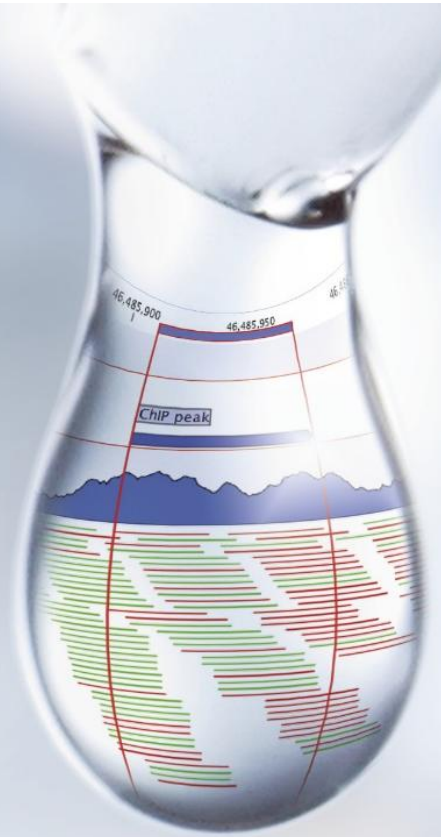
Ingenuity Pathway Analysis (IPA) Advanced Workshop II
Practical Integration of Metabolomic and Genomic Pathway Analysis
Case Study: Integrative Mechanisms Linking COVID-19–Related Metabolic Dysregulation and COPD Genetic Risk



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Training account

Training account activation code and link by e-mail, please notices your mailbox

Dear

Reminder: You have 33 days remaining to activate your QIAGEN IPA trial.

Your 14-day trial license activation code is: xUJSRVV2bf2VNllV.

Once activated, your QIAGEN IPA trial will be valid for 14 days. Please be aware that this is an evaluation license and there are limitations on the number of uploads, exports and analyses that can be performed during the trial period.

To activate your trial, click here or copy paste this text to a browser https://apps.ingenuity.com/isa/account/protected/signup/ipa?coupon=tpd3U2Yyn1NPSXX4Zt1ZIEhWDjAgqiZK63TVMtzy_Mw-FHZhISQKdPVlgaaJjuTR. The trial can be activated to begin anytime within the next 33 days, and after that the code will expire.

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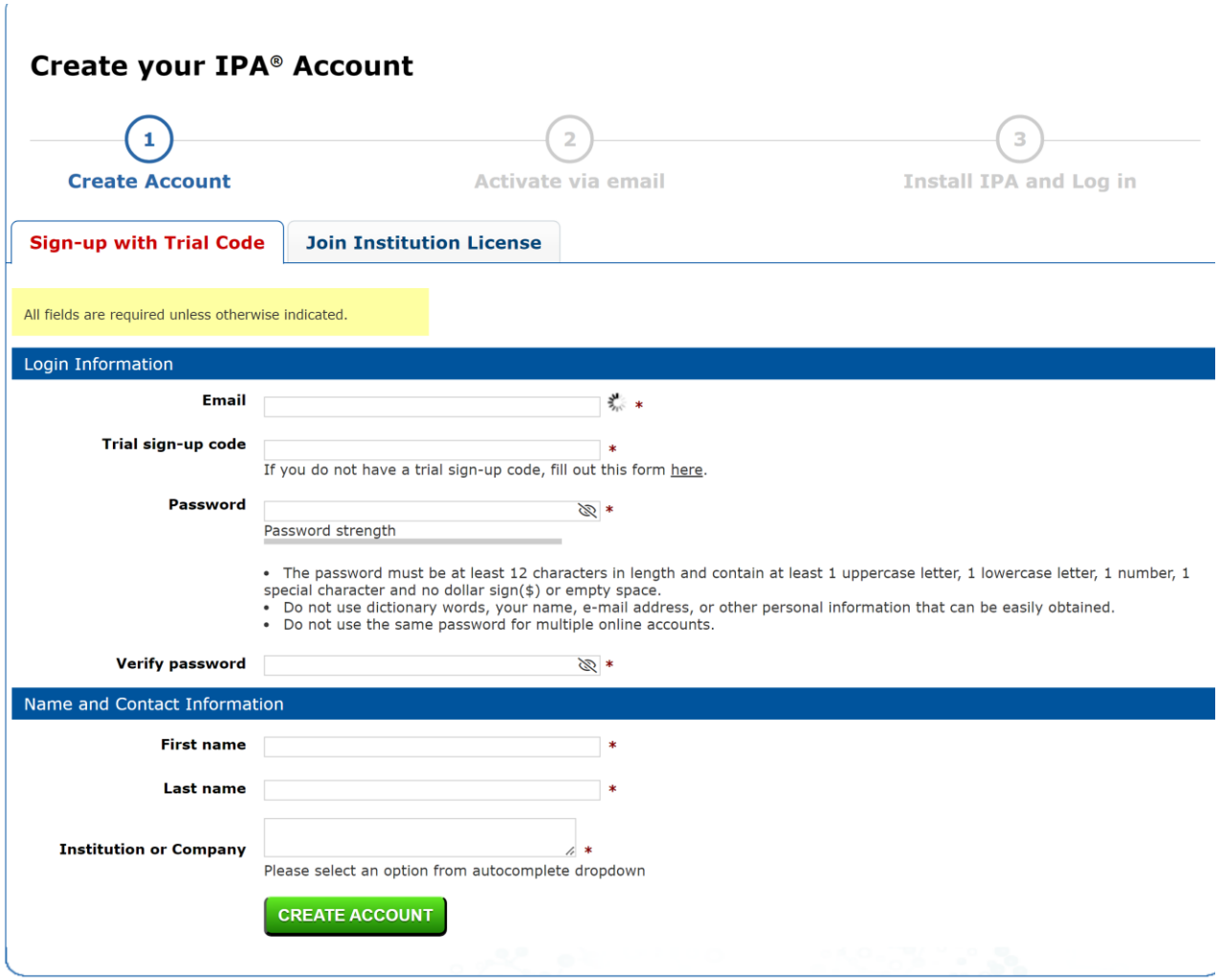
Best regards,
The QIAGEN Digital Insights Team

Activation code and link



Agenda

Introduction to pathway analysis

What is QIAGEN Ingenuity Pathway Analysis

- Introduction of Ingenuity Pathway Analysis
- What's new in Ingenuity Pathway Analysis

Create networks from scratch and path designer

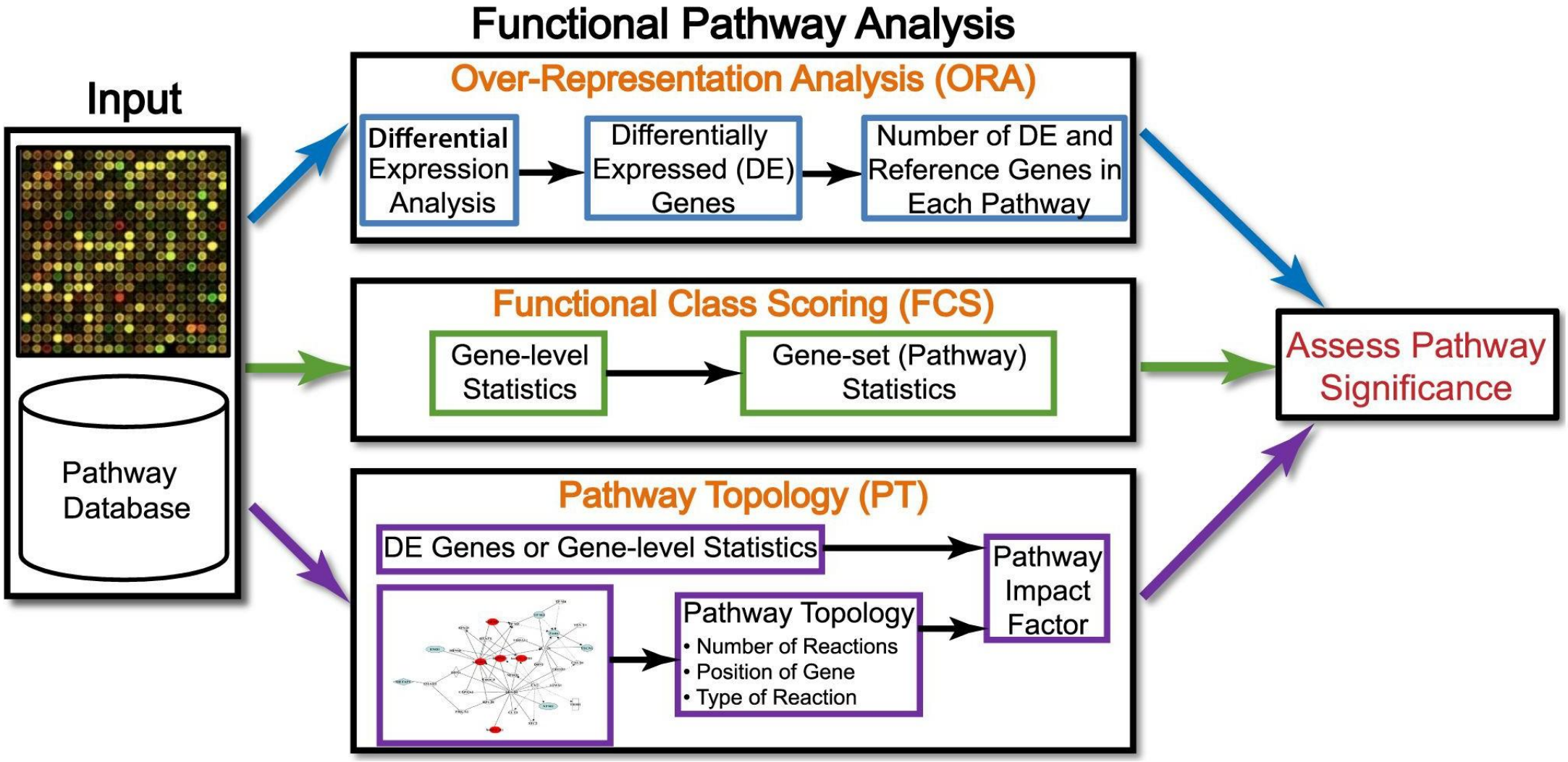
Interpreting your data using IPA

- Data upload and analysis setup
- Canonical pathways and upstream regulators
- Comparison analysis
- Diseases and functions
- Two case studies

- **Comparison analysis and compare analysis**

Summary

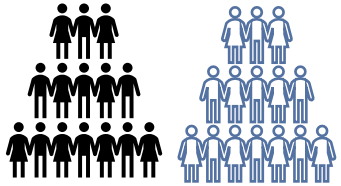
Introduction of pathway analysis

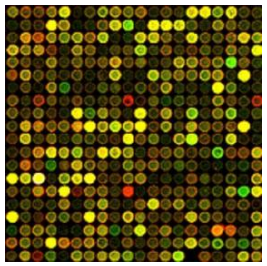


Khatri, Sirota, and Butte. *PLoS Comp Bio*. 2012.

Why are we using Qiagen Ingenuity Pathway analysis?

Your dataset





PDE6A
SLC6A14
LPCAT1
C2
CFB
REG4
CD55
TIMP1
DPP10
PDIA4
PRKG2
NAT8B
SHISA5
LCN2
CDH3
ACAT1
NAALADL1
APOBEC3B
NMT2
KYNU
TMEM63C
S100A11
PI3
CDC25B
CNNM2
CHRNA1
LRRN2
RMDN2
CNTFR
CDC14A
C7orf31
BACE2
CXCL1
SLC36A1
WDR78
PKM

Public /commercial database

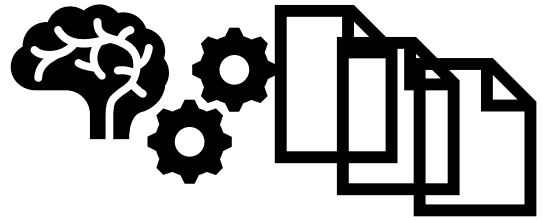
Drugs and chemicals

Pathway

Disease

Function

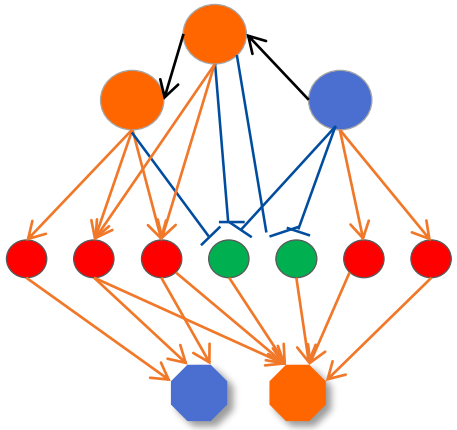
Network



ORA/FCS/Topology Pathway Analysis

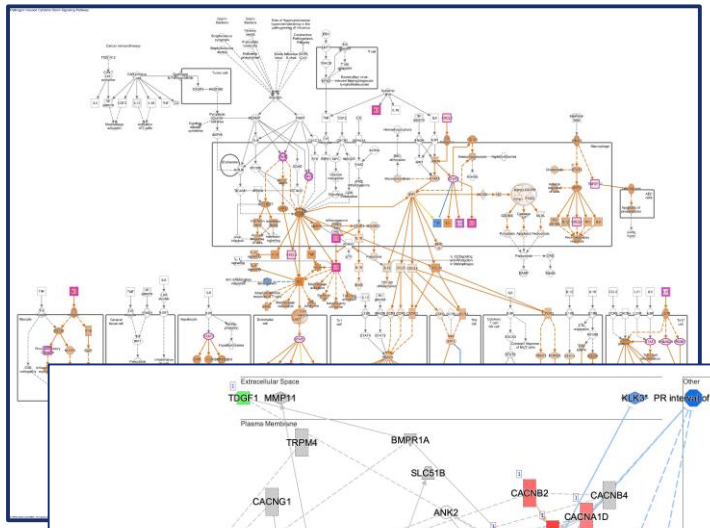
Machine learning

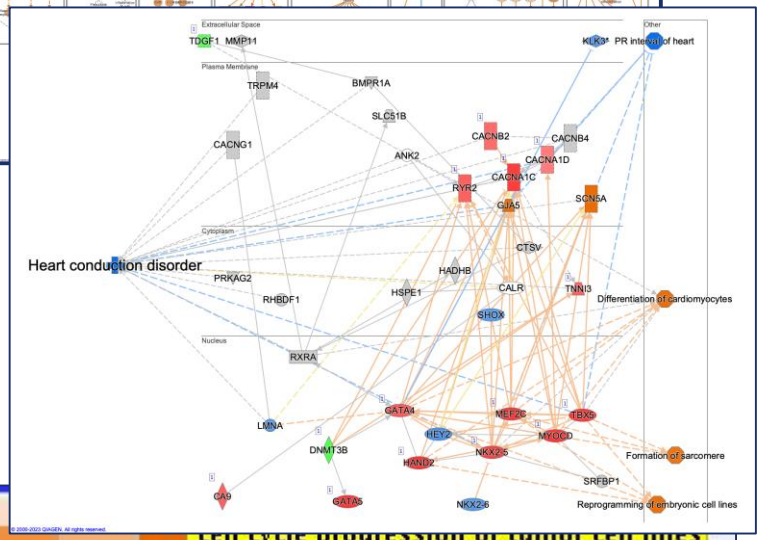
What do they relate to each other?

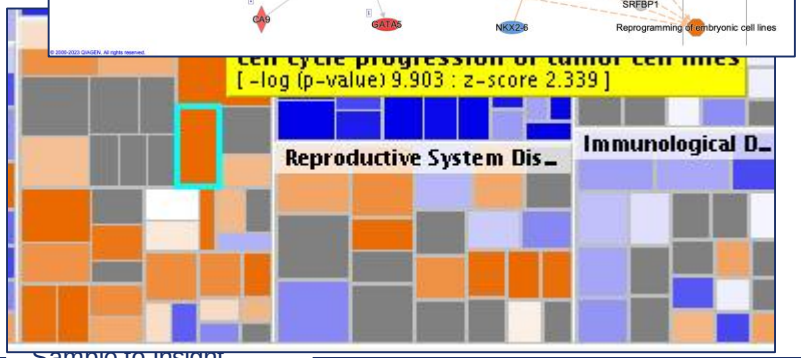


What are the relationship between each molecules?

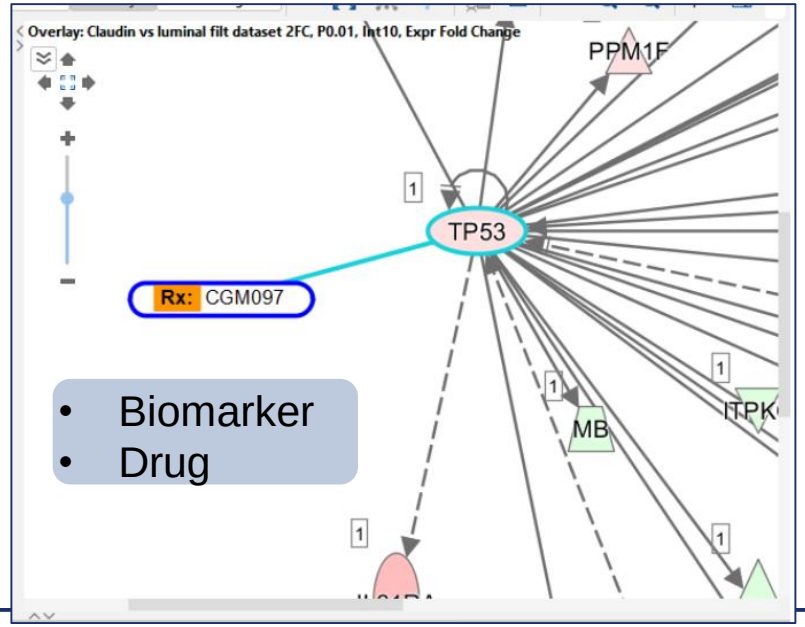
What Can We Achieve with IPA?

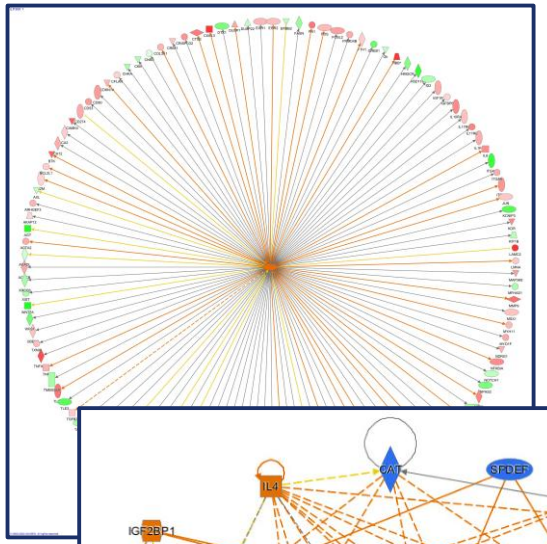


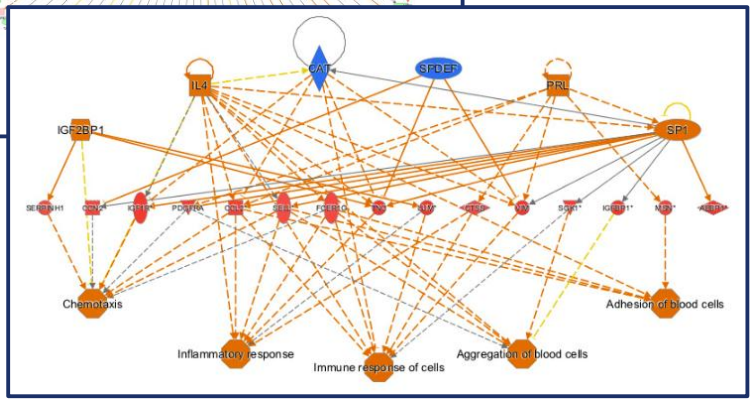


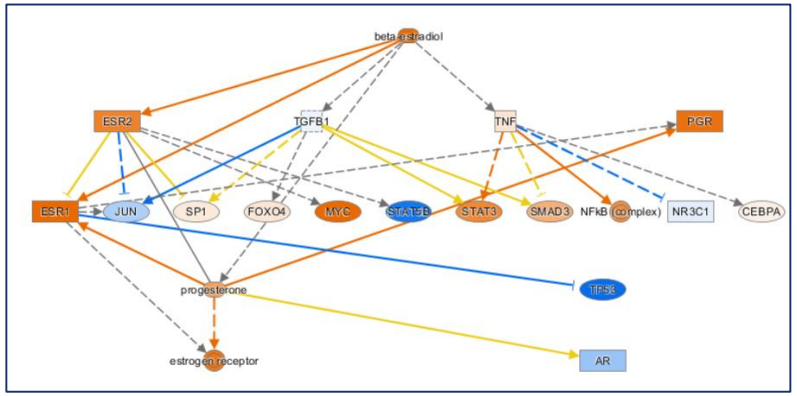


1. Canonical pathway
2. Machine Learning disease pathway
3. Disease and function
4. Upstream regulator
5. Regulate effect
6. Network









Publication using Qiagen Ingenuity Pathway Analysis

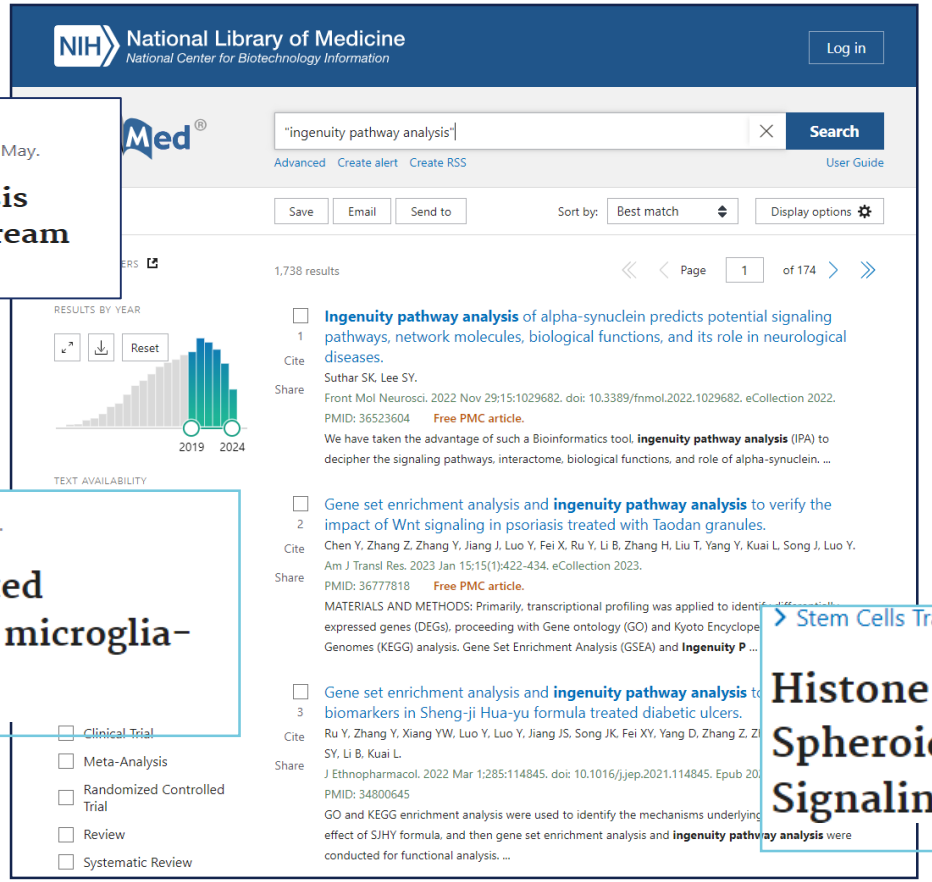
訊聯基因數位

From 2019-2025
2,127literatures

> Hepatol Commun. 2020 Mar 15;4(5):724-738. doi: 10.1002/hep4.1497. eCollection 2020 May.

Integrated GWAS and mRNA Microarray Analysis Identified IFNG and CD40L as the Central Upstream Regulators in Primary Biliary Cholangitis

GWAS



> J Neuroinflammation. 2024 Mar 20;21(1):69. doi: 10.1186/s12974-024-03065-z.

Deletion of Slc9a1 in Cx3cr1^{+} cells stimulated microglial subcluster CREB1 signaling and microglia–oligodendrocyte crosstalk

transcriptomic

> Stem Cells Transl Med. 2024 Mar 15;13(3):293-308. doi: 10.1093/stcltm/szad090.

Histone Trimethylations and HDAC5 Regulate Spheroid Subpopulation and Differentiation Signaling of Human Adipose–Derived Stem Cells

Single-cell RNA-seq

> J Allergy Clin Immunol. 2024 May;153(5):1268-1281. doi: 10.1016/j.jaci.2023.12.030. Epub 2024 Mar 29.

Galectin–10 in serum extracellular vesicles reflects asthma pathophysiology

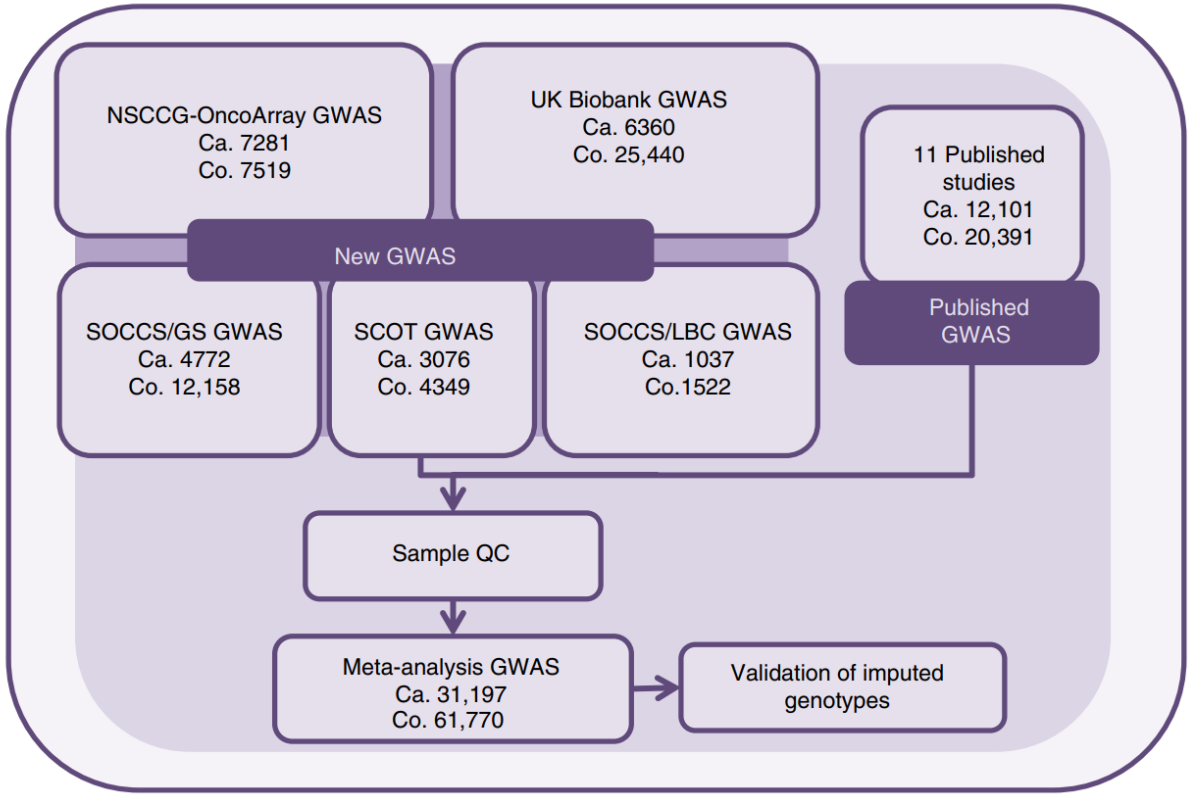
proteinomics

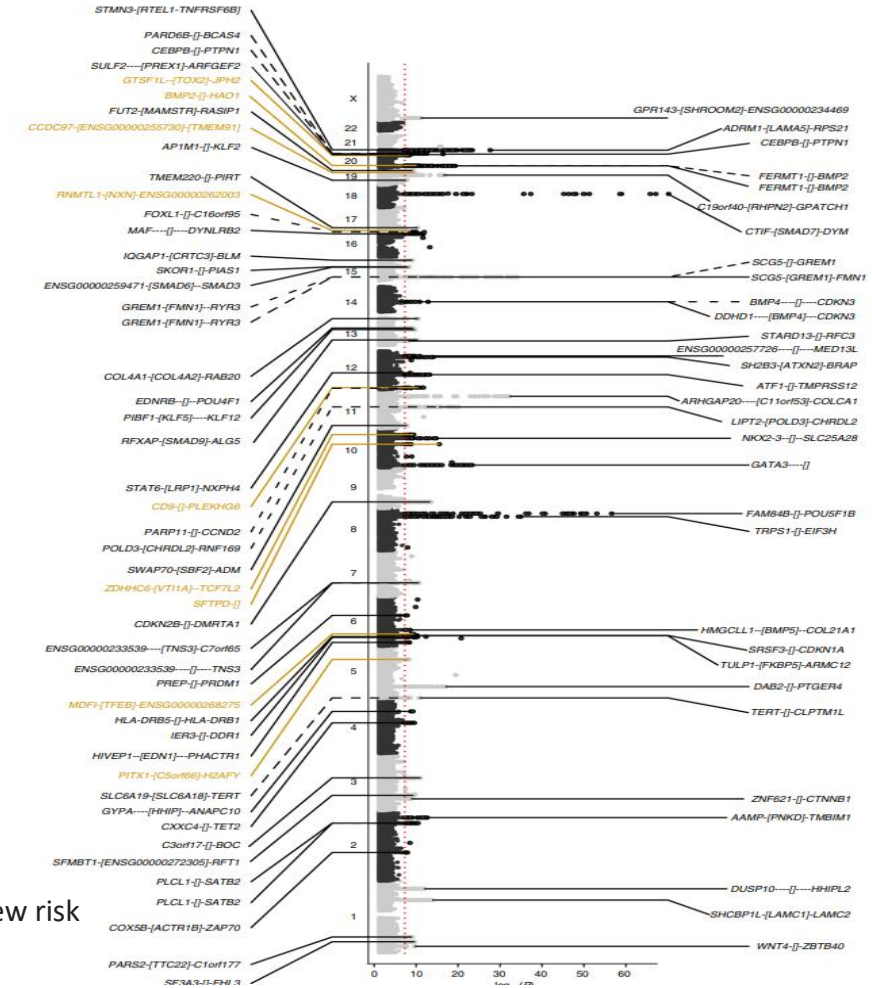
> Chin Med. 2022 Jun 15;17(1):71. doi: 10.1186/s13020-022-00632-5.

Serum metabolomics analysis of deficiency pattern and excess pattern in patients with rheumatoid arthritis

metabolomics

A genome-wide association study (GWA study, or GWAS), is an observational study of a genome-wide set of genetic variants in different individuals to see if any variant is associated with a trait. GWAS typically focus on associations between single-nucleotide polymorphisms (SNPs) and traits like major human diseases, but can equally be applied to any other genetic variants and any other organisms.





Law, P.J., Timofeeva, M., Fernandez-Rozadilla, C. *et al.* Association analyses identify 31 new risk loci for colorectal cancer susceptibility. *Nat Commun* **10**, 2154 (2019). https://doi.org/10.1038/s41467-019-09775-w

Ingenuity Pathway Analysis is powered by QIAGEN knowledge base

Over two decades of expert literature curation

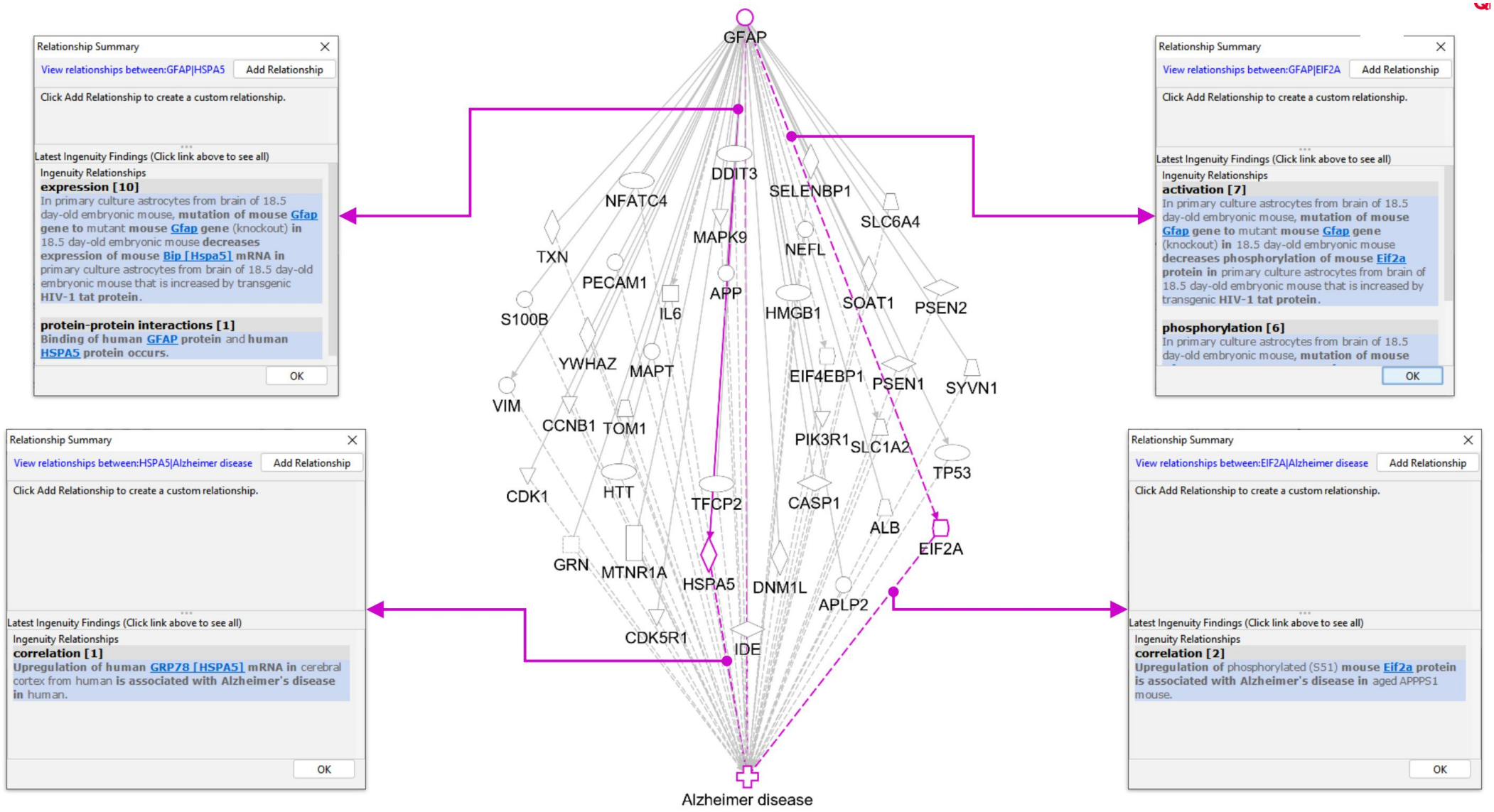
Over 14.2 million research findings accessible to you in **seconds**

Manuscripts, clinical trials and 'omics data obtained from public and commercial sources (TCGA, GTEx, DrugBank, HumanCyc, OMIM, etc.)

Weekly and quarterly updates with the latest disease, genetics, cancer and drug findings

The high-quality, manually curated data allows for **causality prediction**

Every connection in IPA is backed by literature findings



Species Support within IPA

Fully supported:


Human


Mouse


Rat

What species identifiers are accepted for analysis by IPA?

- Atlantic Salmon (*Salmo salar*)
- Thale cress (*Arabidopsis thaliana)*
- Bat (Greater horseshoe bat, *Rhinolophus ferrumequinum*)
- Brewer's yeast (*Saccharomyces cerevisiae)*
- Cat (domestic, *Felis catus*)
- Chicken (*Gallus gallus*)
- Chimpanzee (*Pan troglodytes*)
- Chinese hamster (*Cricetulus griseus*)
- Cow (*Bos taurus*)
- Crab-eating macaque (*Macaca fascicularis*)
- Dog (*Canis lupus familiaris*)
- Fission yeast (*Schizosaccharomyces pombe)*
- Fruit fly (*Drosophila melanogaster*)
- Golden hamster (*Mesocricetus auratus*)
- ✓ Guinea pig, domestic (*Cavia porcellus*)
- ✓ Horse (*Equus caballus*)
- ✓ Human (*Homo sapiens*)
- ✓ Mouse (*Mus musculus*)
- ✓ Pig (*Sus scrofa*)
- ✓ Rabbit (*Oryctolagus cuniculus*)
- ✓ Rainbow trout (*Oncorhynchus mykiss*)
- ✓ Rat (*Rattus norvegicus*)
- ✓ Rhesus Monkey (*Macaca mulatta*)
- ✓ Roundworm (*Caenorhabditis elegans)*
- ✓ Sheep (*Ovis aries*)
- ✓ Western clawed frog (*Xenopus tropicalis*)
- ✓ Zebrafish (*Danio rerio*)
- ✓ Domestic goat
- ✓ three-spined stickleback

Orthologs Gene from NCBI Eukaryotic Genome Annotation Pipeline

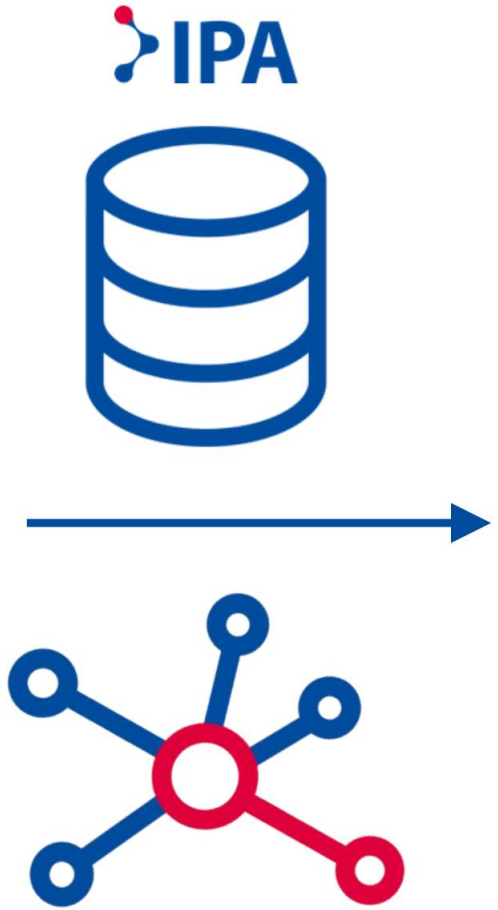
Supported Identifiers for Data Upload

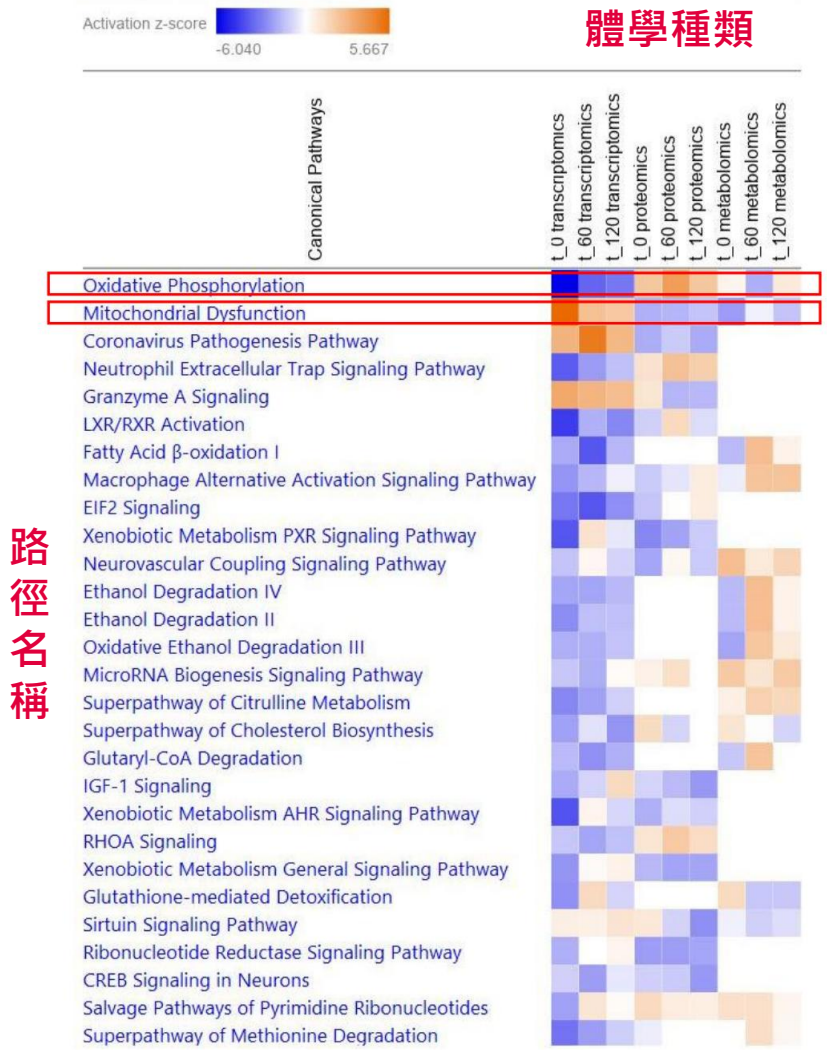
Get more complete mapping during dataset upload!

Vendor IDs	Gene	Protein	Transcript	microRNA	SNP	Chemical
Affymetrix (na36)	Entrez Gene (2023/8)	GenPept	Ensembl (110)	miRbase (mature)	Affy SNP IDs	CAS Registry Number
Agilent	GenBank (257)	International Protein Index (IPI)	RefSeq (human、mouse)	miRBase (stemloop)	dbSNP	HMDB
Life Tech (ABI)	Symbol-human (HUGO/ HGNC, EG)	UniProt/ Swiss-Prot Accession (2022_02)	UCSC (hg18)			KEGG
Codelink	Symbol- mouse (EG)		UCSC (hg19)			PubChem CID
Illumina	Symbol- rat (EG)		UCSC (hg38)			
Ingenuity	GI Number					
	UniGene					

Omics data type

- RNA-seq
- scRNA-seq
- Microarray
- Nanostring
- qPCR
- ChIP-seq
- Proteomics
- Metabolomics
- RNAi
- CRISPR
- WGS/WES etc.



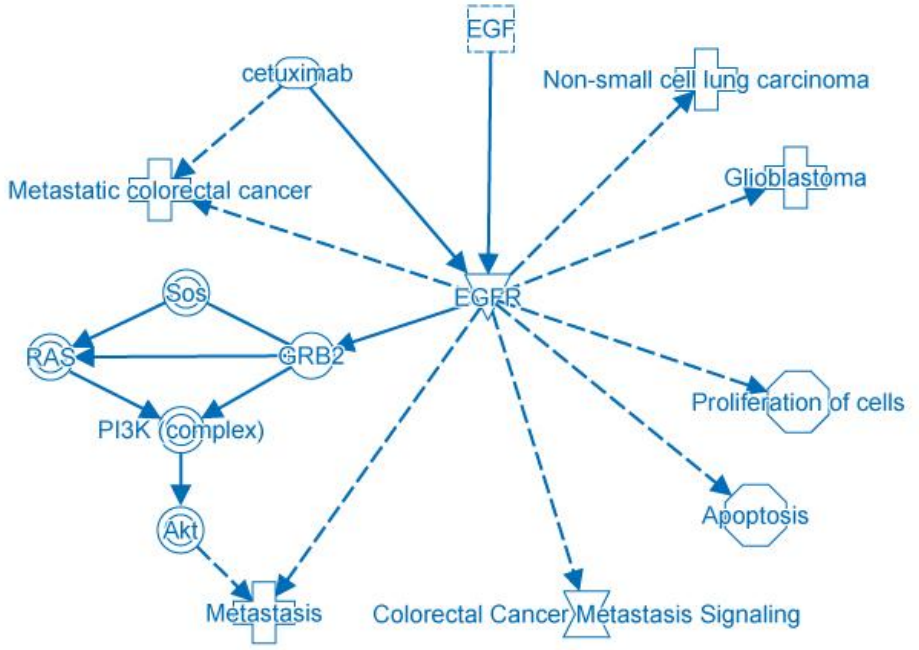


QIAGEN IPA – a dual approach to data analysis

With dataset	Without dataset
• Find connections in your data	• Search and explore the QIAGEN Knowledge Base
• Identify novel biomarkers	• Test hypothesis in silico
• Uncover key targets and regulators	• Identify degree of novelty in a hypothesis
• Discover novel disease mechanisms	
• Compare across experiments	

Example of Biomedical Knowledge Base findings

Selected biomedical relationships between different types of Attributes for selected biomedical relationships entities



Cetuximab is a metastatic colorectal cancer drug. EGFR is a target of cetuximab. Molecular interactions enable you to reconstruct a pathway between EFG, EGFR and the pathological process metastasis. EGFR is a known member of the canonical pathway Colorectal Cancer Metastasis Signaling. In addition to metastatic colorectal cancer, EGFR is involved in other diseases, for example non-small cell lung carcinoma and glioblastoma. Activation of cell proliferation and inhibition of apoptosis by EGFR are known oncology mechanisms.

EGF – EGFR
[one of many]

Type: activation
Direction: directional
Effect: increases
Directness: direct
Tissue or primary cell: epithelial cells
Subcellular location: plasma membrane
Source: PubMed PMID: 17909010

cetuximab – EGFR
[one of many]

Type: phosphorylation
Direction: directional
Effect: decreases
Cell line: CaR1 cells
Organism: human
Experiment: anti-phosphoresidue immunoblot
Source: PubMed PMID: 23213241

EGFR – Proliferation of cells
[one of many]

Type: causation
Direction: directional
Effect: increases
Tissue or primary cell: epithelial cells
Subcellular location: plasma membrane
Source: PubMed PMID: 22674072

EGFR – Glioblastoma
[one of many]

Type: causation
Direction: directional
Effect: increases
Organism: human
Source: PubMed PMID: 24782454

Dig into biology and test hypotheses in silico

OXFORD

Human Molecular Genetics, 2024, Vol. 33, 15, 1367–1377
https://doi.org/10.1093/hmg/ddae076
Advance access publication date 4 May 2024
Original Article

From data to discovery: AI-guided analysis of disease-relevant molecules in spinal muscular atrophy (SMA)

Ines Tapken[1,2], Daniela Kuhn[1,3], Nico Hoffmann[1], Nora T. Detering[1,2], Tobias Schüning[1], Jean-Noël Billaud[4], Stuart Tugendreich[4], Nadine Schlüter[3], Jeff Green[4], Andreas Krämer[4], Peter Claus[1,2,*]

[1]SMATHERIA gGmbH – Non-Profit Biomedical Research Institute, Feodor-Lynen-Str. 31, Hannover 30625, Germany
[2]Center for Systems Neuroscience (ZSN), Bünteweg 2, Hannover 30559, Germany
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[4]QIAGEN Digital Insights, 1001 Marshall Street,Redwood City, CA 94063, United States
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E-mail: peter.claus@smatheria.org

Abstract

Spinal Muscular Atrophy is caused by partial loss of survival of motoneuron (SMN) protein expression. The numerous interaction partners and mechanisms influenced by SMN loss result in a complex disease. Current treatments restore SMN protein levels to a certain extent, but do not cure all symptoms. The prolonged survival of patients creates an increasing need for a better understanding of SMA. Although many SMN-protein interactions, dysregulated pathways, and organ phenotypes are known, the connections among them remain largely unexplored. Monogenic diseases are ideal examples for the exploration of cause-and-effect relationships to create a network describing the disease-context. Machine learning tools can utilize such knowledge to analyze similarities between disease-relevant molecules and molecules not described in the disease so far. We used an artificial intelligence-based algorithm to predict new genes of interest. The transcriptional regulation of 8 out of 13 molecules selected from the predicted set were successfully validated in an SMA mouse model. This bioinformatic approach, using the given experimental knowledge for relevance predictions, enhances efficient targeted research in SMA and potentially in other disease settings.

Keywords: spinal muscular atrophy; SMA; network biology; artificial intelligence; motoneuron disease

Introduction

Spinal Muscular Atrophy (SMA) is a rare monogenic disease caused by mutations or deletions of the Survival of Motoneuron 1 (*SMN1*) gene [1]. Ubiquitous reduction of the SMN protein results primarily in the degeneration of alpha-motoneurons in the brain stem and spinal cord followed by muscular atrophy [2, 3]. Untreated patients with the most common subtype, SMA type I, die within the first two years of life [4]. Current treatments enhance SMN protein levels in the central nervous system (CNS) or systemically, respectively, prolonging survival of patients [5–10].

Although SMA is monogenic, it is a disease involving several molecular, cellular, and systemic networks: On the genetic level (I), SMN is encoded by a second gene, *SMN2*, which differs from *SMN1* by a crucial base transition resulting in about 20% residual functional full-length SMN [1, 11]. The *SMN2* copy number varies (CNV) from 0–8 copies leading to an inverse correlation of copy number and disease severity, formerly clinically classified in types 0-IV [4, 12]. At the protein level (II), SMN interacts with proteins via several binding domains and forms complexes in different cellular compartments [13]. It has multiple functions involved in basal cellular processes, e.g. snRNP assembly [14–16], translation [17, 18], transcription [19, 20], R-loop resolution [21], and cytoskeleton regulation [22–26]. On a systemic level (III), SMA affects peripheral organs resulting in a multi-organ disease [27–29]. At phenotypic or clinical level (IV) the complexity increases since patients differ in disease severity, disease onset, development, and genetic modifiers [4, 12, 30–32]. Unfortunately, no available treatments cure SMA, due to limitations in timing, dosage, and response [32, 33].

The pathological mechanisms after SMN loss are still elusive. Although several dysregulated pathways in SMA are known, the molecular network behind this cause-and-effect relationship remains largely unexplored. The integration and interpretation of single experimental observations in a network of molecular disease mechanisms is challenging. Bioinformatic tools enable integration of scattered observations into a network. Prime examples for this conceptual approach are rare diseases such as SMA caused by a single gene defect, which enables the analysis of the relationship between the genetic cause, molecular alterations, and phenotypic outcome. Disease-specific molecular networks can represent the current knowledge of the disease. We hypothesize that we could use a machine-learning based algorithm to assemble new molecular networks that identify novel disease-specific molecules and molecular relationships. This approach could help explain the pathogenesis and help identify new potential targets of interest. In this study, an artificial intelligence (AI)-based approach was used to analyze causal relationships in SMA

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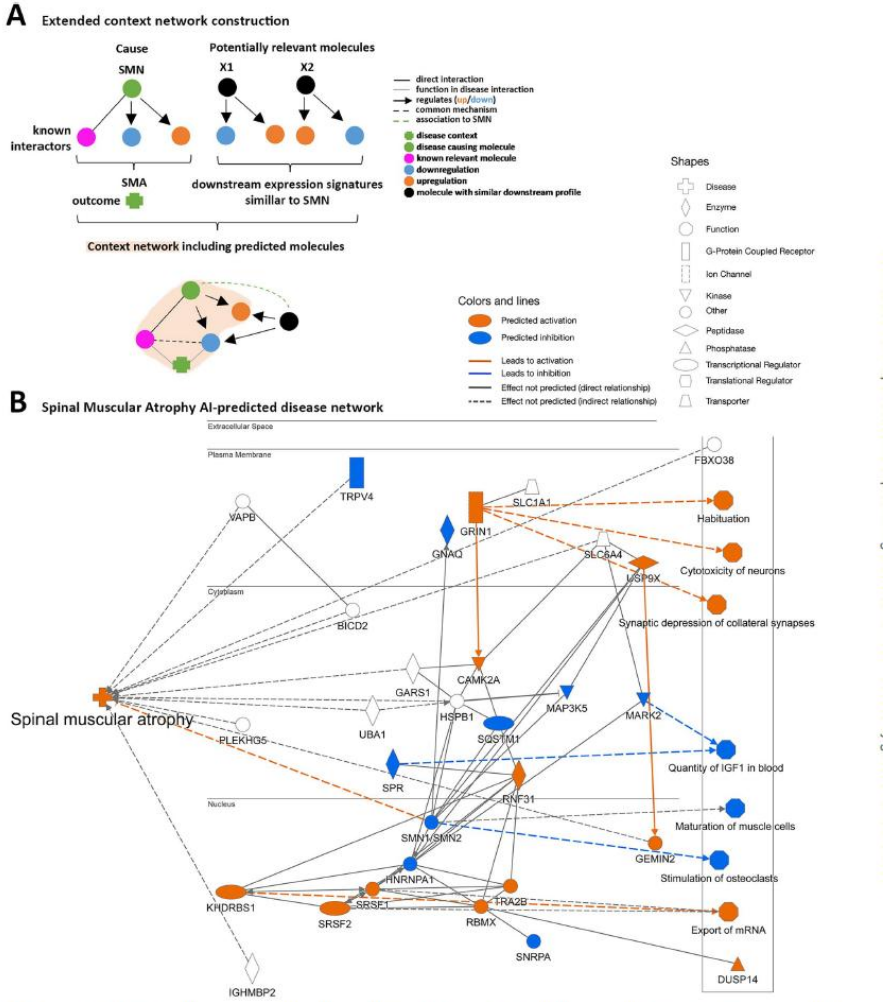
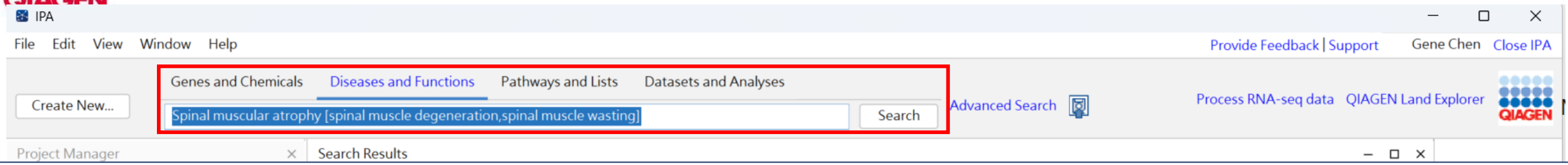


Figure 1. Artificial intelligence-predicted context network for spinal muscular atrophy. (A) Schematic representation of the AI-prediction algorithm and network construction. SMN (green circle) is the genetic cause and SMA (green cross) the disease outcome. In the QIAGEN Knowledge Base (QKB), interactors (pink circle) and causal relationships (black line: protein-protein interaction (PPI); grey line: Function), and dependency keywords (arrow: Direction; orange circle: Increases; blue circle: Decreases) are curated. The downstream profile of the disease-causing molecule is compared to other molecules (X) and similarities are ranked for potential relevance in the disease context. A context network is displayed including known and predicted disease-relevant molecules. Those were selected based on their connectivity to present a network to a size that could be reasonably interpreted. (B) IPA context network for SMA. The network includes known disease relevant molecules (connected to SMA) and predicted potentially relevant molecules with their direction of regulation (orange, blue). Functional outcomes are displayed on the right. Prediction activation (orange)/inhibition (blue): Regulation is predicted from interacting molecule measurements. Color codes for lines are based on the same concept. Molecule shapes represent their type.

Diseases and Function



Molecule Annotations

Add To My Pathway | Add To My List | Create Dataset | Customize Table | Symbol: AARS1 - NEFL (1/2)

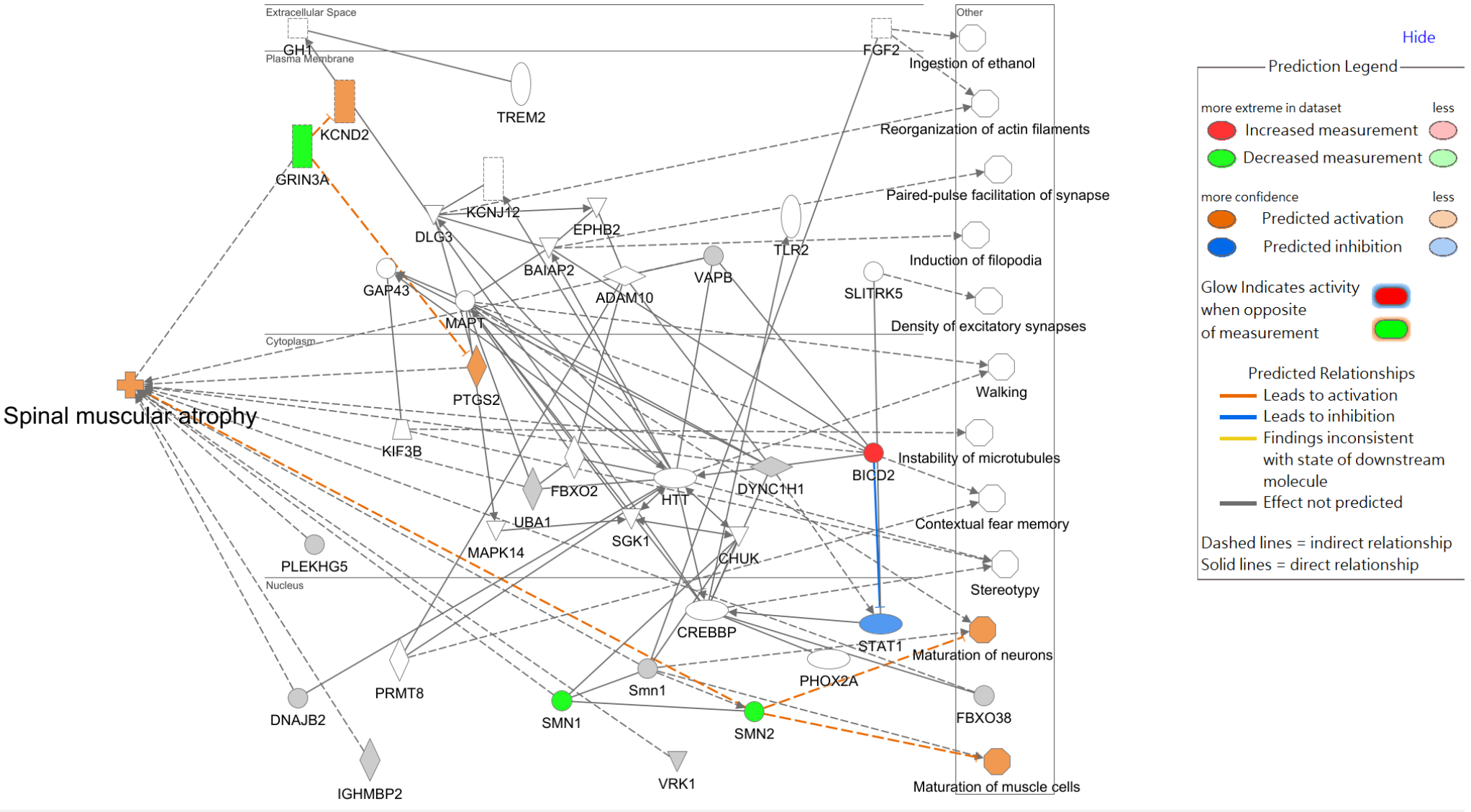
Symbol	Entrez Gene Name	Location	Type(s)	Biomarker Application(s)	Drug(s)
AARS1	alanyl-tRNA synthetase 1	Cytoplasm	enzyme		
acetaminophen	--	Other	chemical drug		
ALT (family)	--	Other	group	efficacy, safety	
amantadine	--	Other	chemical drug		
apitegromab	--	Other	biologic drug		
AR	androgen receptor	Nucleus	ligand-dependent nuclear receptor	diagnosis, disease progression,	clascoterone, nandrolone phenpro...
ASAH1	N-acylsphingosine amidohydrolase 1	Cytoplasm	enzyme	unspecified application	
ASCC1	activating signal cointegrator 1 complex s...	Nucleus	transcription regulator		
ATP2A1	ATPase sarcoplasmic/endoplasmic reticul...	Cytoplasm	transporter	unspecified application	
ATP7A	ATPase copper transporting alpha	Plasma Membrane	transporter		
BAG3	BAG cochaperone 3	Cytoplasm	other		
BCL2L1	BCL2 like 1	Cytoplasm	other	efficacy, prognosis	LP-118, AZD0466
BICD2	BICD cargo adaptor 2	Cytoplasm	other		
BSCL2	BSCL2 lipid droplet biogenesis associated,...	Cytoplasm	other		
butyric acid	--	Other	chemical - endogenous mammalian		
C1QB	complement C1q B chain	Extracellular Space	other		
CASQ1	calsequestrin 1	Cytoplasm	other	unspecified application	
ceramide	--	Other	chemical - endogenous mammalian		
CHCHD10	coiled-coil-helix-coiled-coil-helix domain c...	Cytoplasm	other		
CHMP1A	charged multivesicular body protein 1A	Extracellular Space	peptidase		
creatine	--	Other	chemical - endogenous mammalian	efficacy, safety	
CREATINE KINASE (family)	--	Other	group	efficacy, safety	

Selected/Total molecules: 0/144

Machine learning pathway

Download the related Genes of disease

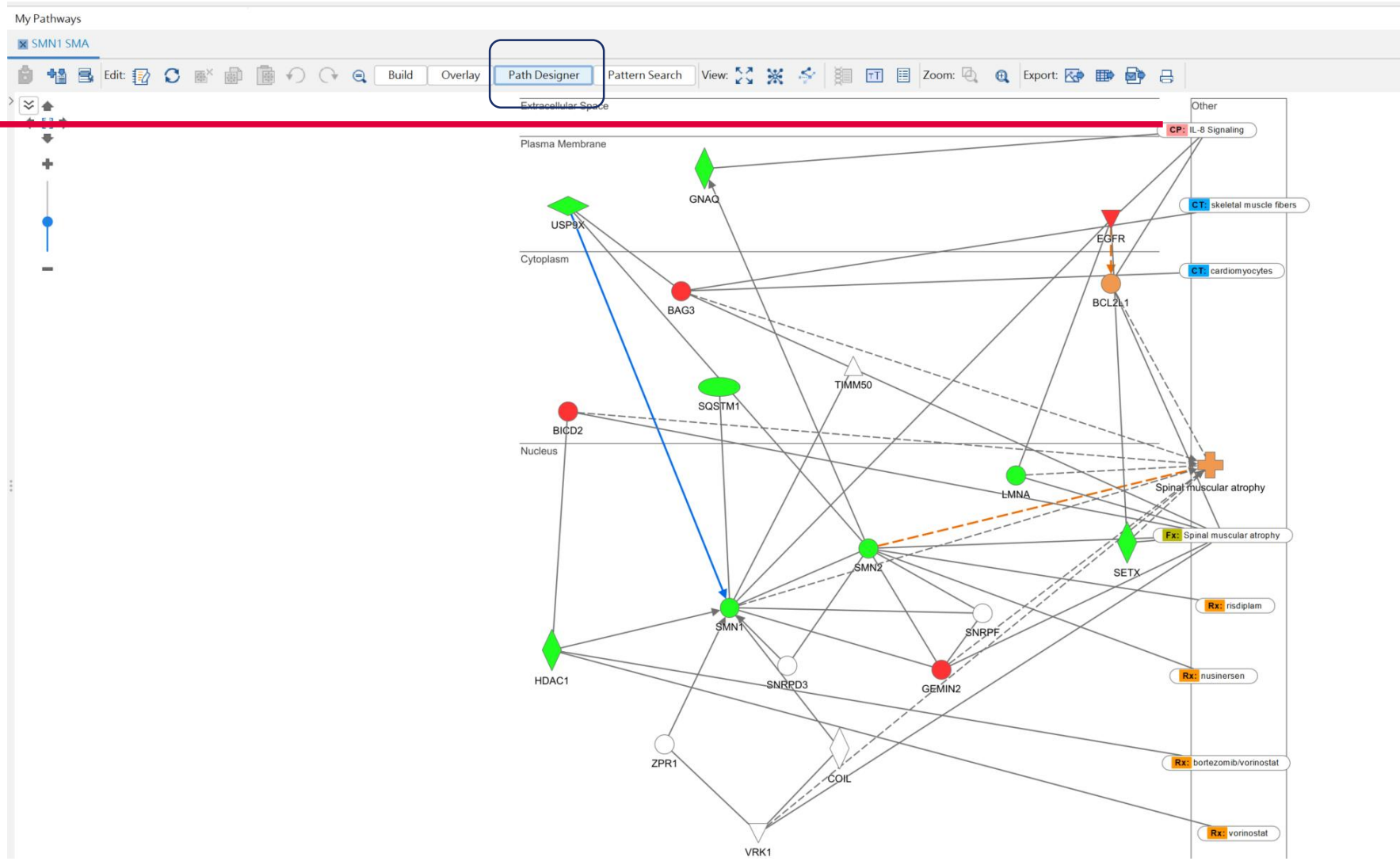
Upload dataset and Core analysis



Create networks from scratch and test activity in silico

New feature:
Cells and Tissues overlay

Predict cell types associated with the genes on your network or pathway using data from The Human Protein Atlas



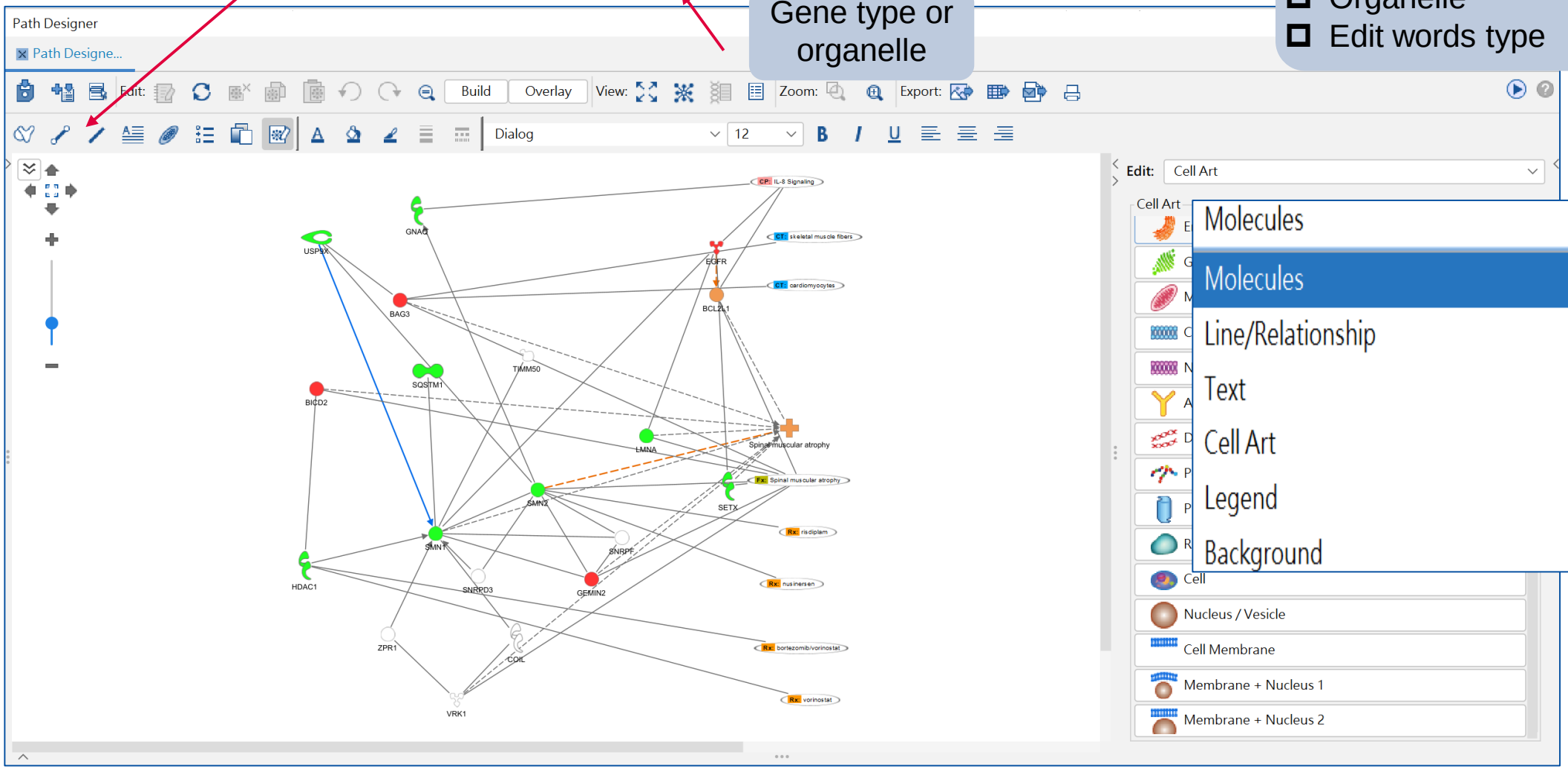
- Search for genes
- Build: grow (molecular or disease a function)
- Search for disease
- Path explore
- Overlay: Molecule activity predictor, Drug, Cells & Tissues
- Drug: IPA Chem View

Path Designer

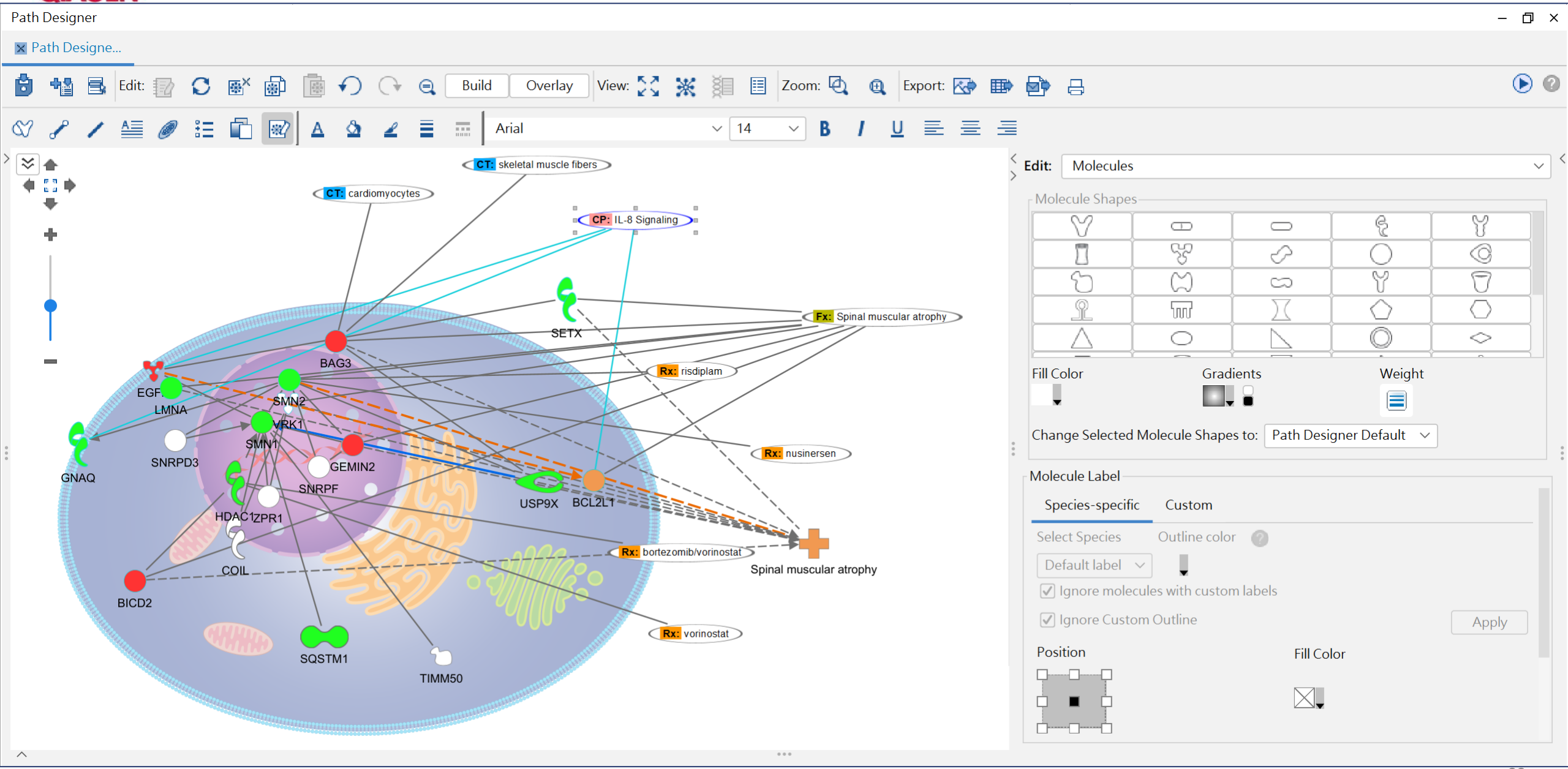
Figure legend

Gene type or organelle

We can add the
- molecules
- Organelle
- Edit words type



Path Designer



QIAGEN IPA Analysis Match and Land Explorer

ArrayExpress, GEO, TCGA, SRA, LINCS, etc.

Processing, curation and QA

Journal articles and databases such as Clinical Trials, COSMIC, MGD,OMIM , etc.

Curated Findings

- Explore gene expression levels
- Determine where a target is differentially expressed
- Understand how 'omics data influences survival
- Identify mutation status of a target

QIAGEN OmicSoft Studio

141,000+ comparison

Ingenuity Pathway Analysis

- Explore biological findings in public datasets
- Build confidence in your analysis results
- Make unexpected insights into shared mechanisms between studies
- "Anti-matches" may provide insights

266,592 total datasets from OmicSoft (10,159 newly added).

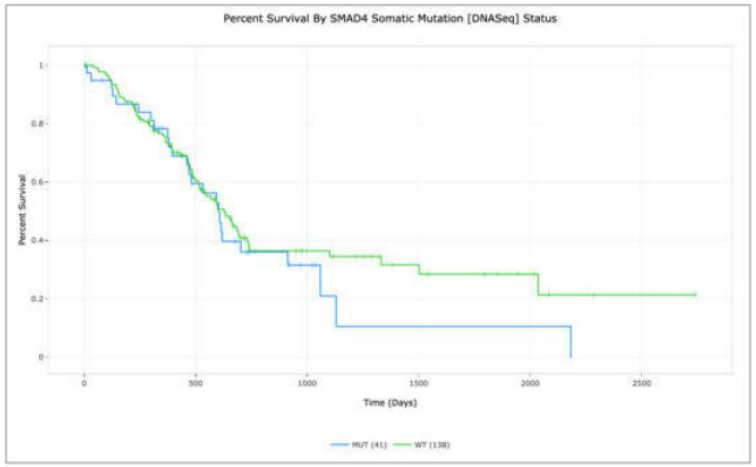
Land	Repository	Datasets Q2 2025	Datasets Q3 2025	Increase
DiseaseLand	HumanDisease	39,650	40,155	505
	MouseDisease	29,564	30,234	670
	RatDisease	10,269	10,269	
	LINCS	25,880	25,880	
OncoLand	OncoHuman	25,472	26,533	791
	OncoMouse	1516	1516	
	TCGA	4854	4854	
	ENCODE RNA Binding	486	486	
	ClinicalProteomicTumor	3090	3419	
	NCI Patient-Derived Models	552	552	
Single Cell Land	SingleCellHuman	194	194	
	SingleCellHumanUmi	89,283	88,525	-758*
	SingleCellHumanHCL	1476	1476	
	SingleCellMouse	81	81	
	SingleCellMouseUmi	23,242	29,481	6239
Normal Cells and Tissues	Human Tissues (GTEx)	1312	2937	1625

*Duplicate datasets removed in Q3

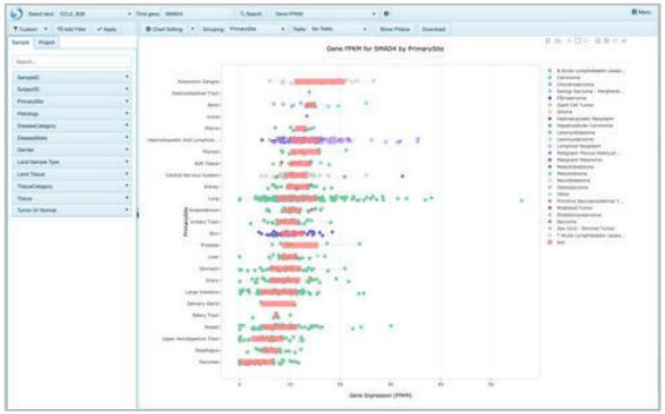
IPA with OmicSoft Land Explorer

Expression in Rat, Mouse, and Human Disease

Mutation frequency

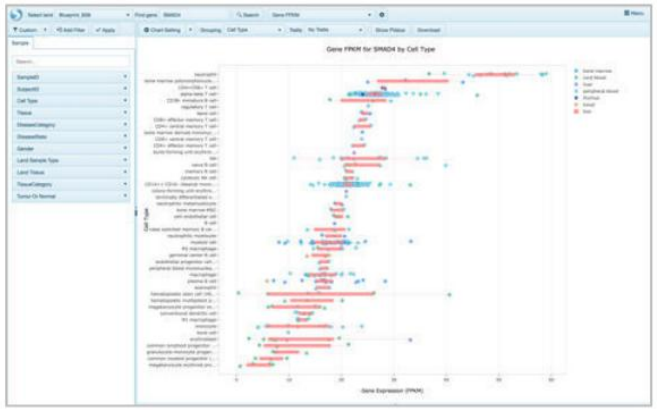


Survival plots



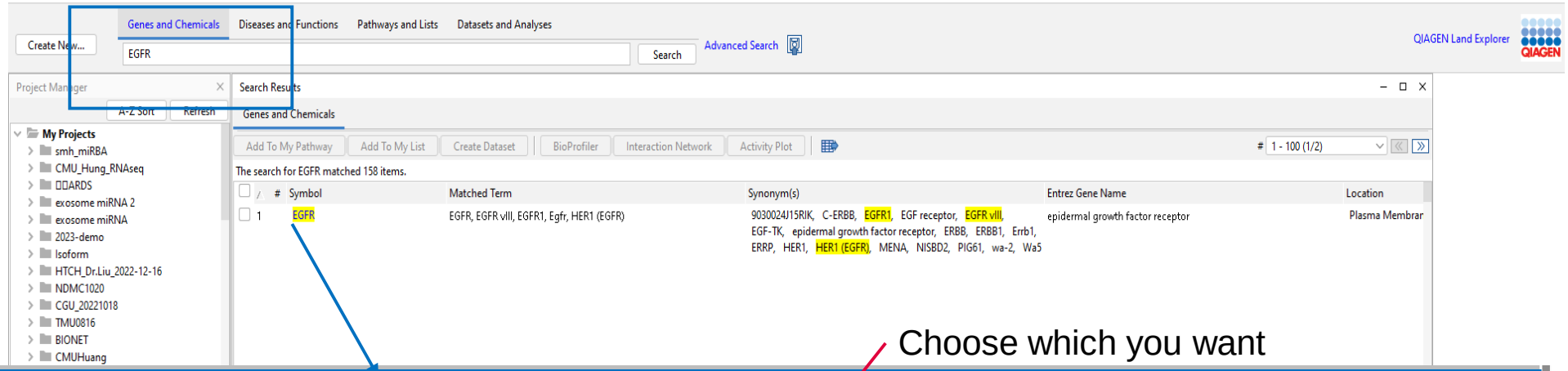
Cell line expression

Tumor expression



Hematopoietic expression (BluePrint)

IPA with OmicSoft Land Explorer



Choose which you want

OmicSoft Land Explorer: Sample-level experimental data

Data Type / Data Source	Normal Tissue	Cell Lines	Oncology Consortia	Oncology Studies	Disease Studies
RNA-seq expression:	Solid tissue (GTEx), Solid tissue (HPA), Blueprint	Cancer cell lines (CCLE)	TCGA, TARGET, BeatAML, ICGC, CGCI, CCLE+GTEx+TCGA, ENCODE RNA-associated gene knockdown	General oncology, Mouse studies	Human disease, Mouse disease, Rat disease
Microarray expression:	Solid tissue (GTEx)	Cancer cell lines (CCLE), Cell lines (Other)	TARGET, expO, METABRIC, CCLE+GTEx	General oncology, Metastasis, Mouse studies	Human disease, Mouse disease, Rat disease
Differential regulation:	Solid tissue (GTEx)	Treated cells (LINCS)	TCGA, TARGET, ENCODE RNA-associated gene knockdown	General oncology, Metastasis, Mouse studies	Human disease, Mouse disease, Rat disease
Alteration frequency:		Cancer cell lines (CCLE), Cell lines (Other)	TCGA, TRACERx, BeatAML, ICGC, TARGET, METABRIC	General oncology, Metastasis	
Survival by expression:			TCGA, BeatAML, TARGET, CGCI	General oncology, Clinical outcomes	
Single Cell differential regulation:	Human Cell Landscape (HCL), Tabula Sapiens			Human Disease (UMI), Human Disease (non-UMI), Mouse Disease (UMI), Mouse Disease (non-UMI)	Human Disease (UMI), Human Disease (non-UMI), Mouse Disease (UMI), Mouse Disease (non-UMI)
Protein expression:	Solid tissue (GTEx)	Cancer cell lines (CCLE)		General oncology	

IPA Gene View :OmicSoft Land Explorer

Find projects by curated metadat

https://omicsoft-explorer.ingenuity.com/overview/0

OmicSoft Explorer

Help Gene Chen

Saved queries

There are no saved queries

Saved gene analyses

There are no saved gene analyses

Saved comparison analyses

There are no saved comparison analyses

Saved differential expression match analyses

There are no saved differential expression match analyses

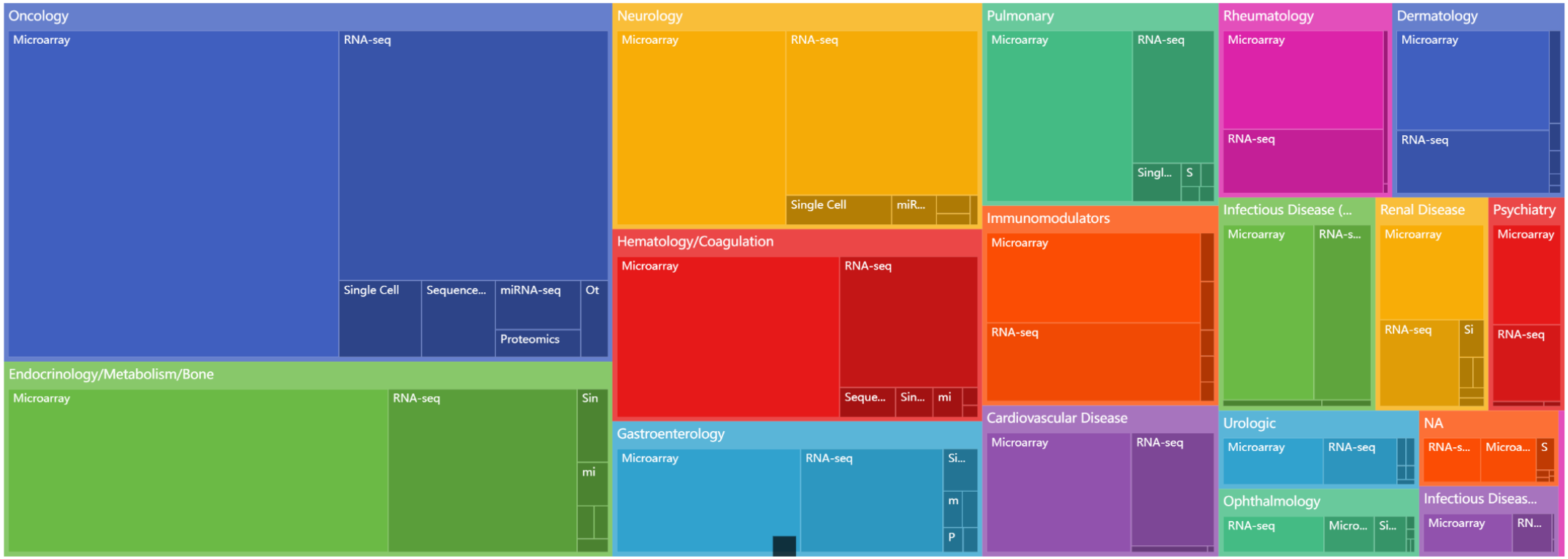
Find projects by curated metadata

Experiment themes | Data types | Database groups

Add keywords to build the search query

Project distribution Group by Therapeutic area | Subgroup by Data type

See 11421 projects

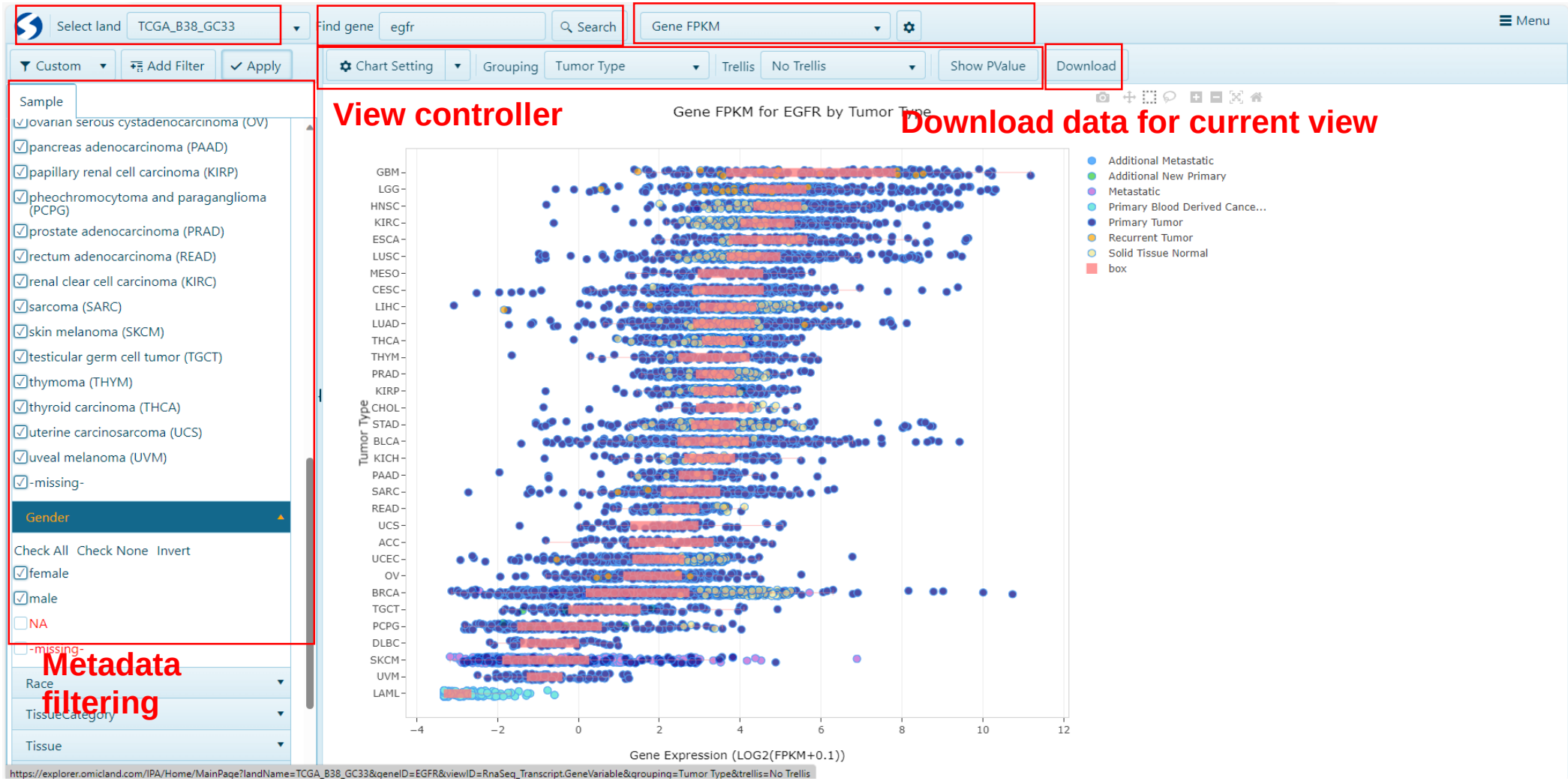


Example searches:

Normal tissue expression with RNA-seq data, in human tissue

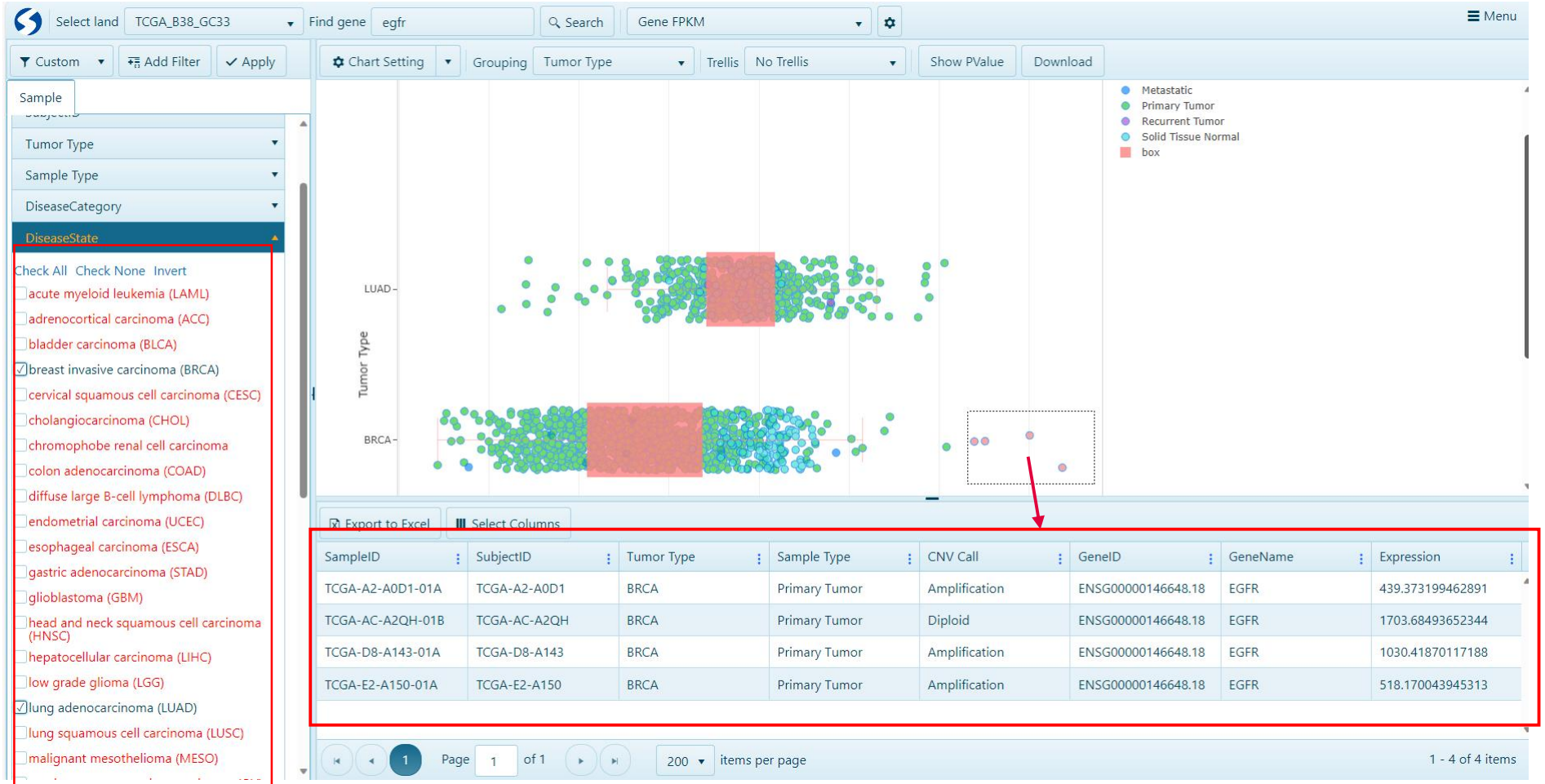
Experiments in normal human lung tissue (clinical samples)

- **TCGA-B38-G33**


Land selection
Search bar
View selection
Select land
TCGA_B38_GC33
Find gene
egfr
Search
Gene FPKM
Menu
Custom
Add Filter
Apply
Chart Setting
Grouping
Tumor Type
Trellis
No Trellis
Show PValue
Download
View controller
Download data for current view
Gene FPKM for EGFR by Tumor Type
Sample
ovarian serous cystadenocarcinoma (OV)
pancreas adenocarcinoma (PAAD)
papillary renal cell carcinoma (KIRP)
pheochromocytoma and paraganglioma (PCPG)
prostate adenocarcinoma (PRAD)
rectum adenocarcinoma (READ)
renal clear cell carcinoma (KIRC)
sarcoma (SARC)
skin melanoma (SKCM)
testicular germ cell tumor (TGCT)
thymoma (THYM)
thyroid carcinoma (THCA)
uterine carcinosarcoma (UCS)
uveal melanoma (UVM)
-missing-
Gender
Check All Check None Invert
female
male
NA
-missing-
Race
TissueCategory
Tissue
Metadata filtering
GBM
LGG
HNSC
KIRC
ESCA
LUSC
MESO
CESC
LIHC
LUAD
THCA
THYM
PRAD
KIRP
CHOL
STAD
BLCA
KICH
PAAD
SARC
READ
UCS
ACC
UCEC
OV
BRCA
TGCT
PCPG
DLBC
SKCM
UVM
LAML
Tumor Type
−4
−2
0
2
4
6
8
10
12
Gene Expression (LOG2(FPKM+0.1))
Additional Metastatic
Additional New Primary
Metastatic
Primary Blood Derived Cance...
Primary Tumor
Recurrent Tumor
Solid Tissue Normal
box
https://explorer.omicland.com/IPA/Home/MainPage?landName=TCGA_B38_GC33&geneID=EGFR&viewID=RnaSeq_Transcript.GeneVariable&grouping=Tumor Type&trellis=No Trellis

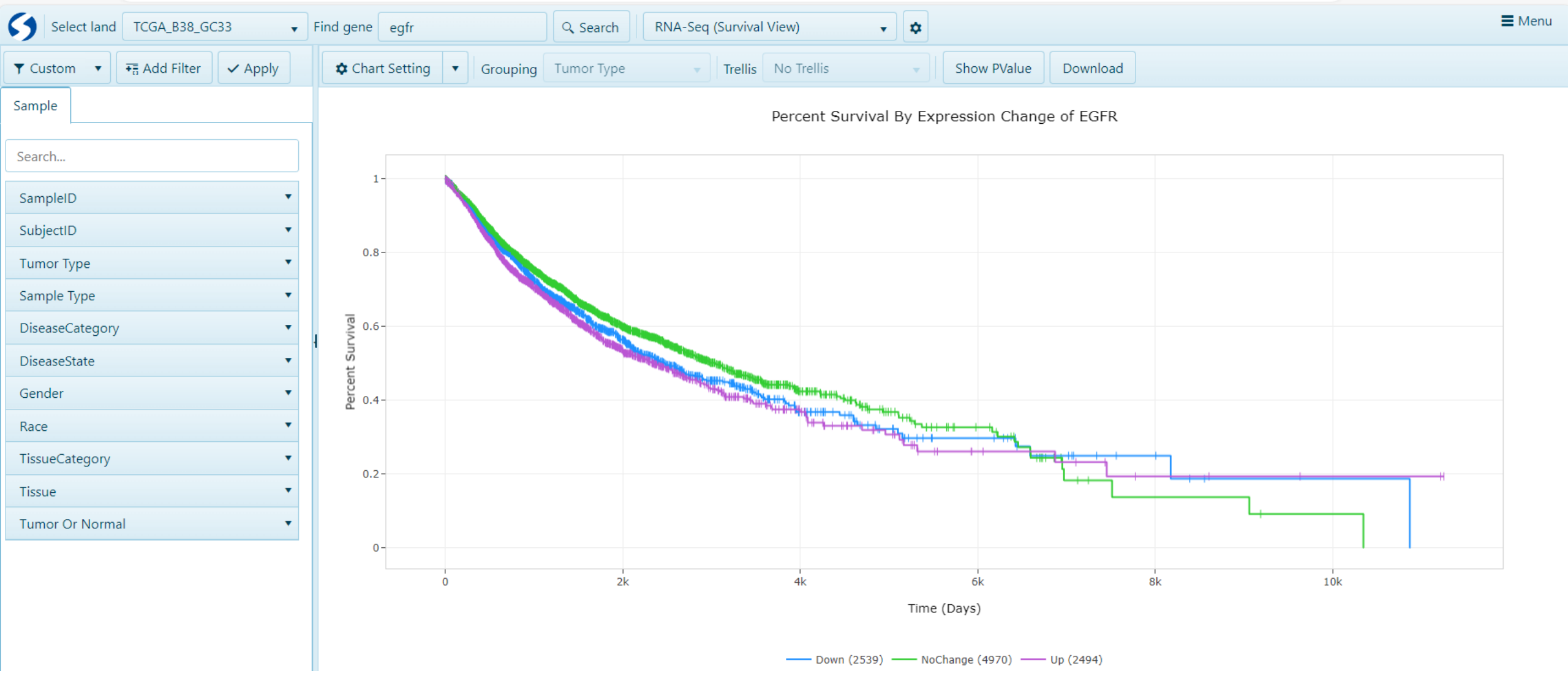
IPA with OmicSoft Land Explorer

- Through DiseaseState filter, to observe the expression difference of EGFR gene in cancer type in TCGA
- Select a specific experimental group to view more detailed information.



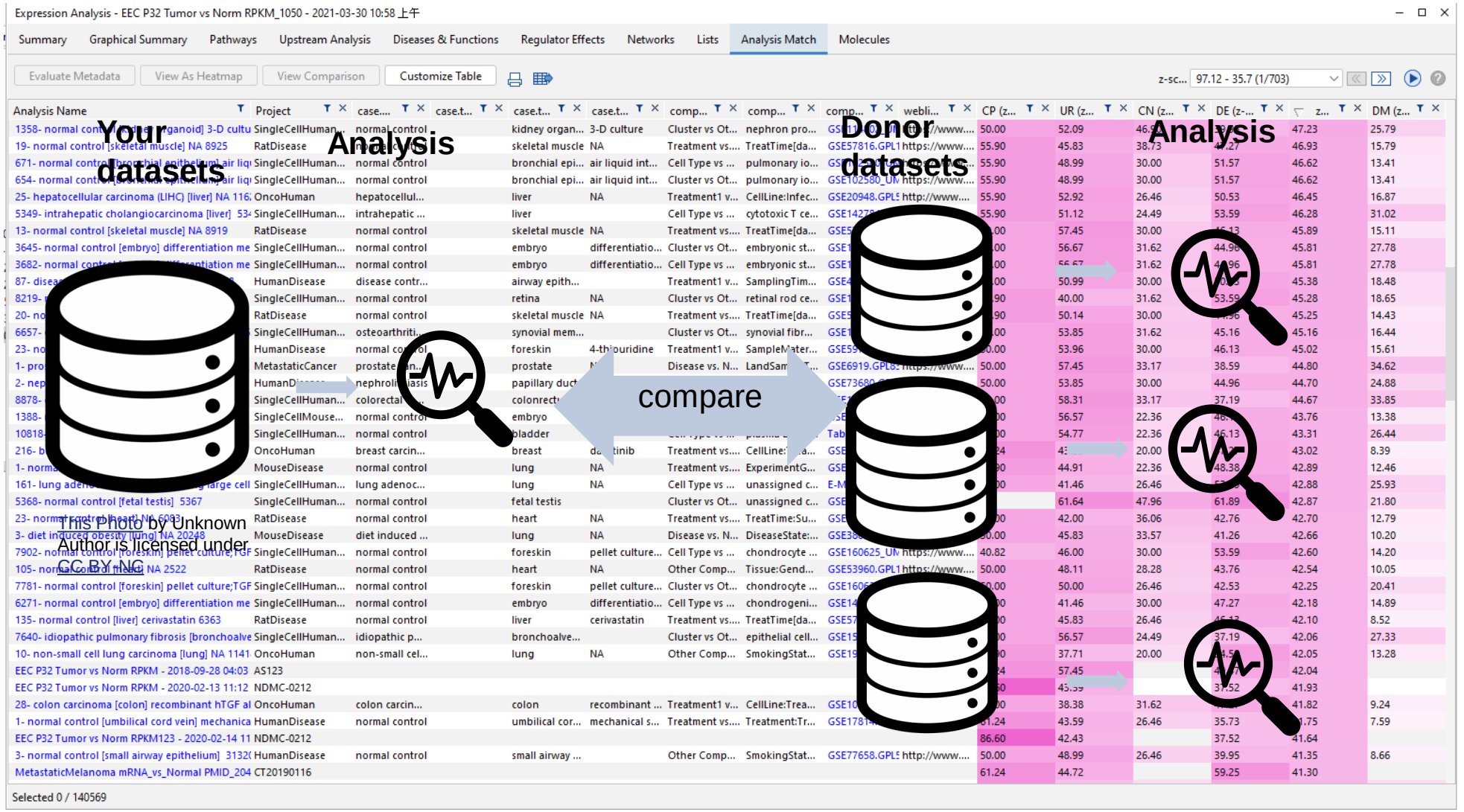
SURVIVAL ANALYSIS RESULT IN TCGA DATASET

TCGA_B38_GC33



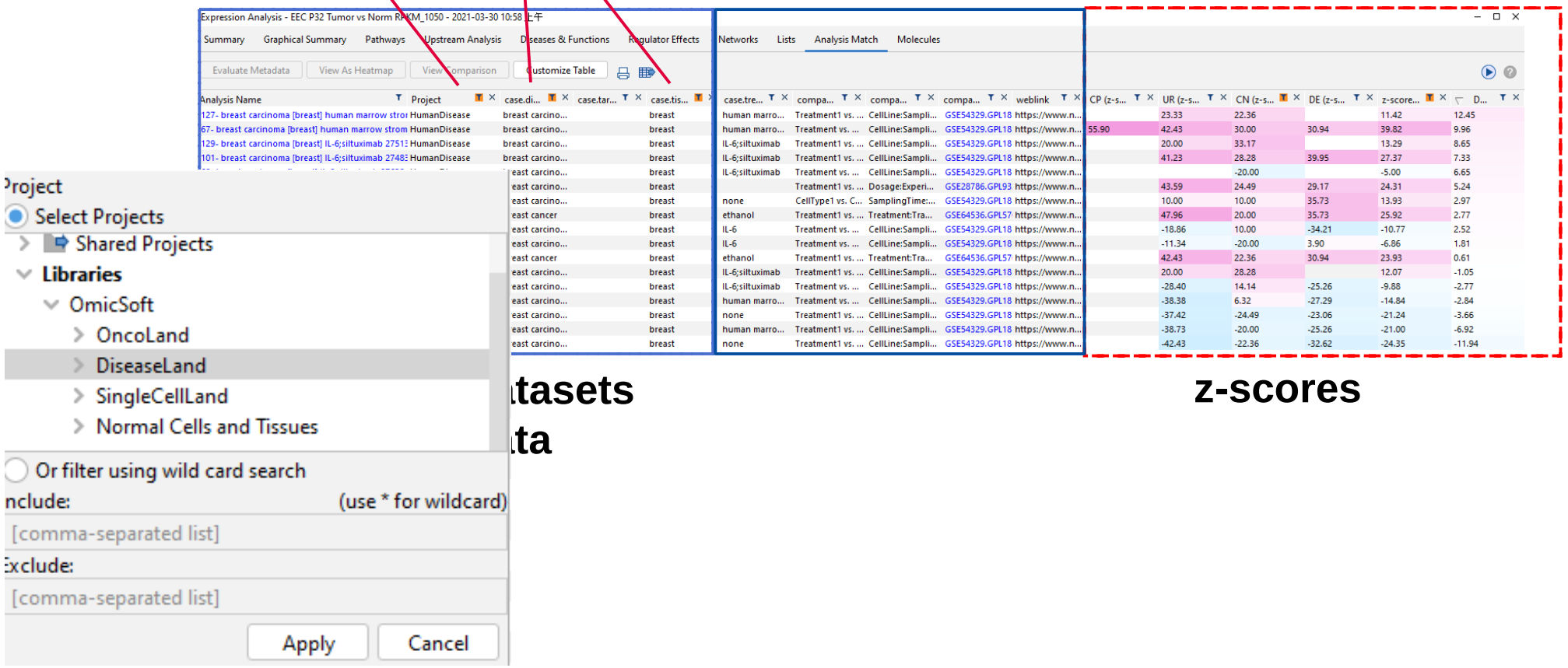
Analysis matching

Automatically discover other IPA Core Analyses with similar (or opposite) biological results as compared to yours, to help confirm your interpretation of the results or to provide unexpected insights into underlying shared biological mechanisms

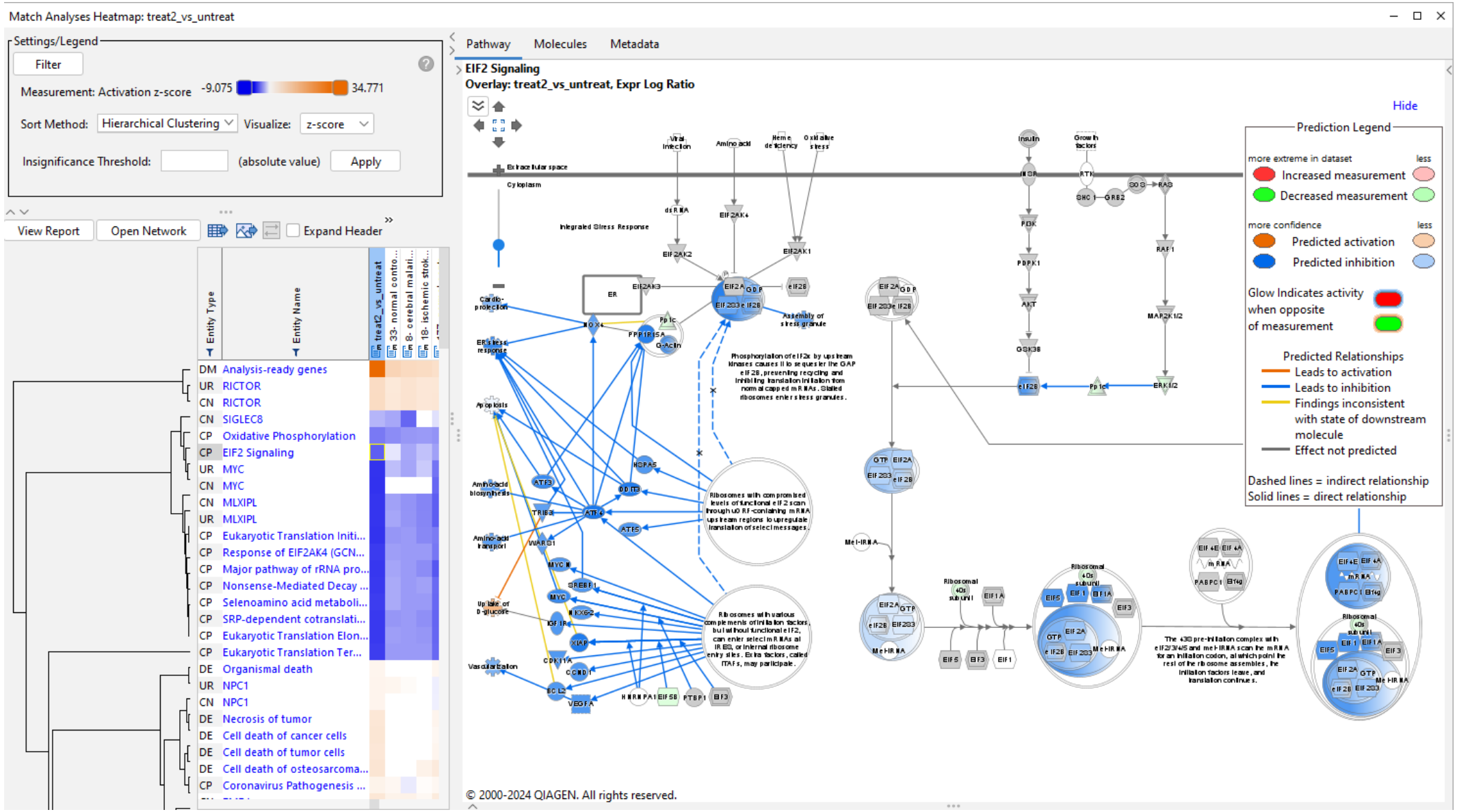


Mapping Your Results to OmicSoft Datasets by IPA Analysis Match

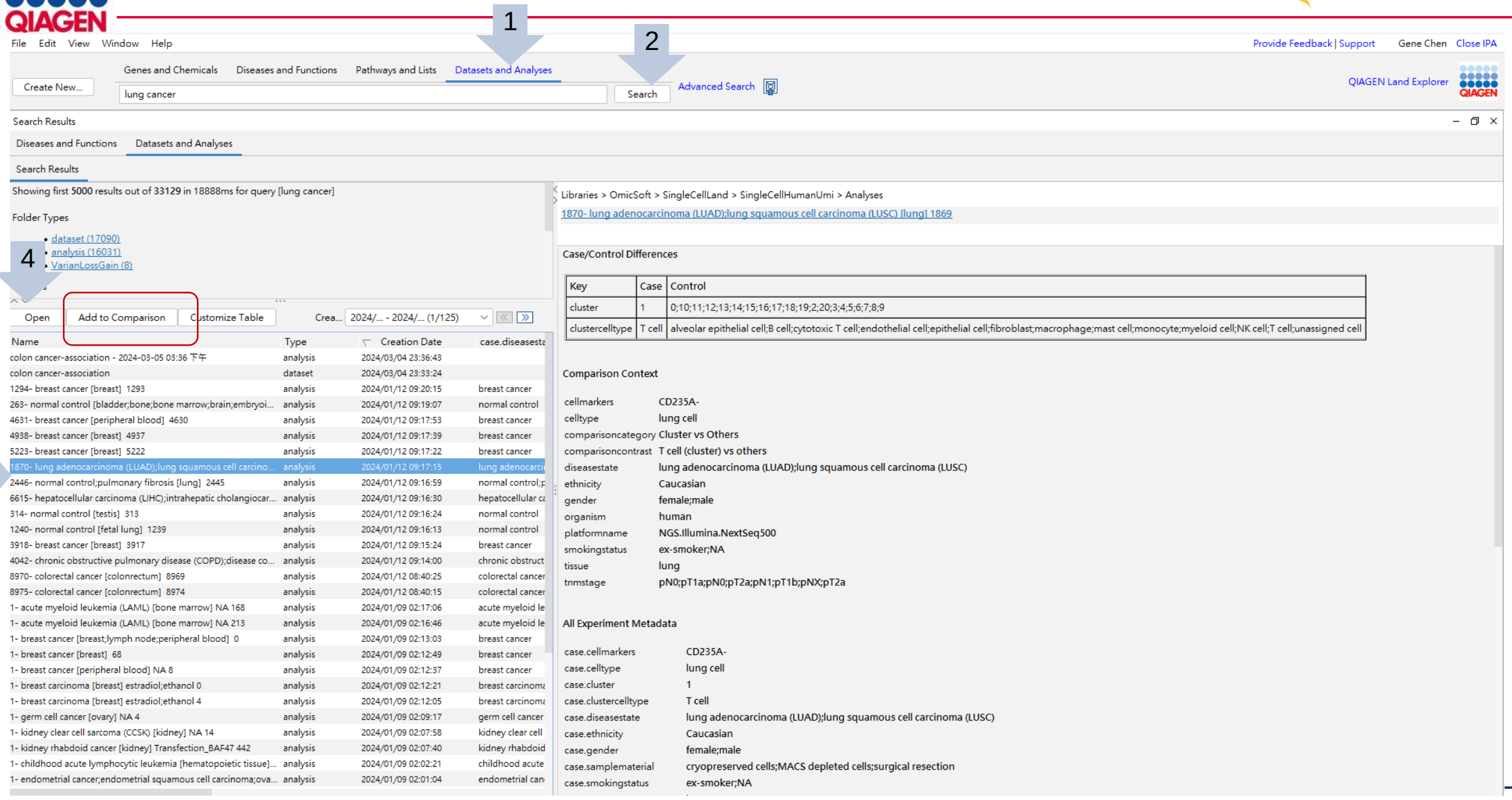
Project **Cell & Tissue** Datasets information **similar** **opposite**



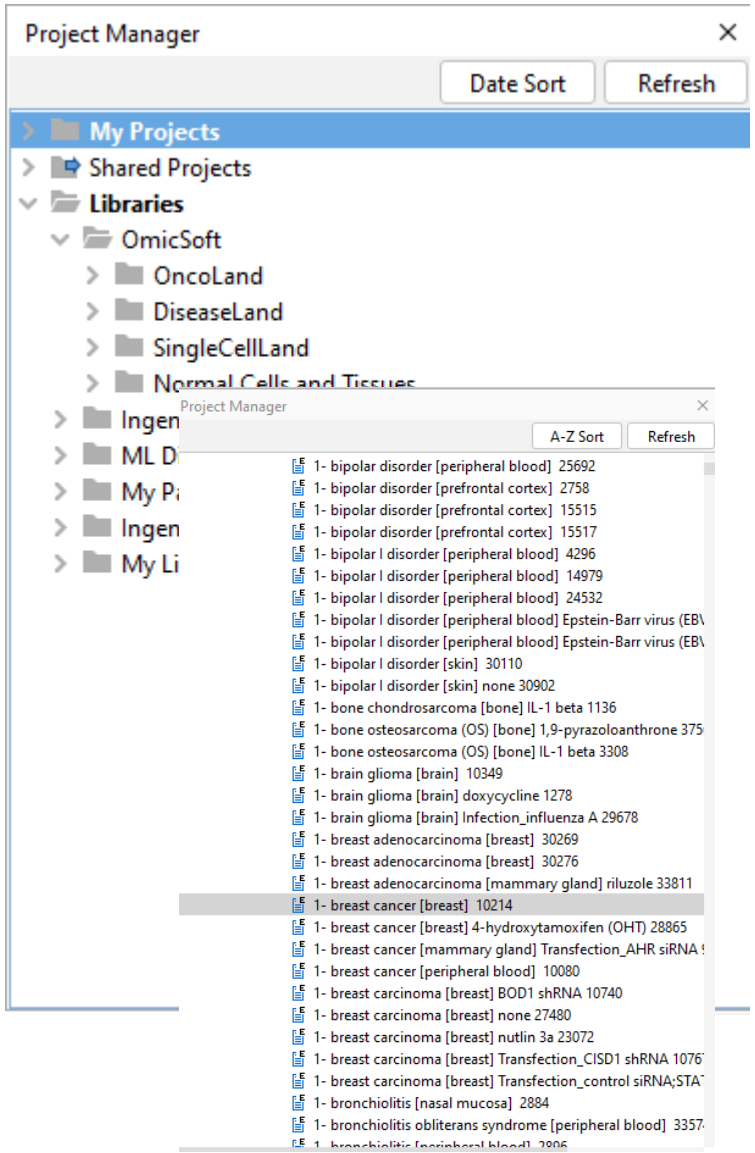
Analysis Match



Dataset and analysis search

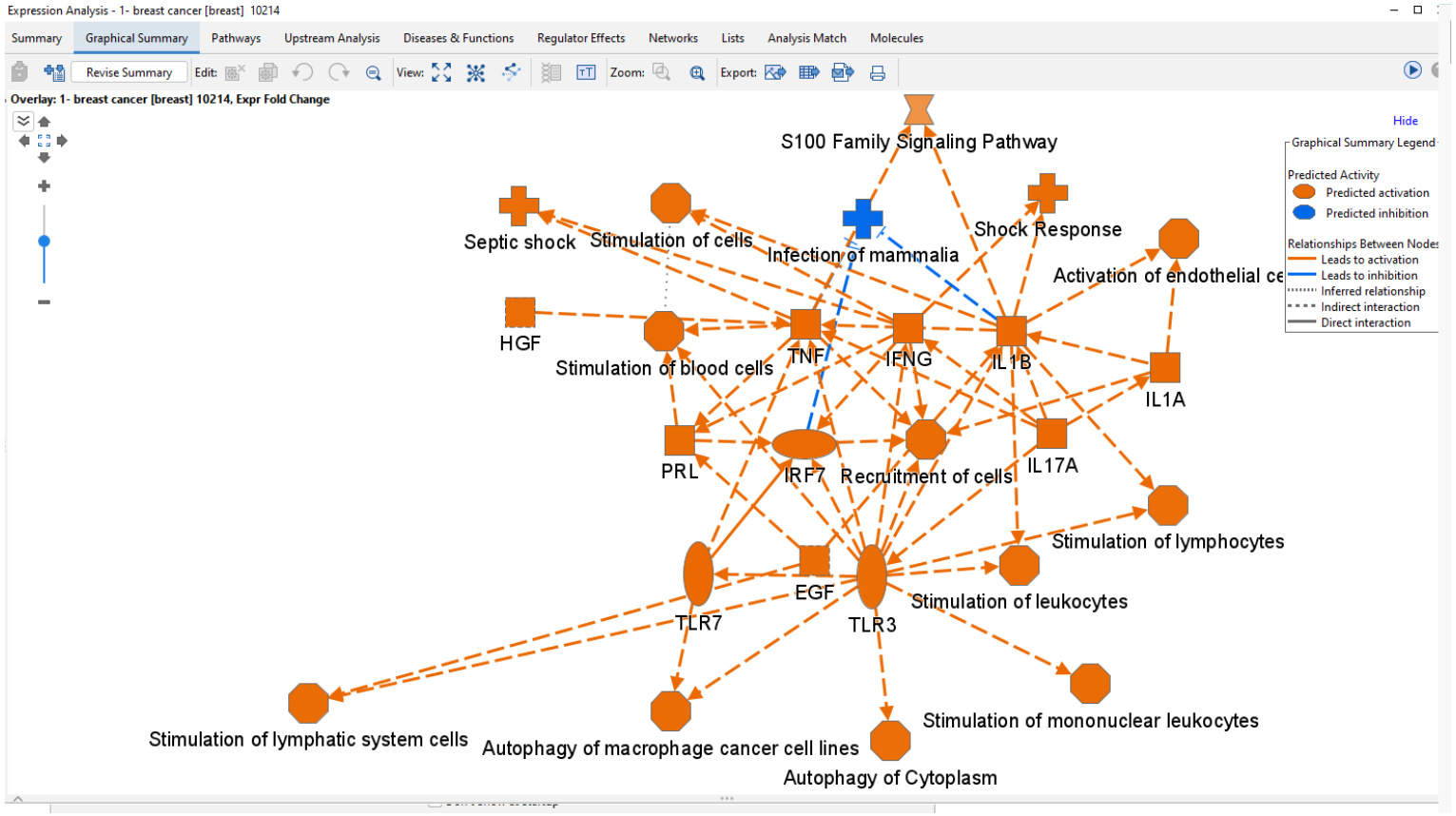


OmicSoft data storage and analysis in IPA



You can also use the repository without your own analysis, just by searching for available analyses of interest.

Graphical summary



What's new in the QIAGEN® Ingenuity Pathway Analysis Fall Release (2024)

IPA interpret

QIAGEN IPA Interpret

Want to analyze your own data? Gene Chen Logout

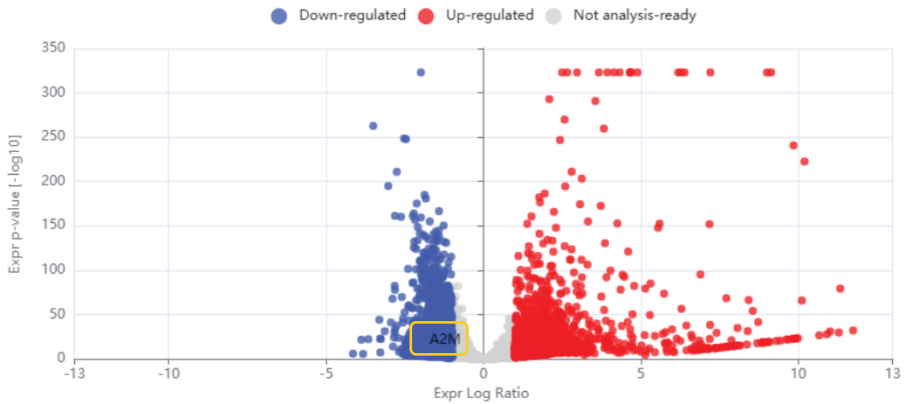
View Details →

Dataset

3891 genes passed cutoffs (1706 down and 2185 up)

Cutoffs: Expr Log Ratio <-1.0, >1.0, Expr False Discovery Rate (q-value) <0.05

X Axis: Expr Log Ratio Y Axis: Expr p-value Clear Labels

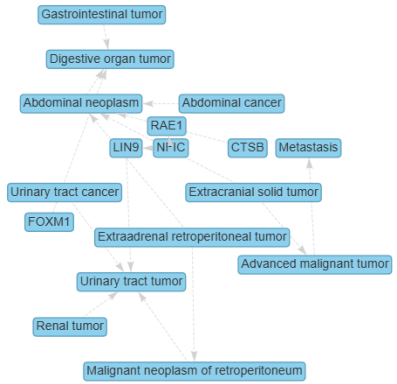


Dataset molecules

Name ▲	Entrez Gene	Identifier	Expr p-value	Expr Log Ratio	Molecule Type
Filter	Filter	Filter	Filter ≤	Filter abs. ≥	Select items
A1BG-AS1	A1BG antisense RNA 1	A1BG-AS1	0.47	0.15	other
A2M	alpha-2-macroglobulin	A2M	9.39e-6	-1.21	other
A4GALT	alpha 1,4-galactosyltransferase (P1PK blood group)	A4GALT	1.69e-7	1.07	enzyme
AAAS	aladin WD repeat nucleoporin	AAAS	4.85e-17	-1.47	other
AACS	acetoacetyl-CoA	AACS	0.82	-0.04	enzyme

View Details →

Graphical Summary



AI suggests the following synopsis of this network:

Top Biological Themes

Theme 1: Tumor Hierarchy and Progression

This network showcases the interconnected nature of different types and stages of tumors, particularly focusing on abdominal, gastrointestinal, digestive organ, and urinary tract tumors. Each link in the network indicates a progression or regression in the severity or spread of the cancer tissues, highlighting the multi-layered hierarchy of tumor development.

Theme 2: Cancer Metastasis Dynamics

The decrease in advanced malignant tumors leading to a decrease in metastasis illustrates the dynamic nature of cancer spreading processes within the body. By identifying key factors in malignant tumor progression such as extracranial solid tumors and gastro intestinal

Sample t

IPA interpret Canonical Pathway Bubble Plot (2025 summer release)

IPA interpret

In canonical pathway, could show volcano bubble plot

1. Z-score
2. P-value
3. Overlay molecules
4. Percentage overlap
5. Pathway type
6. Total pathway size

IPA interpret Canonical Pathway Bubble Plot (2025 summer release)

IPA interpret

In canonical pathway, could show each molecules overlap in this pathway

Dataset molecules for Cerebral Malformation Signaling Pathway

Showing all **19** molecules

Name ▲	Entrez Gene	Identifier	Expr p-value	Expr Log Ratio	Expected	Molecule Type	Location
Filter	Filter	Filter	Filter ≤	Filter abs. ≥	Select	Select	Select
AKT1	AKT serine/threonine kinase 1	AKT1	1.44e-4	-0.63	Up	kinase	Cytoplasm
AKT2	AKT serine/threonine kinase 2	AKT2	7.32e-12	-4.42	Up	kinase	Cytoplasm
AKT3	AKT serine/threonine kinase 3	AKT3	3.05e-3	-0.82	Up	kinase	Cytoplasm
CCM2	CCM2 scaffold protein	CCM2	6.84e-3	-4.77	Down	other	Cytoplasm
CDKN1A	cyclin dependent kinase inhibitor 1A	CDKN1A	0.05	-4.64	Up	kinase	Nucleus
CKS1B	CDC28 protein kinase regulatory subunit 1B	CKS1B	2.95e-4	-5.17	Down	kinase	Unknown
CTNNA1	catenin alpha 1	CTNNA1	1.40e-21	-0.62	Down	other	Plasma Membrane
CTNNB1	catenin beta 1	CTNNB1	1.30e-25	-1.25	Down		Nucleus
F2	coagulation factor II, thrombin	F2	2.15e-19	0.87	Up	peptidase	Extracellular Space
F5	coagulation factor V	F5	6.71e-4	0.86	Down	other	Extracellular Space

Canonical_Pathways_Dataset_Molecules

IPA interpret in upstream regulator

QIAGEN IPA Interpret

Want to analyze your own data? Kristin O'Malley Logout

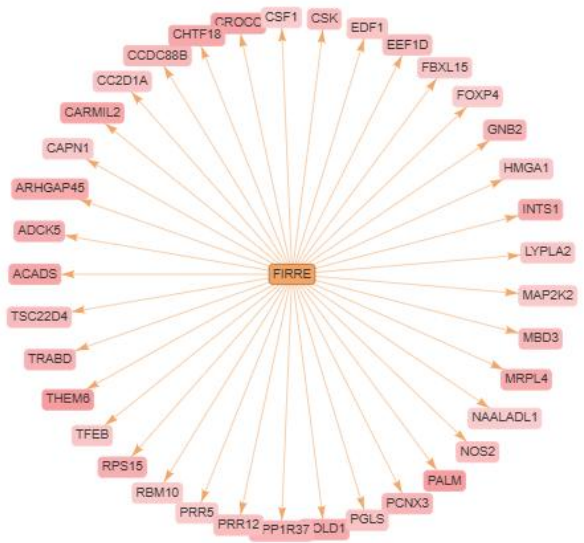
Upstream Regulators

Potentially activated or inhibited upstream molecules driving differential changes in the dataset

Regulator	Molecule Type	P-value ▲	Activation z-score	Percentage overlap	Overlapping molecules	Total known targets
Filter	Select items	Filter <	Filter abs. >	Filter >	Filter >	Filter >
FIRRE	other	2.52e-20	6.08	40.22	37	92
PTPRR	phosphatase	1.42e-16	-5.91	33.98	35	103
miR-3648 (miRNAs w/seed GCCGCGG)	mature microRNA	3.56e-10	-5.29	25.45	28	110
TP73	transcription regulator	1.91e-8	4.88	13.29	69	519
NTRK1	kinase	6.59e-8	5.98	15.21	47	309
COLQ	other	3.26e-7	-1.80	26.09	18	69

Upstream regulator representation

FIRRE Figure Legend OFF



FIRRE network

AI suggests the following synopsis of this network:

Top Biological Themes in the given Biological Network

Gene Regulation and Expression

The relationships suggest that FIRRE (Functional Intergenic Repeating RNA Element) is a significant regulator of various genes, affecting their expression. The broad range of genes influenced by FIRRE indicates a complex regulatory role.

Metabolic Pathways

Several of the genes such as ACADS (Acyl-CoA Dehydrogenase) and PGLS (6-Phosphogluconolactonase) are involved in metabolic processes. The increase of these genes implies FIRRE may play a role in regulating metabolic pathways.

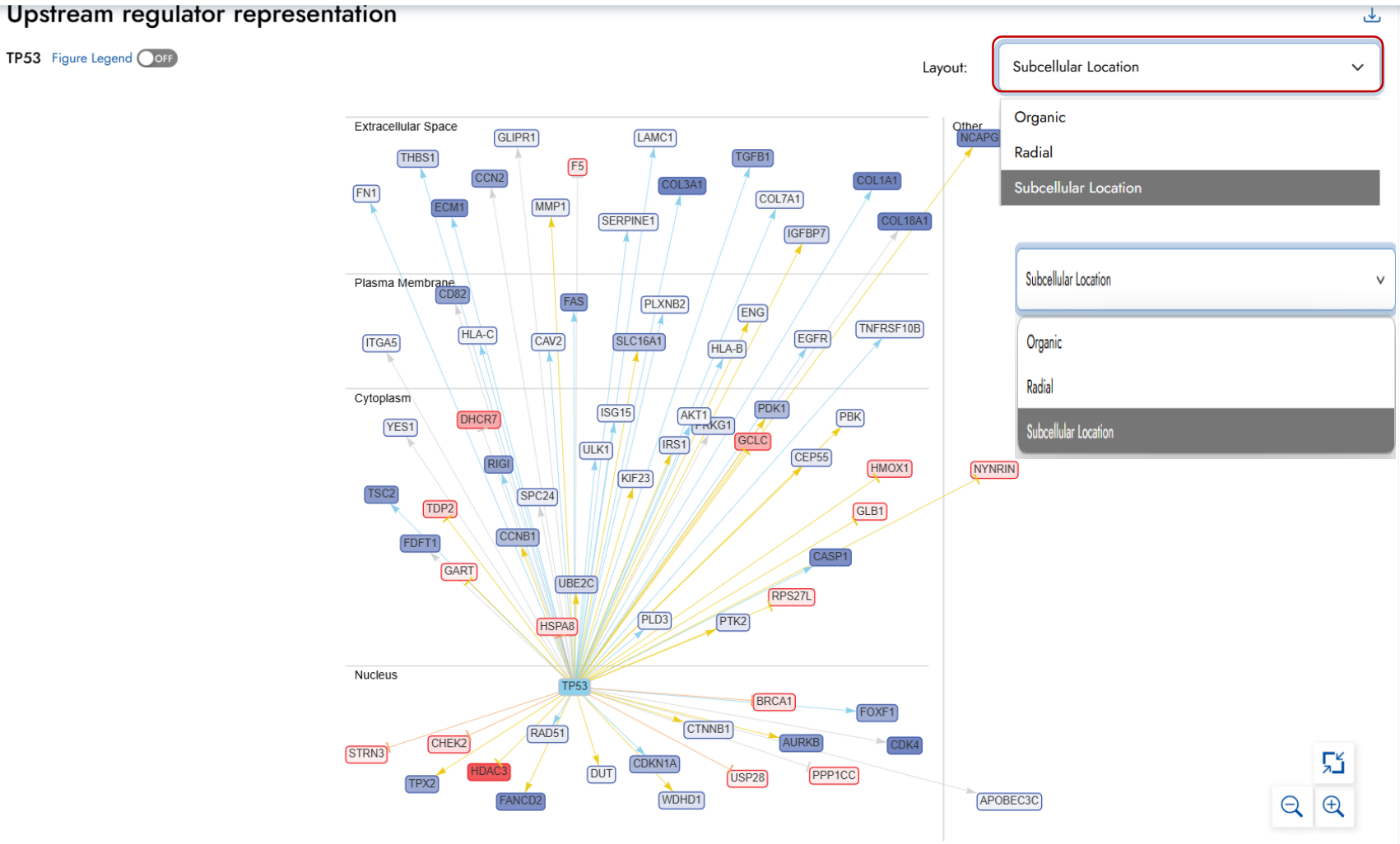
Signal Transduction

Genes like MAP2K2 (Mitogen-Activated Protein Kinase Kinase 2) and CSK (C-Src Tyrosine Kinase) are key components of signal transduction pathways. FIRRE's impact on their activity suggests a role in cellular response mechanisms.

Immune Response

CSF1 (Colony Stimulating Factor 1) and NOS2 (Nitric Oxide Synthase 2) are crucial for immune system

IPA interpret in upstream regulator



TP53

The Role of TP53 in Cellular Regulation and Tumor Suppression AI-Suggested

Cell Cycle Regulation

The decrease of TP53 leads to a decrease in genes such as CDK4, CCNB1, and AURKB, which are crucial for cell cycle progression. This suggests that TP53 plays a significant role in regulating the cell cycle, preventing uncontrolled cell division, a hallmark of cancer.

DNA Damage Response and Repair

TP53 is known to be involved in DNA damage response. The decrease of TP53 results in decreased activity of genes like RAD51 and FANCD2, which are essential for DNA repair processes, indicating TP53's role in maintaining genomic stability.

Apoptosis and Cell Death

The decrease of TP53 leads to decreased activity of CASP1 and FAS, both of which are involved in apoptotic pathways. This highlights TP53's role in promoting apoptosis, a critical mechanism for eliminating damaged or cancerous cells.

Tumor Suppression and Oncogenesis

The network shows that a decrease in TP53 causes an increase in BRCA1 and CHEK2, both of which are involved in tumor suppression pathways. This suggests that TP53 is a central player in preventing oncogenesis by regulating other tumor suppressor genes.

Metabolic Regulation and Stress Response

The increase in genes like HMOX1 and GCLC upon TP53 decrease suggests a role in metabolic regulation and oxidative stress response. TP53 may influence cellular metabolism and the antioxidant response, which are crucial for cell survival under stress conditions.

This AI summary is based on the pairs of connected molecules or other entities in the network and

IPA interpret in Upstream Regulator

We can change the X-axis Y-axis

Color showed the Z-score

Upstream Regulators

Potentially activated or inhibited upstream molecules driving differential cha s in the dataset

Upstream Regulators

Potentially activated or inhibited upstream molecules driving differential changes in the dataset

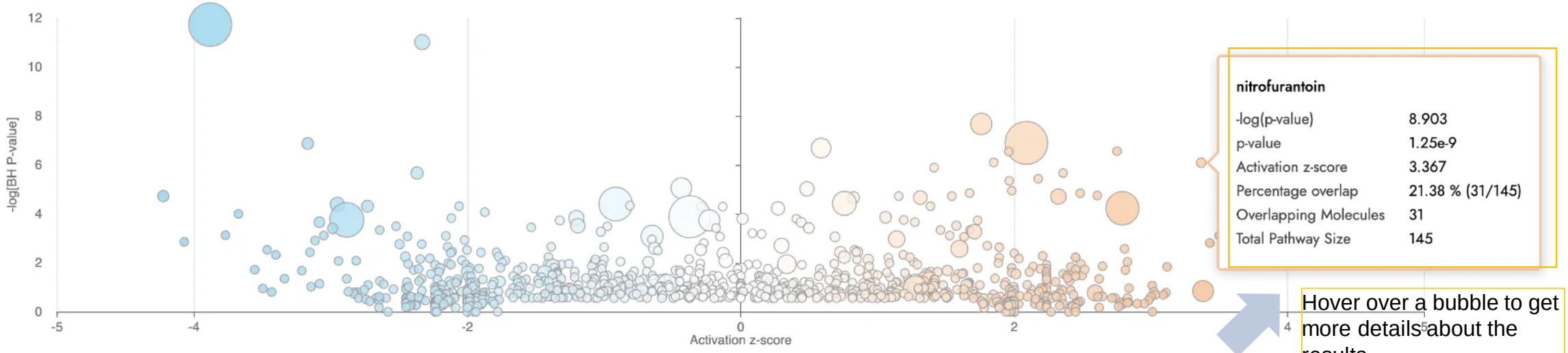
Table | Bar Chart | **Bubble Chart**

Chart Type: Bubble volcano chart | X-axis: Activation z-score | Y-axis: -log[BH P-value] | Bubble size: Overlapping molecules | Bubble color: Activation z-score | Data display: Select Range... | More filters

Figure Legend ON

Z-Score: Positive | Negative | Zero | Neutral or No Prediction

Overlapping molecules 54 108 215



nitrofurantoin

-log(p-value)	8.903
p-value	1.25e-9
Activation z-score	3.367
Percentage overlap	21.38 % (31/145)
Overlapping Molecules	31
Total Pathway Size	145

Hover over a bubble to get more details about the results

IPA interpret Canonical Pathway Bubble Plot (2025 summer release)

IPA interpret in Upstream Regulator

If we selected a upstream regulator, there was show molecules which affected by FGF7

Dataset molecules for TP53

Showing all **72** molecules

Name ▲	Entrez Gene	Identifier	Expr p-value	Expr Log Ratio	Expected	Molecule Type	Location
Filter	Filter	Filter	Filter ≤	Filter abs. ≥	Select	Select	Select
AKT1	AKT serine/threonine kinase 1	AKT1	1.44e-4	-0.63	Up	kinase	Cytoplasm
APOBEC3C	apolipoprotein B mRNA editing enzyme catalytic subunit 3C	APOBEC3C	7.69e-20	-0.90	--	enzyme	Unknown
AURKB	aurora kinase B	AURKB	1.62e-22	-6.69	Down	kinase	Nucleus
BRCA1	BRCA1 DNA repair associated	BRCA1	0.04	0.97	Down	transcription regulator	Nucleus
CASP1	caspase 1	CASP1	2.00e-30	-7.39	Up	peptidase	Cytoplasm
CAV2	caveolin 2	CAV2	4.84e-3	-0.83	Up	other	Plasma Membrane
CCN2	cellular communication network factor 2	CCN2	1.41e-11	-6.04	--	growth factor	Extracellular Space
CCNB1	cyclin B1	CCNB1	0.04	-4.32	Down	enzyme	Cytoplasm
CD82	CD82 molecule	CD82	1.13e-4	-6.00	--	other	Plasma Membrane
CDK4	cyclin dependent kinase 4	CDK4	2.00e-30	-9.17	--	kinase	Nucleus

IPA interpret in Disease and Function

In disease and functional, It also could show Bubble Chart

For Disease and Function
We could use more filter to select our interested disease and function

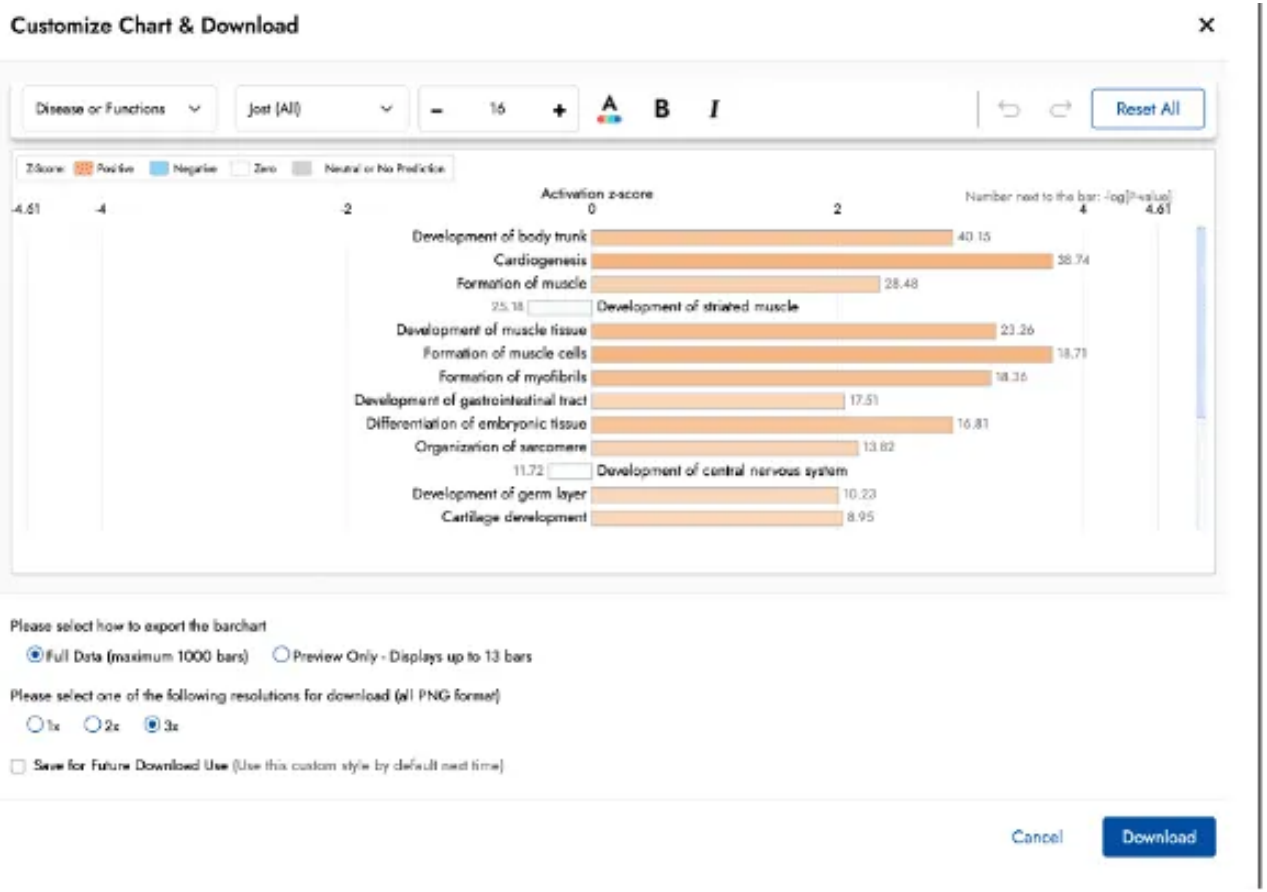
Customize bar charts for image export

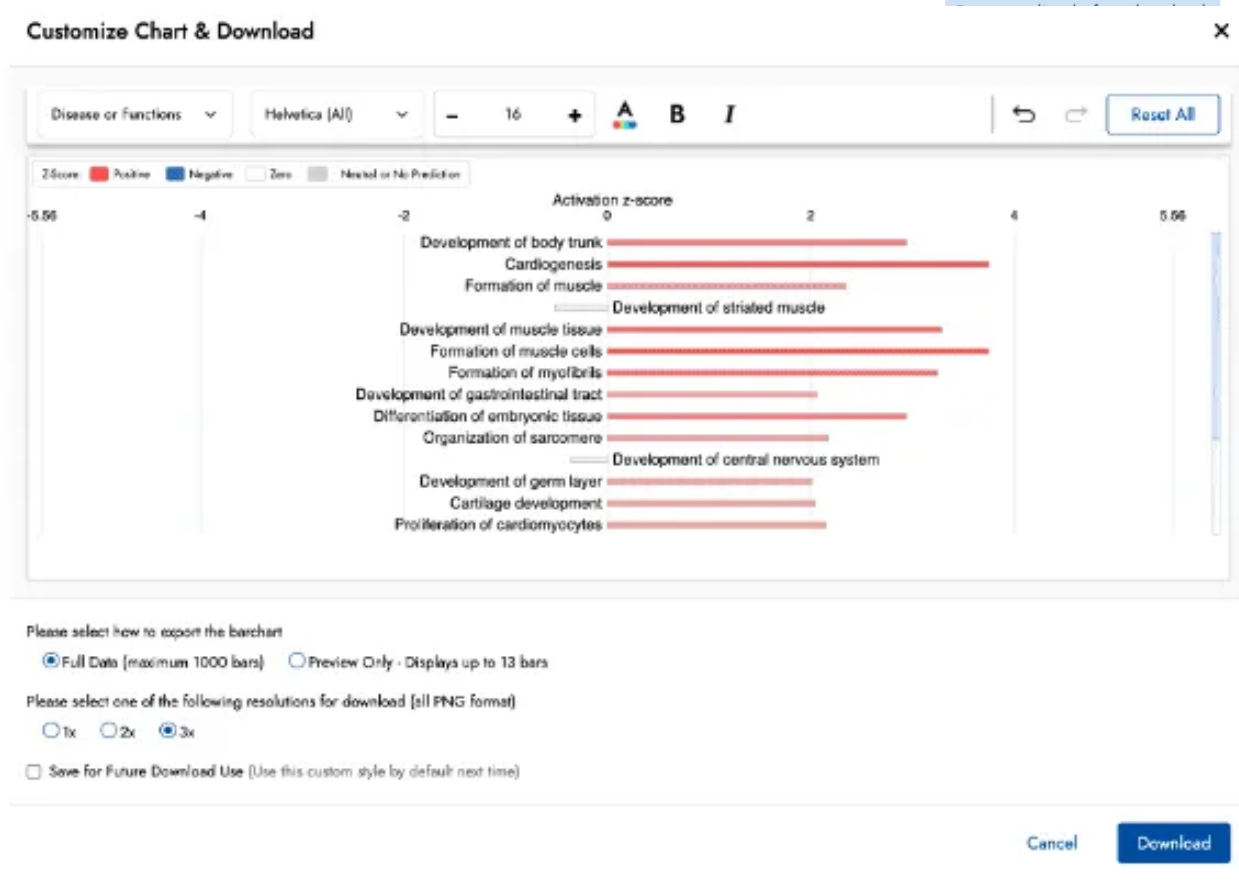
protein.24 / Canonical Pathways

Canonical Pathways

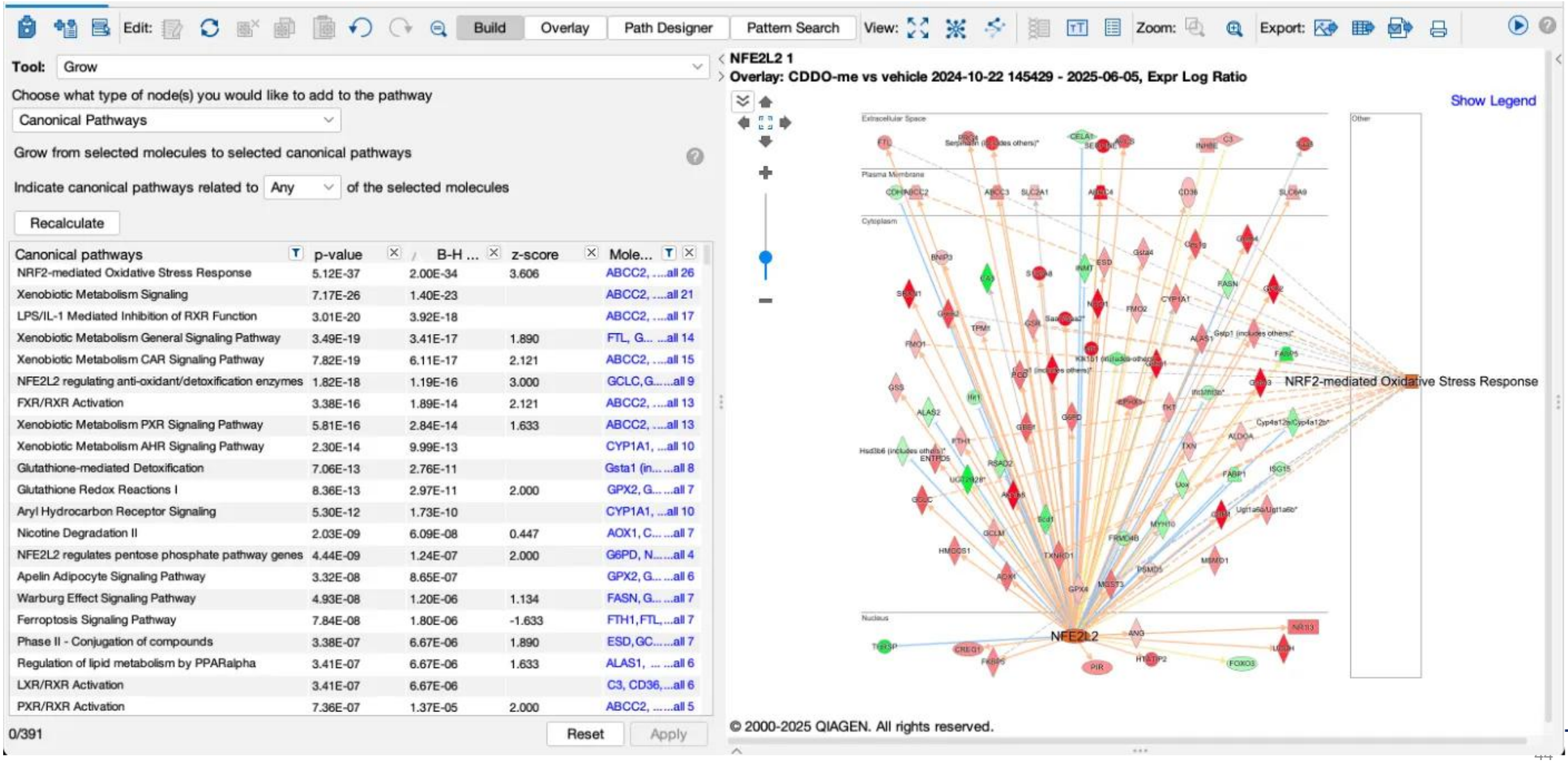
Signaling and metabolic pathways that are potentially activated or inhibited in the dataset

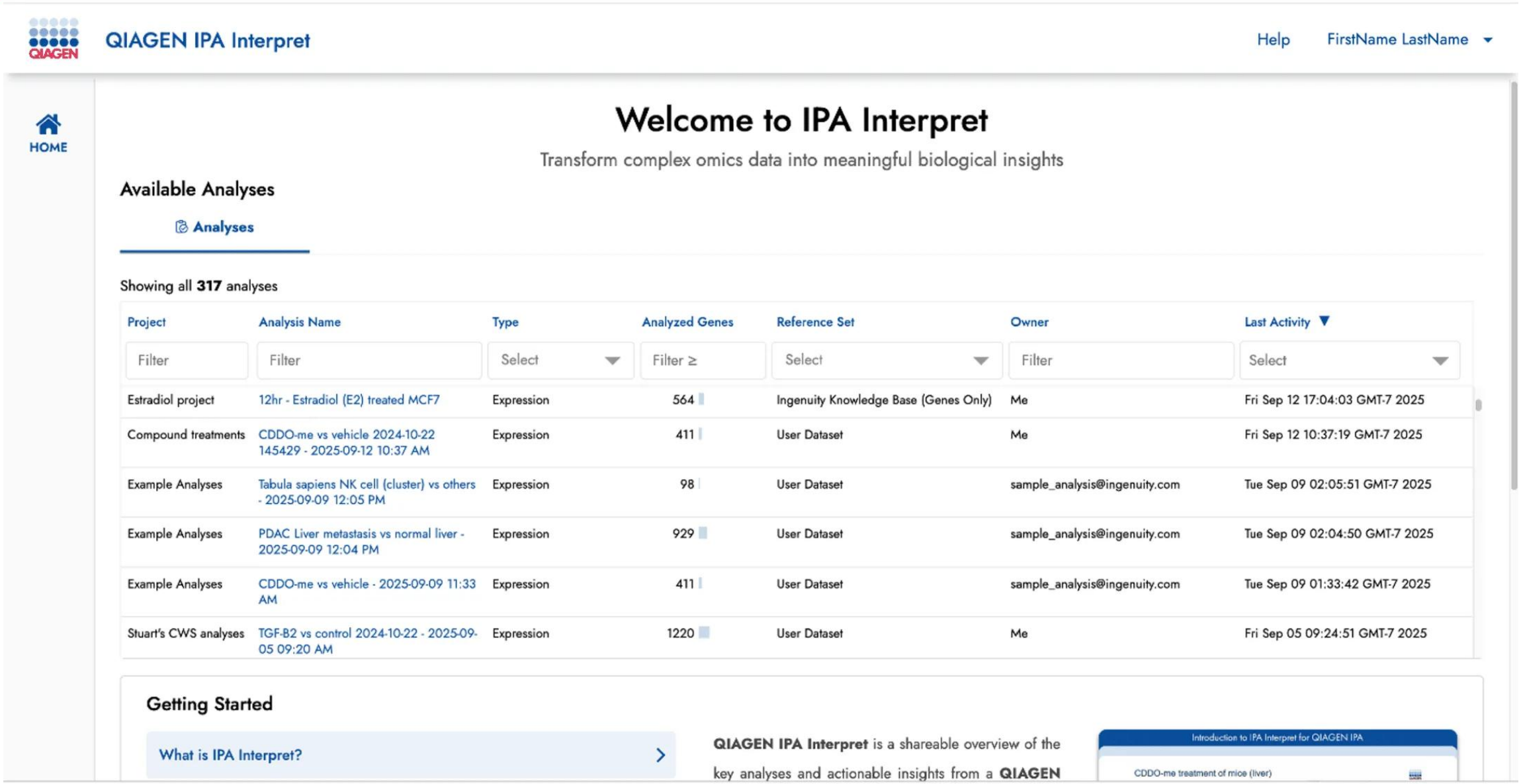
Download current chart





Grow function




QIAGEN IPA Interpret
Help
FirstName LastName
HOME
Welcome to IPA Interpret
Transform complex omics data into meaningful biological insights
Available Analyses
Analyses
Showing all 317 analyses
Project
Analysis Name
Type
Analyzed Genes
Reference Set
Owner
Last Activity
Filter
Filter
Select
Filter ≥
Select
Filter
Select
Estradiol project
12hr - Estradiol (E2) treated MCF7
Expression
564
Ingenuity Knowledge Base (Genes Only)
Me
Fri Sep 12 17:04:03 GMT-7 2025
Compound treatments
CDDO-me vs vehicle 2024-10-22 145429 - 2025-09-12 10:37 AM
Expression
411
User Dataset
Me
Fri Sep 12 10:37:19 GMT-7 2025
Example Analyses
Tabula sapiens NK cell (cluster) vs others - 2025-09-09 12:05 PM
Expression
98
User Dataset
sample_analysis@ingenuity.com
Tue Sep 09 02:05:51 GMT-7 2025
Example Analyses
PDAC Liver metastasis vs normal liver - 2025-09-09 12:04 PM
Expression
929
User Dataset
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Tue Sep 09 02:04:50 GMT-7 2025
Example Analyses
CDDO-me vs vehicle - 2025-09-09 11:33 AM
Expression
411
User Dataset
sample_analysis@ingenuity.com
Tue Sep 09 01:33:42 GMT-7 2025
Stuart's CWS analyses
TGF-B2 vs control 2024-10-22 - 2025-09-05 09:20 AM
Expression
1220
User Dataset
Me
Fri Sep 05 09:24:51 GMT-7 2025
Getting Started
What is IPA Interpret?
QIAGEN IPA Interpret is a shareable overview of the key analyses and actionable insights from a QIAGEN
Introduction to IPA Interpret for QIAGEN IPA
CDDO-me treatment of mice (liver)
Powered by QIAGEN Digital Insights
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Privacy Policy
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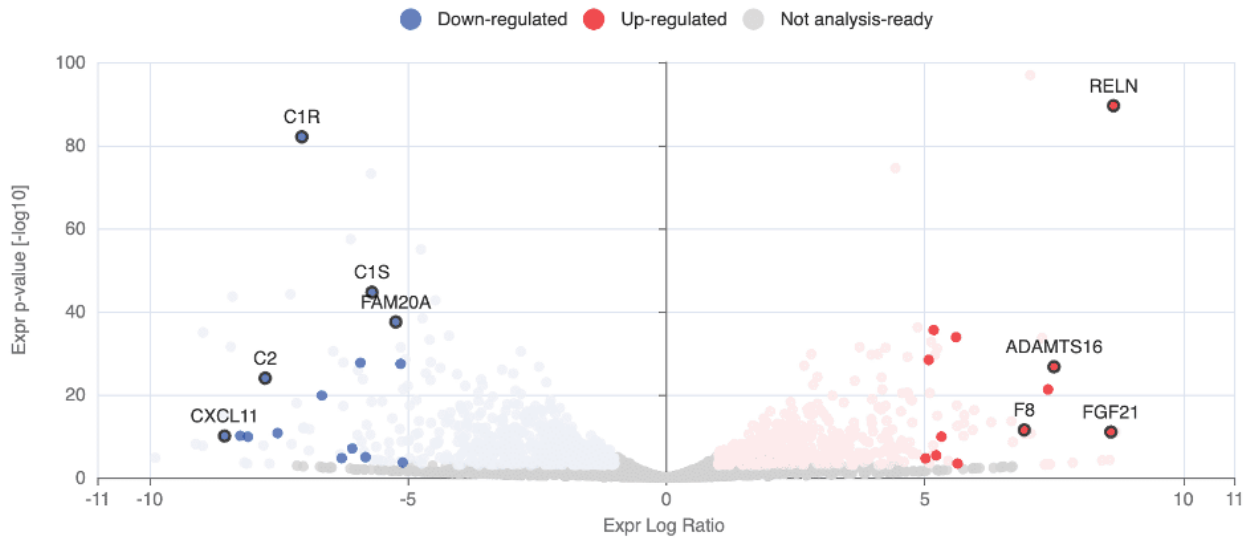
Cutoffs: Expr False Discovery Rate (q-value) <0.01, Expr Fold Change <-2.0, >2.0

X Axis: Expr Log Ratio Y Axis: Expr p-value Clear Selection



ADAMTS16

Entrez Gene Summary:

This gene encodes a member of the ADAMTS (a disintegrin and metalloproteinase with thrombospondin motifs) protein family. ADAMTS family members share several distinct protein modules, including a propeptide region, a metalloproteinase domain, a disintegrin-like domain, and a thrombospondin type 1 (TS) motif. Individual members of this family differ in the number of C-terminal TS motifs, and some have unique C-terminal domains. The encoded preproprotein is proteolytically processed to generate the mature protein, which may inhibit chondrosarcoma cell proliferation and migration. This gene may regulate blood pressure. [provided by RefSeq, May 2016]

Entrez Gene Name:

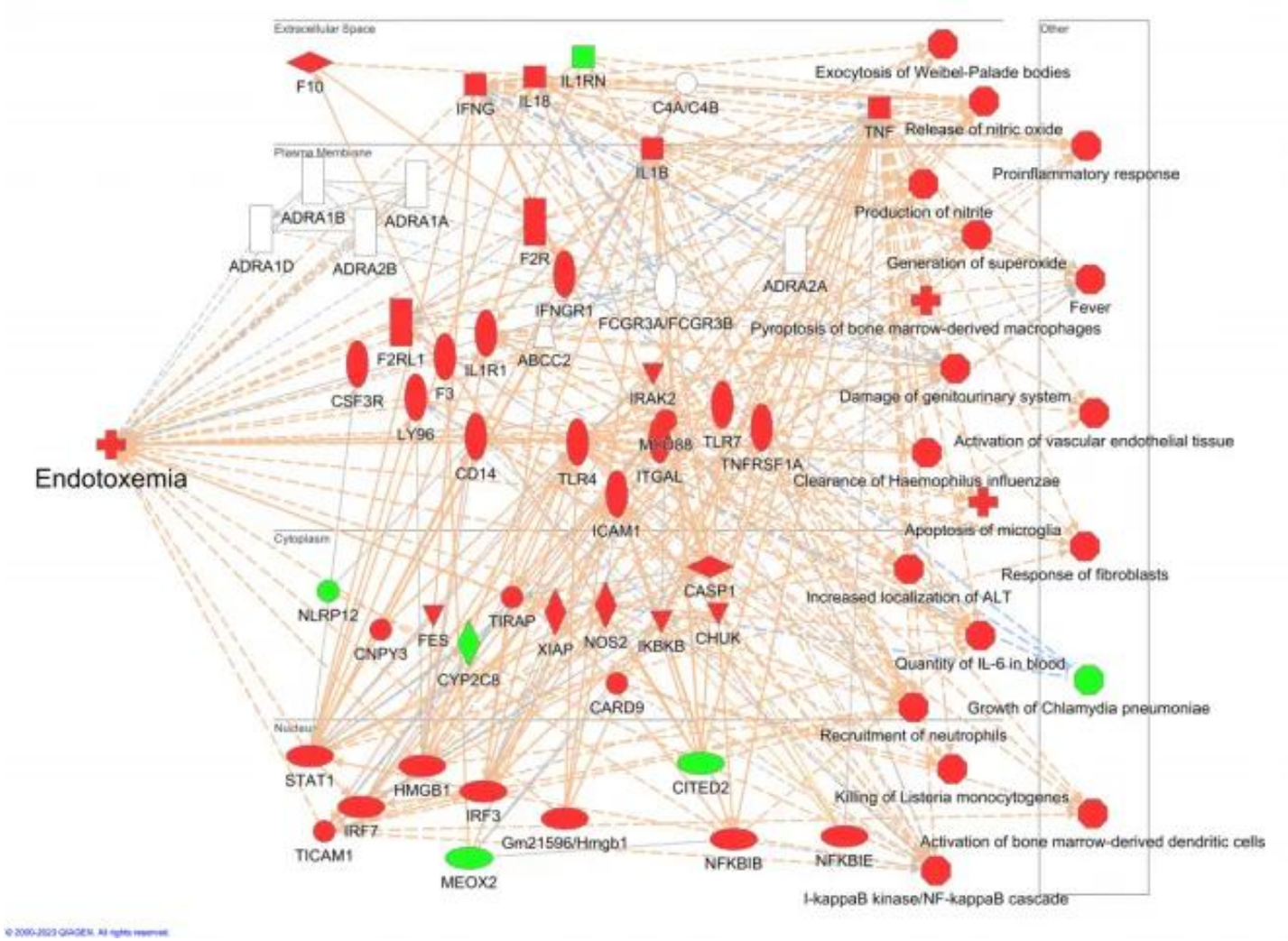
ADAM metallopeptidase with thrombospondin type 1 motif 16

Dataset molecules

Showing **32** of 13406 molecules

Name ▲	Entrez Gene	Identifier	Expr p-value	Expr p-value	Expr False Discovery Rate (q-value)	Expr Fold Change	Expr Log Ratio	Expr Other	Molecule Type	Location	Analyzed
Filter	Filter	Filter	Filter ≤	Filter ≤	Filter ≤	abs. ≥ 30	Filter abs. ≥	Filter ≤	Select	+1	Select
APOL6	apolipoprotein L6	ENSECAG00000018752	8.01e-11	1.43e-6	4.02e-9	-303.79	-8.25	3	transporter	Extracellular Space	Yes
BPIFB4	BPI fold containing family B member 4	ENSECAG00000017316	4.29e-6	0.08	8.50e-5	37.24	5.22	3	other	Extracellular Space	Yes

Using machine learning (ML) to mine the QIAGEN Knowledge Base, creating ~1500 disease, phenotype and function pathways all within the Ingenuity Pathway Analysis (IPA) software.



Formatting ‘omics data before uploading to IPA

Observation 1

Observation 2

	A	B	C	D	E
1	**geneid**	**UCvsNormal.Log2FoldChange**	**UCvsNormal.pval**	**52wksVedolizumabvsBaseline.Log2FoldChange**	**52wksVedolizumabvsBaseline.pval**
2	DDX11L1	-0.1067	0.2878	0.1183	0.1624
3	WASH7P	-0.1883	0.0097	0.3063	0.0006
4	FAM138F	-0.0761	0.4699	0.2466	0.0191
5	OR4F5	0.1474	0.5311	0.1713	0.2913
6	LOC729737	0.4789	0.0017	0.029	0.8331
7	LOC100133331	0.4789	0.0017	0.029	0.8331
8	LOC100132062	0.4789	0.0017	0.029	0.8331
9	OR4F29	0.2495	0.2389	0.2181	0.1887
10	JA429831	0.1215	0.3338	0.2556	0.0004

Analyte identifier REQUIRED to explore enrichment

RNA examples: Gene symbols, array identifiers from Affymetrix, Ensembl, etc.

Protein examples: UniProt, GenPept, Gene symbols, Ensembl. etc.

Metabolite examples: KEGG, CAS registry number, etc. **add multiple columns of ids to ensure best mapping*

Change values needed to calculate activity predictions

Change value examples: fold changes, ratios, etc.

Significance values: P-values **optional but recommended to enable filtering for significance*

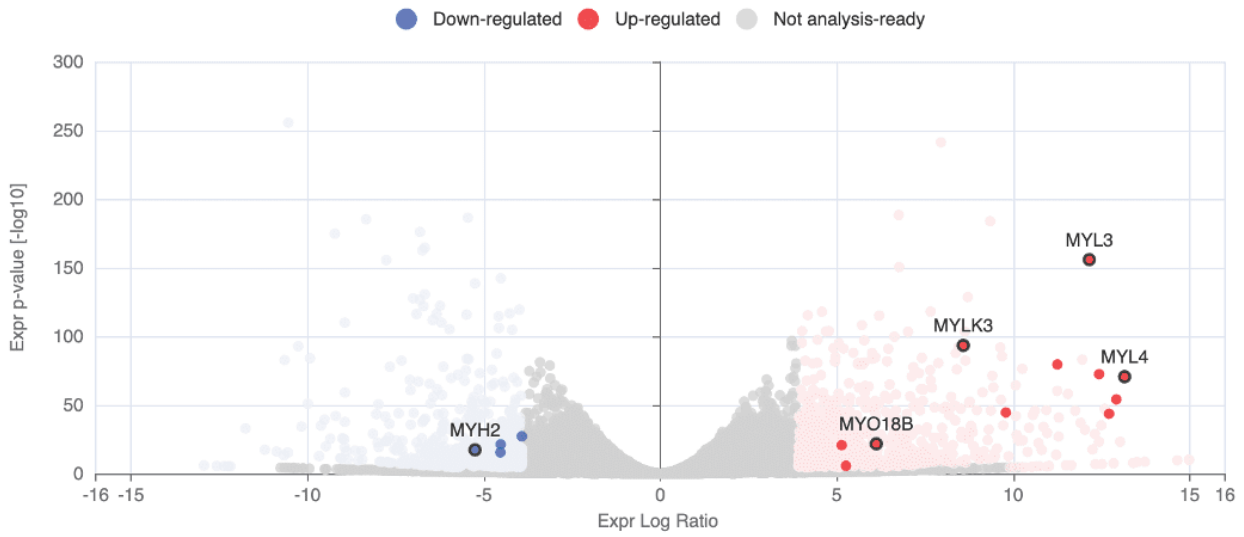
Accepted file formats:

- ✓ .txt (tab-delimited text files)
- ✓ .xls, .xlsx, .csv (Excel tables
- ✓ .diff (Cuffdiff output

Multiple comparisons or observations may be uploaded in one file

What's new in the QIAGEN® Ingenuity Pathway Analysis Fall Release (2025)

X Axis: Expr Log Ratio Y Axis: Expr p-value Clear Selection



MYL3

Entrez Gene Summary:

MYL3 encodes myosin light chain 3, an alkali light chain also referred to in the literature as both the ventricular isoform and the slow skeletal muscle isoform. Mutations in MYL3 have been identified as a cause of mid-left ventricular chamber type hypertrophic cardiomyopathy. [provided by RefSeq, Jul 2008]

Entrez Gene Name:

myosin light chain 3

Synonyms:

Alkali Myosin Light Chain 1, CMH8, Cmlc1, ELC, Elc1v, Elcv1, MLC1s, MLC1SB, MLC1V, MLClV, MLC-lV/sb, Mylc, Mylc1v, myosin light chain 3, myosin, light polypeptide 3, rVMLC1, VELC, Ventricular Myosin Essential Light Chain, VLC1, VLCl

Member of:

Dataset molecules

Showing **73** of 27087 molecules

Name ▲	Entrez Gene	Identifier	Expr p-value	Expr p-value	Expr False Discovery Rate (q-value)	Expr Fold Change	Expr Log Ratio	Expr Other	Molecule Type	Location	Analyzed
Filter	myosin	Filter	Filter ≤	Filter ≤	Filter ≤	Filter abs. ≥	Filter abs. ≥	Filter ≤	Select	Select	Select
	protein C3	1									
MYBPH	myosin binding protein H	ENSG00000133055	3.53e-3	1.00	9.24e-3	115.20	6.85	1	other	Cytoplasm	No
MYBPHL	myosin binding protein H like	ENSG00000221986	2.06e-3	1.00	5.69e-3	9.46	3.24	1	other	Cytoplasm	No

Formatting proteomics data before uploading to IPA

IDs (required)

	A	B	C	D
1	**Proteins**	**Fold change**	**P_value**	**P_value_adjust**
2	P00738	0.592740341	0.000671209	0.016736513
3	P01008	0.25826353	0.000155027	0.006454004
4	P01011	0.47378079	0.000628734	0.016577608
5	P04003	0.312321917	2.2507E-05	0.001618456
6	P06681	0.272046102	0.001374078	0.027869114
7	P05155	0.429462469	4.19294E-05	0.002551241
8	P02748	0.580232999	0.002252137	0.038734209
9	P02763	0.555940063	0.00014192	0.006236575
10	Q14520	0.368464274	9.75518E-05	0.004786156
11	Q08380	0.536007179	0.000258392	0.009290371
12	Q9BXR6	0.332814513	0.00075662	0.01813594
13	P03951	0.306633696	0.000594476	0.016236342
14	P08185	0.304349939	1.12204E-05	0.000914984
15	P05090	0.302847519	0.000817844	0.018730825

Ratio, fold change, etc. (recommended)

Significance (optional)

Common protein IDs

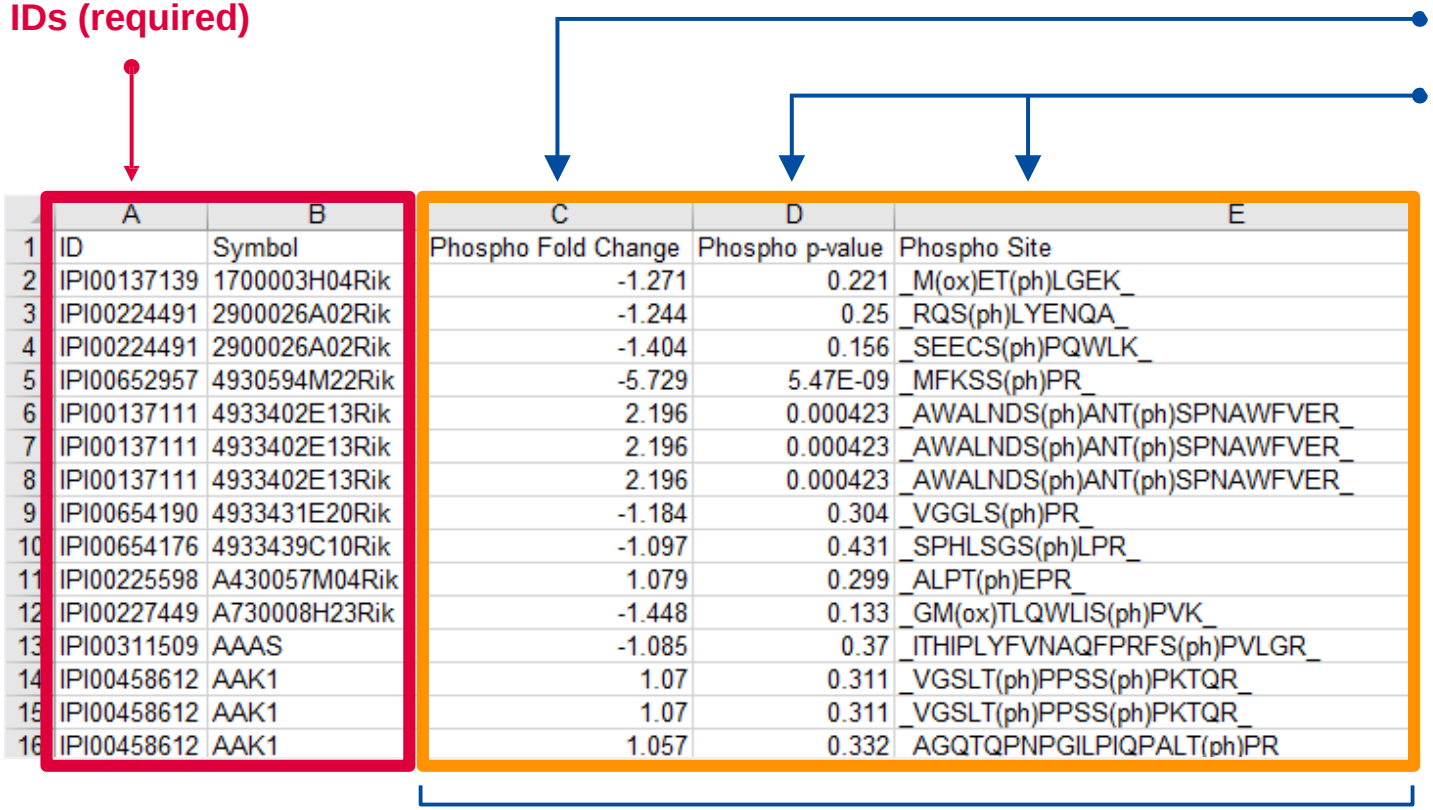
- Ensembl
- Gene symbols (Entrez or HUGO)
- GenPept and GenBank
- International Protein Index
- UniProt and SwissProt

UniProt ID conversion tool:

- https://www.uniprot.org/mapping/

Formatting proteomics data before uploading to IPA

IDs (required)



	A	B	C	D	E
1	ID	Symbol	Phospho Fold Change	Phospho p-value	Phospho Site
2	IPI00137139	1700003H04Rik	-1.271	0.221	_M(ox)ET(ph)LGEK_
3	IPI00224491	2900026A02Rik	-1.244	0.25	_RQS(ph)LYENQA_
4	IPI00224491	2900026A02Rik	-1.404	0.156	_SEECS(ph)PQWLK_
5	IPI00652957	4930594M22Rik	-5.729	5.47E-09	_MFKSS(ph)PR_
6	IPI00137111	4933402E13Rik	2.196	0.000423	_AWALNDS(ph)ANT(ph)SPNAWFVER_
7	IPI00137111	4933402E13Rik	2.196	0.000423	_AWALNDS(ph)ANT(ph)SPNAWFVER_
8	IPI00137111	4933402E13Rik	2.196	0.000423	_AWALNDS(ph)ANT(ph)SPNAWFVER_
9	IPI00654190	4933431E20Rik	-1.184	0.304	_VGGLS(ph)PR_
10	IPI00654176	4933439C10Rik	-1.097	0.431	_SPHLSGS(ph)LPR_
11	IPI00225598	A430057M04Rik	1.079	0.299	_ALPT(ph)EPR_
12	IPI00227449	A730008H23Rik	-1.448	0.133	_GM(ox)TLQWLIS(ph)PVK_
13	IPI00311509	AAAS	-1.085	0.37	_ITHIPLYFVNAQFPRFS(ph)PVLGR_
14	IPI00458612	AAK1	1.07	0.311	_VGSLT(ph)PPSS(ph)PKTQR_
15	IPI00458612	AAK1	1.07	0.311	_VGSLT(ph)PPSS(ph)PKTQR_
16	IPI00458612	AAK1	1.057	0.332	AGQTQPNPGILPIQPALT(ph)PR

Observation 1

Ratio, fold change, etc. (recommended)

Significance (optional)

Common protein IDs

- Ensembl
- Gene symbols (Entrez or HUGO)
- GenPept and GenBank
- International Protein Index
- UniProt and SwissProt

UniProt ID conversion tool:

- https://www.uniprot.org/mapping/

Formatting metabolomics data before uploading to IPA

Multiple ID columns

Ratio, fold change, etc. (recommended)

(optional)

Significance (optional)

	A	B	C	D	E	F	G	H
1	**Pubchem**	**Kegg**	**HMDB**	**CAS**	**Metabolites**	**Fold change**	**P_value**	**P_value_adjust**
2					(2 or 3)-decenoate (10:1n7 or n8)	1.212936133	4.44028E-05	0.000585189
3	6443013	C14762	HMDB0004667	29623-28-7	13-HODE + 9-HODE	0.584109411	0.003698077	0.016919182
4	10111	C02294	HMDB01522	471-29-4	1-methylguanidine	1.219937764	0.015399637	0.049446834
5	5462190	C15606	HMDB0012134	746507-19-7	2,3-dihydroxy-5-methylthio-4-pentenoate (DMTPA)*	1.566518315	0.002802172	0.013670263
6	80283	C02356	HMDB00452	1492-24-6	2-aminobutyrate	0.633800292	0.011016709	0.038805594
7	10796774		HMDB00317	488-15-3	2-hydroxy-3-methylvalerate	0.997343835	0.006172648	0.024774766
8	11427		HMDB37115	120-91-2	2-hydroxy-4-(methylthio)butanoic acid	1.294720456	0.000305912	0.002622524

Observation 1

Common metabolite IDs

- CAS registry number
- Human Metabolome Database
- KEGG
- PubChem CID

Metabolite ID conversion tools:

- https://biodbnet-abcc.ncifcrf.gov/db/db2db.php
- https://cts.fiehnlab.ucdavis.edu/batch
- http://csbg.cnb.csic.es/mbrole2/conversion.php

Analyzing GWAS risk loci using IPA

Hand on Case Study

nature genetics

Article

https://doi.org/10.1038/s41588-023-01314-0

Multi-ancestry genome-wide association analyses improve resolution of genes and pathways influencing lung function and chronic obstructive pulmonary disease risk

Received: 12 May 2022

Accepted: 25 January 2023

Published online: 13 March 2023

Check for updates

A list of authors and their affiliations appears at the end of the paper

Lung-function impairment underlies chronic obstructive pulmonary disease (COPD) and predicts mortality. In the largest multi-ancestry genome-wide association meta-analysis of lung function to date, comprising 588,452 participants, we identified 1,020 independent association signals implicating 559 genes supported by ≥2 criteria from a systematic variant-to-gene mapping framework. These genes were enriched in 29 pathways. Individual variants showed heterogeneity across ancestries, age and smoking groups, and collectively as a genetic risk score showed strong association with COPD across ancestry groups. We undertook phenome-wide association studies for selected associated variants as well as trait and pathway-specific genetic risk scores to infer possible consequences of intervening in pathways underlying lung function. We highlight new putative causal variants, genes, proteins and pathways, including those targeted by existing drugs. These findings bring us closer to understanding the mechanisms underlying lung function and COPD, and should inform functional genomics experiments and potentially future COPD therapies.

Lung-function abnormality predicts mortality and is a diagnostic criterion for chronic obstructive pulmonary disease (COPD)[1], which is the most prevalent respiratory disease globally[2] and lacks disease-modifying treatments. Although smoking and other environmental risk factors for COPD are well known and genetic susceptibility is recognized, the molecular pathways underlying COPD are incompletely understood. As with other complex traits there has been a lack of ancestral diversity in genome-wide association studies (GWAS)[3] of lung function[4–6]. Multi-ancestry studies improve the power and fine-mapping resolution of GWAS and increase the prospects for prediction, prevention, diagnosis and treatment in diverse populations[3,4,7].

Understanding of the genes, proteins and pathways involved in disease-related traits underpins modern drug development. A high yield of genetic-association signals, improved signal resolution and integration with functional evidence assist confident identification of causal genes as well as the variants and pathways that impact gene function and regulation. Although datasets and in silico tools to connect GWAS signals to causal genes are improving, the findings from different datasets and tools have lacked consensus[8,9], highlighting a need for frameworks to integrate functional evidence types and compare findings[10].

Aggregation of lung-function-associated genetic variants into a genetic risk score (GRS) provides a tool for COPD prediction[5]. When a GRS comprises many variants, partitioning the GRS according to the biological pathways the variants influence could provide a tool to explore their aggregated consequences across different traits through phenome-wide association studies (PheWAS). Just as PheWAS of individual genetic variants predicts the consequences of perturbations of specific protein targets, informing assessment of drug efficacy, drug safety and drug repurposing[11], PheWAS of pathway-partitioned GRS

e-mail: nick.shrine@leicester.ac.uk; martin.tobin@leicester.ac.uk

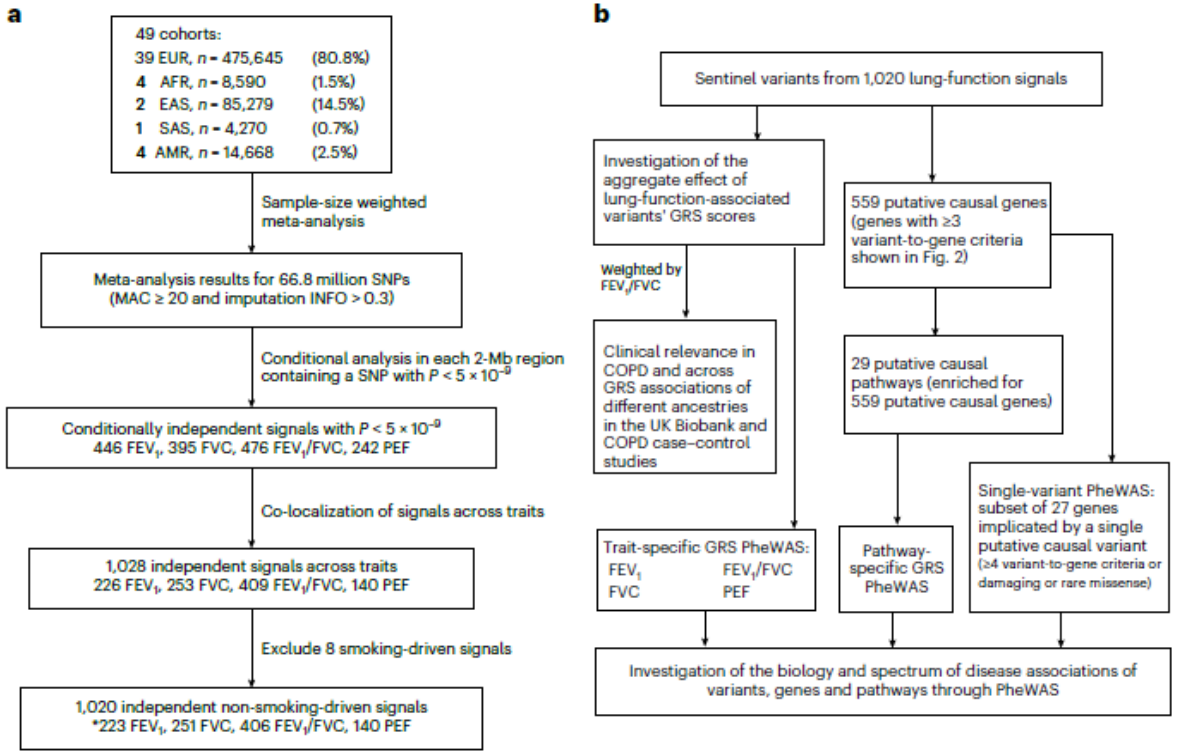


Fig. 1 | Study overview. a, Discovery meta-analysis. *For signals present in more than one trait, the signal is only counted once (for the most significant trait). **b**, Pathway analyses, GRS analyses and PheWAS studies.

Input dataset

	A	B	C
1	Molecules	rsid	P_cP
2	ADAMTS1	rs13615	7.62E-13
3	AEBP2	rs10841302	7.93E-13
4	BRAF	rs13227429	1.32E-14
5	CCND1	rs2510461	1.53E-12
6	COL11A1	rs2376280	6.76E-15
7	COL11A2	rs9277934	2.15E-15
8	COL15A1	rs7874187	4.76E-09
9	COL15A1	rs911930	2.67E-12
10	COL2A1	rs3809324	5.61E-24
11	COL4A2	rs4103	1.66E-11
12	COL4A2	rs61963203	4.75E-11
13	COL6A3	rs11677932	2.75E-16
14	FGF18	rs10059996	2.49E-41
15	FGFR1	rs881299	4.75E-10
16	FGFR2	rs4265539	3.18E-09
17	FGFR2	rs6585739	1.02E-11
18	FGFR2	rs7920383	1.06E-11
19	FGFR3	rs3135877	7.98E-17
20	FOXO3	rs2153960	1.54E-10
21	GNA12	rs11420712	9.37E-14
22	ITGA2	rs34865297	4.35E-21
23	ITGAV	rs9333290	2.45E-18
24	MAP2K4	rs750065349	5.49E-19
25	MMP14	rs1004030	9.73E-10
26	MMP15	rs41390948	3.38E-12
27	MMP15	rs4784886	7.06E-48
28	MUC1	rs2070803	3.19E-10
29	NOX4	rs12290257	2.28E-12
30	PDGFB	rs77516118	1.91E-15
31	PDGFRA	rs6831380	8.83E-11
32	PIK3C2B	rs1008833	1.69E-22
33	PMAIP1	rs145951492	4.93E-13

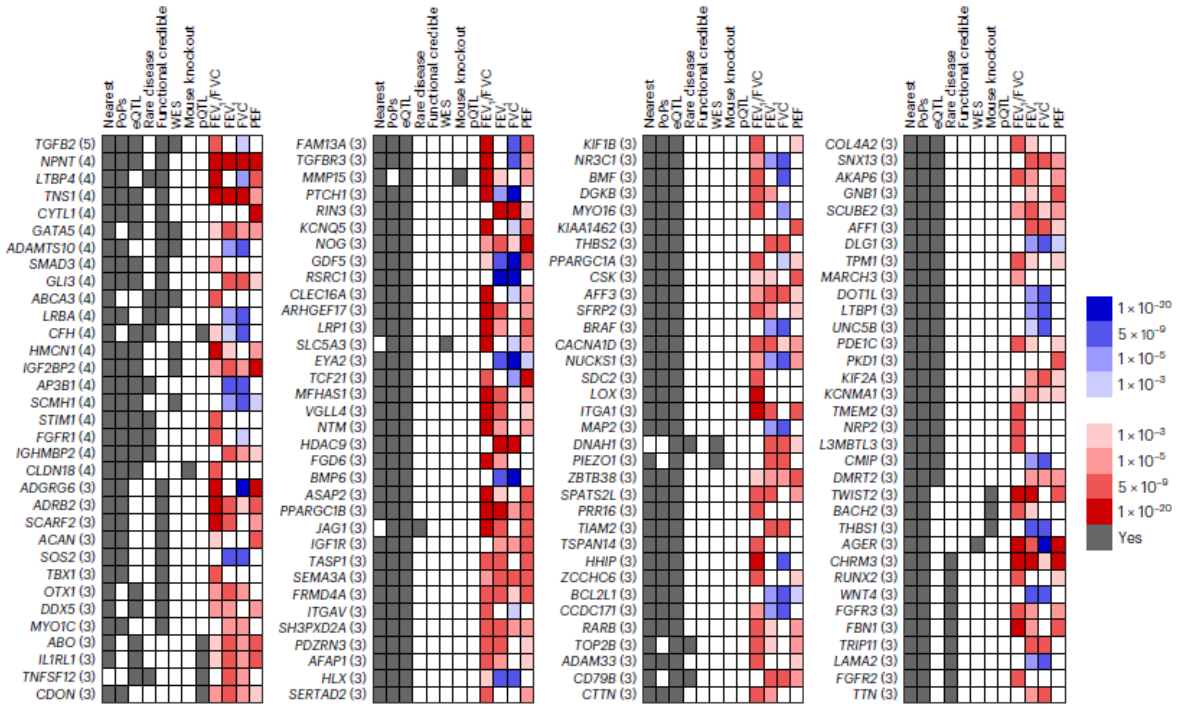
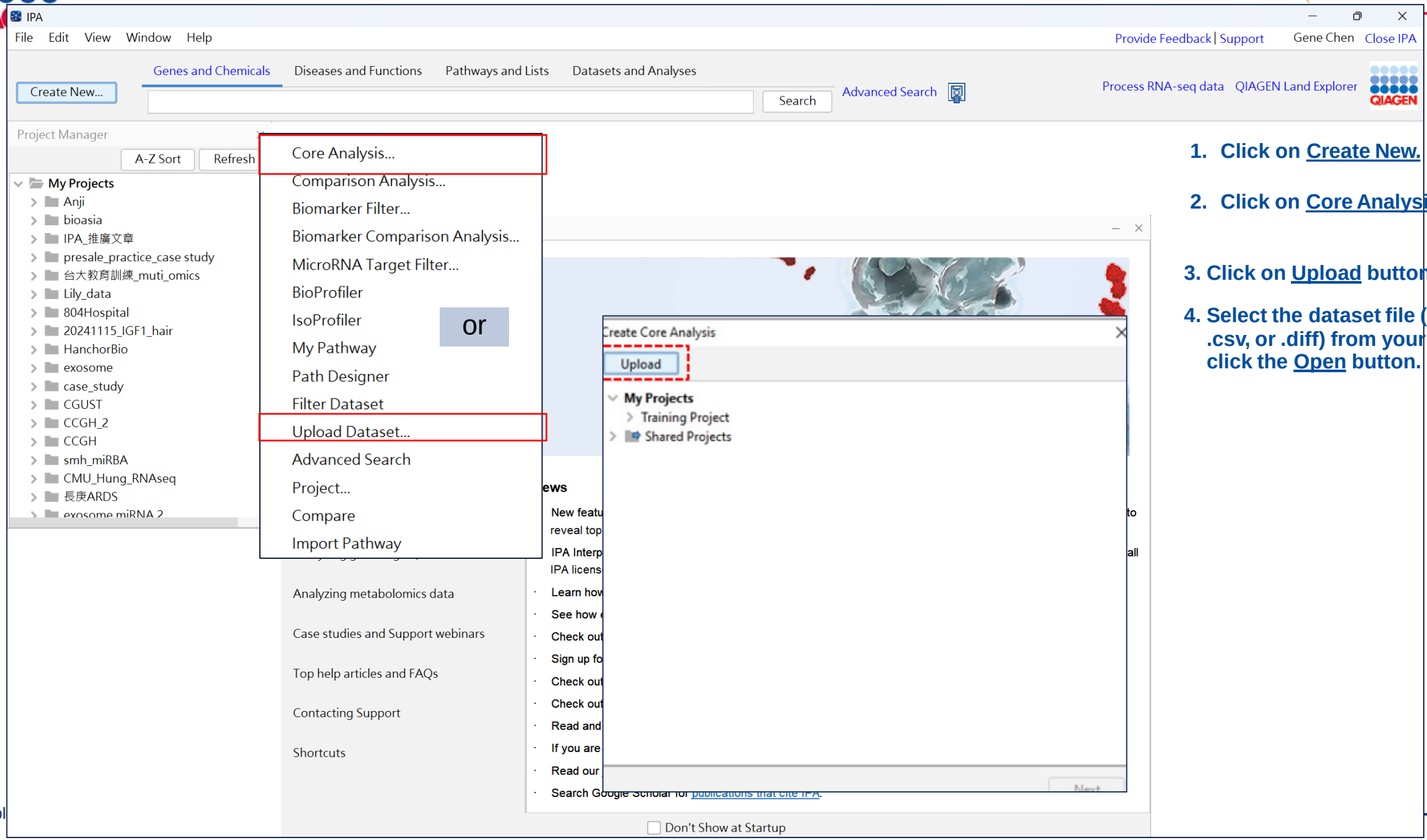
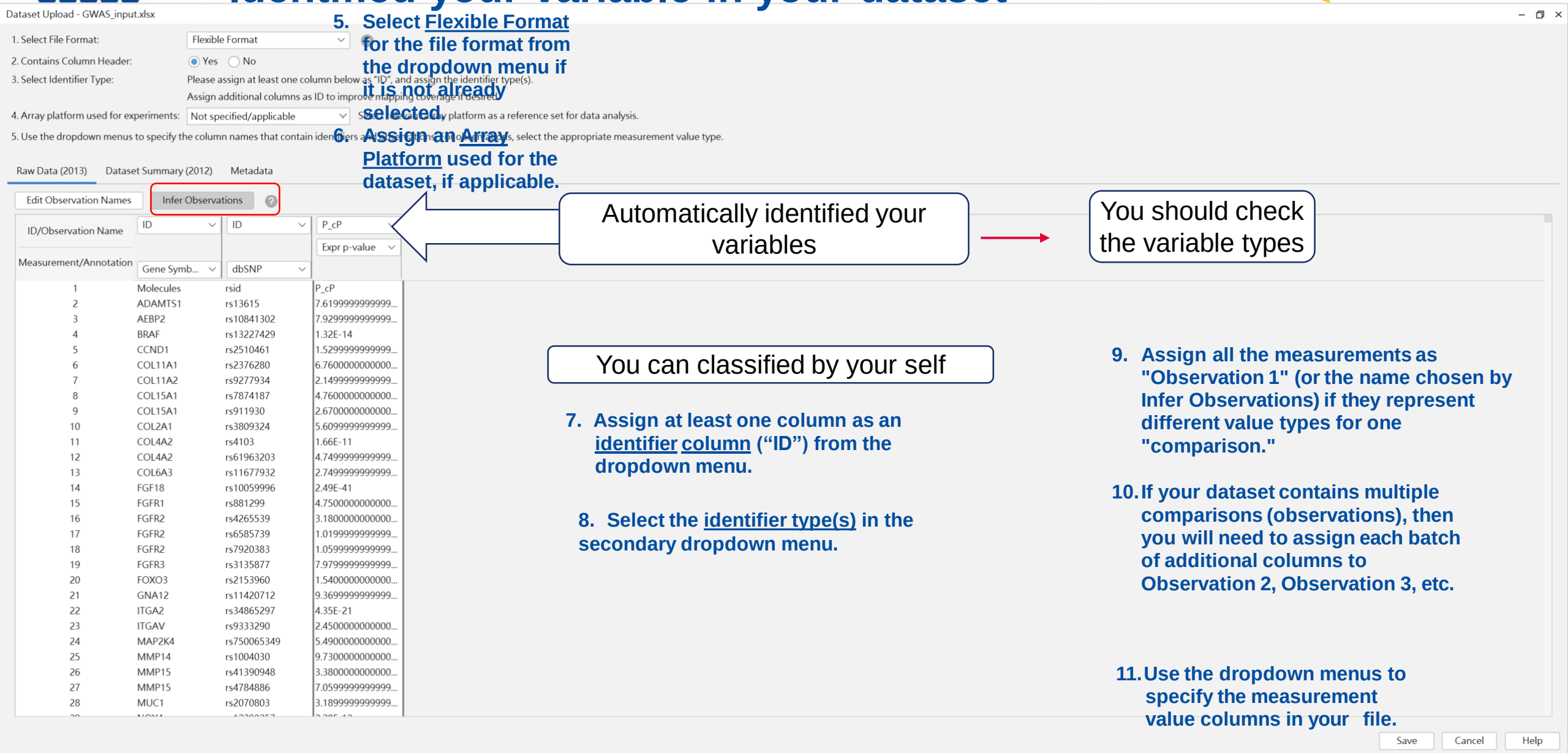


Fig. 2 | 135 genes prioritized with ≥3 variant-to-gene criteria. The number of variant-to-gene criteria implicating the gene is in brackets after the gene name. The gray in the first eight columns indicates that at least one variant implicates the gene as causal via the evidence for that column. The last four columns indicate the level of association of the most significant variant implicating the gene as causal with respect to the FEV_1/FVC decreasing allele; red indicates that this association is in the same direction of effect as the FEV_1/FVC decreasing allele and blue indicates the opposite direction with the shade indicating $P <$ the corresponding value in the legend.



1. Click on Create New.
2. Click on Core Analysis.
3. Click on Upload button.
4. Select the dataset file (.txt, .xls, .xlsx .csv, or .diff) from your computer and click the Open button.

Identified your variable in your dataset



5. Select Flexible Format for the file format from the dropdown menu if it is not already selected.
6. Assign an Array Platform used for the dataset, if applicable.

Automatically identified your variables

You should check the variable types

You can classified by your self

7. Assign at least one column as an identifier column ("ID") from the dropdown menu.

8. Select the identifier type(s) in the secondary dropdown menu.

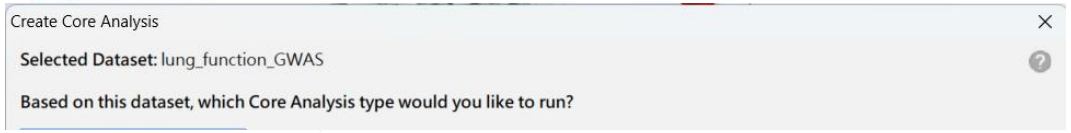
9. Assign all the measurements as "Observation 1" (or the name chosen by Infer Observations) if they represent different value types for one "comparison."

10. If your dataset contains multiple comparisons (observations), then you will need to assign each batch of additional columns to Observation 2, Observation 3, etc.

11. Use the dropdown menus to specify the measurement value columns in your file.

12. Click the Save button to proceed.

Setup Cut off and Biological filter



16. Specify the desired type of analysis to apply and

Create Expression Analysis - [analysis : Glioblastoma_CL3_DEG]

Set Cutoffs | Biological Filters

Use cutoffs to select a set of molecules from your dataset to analyze. Ideally choose between 100 and 3000 significantly regulated molecules, and not more than 8000. Include *both* up-regulated and down-regulated, if possible, to obtain causal predictions.

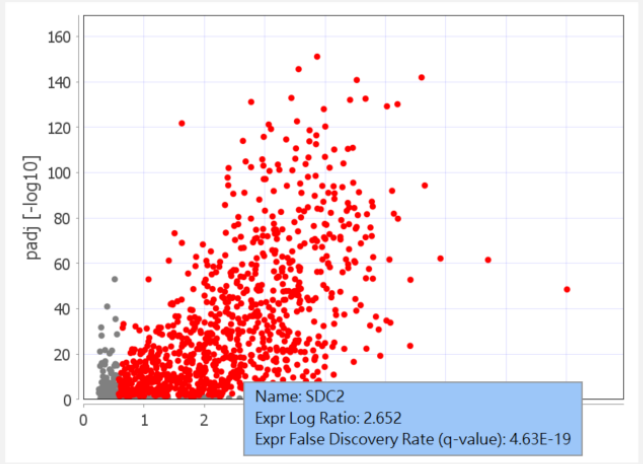
Set Cutoffs

Dataset Column	Measurement Value Type	Range	Cutoff
avg_log2FC	Expr Log Ratio	0.252 to 8.007	Down: [ ] Up: 0.58
padj	Expr False Discovery Rate (q-value)	0.0 to 1.0	0.05

17. In the Set Cutoffs section, enter cutoff values that are suited to your particular dataset. For example, you might enter 0.05 as a p-val cutoff.

18. The final number of "analysis-ready" molecules that pass your cutoffs ideally does not exceed approximately 3000 and must not exceed 8000.

Select molecules by clicking or dragging to label them with their names.
Note that fold changes are converted to log2 for charting purposes.



avg_log2FC | padj [-log10] | Update Axes | Clear Molecule Names

Advanced | Recalculate | **938** analysis-ready molecules (**0** Down and **938** Up)

Preview Dataset Glioblastoma_CL3_DEG

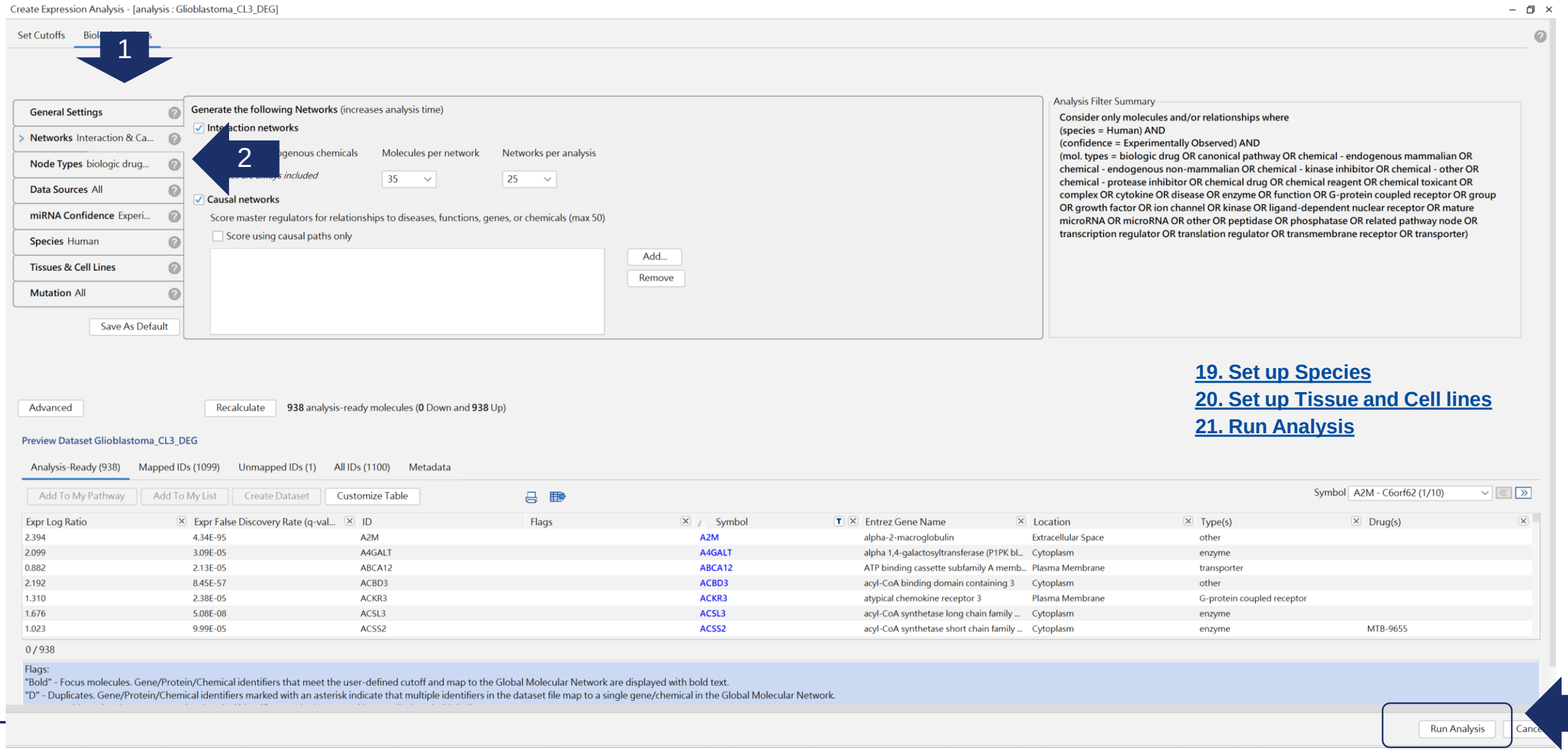
Analysis-Ready (938) | Mapped IDs (1099) | Unmapped IDs (1) | All IDs (1100) | Metadata

Add To My Pathway | Add To My List | Create Dataset | Customize Table

Symbol: A2M - C6orf62 (1/10)

Expr Log Ratio	Expr False Discovery Rate (q-val...	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
2.394	4.34E-95	A2M		A2M	alpha-2-macroglobulin	Extracellular Space	other	
2.099	3.09E-05	A4GALT		A4GALT	alpha 1,4-galactosyltransferase (P1PK bl...	Cytoplasm	enzyme	
0.882	2.13E-05	ABCA12		ABCA12	ATP binding cassette subfamily A memb...	Plasma Membrane	transporter	
2.192	8.45E-57	ACBD3		ACBD3	acyl-CoA binding domain containing 3	Cytoplasm	other	
1.310	2.38E-05	ACKR3		ACKR3	atypical chemokine receptor 3	Plasma Membrane	G-protein coupled receptor	
1.676	5.08E-08	ACSL3		ACSL3	acyl-CoA synthetase long chain family ...	Cytoplasm	enzyme	
1.023	9.99E-05	ACSS2		ACSS2	acyl-CoA synthetase short chain family ...	Cytoplasm	enzyme	MTB-9655

0 / 938


Create Expression Analysis - [analysis : Glioblastoma_CL3_DEG]
Set Cutoffs
1
General Settings
Networks Interaction & Ca...
Node Types biologic drug...
Data Sources All
miRNA Confidence Experi...
Species Human
Tissues & Cell Lines
Mutation All
Save As Default
Generate the following Networks (increases analysis time)
Interaction networks
2
Molecules per network
Networks per analysis
35
25
Causal networks
Score master regulators for relationships to diseases, functions, genes, or chemicals (max 50)
Score using causal paths only
Add...
Remove
Analysis Filter Summary
Consider only molecules and/or relationships where
(species = Human) AND
(confidence = Experimentally Observed) AND
(mol. types = biologic drug OR canonical pathway OR chemical - endogenous mammalian OR chemical - endogenous non-mammalian OR chemical - kinase inhibitor OR chemical - other OR chemical - protease inhibitor OR chemical drug OR chemical reagent OR chemical toxicant OR complex OR cytokine OR disease OR enzyme OR function OR G-protein coupled receptor OR group OR growth factor OR ion channel OR kinase OR ligand-dependent nuclear receptor OR mature microRNA OR microRNA OR other OR peptidase OR phosphatase OR related pathway node OR transcription regulator OR translation regulator OR transmembrane receptor OR transporter)
19. Set up Species
20. Set up Tissue and Cell lines
21. Run Analysis
Advanced
Recalculate
938 analysis-ready molecules (0 Down and 938 Up)
Preview Dataset Glioblastoma_CL3_DEG
Analysis-Ready (938)
Mapped IDs (1099)
Unmapped IDs (1)
All IDs (1100)
Metadata
Add To My Pathway
Add To My List
Create Dataset
Customize Table
Symbol A2M - C6orf62 (1/10)
Expr Log Ratio | Expr False Discovery Rate (q-val... | ID | Flags | Symbol | Entrez Gene Name | Location | Type(s) | Drug(s)
2.394 | 4.34E-95 | A2M | A2M | alpha-2-macroglobulin | Extracellular Space | other
2.099 | 3.09E-05 | A4GALT | A4GALT | alpha 1,4-galactosyltransferase (P1PK bl... | Cytoplasm | enzyme
0.882 | 2.13E-05 | ABCA12 | ABCA12 | ATP binding cassette subfamily A memb... | Plasma Membrane | transporter
2.192 | 8.45E-57 | ACBD3 | ACBD3 | acyl-CoA binding domain containing 3 | Cytoplasm | other
1.310 | 2.38E-05 | ACKR3 | ACKR3 | atypical chemokine receptor 3 | Plasma Membrane | G-protein coupled receptor
1.676 | 5.08E-08 | ACSL3 | ACSL3 | acyl-CoA synthetase long chain family ... | Cytoplasm | enzyme
1.023 | 9.99E-05 | ACSS2 | ACSS2 | acyl-CoA synthetase short chain family ... | Cytoplasm | enzyme | MTB-9655
0 / 938
Flags:
"Bold" - Focus molecules. Gene/Protein/Chemical identifiers that meet the user-defined cutoff and map to the Global Molecular Network are displayed with bold text.
"D" - Duplicates. Gene/Protein/Chemical identifiers marked with an asterisk indicate that multiple identifiers in the dataset file map to a single gene/chemical in the Global Molecular Network.
Run Analysis
3

Canonical Pathway

Supplementary table 19

Ingenuity_Canonical_Pathways	P_value	Ratio
Pulmonary Fibrosis Idiopathic Signaling Pathway	1.00E-18	0.134
Hepatic Fibrosis Signaling Pathway	7.94E-17	0.111

Canonical Pathways

Signaling and metabolic pathways that are potentially activated or inhibited in the dataset

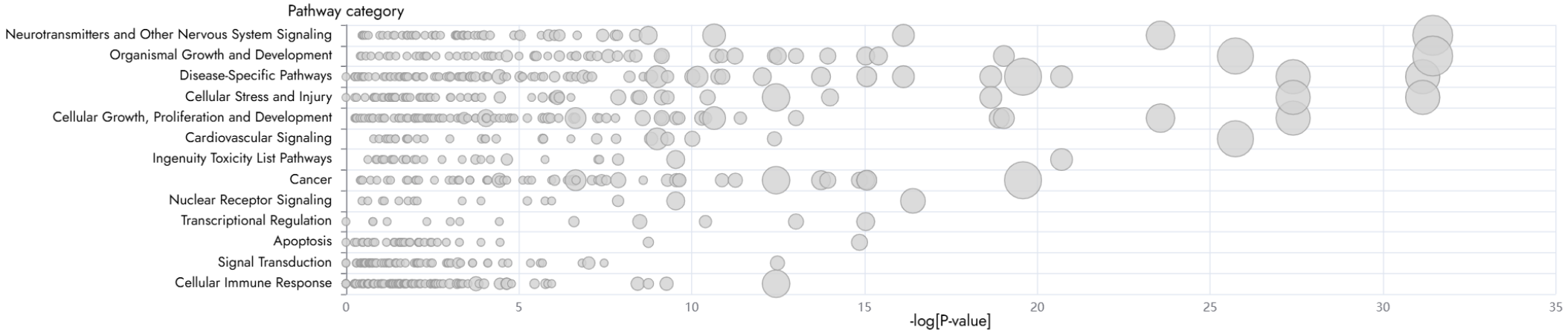
Table | Bar Chart | **Bubble Chart**

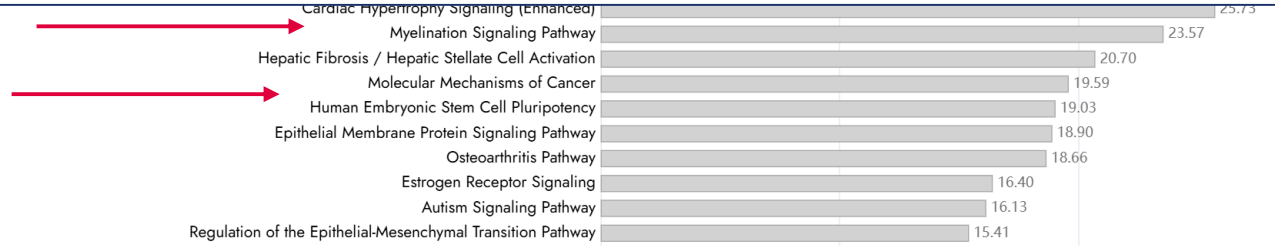
Chart Type: Bubble chart | X-axis: -log[P-value] | Y-axis: Pathway category | Sort by: -log[P-value] | Bubble size: Overlapping molecules | Bubble color: Activation z-score | Data display: Select Range... | More filters

Figure Legend ON

Z-Score: Positive | Negative | Zero | Neutral or No Prediction

Overlapping molecules: 11 | 21 | 42

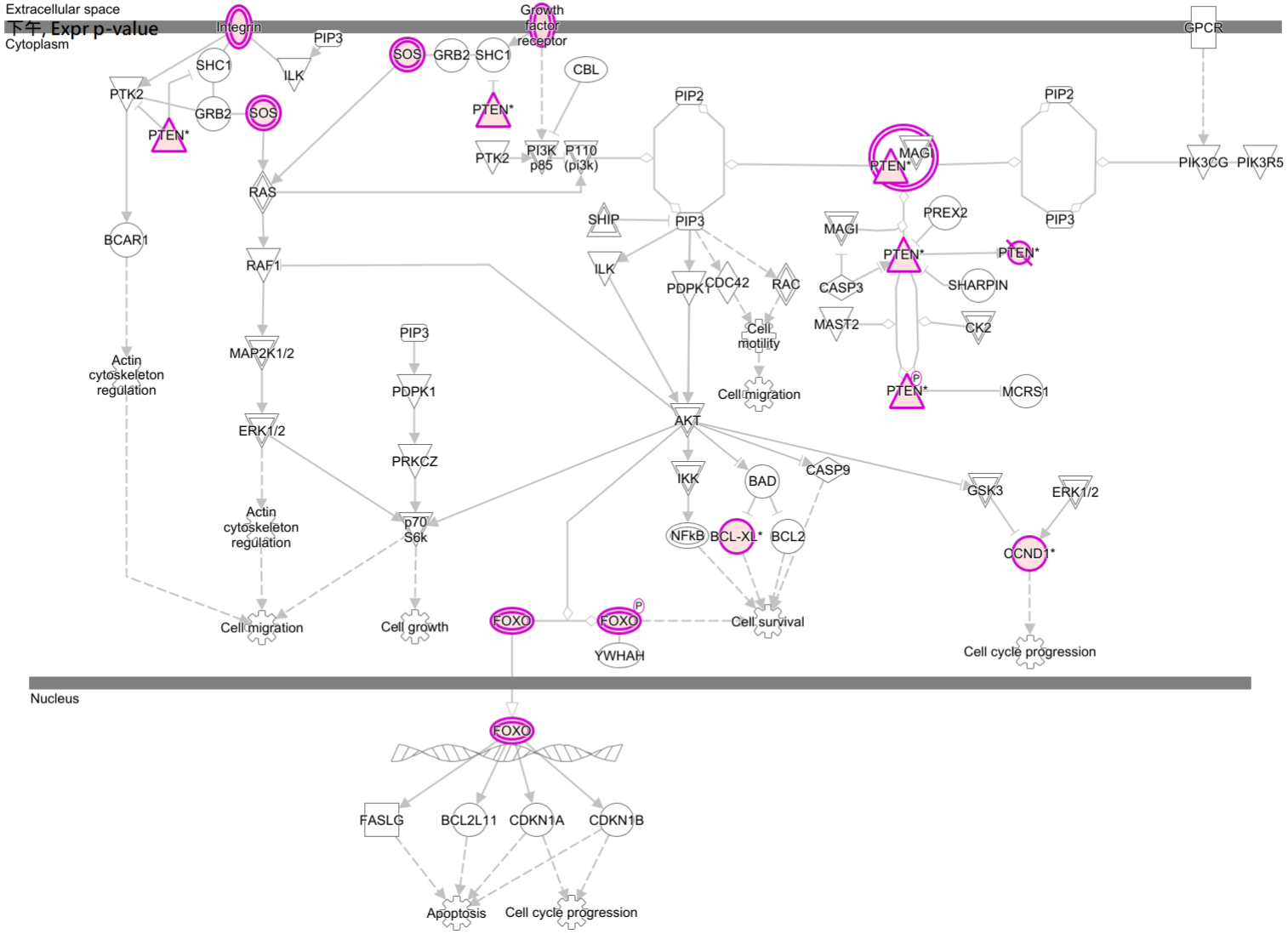




PTEN pathway

Edit: Build Overlay Path Designer Pattern Search View: Zoom: Export:

PTEN Signaling
Overlay: lung_function_GWAS - 2025-11-24 07:11 下午, Expr p-value



Hide

Prediction Legend

more extreme in dataset — less
Increased measurement
Decreased measurement

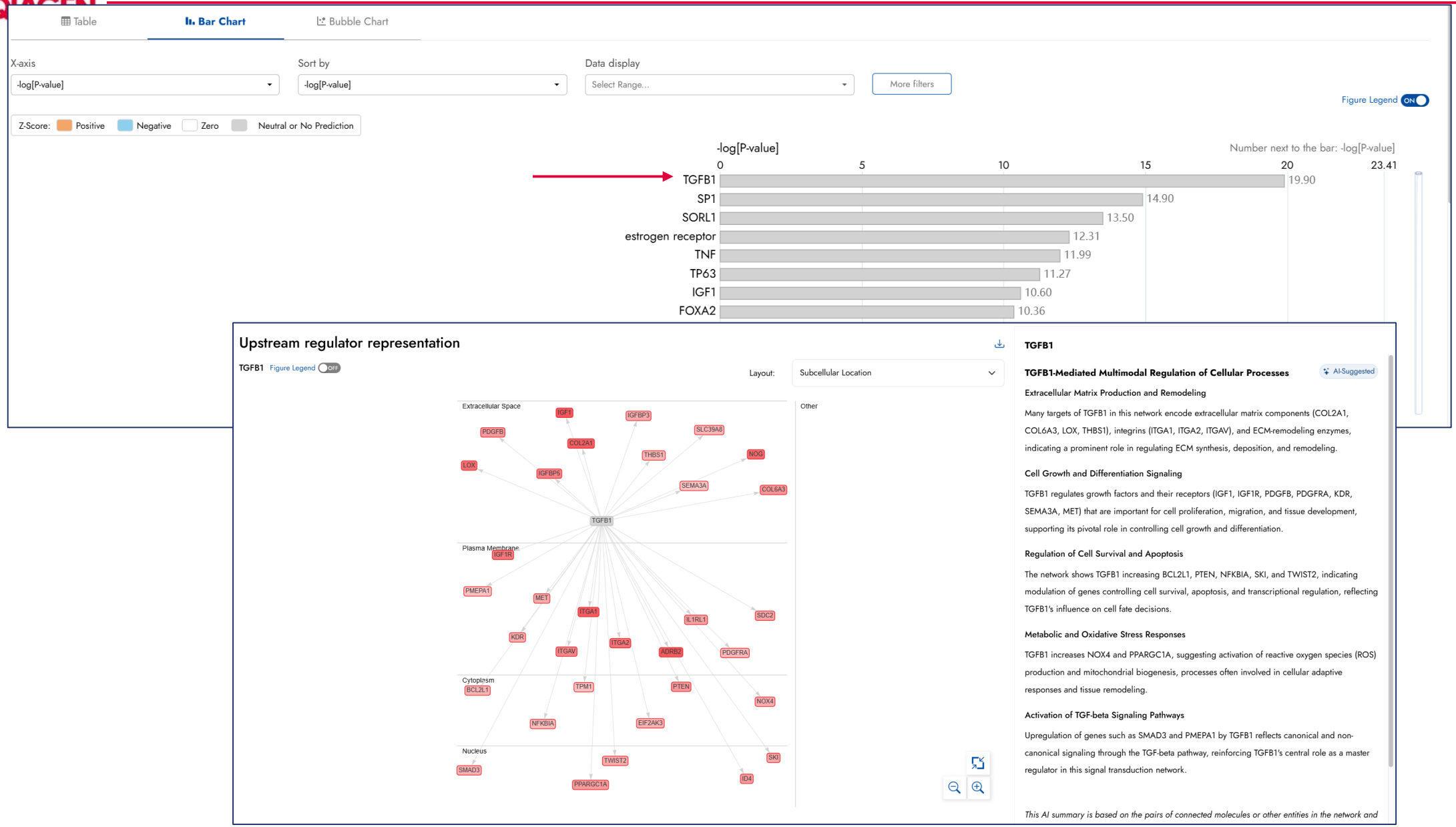
more confidence — less
Predicted activation
Predicted inhibition

Glow Indicates activity when opposite of measurement

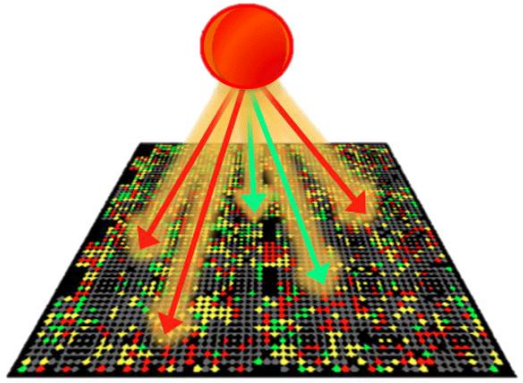
Predicted Relationships
Leads to activation
Leads to inhibition
Findings inconsistent with state of downstream molecule
Effect not predicted

Dashed lines = indirect relationship
Solid lines = direct relationship

Upstream regulator



Upstream Regulator Analysis: *How does it work?*



- Use experimentally observed relationships (vs. Predicted event) between Upstream Regulators and genes to predict potential regulator and activation

- Predict activation or inhibition of regulator to explain the changes in gene expression in your dataset
- Calculates two complementary statistical measures:
  - Activation z-score
  - Overlap p-value

Disease and function

lung_function_GWAS - 2025-11-24 07:11 下午 / Diseases and Functions / Bar Chart

Diseases and Functions

Diseases and biological processes predicted to be impacted in the dataset

Table | **Bar Chart** | Bubble Chart

X-axis: -log[P-value]

Sort by: -log[P-value]

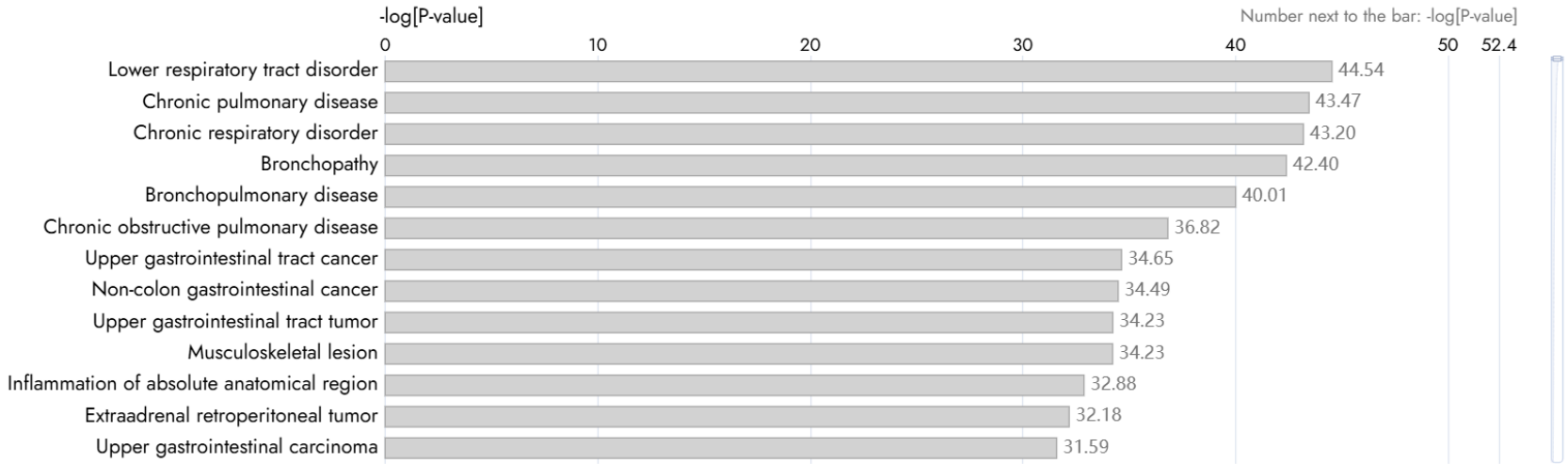
Data display: Select Range...

More filters

Figure Legend ON

Z-Score: Positive | Negative | Zero | Neutral or No Prediction

Lung function/disease



Diseases & Functions Tab

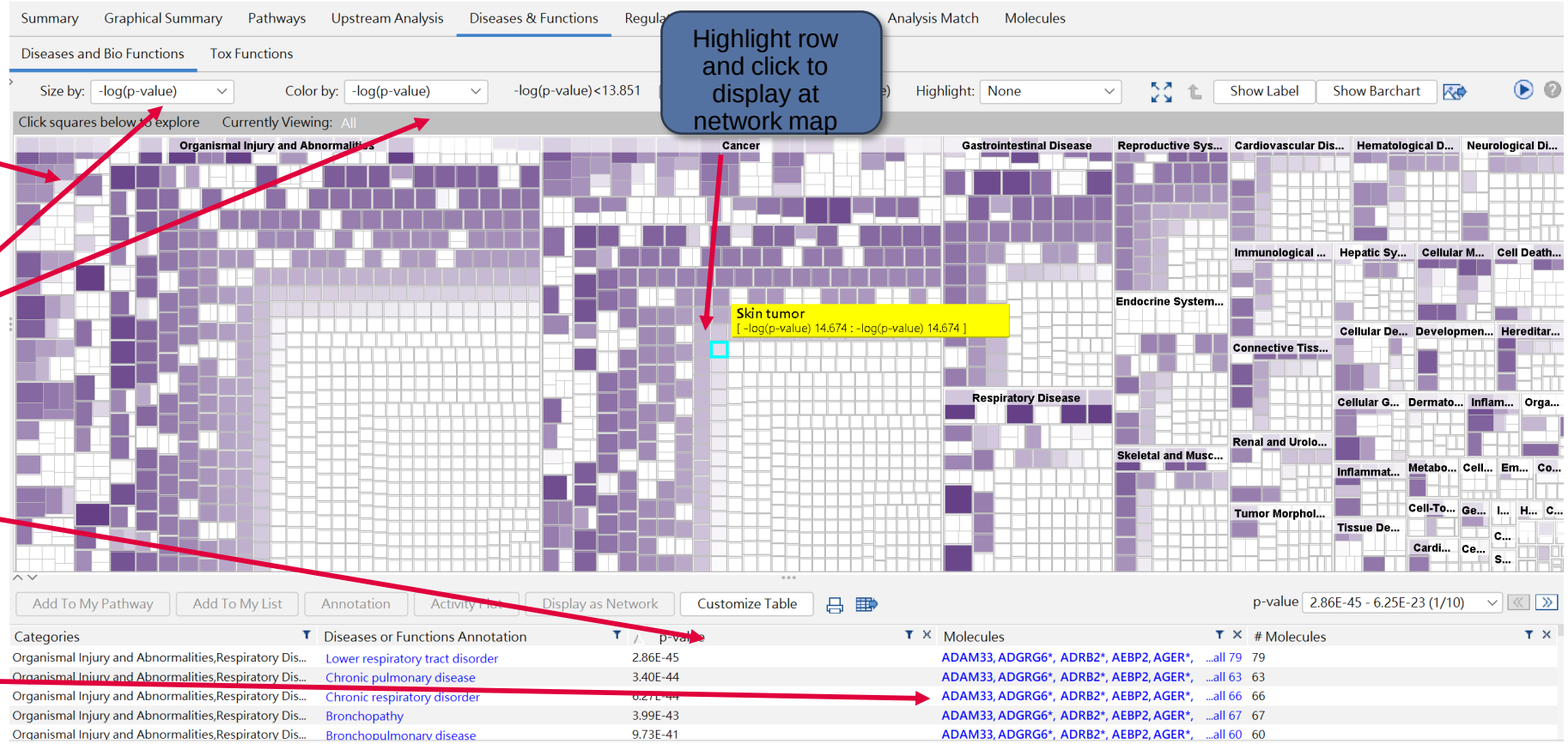
Color is activity prediction; size of square is p-value but can be changed

Organized by biological themes

Significance of enrichment

Genes from dataset involved in disease or function

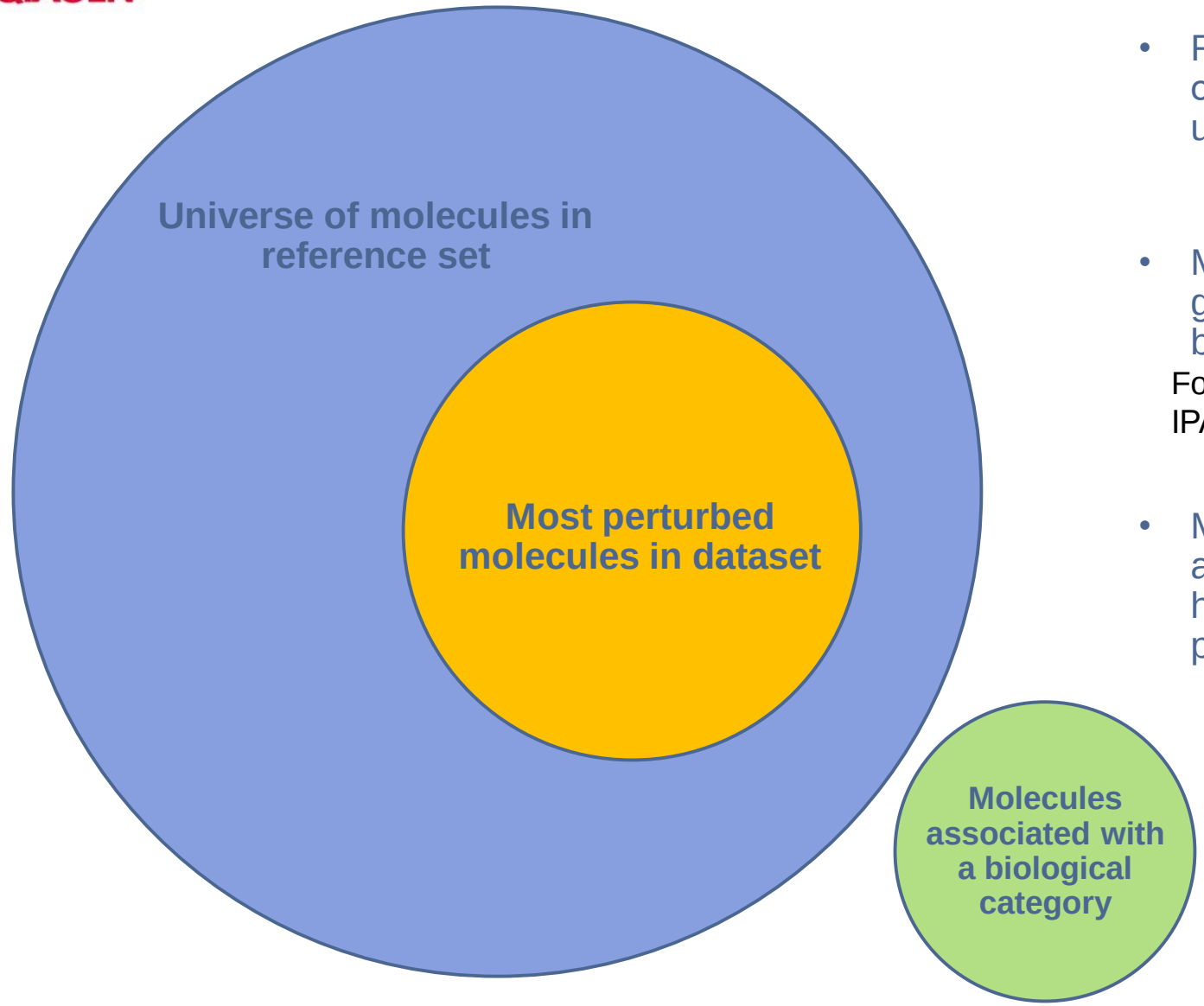
Highlight row and click to display at network map



Diseases and functions that may be key to the biology in your experimental data based on patterns of expression observed

Enrichment in IPA

Pathway enrichment: P-value of overlap

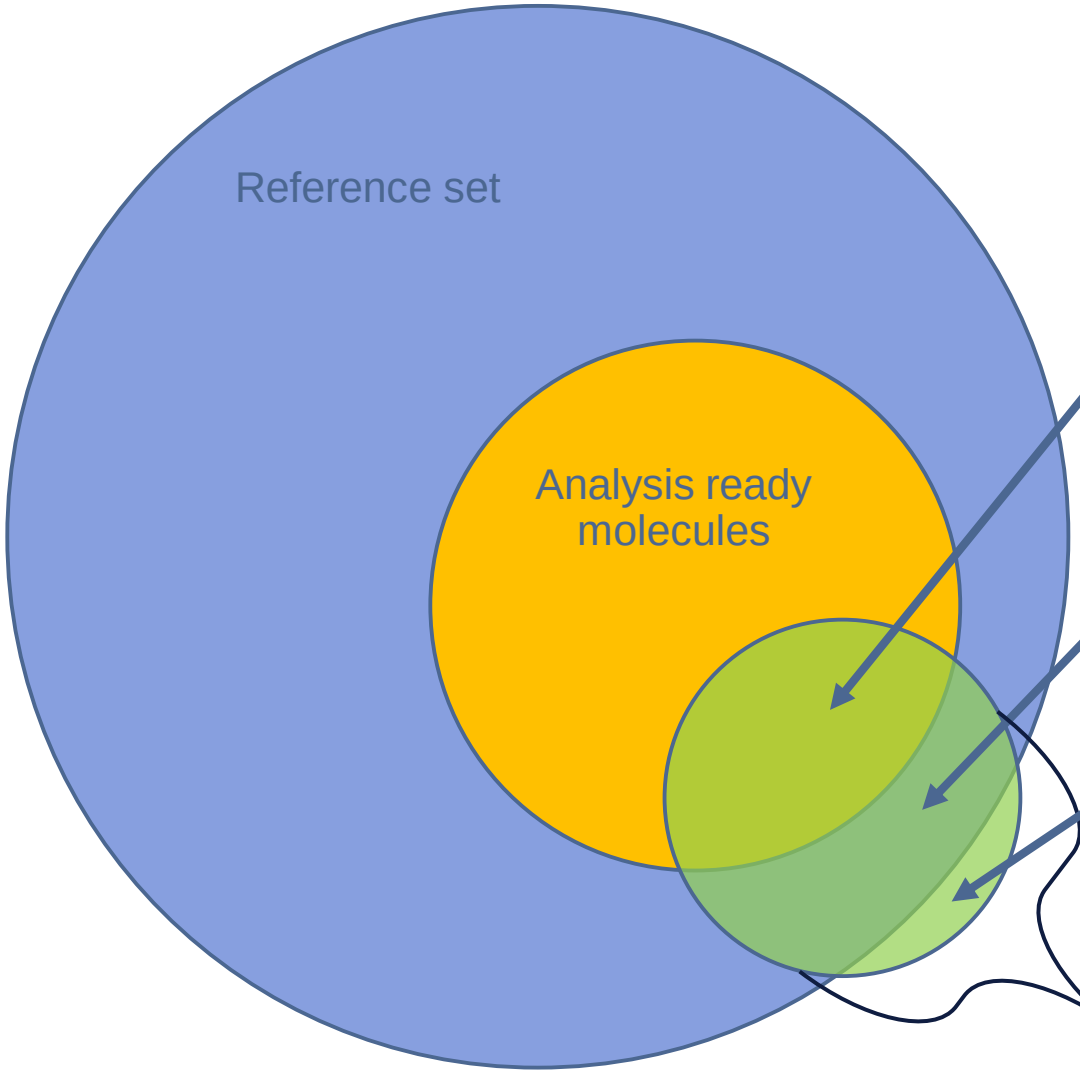


- Reference set is typically all genes or proteins that can be reliably detected by the ‘omics technology used
- Most perturbed is a subset of measured genes/proteins that were significantly different between experimental groups

  Fold change cut offs and p-value cut offs used

  IPA calls these “Analysis-ready molecules”
- Molecules associated with a biological category are a set of genes/proteins that the IPA knowledgebase has annotated to be important for a biological pathway, function, or disease.

Testing for Enrichment using the Fisher's Exact Test



Overlapping molecules

Non-analysis-ready molecules that have been annotated to a biological category

i.e. genes that did not pass cut offs

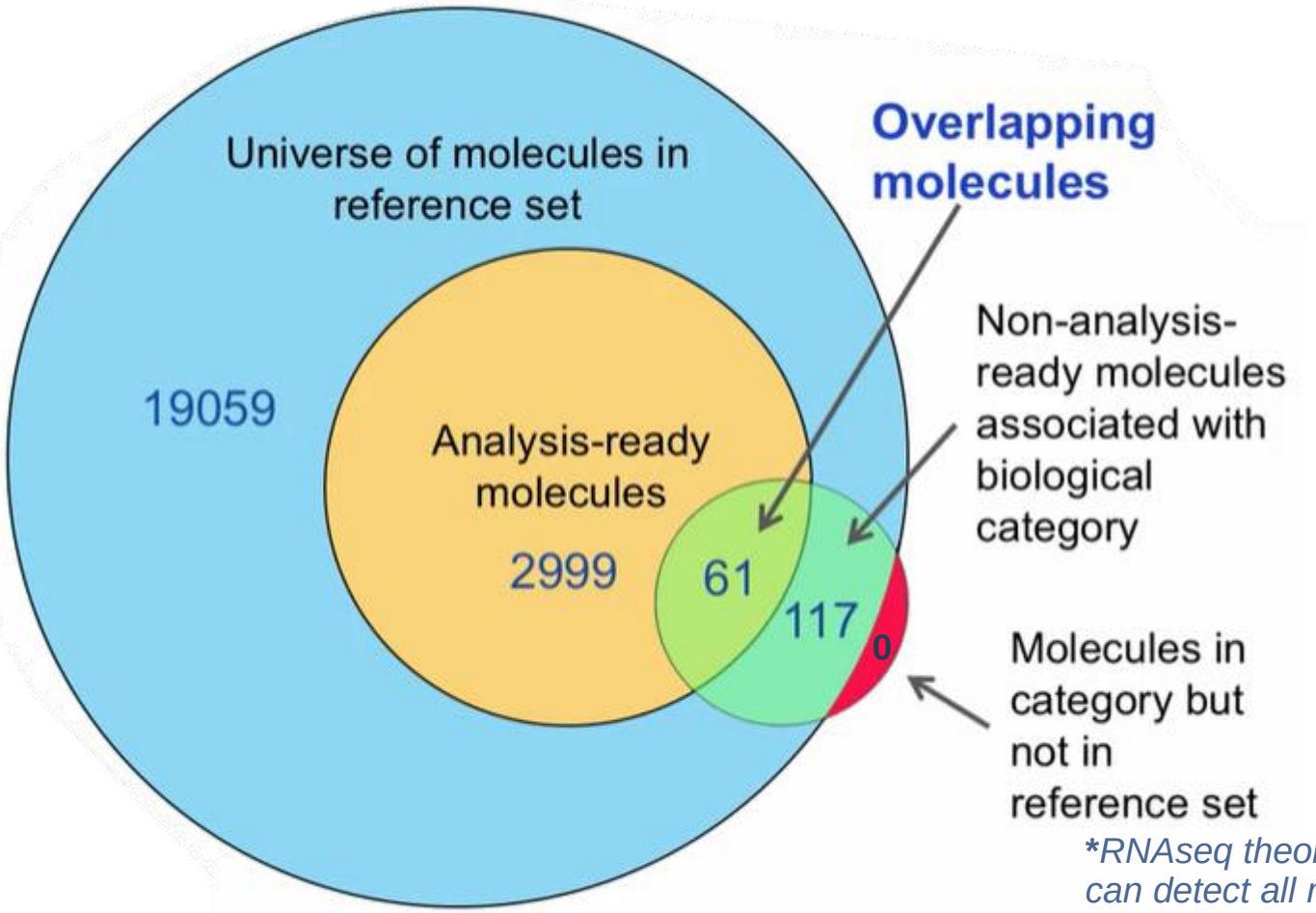
Genes not detected by the technology used and are annotated to a biological category

Molecules associated with a biological category

Is this overlap larger than expected by random sampling?

P-Value from the Right-tailed Fisher's Exact Test

p-value: the probability of observing a result as extreme or more extreme, if the null hypothesis is true



*RNAseq theoretically can detect all molecules

H_o = Overlap of molecules for a particular biological category is due to chance

α (significance level) = 0.05

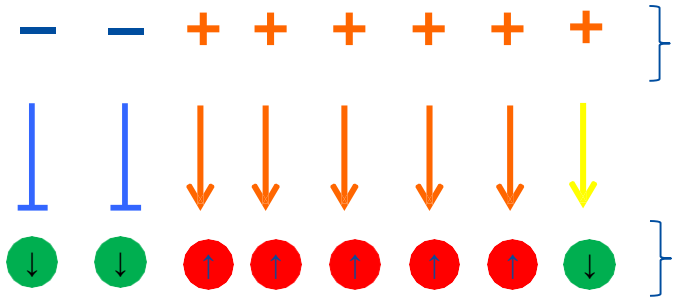
		Category 1		
		Group 1	Group 2	Total
Category 2	Group 1	a	b	a+b
	Group 2	c	d	c+d
	Total	a+c	b+d	a+b+c+d = n

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

P-value = 2.08×10^{-12}

We can reject the null hypothesis

z-score: Activation prediction



Gene expression from QIAGEN Knowledge Base (literature)

Gene expression in your dataset

+1 score for consistent relationships
and –1 for inconsistent relationships

$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}} = (7\text{-}1)/\sqrt{8} = 2.12\ (= \text{predicted activation})$$

- z-score is a statistical measure of the match between expected relationship direction and observed gene expression
- z-score greater than 2 or less than –2 is considered significant
- Note that the actual z-score is weighted by the underlying findings, the relationship bias and dataset bias

Examples of z-scores

Symbol	Measurement Expr Log Ratio	Expected
NR5A2	-1.002	Down
ABCB11	-1.056	Down
CYP2B6	-3.063	Down
PPARGC1A	-2.495	Down
ACOX1	-1.727	Down
SLCO1B3	3.223	Down
TLR4	1.213	Up
LY96	1.189	Up
IL1R1	1.634	Up
IL1RAP	1.046	Up
IL1B	3.890	Up
LIPC	-1.375	Up

Z-score = 2.4

10/12 measurements match expected

Mostly matching

Signal predominantly points to predicted activation

Symbol	Measurement Expr Log Ratio	Expected
CREB3L3	-1.536	Up
IHH	-1.173	Up
PBX1	-1.037	Up
CD86	1.016	Down
IL1RAP	1.046	Down
PKM	1.082	Up
HLA-DMB	1.106	Down
IL18RAP	1.124	Down
CREB5	1.148	Up
CREB3L2	1.179	Up
CCN4	1.204	Up
TLR4	1.213	Down

Z-score = -2.236

4/12 measurements match expected

Mostly anti-matching

Signal predominantly points to predicted inhibition

Analyzing protein and metabolites via IPA

Hand on Case Study

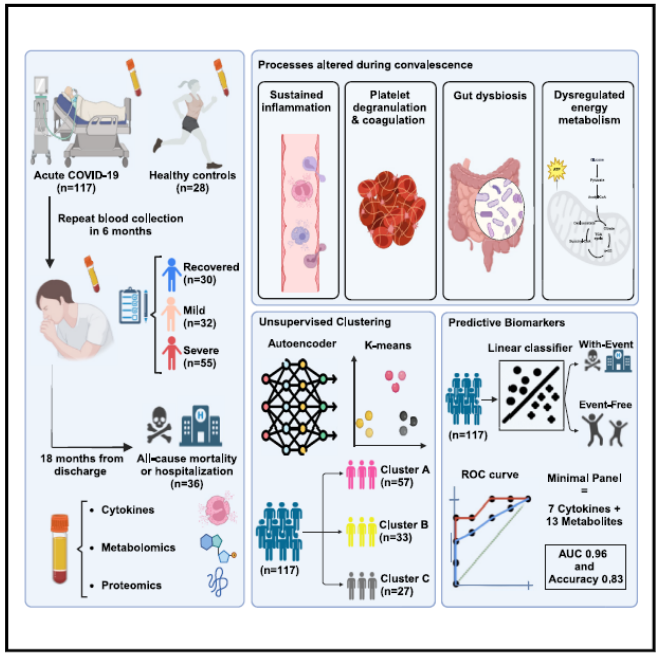
Multi-omics Case Study

Cell Reports Medicine

Article

Sequential multi-omics analysis identifies clinical phenotypes and predictive biomarkers for long COVID

Graphical abstract



Highlights

- Sequential multi-omics profiling of plasma during acute infection and convalescence
- Inflammation, platelet degranulation, and metabolic perturbations at convalescence
- Three distinct disease phenotypes based on unsupervised clustering of omics profile

Authors

Kaiming Wang, Mobin Khoramjoo, Karthik Srinivasan, ..., David S. Wishart, Vinay Prasad, Gavin Y. Oudit

Correspondence

gavin.oudit@ualberta.ca

In brief

Wang et al. conduct a comprehensive multi-omics analysis to identify pathways differentially altered during acute SARS-CoV-2 infection and convalescence. This study provides clues into the heterogeneity of the post-acute COVID-19 symptoms and unveils potential therapeutic targets for long COVID.

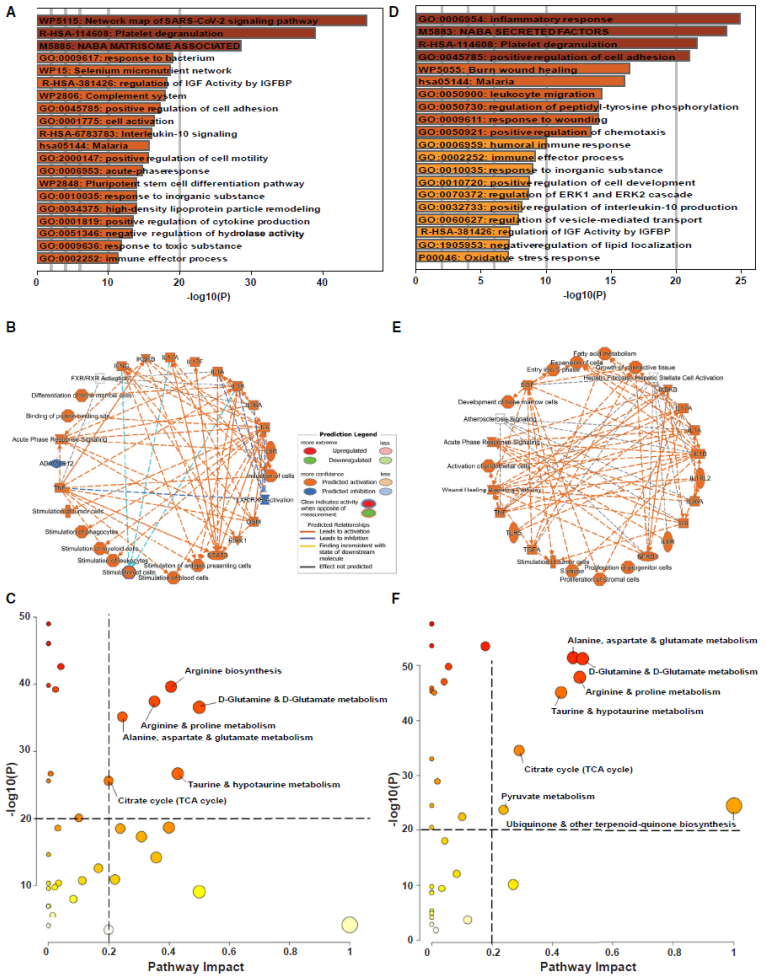


Figure 3. Pathways dysregulated during acute infection and convalescence

(A) Enriched Gene Ontology (GO) terms of differentially expressed proteins and cytokines on Metascape for acute COVID-19 compared to healthy controls, colored based on p values.

(B) Top regulatory effects of molecules and functions in acute COVID-19 based on Ingenuity Pathway Analysis (IPA).

(C) Pathways associated with metabolic alterations in acute COVID-19 compared to healthy controls. Pathway impact indicates the sum of importance of the altered metabolites in the impacted pathway based on pathway topology; the −log(P) are test statistics for quantitative pathway enrichment analysis based on concentration differences between groups. Notable impacted pathways are above the dashed lines (impact >0.2 and −log(P) > 20).

(D) Enriched GO terms of differentially expressed proteins and cytokines on Metascape for convalescence phase compared to healthy controls, colored based on p values.

(E) Top regulatory effects of molecules and functions during convalescence based on Ingenuity Pathway Analysis (IPA).

(F) Pathways associated with metabolic alterations during convalescence compared to healthy controls.

Upload dataset protein and metabolite

Acute vs Control | Covlanvance vs Control | Covlanvance vs Acute | Recover vs Control

	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	Identifier	Log2FoldC	LOG10_A	Adj_P_vali	Type_Cov	Log2FoldC	LOG10_A	Adj_P_vali	Log2FoldC	LOG10_A	Adj_P_vali	Log2FoldC	LOG10_A	Adj_P_valu
2	CCL22	-0.59255	2.14246	0.007203	cytokine	0.87785	8.10959	7.77E-09	NA	NA	NA	NA	NA	NA
3	IL15	0.62343	10.17656	6.66E-11	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
4	IL27	0.75691	1.56589	0.027171	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
5	IFNB2	NA	NA	NA	cytokine	-2.8755	8.31512	4.84E-09	NA	NA	NA	NA	NA	NA
6	CCL4	0.91855	2.1882	0.006483	NA	NA	NA	NA	1.1692	6.71627	1.92E-07	1.1692	6.71627	1.92E-07
7	CD40LG	3.2722	18.03133	9.30E-19	NA	NA	NA	NA	3.7221	38.84747	1.42E-39	3.7221	38.84747	1.42E-39
8	CXCL1	2.6265	16.81206	1.54E-17	NA	NA	NA	NA	2.962	22.58921	2.58E-23	2.962	22.58921	2.58E-23
9	CXCL10	3.9462	4.00972	9.78E-05	cytokine	-3.4598	8.31512	4.84E-09	NA	NA	NA	NA	NA	NA
10	CXCL8	1.2064	8.1271	7.46E-09	NA	NA	NA	NA	1.7062	11.15951	6.93E-12	1.7062	11.15951	6.93E-12
11	CXCL9	0.72302	1.59385	0.025477	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
12	EGF	3.81	19.0099	9.77E-20	cytokine	0.89458	3.8323	0.000147	4.7046	28.41106	3.88E-29	4.7046	28.41106	3.88E-29
13	FGF2	1.2964	6.99136	1.02E-07	NA	NA	NA	NA	1.4117	9.37633	4.20E-10	1.4117	9.37633	4.20E-10
14	FLT3LG	0.78975	3.87034	0.000135	NA	NA	NA	NA	0.97072	6.32806	4.70E-07	0.97072	6.32806	4.70E-07
15	HMDB00(	1.6541	9.60216	2.50E-10	Metabolite	-1.2633	14.89963	1.26E-15	NA	NA	NA	NA	NA	NA
16	HMDB00(	-0.62984	7.39823	4.00E-08	NA	NA	NA	NA	-0.62157	7.34581	4.51E-08	-0.62157	7.34581	4.51E-08
17	HMDB00(	NA	NA	NA	NA	NA	NA	NA	3.1319	2.55156	0.002808	3.1319	2.55156	0.002808
18	HMDB00(	0.8291	5.62302	2.38E-06	Metabolite	-0.80725	11.22915	5.90E-12	NA	NA	NA	NA	NA	NA
19	HMDB00(	0.64911	3.29354	0.000509	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
20	HMDB00(	1.437	4.5433	2.86E-05	NA	NA	NA	NA	0.87763	3.97127	0.000107	0.87763	3.97127	0.000107

Upload dataset

Create New

Upload dataset

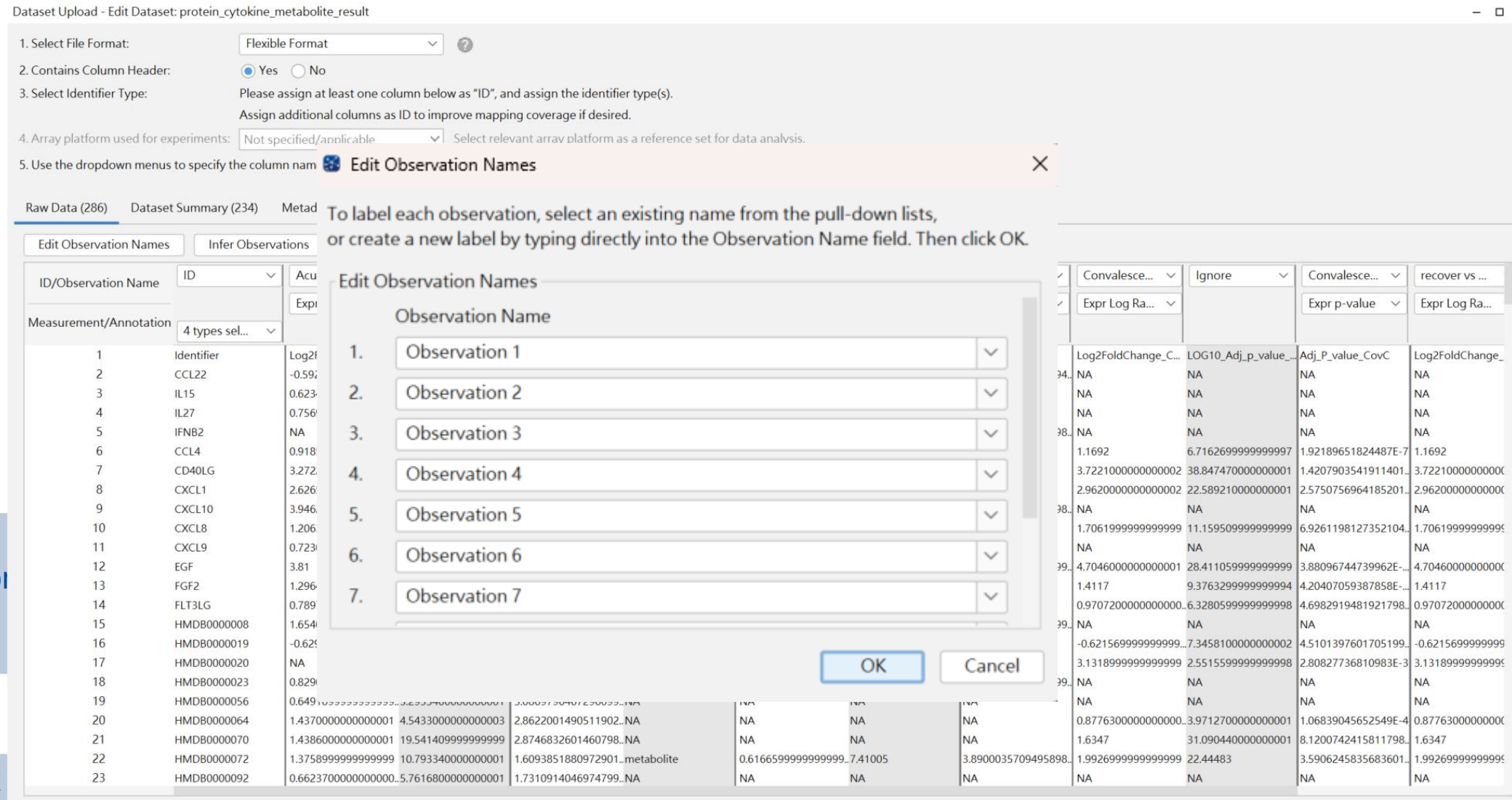
Choose your file

Edit observation name

Infer observation

Select variable type

Check variable type



Core analysis

Analyze filter dataset

Core analysis

Set cut off

Annotated Dataset: protein_cytokine_metabolite_result

Preview Dataset protein_cytokine_metabolite_result Observation: Acute_vs_Control (224)

Mapped IDs (234) | Unmapped IDs (51) | All IDs (285) | Metadata

Add To My Pathway | Add To My List | Create Dataset | Customize Table

Symbol (S)-2-hydroxybut... (1/3)

Expr Log Ratio	Expr p-value	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
1.654	2.50E-10	HMDB0000008		(S)-2-hydroxybutyric acid		Other	chemical - endogenous ma...	
0.829	2.38E-06	HMDB0000023		(S)-3-hydroxy-2-methylpropa		Other	chemical - endogenous ma...	
		HMDB0000671		(S)-indole-3-lactic acid		Other	chemical - endogenous ma...	
		HMDB07014		1-14:0/2-18:1(11Z) diacylglyce		Other	chemical - endogenous ma...	
		HMDB0010383		1-16:1(9Z) lysophosphatidylcl		Other	chemical - endogenous ma...	
		HMDB0010384		1-18:0 lysophosphatidylcholir		Other	chemical - endogenous ma...	
0.745	1.82E-03	HMDB07190		1-18:1(11Z)/2-18:2(9Z,12Z) di		Other	chemical - endogenous ma...	
-0.937	3.92E-09	HMDB0010386		1-18:2(9Z,12Z) lysophosphati		Other	chemical - endogenous ma...	
1.010	1.39E-03	HMDB07248		1-18:2(9Z,12Z)/2-18:2(9Z,12Z)		Other	chemical - endogenous ma...	
		HMDB0012108		1-heptadecanoyl-2-hydroxy-s		Other	chemical - endogenous ma...	
		HMDB0002815		1-oleoyl lysophosphatidylcho		Other	chemical - endogenous ma...	
-0.856	2.13E-07	HMDB0007883		14:0/20:4(5Z,8Z,11Z,14Z) pho		Other	chemical - endogenous ma...	
		HMDB0007884		14:0/20:4(8Z,11Z,14Z,17Z) ph		Other	chemical - endogenous ma...	
		HMDB0005359		16:0/16:0/16:1(9Z)[iso3] triacy		Other	chemical - endogenous ma...	
		HMDB0005357		16:0/16:0/18:0[iso3] triacylgly		Other	chemical - endogenous ma...	
0.769	1.28E-02	HMDB0005363		16:0/16:0/20:4(5Z,8Z,11Z,14Z)		Other	chemical - endogenous ma...	
		HMDB0005376		16:0/16:1(9Z)/16:1(9Z)[iso3] tr		Other	chemical - endogenous ma...	
0.854	1.90E-05	HMDB0005369		16:0/18:0/18:2(9Z,12Z)[iso6] t		Other	chemical - endogenous ma...	
0.864	1.06E-04	HMDB0005384		16:0/18:1(9Z)/18:2(9Z,12Z)[isc		Other	chemical - endogenous ma...	
0.597	2.04E-02	HMDB0005392		16:0/20:4(5Z,8Z,11Z,14Z)/20:4		Other	chemical - endogenous ma...	
		HMDB0007984		16:0/20:5(5Z,8Z,11Z,14Z,17Z)		Other	chemical - endogenous ma...	
		HMDB0010426		18:0/14:0/16:1(9Z)[iso6] triacy		Other	chemical - endogenous ma...	

0 / 234

Flags:
"D" - Duplicates. Gene/Protein/Chemical identifiers marked with an asterisk indicate that multiple identifiers in the dataset file map to a single gene/chemical in the Global Molecular Network.
"O" - Override molecules. Gene/Protein/Chemical identifiers marked as "Override" are displayed with italic text.
"A" - Gene/Protein/Chemical ID marked as Absent. The gene/protein/chemical will not be used as a focus molecule or appear in networks unless you also explicitly override this flag with the Override column.

Edit Dataset Settings | Analyze/Filter Dataset | Close

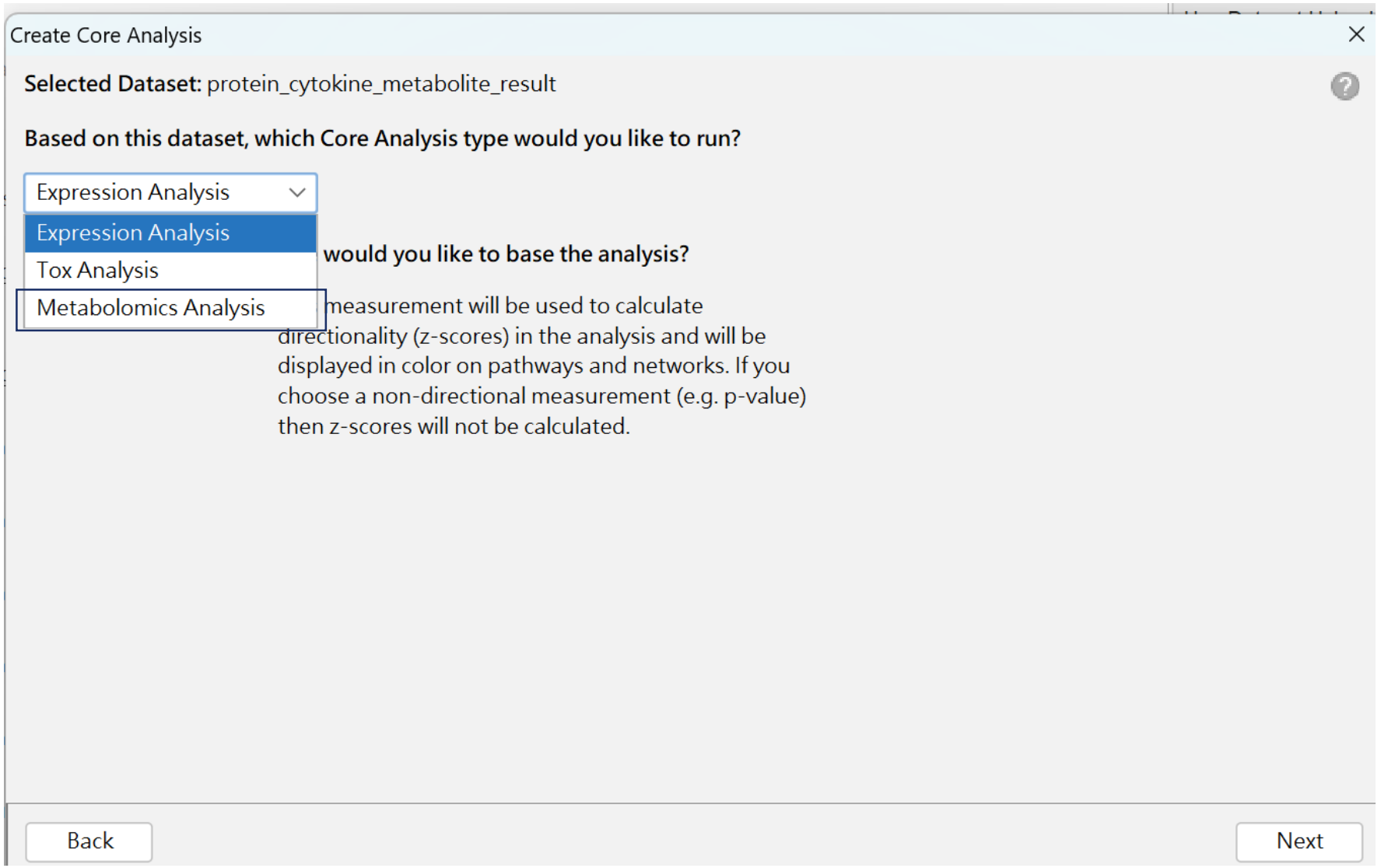
Choose which analysis do you want

Analyze filter dataset

Core analysis

Choose which analysis

Set cut off



Set Cutoff

Analyze filter dataset

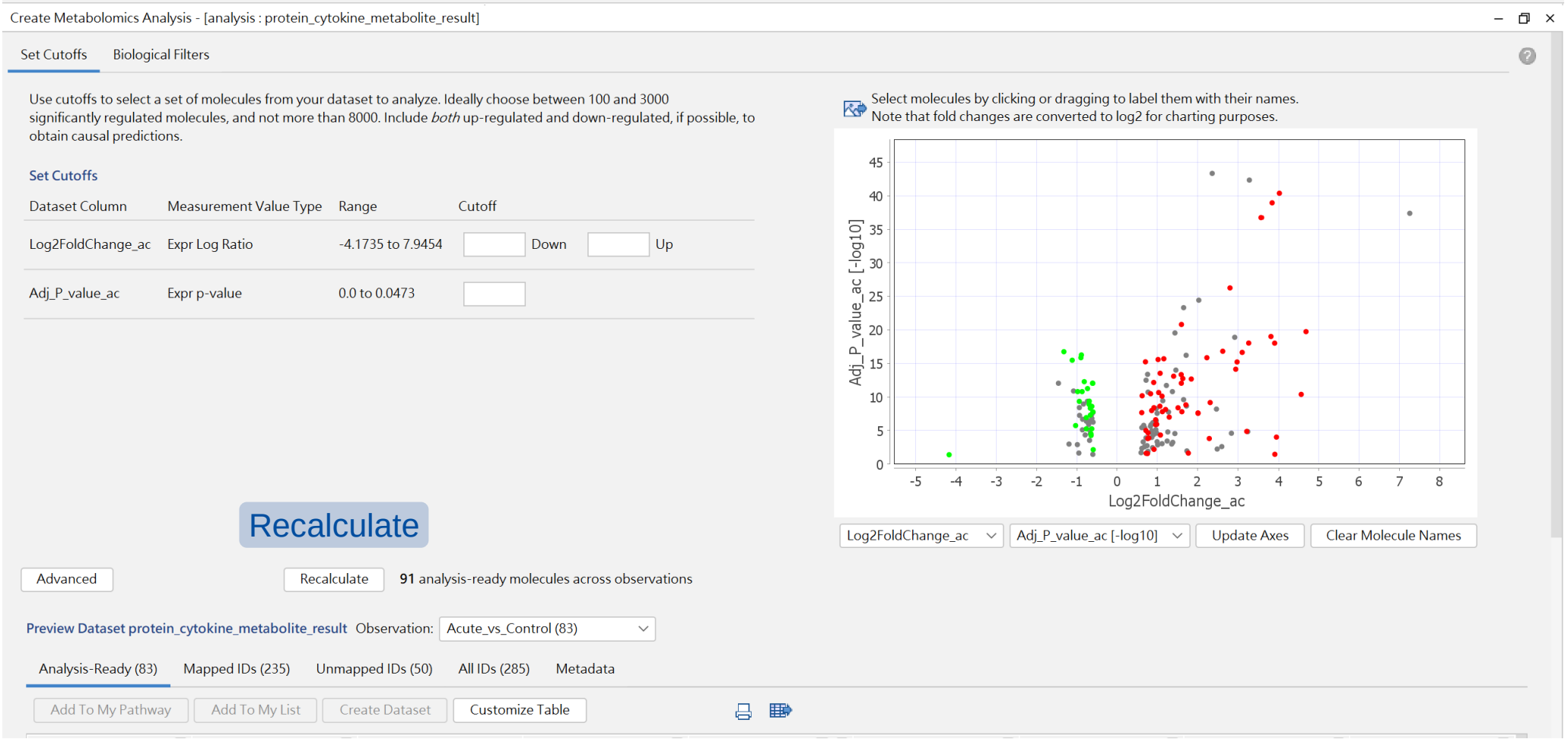
↓

Core analysis

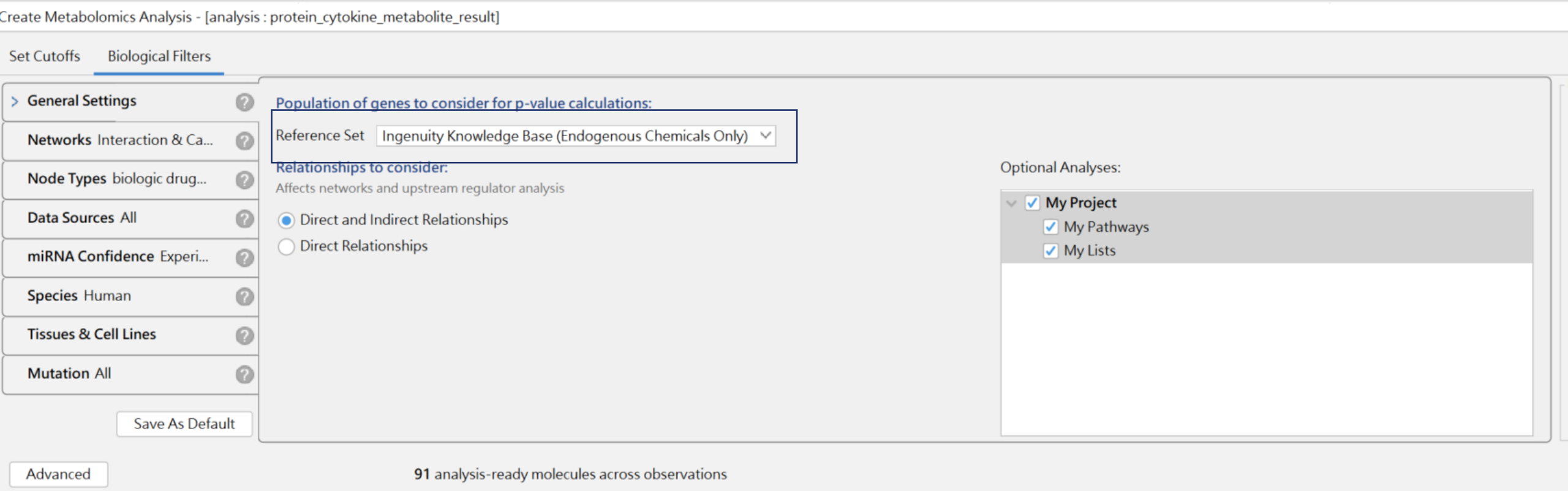
↓

Set cut off

Volcano plot



Biological Filter in metabolite



Casual network

Create Metabolomics Analysis - [analysis : protein_cytokine_metabolite_result]

Set Cutoffs | Biological Filters

General Settings
Networks Interaction & Ca...
Node Types biologic drug...
Data Sources All
miRNA Confidence Experi...
Species Human
Tissues & Cell Lines
Mutation All

Save As Default

Generate the following Networks (increases analysis time)

☑ **Interaction networks**

☑ Include endogenous chemicals — Molecules per network: 35 — Networks per analysis: 25

Genes are always included

☑ **Causal networks**

Score master regulators for relationships to diseases, functions, genes, or chemicals (max 50)

☐ Score using causal paths only

Long-haul COVID-19 [long COVID-19 syndrome,post-acute COVID-19 syndrome,...]

Add...
Remove

Filter Summary

Consider only molecules and/or relationships where
(species = Human) AND
(confidence = Experimentally Observed) AND
(mol. types = biologic drug OR canonical pathway OR chemical - endogenous mammalian OR chemical - endogenous non-mammalian OR chemical - kinase inhibitor OR chemical - other OR chemical - protease inhibitor OR chemical drug OR chemical reagent OR chemical toxicant OR complex OR cytokine OR disease OR enzyme OR function OR G-protein coupled receptor OR group OR growth factor OR ion channel OR kinase OR ligand-dependent nuclear receptor OR mature microRNA OR microRNA OR other OR peptidase OR phosphatase OR related pathway node OR transcription regulator OR translation

You can put interesting disease or gene

Advanced | Recalculate | **91** analysis-ready molecules across observations

Preview Dataset protein_cytokine_metabolite_result Observation: Acute_vs_Control (83)

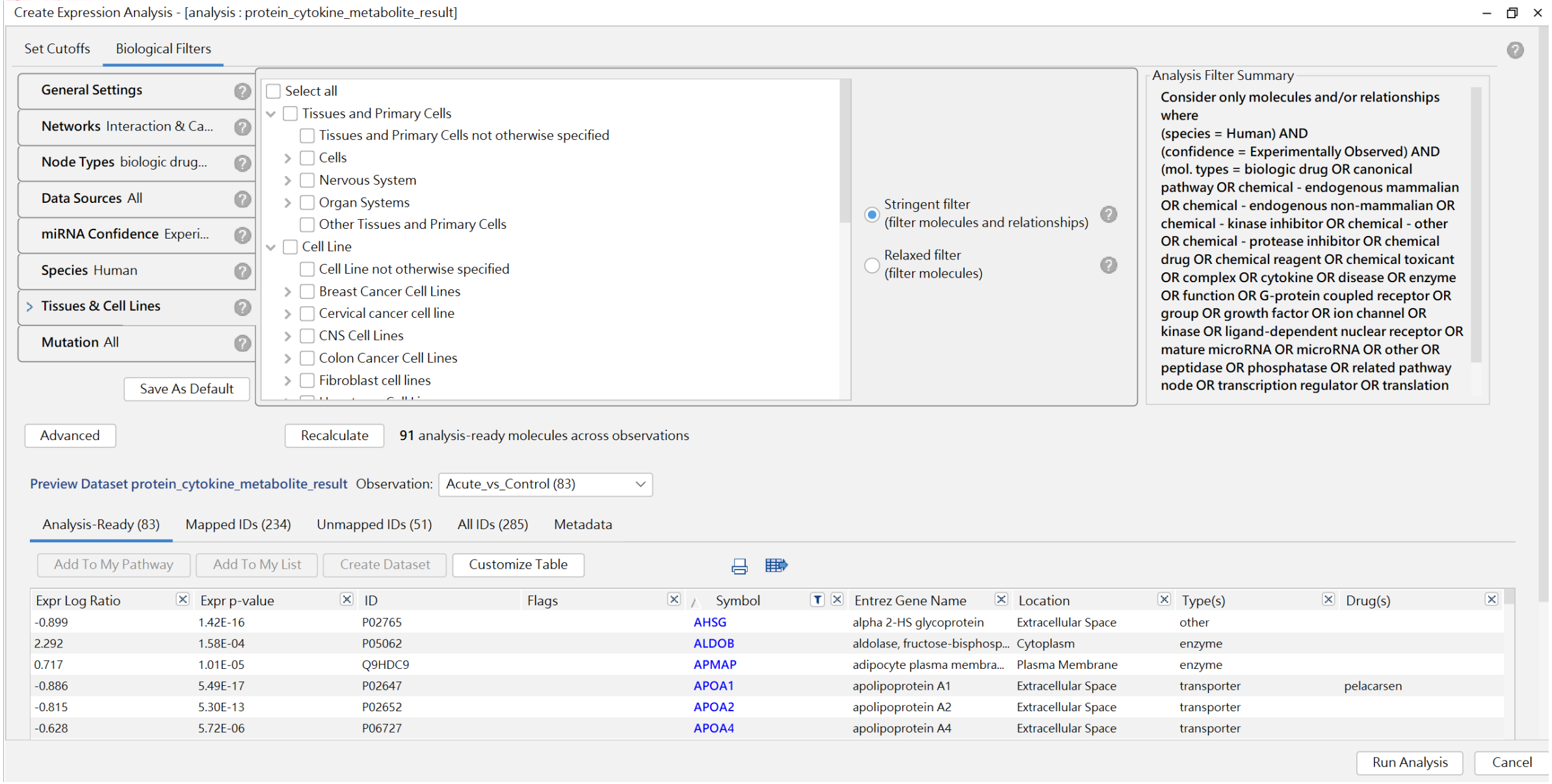
Analysis-Ready (83) | Mapped IDs (235) | Unmapped IDs (50) | All IDs (285) | Metadata

Add To My Pathway | Add To My List | Create Dataset | Customize Table

Expr Log Ratio	Expr p-value	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)

Run Analysis | Cancel

Tissue and Cell lines

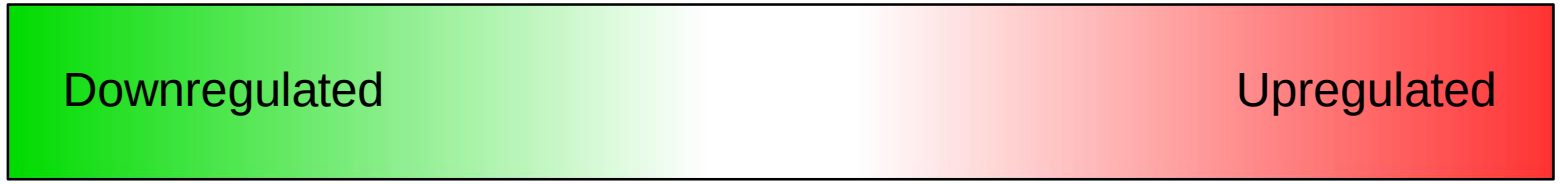


Expr Log Ratio	Expr p-value	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
-0.899	1.42E-16	P02765		AHSG	alpha 2-HS glycoprotein	Extracellular Space	other	
2.292	1.58E-04	P05062		ALDOB	aldolase, fructose-bisphosp...	Cytoplasm	enzyme	
0.717	1.01E-05	Q9HDC9		APMAP	adipocyte plasma membra...	Plasma Membrane	enzyme	
-0.886	5.49E-17	P02647		APOA1	apolipoprotein A1	Extracellular Space	transporter	pelacarsen
-0.815	5.30E-13	P02652		APOA2	apolipoprotein A2	Extracellular Space	transporter	
-0.628	5.72E-06	P06727		APOA4	apolipoprotein A4	Extracellular Space	transporter	

What do colors mean in IPA?

Pathway or gene activity predicted by IPA

Actual measurement of gene expression in your dataset



What do z-scores mean in IPA?

Actual dataset measurement **VS.** **What IPA expects if pathway is activated**

Symbol	Measurement Expr Log Ratio	Expected
CCL2	↓-2.030	↑ Up
CD44	↓-1.634	↑ Up
CD274	↓-2.218	↑ Up
COL1A1	↓-2.040	↑ Up
COL1A2	↓-1.920	↑ Up

Pathway inhibited

- Z score

Symbol	Measurement Expr Log Ratio	Expected
CCL2	↓-2.030	↑ Up
CD44	↑1.634	↑ Up
CD274	↓-2.218	↑ Up
COL1A1	↑2.040	↑ Up
COL1A2	↓-1.920	↑ Up

No clear signal for prediction Z score = 0

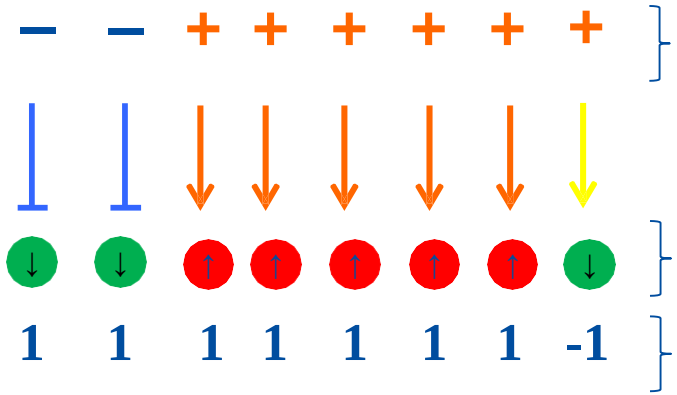
Symbol	Measurement Expr Log Ratio	Expected
CCL2	↑2.030	↑ Up
CD44	↑1.634	↑ Up
CD274	↑2.218	↑ Up
COL1A1	↑2.040	↑ Up
COL1A2	↑1.920	↑ Up

Pathway activated

+ Z score

How well do the actual measurements match the expected measurements?

z-score: Activation prediction



Gene expression from QIAGEN Knowledge Base (literature)

Gene expression in your dataset

+1 score for consistent relationships
and –1 for inconsistent relationships

$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}} = (7\text{-}1)/\sqrt{8} = 2.12\ (= \text{predicted activation})$$

- z-score is a statistical measure of the match between expected relationship direction and observed gene expression
- z-score greater than 2 or less than –2 is considered significant
- Note that the actual z-score is weighted by the underlying findings, the relationship bias and dataset bias

Examples of z-scores

Symbol	Measurement Expr Log Ratio	Expected
NR5A2	-1.002	Down
ABCB11	-1.056	Down
CYP2B6	-3.063	Down
PPARGC1A	-2.495	Down
ACOX1	-1.727	Down
SLCO1B3	3.223	Down
TLR4	1.213	Up
LY96	1.189	Up
IL1R1	1.634	Up
IL1RAP	1.046	Up
IL1B	3.890	Up
LIPC	-1.375	Up

Z-score = 2.4

10/12 measurements match expected

Mostly matching

Signal predominantly points to predicted activation

Symbol	Measurement Expr Log Ratio	Expected
CREB3L3	-1.536	Up
IHH	-1.173	Up
PBX1	-1.037	Up
CD86	1.016	Down
IL1RAP	1.046	Down
PKM	1.082	Up
HLA-DMB	1.106	Down
IL18RAP	1.124	Down
CREB5	1.148	Up
CREB3L2	1.179	Up
CCN4	1.204	Up
TLR4	1.213	Down

Z-score = -2.236

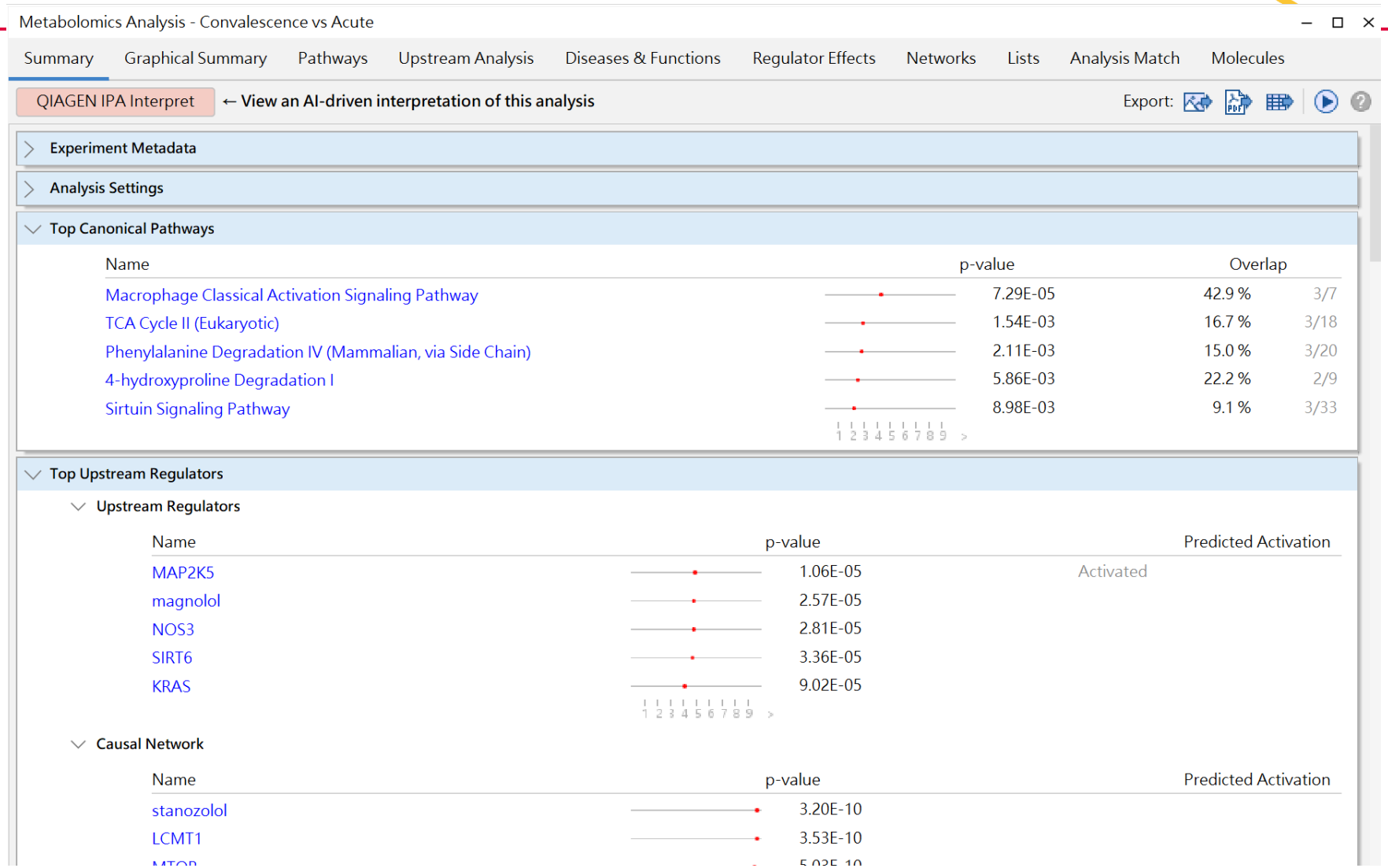
4/12 measurements match expected

Mostly anti-matching

Signal predominantly points to predicted inhibition

IPA Analysis Tabs

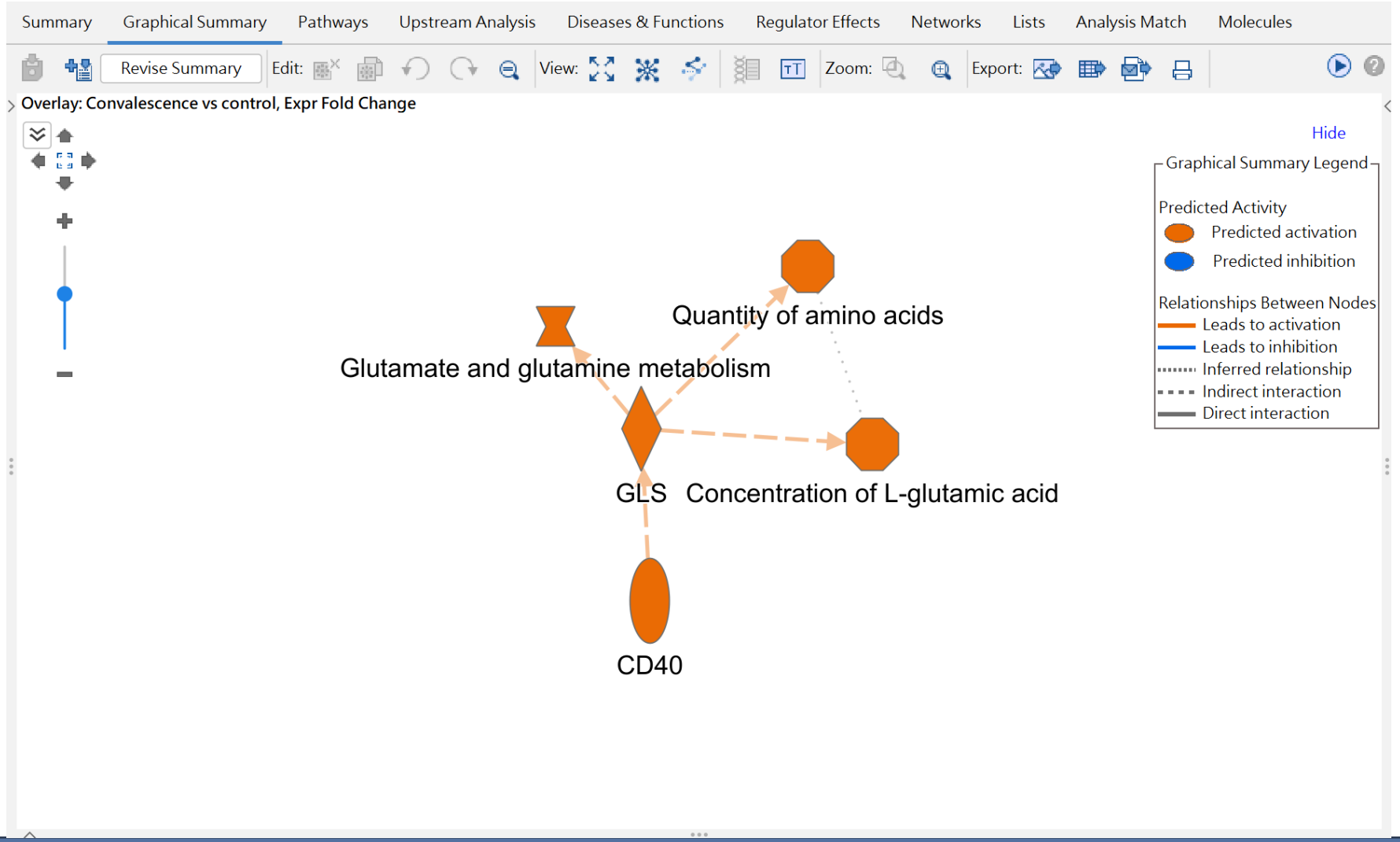
Summary Tab



Top 5 for all analysis modules and a quick high-level look at your data

Graphical Summary Tab

Metabolomics Analysis - Convalescence vs control



Graphical display of the top biological themes and features within your data with added AI inferences (dotted lines)

Change chart characteristics

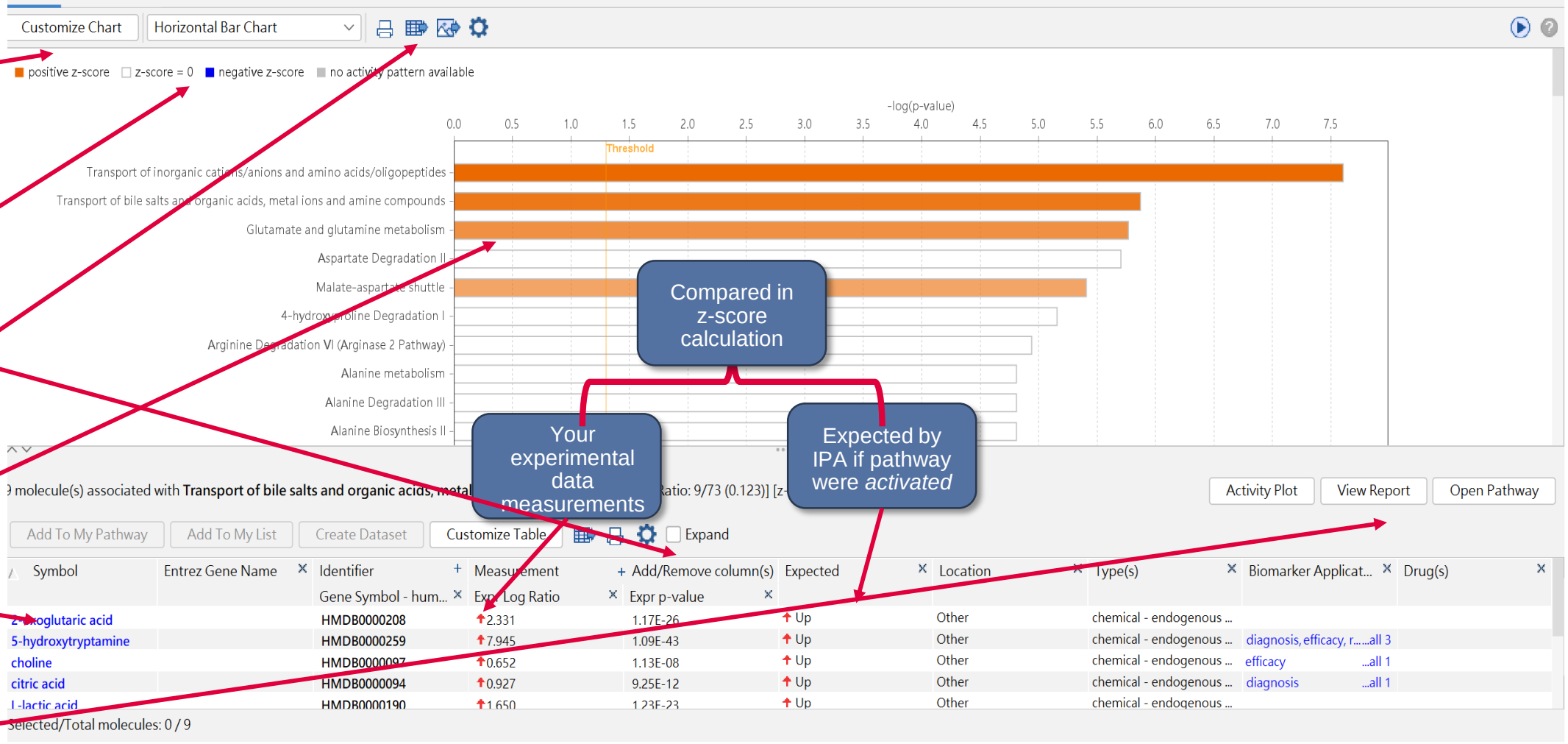
Change chart view

Export data or picture

Click on bar to display chart below

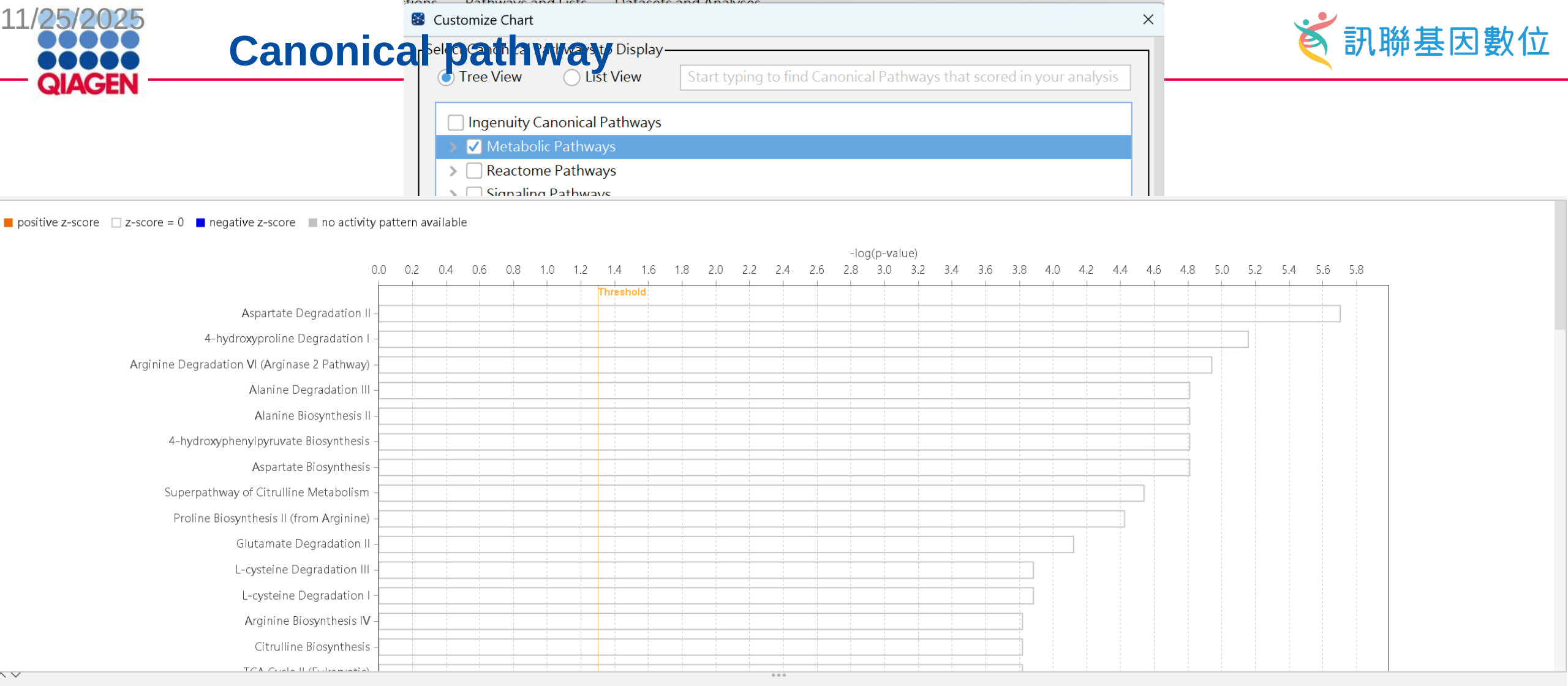
Genes in data set annotated to selected pathway

View network map of pathway



Metabolic and cell signaling pathways that are enriched in your data with activity prediction

Canonical pathway



Upstream Analysis Tab

Immediately upstream of dataset genes regulators

One additional level upstream of regulatory networks

Regulator predicted by IPA using patterns seen in your data (no measurement)

Highlight row and click to display at network map

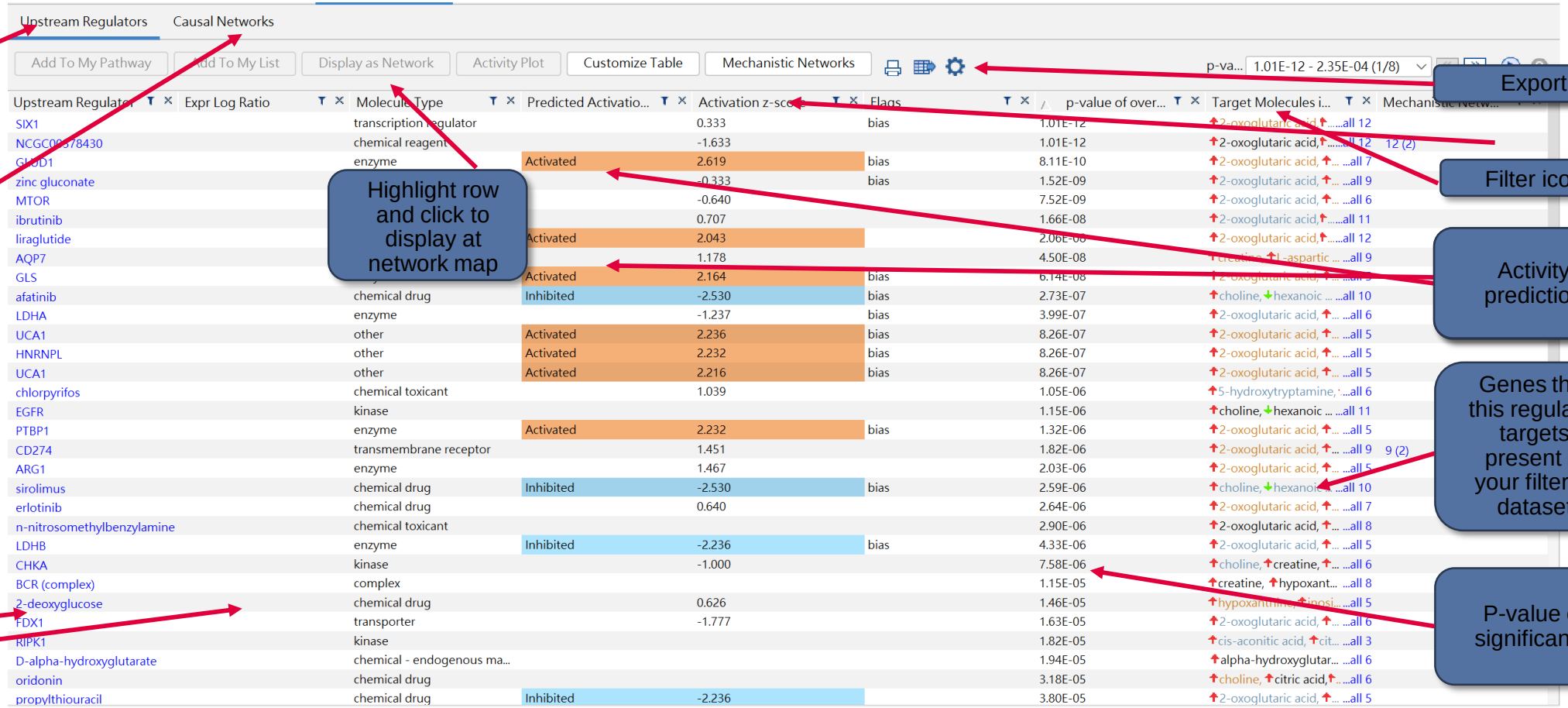
Export

Filter icons

Activity prediction

Genes that this regulator targets present in your filtered dataset

P-value of significance

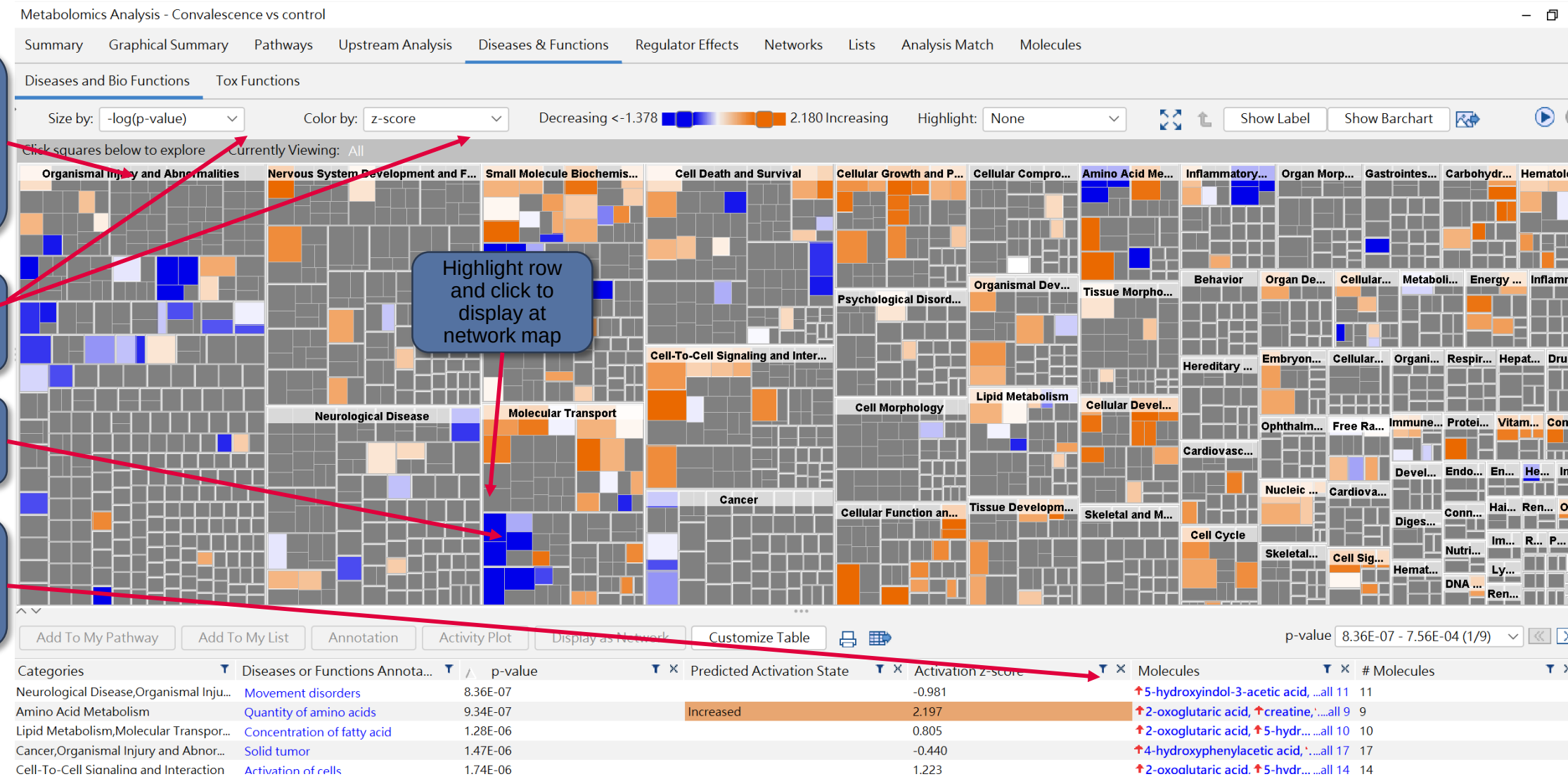


Upstream Regulator	Expr Log Ratio	Molecule Type	Predicted Activatio...	Activation z-score	Flags	p-value of over...	Target Molecules i...	Mechanistic Netw...
SIX1		transcription regulator		0.333	bias	1.01E-12	↑2-oxoglutaric acid,↑ ...all 12	
NCGC00378430		chemical reagent		-1.633		1.01E-12	↑2-oxoglutaric acid,↑ ...all 12	12 (2)
GUSD1		enzyme	Activated	2.619	bias	8.11E-10	↑2-oxoglutaric acid,↑ ...all 7	
zinc gluconate				-0.333	bias	1.52E-09	↑2-oxoglutaric acid,↑ ...all 9	
MTOR				-0.640		7.52E-09	↑2-oxoglutaric acid,↑ ...all 6	
ibrutinib				0.707		1.66E-08	↑2-oxoglutaric acid,↑ ...all 11	
liraglutide			Activated	2.043		2.06E-08	↑2-oxoglutaric acid,↑ ...all 12	
AQP7				1.178		4.50E-08	↑creatine,↑L-aspartic ...all 9	
GLS			Activated	2.164	bias	6.14E-08	↑2-oxoglutaric acid,↑ ...all 5	
afatinib		chemical drug	Inhibited	-2.530	bias	2.73E-07	↑choline,↓hexanoic ... ...all 10	
LDHA		enzyme		-1.237	bias	3.99E-07	↑2-oxoglutaric acid,↑ ... ...all 6	
UCA1		other	Activated	2.236	bias	8.26E-07	↑2-oxoglutaric acid,↑ ... ...all 5	
HNRNPL		other	Activated	2.232	bias	8.26E-07	↑2-oxoglutaric acid,↑ ... ...all 5	
UCA1		other	Activated	2.216	bias	8.26E-07	↑2-oxoglutaric acid,↑ ... ...all 5	
chlorpyrifos		chemical toxicant		1.039		1.05E-06	↑5-hydroxytryptamine,↑ ...all 6	
EGFR		kinase				1.15E-06	↑choline,↓hexanoic ... ...all 11	
PTBP1		enzyme	Activated	2.232	bias	1.32E-06	↑2-oxoglutaric acid,↑ ... ...all 5	
CD274		transmembrane receptor		1.451		1.82E-06	↑2-oxoglutaric acid,↑ ... ...all 9	9 (2)
ARG1		enzyme		1.467		2.03E-06	↑2-oxoglutaric acid,↑ ... ...all 5	
sirolimus		chemical drug	Inhibited	-2.530	bias	2.59E-06	↑choline,↓hexanoic ... ...all 10	
erlotinib		chemical drug		0.640		2.64E-06	↑2-oxoglutaric acid,↑ ... ...all 7	
n-nitrosomethylbenzylamine		chemical toxicant				2.90E-06	↑2-oxoglutaric acid,↑ ... ...all 8	
LDHB		enzyme	Inhibited	-2.236	bias	4.33E-06	↑2-oxoglutaric acid,↑ ... ...all 5	
CHKA		kinase		-1.000		7.58E-06	↑choline,↑creatine,↑ ... ...all 6	
BCR (complex)		complex				1.15E-05	↑creatine,↑hypoxant... ...all 8	
2-deoxyglucose		chemical drug		0.626		1.46E-05	↑hypoxanthine,↑inosi... ...all 5	
FDX1		transporter		-1.777		1.63E-05	↑2-oxoglutaric acid,↑ ... ...all 6	
RIPK1		kinase				1.82E-05	↑cis-aconitic acid,↑cit... ...all 3	
D-alpha-hydroxyglutarate		chemical - endogenous ma...				1.94E-05	↑alpha-hydroxyglutar... ...all 6	
oridonin		chemical drug				3.18E-05	↑choline,↑citric acid,↑ ... ...all 6	
propylthiouracil		chemical drug	Inhibited	-2.236		3.80E-05	↑2-oxoglutaric acid,↑ ... ...all 5	

Regulators that may be contributing to the signal observed in your data. Some have been measured in your dataset and some have been predicted by IPA

**** ALL COLUMNS ARE FILTERABLE****

Diseases & Functions Tab



Color is activity prediction; size of square is p-value but can be changed

Organized by biological themes

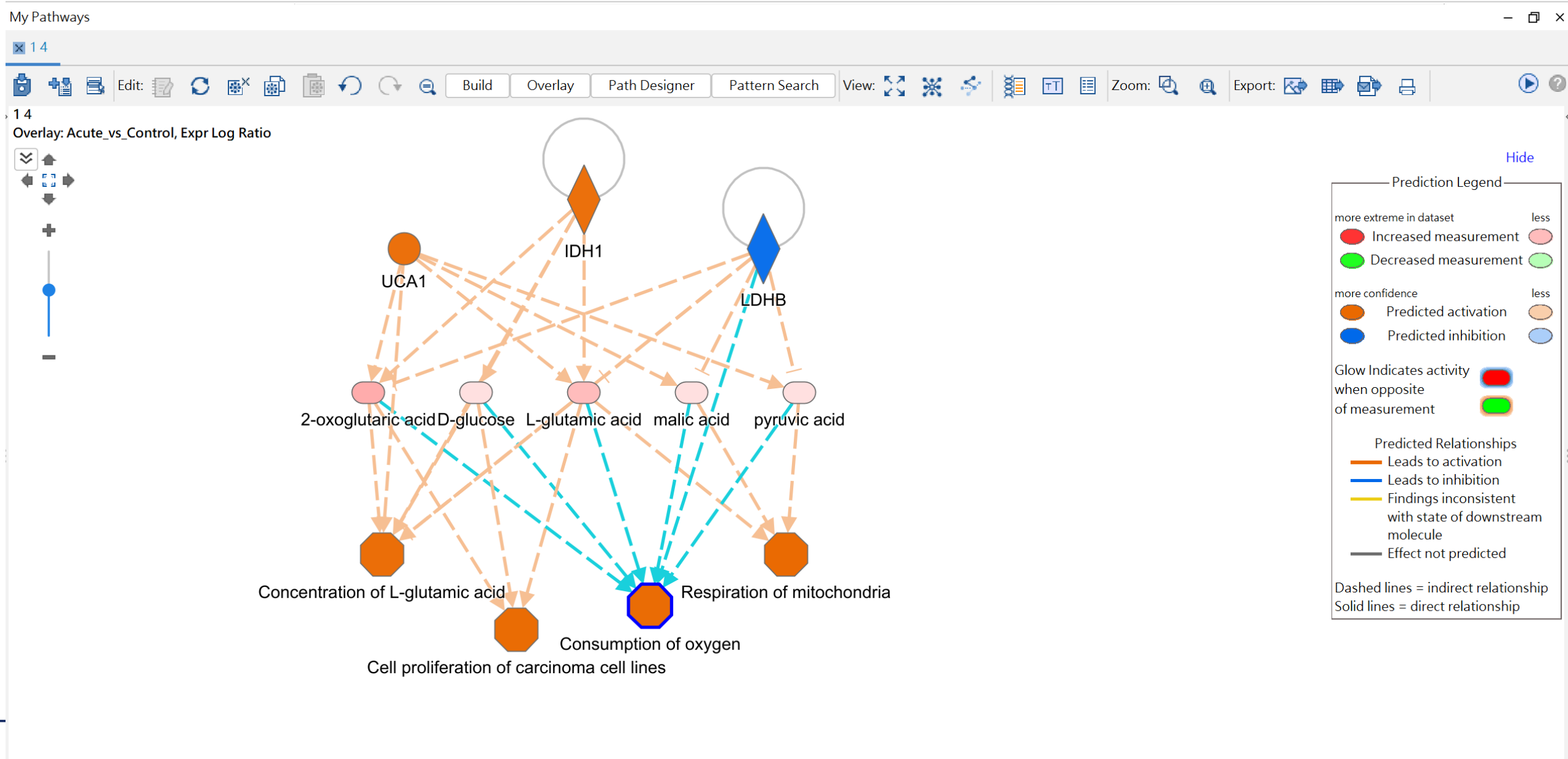
Significance of enrichment

Genes from dataset involved in disease or function

Highlight row and click to display at network map

Diseases and functions that may be key to the biology in your experimental data based on patterns of expression observed

Regulate Effect



Network of highly connected molecules, click to open network map

Molecule in **bold** is in your dataset; unbolded have been added to maximize connectivity

Based on a p-value calculation how likely molecules exist as part of a network than chance alone

Disease or function predicted to be an outcome

Metabolomics Analysis - Acute_vs_Control

Summary | Graphical Summary | Pathways | Upstream Analysis | Diseases & Functions | Regulator Effects | Networks | Lists | Analysis Match | Molecules

Networks | Overlapping Networks

View Networks | Add To My Pathway | Add To My List | Merge Networks | Functions | Annotation | Customize Table | Expand

The analysis is composed of 18 networks. To view a network, select the appropriate network(s) and click View Networks. To merge selected networks, click Merge Networks. Total selected molecules: 0

	Molecules in Network			Top Diseases and Functions
1	actin, activated RAF:scaffold:MAP2K:MAPK:single mechanism MAPK inhibitors, ↑**ALDOB**, ↑**alpha-hydroxyglutarate**, casp... ...all 35	24	13	Digestive System Development and Function, Fr... ...all 3
2	↑**(S)-3-hydroxy-2-methylpropanoic acid**, ↓**14:0/20:4(5Z,8Z,11Z,14Z) phosphatidylcholine**, ↓**4-cresol sulfate**, 8,9-epoxy... ...all 35	24	13	Lipid Metabolism, Molecular Transport, Small M... ...all 3
3	aconitase, ↓**AHSG**, Amyloid fibril main peptide chains, Amyloid fibrils, ↓**APOA1**, ↓**APOA4**, ↑**APOC3**, apolipoprotein, ↓... ...all 35	22	12	Cardiac Dysfunction, Cardiovascular Disease, Pro... ...all 3
4	Activator:PI3K, ↑**APMAP**, arylesterase, ↑**CA1**, calpain, CD1, Complement, ↑**FLT3LG**, HDL, IFN ...all 35	22	12	Cellular Development, Cellular Growth and Proli... ...all 3
5	Ap1, ↓**CCL22**, ↑**CCL4**, CD3 (complex), ↑**CD40LG**, ↑**CXCL1**, ↑**CXCL10**, ↑**CXCL8**, ↑**CXCL9**, GPCR ...all 35	22	12	Cell-To-Cell Signaling and Interaction, Hematolo... ...all 3
6	17-epi-resolvin D1, ↑**2-hydroxy-3-methylvaleric acid**, ↑**2-hydroxyisovaleric acid**, ↑**4-hydroxyhippuric acid**, ↑**4-hydrox...** ...all 35	22	12	Cell-To-Cell Signaling and Interac... ...all 3
7	↑**2-oxoglutaric acid**, ↑**5-hydroxytryptamine**, ADRB, ↓**cholesteryl myristate**, collagen, collagenase, cytochrome C, cytoc... ...all 35	19	11	Cellular Function and Maintenan...
8	26S proteasome, ADCY, AMPK, ↓**APOC1**, BCR (complex), ↑**beta-alanine**, CK2 alpha, cytokine, ↑**D-glucose**, ERM ...all 35	17	10	Inflammatory Disease, Inflammat...
9	antioxidant, arginase, ↑**beta-hydroxyisovaleric acid**, C/EBP, cyclooxygenase, eotaxin, ERK1/2, ETS, Ferritin, glutathione p... ...all 35	13	8	Amino Acid Metabolism, Cell Cyc...
10	ACAC, Activated TLR1:2 or TLR 2:6 heterodimers or TLR4 homodimer, activated TLR2/4:TIRAP:PI(4,5)P2:BTK, C1Q (family), ...all 35	13	8	Cancer, Gastrointestinal Disease, ...
11	acute phase, alpha 1 antitrypsin, ↓**APOA2**, C4BP, casein, Cebp, chymotrypsin, coagulation factor, DAF,FAM20C:FAM20C s... ...all 35	7	5	Immunological Disease, Metabolic Disease, Orga... ...all 3
12	activin (family), ALP, BCAR1:Talin:RIAM:ECM ligands:alphaIIb beta3:SRC:PTK2, C1Q, collagen alpha1, collagen type i (family), ...all 35	7	5	Cardiovascular Disease, Organismal Injury and A... ...all 3
13	angiotensin II receptor type 1, AP2, apyrase, C-SRC, ↑**C9**, cathepsin, CD3 (family), CPLA2, elastase, ENaC ...all 35	5	4	Cell Cycle, Cell-To-Cell Signaling and Interaction, ...all 3
14	aldose reductase, ALT, CD8 (family), CLASP proteins:cargo, ↑**EGF**, Fc receptor, fibrinogen (family), FOS (family), GNRH, GOT ...all 35	5	4	Cancer, Cell-To-Cell Signaling and Interaction, C... ...all 3
15	alpha catenin, ↑**B2M**, Calcineurin (complex), calmodulin, CG, CK2, CSF, ↑**F5**, focal adhesion kinase, FSH ...all 35	5	4	Cellular Development, Cellular Growth and Proli... ...all 3
16	↓**1-18:2(9Z,12Z) lysophosphatidylcholine**, ARHGEF2, ARSB, Autophagy, BCHE, BNIP3, ↓**BTD**, BUB1B, ELOVL6, FAT1 ...all 35	5	4	Cell Death and Survival, Cellular Development, ...all 3
17	activated RAF:scaffold:MAP2K:MAPK, activated RAF:scaffold:MAP2K:MAPK complex:dual mechanism MAP2K inhibitors, act... ...all 35	4	3	Connective Tissue Disorders, Inflammatory Dise... ...all 3

Networks constructed from your dataset with level of connectivity prioritized

Analysis Match

How signatures are created and compared

- Data source from Omicsoft datalands

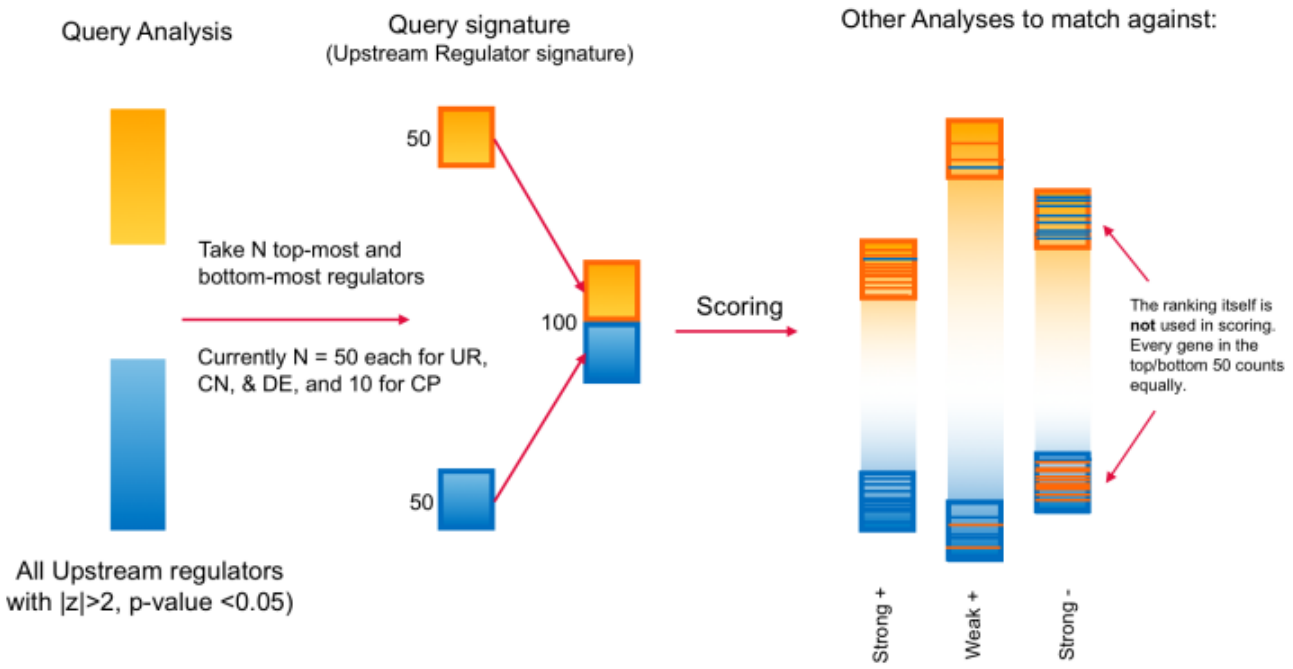
Canonical Pathways (up to 20 pathways)

Upstream Regulators (up to 100 regulators)

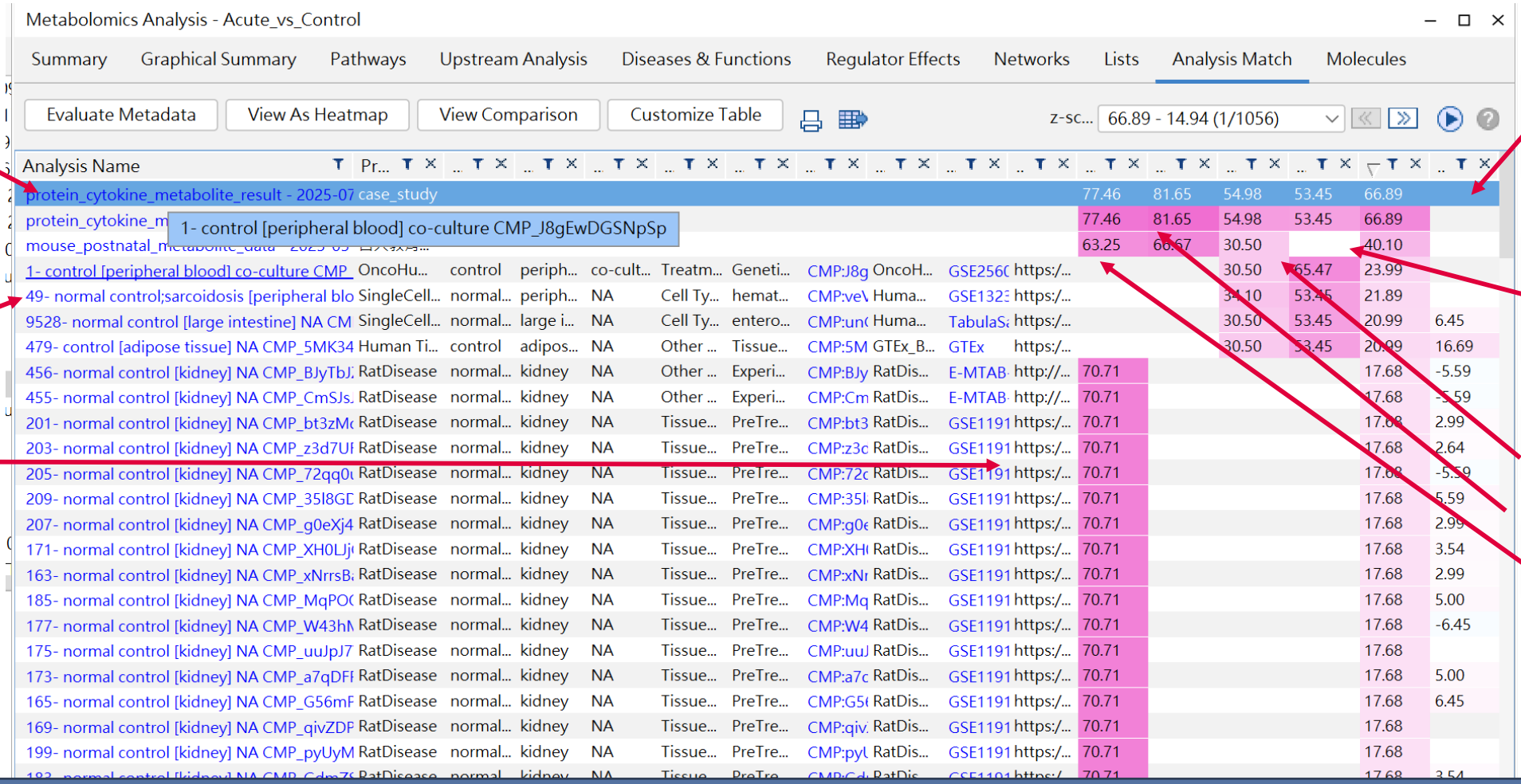
Causal Networks (up to 100 master regulators)

Diseases & Functions (up to 100 diseases or functions)

Example



Analysis Match Tab



Public and previously run analyses with matching or antimatching results

Double click to open core analysis

Link to Land Explorer to view volcano plot of comparison

Average z-score from all 4 analysis features

DE: Downstream effects (i.e. diseases and functions

CN: Causal Networks

UR: Upstream Regulators

CP: Canonical Pathways

Matches your core analysis against public datasets in IPA as well as previously run core analyses and returns similar and dissimilar datasets based on 4 core analysis features: CP, UR, CN, DE

****All columns are filterable****

Positive z-score: Pink: matching ***Negative z-score: Blue: antimatching***

Molecules

訊聯基因數位

Biomarker Application

Drug

Metabolomics Analysis - Acute_vs_Control

Summary | Graphical Summary | Pathways | Upstream Analysis | Diseases & Functions | Regulator Effects | Networks | Lists | Analysis Match | Molecules

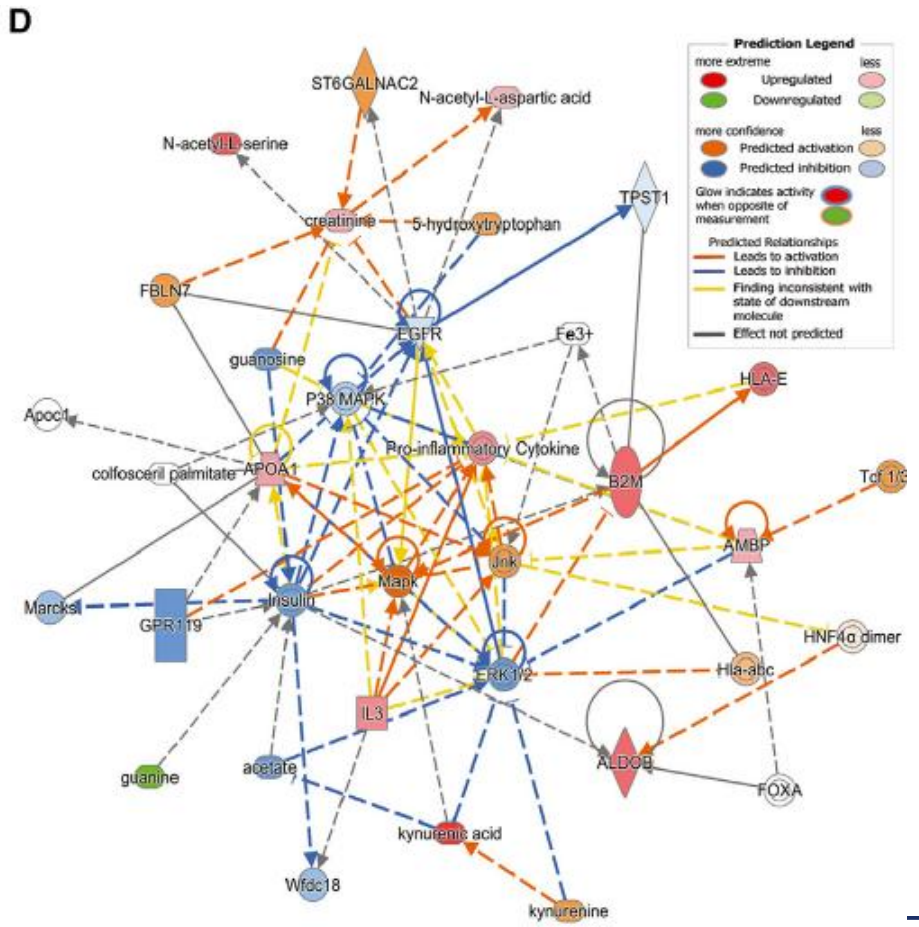
Add To My Pathway | Add To My List | Create Dataset | Customize Table | Symbol (S)-2-hydroxybut... (1/3)

Symbol	Entrez Gen...	Identifier / Gene Symb...	Measurem... / Expr Log Ra...	Add/Remove column(s) / Expr p-value	Location	Type(s)	Biomarker ...	Drug(s)
(S)-2-hydroxybutyric	--	**HMDB0000008**	↑1.654	2.50E-10	Other	chemical - endogen...		
(S)-3-hydroxy-2-methl	--	**HMDB0000023**	↑0.829	2.38E-06	Other	chemical - endogen...		
(S)-indole-3-lactic aci	--	HMDB0000671			Other	chemical - endogen...		
1-14:0/2-18:1(11Z) di	--	HMDB07014			Other	chemical - endogen...		
1-16:1(9Z) lysophosp	--	HMDB0010383			Other	chemical - endogen...		
1-18:0 lysophosphati	--	HMDB0010384			Other	chemical - endogen...		
1-18:1(11Z)/2-18:2(9Z	--	**HMDB07190**	↑0.745	1.82E-03	Other	chemical - endogen...		
1-18:2(9Z,12Z) lysoph	--	**HMDB0010386**	↓-0.937	3.92E-09	Other	chemical - endogen...		
1-18:2(9Z,12Z)/2-18:2	--	**HMDB07248**	↑1.010	1.39E-03	Other	chemical - endogen...		
1-heptadecanoyl-2-h	--	HMDB0012108			Other	chemical - endogen...		
1-oleoyl lysophospha	--	HMDB0002815			Other	chemical - endogen...		
14:0/20:4(5Z,8Z,11Z,1	--	**HMDB0007883**	↓-0.856	2.13E-07	Other	chemical - endogen...		
14:0/20:4(8Z,11Z,14Z,	--	HMDB0007884			Other	chemical - endogen...		
16:0/16:0/16:1(9Z)[isc	--	HMDB0005359			Other	chemical - endogen...		
16:0/16:0/18:0[iso3] t	--	HMDB0005357			Other	chemical - endogen...		
16:0/16:0/20:4(5Z,8Z,	--	**HMDB0005363**	↑0.769	1.28E-02	Other	chemical - endogen...		
16:0/16:1(9Z)/16:1(9Z	--	HMDB0005376			Other	chemical - endogen...		
16:0/18:0/18:2(9Z,12Z	--	**HMDB0005369**	↑0.854	1.90E-05	Other	chemical - endogen...		
16:0/18:1(9Z)/18:2(9Z	--	**HMDB0005384**	↑0.864	1.06E-04	Other	chemical - endogen...		
16:0/20:4(5Z,8Z,11Z,1	--	**HMDB0005392**	↑0.597	2.04E-02	Other	chemical - endogen...		
16:0/20:5(5Z,8Z,11Z,1	--	HMDB0007984			Other	chemical - endogen...		
18:0/14:0/16:1(9Z)[isc	--	HMDB0010426			Other	chemical - endogen...		
18:0/14:0/18:1(11Z)[is	--	HMDB0010428			Other	chemical - endogen...		
18:0/14:0/18:2(9Z,12Z	--	HMDB0010430			Other	chemical - endogen...		
18:0/16:0/18:3(9Z,12Z	--	**HMDB0010432**	↑0.617	4.64E-03	Other	chemical - endogen...		
18:0/18:1(9Z)/18:2(9Z	--	**HMDB0005405**	↑0.682	2.72E-03	Other	chemical - endogen...		
2,5-furandicarboxylic	--	**HMDB0004812**	↓-0.986	1.28E-03	Other	chemical - endogen...		
2-hydroxy-3-methylv	--	**HMDB0000317**	↑0.964	7.62E-06	Other	chemical - endogen		

Selected/Total molecules: 0 / 224

Constructed Gene/Metabolite network

Unsupervised method
Separate COVID19 patients to 3 cluster
Cluster 3 poor status



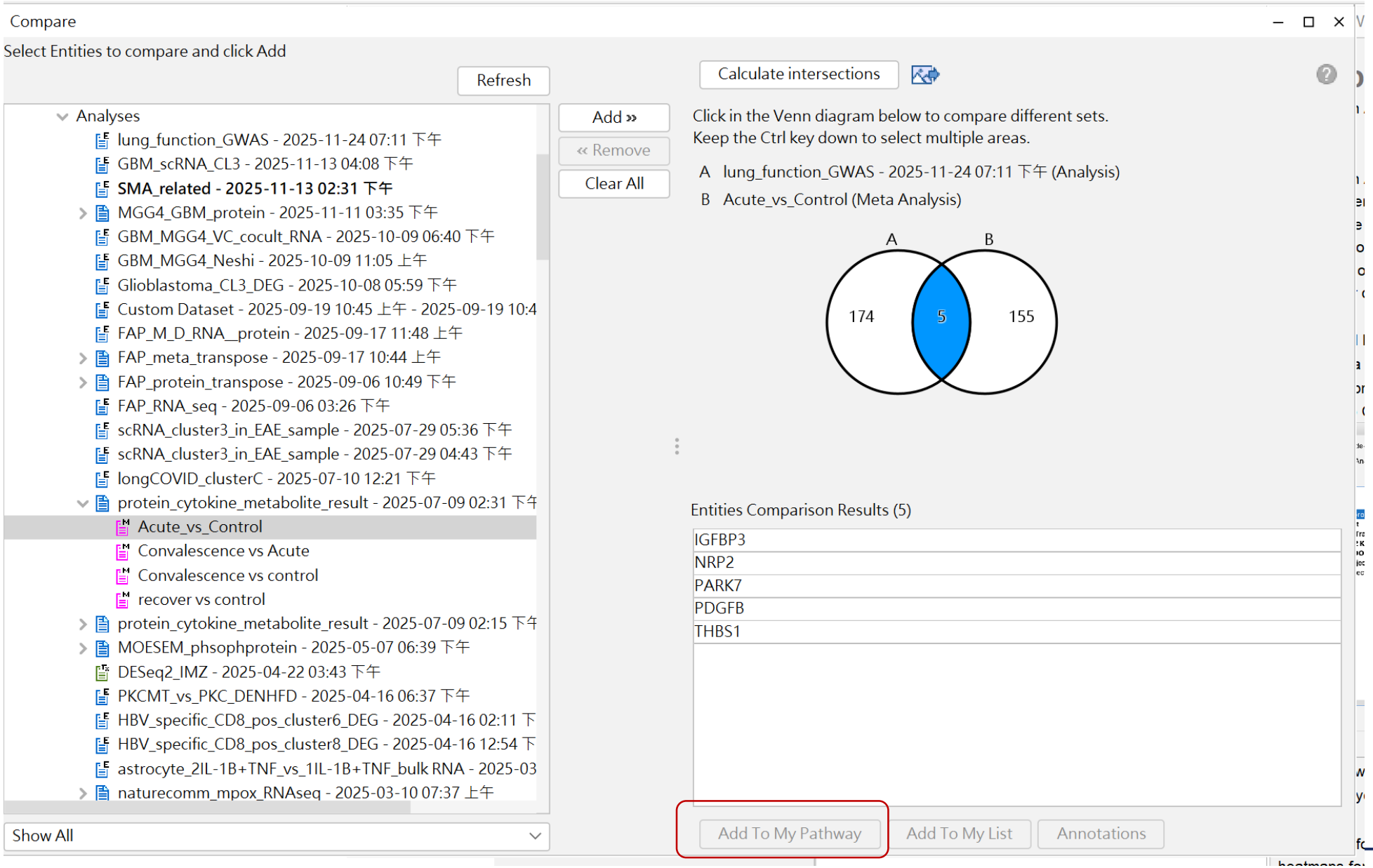
	A	B	C
1	Biomarker name	indentifier	Percentage Deviation
2	TG(18:2_36:3)	NA	65.15435
3	TG(18:2_36:4)	NA	70.42088
4	TG(18:3_36:4)	NA	70.85822
5	N-Acetyl-Aspartic acid	HMDB0000201	71.30437
6	TG(18:2_36:5)	NA	71.62724
7	Guanine	HMDB0000132	-71.83251
8	Protein AMBP	P02760	76.56766
9	Creatinine	HMDB0000562	79.54263
10	Apolipoprotein(a)	P08519	83.2135
11	Methylmalonic acid	HMDB0000845	94.58442
12	p-Hydroxyhippuric acid	HMDB0000715	99.0861
13	IL-3	P08700	99.81049
14	Cystathionine	HMDB0000675	101.45969
15	Phenylacetylglutamine	HMDB0001961	103.17527
16	N-Acetyl-Tryptophan	HMDB0013713	106.88627
17	Trimethylamine N-Oxide	HMDB0001965	107.73705
18	Methylhistidine	HMDB0001331	111.25071
19	Fructose-bisphosphate aldolase B	P05062	121.84065
20	Beta-2-microglobulin	P61769	122.31938
21	N-Acetyl-Serine	HMDB0002180	136.2814
22	2-Hydroxyphenylacetic acid	HMDB0000669	136.72478
23	Hippuric acid	HMDB0000714	157.83553
24	Kynurenic acid	HMDB0000684	163.77833
25	4-Hydroxyphenylacetic acid	HMDB0000668	177.55187

Network

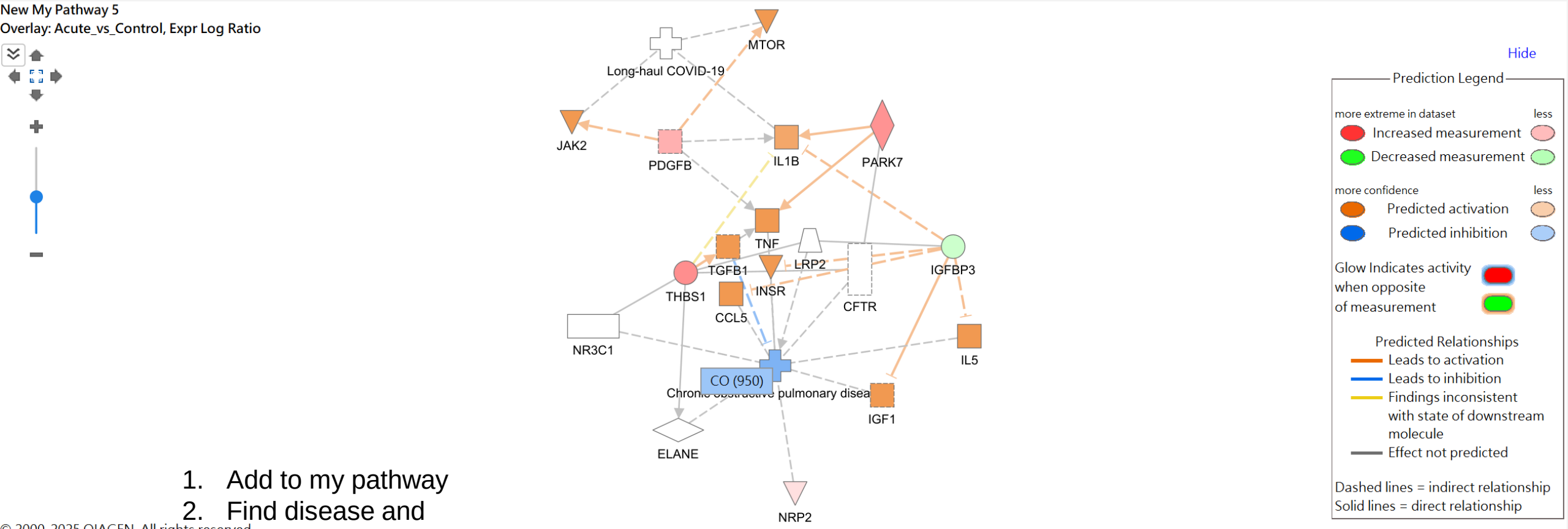
3 step

1. Constructed network
2. Overlap dataset

Compare

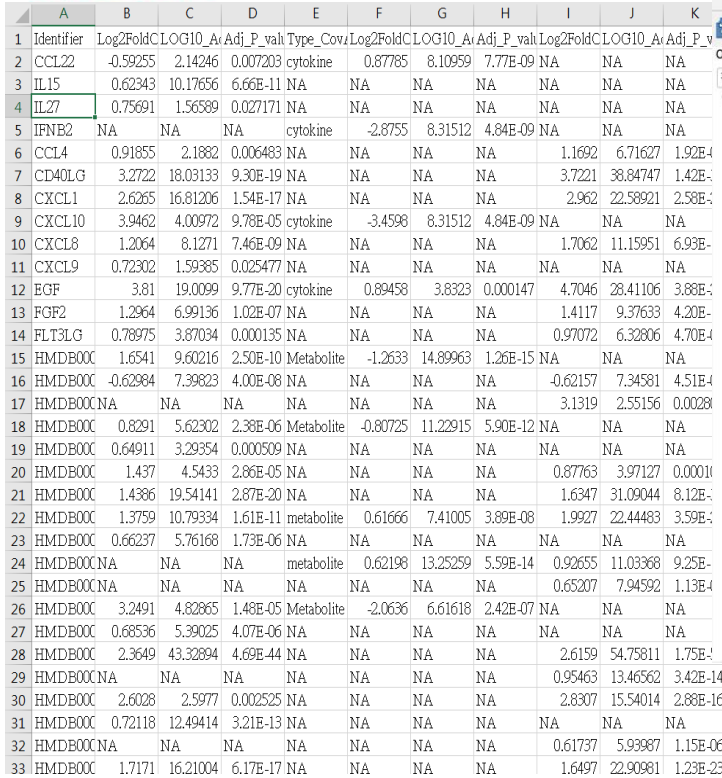

Compare
Select Entities to compare and click Add
Refresh
Analyses
lung_function_GWAS - 2025-11-24 07:11 下午
GBM_scRNA_CL3 - 2025-11-13 04:08 下午
SMA_related - 2025-11-13 02:31 下午
MGG4_GBM_protein - 2025-11-11 03:35 下午
GBM_MGG4_VC_cocult_RNA - 2025-10-09 06:40 下午
GBM_MGG4_Neshi - 2025-10-09 11:05 上午
Glioblastoma_CL3_DEG - 2025-10-08 05:59 下午
Custom Dataset - 2025-09-19 10:45 上午 - 2025-09-19 10:4
FAP_M_D_RNA__protein - 2025-09-17 11:48 上午
FAP_meta_transpose - 2025-09-17 10:44 上午
FAP_protein_transpose - 2025-09-06 10:49 下午
FAP_RNA_seq - 2025-09-06 03:26 下午
scRNA_cluster3_in_EAE_sample - 2025-07-29 05:36 下午
scRNA_cluster3_in_EAE_sample - 2025-07-29 04:43 下午
longCOVID_clusterC - 2025-07-10 12:21 下午
protein_cytokine_metabolite_result - 2025-07-09 02:31 下午
Acute_vs_Control
Convalescence vs Acute
Convalescence vs control
recover vs control
protein_cytokine_metabolite_result - 2025-07-09 02:15 下午
MOESEM_phsophprotein - 2025-05-07 06:39 下午
DESeq2_IMZ - 2025-04-22 03:43 下午
PKCMT_vs_PKC_DENHFD - 2025-04-16 06:37 下午
HBV_specific_CD8_pos_cluster6_DEG - 2025-04-16 02:11 下
HBV_specific_CD8_pos_cluster8_DEG - 2025-04-16 12:54 下
astrocyte_2IL-1B+TNF_vs_1IL-1B+TNF_bulk RNA - 2025-03
naturecomm_mpox_RNAseq - 2025-03-10 07:37 上午
Show All
Add »
« Remove
Clear All
Calculate intersections
Click in the Venn diagram below to compare different sets.
Keep the Ctrl key down to select multiple areas.
A lung_function_GWAS - 2025-11-24 07:11 下午 (Analysis)
B Acute_vs_Control (Meta Analysis)
A
B
174
5
155
Entities Comparison Results (5)
IGFBP3
NRP2
PARK7
PDGFB
THBS1
Add To My Pathway
Add To My List
Annotations

Construct your self network

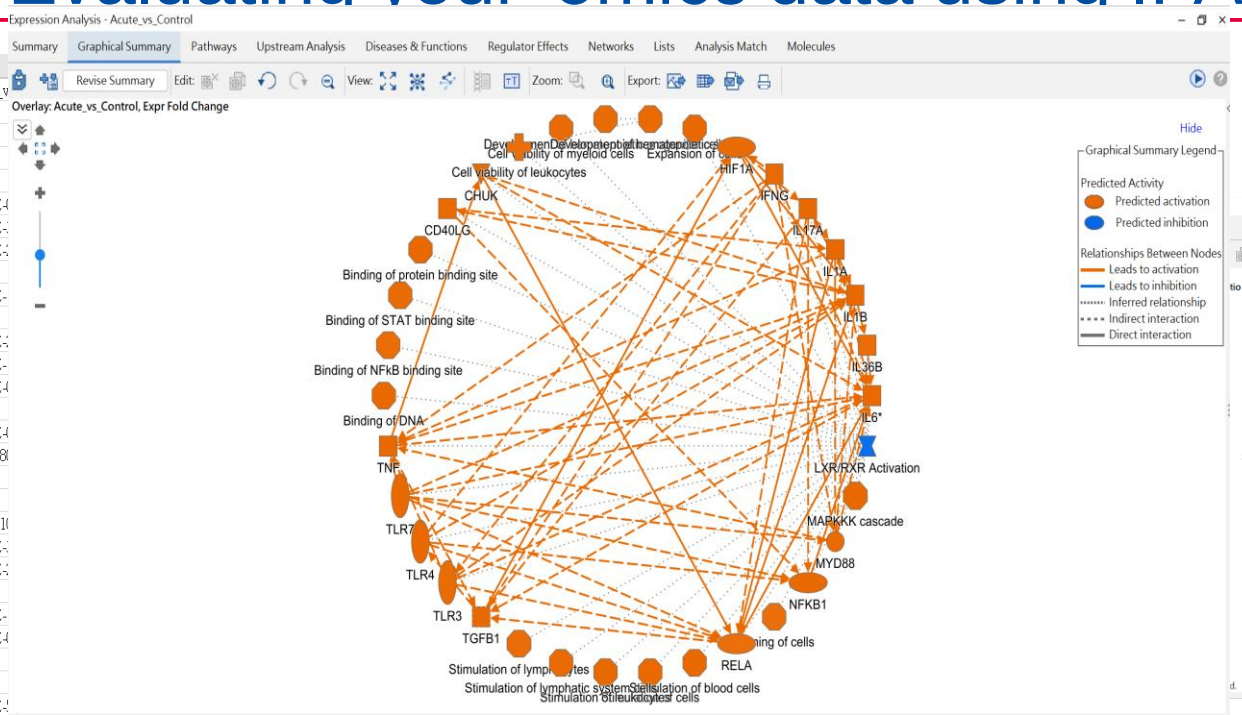


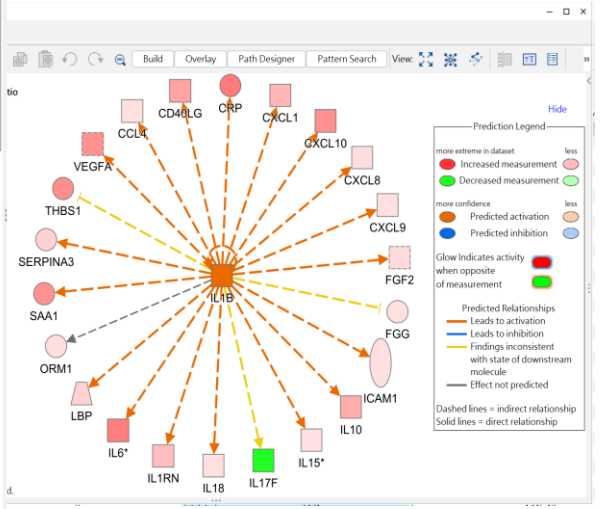
1. Add to my pathway
2. Find disease and function
3. Build -> path explore
4. Overlap analysis and datasets

Summary: Evaluating your 'omics data using IPA



	A	B	C	D	E	F	G	H	I	J	K
1	Identifier	Log2FoldC	LOG10_A	Adj_P_valu	Type_Cova	Log2FoldC	LOG10_A	Adj_P_valu	Log2FoldC	LOG10_A	Adj_P_v
2	CCL22	-0.59255	2.14246	0.007203	cytokine	0.87785	8.10959	7.77E-09	NA	NA	NA
3	IL15	0.62343	10.17656	6.66E-11	NA	NA	NA	NA	NA	NA	NA
4	IL27	0.75691	1.56589	0.027171	NA	NA	NA	NA	NA	NA	NA
5	IFNB2	NA	NA	NA	cytokine	-2.8755	8.31512	4.84E-09	NA	NA	NA
6	CCL4	0.91855	2.1882	0.006483	NA	NA	NA	NA	1.1692	6.71627	1.92E-4
7	CD40LG	3.2722	18.03133	9.30E-19	NA	NA	NA	NA	3.7221	38.84747	1.42E-1
8	CXCL1	2.6265	16.81206	1.54E-17	NA	NA	NA	NA	2.962	22.58921	2.58E-1
9	CXCL10	3.9462	4.00972	9.78E-05	cytokine	-3.4598	8.31512	4.84E-09	NA	NA	NA
10	CXCL8	1.2064	8.1271	7.46E-09	NA	NA	NA	NA	1.7062	11.15951	6.93E-
11	CXCL9	0.72302	1.59385	0.025477	NA	NA	NA	NA	NA	NA	NA
12	EGF	3.81	19.0099	9.77E-20	cytokine	0.89458	3.8323	0.000147	4.7046	28.41106	3.88E-1
13	FGF2	1.2964	6.99136	1.02E-07	NA	NA	NA	NA	1.4117	9.37633	4.20E-
14	FLT3LG	0.78975	3.87034	0.000135	NA	NA	NA	NA	0.97072	6.32806	4.70E-4
15	HMDB000	1.6541	9.60216	2.50E-10	Metabolite	-1.2633	14.89963	1.26E-15	NA	NA	NA
16	HMDB000	-0.62984	7.39823	4.00E-08	NA	NA	NA	NA	-0.62157	7.34581	4.51E-4
17	HMDB000	NA	NA	NA	NA	NA	NA	NA	3.1319	2.55156	0.00288
18	HMDB000	0.8291	5.62302	2.38E-06	Metabolite	-0.80725	11.22915	5.90E-12	NA	NA	NA
19	HMDB000	0.64911	3.29354	0.000509	NA	NA	NA	NA	NA	NA	NA
20	HMDB000	1.437	4.5433	2.86E-05	NA	NA	NA	NA	0.87763	3.97127	0.00010
21	HMDB000	1.4386	19.54141	2.87E-20	NA	NA	NA	NA	1.6347	31.09044	8.12E-1
22	HMDB000	1.3759	10.79334	1.61E-11	metabolite	0.61666	7.41005	3.89E-08	1.9927	22.44483	3.59E-1
23	HMDB000	0.66237	5.76168	1.73E-06	NA	NA	NA	NA	NA	NA	NA
24	HMDB000	NA	NA	NA	metabolite	0.62198	13.25259	5.59E-14	0.92655	11.03368	9.25E-
25	HMDB000	NA	NA	NA	NA	NA	NA	NA	0.65207	7.94592	1.13E-4
26	HMDB000	3.2491	4.82865	1.48E-05	Metabolite	-2.0636	6.61618	2.42E-07	NA	NA	NA
27	HMDB000	0.68536	5.39025	4.07E-06	NA	NA	NA	NA	NA	NA	NA
28	HMDB000	2.3649	43.32894	4.69E-44	NA	NA	NA	NA	2.6159	54.75811	1.75E-1
29	HMDB000	NA	NA	NA	NA	NA	NA	NA	0.95463	13.46562	3.42E-14
30	HMDB000	2.6028	2.5977	0.002525	NA	NA	NA	NA	2.8307	15.54014	2.88E-16
31	HMDB000	0.72118	12.49414	3.21E-13	NA	NA	NA	NA	NA	NA	NA
32	HMDB000	NA	NA	NA	NA	NA	NA	NA	0.61737	5.93987	1.15E-06
33	HMDB000	1.7171	16.21004	6.17E-17	NA	NA	NA	NA	1.6497	22.90981	1.23E-23





- Data upload and analysis setup
- Canonical pathways
- Upstream regulators
- Diseases and functions
- Comparison analysis

Better Care with Better Knowledge

若有需要進一步的資訊或在使用軟體上遇到問題歡迎聯繫以下窗口:

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