [liver] NA 9311	HumanDisease	normal control	liver	Treatment1 vs. ...	Infection:TreatT...	55.90	29.96		63.62	37.37
7- lung adenocarcinoma (LUAD) [bronchial epitheli	HumanDisease	lung adenocarc...	bronchial epith...	Treatment vs. C...	SamplingTime[...	61.24	27.74		59.76	37.18
23- lung adenocarcinoma (LUAD) [bronchial epithe	HumanDisease	lung adenocarc...	bronchial epith...	Treatment1 vs. ...	ExperimentGro...	55.90	32.03		59.76	36.92
12- normal control [lung] S_ pneumoniae 2914	MouseDisease	normal control	lung	Treatment vs. C...	PreTreatment:T...	50.00	29.96	14.64	51.18	36.44
16- normal control [skeletal muscle] NA 3721	RatDisease	normal control	skeletal muscle	Treatment vs. C...	TreatTime[days...	50.00	35.81		59.76	36.39
1- normal control [peripheral blood] pneumonia pa	HumanDisease	normal control	peripheral blood	Treatment1 vs. ...	Treatment => p...	55.90	27.74		61.72	36.34
1- normal control [liver] NA 9305	HumanDisease	normal control	liver	Treatment1 vs. ...	Infection:TreatT...	55.90	27.74		61.72	36.34

Unprecedented discovery, together

Array Express

GEO

SRA

TCGA

Etc.

Journal articles

Clinical Trials

COSMIC

OMIM

MGD

Etc.

Curation, Processing, & QA

Curation & QA

Datasets integrated into OmicSoft Lands

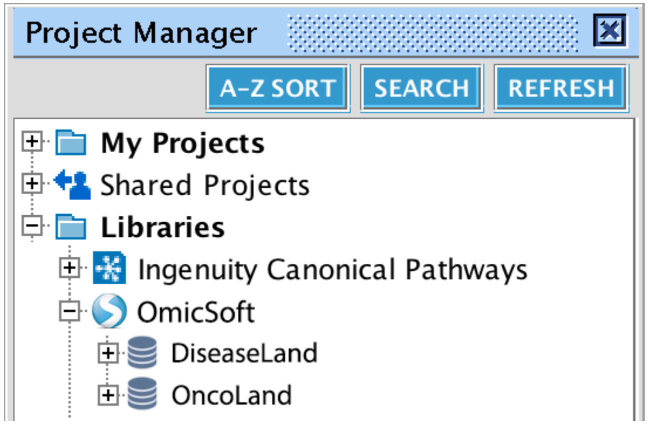
Curated Findings

OmicSoft Array Suite

OncoLand
DiseaseLand

73,000+ Expression comparison datasets

INGENUITY PATHWAY ANALYSIS

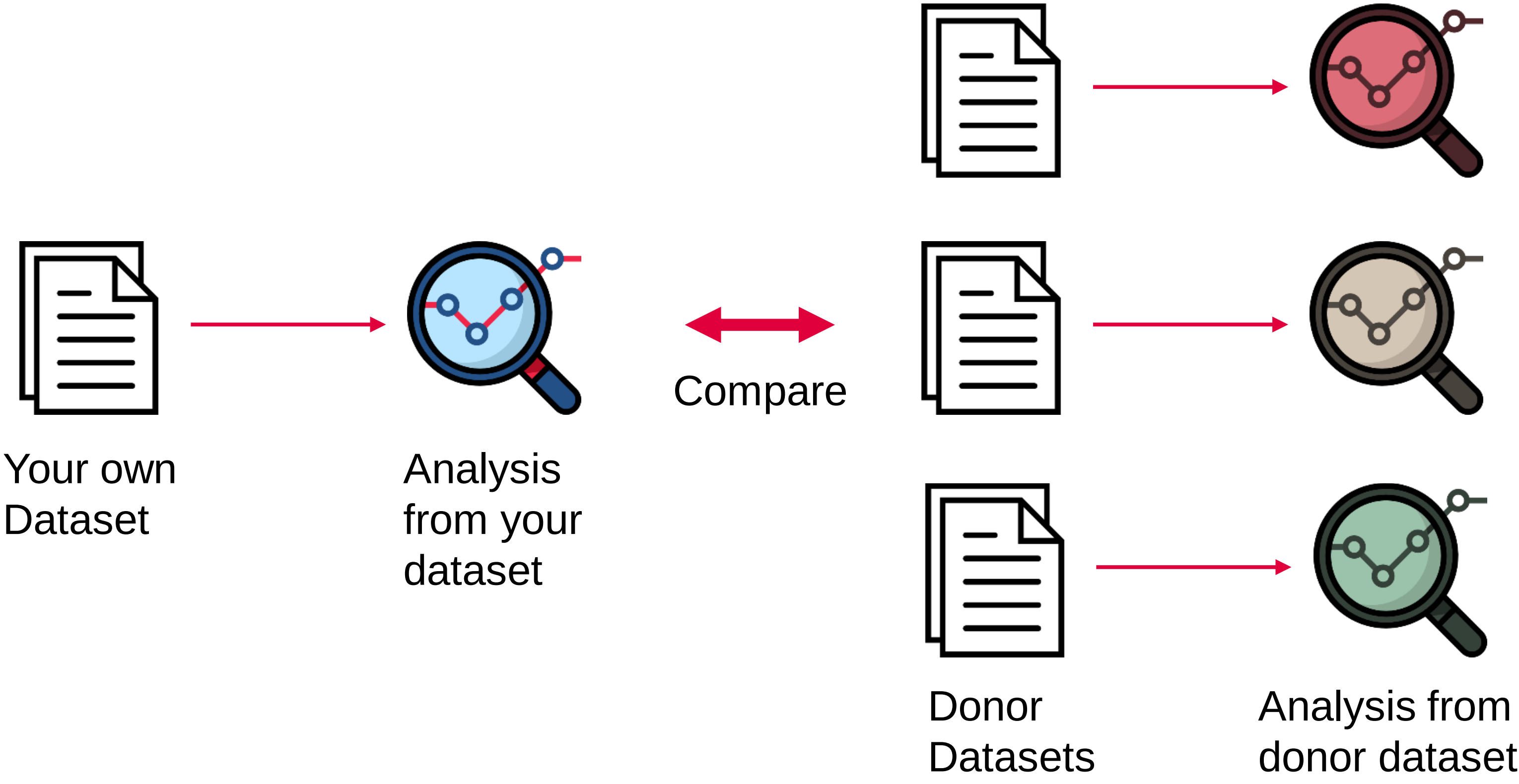


- Biological analyses of each dataset
- Compare your analysis to all OmicSoft analyses

Analysis Match

截至今日，本次更新增加了19,000組分析完成的數據至Analysis Match分析功能中，您可以在Analysis Match分析模組當中，比較您的實驗資料與外部資料庫如TCGA、LINCS等，在不同的癌症類型，疾病類型與實驗組中分析其相似及相異關係度。

並自**LINCS（NIH Library of Integrated Network-Based Cellular Signatures）**再添加大約**28,000**個分析組，總數將超過**73,000**個



Analysis Match

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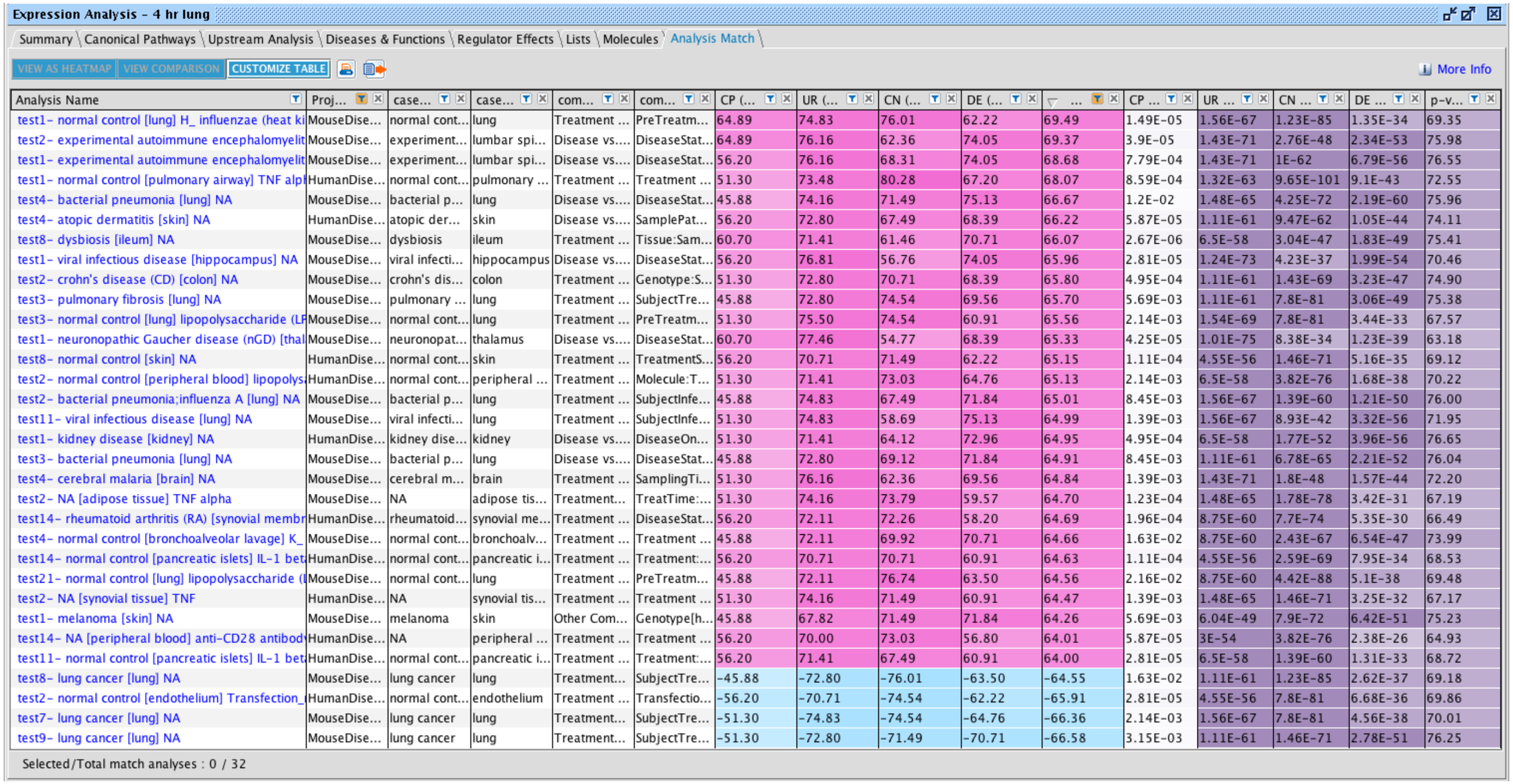
並自**DiseaseLand & OncoLand**再添加大約**6,900**個分析組，總數將超過**80,000**個!

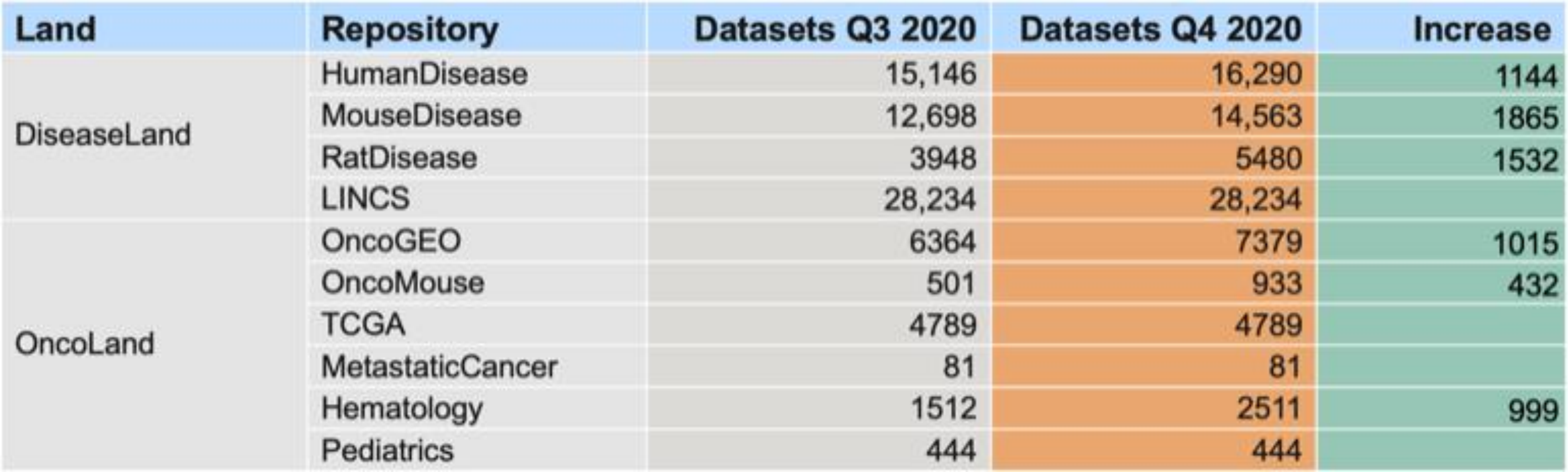


Analysis Name	Proj...	case...	case...	com...	com...	CP (...	UR (...	CN (...	DE (...	...	CP ...	UR ...	CN ...	DE ...	p-v...
test1- normal control [lung] H_ influenzae (heat ki	MouseDise...	normal cont...	lung	Treatment ...	PreTreatm...	64.89	74.83	76.01	62.22	69.49	1.49E-05	1.56E-67	1.23E-85	1.35E-34	69.35
test2- experimental autoimmune encephalomyelit	MouseDise...	experiment...	lumbar spi...	Disease vs....	DiseaseStat...	64.89	76.16	62.36	74.05	69.37	3.9E-05	1.43E-71	2.76E-48	2.34E-53	75.98
test1- experimental autoimmune encephalomyelit	MouseDise...	experiment...	lumbar spi...	Disease vs....	DiseaseStat...	56.20	76.16	68.31	74.05	68.68	7.79E-04	1.43E-71	1E-62	6.79E-56	76.55
test1- normal control [pulmonary airway] TNF alph	HumanDise...	normal cont...	pulmonary ...	Treatment ...	Treatment ...	51.30	73.48	80.28	67.20	68.07	8.59E-04	1.32E-63	9.65E-101	9.1E-43	72.55
test4- bacterial pneumonia [lung] NA	MouseDise...	bacterial p...	lung	Disease vs....	DiseaseStat...	45.88	74.16	71.49	75.13	66.67	1.2E-02	1.48E-65	4.25E-72	2.19E-60	75.96
test4- atopic dermatitis [skin] NA	HumanDise...	atopic der...	skin	Disease vs....	SamplePat...	56.20	72.80	67.49	68.39	66.22	5.87E-05	1.11E-61	9.47E-62	1.05E-44	74.11
test8- dysbiosis [ileum] NA	MouseDise...	dysbiosis	ileum	Treatment ...	Tissue:Sam...	60.70	71.41	61.46	70.71	66.07	2.67E-06	6.5E-58	3.04E-47	1.83E-49	75.41
test1- viral infectious disease [hippocampus] NA	MouseDise...	viral infecti...	hippocampus	Disease vs....	DiseaseStat...	56.20	76.81	56.76	74.05	65.96	2.81E-05	1.24E-73	4.23E-37	1.99E-54	70.46
test2- crohn's disease (CD) [colon] NA	MouseDise...	crohn's dis...	colon	Treatment ...	Genotype:S...	51.30	72.80	70.71	68.39	65.80	4.95E-04	1.11E-61	1.43E-69	3.23E-47	74.90
test3- pulmonary fibrosis [lung] NA	MouseDise...	pulmonary ...	lung	Treatment ...	SubjectTre...	45.88	72.80	74.54	69.56	65.70	5.69E-03	1.11E-61	7.8E-81	3.06E-49	75.38
test3- normal control [lung] lipopolysaccharide (LP	MouseDise...	normal cont...	lung	Treatment ...	PreTreatm...	51.30	75.50	74.54	60.91	65.56	2.14E-03	1.54E-69	7.8E-81	3.44E-33	67.57
test1- neuronopathic Gaucher disease (nGD) [thal	MouseDise...	neuronopat...	thalamus	Disease vs....	DiseaseStat...	60.70	77.46	54.77	68.39	65.33	4.25E-05	1.01E-75	8.38E-34	1.23E-39	63.18
test8- normal control [skin] NA	HumanDise...	normal cont...	skin	Treatment ...	TreatmentS...	56.20	70.71	71.49	62.22	65.15	1.11E-04	4.55E-56	1.46E-71	5.16E-35	69.12
test2- normal control [peripheral blood] lipopolys	HumanDise...	normal cont...	peripheral ...	Treatment ...	Molecule:T...	51.30	71.41	73.03	64.76	65.13	2.14E-03	6.5E-58	3.82E-76	1.68E-38	70.22
test2- bacterial pneumonia;influenza A [lung] NA	MouseDise...	bacterial p...	lung	Treatment ...	SubjectInfe...	45.88	74.83	67.49	71.84	65.01	8.45E-03	1.56E-67	1.39E-60	1.21E-50	76.00
test11- viral infectious disease [lung] NA	MouseDise...	viral infecti...	lung	Treatment ...	SubjectInfe...	51.30	74.83	58.69	75.13	64.99	1.39E-03	1.56E-67	8.93E-42	3.32E-56	71.95
test1- kidney disease [kidney] NA	HumanDise...	kidney dise...	kidney	Disease vs....	DiseaseOn...	51.30	71.41	64.12	72.96	64.95	4.95E-04	6.5E-58	1.77E-52	3.96E-56	76.65
test3- bacterial pneumonia [lung] NA	MouseDise...	bacterial p...	lung	Disease vs....	DiseaseStat...	45.88	72.80	69.12	71.84	64.91	8.45E-03	1.11E-61	6.78E-65	2.21E-52	76.04
test4- cerebral malaria [brain] NA	MouseDise...	cerebral m...	brain	Treatment ...	SamplingTi...	51.30	76.16	62.36	69.56	64.84	1.39E-03	1.43E-71	1.8E-48	1.57E-44	72.20
test2- NA [adipose tissue] TNF alpha	MouseDise...	NA	adipose tis...	Treatment...	TreatTime:...	51.30	74.16	73.79	59.57	64.70	1.23E-04	1.48E-65	1.78E-78	3.42E-31	67.19
test14- rheumatoid arthritis (RA) [synovial membr	HumanDise...	rheumatoid...	synovial me...	Treatment ...	DiseaseStat...	56.20	72.11	72.26	58.20	64.69	1.96E-04	8.75E-60	7.7E-74	5.35E-30	66.49
test4- normal control [bronchoalveolar lavage] K_	MouseDise...	normal cont...	bronchoalv...	Treatment ...	Treatment ...	45.88	72.11	69.92	70.71	64.66	1.63E-02	8.75E-60	2.43E-67	6.54E-47	73.99
test14- normal control [pancreatic islets] IL-1 bet	HumanDise...	normal cont...	pancreatic i...	Treatment ...	Treatment:...	56.20	70.71	70.71	60.91	64.63	1.11E-04	4.55E-56	2.59E-69	7.95E-34	68.53
test21- normal control [lung] lipopolysaccharide (I	MouseDise...	normal cont...	lung	Treatment ...	PreTreatm...	45.88	72.11	76.74	63.50	64.56	2.16E-02	8.75E-60	4.42E-88	5.1E-38	69.48
test2- NA [synovial tissue] TNF	HumanDise...	NA	synovial tis...	Treatment ...	Treatment ...	51.30	74.16	71.49	60.91	64.47	1.39E-03	1.48E-65	1.46E-71	3.25E-32	67.17
test1- melanoma [skin] NA	MouseDise...	melanoma	skin	Other Com...	Genotype[h...	45.88	67.82	71.49	71.84	64.26	5.69E-03	6.04E-49	7.9E-72	6.42E-51	75.23
test14- NA [peripheral blood] anti-CD28 antibod	HumanDise...	NA	peripheral ...	Treatment ...	Treatment ...	56.20	70.00	73.03	56.80	64.01	5.87E-05	3E-54	3.82E-76	2.38E-26	64.93
test11- normal control [pancreatic islets] IL-1 bet	HumanDise...	normal cont...	pancreatic i...	Treatment ...	Treatment:...	56.20	71.41	67.49	60.91	64.00	2.81E-05	6.5E-58	1.39E-60	1.31E-33	68.72
test8- lung cancer [lung] NA	MouseDise...	lung cancer	lung	Treatment...	SubjectTre...	-45.88	-72.80	-76.01	-63.50	-64.55	1.63E-02	1.11E-61	1.23E-85	2.62E-37	69.18
test2- normal control [endothelium] Transfection_	HumanDise...	normal cont...	endothelium	Treatment ...	Transfectio...	-56.20	-70.71	-74.54	-62.22	-65.91	2.81E-05	4.55E-56	7.8E-81	6.68E-36	69.86
test7- lung cancer [lung] NA	MouseDise...	lung cancer	lung	Treatment...	SubjectTre...	-51.30	-74.83	-74.54	-64.76	-66.36	2.14E-03	1.56E-67	7.8E-81	4.56E-38	70.01
test9- lung cancer [lung] NA	MouseDise...	lung cancer	lung	Treatment...	SubjectTre...	-51.30	-72.80	-71.49	-70.71	-66.58	3.15E-03	1.11E-61	1.46E-71	2.78E-51	76.25

Selected/Total match analyses : 0 / 32

Analysis Match Database

>80,000 OmicSoft Analyses available in Analysis Match and Activity Plot



Land	Repository	Datasets Q3 2020	Datasets Q4 2020	Increase
DiseaseLand	HumanDisease	15,146	16,290	1144
	MouseDisease	12,698	14,563	1865
	RatDisease	3948	5480	1532
	LINCS	28,234	28,234	
OncoLand	OncoGEO	6364	7379	1015
	OncoMouse	501	933	432
	TCGA	4789	4789	
	MetastaticCancer	81	81	
	Hematology	1512	2511	999
	Pediatrics	444	444	

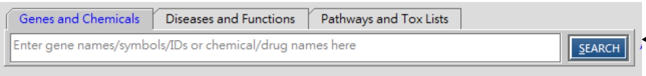
Entry Points in IPA

Biological Questions

Search

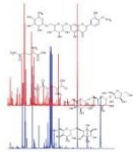
Experiment Data

Custom Pathway



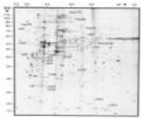
Enter gene names/symbols/IDs or chemical/drug names here

Expression arrays

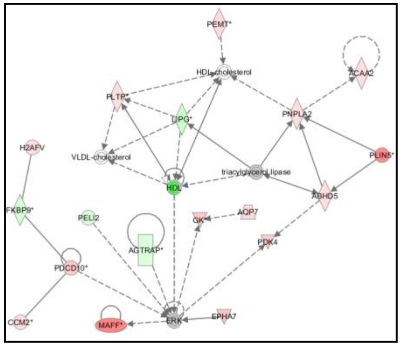


Mass spec

Protein arrays



2D Gel electrophoresis



Networks

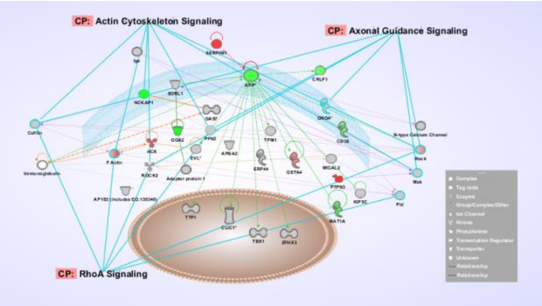
Core

IPA-Biomarker

IPA-Tox

IPA-Metabolomics

Bio/Tox Functions
Diseases/Disorders
Canonical Pathways
Upstream regulators
Mechanistic/Casual Network
Interaction Network



Communicate & Collaborate

Basic Module and Advanced module on IPA

Basic Module

- Gene and Chem View
- Isoform View
- Disease View
- Canonical Pathway
- BioProfiler
- Upload Dataset
- Molecule Activity Predictor (MAP)
- Tox Lists and Tox Functions
- Interactive Disease and Functions Nodes
- Biomarker filter
- Path Designer

https://www.qiagenbioinformatics.com/products/features/

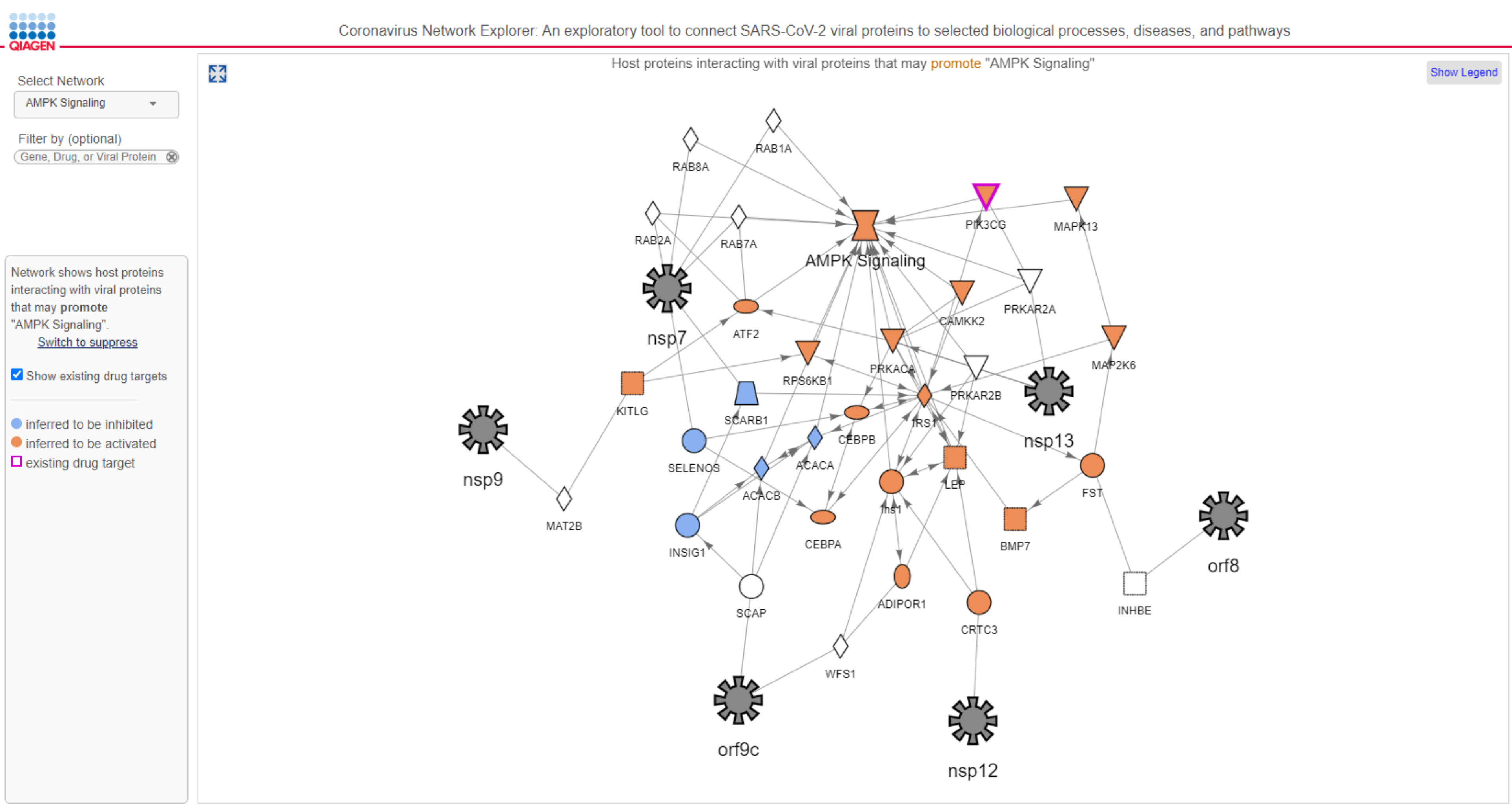
Advanced Analytics (AA)

- Causal Network Analysis
- Upstream regulator Analysis
- Downstream Effects Analysis
- Regulator Effects
- Network Analysis
- Mechanistic Network
- Activity Plot
- Graphic Summary
- Analysis Match

- MicroRNA Target Filter
- Relationship Export
- IsoProfiler
- Comparison Analysis
- PhosphoProteomics Analysis

https://www.qiagenbioinformatics.com/files/flyers/IPA_Advanced_Analytics_WEB.pdf

Coronavirus Network Explorer



Coronavirus Network Explorer: An exploratory tool to connect SARS-CoV-2 viral proteins to selected biological processes, diseases, and pathways

Select Network: AMPK Signaling

Filter by (optional): Gene, Drug, or Viral Protein

Network shows host proteins interacting with viral proteins that may **promote** "AMPK Signaling".

Switch to suppress

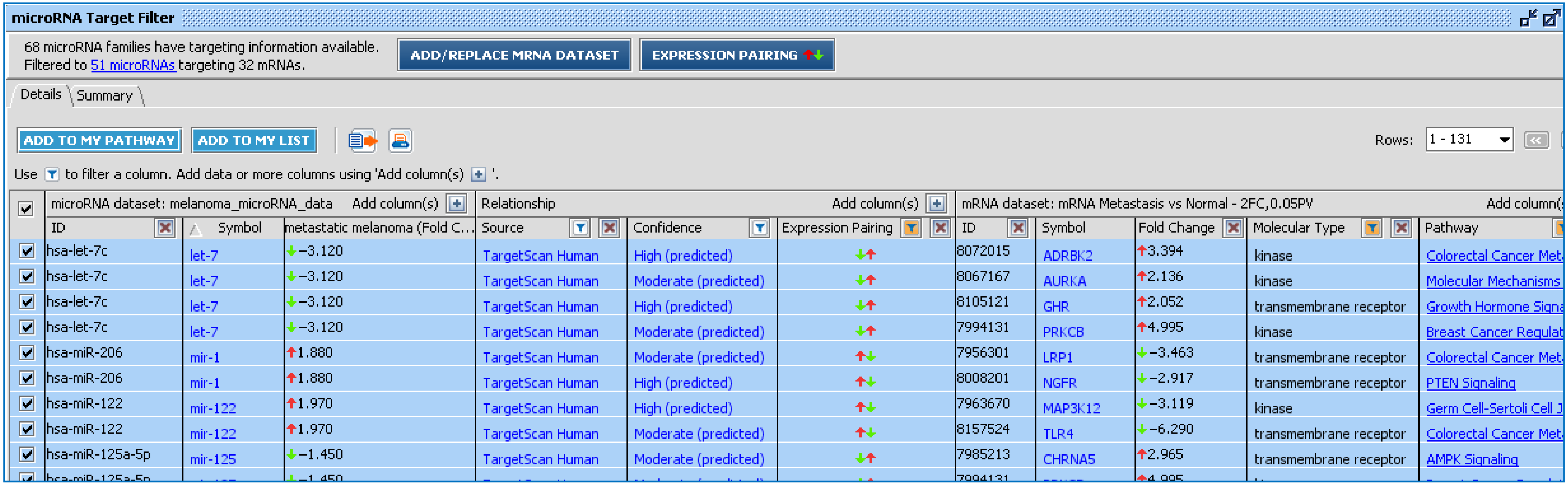
☑ Show existing drug targets

- 🔵 inferred to be inhibited
- 🟠 inferred to be activated
- ☐ existing drug target

Host proteins interacting with viral proteins that may promote "AMPK Signaling"

https://digitalinsights.qiagen.com/coronavirus-network-explorer/

Filter Datasets for Biomarkers or miRNA Targets



68 microRNA families have targeting information available.
Filtered to 51 microRNAs targeting 32 mRNAs.

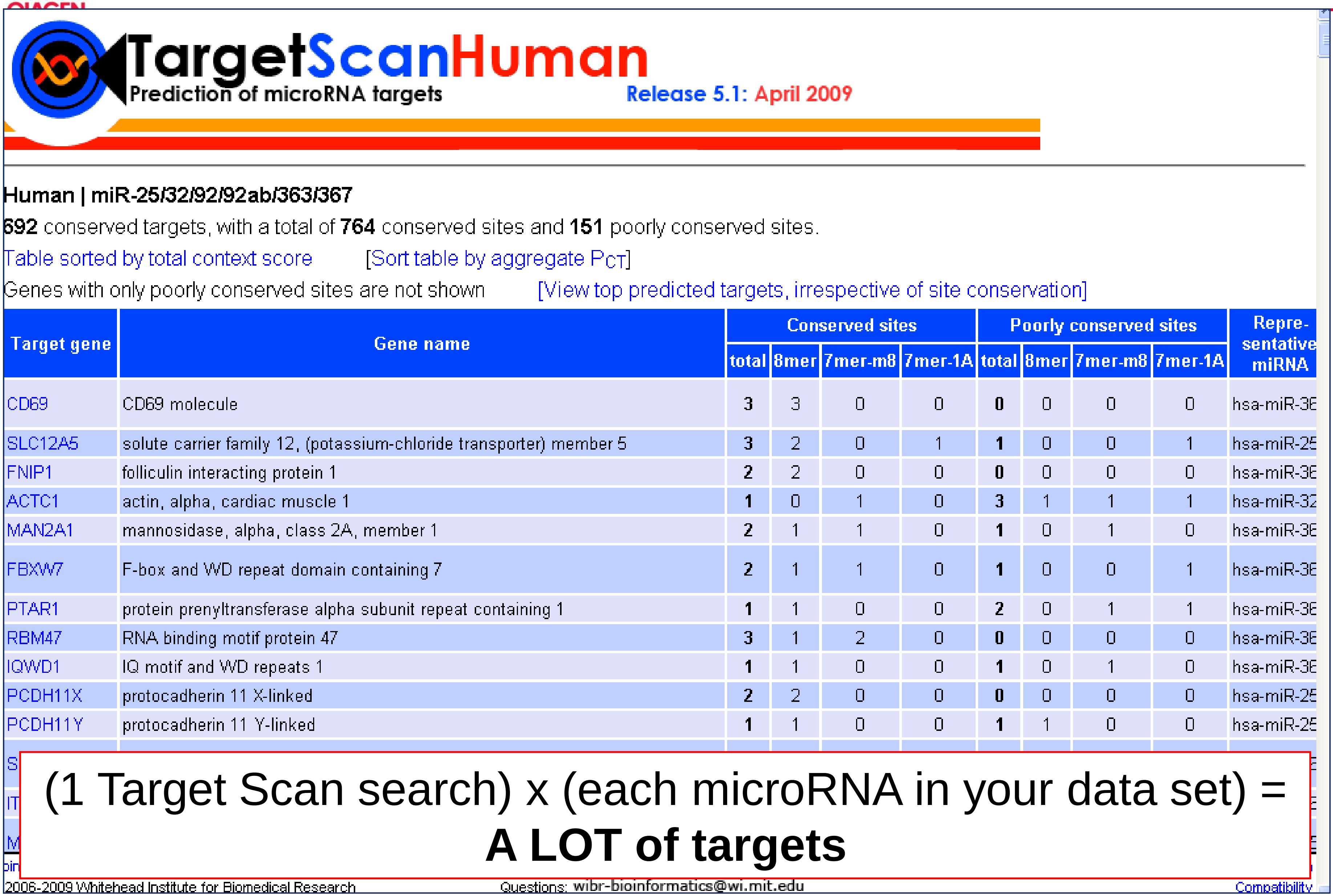
Use to filter a column. Add data or more columns using 'Add column(s) '.

	microRNA dataset: melanoma_microRNA_data Add column(s)			Relationship Add column(s)			mRNA dataset: mRNA Metastasis vs Normal - 2FC,0.05PV Add column(				
☑	ID	Symbol	metastatic melanoma (Fold C...	Source	Confidence	Expression Pairing	ID	Symbol	Fold Change	Molecular Type	Pathway
☑	hsa-let-7c	let-7	↓-3.120	TargetScan Human	High (predicted)	↓↑	8072015	ADRBK2	↑3.394	kinase	Colorectal Cancer Met
☑	hsa-let-7c	let-7	↓-3.120	TargetScan Human	Moderate (predicted)	↓↑	8067167	AURKA	↑2.136	kinase	Molecular Mechanisms
☑	hsa-let-7c	let-7	↓-3.120	TargetScan Human	High (predicted)	↓↑	8105121	GHR	↑2.052	transmembrane receptor	Growth Hormone Signa
☑	hsa-let-7c	let-7	↓-3.120	TargetScan Human	Moderate (predicted)	↓↑	7994131	PRKCB	↑4.995	kinase	Breast Cancer Regulat
☑	hsa-miR-206	mir-1	↑1.880	TargetScan Human	Moderate (predicted)	↑↓	7956301	LRP1	↓-3.463	transmembrane receptor	Colorectal Cancer Met
☑	hsa-miR-206	mir-1	↑1.880	TargetScan Human	High (predicted)	↑↓	8008201	NGFR	↓-2.917	transmembrane receptor	PTEN Signaling
☑	hsa-miR-122	mir-122	↑1.970	TargetScan Human	High (predicted)	↑↓	7963670	MAP3K12	↓-3.119	kinase	Germ Cell-Sertoli Cell J
☑	hsa-miR-122	mir-122	↑1.970	TargetScan Human	Moderate (predicted)	↑↓	8157524	TLR4	↓-6.290	transmembrane receptor	Colorectal Cancer Met
☑	hsa-miR-125a-5p	mir-125	↓-1.450	TargetScan Human	Moderate (predicted)	↓↑	7985213	CHRNA5	↑2.965	transmembrane receptor	AMPK Signaling

miRNA Data → miRNA Target Filter → Molecule Type → Pathways (Cancer/ Growth) → mRNA → ↑↓ ↓↑ → ?

miRNA Data	miRNA Target Filter	Molecule Type	Pathways (Cancer/ Growth)	mRNA	↑↓ ↓↑
88 data points	13,690 targets	1,090 targets	333 targets	39 targets	32 targets

Use Pathway tools to build hypothesis for microRNA to mRNA target association



Human | miR-25/32/92/92ab/363/367

692 conserved targets, with a total of **764** conserved sites and **151** poorly conserved sites.

Table sorted by total context score [Sort table by aggregate P_{CT}]

Genes with only poorly conserved sites are not shown [View top predicted targets, irrespective of site conservation]

Target gene	Gene name	Conserved sites				Poorly conserved sites				Repre-sentative miRNA
		total	8mer	7mer-m8	7mer-1A	total	8mer	7mer-m8	7mer-1A	
CD69	CD69 molecule	**3**	3	0	0	**0**	0	0	0	hsa-miR-3
SLC12A5	solute carrier family 12, (potassium-chloride transporter) member 5	**3**	2	0	1	**1**	0	0	1	hsa-miR-2
FNIP1	folliculin interacting protein 1	**2**	2	0	0	**0**	0	0	0	hsa-miR-3
ACTC1	actin, alpha, cardiac muscle 1	**1**	0	1	0	**3**	1	1	1	hsa-miR-3
MAN2A1	mannosidase, alpha, class 2A, member 1	**2**	1	1	0	**1**	0	1	0	hsa-miR-3
FBXW7	F-box and WD repeat domain containing 7	**2**	1	1	0	**1**	0	0	1	hsa-miR-3
PTAR1	protein prenyltransferase alpha subunit repeat containing 1	**1**	1	0	0	**2**	0	1	1	hsa-miR-3
RBM47	RNA binding motif protein 47	**3**	1	2	0	**0**	0	0	0	hsa-miR-3
IQWD1	IQ motif and WD repeats 1	**1**	1	0	0	**1**	0	1	0	hsa-miR-3
PCDH11X	protocadherin 11 X-linked	**2**	2	0	0	**0**	0	0	0	hsa-miR-2
PCDH11Y	protocadherin 11 Y-linked	**1**	1	0	0	**1**	1	0	0	hsa-miR-2

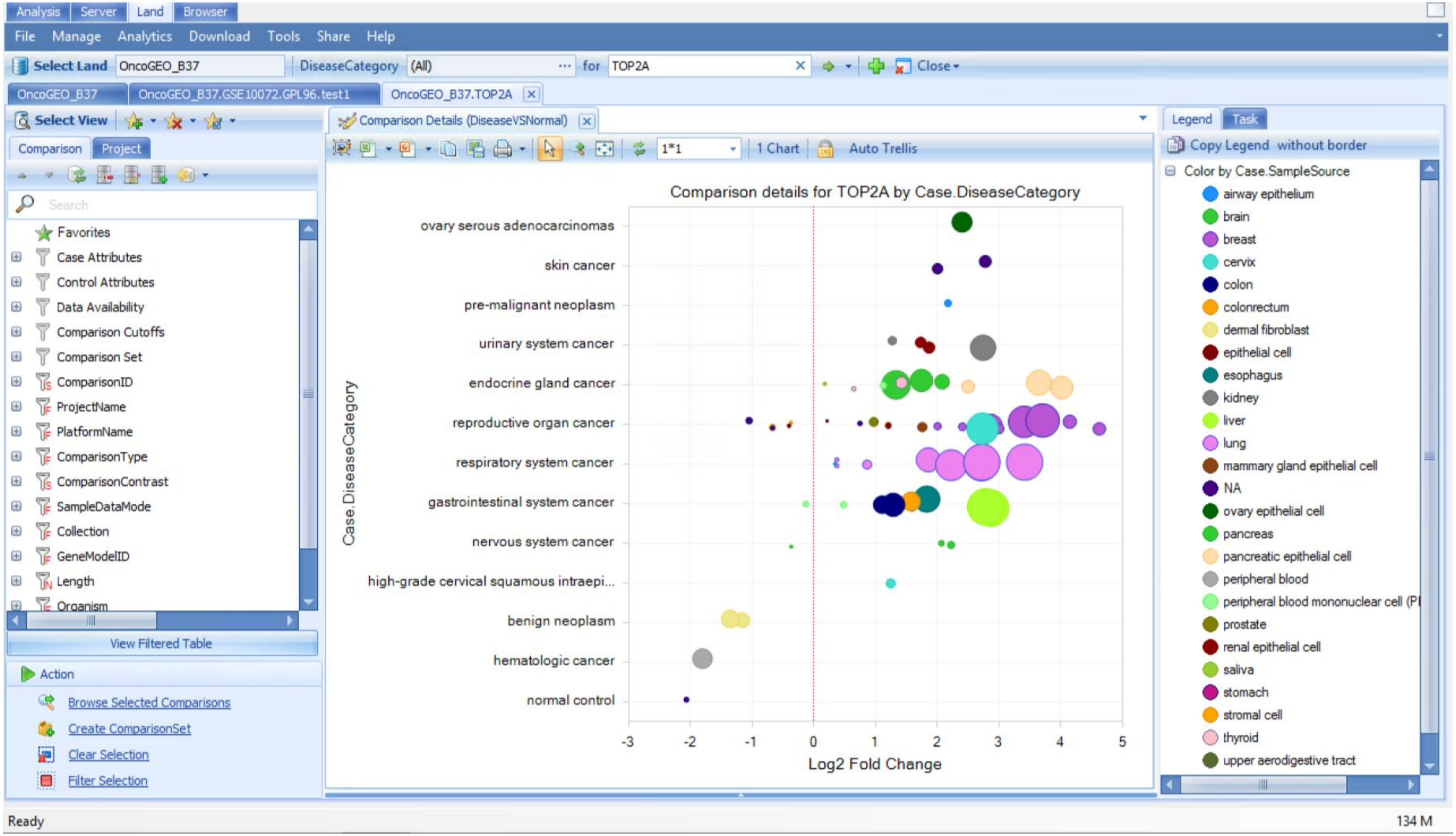
2006-2009 Whitehead Institute for Biomedical Research Questions: wibr-bioinformatics@wi.mit.edu Compatibility

(1 Target Scan search) x (each microRNA in your data set) =

A LOT of targets

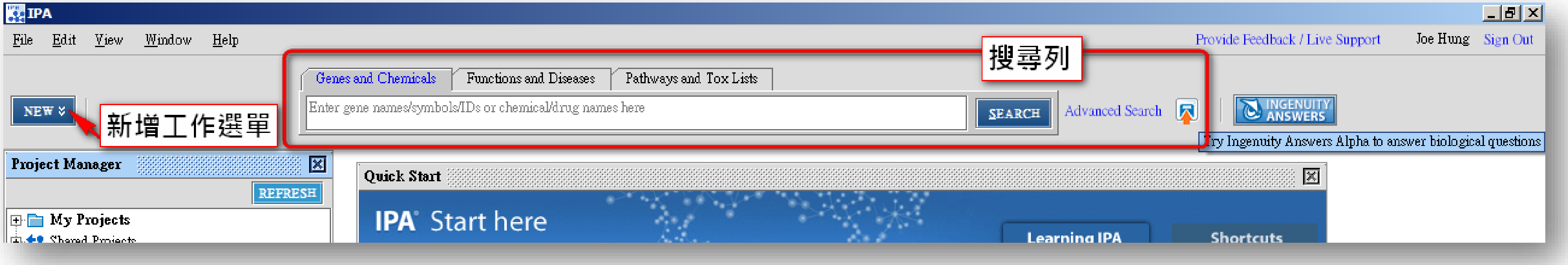
OmicSoft Array Suite provides detailed view of underlying data

Visualizing an individual gene across comparisons



Searching

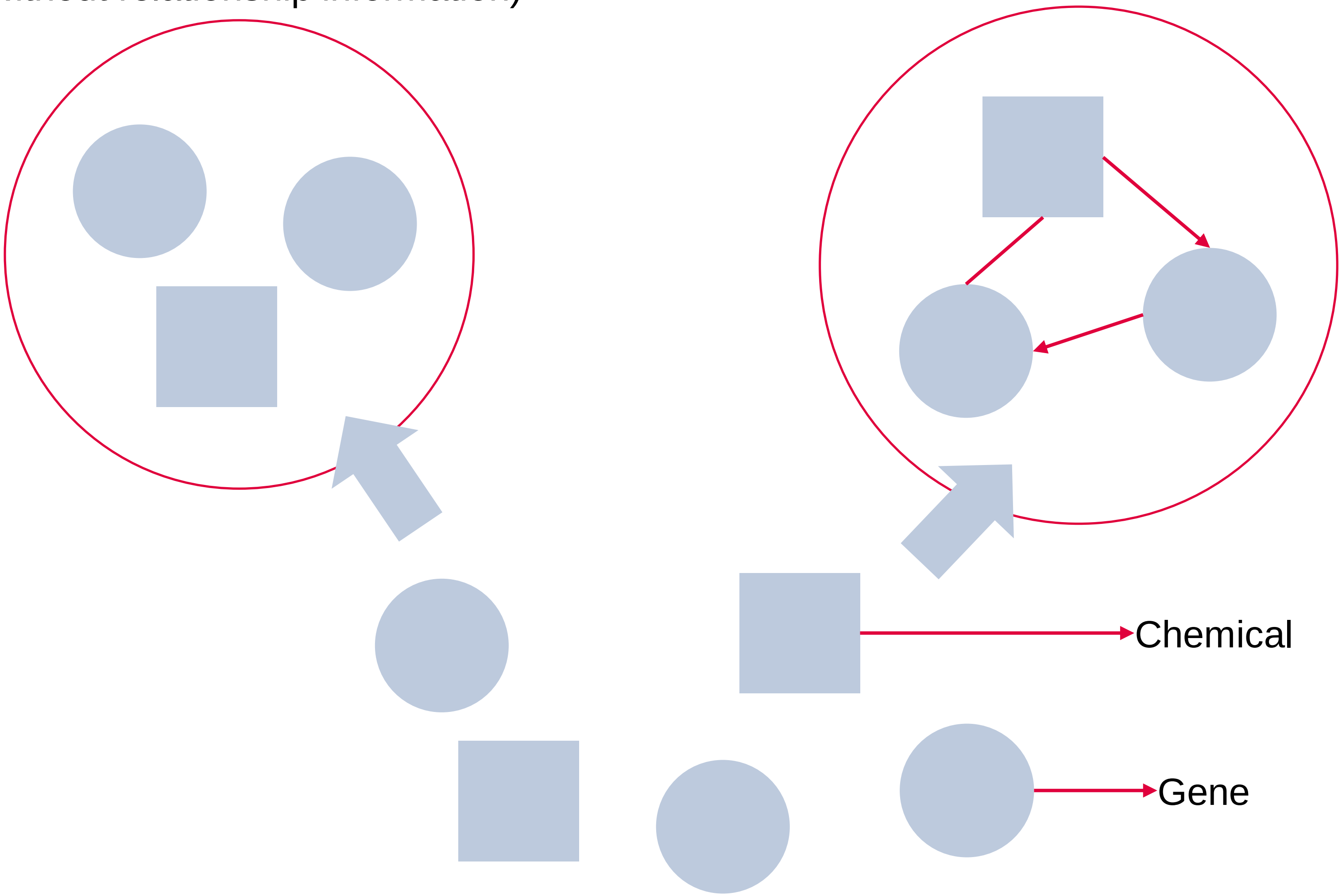
- **Genes and chemicals**
- **Diseases and Functions**
- **Pathways and tox lists**
- Advanced search: Limiting results to a molecule type, family or subcellular location



搜尋列

新增工作選單

Scales for Gene/Chemical, Disease, Pathway

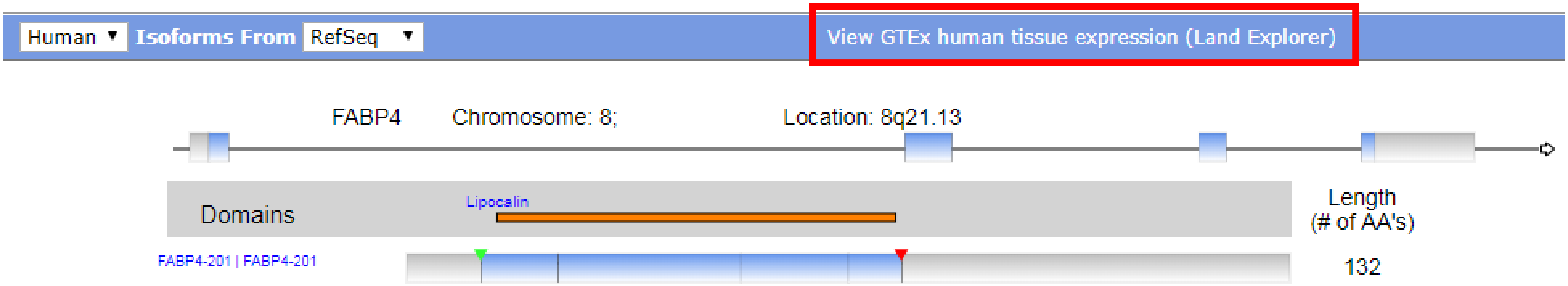


Set of Genes and Chemicals associated with Disease/Function (without relationship information)

Set of Genes and Chemicals associated with Disease/Function (with relationship information)

Gene View

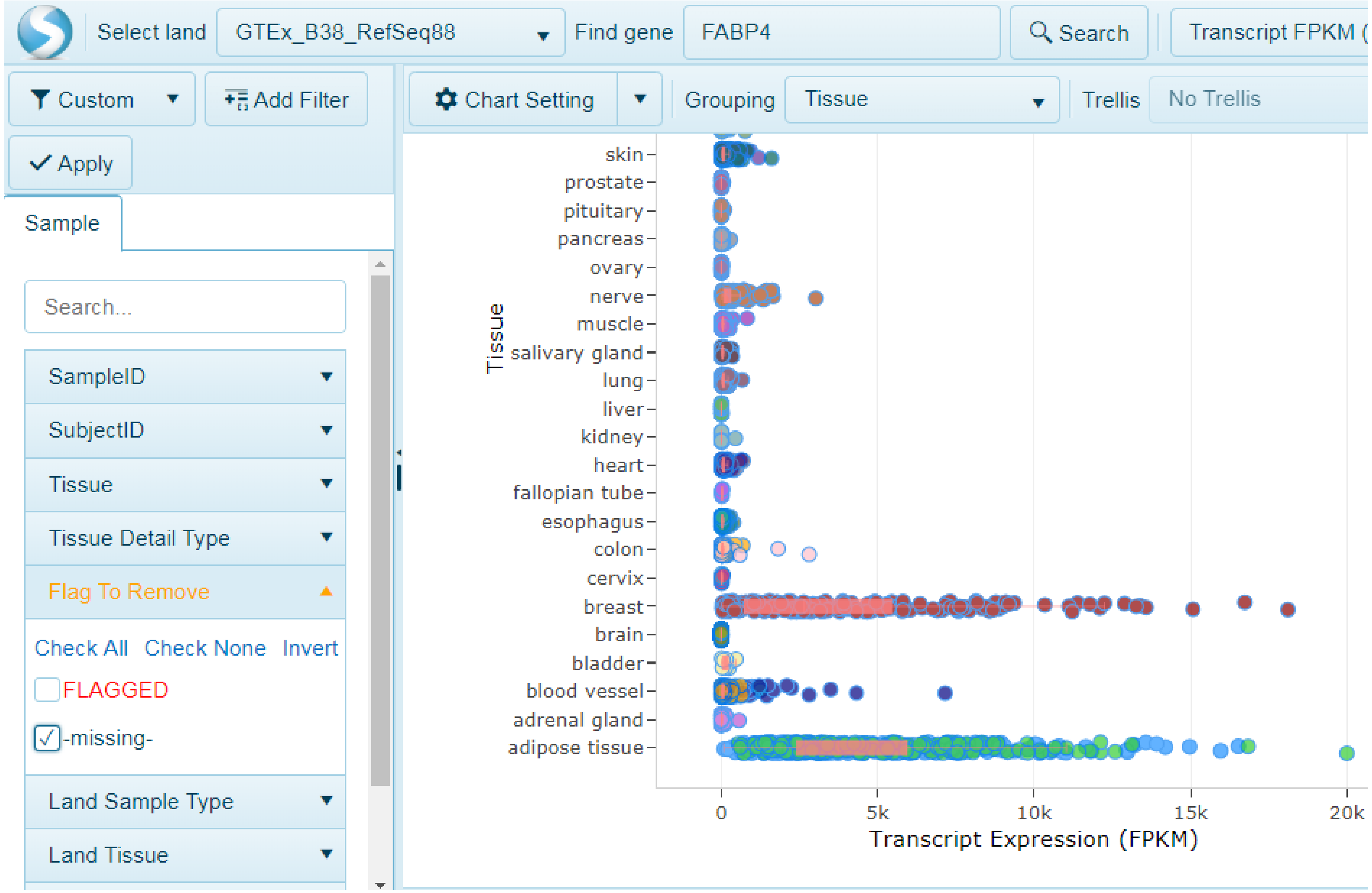
- **Explore sample-level human tissue expression through OmicSoft Land Explorer**



Now you can examine detailed expression patterns across human tissues directly from IPA’s Isoform Views. IPA now offers access to a lite version of OmicSoft Land Explorer. With this new feature, you can provide interactive plots of gene expression in 51 different human tissues from the GTEx project, for both gene level and individual splice variants. You can filter the view for a particular tissue, or filter on metadata, such as tissue donor age or gender. You can also download the detailed sample-level expression data for the gene.

Gene View

- **View of human isoform-level expression in human tissue samples for FABP4**



Select land GTEx_B38_RefSeq88

Find gene FABP4

Transcript FPKM (

Grouping Tissue

Trellis No Trellis

☐ FLAGGED

☑ -missing-

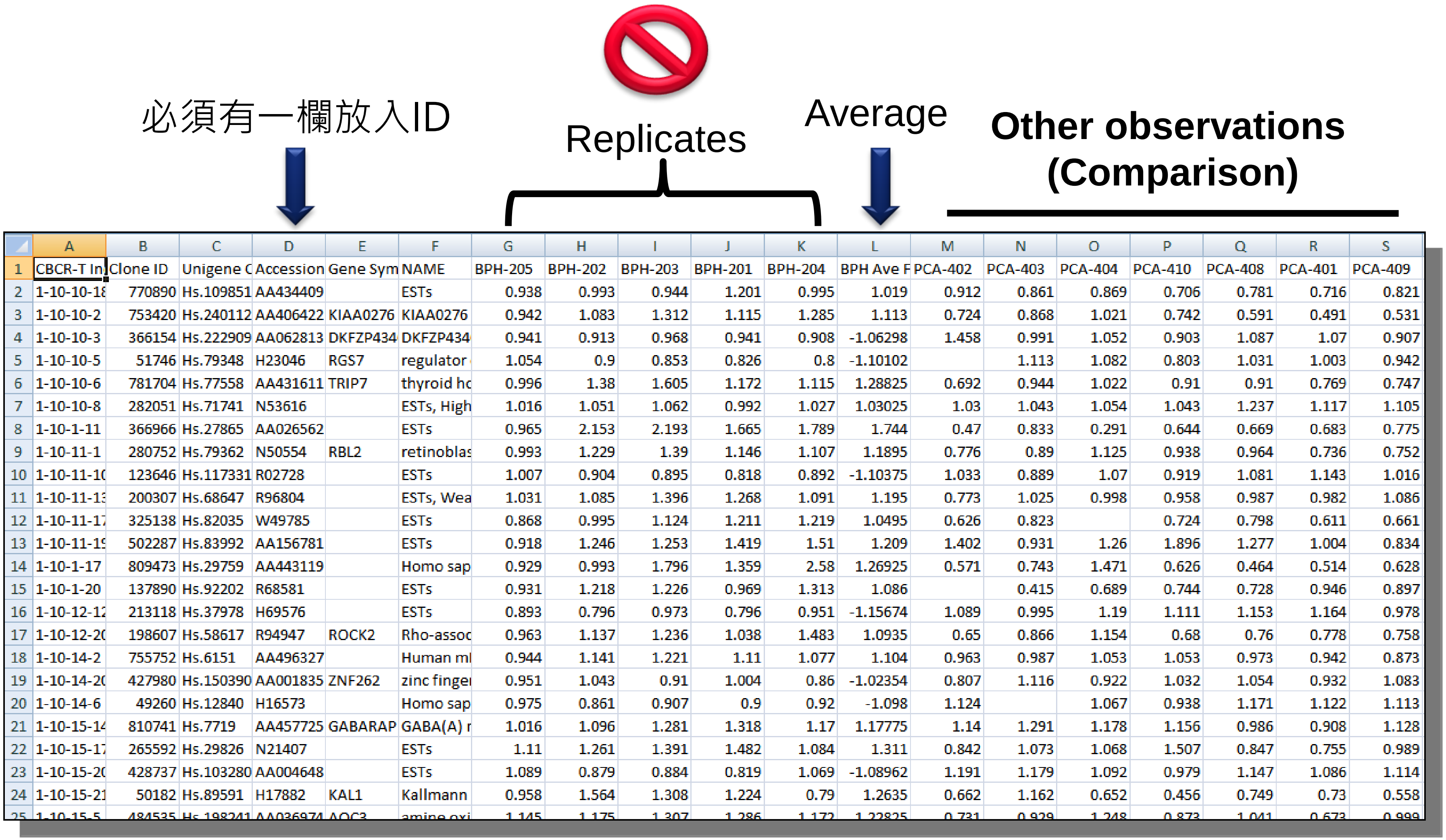
Key Terminology

- **Finding:6.6 million**
  - A single piece of evidence from a literature source or database in the **Ingenuity Knowledge Base**
  - Includes context of the fact such as experiment type, species, tissue/cell location, etc.

- **Canonical Pathway (Signaling and Metabolic)**
  - Are generated prior to data input, based on the literature
  - Do NOT change upon data input
  - Do have directionality

Live Demo

準備IPA分析用的Dataset



必須有一欄放入ID

Replicates

Average

Other observations (Comparison)

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S
1	CBCR-T In	Clone ID	Unigene C	Accession	Gene Sym	NAME	BPH-205	BPH-202	BPH-203	BPH-201	BPH-204	BPH Ave F	PCA-402	PCA-403	PCA-404	PCA-410	PCA-408	PCA-401	PCA-409
2	1-10-10-18	770890	Hs.109851	AA434409		ESTs	0.938	0.993	0.944	1.201	0.995	1.019	0.912	0.861	0.869	0.706	0.781	0.716	0.821
3	1-10-10-2	753420	Hs.240112	AA406422	KIAA0276	KIAA0276	0.942	1.083	1.312	1.115	1.285	1.113	0.724	0.868	1.021	0.742	0.591	0.491	0.531
4	1-10-10-3	366154	Hs.222909	AA062813	DKFZP434	DKFZP434	0.941	0.913	0.968	0.941	0.908	-1.06298	1.458	0.991	1.052	0.903	1.087	1.07	0.907
5	1-10-10-5	51746	Hs.79348	H23046	RGS7	regulator	1.054	0.9	0.853	0.826	0.8	-1.10102		1.113	1.082	0.803	1.031	1.003	0.942
6	1-10-10-6	781704	Hs.77558	AA431611	TRIP7	thyroid hc	0.996	1.38	1.605	1.172	1.115	1.28825	0.692	0.944	1.022	0.91	0.91	0.769	0.747
7	1-10-10-8	282051	Hs.71741	N53616		ESTs, High	1.016	1.051	1.062	0.992	1.027	1.03025	1.03	1.043	1.054	1.043	1.237	1.117	1.105
8	1-10-1-11	366966	Hs.27865	AA026562		ESTs	0.965	2.153	2.193	1.665	1.789	1.744	0.47	0.833	0.291	0.644	0.669	0.683	0.775
9	1-10-11-1	280752	Hs.79362	N50554	RBL2	retinoblas	0.993	1.229	1.39	1.146	1.107	1.1895	0.776	0.89	1.125	0.938	0.964	0.736	0.752
10	1-10-11-10	123646	Hs.117331	R02728		ESTs	1.007	0.904	0.895	0.818	0.892	-1.10375	1.033	0.889	1.07	0.919	1.081	1.143	1.016
11	1-10-11-13	200307	Hs.68647	R96804		ESTs, Wea	1.031	1.085	1.396	1.268	1.091	1.195	0.773	1.025	0.998	0.958	0.987	0.982	1.086
12	1-10-11-17	325138	Hs.82035	W49785		ESTs	0.868	0.995	1.124	1.211	1.219	1.0495	0.626	0.823		0.724	0.798	0.611	0.661
13	1-10-11-19	502287	Hs.83992	AA156781		ESTs	0.918	1.246	1.253	1.419	1.51	1.209	1.402	0.931	1.26	1.896	1.277	1.004	0.834
14	1-10-1-17	809473	Hs.29759	AA443119		Homo sap	0.929	0.993	1.796	1.359	2.58	1.26925	0.571	0.743	1.471	0.626	0.464	0.514	0.628
15	1-10-1-20	137890	Hs.92202	R68581		ESTs	0.931	1.218	1.226	0.969	1.313	1.086		0.415	0.689	0.744	0.728	0.946	0.897
16	1-10-12-12	213118	Hs.37978	H69576		ESTs	0.893	0.796	0.973	0.796	0.951	-1.15674	1.089	0.995	1.19	1.111	1.153	1.164	0.978
17	1-10-12-20	198607	Hs.58617	R94947	ROCK2	Rho-assoc	0.963	1.137	1.236	1.038	1.483	1.0935	0.65	0.866	1.154	0.68	0.76	0.778	0.758
18	1-10-14-2	755752	Hs.6151	AA496327		Human ml	0.944	1.141	1.221	1.11	1.077	1.104	0.963	0.987	1.053	1.053	0.973	0.942	0.873
19	1-10-14-20	427980	Hs.150390	AA001835	ZNF262	zinc finge	0.951	1.043	0.91	1.004	0.86	-1.02354	0.807	1.116	0.922	1.032	1.054	0.932	1.083
20	1-10-14-6	49260	Hs.12840	H16573		Homo sap	0.975	0.861	0.907	0.9	0.92	-1.098	1.124		1.067	0.938	1.171	1.122	1.113
21	1-10-15-14	810741	Hs.7719	AA457725	GABARAP	GABA(A) r	1.016	1.096	1.281	1.318	1.17	1.17775	1.14	1.291	1.178	1.156	0.986	0.908	1.128
22	1-10-15-17	265592	Hs.29826	N21407		ESTs	1.11	1.261	1.391	1.482	1.084	1.311	0.842	1.073	1.068	1.507	0.847	0.755	0.989
23	1-10-15-20	428737	Hs.103280	AA004648		ESTs	1.089	0.879	0.884	0.819	1.069	-1.08962	1.191	1.179	1.092	0.979	1.147	1.086	1.114
24	1-10-15-21	50182	Hs.89591	H17882	KAL1	Kallmann	0.958	1.564	1.308	1.224	0.79	1.2635	0.662	1.162	0.652	0.456	0.749	0.73	0.558
25	1-10-15-5	484535	Hs.198241	AA036974	AOC3	amine oxi	1.145	1.175	1.307	1.286	1.172	1.22825	0.731	0.929	1.248	0.873	1.041	0.673	0.999

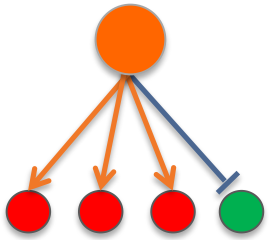
準備IPA分析用的Dataset

- **重複性實驗的數值平均、p-vlaue或fold-change等統計計算，要先在IPA分析之前完成。**

- **將實驗資料用 Excel 表格檔案儲存，檔案裡面只能有一個Sheet存在。**
  - □ Excel Sheet當中必須要有一欄是列出**分子的ID** (如Gene Symbol, Refseq number, Uniprot number, HMDB等常用命名皆支援)
  - □ 每個Excel Sheet 最多可以放入 **20個 observations** (即20個實驗變因的資料欄的意思)
  - □ 每個Observation可以有3個不同的表現值種類 (ex. p-Value，fold-change等)
  - □ **表格欄位最上方只能有一個Head row (首行)**
  - □ 資料上傳到IPA後，可以在cut-off 值欄位進行設定，讓使用者決定門檻來決定**表現顯著有差異**的生物分子。意味著原始實驗資料中有些分子的數值不夠顯著，可以用cut-off值作為門檻排除於分析運算中。那些通過cut-off值的分子們在IPA中稱之為Analysis-Ready Molecules。

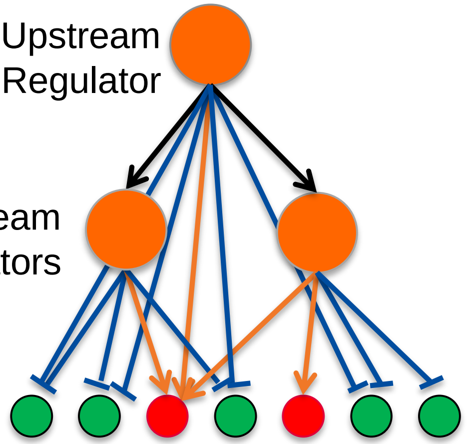
Network types in IPA

Upstream Analysis



Dataset Molecules

Mechanistic Network of Upstream Regulators



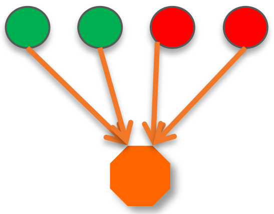
Upstream Regulator

Other upstream regulators

Dataset Molecules

Function Analysis

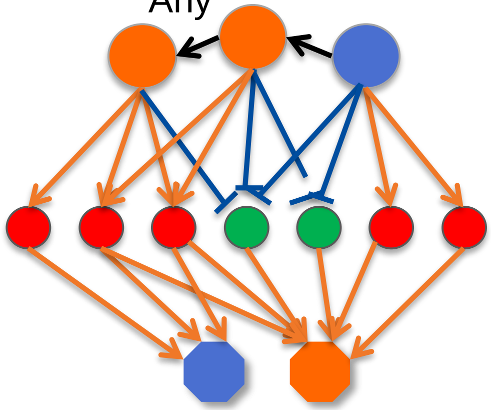
Dataset Molecules



Diseases / functions

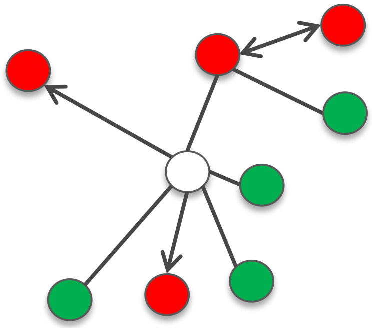
Regulator Effect Network

Any



Diseases / functions

Interaction Network



Dataset Molecules

IPA 分析結果

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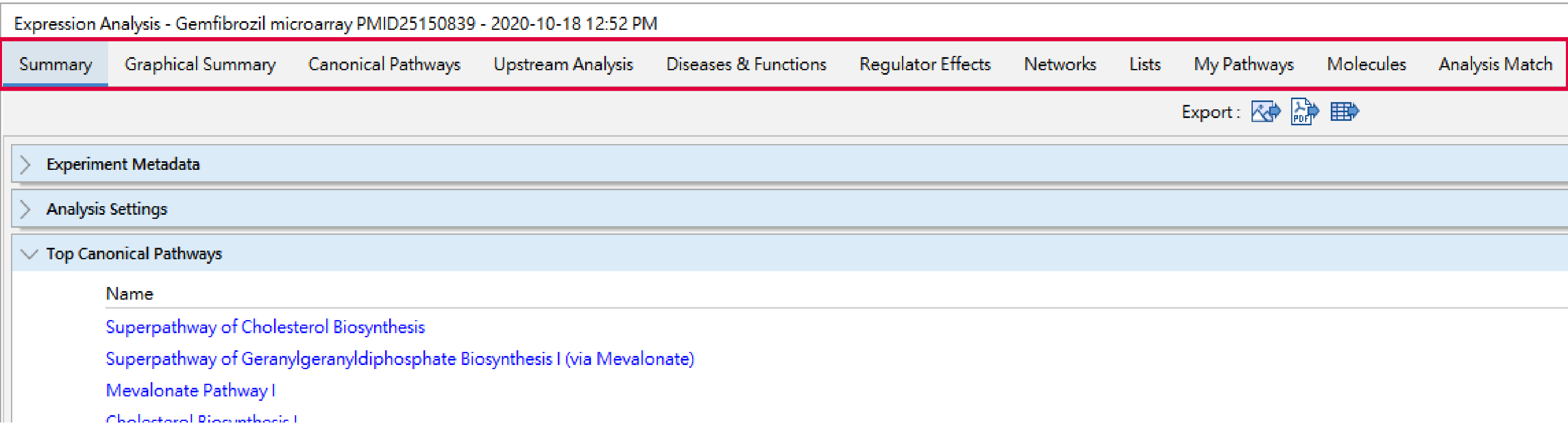

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Name
Superpathway of Cholesterol Biosynthesis
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)
Mevalonate Pathway I
Cholesterol Biosynthesis I

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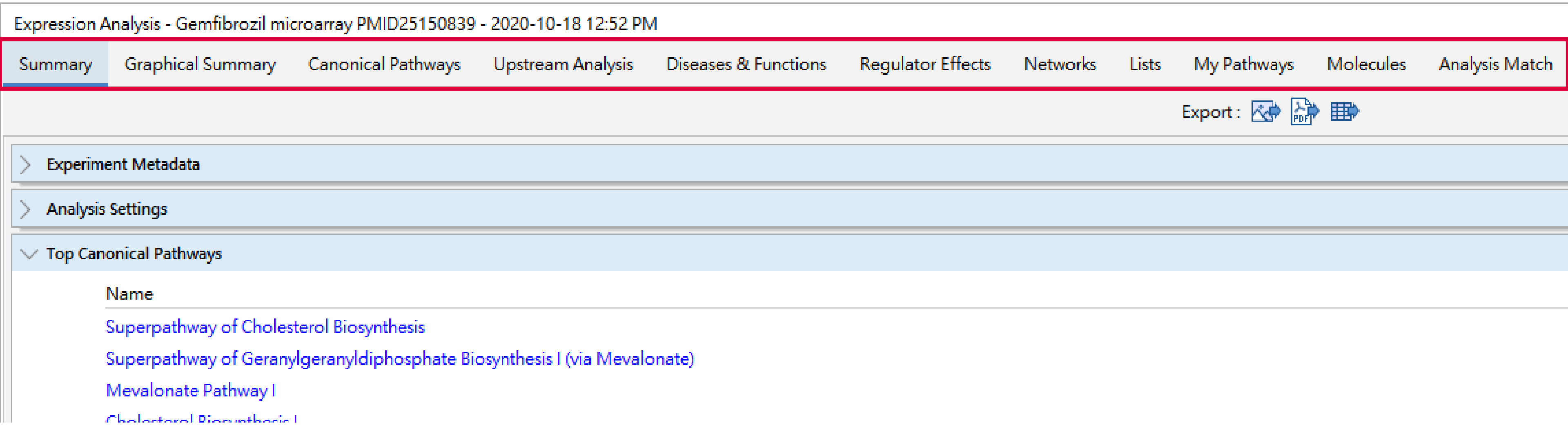

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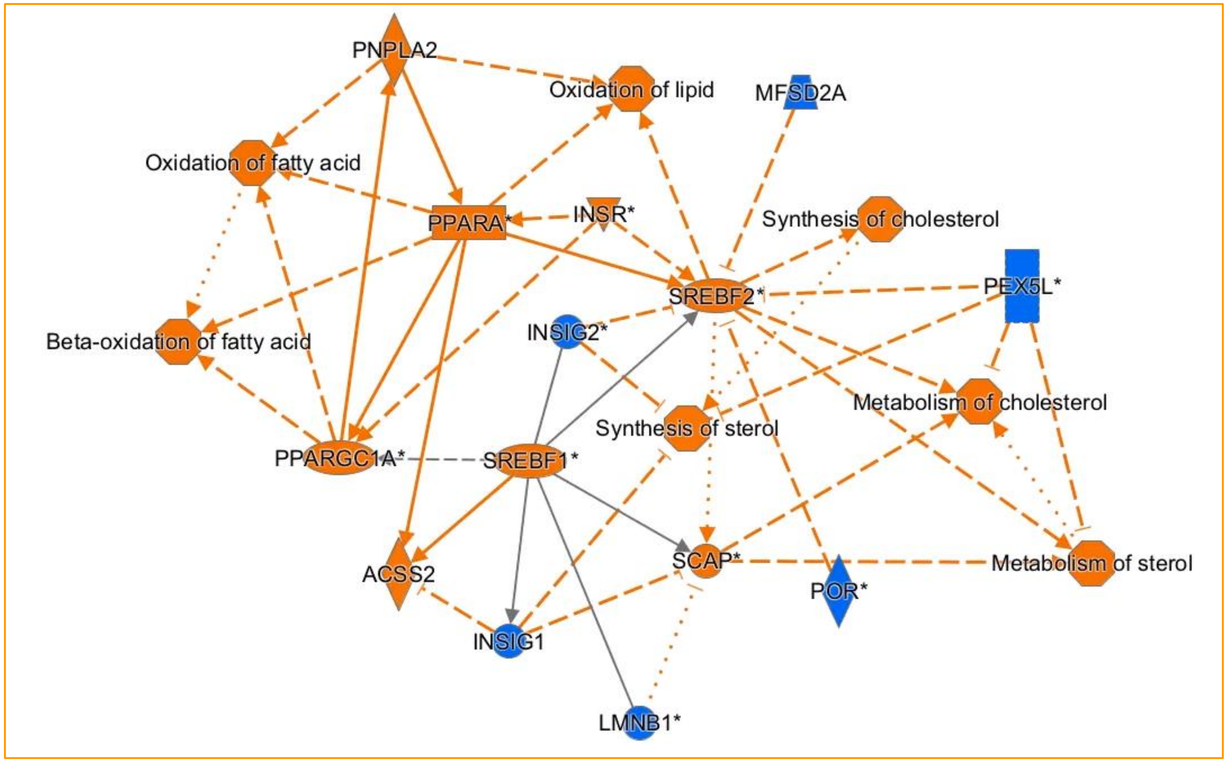
Graphical Summary

Graphical Summary結果:
將資料集最相關的生物主題以網路圖像呈現
(canonical pathways, upstream regulators, causal network master regulators, diseases, and biological functions)



Criteria for selection

- □ All entities:
  p-value < 0.05
- □ Diseases、Functions、Upstream regulators:
  z-score ≧ 2
- □ All molecules types
  (except chemicals)

- □ Activated nodes
  z-score ≧ 2
- □ Inhibited nodes
  z-score ≦ -2

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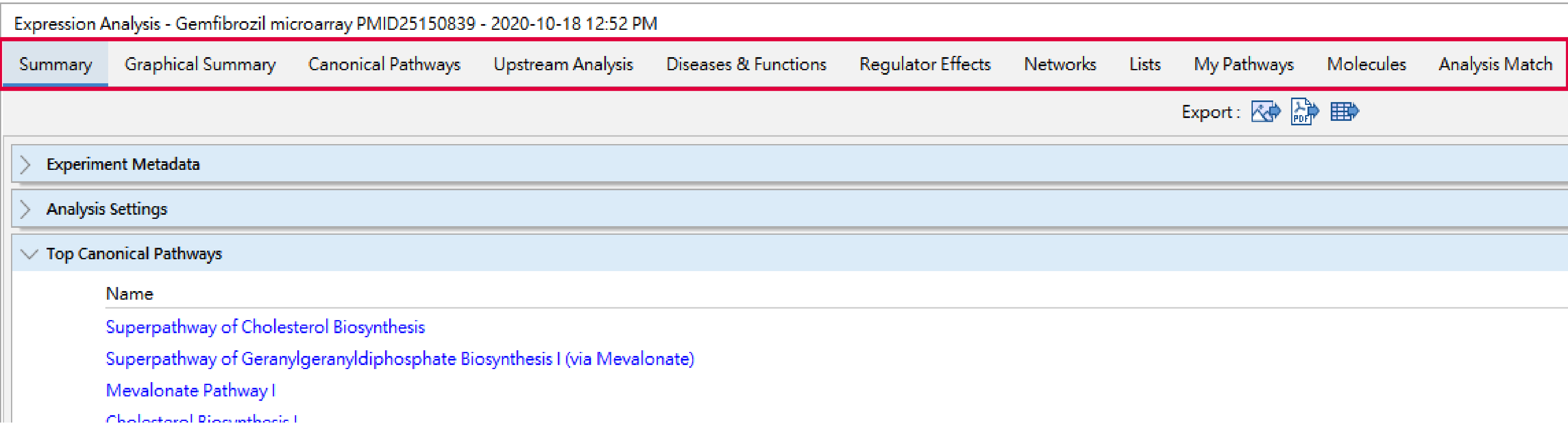

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Experiment Metadata

Analysis Settings

Top Canonical Pathways

Name
Superpathway of Cholesterol Biosynthesis
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)
Mevalonate Pathway I
Cholesterol Biosynthesis I

Canonical Pathway Analysis

Canonical Pathways結果標籤:
受影響的Signaling Pathway與Metabolic Pathway 依照顯著性用條狀圖**排列**

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

點擊特定Canonical Pathway名稱上方的Bar條，下方視窗會出現dataset 中有參與組成該 pathway的分子 ID

10 molecule(s) associated with **Cholesterol Biosynthesis III (via Desmosterol) at Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM** [Ratio: 10/13 (0.769)] [z-score: 3.16

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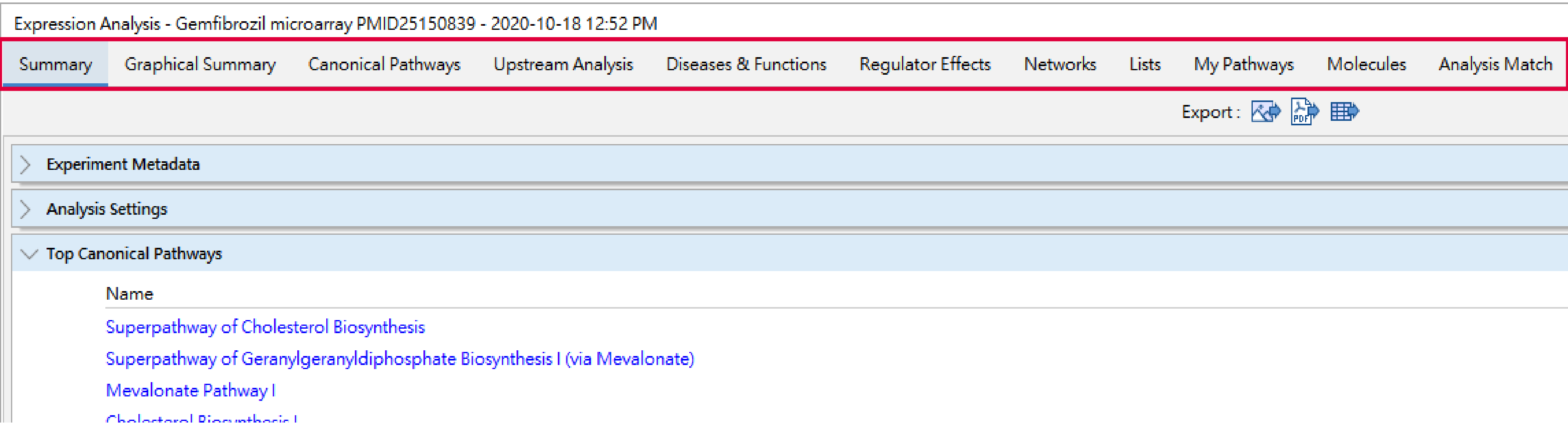

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

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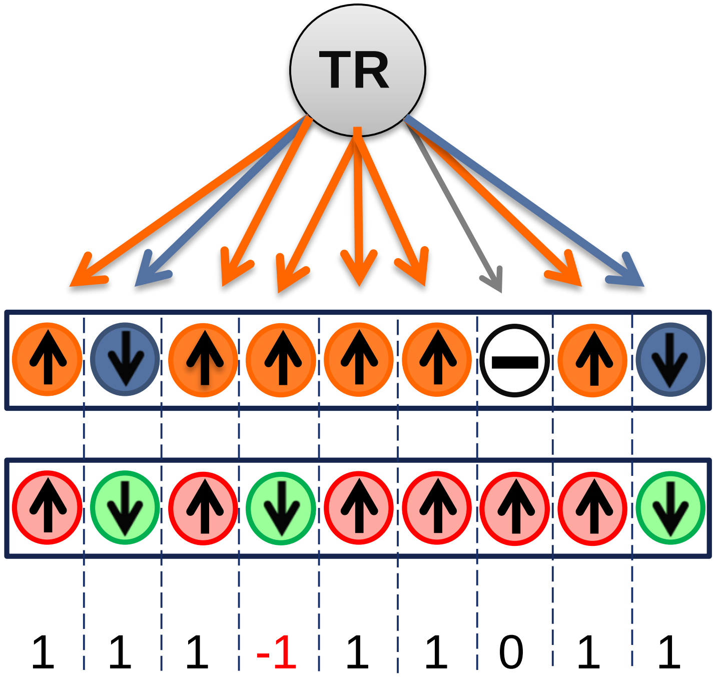
Upstream Analysis Activation z–score

Statistical measure of correlation between the transcription regulator (TR) and resulting gene expression



N = 8 genes

TR effect on downstream genes
(Literature)

Differential gene expression
(Uploaded Data)

z-score > 2 or < -2 is considered significant

Actual z-score *can* be weighted by relationship types, relationship bias, data bias

Upstream Analysis Activation z–score

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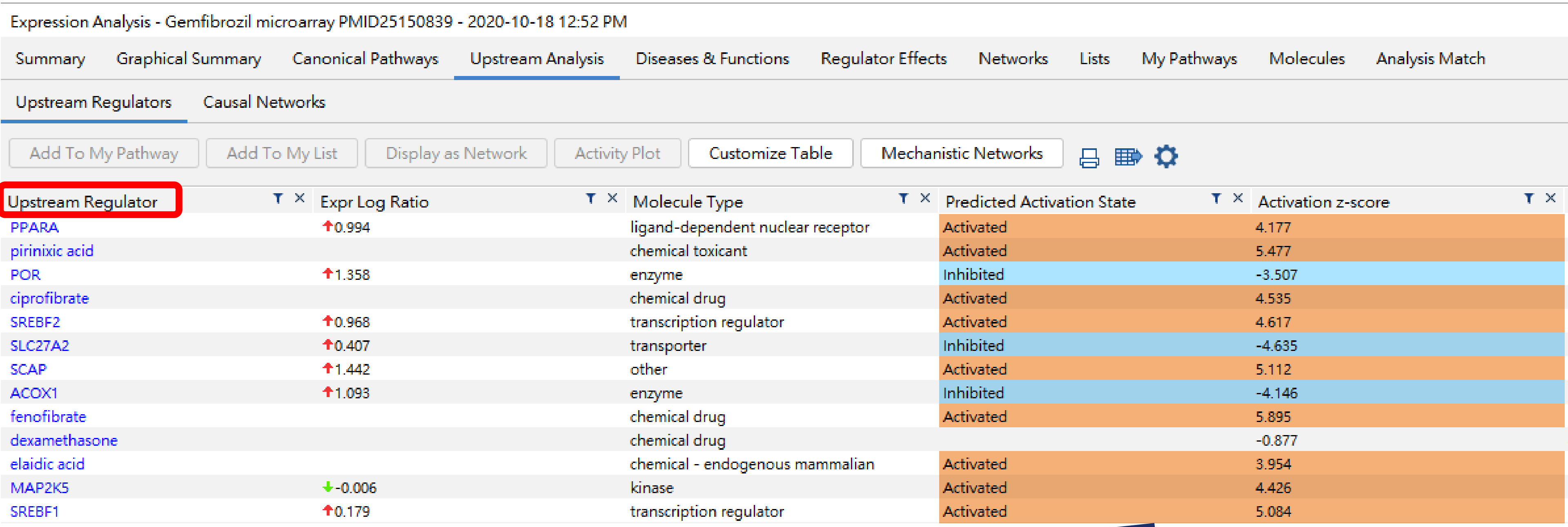

Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activation State	Activation z-score
PPARA	↑0.994	ligand-dependent nuclear receptor	Activated	4.177
pirinixic acid		chemical toxicant	Activated	5.477
POR	↑1.358	enzyme	Inhibited	-3.507
ciprofibrate		chemical drug	Activated	4.535
SREBF2	↑0.968	transcription regulator	Activated	4.617
SLC27A2	↑0.407	transporter	Inhibited	-4.635
SCAP	↑1.442	other	Activated	5.112
ACOX1	↑1.093	enzyme	Inhibited	-4.146
fenofibrate		chemical drug	Activated	5.895
dexamethasone		chemical drug		-0.877
elaidic acid		chemical - endogenous mammalian	Activated	3.954
MAP2K5	↓-0.006	kinase	Activated	4.426
SREBF1	↑0.179	transcription regulator	Activated	5.084

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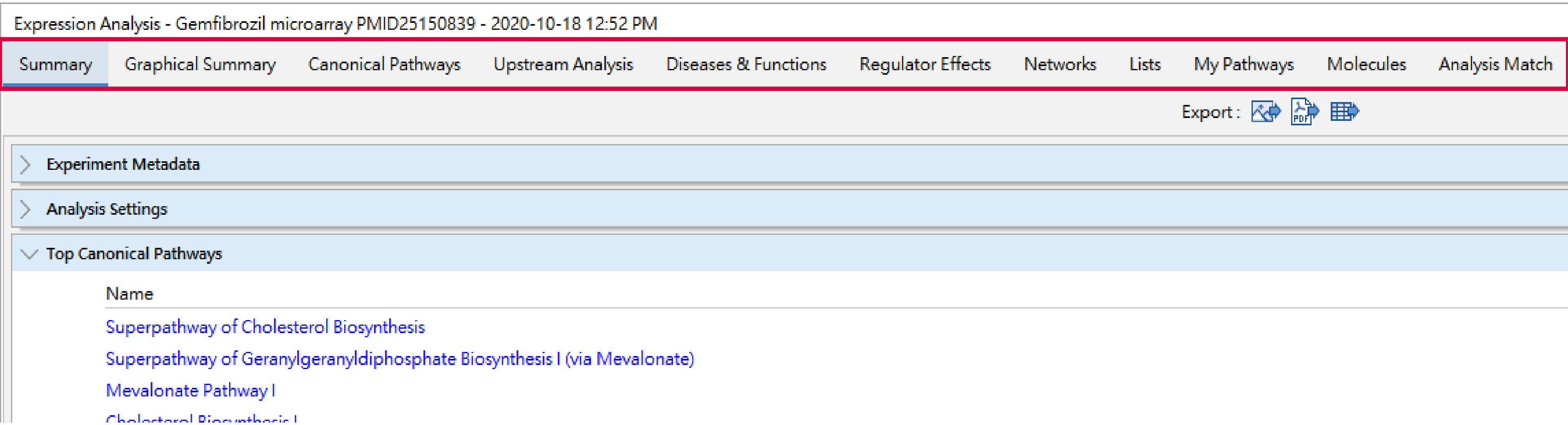


Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

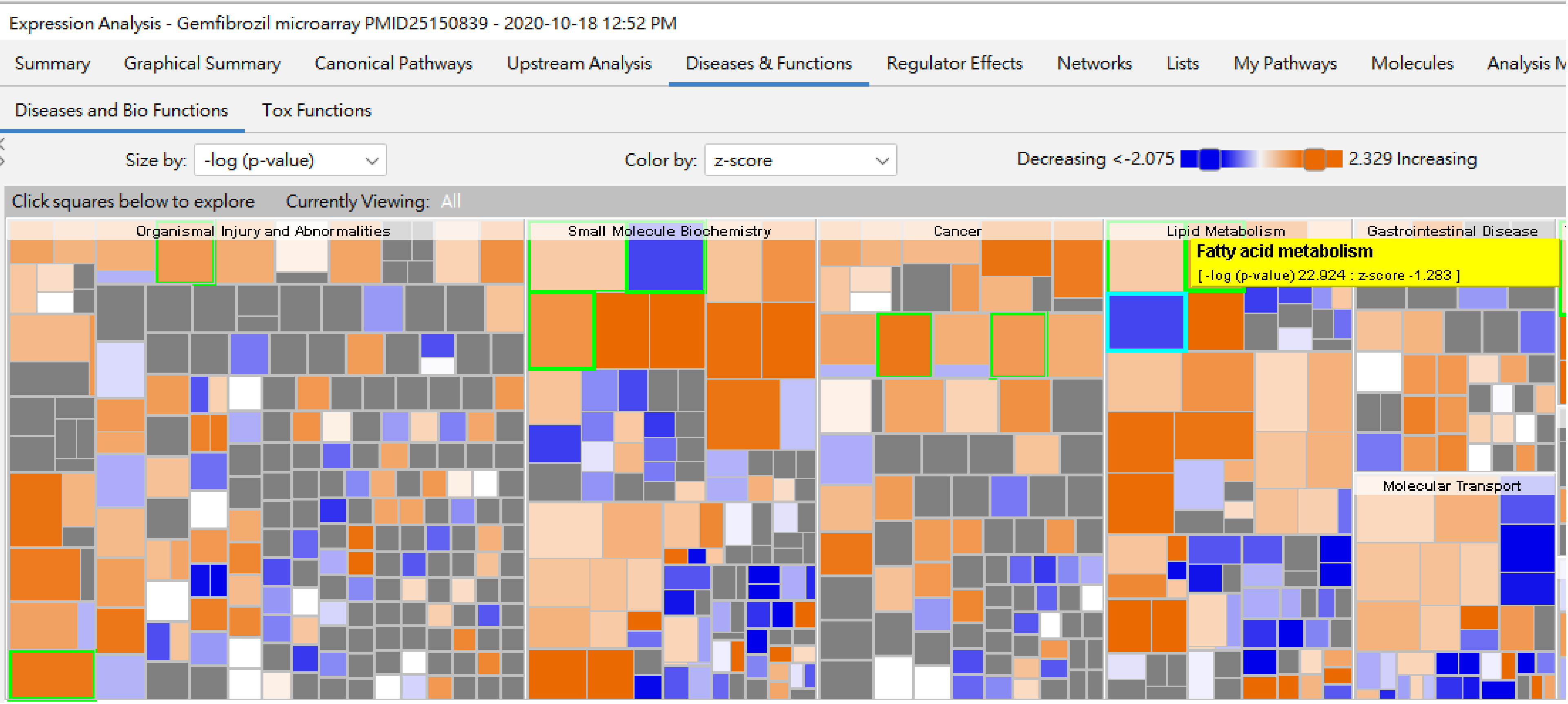
Superpathway of Cholesterol Biosynthesis

Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)

Mevalonate Pathway I

Diseases and functions

Diseases and functions結果標籤:
了解實驗結果在各分析疾病調控上之結果



Expression Analysis - Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM

Size by: -log (p-value)

Color by: z-score

Decreasing <-2.075 2.329 Increasing

Click squares below to explore Currently Viewing: All

Fatty acid metabolism
[-log (p-value) 22.924 : z-score -1.283]

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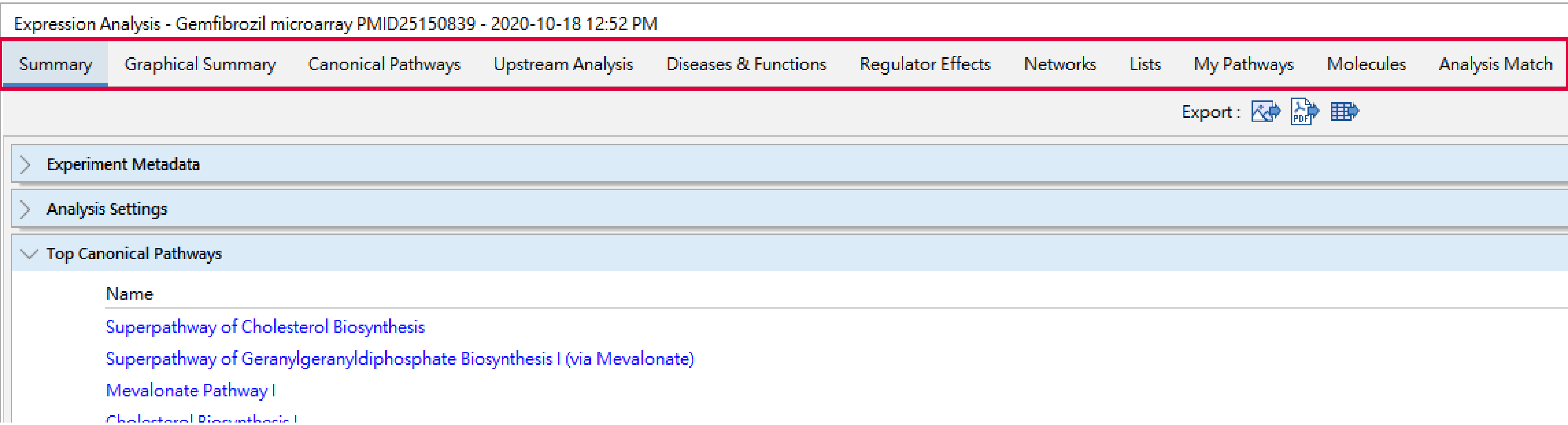

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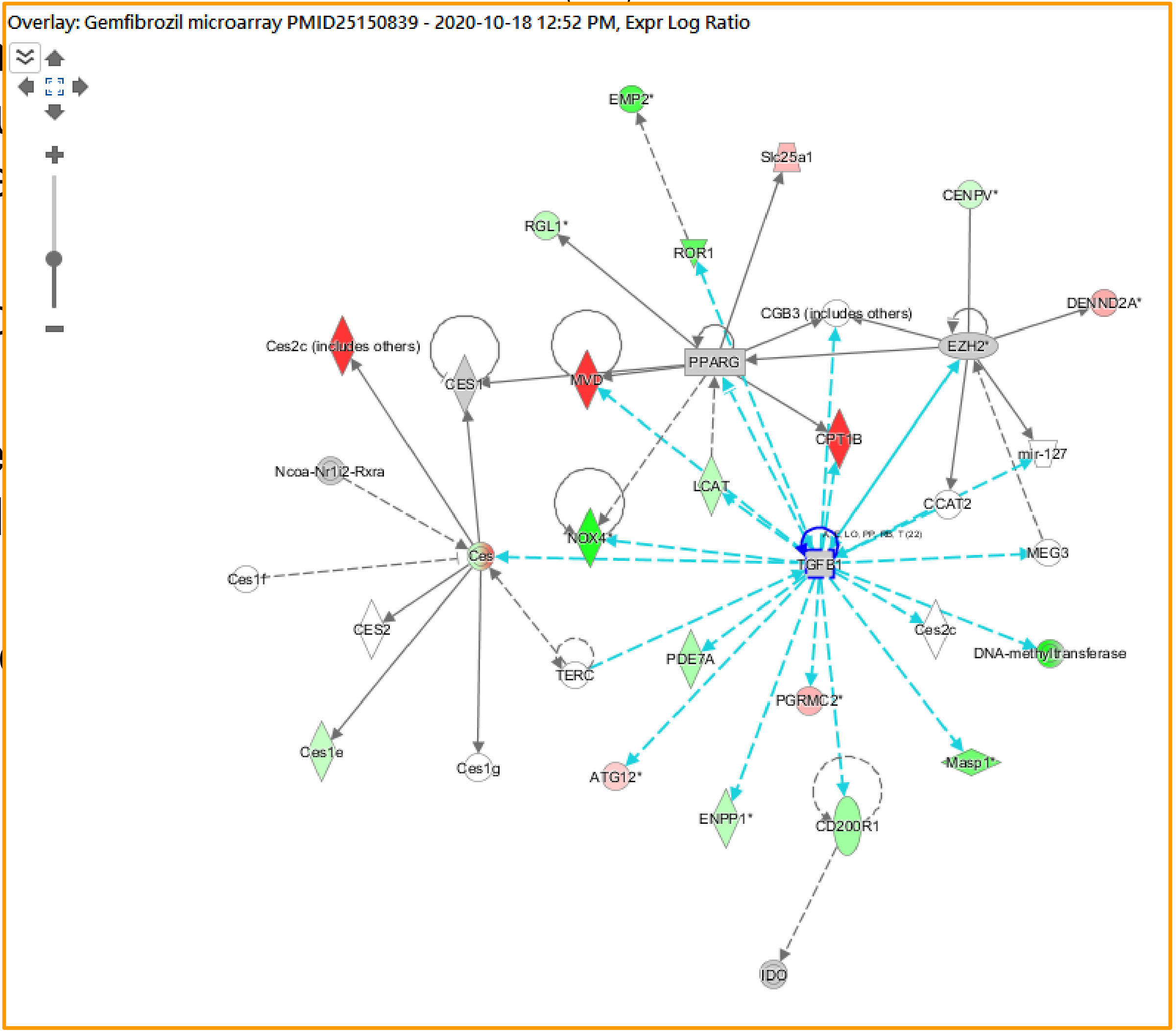
Superpathway of Cholesterol Biosynthesis
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)
Mevalonate Pathway I
Cholesterol Biosynthesis I

How Networks Are Generated

1. Focus molecules are “seeds”
2. Focus molecules with th
   interactions to other focu
   are then connected toge
   network
3. Non-focus molecules fro
   dataset are then added
4. Molecules from the Inge
   Knowledge Base are ad
5. Resulting Networks are
   then sorted based on the



Overlay: Gemfibrozil microarray PMID25150839 - 2020-10-18 12:52 PM, Expr Log Ratio

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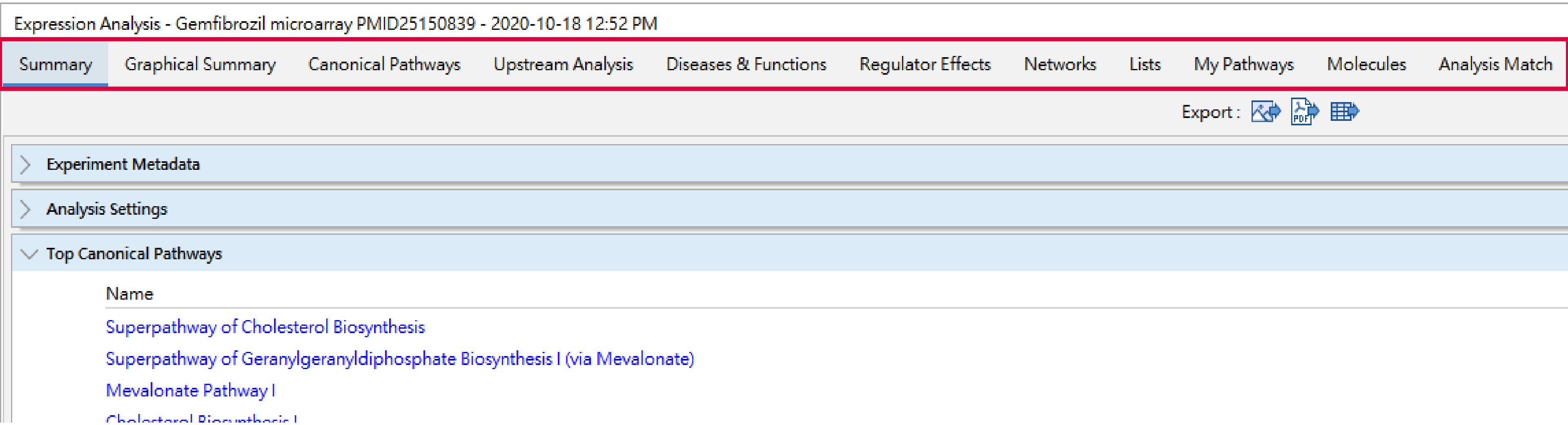
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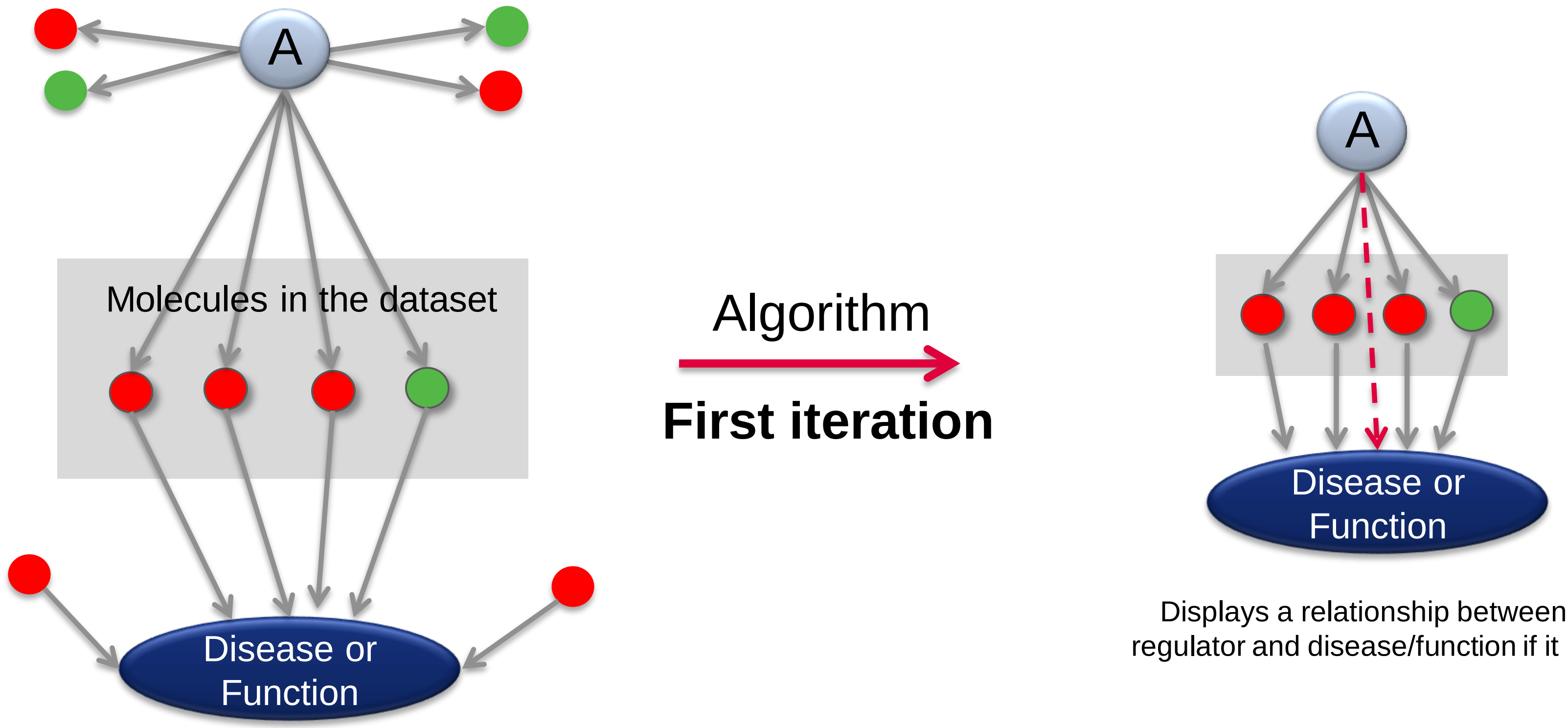
Concept of “Regulator Effects”

Hypotheses for how activated or inhibited upstream regulators cause downstream effects on biology

Upstream Regulators

Simplest Regulator Effects result



Displays a relationship between the regulator and disease/function if it exists

Downstream Effects Analysis

Causally consistent networks score higher

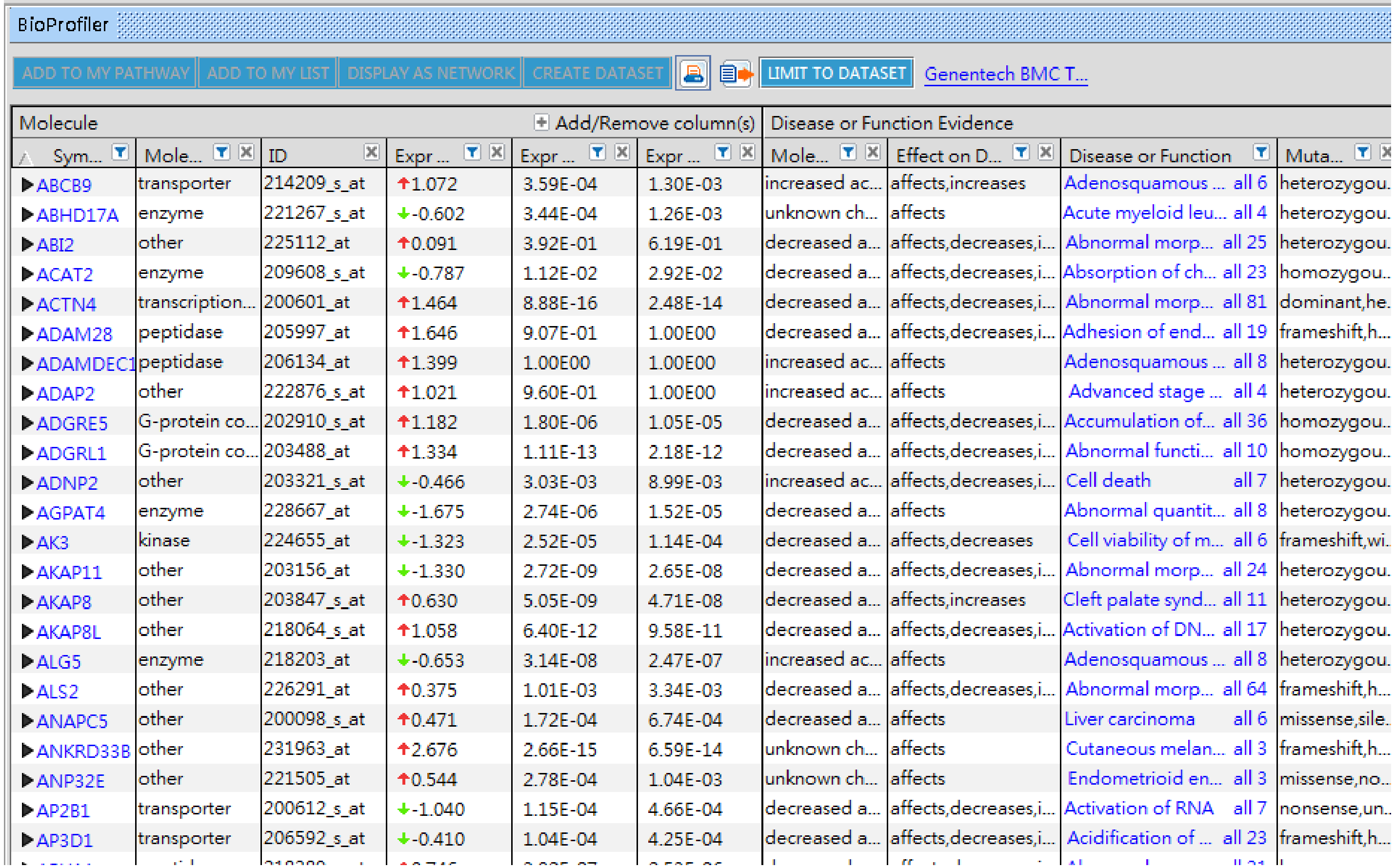
The algorithm runs iteratively to merge additional regulators with diseases and functions

Live Demo

BioProfiler

BioProfiler

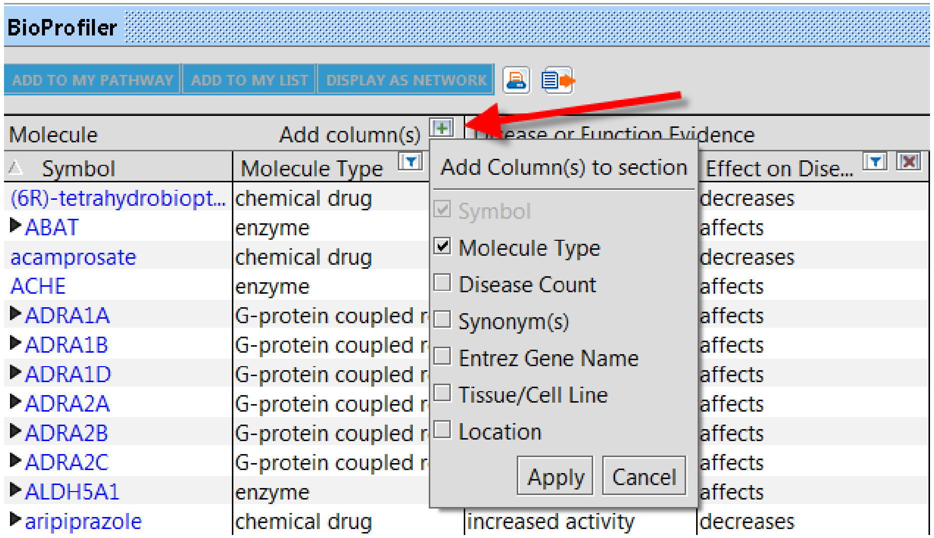
BioProfiler allows you to make novel discoveries by providing you the ability to filter the fine-grained relationships between molecules (genes, RNAs, proteins, and chemicals) and diseases or functions.



Molecule					Add/Remove column(s)	Disease or Function Evidence			
Sym...	Mole...	ID	Expr ...	Expr ...	Expr ...	Mole...	Effect on D...	Disease or Function	Muta...
▶ABCB9	transporter	214209_s_at	↑1.072	3.59E-04	1.30E-03	increased ac...	affects,increases	Adenosquamous ... all 6	heterozygou.
▶ABHD17A	enzyme	221267_s_at	↓-0.602	3.44E-04	1.26E-03	unknown ch...	affects	Acute myeloid leu... all 4	heterozygou.
▶ABI2	other	225112_at	↑0.091	3.92E-01	6.19E-01	decreased a...	affects,decreases,i...	Abnormal morp... all 25	heterozygou.
▶ACAT2	enzyme	209608_s_at	↓-0.787	1.12E-02	2.92E-02	decreased a...	affects,decreases,i...	Absorption of ch... all 23	homozygou..
▶ACTN4	transcription...	200601_at	↑1.464	8.88E-16	2.48E-14	decreased a...	affects,decreases,i...	Abnormal morp... all 81	dominant,he.
▶ADAM28	peptidase	205997_at	↑1.646	9.07E-01	1.00E00	decreased a...	affects,decreases,i...	Adhesion of end... all 19	frameshift,h...
▶ADAMDEC1	peptidase	206134_at	↑1.399	1.00E00	1.00E00	increased ac...	affects	Adenosquamous ... all 8	heterozygou.
▶ADAP2	other	222876_s_at	↑1.021	9.60E-01	1.00E00	increased ac...	affects	Advanced stage ... all 4	heterozygou.
▶ADGRE5	G-protein co...	202910_s_at	↑1.182	1.80E-06	1.05E-05	decreased a...	affects,decreases,i...	Accumulation of... all 36	homozygou..
▶ADGRL1	G-protein co...	203488_at	↑1.334	1.11E-13	2.18E-12	decreased a...	affects,decreases,i...	Abnormal functi... all 10	homozygou..
▶ADNP2	other	203321_s_at	↓-0.466	3.03E-03	8.99E-03	increased ac...	affects,decreases,i...	Cell death all 7	heterozygou.
▶AGPAT4	enzyme	228667_at	↓-1.675	2.74E-06	1.52E-05	decreased a...	affects	Abnormal quantit... all 8	heterozygou.
▶AK3	kinase	224655_at	↓-1.323	2.52E-05	1.14E-04	decreased a...	affects,decreases	Cell viability of m... all 6	frameshift,wi..
▶AKAP11	other	203156_at	↓-1.330	2.72E-09	2.65E-08	decreased a...	affects,decreases,i...	Abnormal morp... all 24	heterozygou.
▶AKAP8	other	203847_s_at	↑0.630	5.05E-09	4.71E-08	decreased a...	affects,increases	Cleft palate synd... all 11	heterozygou.
▶AKAP8L	other	218064_s_at	↑1.058	6.40E-12	9.58E-11	decreased a...	affects,decreases,i...	Activation of DN... all 17	heterozygou.
▶ALG5	enzyme	218203_at	↓-0.653	3.14E-08	2.47E-07	increased ac...	affects	Adenosquamous ... all 8	heterozygou.
▶ALS2	other	226291_at	↑0.375	1.01E-03	3.34E-03	decreased a...	affects,decreases,i...	Abnormal morp... all 64	frameshift,h...
▶ANAPC5	other	200098_s_at	↑0.471	1.72E-04	6.74E-04	decreased a...	affects	Liver carcinoma all 6	missense,sile..
▶ANKRD33B	other	231963_at	↑2.676	2.66E-15	6.59E-14	unknown ch...	affects	Cutaneous melan... all 3	frameshift,h...
▶ANP32E	other	221505_at	↑0.544	2.78E-04	1.04E-03	unknown ch...	affects	Endometrioid en... all 3	missense,no..
▶AP2B1	transporter	200612_s_at	↓-1.040	1.15E-04	4.66E-04	decreased a...	affects,decreases,i...	Activation of RNA all 7	nonsense,un..
▶AP3D1	transporter	206592_s_at	↓-0.410	1.04E-04	4.25E-04	decreased a...	affects,decreases,i...	Acidification of ... all 23	frameshift,h...

BioProfiler

- Targets of toxicity: Which genes when [decreased] in activity [increase][liver cholestasis]? What types of [genetic] evidence support this?
- Target discovery: What [heterozygous knockouts] in [mouse] can [decrease] [asthma]?
- Which drugs or which targets have been in late stage clinical trials or approved to decrease [diabetes]?
- Biomarker research: Which genes are potential [diagnosis OR prognosis] biomarkers of [breast cancer] and are [upregulated] in breast cancer?

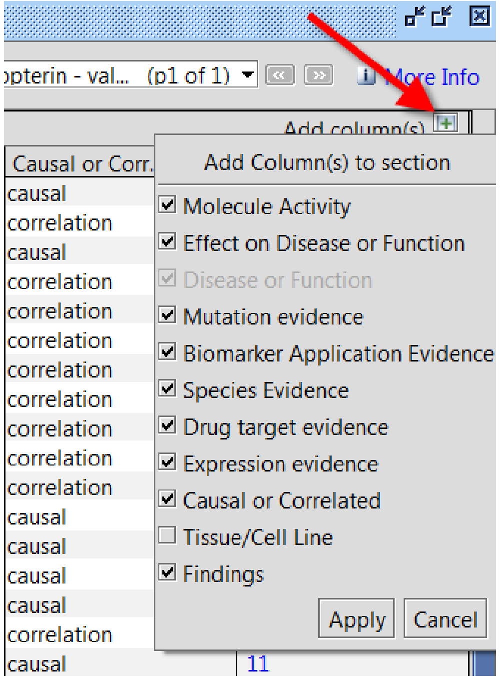


Molecule		ease or Function Evidence	
Symbol	Molecule Type		Effect on Dise...
(6R)-tetrahydrobiopt...	chemical drug		decreases
ABAT	enzyme		affects
acamprosate	chemical drug		decreases
ACHE	enzyme		affects
ADRA1A	G-protein coupled r		affects
ADRA1B	G-protein coupled r		affects
ADRA1D	G-protein coupled r		affects
ADRA2A	G-protein coupled r		affects
ADRA2B	G-protein coupled r		affects
ADRA2C	G-protein coupled r		affects
ALDH5A1	enzyme		affects
aripiprazole	chemical drug	increased activity	decreases

Add Column(s) to section

☑ Symbol
☑ Molecule Type
☐ Disease Count
☐ Synonym(s)
☐ Entrez Gene Name
☐ Tissue/Cell Line
☐ Location

Apply Cancel



Causal or Corr.
causal
correlation
causal
correlation
correlation
correlation
correlation
correlation
correlation
correlation
correlation
causal
causal
causal
causal
correlation
causal

11

Add Column(s) to section

☑ Molecule Activity
☑ Effect on Disease or Function
☑ Disease or Function
☑ Mutation evidence
☑ Biomarker Application Evidence
☑ Species Evidence
☑ Drug target evidence
☑ Expression evidence
☑ Causal or Correlated
☐ Tissue/Cell Line
☑ Findings

Apply Cancel

When will I use BioProfil

BioProfiler

ABCD2

- Type: Transporter
- Location: Cytoplasm
- Tissue: Adipose, Liver
- Disease: Abnormal Conduction by Nerves
- Effect: Decrease

HBZ

- Type: Transporter
- Location: Cytoplasm
- Tissue: Liver, Lung
- Disease: Abnormal Conduction by Nerves
- Effect: Increase

ARTN

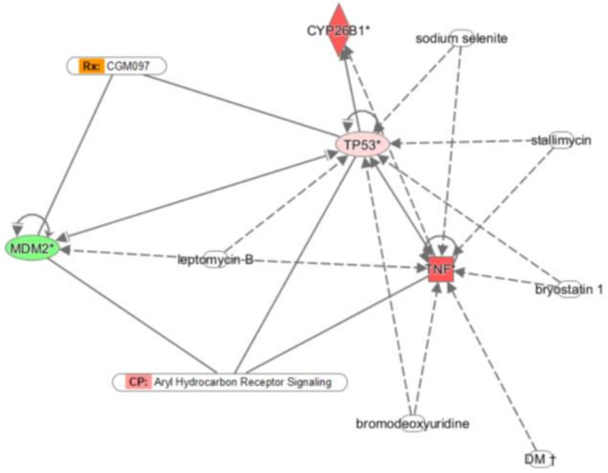
- Type: Growth Factor
- Location: Extracellular Space
- Tissue: Adrenal
- Disease: Abnormal Conduction by Nerves
- Effect: Decrease

- What kind of **Transporter** express in **Liver**?
  - ABCD2, HBZ

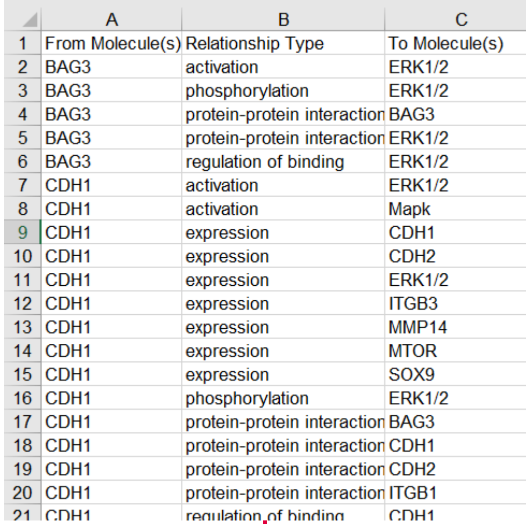
Relationship Export

The new Relationship Export capability in IPA enables you to export the structural information contained within IPA networks or pathways for visualization in other tools such as Cytoscape.

The export format contains relationships modeled as triples: Node A --> Relationship -->Node B

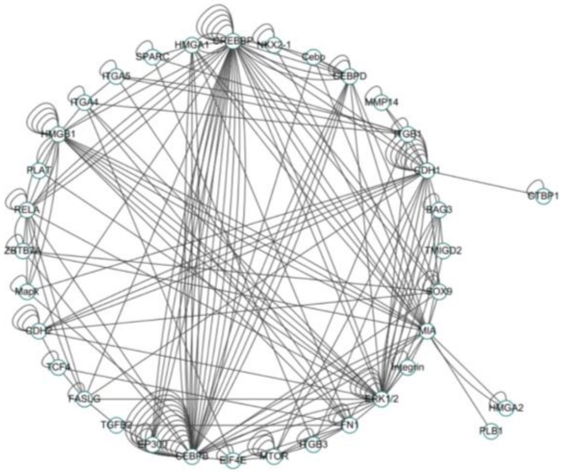


IPA Network



	A	B	C
1	From Molecule(s)	Relationship Type	To Molecule(s)
2	BAG3	activation	ERK1/2
3	BAG3	phosphorylation	ERK1/2
4	BAG3	protein-protein interaction	BAG3
5	BAG3	protein-protein interaction	ERK1/2
6	BAG3	regulation of binding	ERK1/2
7	CDH1	activation	ERK1/2
8	CDH1	activation	Mapk
9	CDH1	expression	CDH1
10	CDH1	expression	CDH2
11	CDH1	expression	ERK1/2
12	CDH1	expression	ITGB3
13	CDH1	expression	MMP14
14	CDH1	expression	MTOR
15	CDH1	expression	SOX9
16	CDH1	phosphorylation	ERK1/2
17	CDH1	protein-protein interaction	BAG3
18	CDH1	protein-protein interaction	CDH1
19	CDH1	protein-protein interaction	CDH2
20	CDH1	protein-protein interaction	ITGB1
21	CDH1	regulation of binding	CDH1

Relationship Export

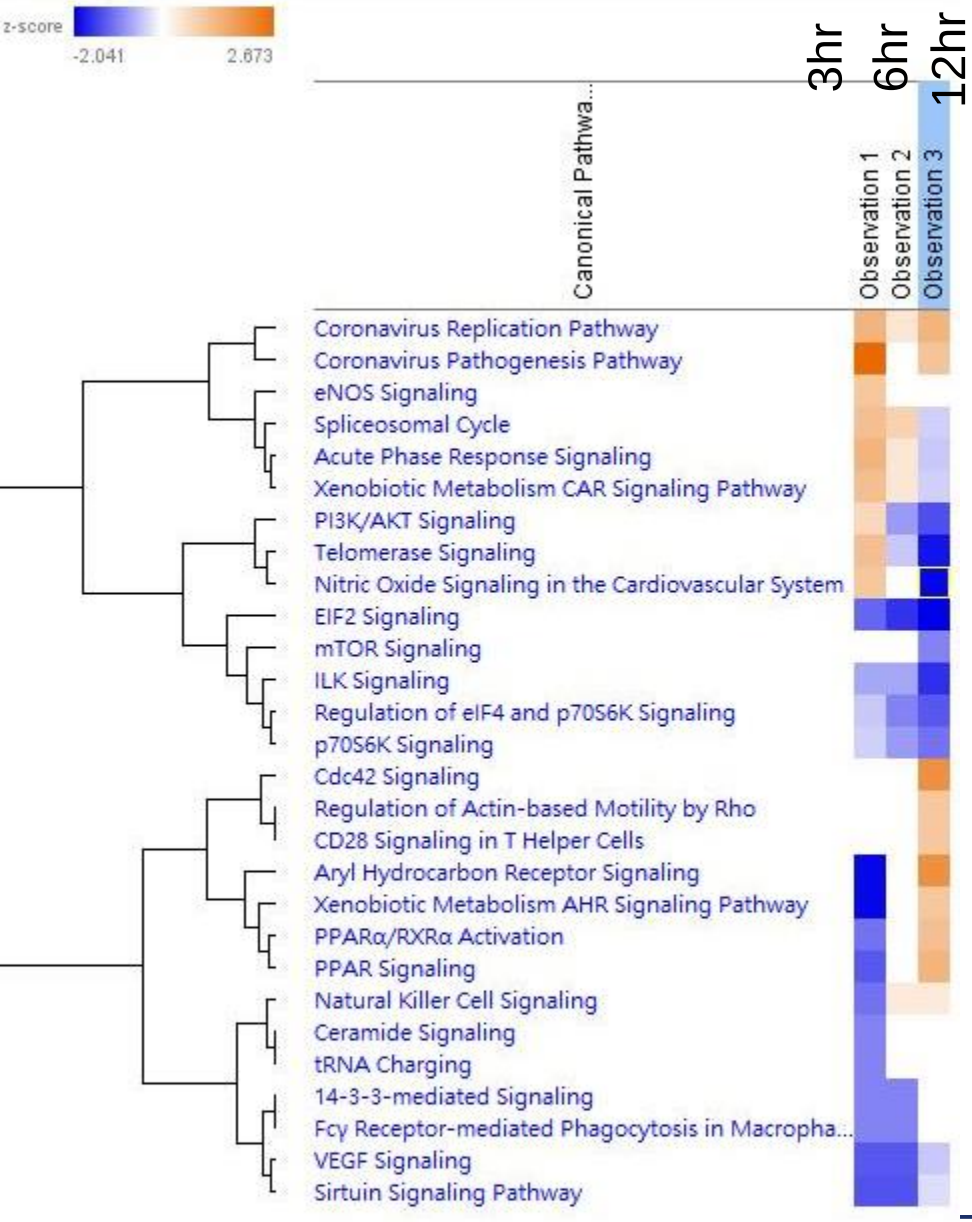


Cytoscape

Live Demo

Case Study

Case Study of ITRAq data



Comparison Analysis of Canonical Pathways

Coronavirus Pathway activated

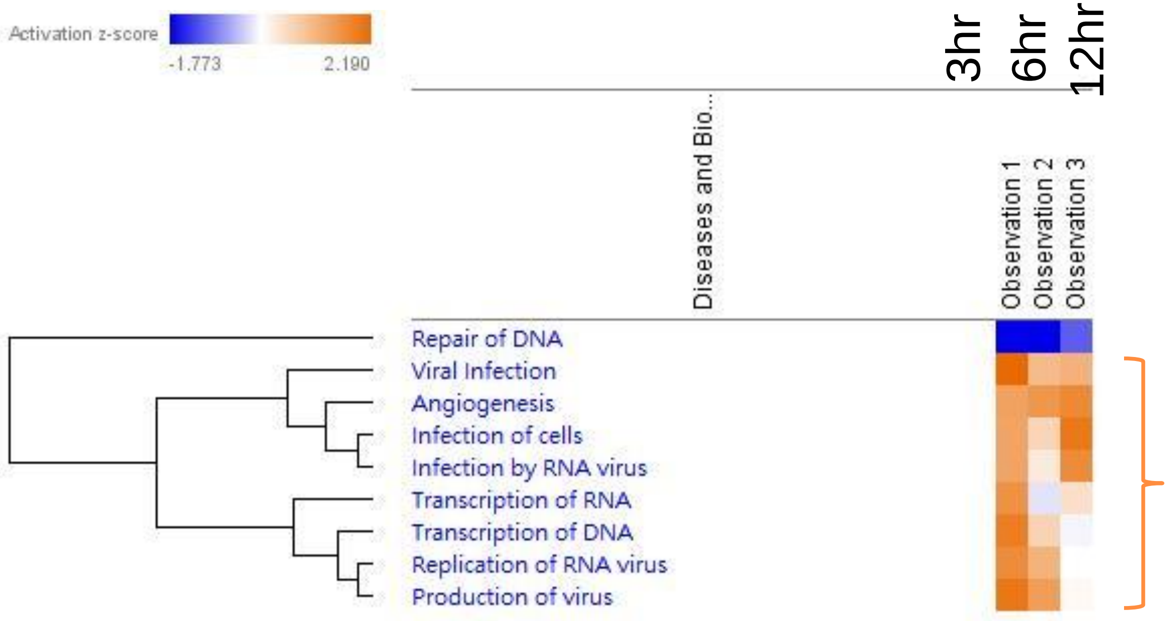
Cardiovascular System inhibited

PPAR Signaling activated

Case Study of ITRAq data

Comparison Analysis of Disease and Function

| Z-score | > 1.5



Virus function activated

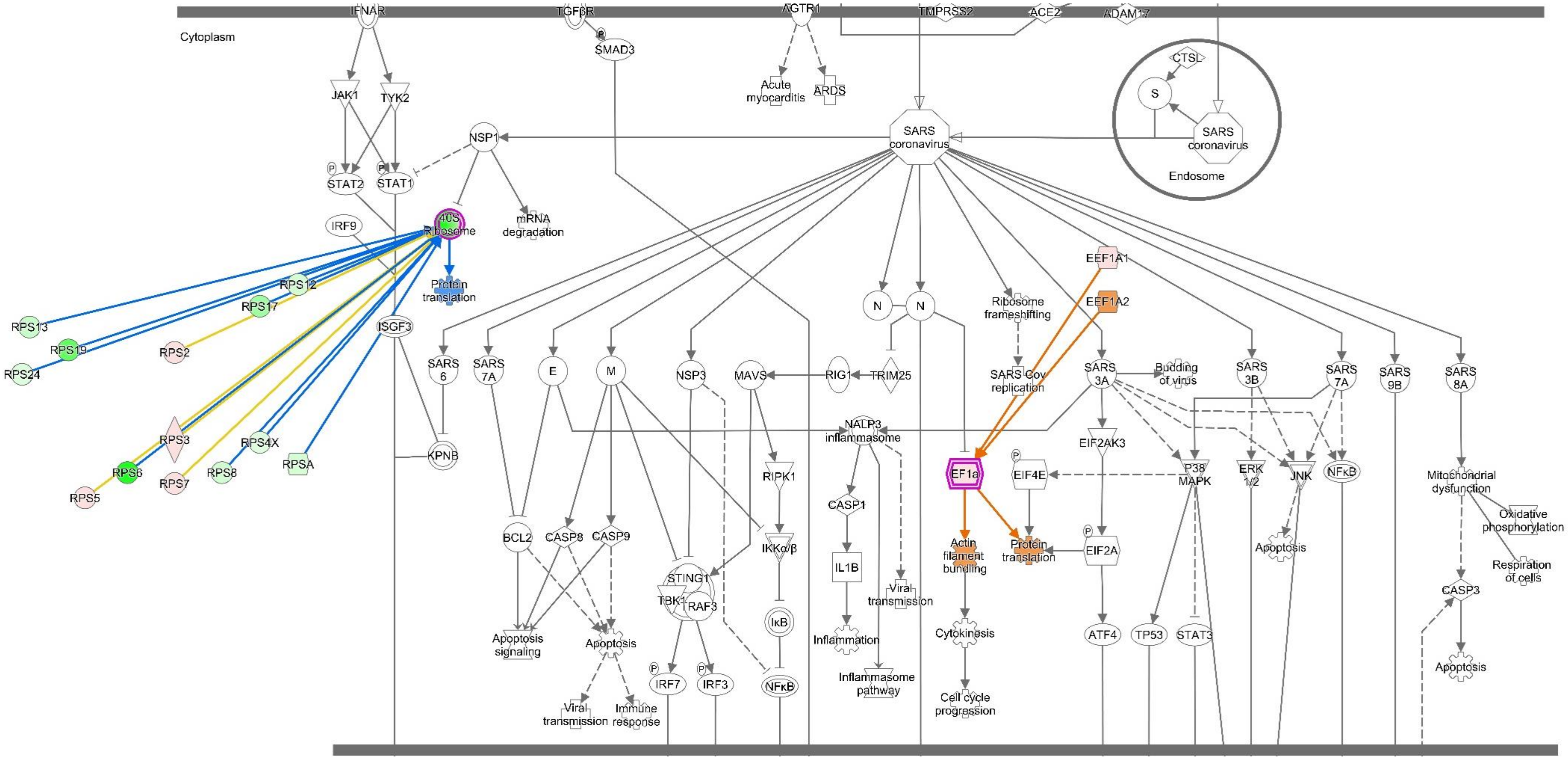
Case Study of ITRAq data

Coronavirus Pathogenesis Pathway

Z-score = 2.67

-log P-value = 8.5

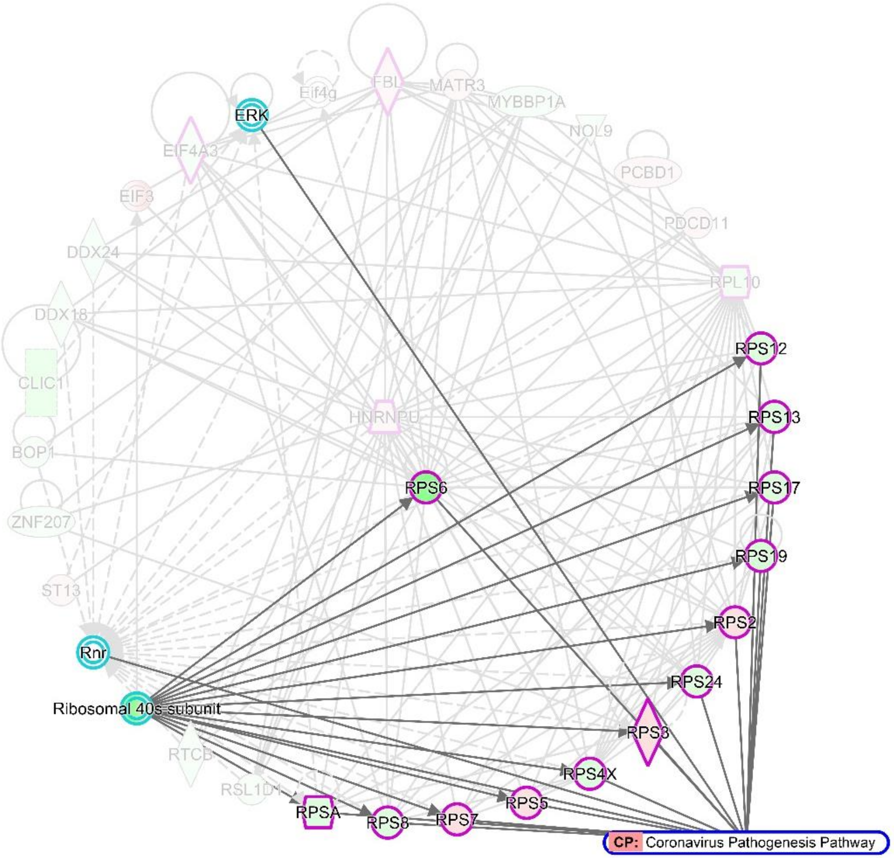
Molecules = 15

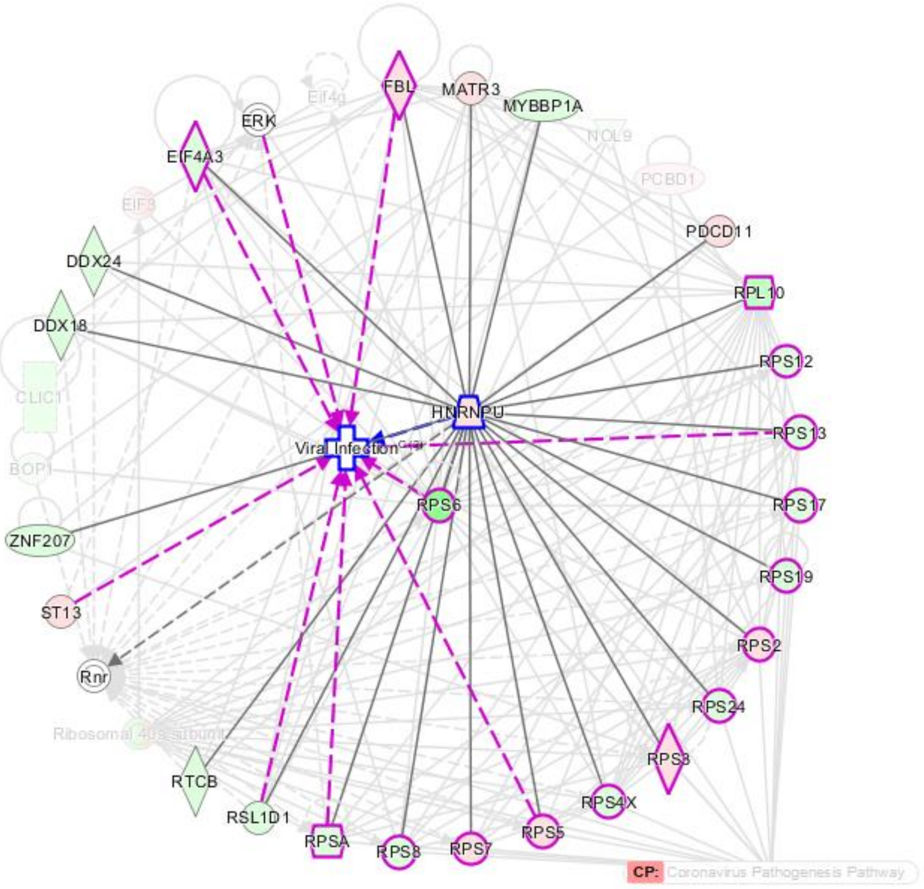


Case Study of ITRAq data

Key:
- 40s Ribosome
- Coronavirus Pathogenesis Pathway

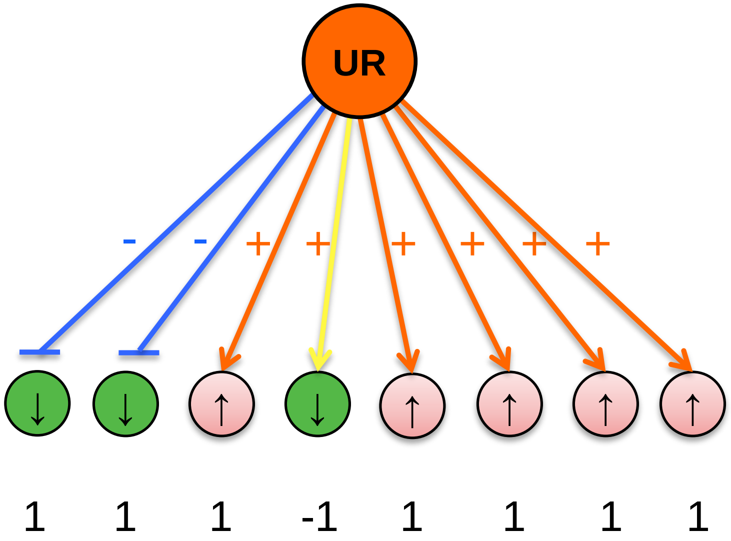
Key:
- HNRNPU
- Viral Infection





Q&A

Predicting upstream regulators of a dataset



← Every possible TF & Upstream Regulator in the Ingenuity Knowledge Base is analyzed

← Literature-based effect TF/UR has on downstream genes

← Differential Gene Expression (Uploaded Data)

← Predicted activation state of TF/UR:

1 = Consistent with activation of UR

-1 = Consistent with inhibition of UR

$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}}$$

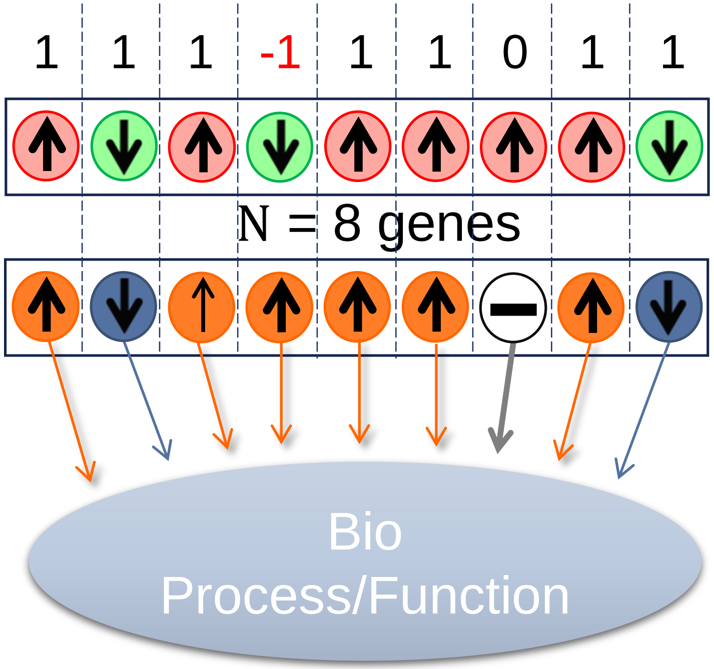
$=(7-1)/\sqrt{8} = 2.12$ (=predicted activation)

- z-score is a statistical measure of the match between expected relationship direction and observed gene expression
- z-score > 2 or < -2 is considered significant

Note that the actual z-score is weighted by the underlying findings, the relationship bias, and dataset bias

Downstream Effect Activation z–score

Statistical measure of correlation between the relationship direction and resulting gene expression



Differential gene expression (Uploaded Data)

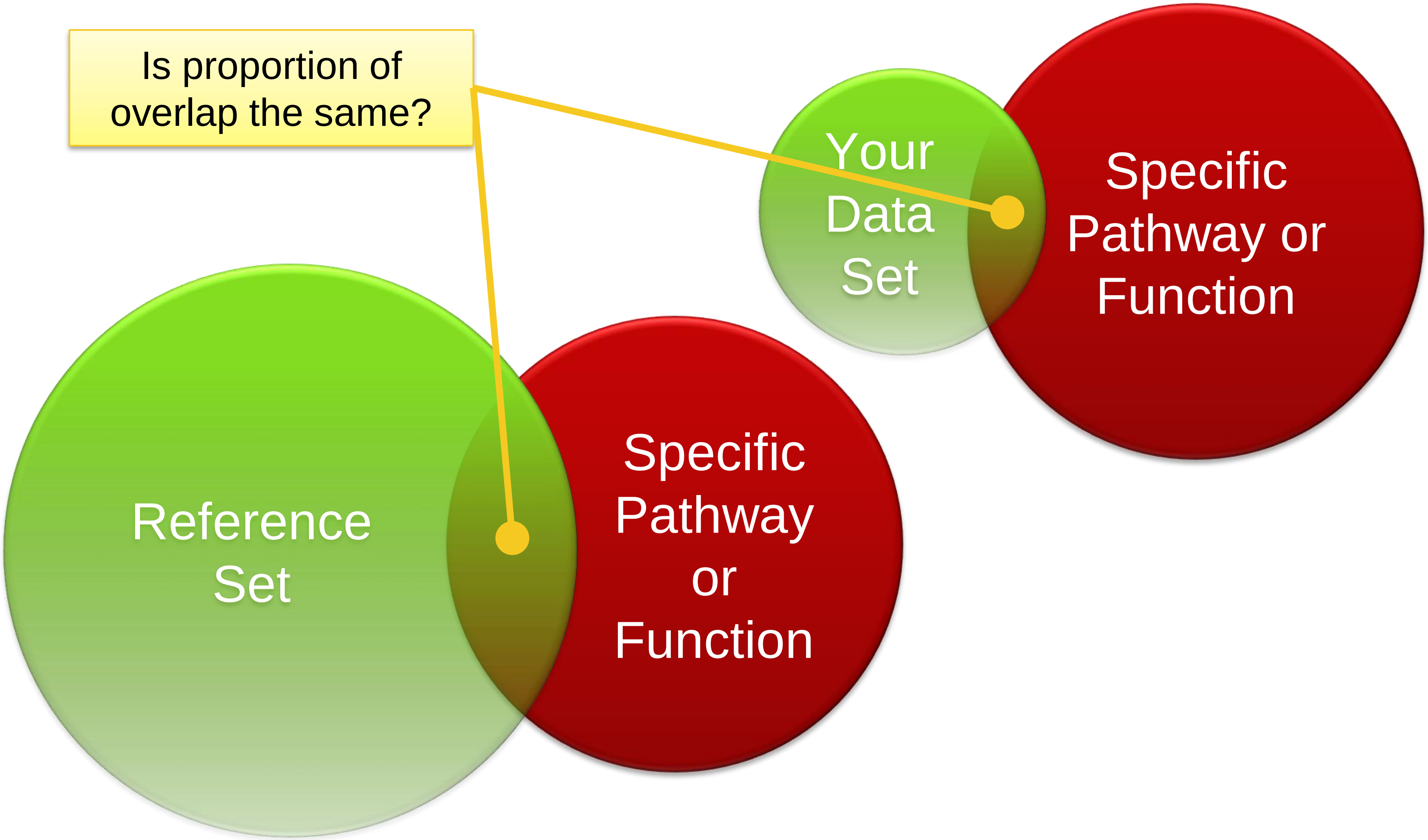
Effect genes have on a process or function (Literature)

$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}}$$

z-score > 2 or < -2 is considered significant

Actual z-score *can* be weighted by relationship types, relationship bias, data bias

Determining Significance of Your Data to IPA



Important note: Statistics in Biology

The Fisher’s Exact Test

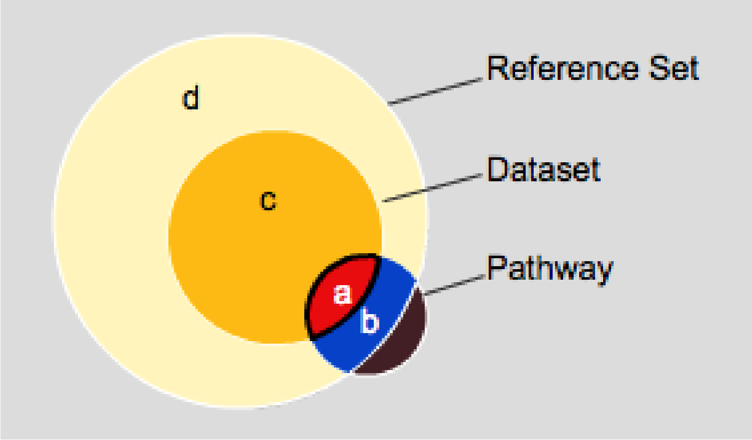
Given a list of differentially expressed genes in a dataset, what is the probability that the overlap with the set of genes on a particular pathway is by random chance?

The null hypothesis is that the association occurs purely by chance.

The Fisher’s Exact Test is a way to test for significant associations

The test looks at the **number** of genes

a. That match between pathway and dataset
b. That are in pathway but did not match dataset
c. That are in dataset but did not match pathway
d. That were possible to assay in the experiment but are not in the pathway or dataset (this is usually called the “reference set” and is ~the set of all genes on the array platform)



The calculation returns a **p-value:**
From 0-1, where values <0.05 are generally considered significant)

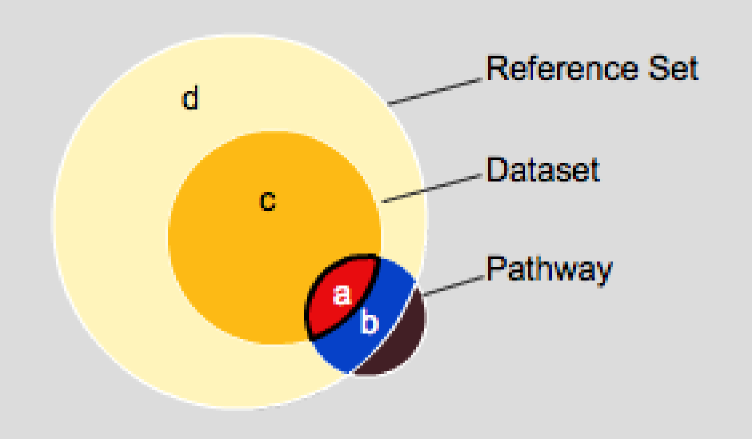
Statistics in Biology: Fisher’s Exact, continued

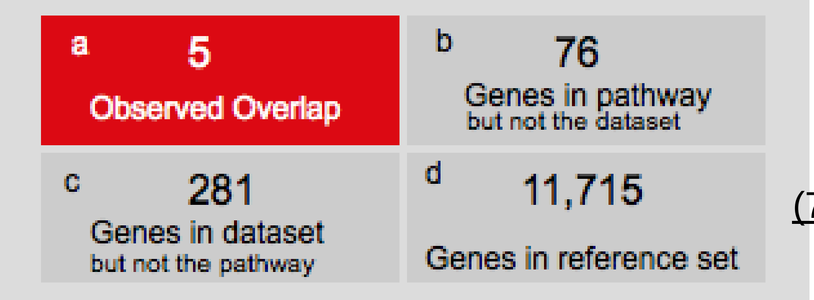
If you had this situation:

- Dataset (significantly differentially expressed) of 286 genes
- Pathway of 81 genes
- Where 5 of the dataset genes overlap those in the pathway
- And the platform measured about 12,000 genes

What is the significance of that overlap?

$$\text{p-value} = \frac{(a+b)!(c+d)!(a+c)!(b+d)!}{(a+b+c+d)!a!b!c!d!}$$





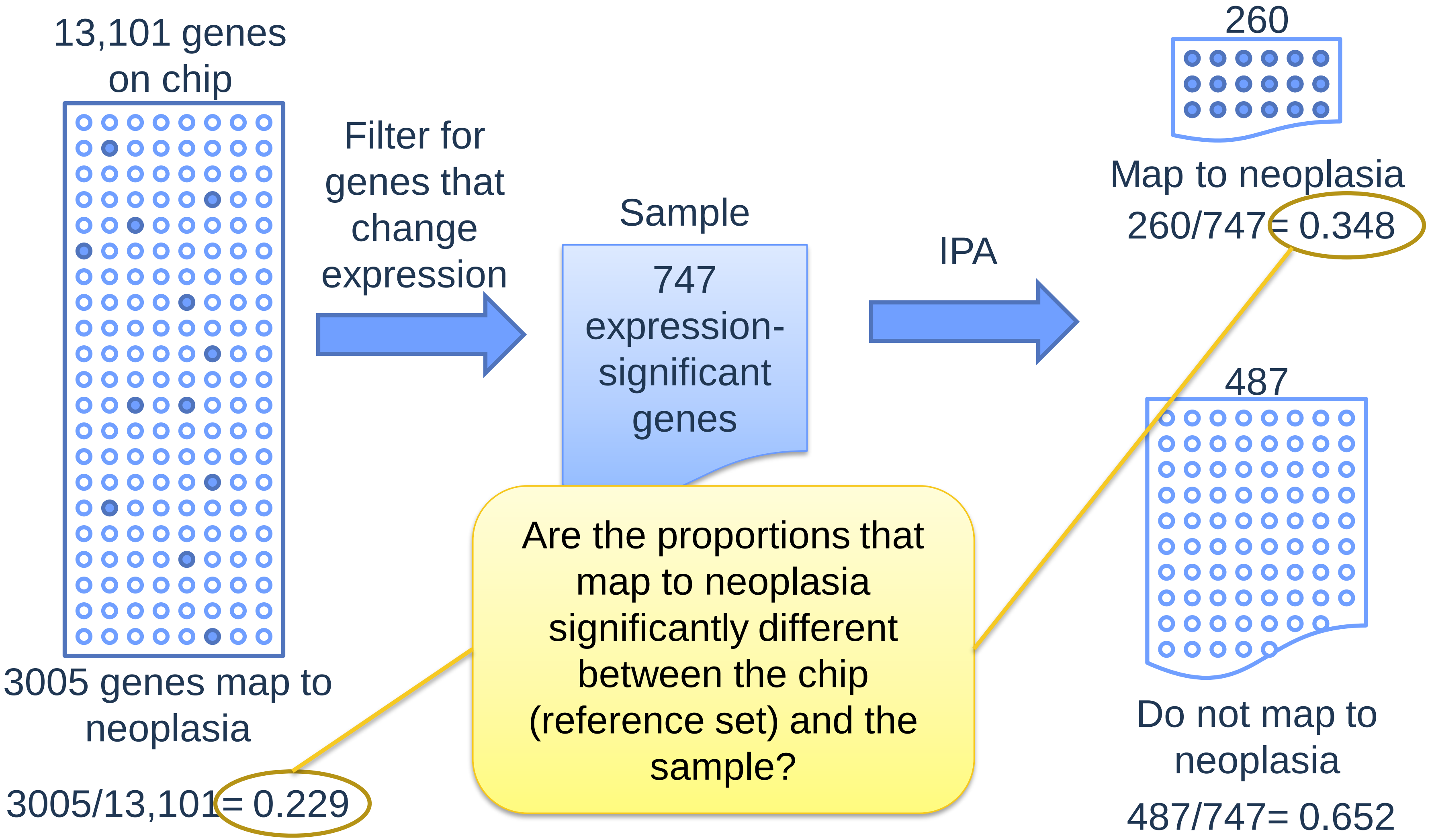
a 5 Observed Overlap	b 76 Genes in pathway but not the dataset
c 281 Genes in dataset but not the pathway	d 11,715 Genes in reference set

$$p = \frac{(5+76)!\ (281+11715)!\ (5+281)!\ (76+11715)!}{(5+76+281+11715)!\ 5!\ 76!\ 281!\ 11715!}$$

$$=0.043$$

Note: “!” is the factorial operator, where for example 3! = 3 x 2 x 1 = 6

Mapping Colorectal Cancer Expression Data to the Function “Neoplasia”



13,101 genes on chip

3005 genes map to neoplasia

3005/13,101= 0.229

Filter for genes that change expression

Sample

747 expression-significant genes

IPA

260

Map to neoplasia

260/747= 0.348

487

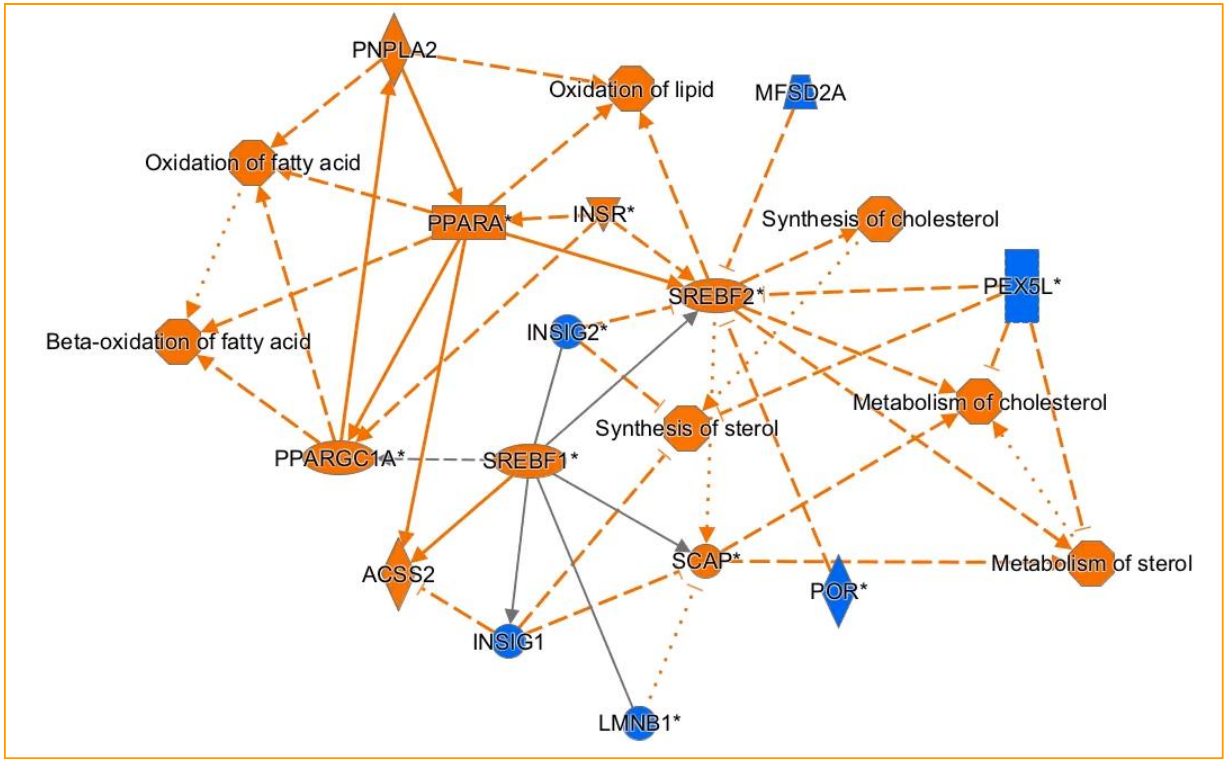
Do not map to neoplasia

487/747= 0.652

Are the proportions that map to neoplasia significantly different between the chip (reference set) and the sample?

Graphical Summary

Graphical Summary結果:
將資料集最相關的生物主題以網路圖像呈現
(canonical pathways, upstream regulators, causal network master regulators, diseases, and biological functions)



Criteria for selection

□ All entities:
p-value < 0.05

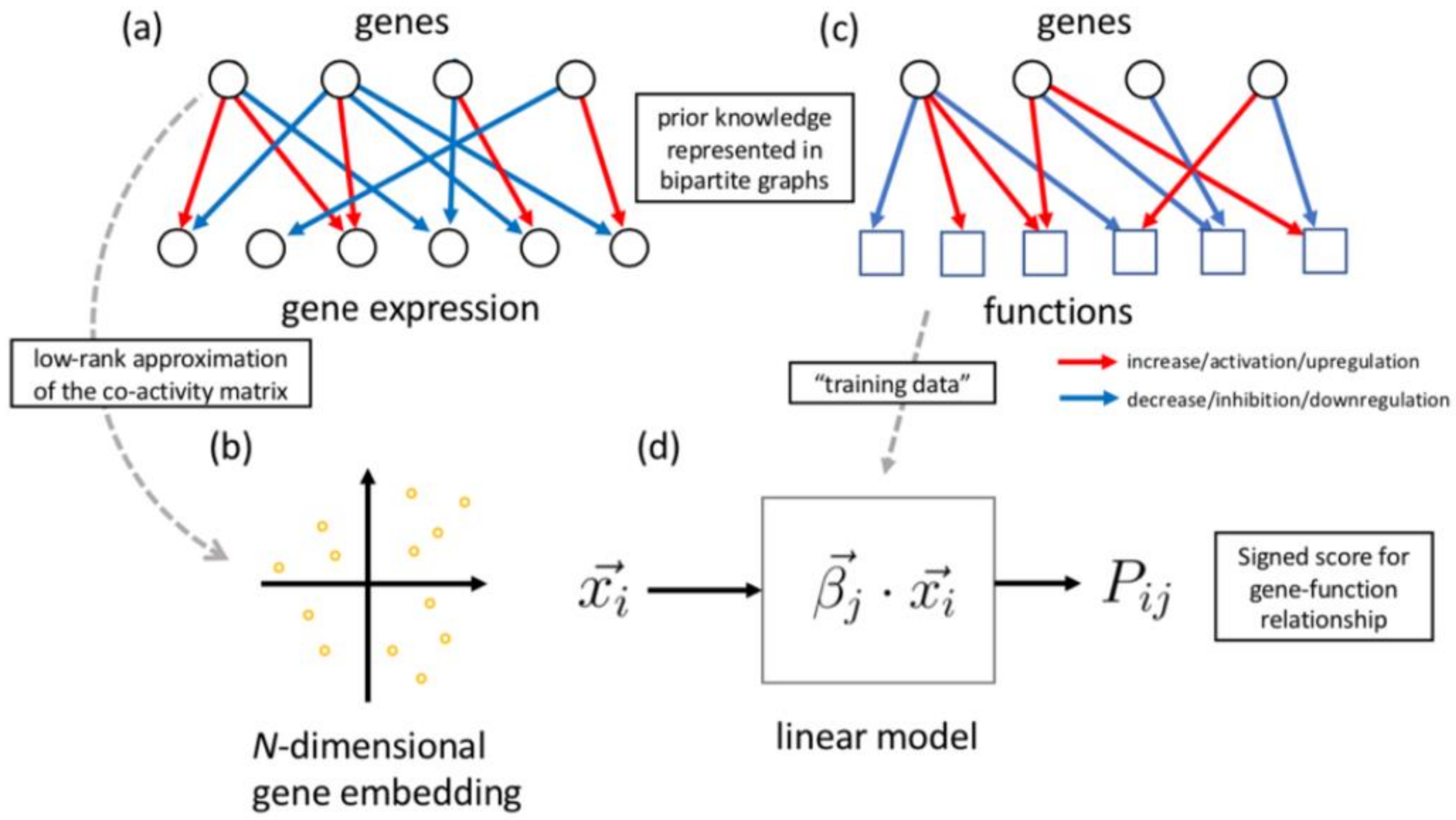
□ Diseases、Functions、Upstream regulators:
z-score≧2

□ All molecules types (except chemicals)

□ Activated nodes
z-score≧2

□ Inhibited nodes
z-score≦-2

Graphical Content-based machine learning



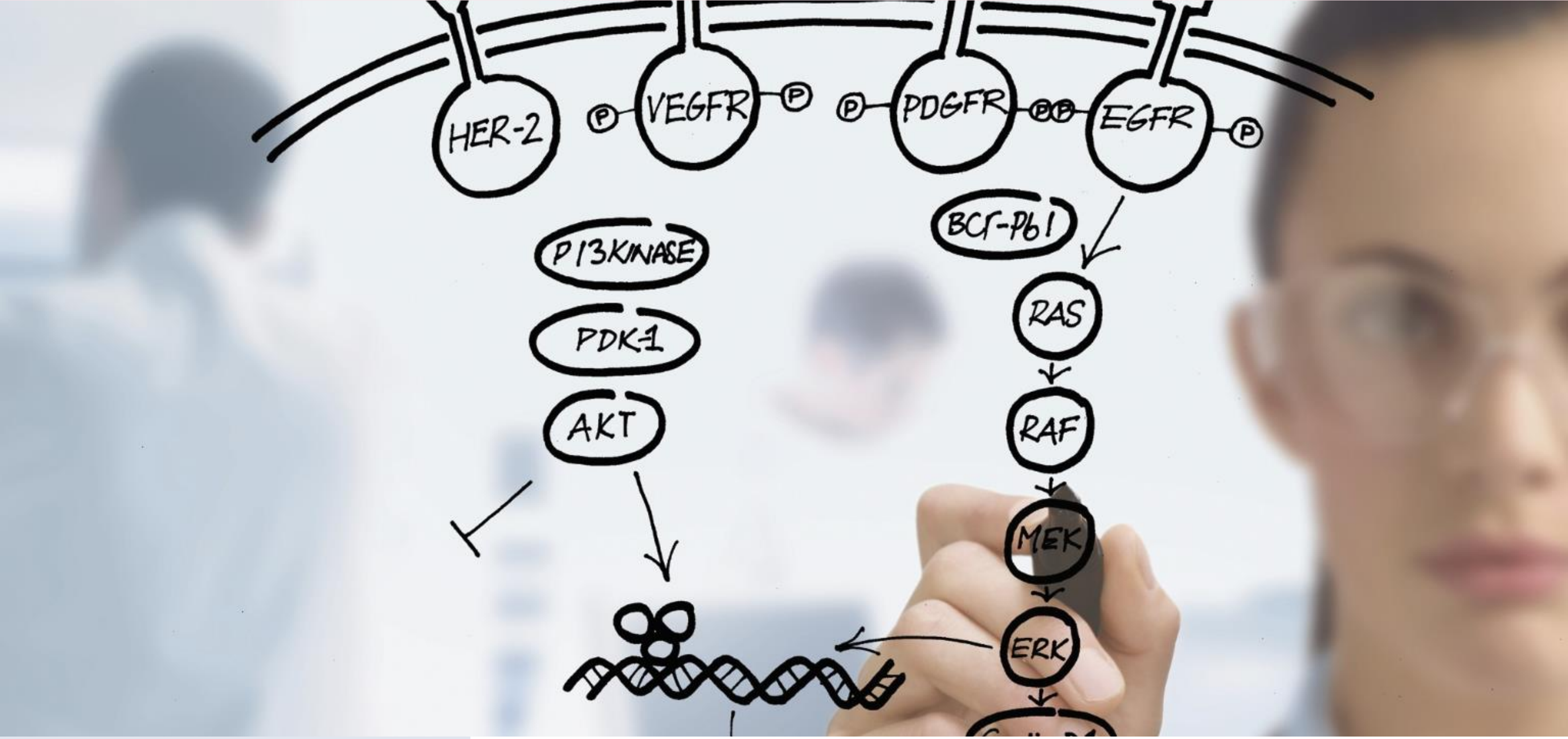
This also applies to inferred **molecule-function relationships**, but in this case the predicted relationships can also be interpreted as being **causal**.

Calculating the Fisher's Exact Test

- For IPA, a 2x2 contingency table is created based on the total population, the sample, and how many genes map to the function/pathway. This table is used to calculate the Fisher's exact test.

	Neoplasia	Not Neoplasia	
In Sample	k	n - k	n
Not in Sample	m - k	N + k - n - m	N - n
	m	N - m	N

m= Total that map to function/pathway
N= Total
k= Number that map to function/pathway in sample
n= Total sample



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