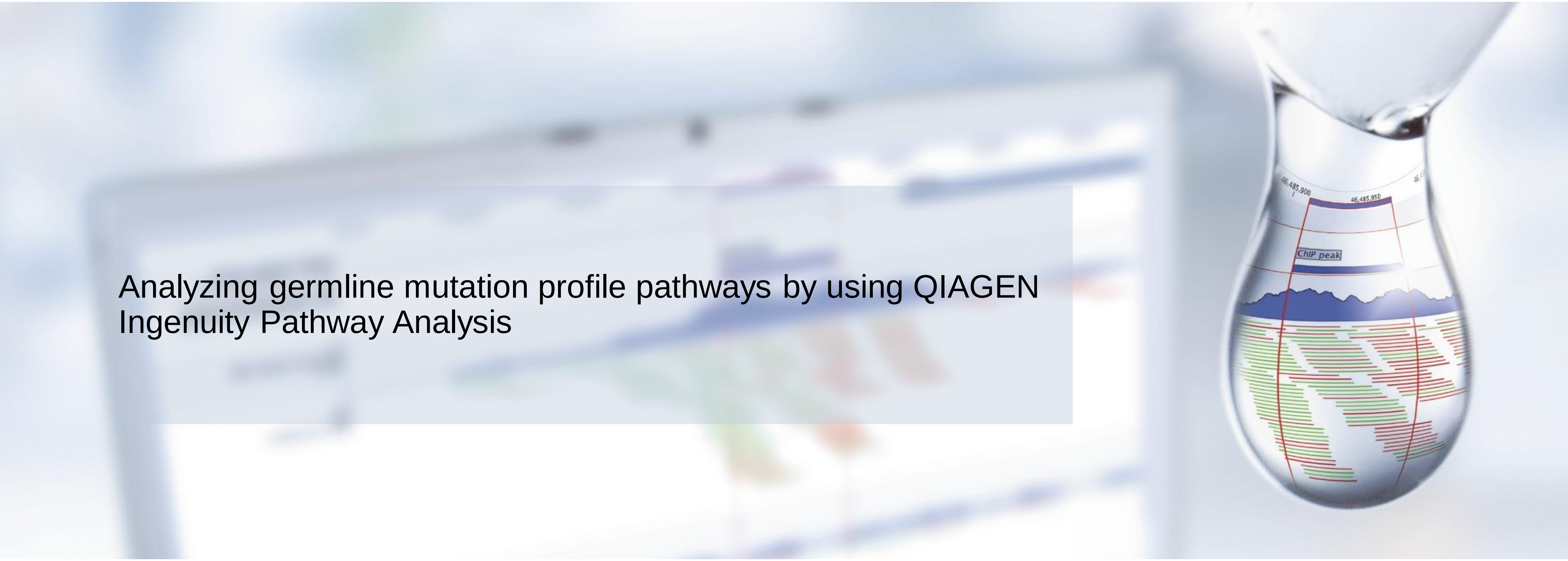


Analyzing germline mutation profile pathways by using QIAGEN Ingenuity Pathway Analysis

Cleo Hsi 席佩妤　業務專員

Christine Hsiung　熊嘉妮 專案主任　Bioinfo@GGA.ASIA

Agenda

- Introduction to QIAGEN Ingenuity Pathway Analysis
- Search in IPA
- Analyzing germline mutation using IPA
  - Data format
  - Data upload and analysis setup
  - Core analysis
- Querying IPA's Knowledge base
  - Custom network construction
  - Contextualization using public data
- Summary

IPA Training Account & Demo Data

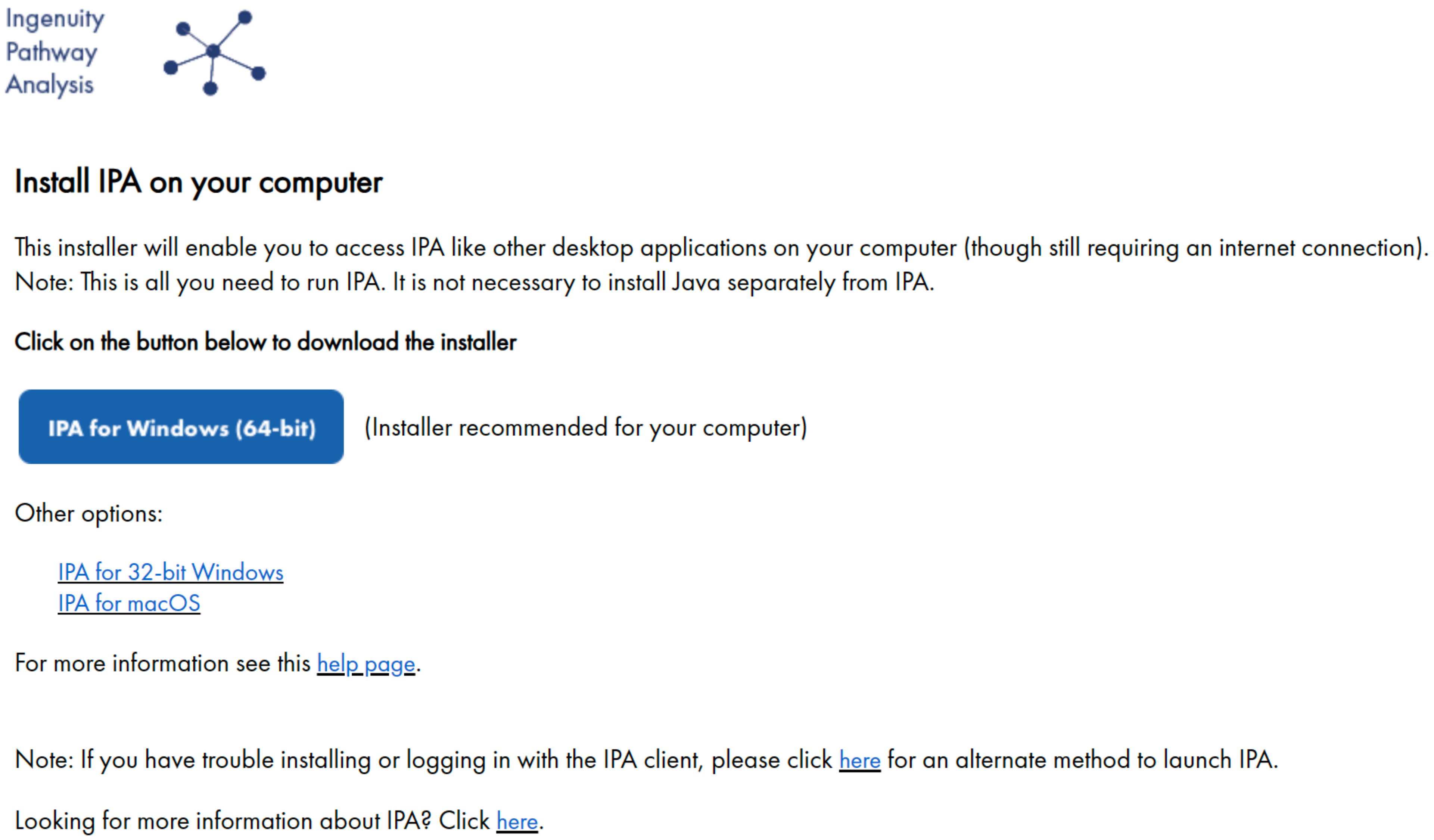
Account: XX@gate.sinica.edu.tw

(xx is your email account)

Password: **your password**

Download website: https://analysis.ingenuity.com/pa/installer/select

Choose your IPA installer



Install IPA on your computer

This installer will enable you to access IPA like other desktop applications on your computer (though still requiring an internet connection).
Note: This is all you need to run IPA. It is not necessary to install Java separately from IPA.

Click on the button below to download the installer

(Installer recommended for your computer)

Other options:

IPA for 32-bit Windows
IPA for macOS

For more information see this help page.

Note: If you have trouble installing or logging in with the IPA client, please click here for an alternate method to launch IPA.

Looking for more information about IPA? Click here.

System requirements

Operating systems

- Windows operating systems:
  - Windows 11, 10, 8
- Mac operating systems:
  - macOS Sonoma, Ventura, Monterey
- Internet browsers:
  - Firefox 91 or later*
  - Safari 16 or later*
  - Chrome 110 or later*
  - Microsoft Edge 94 or later*

*older internet browsers are still likely to work

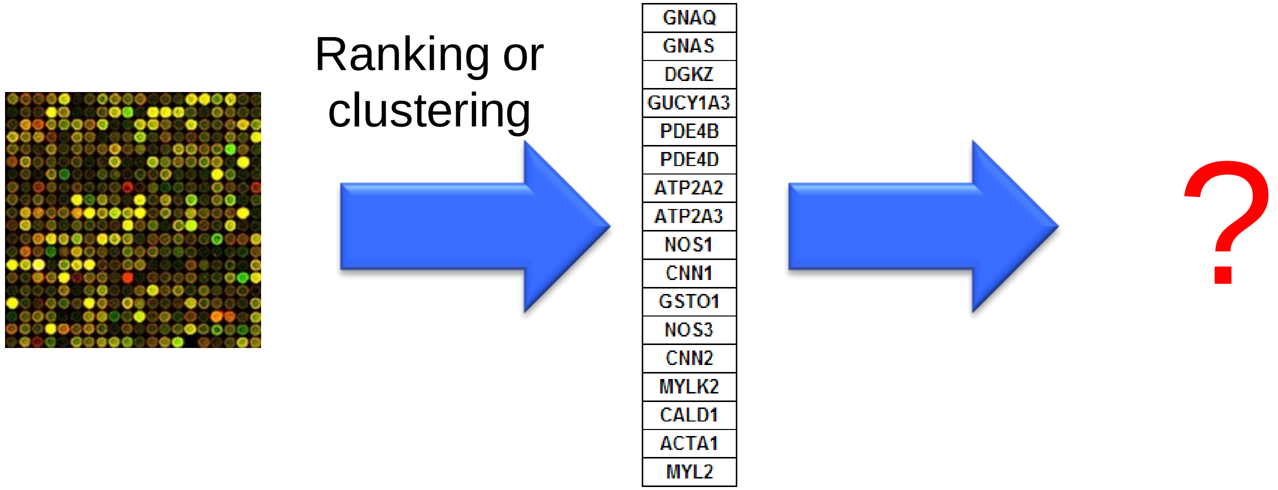
- Java runtime environment (JRE; not needed if you install the IPA client):
  - JRE 8 to 10

Hardware

- CoreTM i5 processor or equivalent running at 2 GHz or higher with 64-bit OS and Java
- Minimum at least 3 GB RAM free for Java

Interpreting gene lists

- Genome-Scale Analysis (Omics)
  - Genomics, Proteomics
- Tell me what's interesting about these genes



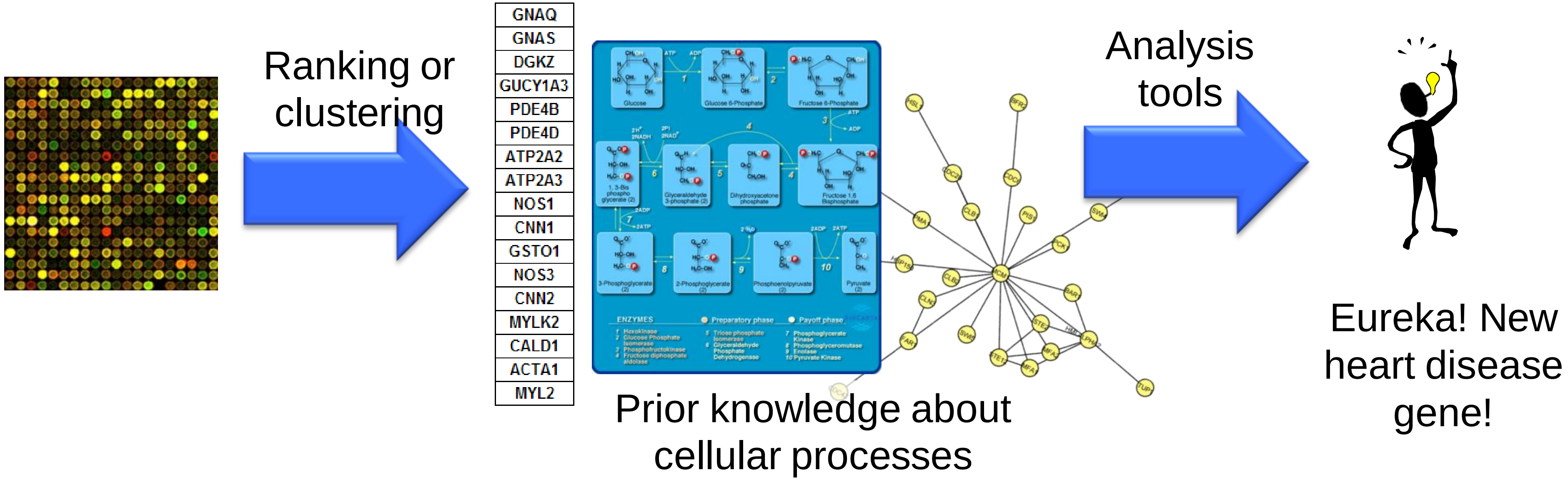
Ranking or clustering

GNAQ
GNAS
DGKZ
GUCY1A3
PDE4B
PDE4D
ATP2A2
ATP2A3
NOS1
CNN1
GSTO1
NOS3
CNN2
MYLK2
CALD1
ACTA1
MYL2

?

Interpreting gene lists

- Genome-Scale Analysis (Omics)
  - Genomics, Proteomics
- Tell me what's interesting about these genes
  - Are they enriched in known pathways, complexes, functions



Ranking or clustering

GNAQ
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GSTO1
NOS3
CNN2
MYLK2
CALD1
ACTA1
MYL2

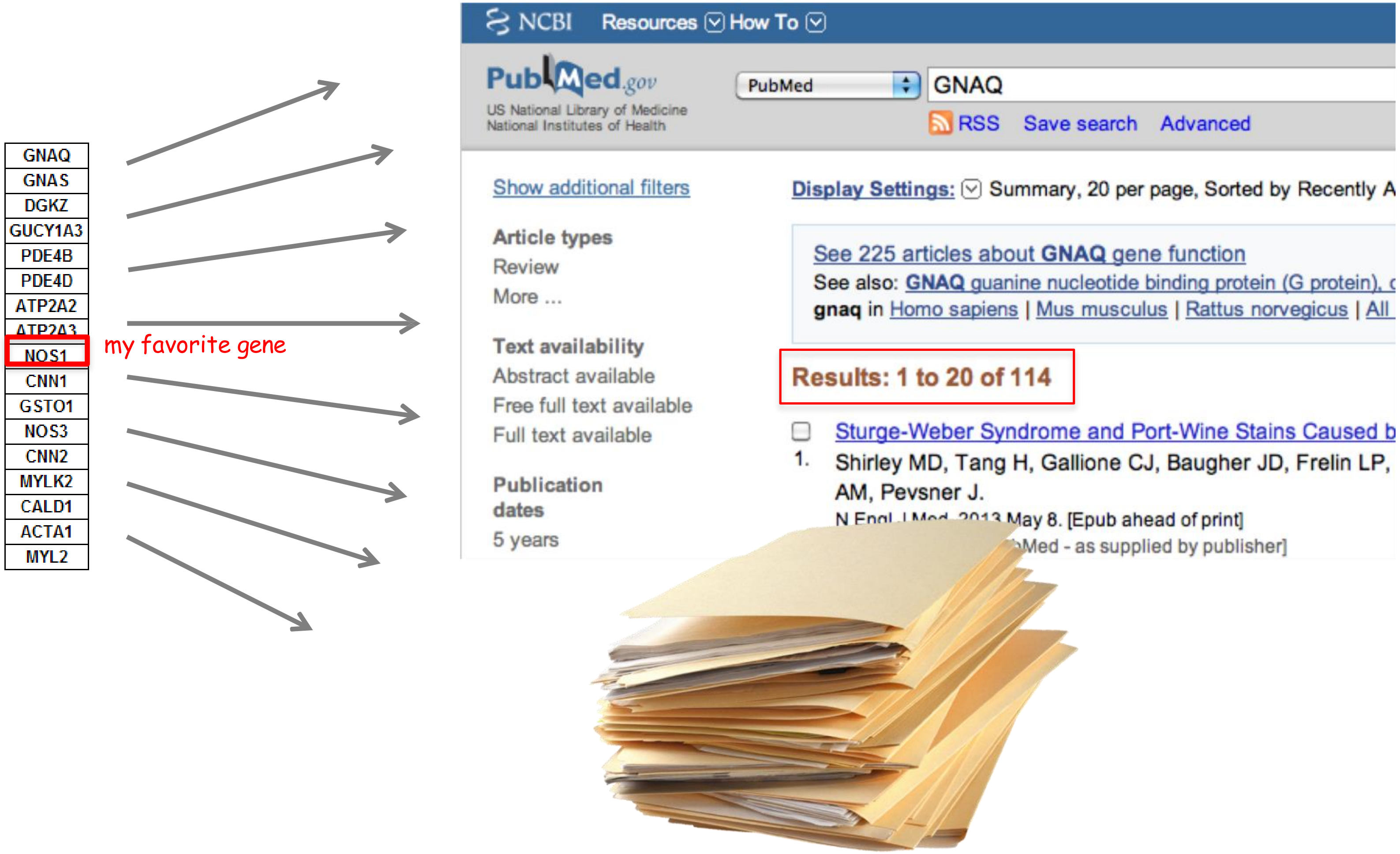
Analysis tools

Prior knowledge about cellular processes

Eureka! New heart disease gene!

Pathway and network analysis

- Save time compared to traditional approach



GNAQ
GNAS
DGKZ
GUCY1A3
PDE4B
PDE4D
ATP2A2
ATP2A3
NOS1
CNN1
GSTO1
NOS3
CNN2
MYLK2
CALD1
ACTA1
MYL2

my favorite gene

Show additional filters

Display Settings: Summary, 20 per page, Sorted by Recently A

Article types
Review
More ...

Text availability
Abstract available
Free full text available
Full text available

Publication dates
5 years

See 225 articles about GNAQ gene function

See also: GNAQ guanine nucleotide binding protein (G protein), c

gnaq in Homo sapiens | Mus musculus | Rattus norvegicus | All

Results: 1 to 20 of 114

☐ 1. Sturge-Weber Syndrome and Port-Wine Stains Caused b

Shirley MD, Tang H, Gallione CJ, Baugher JD, Frelin LP, AM, Pevsner J.

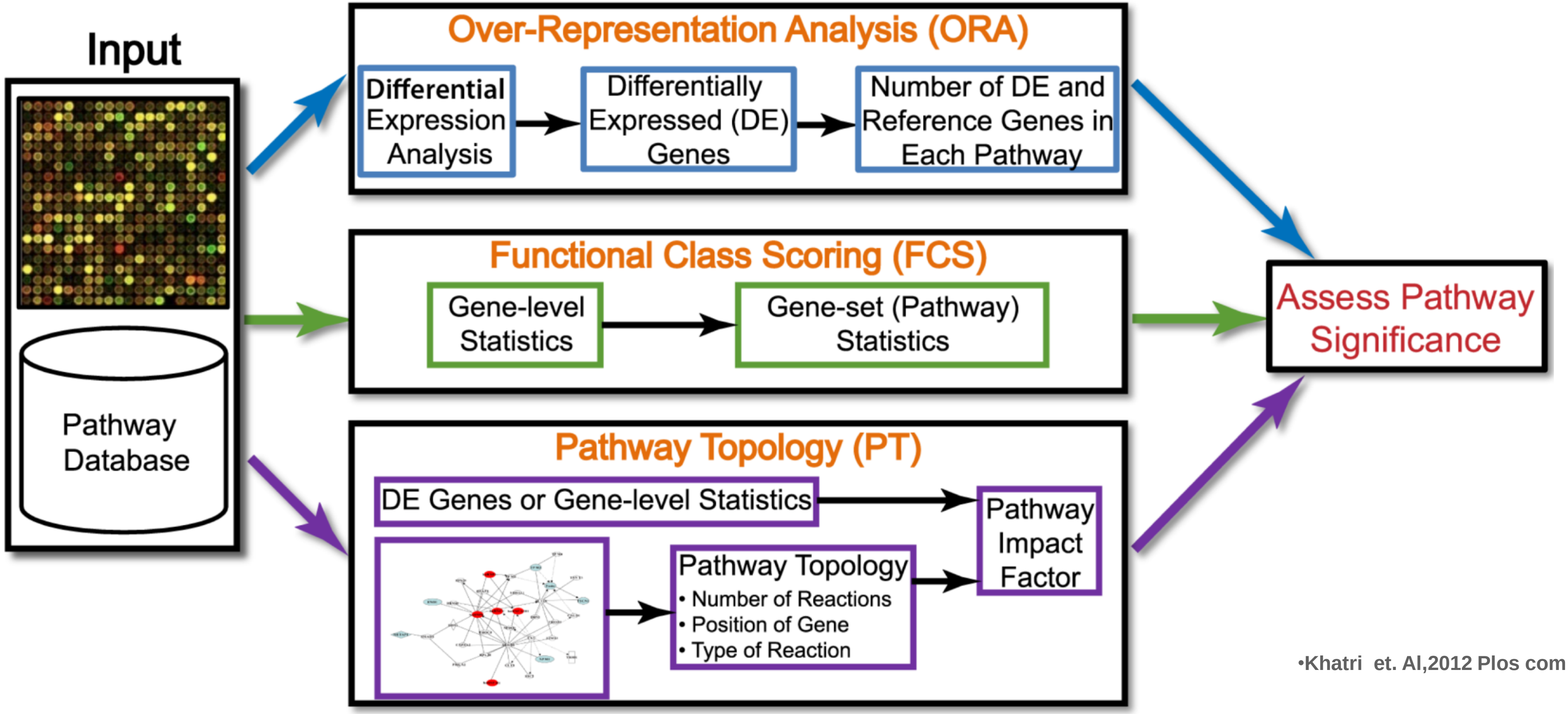
N Engl J Med. 2013 May 8. [Epub ahead of print]

bMed - as supplied by publisher]

Pathway and network analysis

- Helps gain mechanistic insight into ‘omics data
  - Identifying a master regulator, drug targets, characterizing pathways active in a sample
- Any type of analysis that involves pathway or network information
- Most commonly applied to help interpret lists of genes
- Most popular type is pathway enrichment analysis, but many others are useful

Functional Pathway Analysis



Input

Pathway Database

Over-Representation Analysis (ORA)

Differential Expression Analysis → Differentially Expressed (DE) Genes → Number of DE and Reference Genes in Each Pathway

Functional Class Scoring (FCS)

Gene-level Statistics → Gene-set (Pathway) Statistics

Pathway Topology (PT)

DE Genes or Gene-level Statistics → Pathway Impact Factor

Pathway Topology
- Number of Reactions
- Position of Gene
- Type of Reaction

→ Pathway Impact Factor

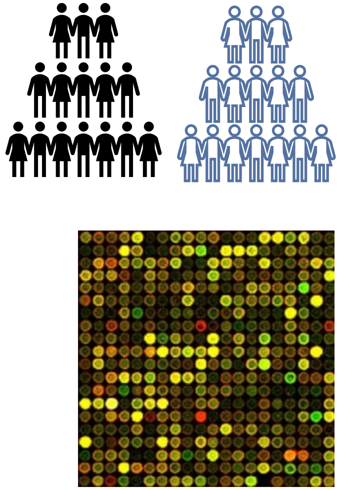
Assess Pathway Significance

•Khatri et. Al,2012 Plos computational biology

- The data generated by an experiment using a high-throughput technology (e.g., microarray, proteomics, metabolomics), along with functional annotations (pathway database) of the corresponding genome, are input to virtually all pathway analysis methods.
- ORA methods require that the input is a list of differentially expressed genes
- FCS methods use the entire data matrix as input
- PT-based methods additionally utilize the number and type of interactions between gene products, which may or may not be a part of a pathway database.
- The result of every pathway analysis method is a list of significant pathways in the condition under study.

Why are we using IPA?

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

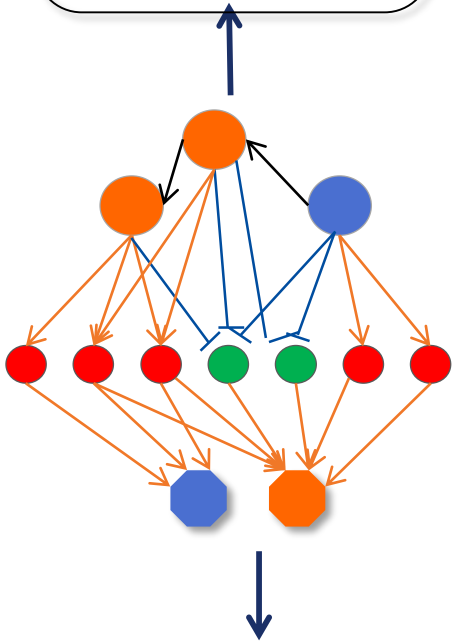
Function

Network

ORA/FCS/Topology Pathway Analysis

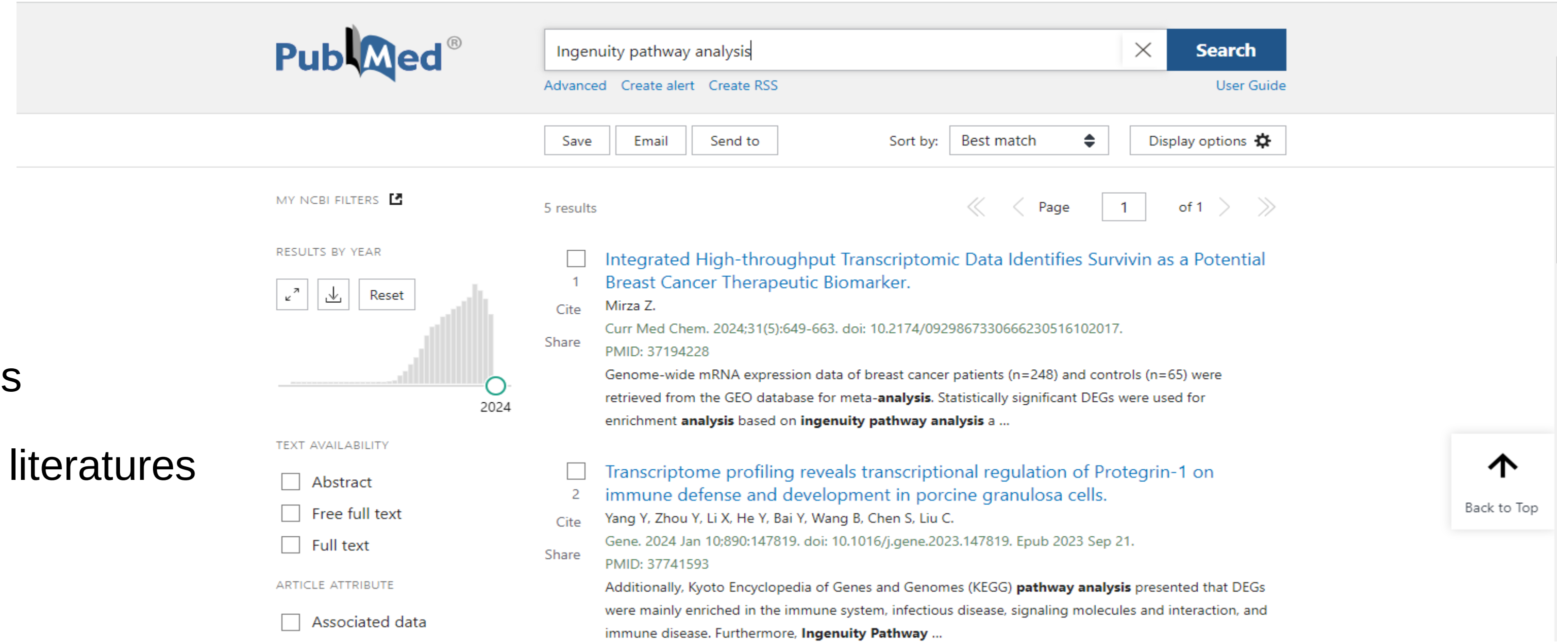
Machine learning

What do they relate to each other?



What are the relationship between each molecules?

Publication of IPA



☐ 1 Cite Share

Integrated High-throughput Transcriptomic Data Identifies Survivin as a Potential Breast Cancer Therapeutic Biomarker.

Mirza Z.

Curr Med Chem. 2024;31(5):649-663. doi: 10.2174/0929867330666230516102017.

PMID: 37194228

Genome-wide mRNA expression data of breast cancer patients (n=248) and controls (n=65) were retrieved from the GEO database for meta-**analysis**. Statistically significant DEGs were used for enrichment **analysis** based on **ingenuity pathway analysis** a ...

☐ 2 Cite Share

Transcriptome profiling reveals transcriptional regulation of Protegrin-1 on immune defense and development in porcine granulosa cells.

Yang Y, Zhou Y, Li X, He Y, Bai Y, Wang B, Chen S, Liu C.

Gene. 2024 Jan 10;890:147819. doi: 10.1016/j.gene.2023.147819. Epub 2023 Sep 21.

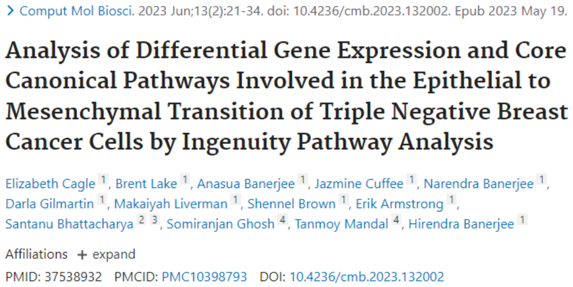
PMID: 37741593

Additionally, Kyoto Encyclopedia of Genes and Genomes (KEGG) **pathway analysis** presented that DEGs were mainly enriched in the immune system, infectious disease, signaling molecules and interaction, and immune disease. Furthermore, **Ingenuity Pathway** ...

4,153 results

In 2023, 303 literatures

Transcriptomics



› Comput Mol Biosci. 2023 Jun;13(2):21-34. doi: 10.4236/cmb.2023.132002. Epub 2023 May 19.

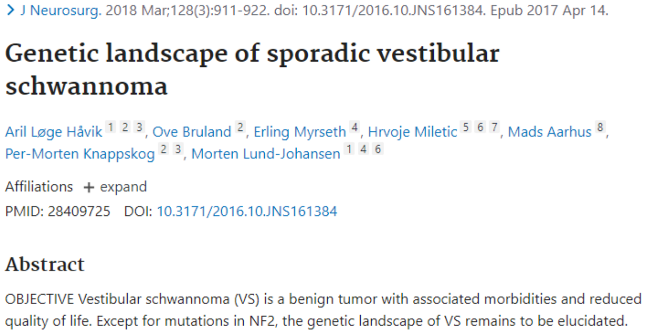
Analysis of Differential Gene Expression and Core Canonical Pathways Involved in the Epithelial to Mesenchymal Transition of Triple Negative Breast Cancer Cells by Ingenuity Pathway Analysis

Elizabeth Cagle[1], Brent Lake[1], Anasua Banerjee[1], Jazmine Cuffee[1], Narendra Banerjee[1], Darla Gilmartin[1], Makaiyah Liverman[1], Shennel Brown[1], Erik Armstrong[1], Santanu Bhattacharya[2] [3], Somiranjan Ghosh[4], Tanmoy Mandal[4], Hirendra Banerjee[1]

Affiliations + expand

PMID: 37538932 PMCID: PMC10398793 DOI: 10.4236/cmb.2023.132002

Genomics



› J Neurosurg. 2018 Mar;128(3):911-922. doi: 10.3171/2016.10.JNS161384. Epub 2017 Apr 14.

Genetic landscape of sporadic vestibular schwannoma

Aril Løge Håvik[1] [2] [3], Ove Bruland[2], Erling Myrseth[4], Hrvoje Miletic[5] [6] [7], Mads Aarhus[8], Per-Morten Knappskog[2] [3], Morten Lund-Johansen[1] [4] [6]

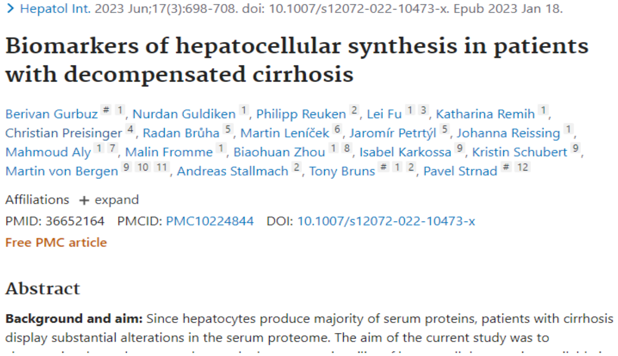
Affiliations + expand

PMID: 28409725 DOI: 10.3171/2016.10.JNS161384

Abstract

OBJECTIVE Vestibular schwannoma (VS) is a benign tumor with associated morbidities and reduced quality of life. Except for mutations in NF2, the genetic landscape of VS remains to be elucidated.

proteomics



› Hepatol Int. 2023 Jun;17(3):698-708. doi: 10.1007/s12072-022-10473-x. Epub 2023 Jan 18.

Biomarkers of hepatocellular synthesis in patients with decompensated cirrhosis

Berivan Gurbuz[#] [1], Nurdan Guldiken[1], Philipp Reuken[2], Lei Fu[1] [3], Katharina Remih[1], Christian Preisinger[4], Radan Brůha[5], Martin Leníček[6], Jaromír Petrtýl[5], Johanna Reissing[1], Mahmoud Aly[1] [7], Malin Fromme[1], Biaohuan Zhou[1] [8], Isabel Karkossa[9], Kristin Schubert[9], Martin von Bergen[9] [10] [11], Andreas Stallmach[2], Tony Bruns[#] [1] [2], Pavel Strnad[#] [12]

Affiliations + expand

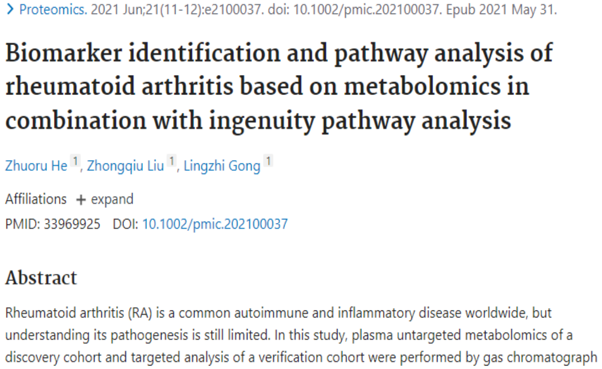
PMID: 36652164 PMCID: PMC10224844 DOI: 10.1007/s12072-022-10473-x

Free PMC article

Abstract

Background and aim: Since hepatocytes produce majority of serum proteins, patients with cirrhosis display substantial alterations in the serum proteome. The aim of the current study was to

metabolomics



› Proteomics. 2021 Jun;21(11-12):e2100037. doi: 10.1002/pmic.202100037. Epub 2021 May 31.

Biomarker identification and pathway analysis of rheumatoid arthritis based on metabolomics in combination with ingenuity pathway analysis

Zhuoru He[1], Zhongqiu Liu[1], Lingzhi Gong[1]

Affiliations + expand

PMID: 33969925 DOI: 10.1002/pmic.202100037

Abstract

Rheumatoid arthritis (RA) is a common autoimmune and inflammatory disease worldwide, but understanding its pathogenesis is still limited. In this study, plasma untargeted metabolomics of a discovery cohort and targeted analysis of a verification cohort were performed by gas chromatograph

Ingenuity Pathway Analysis is powered by QUAIGEN knowledge base

Ingenuity Literature Findings

Ingenuity Expert Findings – manually curated Findings from the full-text with contextual details from top journals

Ingenuity ExpertAssist Findings – automated text Findings that are manually reviewed from abstracts covering a broader range of publications – comprise a small percentage of IPA's findings

Ingenuity Modeled Knowledge

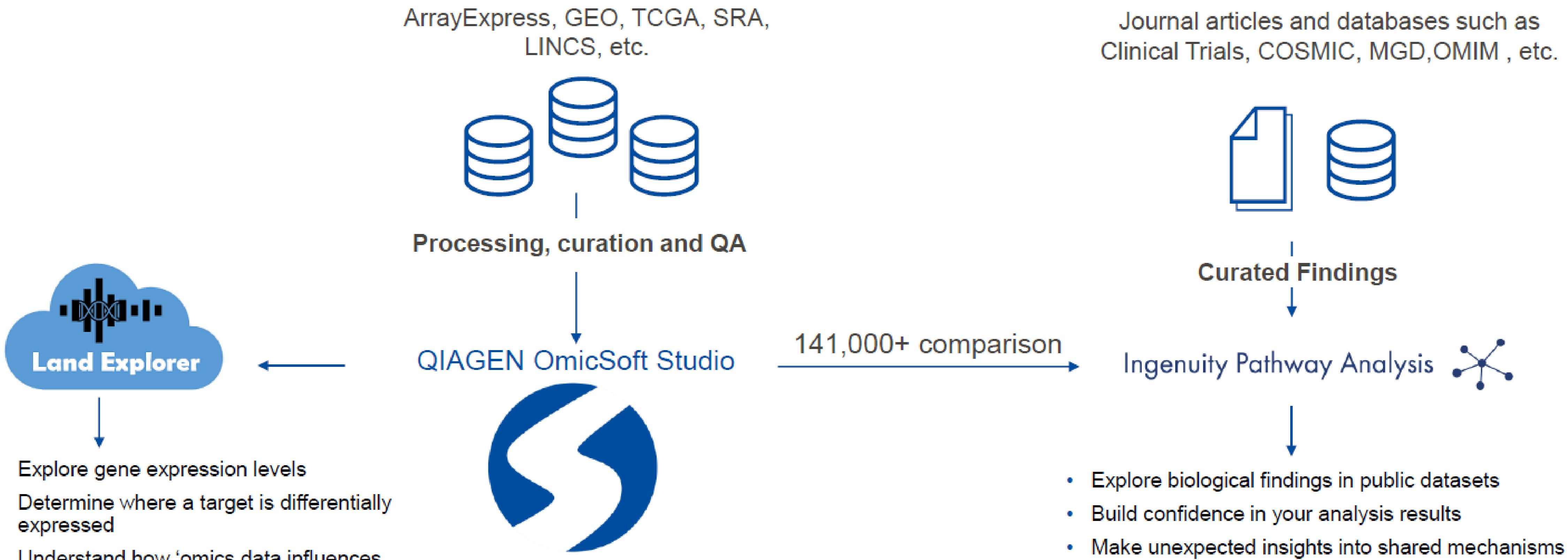
Ingenuity Expert Knowledge – content we model such as canonical pathways, toxicity lists, etc.

Ingenuity-Supported Third-Party Information – content areas include protein-protein, miRNA, biomarker, clinical trial information and others

Databases such as COSMIC, Clinical Trials, OMIM, TargetScan, BioGRID, MGD and HumanCyc

A massive, manually curated Knowledge Base updated weekly for the last ~20 years

QIAGEN IPA Analysis Match and Land Explorer



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

Processing, curation and QA

QIAGEN OmicSoft Studio

141,000+ comparison

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

Curated Findings

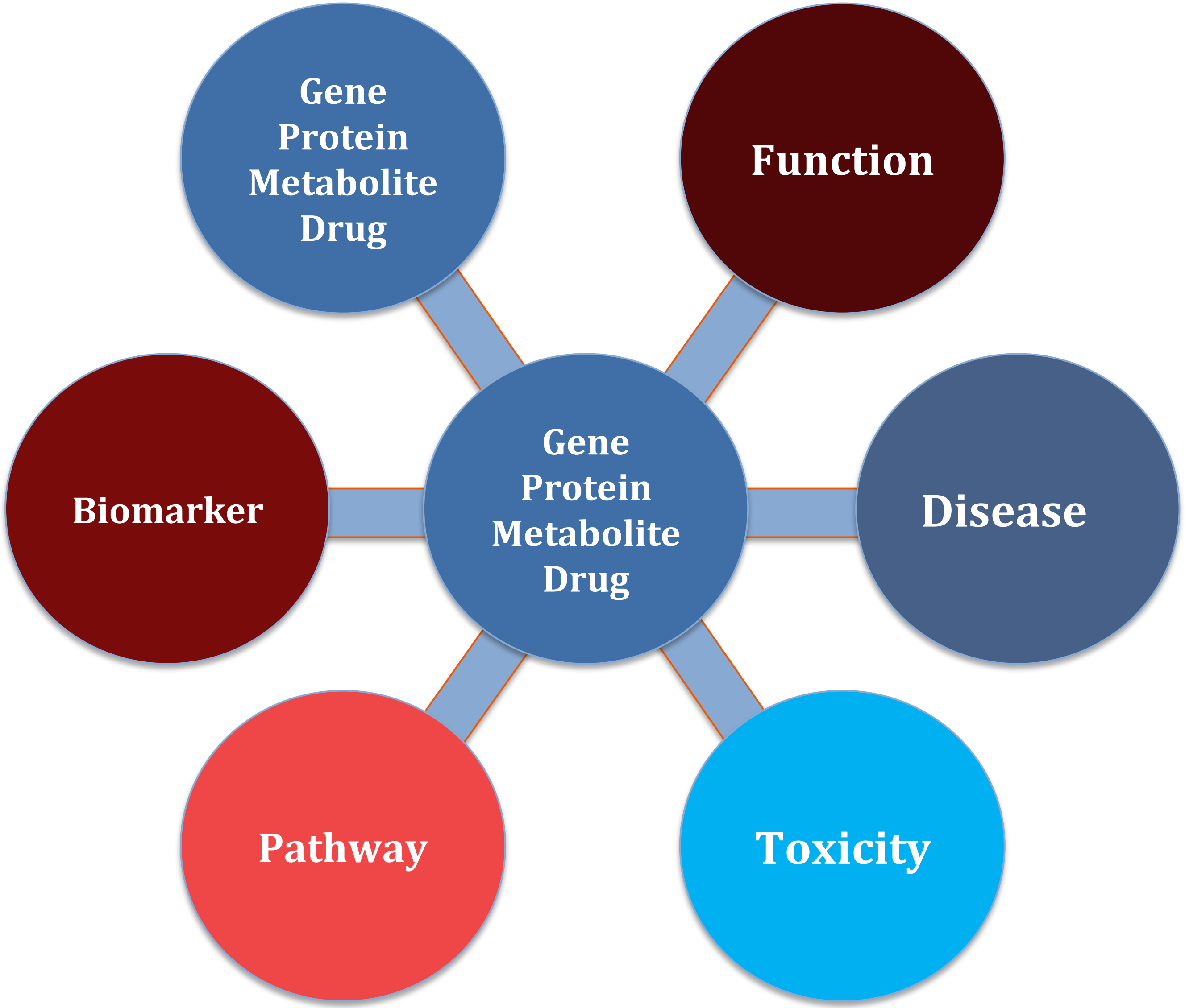
Ingenuity Pathway Analysis

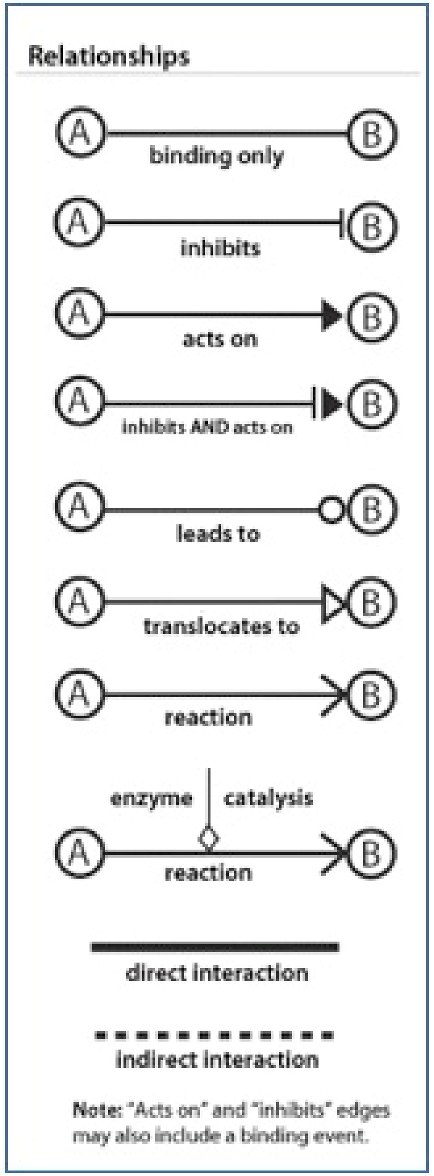
Land Explorer

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

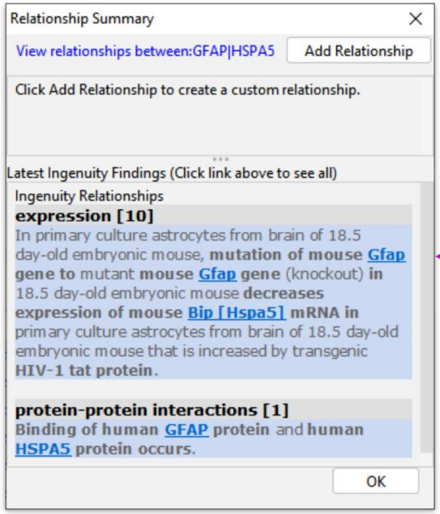
- Explore biological findings in public datasets
- Build confidence in your analysis results
- Make unexpected insights into shared mechanisms between studies
- “Anti-matches” may provide insights

Using IPA to Discover Relationships in Experimental Data





Every connection in IPA is backed by literature findings



View relationships between:GFAP|HSPA5

Click Add Relationship to create a custom relationship.

Latest Ingenuity Findings (Click link above to see all)

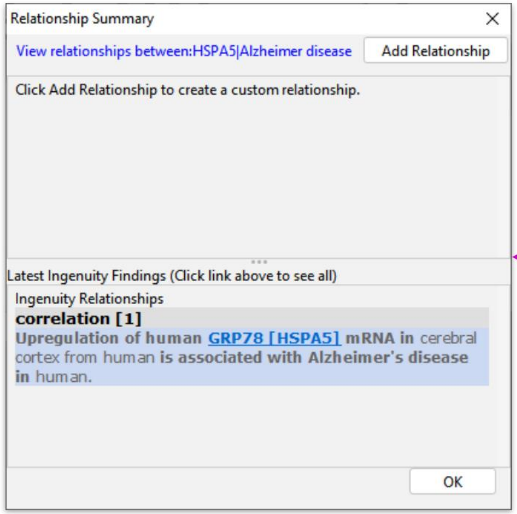
Ingenuity Relationships

expression [10]

In primary culture astrocytes from brain of 18.5 day-old embryonic mouse, **mutation of mouse** Gfap **gene to** mutant **mouse** Gfap **gene** (knockout) **in** 18.5 day-old embryonic mouse **decreases expression of mouse** Bip [Hspa5] **mRNA in** primary culture astrocytes from brain of 18.5 day-old embryonic mouse that is increased by transgenic **HIV-1 tat protein**.

protein-protein interactions [1]

Binding of human GFAP **protein** and **human** HSPA5 **protein occurs.**



View relationships between:HSPA5|Alzheimer disease

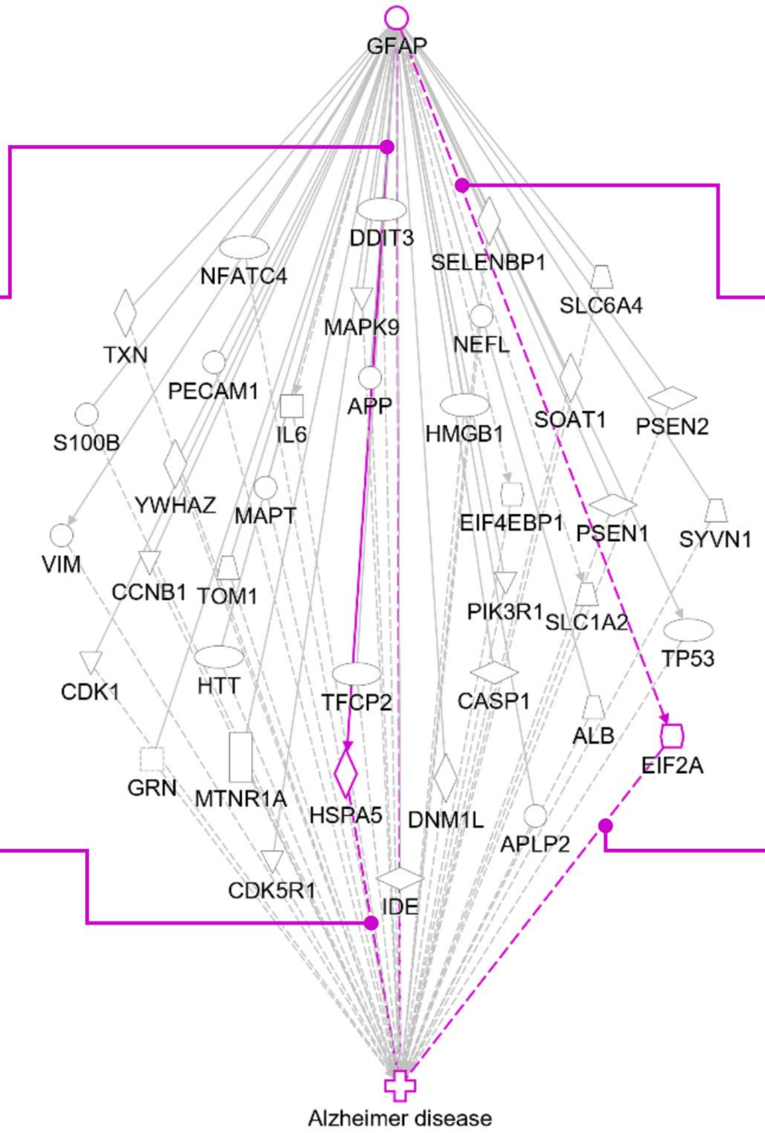
Click Add Relationship to create a custom relationship.

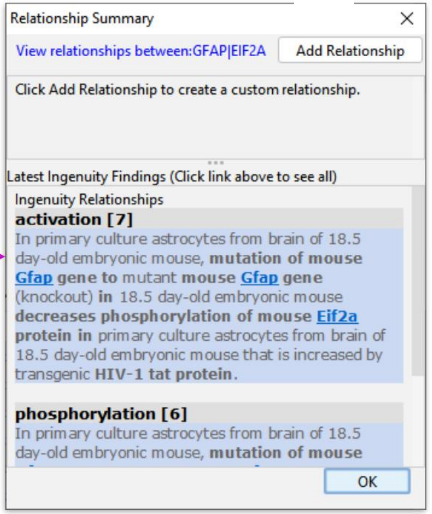
Latest Ingenuity Findings (Click link above to see all)

Ingenuity Relationships

correlation [1]

Upregulation of human GRP78 [HSPA5] **mRNA in** cerebral cortex from human **is associated with Alzheimer's disease in** human.





View relationships between:GFAP|EIF2A

Click Add Relationship to create a custom relationship.

Latest Ingenuity Findings (Click link above to see all)

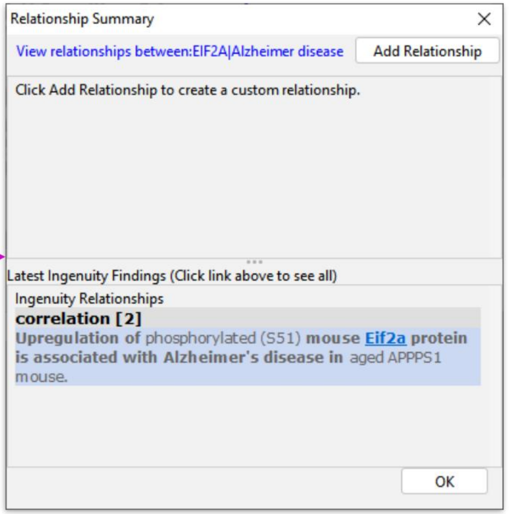
Ingenuity Relationships

activation [7]

In primary culture astrocytes from brain of 18.5 day-old embryonic mouse, **mutation of mouse** Gfap **gene to** mutant **mouse** Gfap **gene** (knockout) **in** 18.5 day-old embryonic mouse **decreases phosphorylation of mouse** Eif2a **protein in** primary culture astrocytes from brain of 18.5 day-old embryonic mouse that is increased by transgenic **HIV-1 tat protein**.

phosphorylation [6]

In primary culture astrocytes from brain of 18.5 day-old embryonic mouse, **mutation of mouse**



View relationships between:EIF2A|Alzheimer disease

Click Add Relationship to create a custom relationship.

Latest Ingenuity Findings (Click link above to see all)

Ingenuity Relationships

correlation [2]

Upregulation of phosphorylated (S51) **mouse** Eif2a **protein is associated with Alzheimer's disease in** aged APPPS1 mouse.

Species support within IPA

What species identifiers are accepted for analysis by IPA?

Fully supported:

Human

Mouse

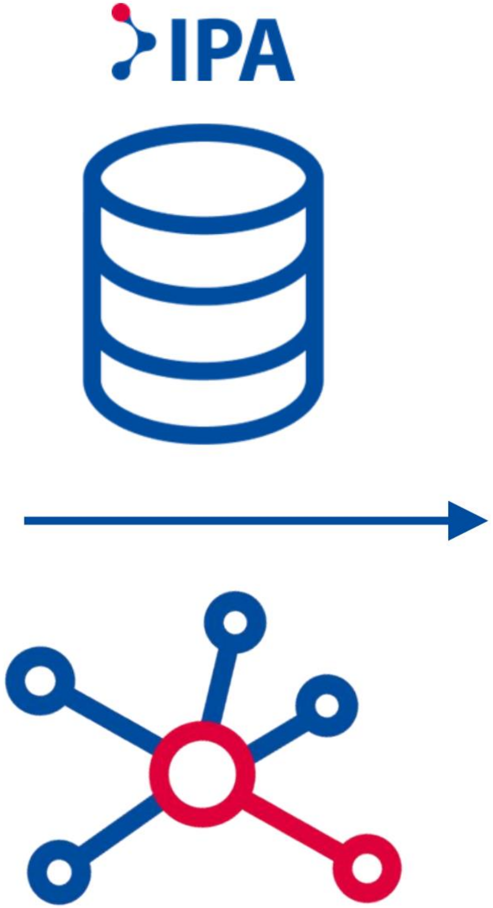
Rat

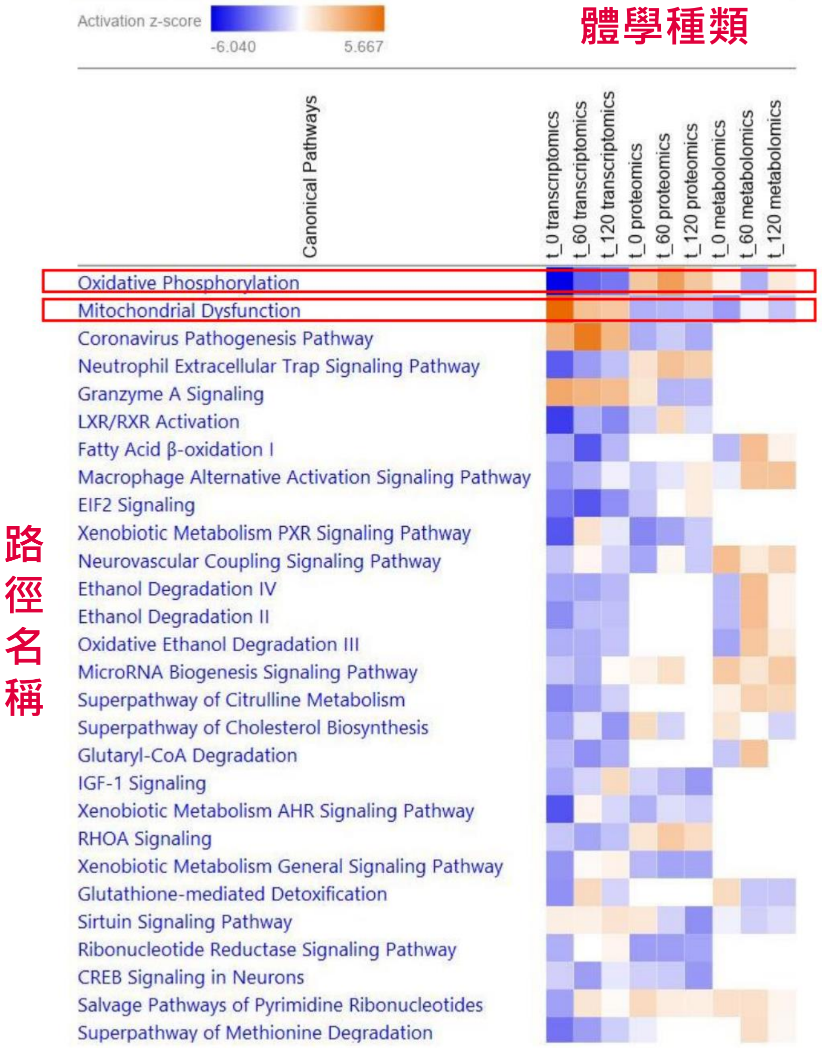
- ✓ Atlantic Salmon (*Salmo salar*)
- ✓ Thale cress (*Arabidopsis thaliana)*
- ✓ Bat (Greater horseshoe bat, *Rhinolophus ferrumequinum*)
- ✓ Brewer's yeast (*Saccharomyces cerevisiae)*
- ✓ Cat (domestic, *Felis catus*)
- ✓ Chicken (*Gallus gallus*)
- ✓ Chimpanzee (*Pan troglodytes*)
- ✓ Chinese hamster (*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*)

Multi-omics data analysis using QIAGEN IPA

Omics data type

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





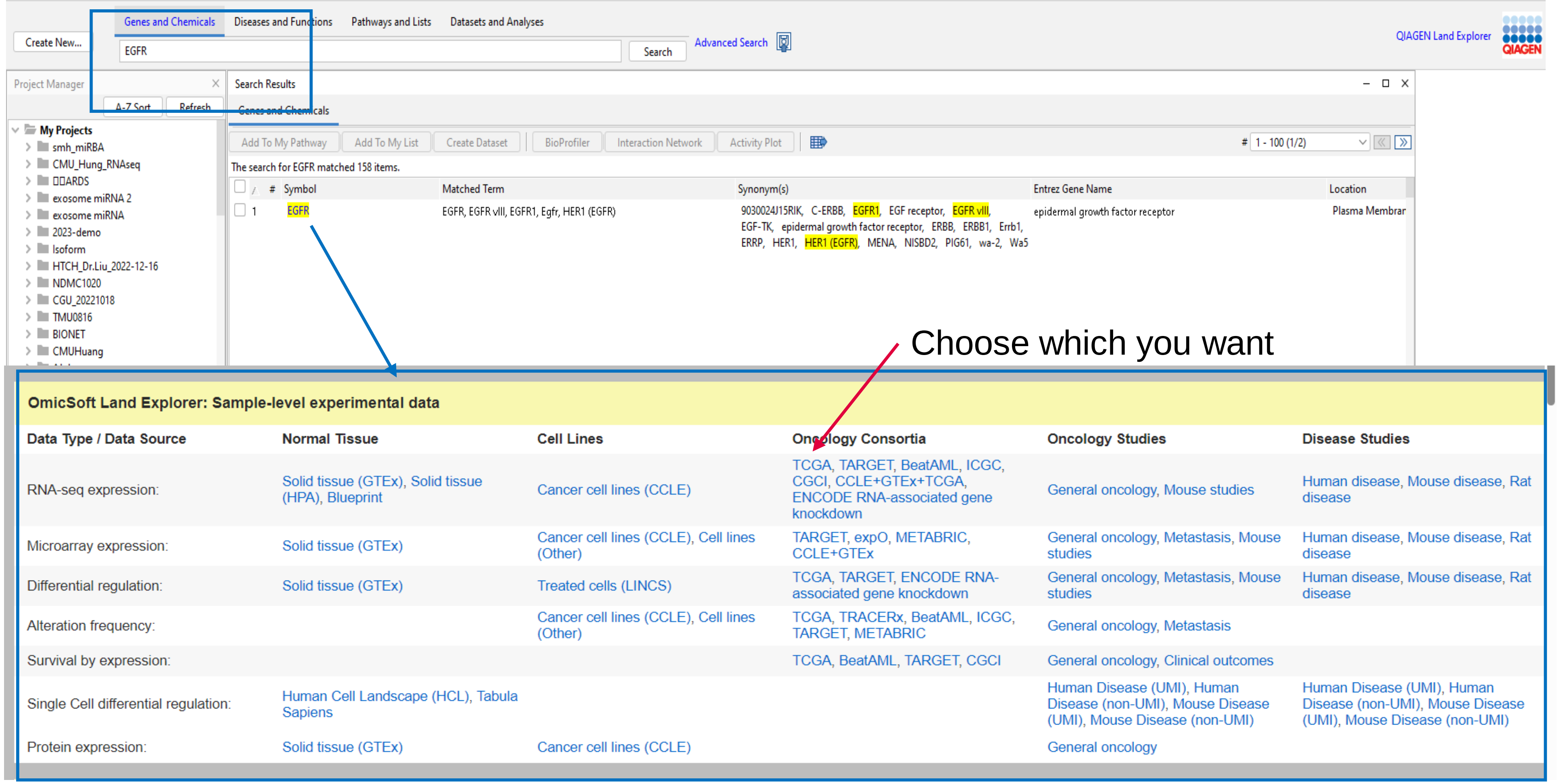
體學種類

路徑名稱

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	

IPA with OmicSoft Land Explorer



The search for EGFR matched 158 items.

☐	#	Symbol	Matched Term	Synonym(s)	Entrez Gene Name	Location
☐	1	EGFR	EGFR, EGFR vIII, EGFR1, Egfr, HER1 (EGFR)	9030024J15RIK, C-ERBB, EGFR1, EGF receptor, EGFR vIII, EGF-TK, epidermal growth factor receptor, ERBB, ERBB1, Errb1, ERRP, HER1, HER1 (EGFR), MENA, NISBD2, PIG61, wa-2, Wa5	epidermal growth factor receptor	Plasma Membrar

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

IPA with OmicSoft Land Explorer

- **TCGA-B38-G33**

Land selection

Search bar

View selection

View controller

Download data for current view

Metadata filtering

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

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

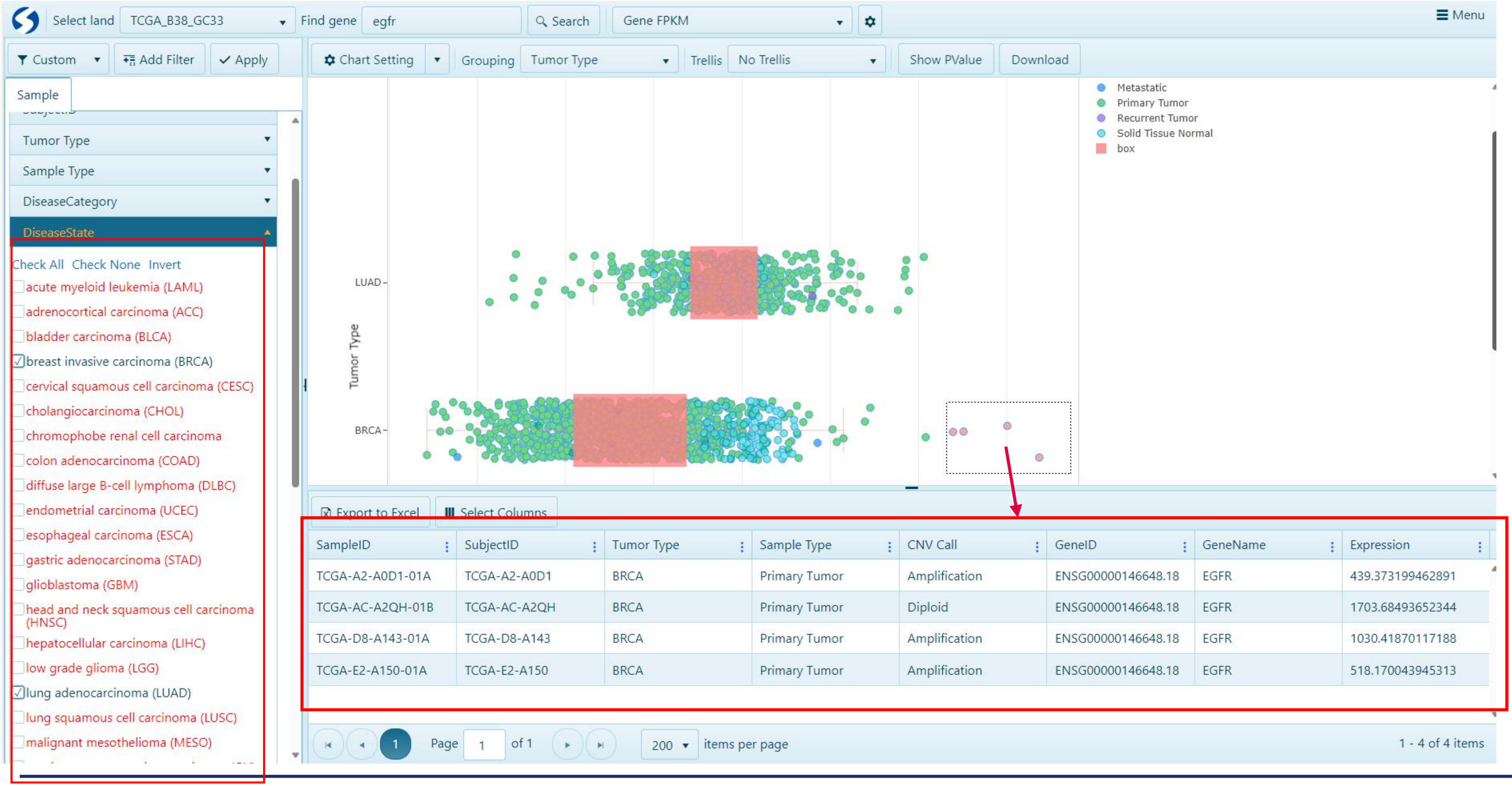
Tissue Category

Tissue

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.



Select land: TCGA_B38_GC33
Find gene: egfr
Gene FPKM
Grouping: Tumor Type
Trellis: No Trellis

DiseaseState:

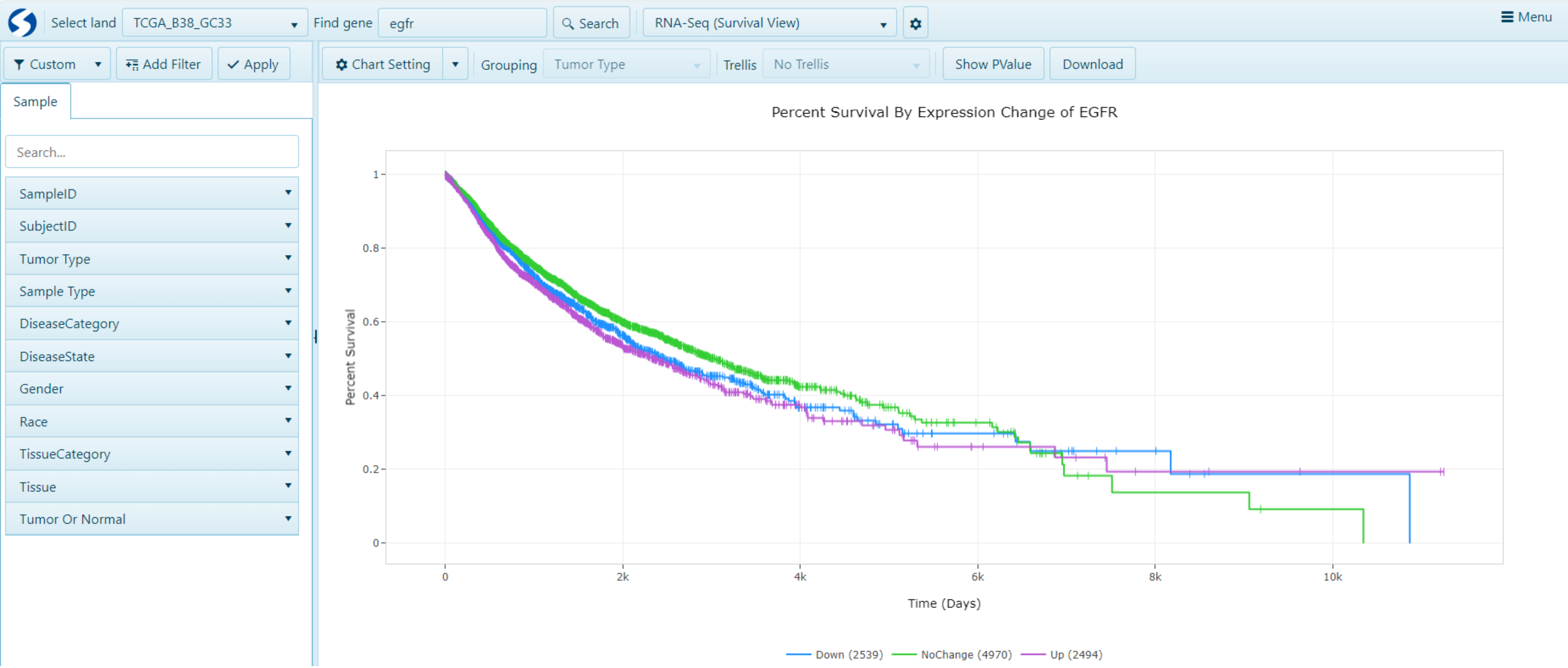
- ☐ acute myeloid leukemia (LAML)
- ☐ adrenocortical carcinoma (ACC)
- ☐ bladder carcinoma (BLCA)
- ☑ breast invasive carcinoma (BRCA)
- ☐ cervical squamous cell carcinoma (CESC)
- ☐ cholangiocarcinoma (CHOL)
- ☐ chromophobe renal cell carcinoma
- ☐ colon adenocarcinoma (COAD)
- ☐ diffuse large B-cell lymphoma (DLBC)
- ☐ endometrial carcinoma (UCEC)
- ☐ esophageal carcinoma (ESCA)
- ☐ gastric adenocarcinoma (STAD)
- ☐ glioblastoma (GBM)
- ☐ head and neck squamous cell carcinoma (HNSC)
- ☐ hepatocellular carcinoma (LIHC)
- ☐ low grade glioma (LGG)
- ☑ lung adenocarcinoma (LUAD)
- ☐ lung squamous cell carcinoma (LUSC)
- ☐ malignant mesothelioma (MESO)

SampleID	SubjectID	Tumor Type	Sample Type	CNV Call	GeneID	GeneName	Expression
TCGA-A2-A0D1-01A	TCGA-A2-A0D1	BRCA	Primary Tumor	Amplification	ENSG00000146648.18	EGFR	439.373199462891
TCGA-AC-A2QH-01B	TCGA-AC-A2QH	BRCA	Primary Tumor	Diploid	ENSG00000146648.18	EGFR	1703.68493652344
TCGA-D8-A143-01A	TCGA-D8-A143	BRCA	Primary Tumor	Amplification	ENSG00000146648.18	EGFR	1030.41870117188
TCGA-E2-A150-01A	TCGA-E2-A150	BRCA	Primary Tumor	Amplification	ENSG00000146648.18	EGFR	518.170043945313

Page 1 of 1
200 items per page
1 - 4 of 4 items

SURVIVAL ANALYSIS RESULT IN TCGA DATASET

TCGA_B38_GC33



Select land: TCGA_B38_GC33

Find gene: egfr

RNA-Seq (Survival View)

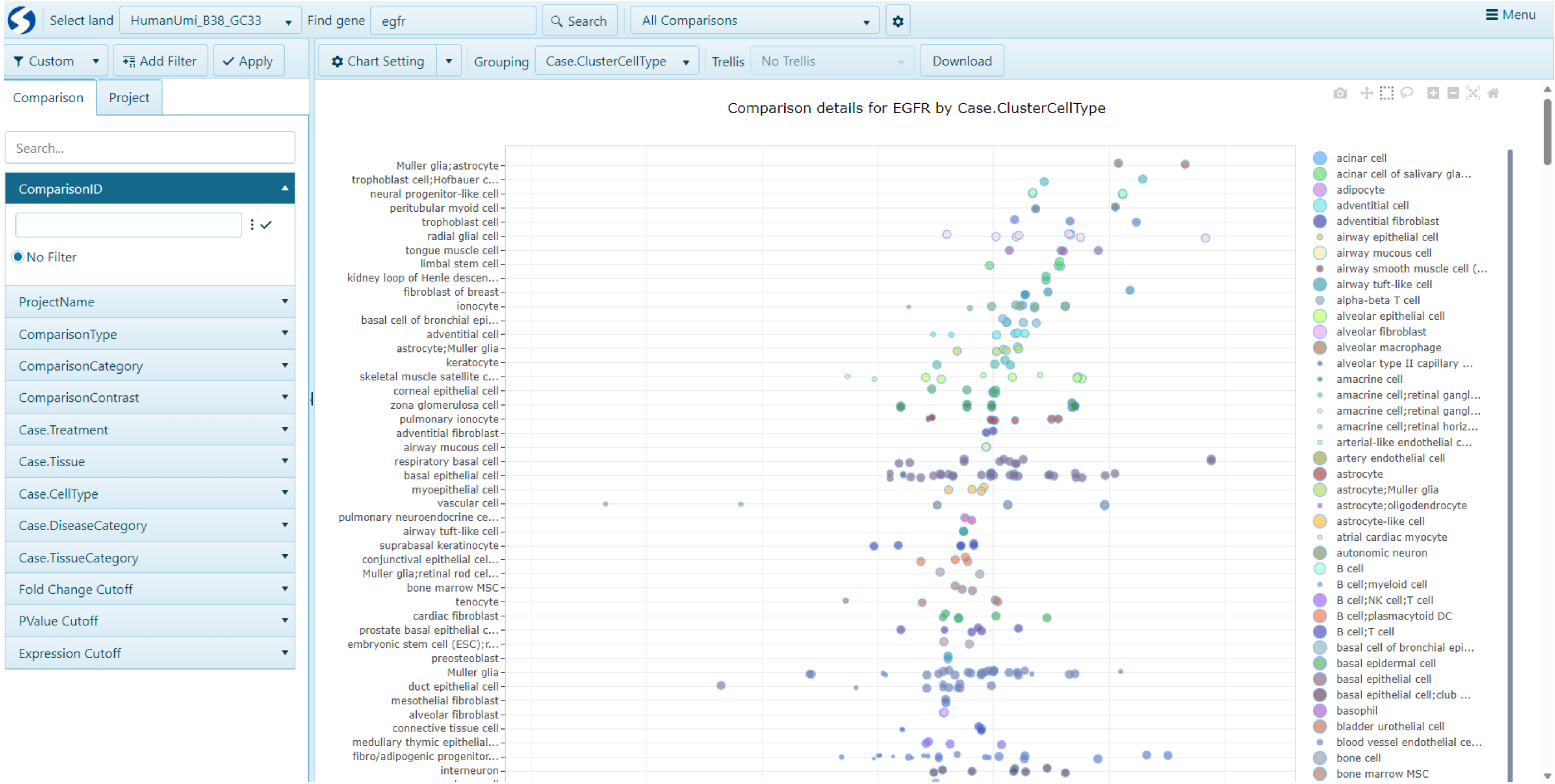
Grouping: Tumor Type

Trellis: No Trellis

Percent Survival By Expression Change of EGFR

Recent update: expression of a gene in single cell data

HumanUMI_B38_GC33



Select land: HumanUmi_B38_GC33

Find gene: egfr

All Comparisons

Grouping: Case.ClusterCellType

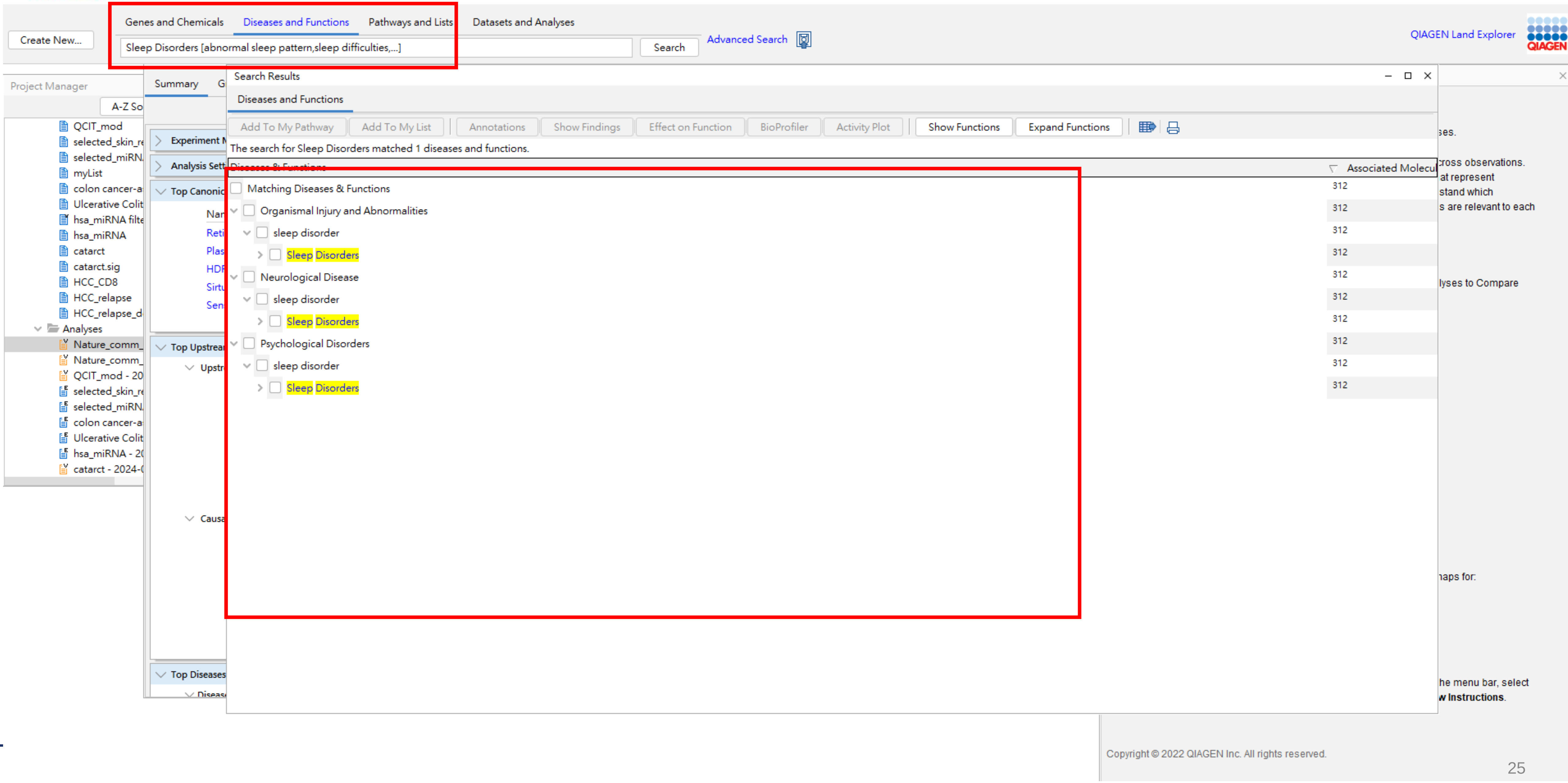
Trellis: No Trellis

● No Filter

Comparison details for EGFR by Case.ClusterCellType

We can choose the project, disease type

Diseases and Fuction

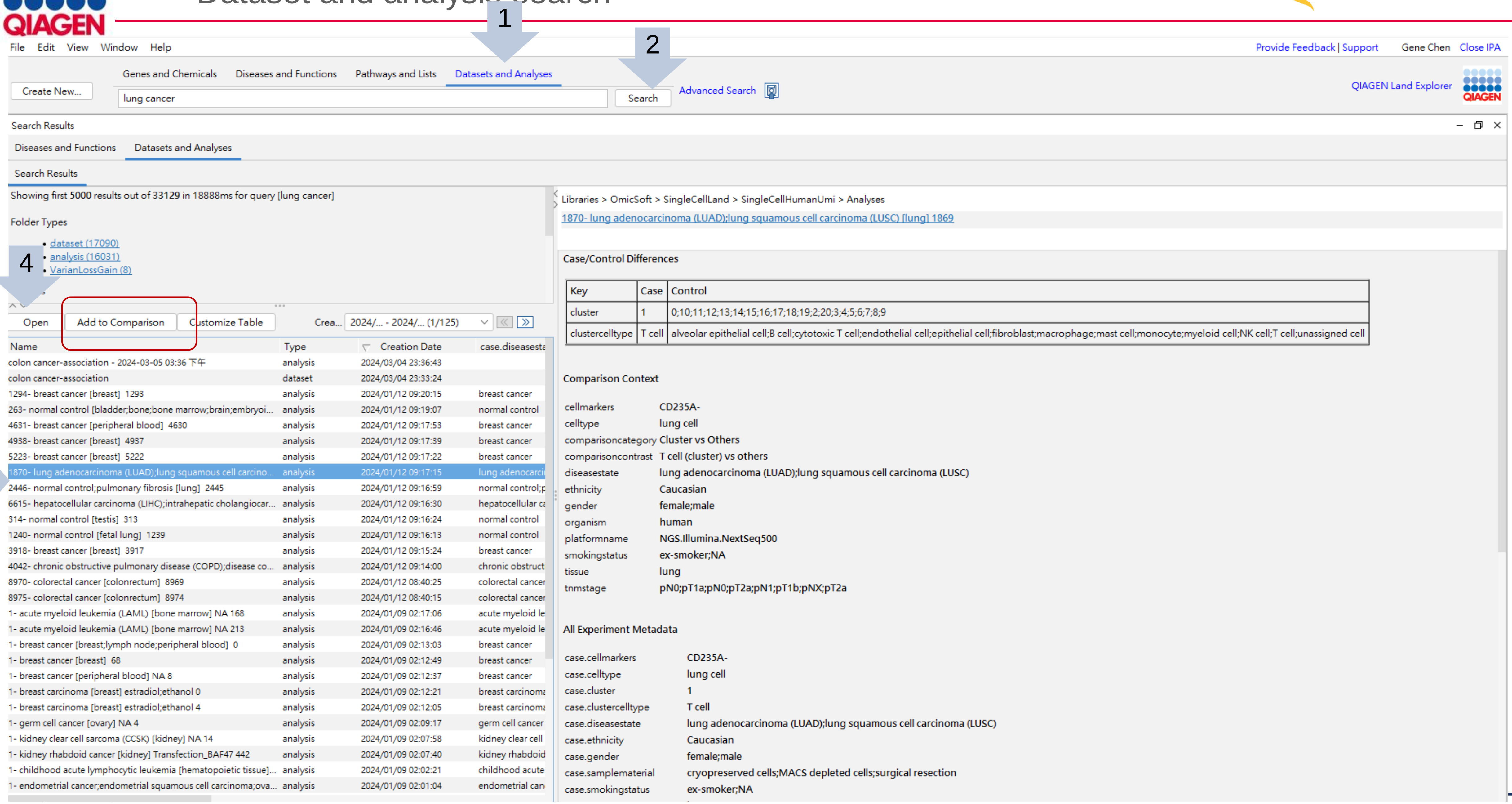


Sleep Disorders [abnormal sleep pattern,sleep difficulties,...]

The search for Sleep Disorders matched 1 diseases and functions.

Diseases & Functions	Associated Molecu
☐ Matching Diseases & Functions	312
☐ Organismal Injury and Abnormalities	312
☐ sleep disorder	312
☐ Sleep Disorders	312
☐ Neurological Disease	312
☐ sleep disorder	312
☐ Sleep Disorders	312
☐ Psychological Disorders	312
☐ sleep disorder	312
☐ Sleep Disorders	312

Dataset and analysis search



lung cancer

Showing first **5000** results out of **33129** in 18888ms for query [lung cancer]

Folder Types

- dataset (17090)
- analysis (16031)
- VarianLossGain (8)

Name	Type	Creation Date	case.diseasesta
colon cancer-association - 2024-03-05 03:36 下午	analysis	2024/03/04 23:36:43	
colon cancer-association	dataset	2024/03/04 23:33:24	
1294- breast cancer [breast] 1293	analysis	2024/01/12 09:20:15	breast cancer
263- normal control [bladder;bone;bone marrow;brain;embryoi...	analysis	2024/01/12 09:19:07	normal control
4631- breast cancer [peripheral blood] 4630	analysis	2024/01/12 09:17:53	breast cancer
4938- breast cancer [breast] 4937	analysis	2024/01/12 09:17:39	breast cancer
5223- breast cancer [breast] 5222	analysis	2024/01/12 09:17:22	breast cancer
1870- lung adenocarcinoma (LUAD);lung squamous cell carcino...	analysis	2024/01/12 09:17:15	lung adenocarci
2446- normal control;pulmonary fibrosis [lung] 2445	analysis	2024/01/12 09:16:59	normal control;p
6615- hepatocellular carcinoma (LIHC);intrahepatic cholangiocar...	analysis	2024/01/12 09:16:30	hepatocellular ca
314- normal control [testis] 313	analysis	2024/01/12 09:16:24	normal control
1240- normal control [fetal lung] 1239	analysis	2024/01/12 09:16:13	normal control
3918- breast cancer [breast] 3917	analysis	2024/01/12 09:15:24	breast cancer
4042- chronic obstructive pulmonary disease (COPD);disease co...	analysis	2024/01/12 09:14:00	chronic obstruct
8970- colorectal cancer [colonrectum] 8969	analysis	2024/01/12 08:40:25	colorectal cancer
8975- colorectal cancer [colonrectum] 8974	analysis	2024/01/12 08:40:15	colorectal cancer
1- acute myeloid leukemia (LAML) [bone marrow] NA 168	analysis	2024/01/09 02:17:06	acute myeloid le
1- acute myeloid leukemia (LAML) [bone marrow] NA 213	analysis	2024/01/09 02:16:46	acute myeloid le
1- breast cancer [breast;lymph node;peripheral blood] 0	analysis	2024/01/09 02:13:03	breast cancer
1- breast cancer [breast] 68	analysis	2024/01/09 02:12:49	breast cancer
1- breast cancer [peripheral blood] NA 8	analysis	2024/01/09 02:12:37	breast cancer
1- breast carcinoma [breast] estradiol;ethanol 0	analysis	2024/01/09 02:12:21	breast carcinoma
1- breast carcinoma [breast] estradiol;ethanol 4	analysis	2024/01/09 02:12:05	breast carcinoma
1- germ cell cancer [ovary] NA 4	analysis	2024/01/09 02:09:17	germ cell cancer
1- kidney clear cell sarcoma (CCSK) [kidney] NA 14	analysis	2024/01/09 02:07:58	kidney clear cell
1- kidney rhabdoid cancer [kidney] Transfection_BAF47 442	analysis	2024/01/09 02:07:40	kidney rhabdoid
1- childhood acute lymphocytic leukemia [hematopoietic tissue]...	analysis	2024/01/09 02:02:21	childhood acute
1- endometrial cancer;endometrial squamous cell carcinoma;ova...	analysis	2024/01/09 02:01:04	endometrial can

Libraries > OmicSoft > SingleCellLand > SingleCellHumanUmi > Analyses

1870- lung adenocarcinoma (LUAD);lung squamous cell carcinoma (LUSC) [lung] 1869

Case/Control Differences

Key	Case	Control
cluster	1	0;10;11;12;13;14;15;16;17;18;19;2;20;3;4;5;6;7;8;9
clustercelltype	T cell	alveolar epithelial cell;B cell;cytotoxic T cell;endothelial cell;epithelial cell;fibroblast;macrophage;mast cell;monocyte;myeloid cell;NK cell;T cell;unassigned cell

Comparison Context

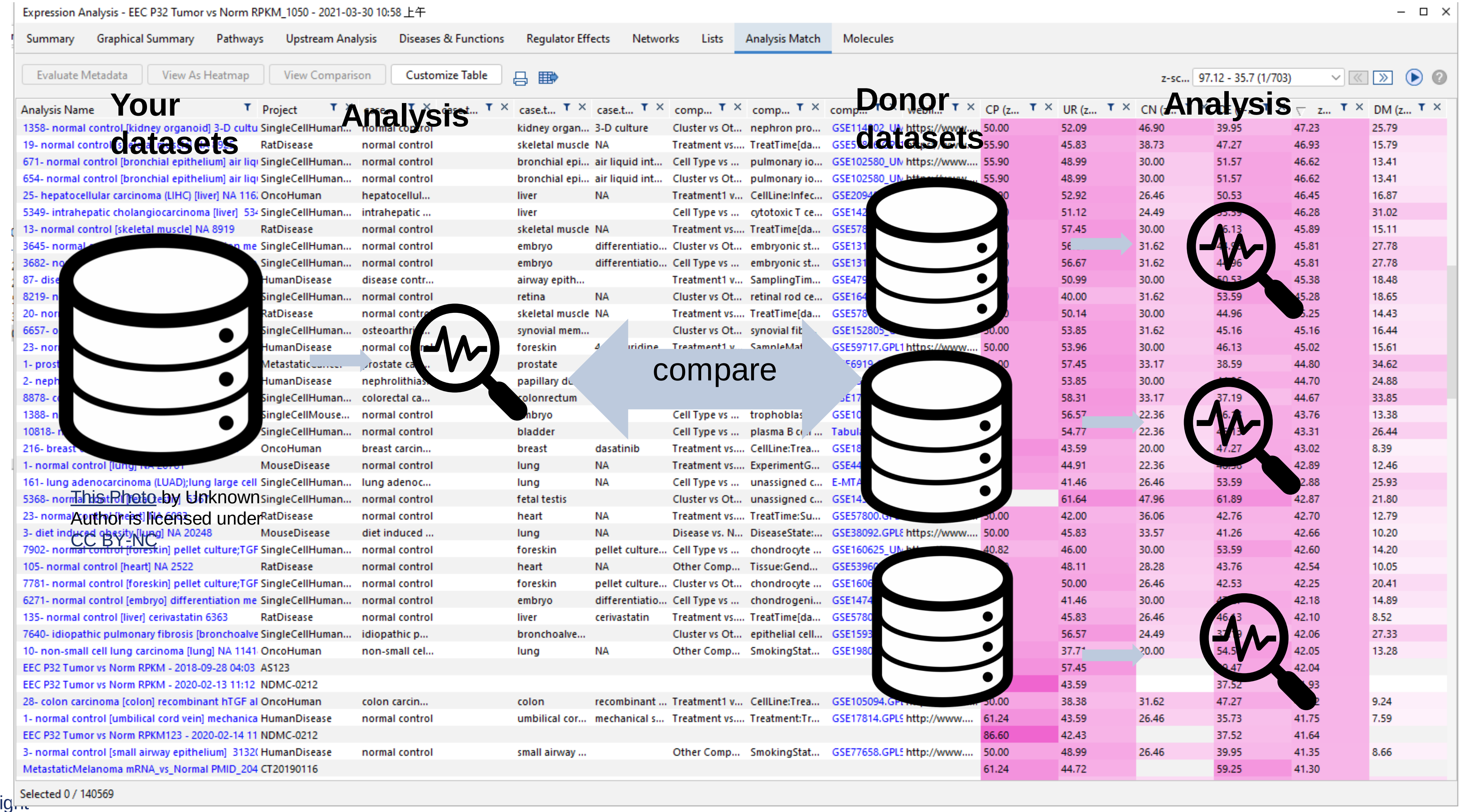
cellmarkers	CD235A-
celltype	lung cell
comparisoncategory	Cluster vs Others
comparisoncontrast	T cell (cluster) vs others
diseasestate	lung adenocarcinoma (LUAD);lung squamous cell carcinoma (LUSC)
ethnicity	Caucasian
gender	female;male
organism	human
platformname	NGS.Illumina.NextSeq500
smokingstatus	ex-smoker;NA
tissue	lung
tnmstage	pN0;pT1a;pN0;pT2a;pN1;pT1b;pNX;pT2a

All Experiment Metadata

case.cellmarkers	CD235A-
case.celltype	lung cell
case.cluster	1
case.clustercelltype	T cell
case.diseasestate	lung adenocarcinoma (LUAD);lung squamous cell carcinoma (LUSC)
case.ethnicity	Caucasian
case.gender	female;male
case.samplematerial	cryopreserved cells;MACS depleted cells;surgical resection
case.smokingstatus	ex-smoker;NA

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



Analysis Name	Project	case...	case.t...	case.t...	case.t...	comp...	comp...	comp...	webl...	CP (z...	UR (z...	CN (z...	[illegible]	z...	DM (z...
1358- normal control [kidney organoid] 3-D cultu	SingleCellHuman...	normal control		kidney organ...	3-D culture	Cluster vs Ot...	nephron pro...	GSE114802_UN	https://www....	50.00	52.09	46.90	39.95	47.23	25.79
19- normal control [illegible]	RatDisease	normal control		skeletal muscle	NA	Treatment vs....	TreatTime[da...	GSE5[illegible]	[illegible]	55.90	45.83	38.73	47.27	46.93	15.79
671- normal control [bronchial epithelium] air liqu	SingleCellHuman...	normal control		bronchial epi...	air liquid int...	Cell Type vs ...	pulmonary io...	GSE102580_UN	https://www....	55.90	48.99	30.00	51.57	46.62	13.41
654- normal control [bronchial epithelium] air liqu	SingleCellHuman...	normal control		bronchial epi...	air liquid int...	Cluster vs Ot...	pulmonary io...	GSE102580_UN	https://www....	55.90	48.99	30.00	51.57	46.62	13.41
25- hepatocellular carcinoma (LIHC) [liver] NA 116	OncoHuman	hepatocellul...		liver	NA	Treatment1 v...	CellLine:Infec...	GSE2094[illegible]	[illegible]	[illegible]	52.92	26.46	50.53	46.45	16.87
5349- intrahepatic cholangiocarcinoma [liver] 534	SingleCellHuman...	intrahepatic ...		liver		Cell Type vs ...	cytotoxic T ce...	GSE142[illegible]	[illegible]	[illegible]	51.12	24.49	[illegible]	46.28	31.02
13- normal control [skeletal muscle] NA 8919	RatDisease	normal control		skeletal muscle	NA	Treatment vs....	TreatTime[da...	GSE578[illegible]	[illegible]	[illegible]	57.45	30.00	[illegible]	45.89	15.11
3645- normal [illegible] me	SingleCellHuman...	normal control		embryo	differentiatio...	Cluster vs Ot...	embryonic st...	GSE131[illegible]	[illegible]	[illegible]	[illegible]	31.62	[illegible]	45.81	27.78
3682- no[illegible]	SingleCellHuman...	normal control		embryo	differentiatio...	Cell Type vs ...	embryonic st...	GSE131[illegible]	[illegible]	[illegible]	56.67	31.62	[illegible]	45.81	27.78
87- dise[illegible]	HumanDisease	disease contr...		airway epith...		Treatment1 v...	SamplingTim...	GSE479[illegible]	[illegible]	[illegible]	50.99	30.00	[illegible]	45.38	18.48
8219- n[illegible]	SingleCellHuman...	normal control		retina	NA	Cluster vs Ot...	retinal rod ce...	GSE164[illegible]	[illegible]	[illegible]	40.00	31.62	53.59	45.28	18.65
20- nor[illegible]	RatDisease	normal contr[illegible]		skeletal muscle	NA	Treatment vs....	TreatTime[da...	GSE578[illegible]	[illegible]	[illegible]	50.14	30.00	44.96	[illegible]	14.43
6657- o[illegible]	SingleCellHuman...	osteoarthri[illegible]		synovial mem...		Cluster vs Ot...	synovial fib[illegible]	GSE152805_[illegible]	[illegible]	[illegible]	53.85	31.62	45.16	45.16	16.44
23- nor[illegible]	HumanDisease	normal co[illegible]		foreskin	4[illegible]uridine	Treatment1 v...	SampleMat[illegible]	GSE59717.GPL1	https://www....	50.00	53.96	30.00	46.13	45.02	15.61
1- prost[illegible]	Metastatic[illegible]	prostate ca[illegible]		prostate	[illegible]	[illegible]	[illegible]	[illegible]6919[illegible]	[illegible]	[illegible]	57.45	33.17	38.59	44.80	34.62
2- neph[illegible]	HumanDisease	nephrolithias[illegible]		papillary d[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	53.85	30.00	[illegible]	44.70	24.88
8878- c[illegible]	SingleCellHuman...	colorectal ca...		colonrectum	[illegible]	[illegible]	[illegible]	[illegible]E17	[illegible]	[illegible]	58.31	33.17	37.19	44.67	33.85
1388- n[illegible]	SingleCellMouse...	normal control		[illegible]mbryo	[illegible]	Cell Type vs ...	trophoblas[illegible]	GSE10[illegible]	[illegible]	[illegible]	56.57	22.36	[illegible]	43.76	13.38
10818- [illegible]	SingleCellHuman...	normal control		bladder	[illegible]	Cell Type vs ...	plasma B c[illegible]	Tabula[illegible]	[illegible]	[illegible]	54.77	22.36	[illegible]	43.31	26.44
216- breast [illegible]	OncoHuman	breast carcin...		breast	dasatinib	Treatment vs....	CellLine:Trea...	GSE18[illegible]	[illegible]	[illegible]	43.59	20.00	47.27	43.02	8.39
1- normal control [lung] [illegible]	MouseDisease	normal control		lung	NA	Treatment vs....	ExperimentG...	GSE44[illegible]	[illegible]	[illegible]	44.91	22.36	[illegible]	42.89	12.46
161- lung adenocarcinoma (LUAD);lung large cell	SingleCellHuman...	lung adenoc...		lung	NA	Cell Type vs ...	unassigned c...	E-MTA[illegible]	[illegible]	[illegible]	41.46	26.46	53.59	[illegible]2.88	25.93
5368- normal control [fetal testis] [illegible]	SingleCellHuman...	normal control		fetal testis		Cluster vs Ot...	unassigned c...	GSE14[illegible]	[illegible]		61.64	47.96	61.89	42.87	21.80
23- normal control [heart] [illegible]	RatDisease	normal control		heart	NA	Treatment vs....	TreatTime:Su...	GSE57800.G[illegible]	[illegible]	[illegible]0.00	42.00	36.06	42.76	42.70	12.79
3- diet induced obesity [lung] NA 20248	MouseDisease	diet induced ...		lung	NA	Disease vs. N...	DiseaseState:...	GSE38092.GPL	https://www....	50.00	45.83	33.57	41.26	42.66	10.20
7902- normal control [foreskin] pellet culture;TGF	SingleCellHuman...	normal control		foreskin	pellet culture...	Cell Type vs ...	chondrocyte ...	GSE160625_UN	[illegible]	40.82	46.00	30.00	53.59	42.60	14.20
105- normal control [heart] NA 2522	RatDisease	normal control		heart	NA	Other Comp...	Tissue:Gend...	GSE5396[illegible]	[illegible]	[illegible]	48.11	28.28	43.76	42.54	10.05
7781- normal control [foreskin] pellet culture;TGF	SingleCellHuman...	normal control		foreskin	pellet culture...	Cluster vs Ot...	chondrocyte ...	GSE1606[illegible]	[illegible]	[illegible]	50.00	26.46	42.53	42.25	20.41
6271- normal control [embryo] differentiation me	SingleCellHuman...	normal control		embryo	differentiatio...	Cell Type vs ...	chondrogeni...	GSE1474[illegible]	[illegible]	[illegible]	41.46	30.00	[illegible]	42.18	14.89
135- normal control [liver] cerivastatin 6363	RatDisease	normal control		liver	cerivastatin	Treatment vs....	TreatTime[da...	GSE5780[illegible]	[illegible]	[illegible]	45.83	26.46	[illegible]	42.10	8.52
7640- idiopathic pulmonary fibrosis [bronchoalve	SingleCellHuman...	idiopathic p...		bronchoalve...		Cluster vs Ot...	epithelial cell...	GSE1593[illegible]	[illegible]	[illegible]	56.57	24.49	[illegible]	42.06	27.33
10- non-small cell lung carcinoma [lung] NA 1141	OncoHuman	non-small cel...		lung	NA	Other Comp...	SmokingStat...	GSE1980[illegible]	[illegible]	[illegible]	37.7[illegible]	[illegible]	[illegible]	42.05	13.28
EEC P32 Tumor vs Norm RPKM - 2018-09-28 04:03	AS123									[illegible]	57.45		[illegible]	42.04	
EEC P32 Tumor vs Norm RPKM - 2020-02-13 11:12	NDMC-0212									[illegible]	43.59		37.52	[illegible]	
28- colon carcinoma [colon] recombinant hTGF al	OncoHuman	colon carcin...		colon	recombinant ...	Treatment1 v...	CellLine:Trea...	GSE105094.GP[illegible]	[illegible]	[illegible]0.00	38.38	31.62	47.27	[illegible]	9.24
1- normal control [umbilical cord vein] mechanica	HumanDisease	normal control		umbilical cor...	mechanical s...	Treatment vs....	Treatment:Tr...	GSE17814.GPL	http://www....	61.24	43.59	26.46	35.73	41.75	7.59
EEC P32 Tumor vs Norm RPKM123 - 2020-02-14 11	NDMC-0212									86.60	42.43		37.52	41.64	
3- normal control [small airway epithelium] 3132(	HumanDisease	normal control		small airway ...		Other Comp...	SmokingStat...	GSE77658.GPL	http://www....	50.00	48.99	26.46	39.95	41.35	8.66
MetastaticMelanoma mRNA_vs_Normal PMID_204	CT20190116									61.24	44.72		59.25	41.30	

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Analysis Match

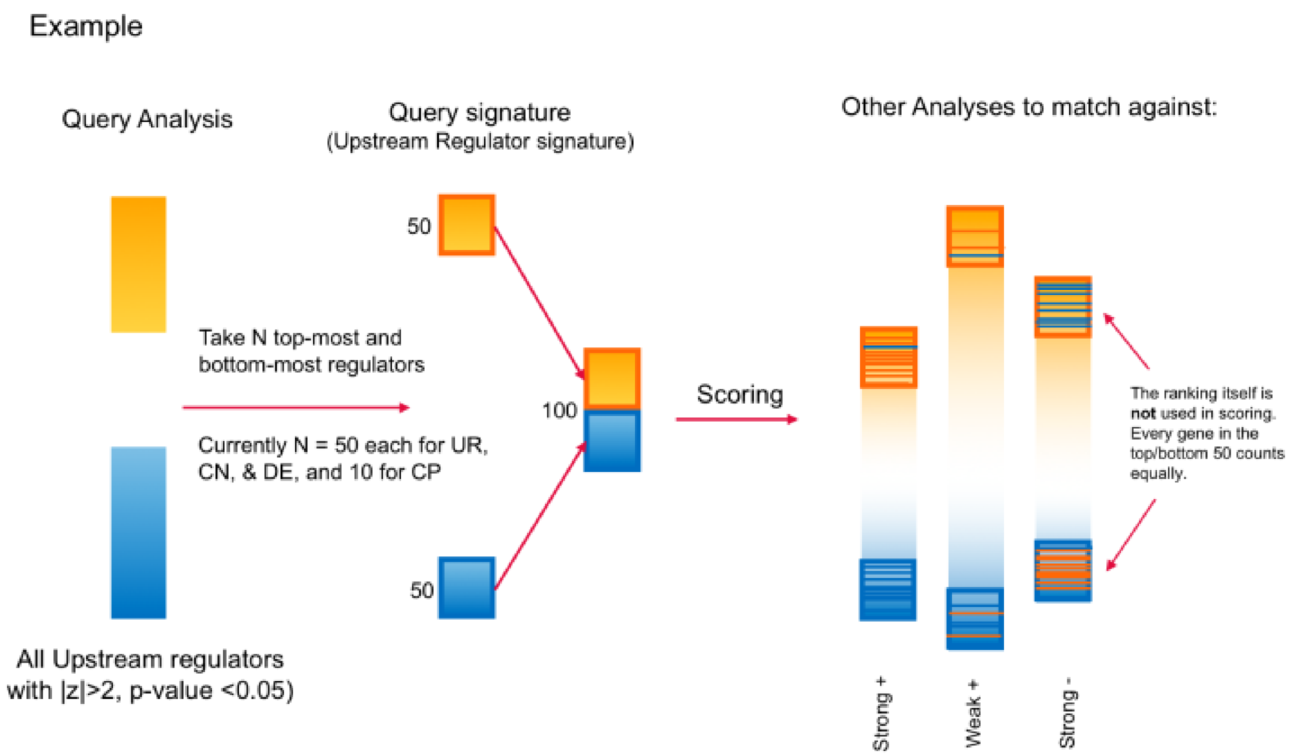
How signatures are created and compared

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

Query Analysis

Query signature
(Upstream Regulator signature)

Other Analyses to match against:

Take N top-most and bottom-most regulators

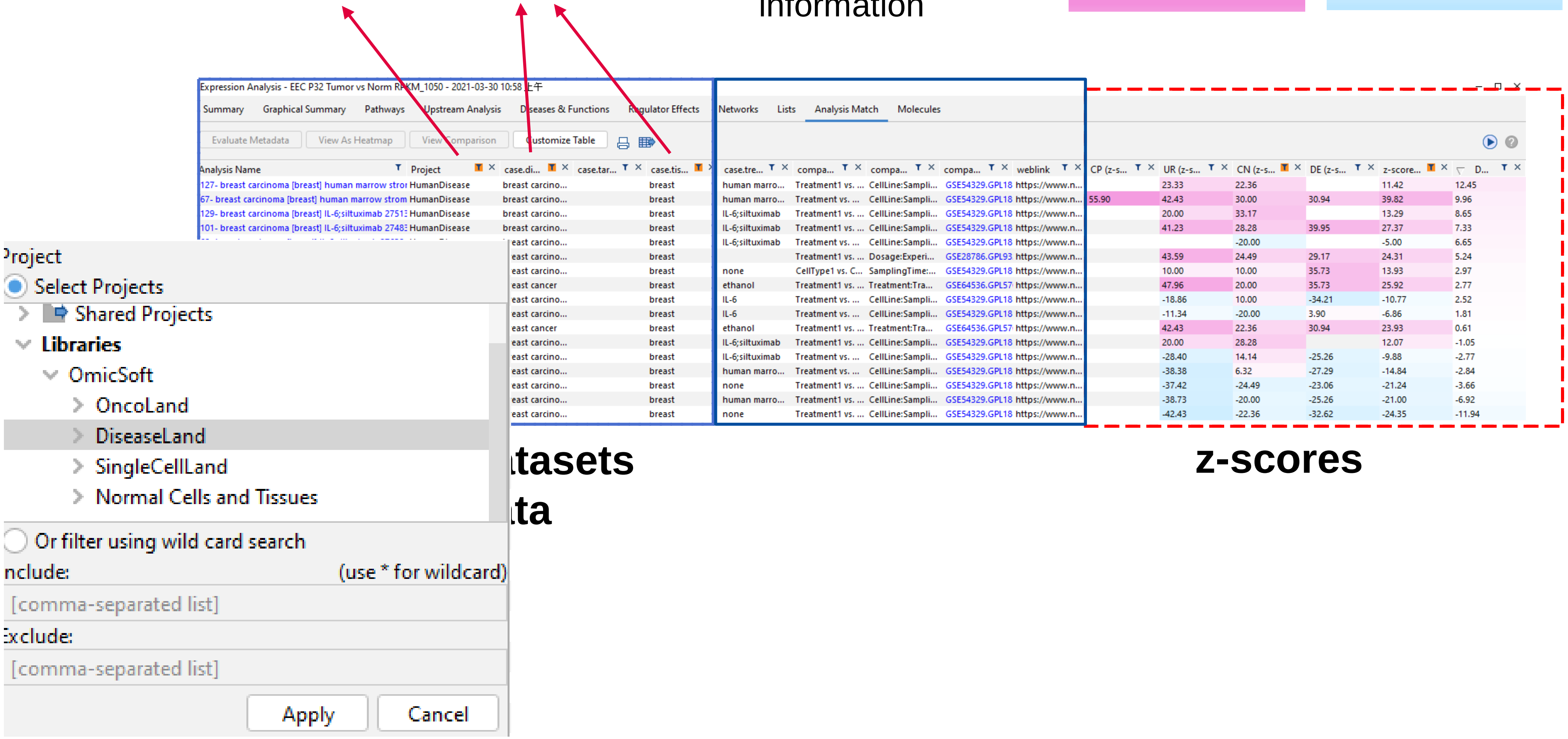
Currently N = 50 each for UR, CN, & DE, and 10 for CP

All Upstream regulators with |z|>2, p-value <0.05)

The ranking itself is **not** used in scoring. Every gene in the top/bottom 50 counts equally.

Analysis matching

Mapping Your Results to OmicSoft Datasets by IPA Analysis Match



Project

Cell & Tissue

Datasets information

similar

opposite

Expression Analysis - EEC P32 Tumor vs Norm RPKM_1050 - 2021-03-30 10:58 上午

Analysis Name	Project	case.di...	case.tar...	case.tis...	case.tre...	compa...	compa...	compa...	weblink	CP (z-s...	UR (z-s...	CN (z-s...	DE (z-s...	z-score...	D...
127- breast carcinoma [breast] human marrow stror	HumanDisease	breast carcino...		breast	human marro...	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		23.33	22.36		11.42	12.45
67- breast carcinoma [breast] human marrow strom	HumanDisease	breast carcino...		breast	human marro...	Treatment vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...	55.90	42.43	30.00	30.94	39.82	9.96
129- breast carcinoma [breast] IL-6;siltuximab 2751:	HumanDisease	breast carcino...		breast	IL-6;siltuximab	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		20.00	33.17		13.29	8.65
101- breast carcinoma [breast] IL-6;siltuximab 2748:	HumanDisease	breast carcino...		breast	IL-6;siltuximab	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		41.23	28.28	39.95	27.37	7.33
		east carcino...		breast	IL-6;siltuximab	Treatment vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...			-20.00		-5.00	6.65
		east carcino...		breast		Treatment1 vs. ...	Dosage:Experi...	GSE28786.GPL93	https://www.n...		43.59	24.49	29.17	24.31	5.24
		east carcino...		breast	none	CellType1 vs. C...	SamplingTime:...	GSE54329.GPL18	https://www.n...		10.00	10.00	35.73	13.93	2.97
		east cancer		breast	ethanol	Treatment1 vs. ...	Treatment:Tra...	GSE64536.GPL57	https://www.n...		47.96	20.00	35.73	25.92	2.77
		east carcino...		breast	IL-6	Treatment vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-18.86	10.00	-34.21	-10.77	2.52
		east carcino...		breast	IL-6	Treatment vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-11.34	-20.00	3.90	-6.86	1.81
		east cancer		breast	ethanol	Treatment1 vs. ...	Treatment:Tra...	GSE64536.GPL57	https://www.n...		42.43	22.36	30.94	23.93	0.61
		east carcino...		breast	IL-6;siltuximab	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		20.00	28.28		12.07	-1.05
		east carcino...		breast	IL-6;siltuximab	Treatment vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-28.40	14.14	-25.26	-9.88	-2.77
		east carcino...		breast	human marro...	Treatment vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-38.38	6.32	-27.29	-14.84	-2.84
		east carcino...		breast	none	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-37.42	-24.49	-23.06	-21.24	-3.66
		east carcino...		breast	human marro...	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-38.73	-20.00	-25.26	-21.00	-6.92
		east carcino...		breast	none	Treatment1 vs. ...	CellLine:Sampli...	GSE54329.GPL18	https://www.n...		-42.43	-22.36	-32.62	-24.35	-11.94

roject

● Select Projects

○ Or filter using wild card search

nclude: (use * for wildcard)

[comma-separated list]

xclude:

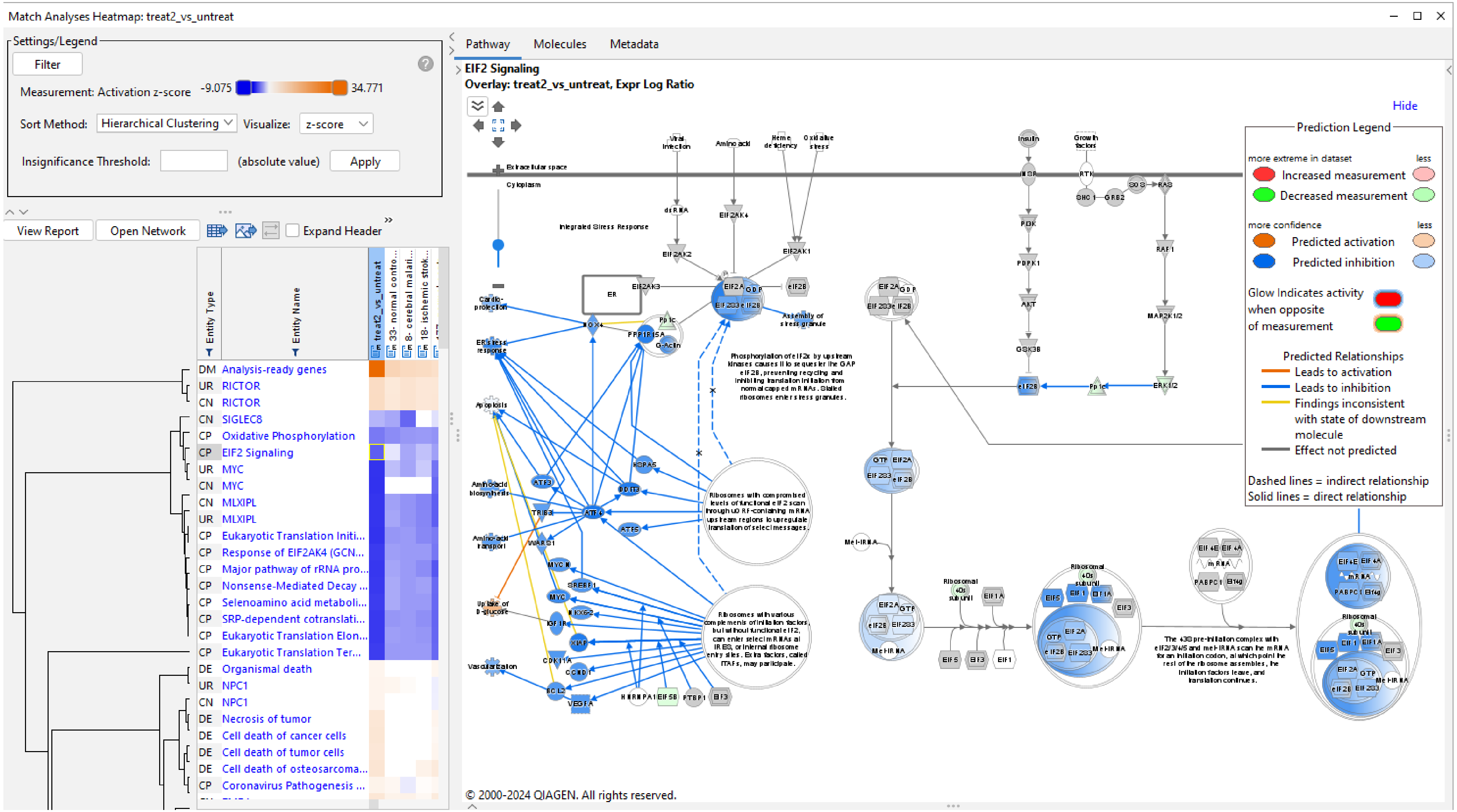
[comma-separated list]

tasets
ta

z-scores

Analysis Match

訊聯基因數位



Match Analyses Heatmap: treat2_vs_untreat

Settings/Legend

Filter

Measurement: Activation z-score -9.075 34.771

Sort Method: Hierarchical Clustering

Visualize: z-score

Insignificance Threshold: (absolute value) Apply

View Report · Open Network · ☐ Expand Header

Entity Type	Entity Name
DM	Analysis-ready genes
UR	RICTOR
CN	RICTOR
CN	SIGLEC8
CP	Oxidative Phosphorylation
CP	EIF2 Signaling
UR	MYC
CN	MYC
CN	MLXIPL
UR	MLXIPL
CP	Eukaryotic Translation Initi...
CP	Response of EIF2AK4 (GCN...
CP	Major pathway of rRNA pro...
CP	Nonsense-Mediated Decay ...
CP	Selenoamino acid metaboli...
CP	SRP-dependent cotranslati...
CP	Eukaryotic Translation Elon...
CP	Eukaryotic Translation Ter...
DE	Organismal death
UR	NPC1
CN	NPC1
DE	Necrosis of tumor
DE	Cell death of cancer cells
DE	Cell death of tumor cells
DE	Cell death of osteosarcoma...
CP	Coronavirus Pathogenesis ...

EIF2 Signaling

Overlay: treat2_vs_untreat, Expr Log Ratio

Phosphorylation of eIF2α by upstream kinases causes it to sequester the GAP eIF2B, preventing recycling and inhibiting translation initiation from normal capped mRNAs. Stalled ribosomes enter stress granules.

Ribosomes with compromised levels of functional eIF2 scan through uORF-containing mRNA upstream regions to upregulate translation of select messages.

Ribosomes with various complements of initiation factors, but without functional eIF2, can enter select mRNAs at IRES, or internal ribosome entry sites. Extra factors, called ITAFs, may participate.

The 43S pre-initiation complex with eIF2/3/4/5 and met-tRNA scan the mRNA for an initiation codon, at which point the rest of the ribosome assembles, the initiation factors leave, and translation continues.

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

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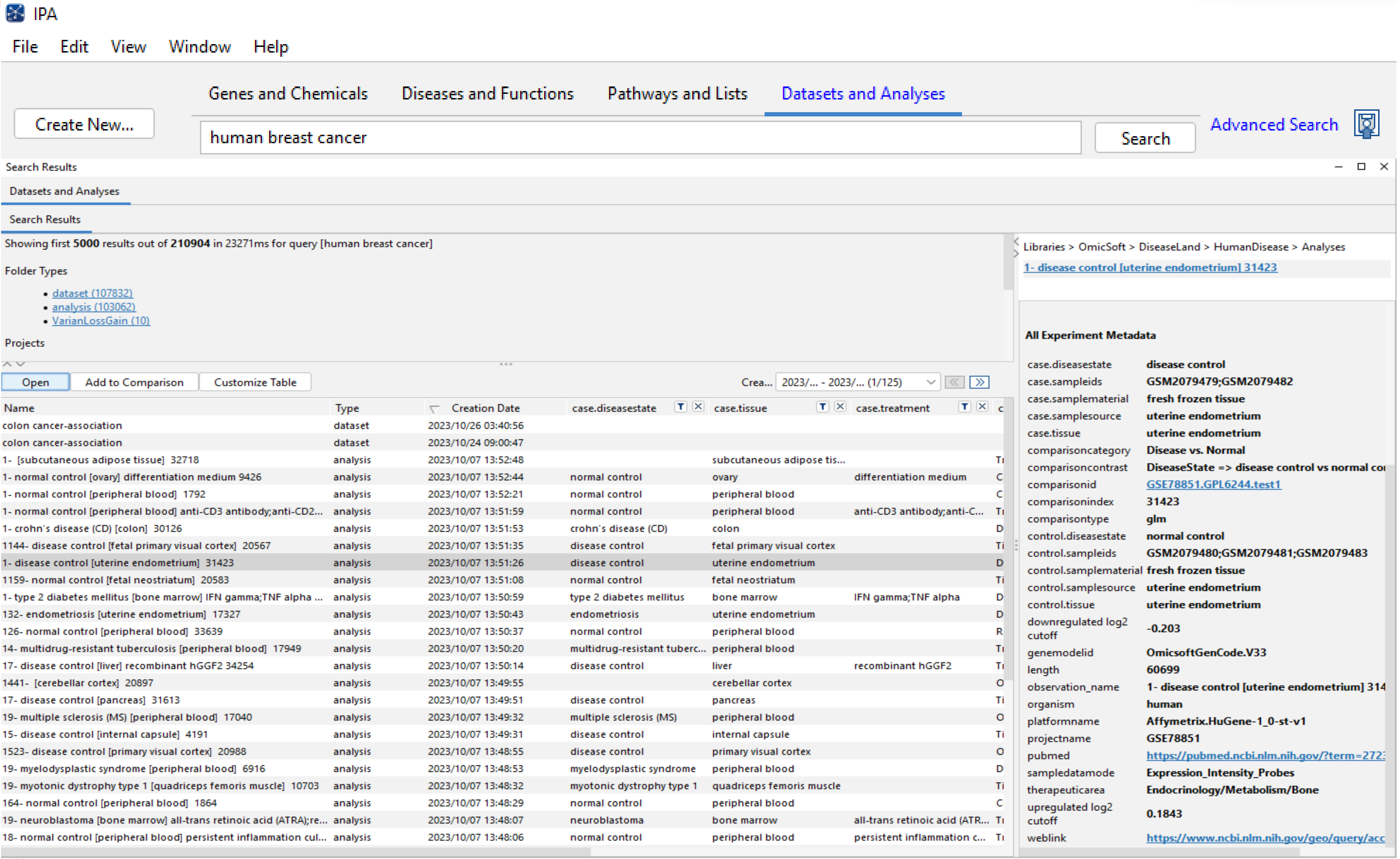
Disease and Analysis search



human breast cancer

Showing first **5000** results out of **210904** in 23271ms for query [human breast cancer]

Folder Types

- dataset (107832)
- analysis (103062)
- VarianLossGain (10)

Projects

Name	Type	Creation Date	case.diseasestate	case.tissue	case.treatment	c
colon cancer-association	dataset	2023/10/26 03:40:56				
colon cancer-association	dataset	2023/10/24 09:00:47				
1- [subcutaneous adipose tissue] 32718	analysis	2023/10/07 13:52:48		subcutaneous adipose tis...		T
1- normal control [ovary] differentiation medium 9426	analysis	2023/10/07 13:52:44	normal control	ovary	differentiation medium	C
1- normal control [peripheral blood] 1792	analysis	2023/10/07 13:52:21	normal control	peripheral blood		C
1- normal control [peripheral blood] anti-CD3 antibody;anti-CD2...	analysis	2023/10/07 13:51:59	normal control	peripheral blood	anti-CD3 antibody;anti-C...	T
1- crohn's disease (CD) [colon] 30126	analysis	2023/10/07 13:51:53	crohn's disease (CD)	colon		D
1144- disease control [fetal primary visual cortex] 20567	analysis	2023/10/07 13:51:35	disease control	fetal primary visual cortex		Ti
1- disease control [uterine endometrium] 31423	analysis	2023/10/07 13:51:26	disease control	uterine endometrium		D
1159- normal control [fetal neostriatum] 20583	analysis	2023/10/07 13:51:08	normal control	fetal neostriatum		Ti
1- type 2 diabetes mellitus [bone marrow] IFN gamma;TNF alpha ...	analysis	2023/10/07 13:50:59	type 2 diabetes mellitus	bone marrow	IFN gamma;TNF alpha	D
132- endometriosis [uterine endometrium] 17327	analysis	2023/10/07 13:50:43	endometriosis	uterine endometrium		D
126- normal control [peripheral blood] 33639	analysis	2023/10/07 13:50:37	normal control	peripheral blood		R
14- multidrug-resistant tuberculosis [peripheral blood] 17949	analysis	2023/10/07 13:50:20	multidrug-resistant tuberc...	peripheral blood		T
17- disease control [liver] recombinant hGGF2 34254	analysis	2023/10/07 13:50:14	disease control	liver	recombinant hGGF2	T
1441- [cerebellar cortex] 20897	analysis	2023/10/07 13:49:55		cerebellar cortex		O
17- disease control [pancreas] 31613	analysis	2023/10/07 13:49:51	disease control	pancreas		Ti
19- multiple sclerosis (MS) [peripheral blood] 17040	analysis	2023/10/07 13:49:32	multiple sclerosis (MS)	peripheral blood		O
15- disease control [internal capsule] 4191	analysis	2023/10/07 13:49:31	disease control	internal capsule		Ti
1523- disease control [primary visual cortex] 20988	analysis	2023/10/07 13:48:55	disease control	primary visual cortex		O
19- myelodysplastic syndrome [peripheral blood] 6916	analysis	2023/10/07 13:48:53	myelodysplastic syndrome	peripheral blood		D
19- myotonic dystrophy type 1 [quadriceps femoris muscle] 10703	analysis	2023/10/07 13:48:32	myotonic dystrophy type 1	quadriceps femoris muscle		Ti
164- normal control [peripheral blood] 1864	analysis	2023/10/07 13:48:29	normal control	peripheral blood		C
19- neuroblastoma [bone marrow] all-trans retinoic acid (ATRA);re...	analysis	2023/10/07 13:48:07	neuroblastoma	bone marrow	all-trans retinoic acid (ATR...	T
18- normal control [peripheral blood] persistent inflammation cul...	analysis	2023/10/07 13:48:06	normal control	peripheral blood	persistent inflammation c...	T

Libraries > OmicSoft > DiseaseLand > HumanDisease > Analyses

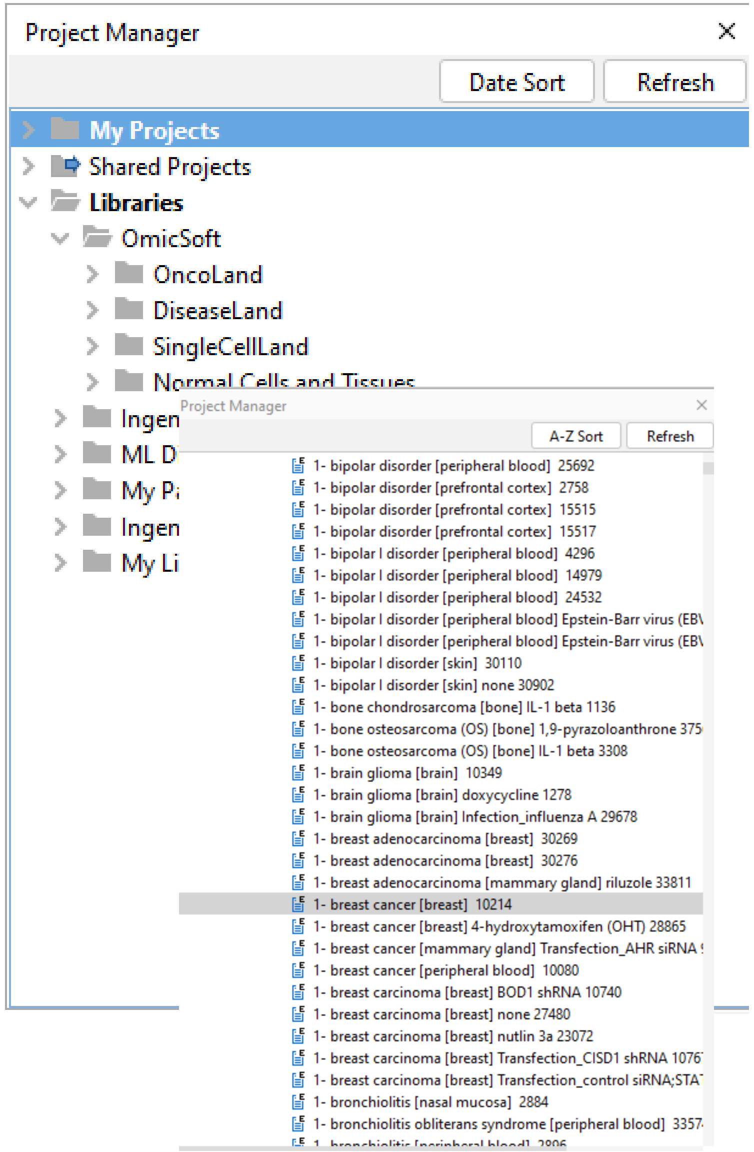
1- disease control [uterine endometrium] 31423

All Experiment Metadata

case.diseasestate	**disease control**
case.sampleids	**GSM2079479;GSM2079482**
case.samplematerial	**fresh frozen tissue**
case.samplesource	**uterine endometrium**
case.tissue	**uterine endometrium**
comparisoncategory	**Disease vs. Normal**
comparisoncontrast	**DiseaseState => disease control vs normal co**
comparisonid	GSE78851.GPL6244.test1
comparisonindex	**31423**
comparisontype	**glm**
control.diseasestate	**normal control**
control.sampleids	**GSM2079480;GSM2079481;GSM2079483**
control.samplematerial	**fresh frozen tissue**
control.samplesource	**uterine endometrium**
control.tissue	**uterine endometrium**
downregulated log2 cutoff	**-0.203**
genemodelid	**OmicsoftGenCode.V33**
length	**60699**
observation_name	**1- disease control [uterine endometrium] 314**
organism	**human**
platformname	**Affymetrix.HuGene-1_0-st-v1**
projectname	**GSE78851**
pubmed	https://pubmed.ncbi.nlm.nih.gov/?term=272
sampledatamode	**Expression_Intensity_Probes**
therapeuticarea	**Endocrinology/Metabolism/Bone**
upregulated log2 cutoff	**0.1843**
weblink	https://www.ncbi.nlm.nih.gov/geo/query/acc

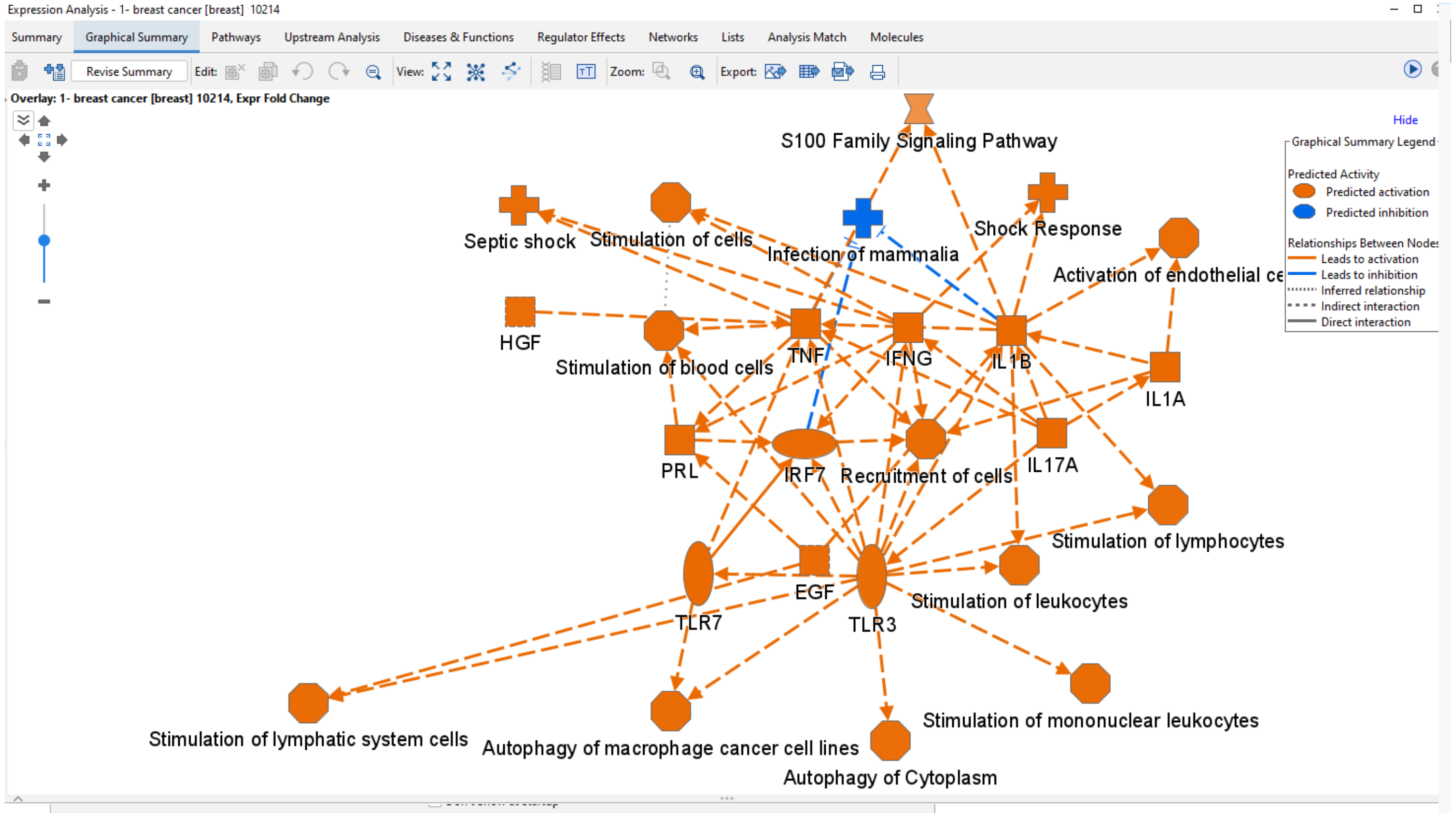
OmicSoft data storage and analysis in IPA

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



1- bipolar disorder [peripheral blood] 25692
1- bipolar disorder [prefrontal cortex] 2758
1- bipolar disorder [prefrontal cortex] 15515
1- bipolar disorder [prefrontal cortex] 15517
1- bipolar I disorder [peripheral blood] 4296
1- bipolar I disorder [peripheral blood] 14979
1- bipolar I disorder [peripheral blood] 24532
1- bipolar I disorder [peripheral blood] Epstein-Barr virus (EB
1- bipolar I disorder [peripheral blood] Epstein-Barr virus (EB
1- bipolar I disorder [skin] 30110
1- bipolar I disorder [skin] none 30902
1- bone chondrosarcoma [bone] IL-1 beta 1136
1- bone osteosarcoma (OS) [bone] 1,9-pyrazoloanthrone 375
1- bone osteosarcoma (OS) [bone] IL-1 beta 3308
1- brain glioma [brain] 10349
1- brain glioma [brain] doxycycline 1278
1- brain glioma [brain] Infection_influenza A 29678
1- breast adenocarcinoma [breast] 30269
1- breast adenocarcinoma [breast] 30276
1- breast adenocarcinoma [mammary gland] riluzole 33811
1- breast cancer [breast] 10214
1- breast cancer [breast] 4-hydroxytamoxifen (OHT) 28865
1- breast cancer [mammary gland] Transfection_AHR siRNA
1- breast cancer [peripheral blood] 10080
1- breast carcinoma [breast] BOD1 shRNA 10740
1- breast carcinoma [breast] none 27480
1- breast carcinoma [breast] nutlin 3a 23072
1- breast carcinoma [breast] Transfection_CISD1 shRNA 1076
1- breast carcinoma [breast] Transfection_control siRNA;STA
1- bronchiolitis [nasal mucosa] 2884
1- bronchiolitis obliterans syndrome [peripheral blood] 3357
1- bronchiolitis [peripheral blood] 2806

Graphical summary



What's new in the IPA winter release (Dec 2023)

Volcano plot

Create Expression Analysis - [analysis : 100- disease control [airway epithelium] 26883]

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			
Log2FoldChange	Expr Log Ratio	-5.3512 to 4.1489	-0.99	Down	0.8	Up
Pvalue	Expr p-value	0.0 to 0.9999				
AdjustedPValue	Expr p-value	0.0 to 0.9999	0.01			
NumeratorValue	Expr Intensity/RPKM/FPKM/Counts	1.7226 to 19.4263				
DenominatorValue	Expr Intensity/RPKM/FPKM/Counts	1.6911 to 19.4031				
ExprOther	Expr Other	0.0 to 1.0		Down		Up

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

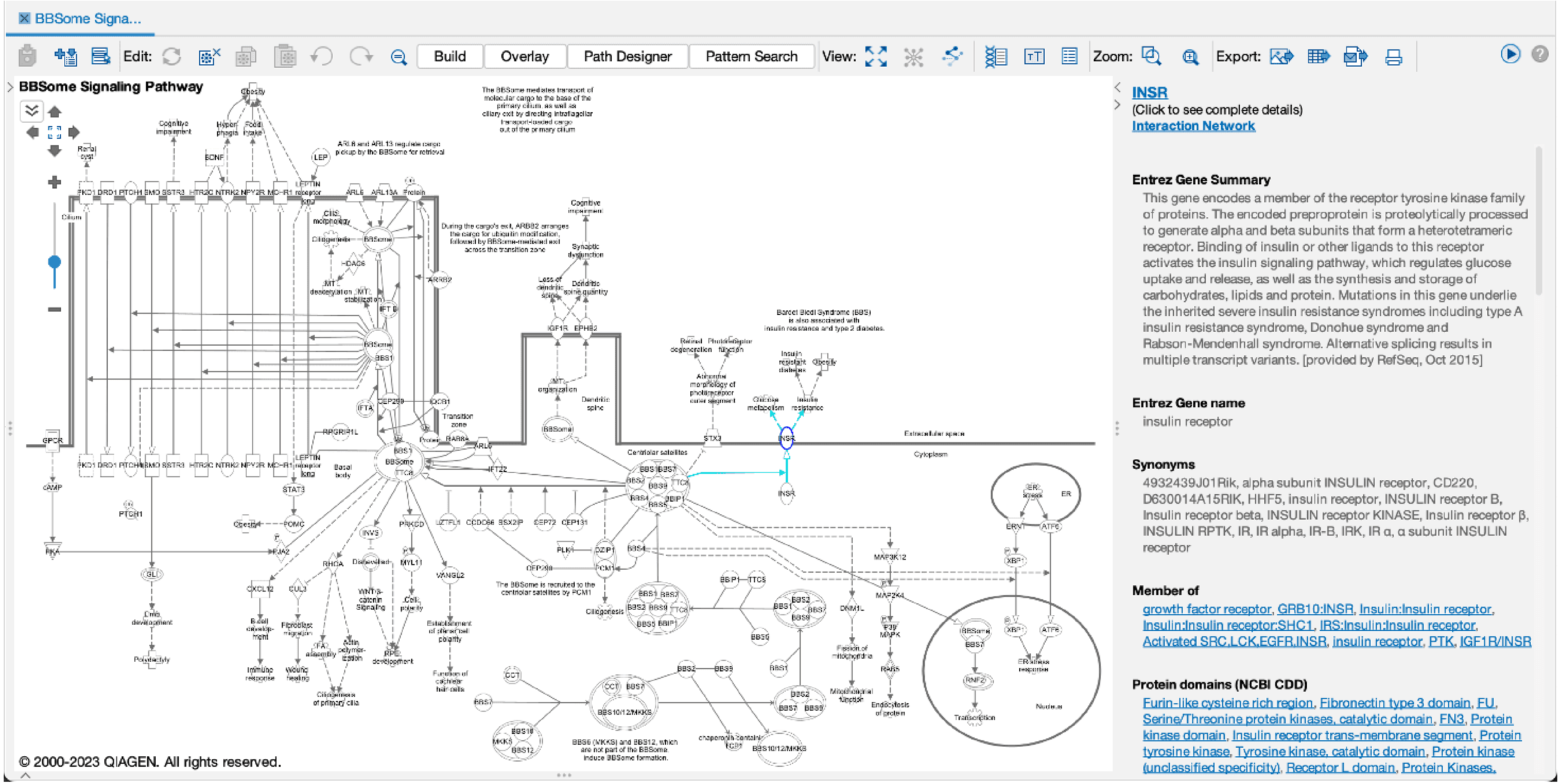
1410 analysis-ready molecules (**748** Down and **662** Up)

Preview Dataset 100- disease control [airway epithelium] 26883

Symbol A1BG-AS1 - BCL10... (1/15)

What's new in the IPA winter release (Dec 2023)

Easy to find relationship summary



INSR
(Click to see complete details)
Interaction Network

Entrez Gene Summary

This gene encodes a member of the receptor tyrosine kinase family of proteins. The encoded preproprotein is proteolytically processed to generate alpha and beta subunits that form a heterotetrameric receptor. Binding of insulin or other ligands to this receptor activates the insulin signaling pathway, which regulates glucose uptake and release, as well as the synthesis and storage of carbohydrates, lipids and protein. Mutations in this gene underlie the inherited severe insulin resistance syndromes including type A insulin resistance syndrome, Donohue syndrome and Rabson-Mendenhall syndrome. Alternative splicing results in multiple transcript variants. [provided by RefSeq, Oct 2015]

Entrez Gene name

insulin receptor

Synonyms

4932439J01Rik, alpha subunit INSULIN receptor, CD220, D630014A15RIK, HHF5, insulin receptor, INSULIN receptor B, Insulin receptor beta, INSULIN receptor KINASE, Insulin receptor β, INSULIN RPTK, IR, IR alpha, IR-B, IRK, IR α, α subunit INSULIN receptor

Member of

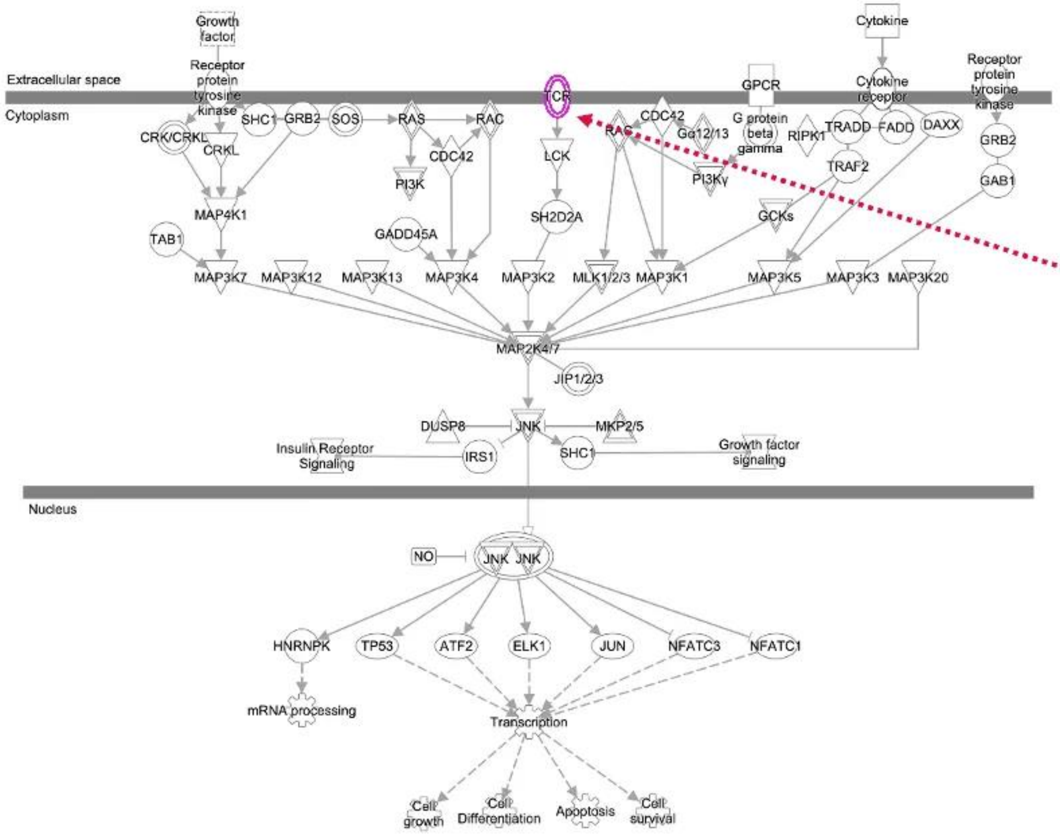
growth factor receptor, GRB10:INSR, Insulin:Insulin receptor, Insulin:Insulin receptor:SHC1, IRS:Insulin:Insulin receptor, Activated SRC,LCK,EGFR,INSR, insulin receptor, PTK, IGF1R/INSR

Protein domains (NCBI CDD)

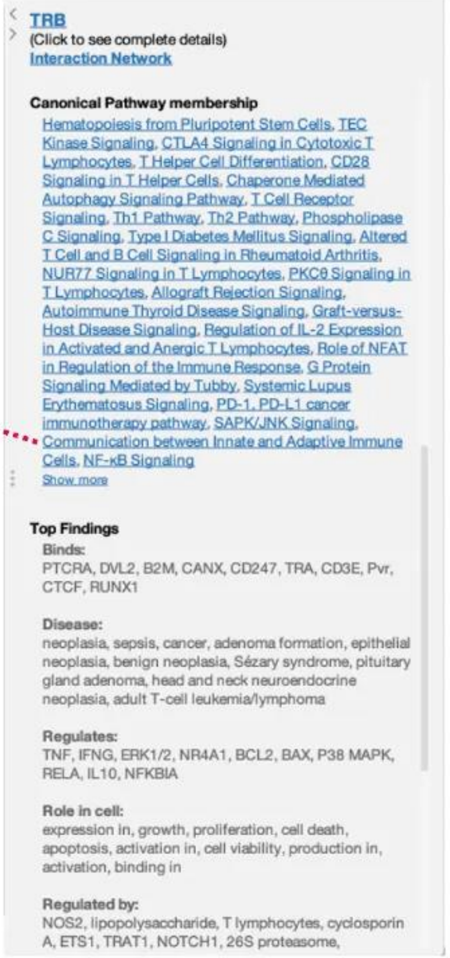
Furin-like cysteine rich region, Fibronectin type 3 domain, FU, Serine/Threonine protein kinases, catalytic domain, FN3, Protein kinase domain, Insulin receptor trans-membrane segment, Protein tyrosine kinase, Tyrosine kinase, catalytic domain, Protein kinase (unclassified specificity), Receptor L domain, Protein Kinases,

What’s new in the IPA winter release (Dec 2023)

Easy to find relationship summary



Opens pathway and highlights the node, even if it is a group for which that gene is a member



TRB
(Click to see complete details)
Interaction Network

Canonical Pathway membership

Hematopoiesis from Pluripotent Stem Cells, TEC Kinase Signaling, CTLA4 Signaling in Cytotoxic T Lymphocytes, T Helper Cell Differentiation, CD28 Signaling in T Helper Cells, Chaperone Mediated Autophagy Signaling Pathway, T Cell Receptor Signaling, Th1 Pathway, Th2 Pathway, Phospholipase C Signaling, Type I Diabetes Mellitus Signaling, Altered T Cell and B Cell Signaling in Rheumatoid Arthritis, NUR77 Signaling in T Lymphocytes, PKCθ Signaling in T Lymphocytes, Allograft Rejection Signaling, Autoimmune Thyroid Disease Signaling, Graft-versus-Host Disease Signaling, Regulation of IL-2 Expression in Activated and Anergic T Lymphocytes, Role of NFAT in Regulation of the Immune Response, G Protein Signaling Mediated by Tubby, Systemic Lupus Erythematosus Signaling, PD-1, PD-L1 cancer immunotherapy pathway, SAPK/JNK Signaling, Communication between Innate and Adaptive Immune Cells, NF-κB Signaling

Show more

Top Findings

Binds:
PTCRA, DVL2, B2M, CANX, CD247, TRA, CD3E, Pvr, CTCF, RUNX1

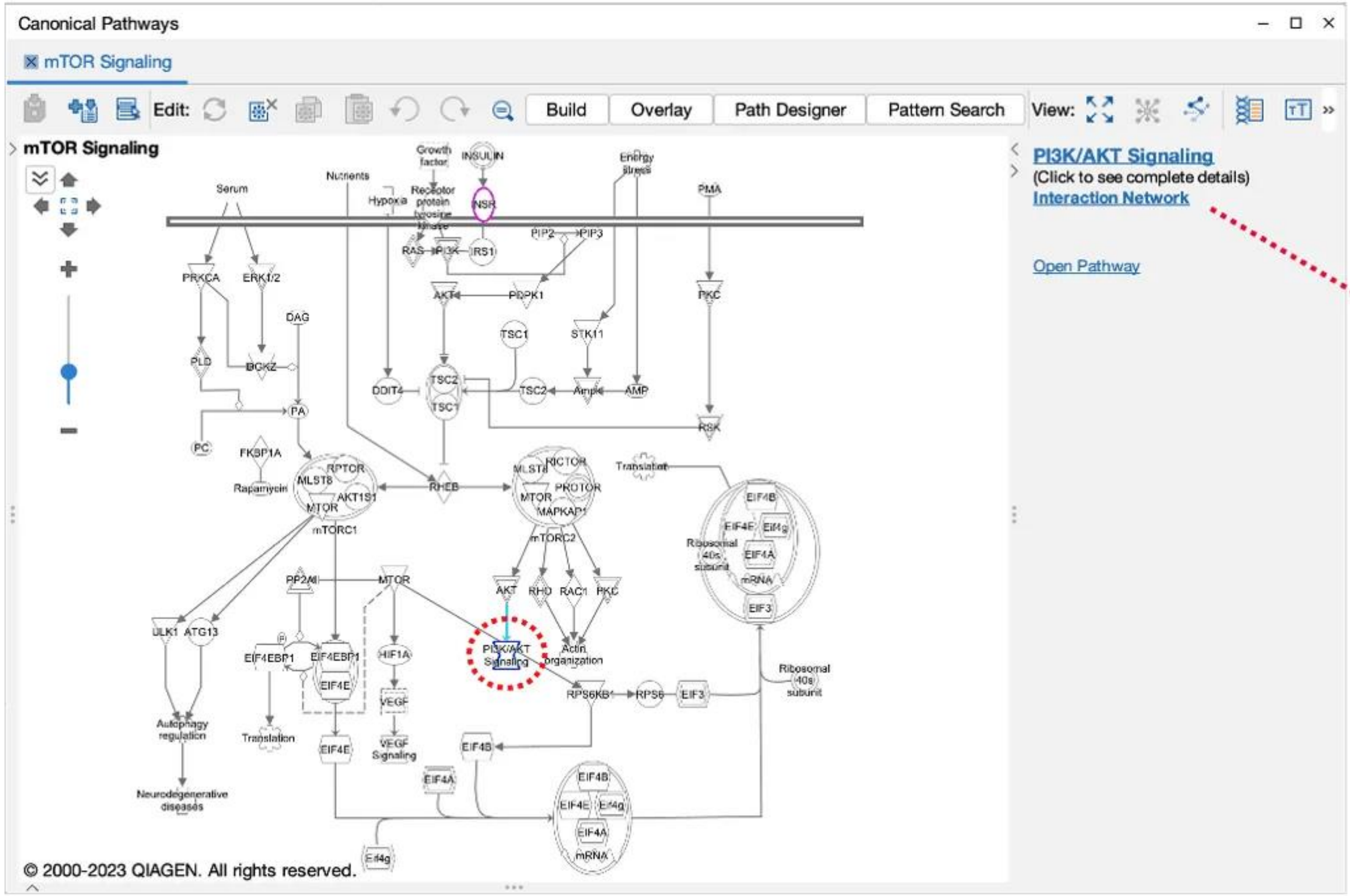
Disease:
neoplasia, sepsis, cancer, adenoma formation, epithelial neoplasia, benign neoplasia, Sézary syndrome, pituitary gland adenoma, head and neck neuroendocrine neoplasia, adult T-cell leukemia/lymphoma

Regulates:
TNF, IFNG, ERK1/2, NR4A1, BCL2, BAX, P38 MAPK, RELA, IL10, NFKBIA

Role in cell:
expression in, growth, proliferation, cell death, apoptosis, activation in, cell viability, production in, activation, binding in

Regulated by:
NOS2, lipopolysaccharide, T lymphocytes, cyclosporin A, ETS1, TRAT1, NOTCH1, 26S proteasome,

What's new in the IPA winter release (Dec 2023)



PI3K/AKT Signaling
(Click to see complete details)
Interaction Network

Open Pathway

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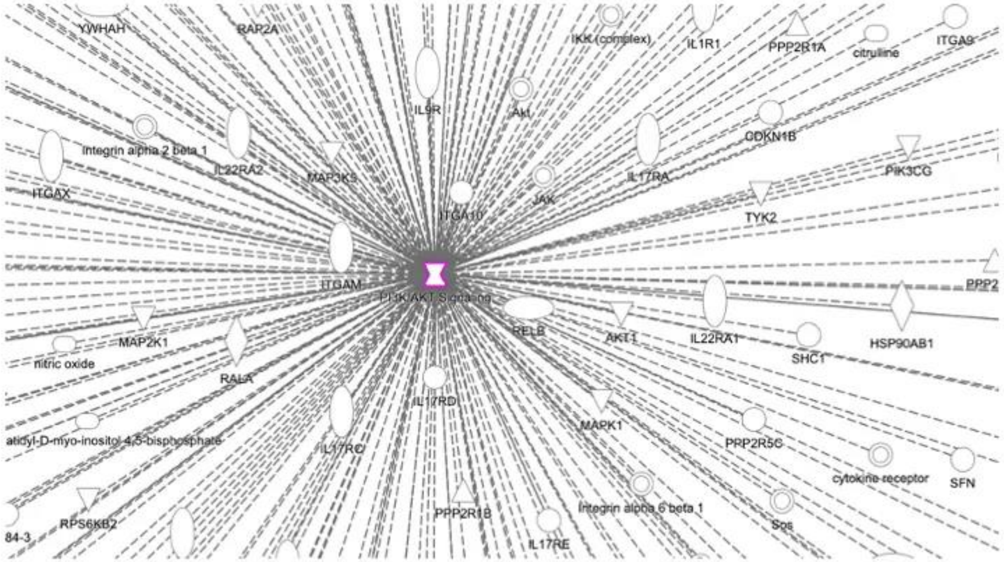
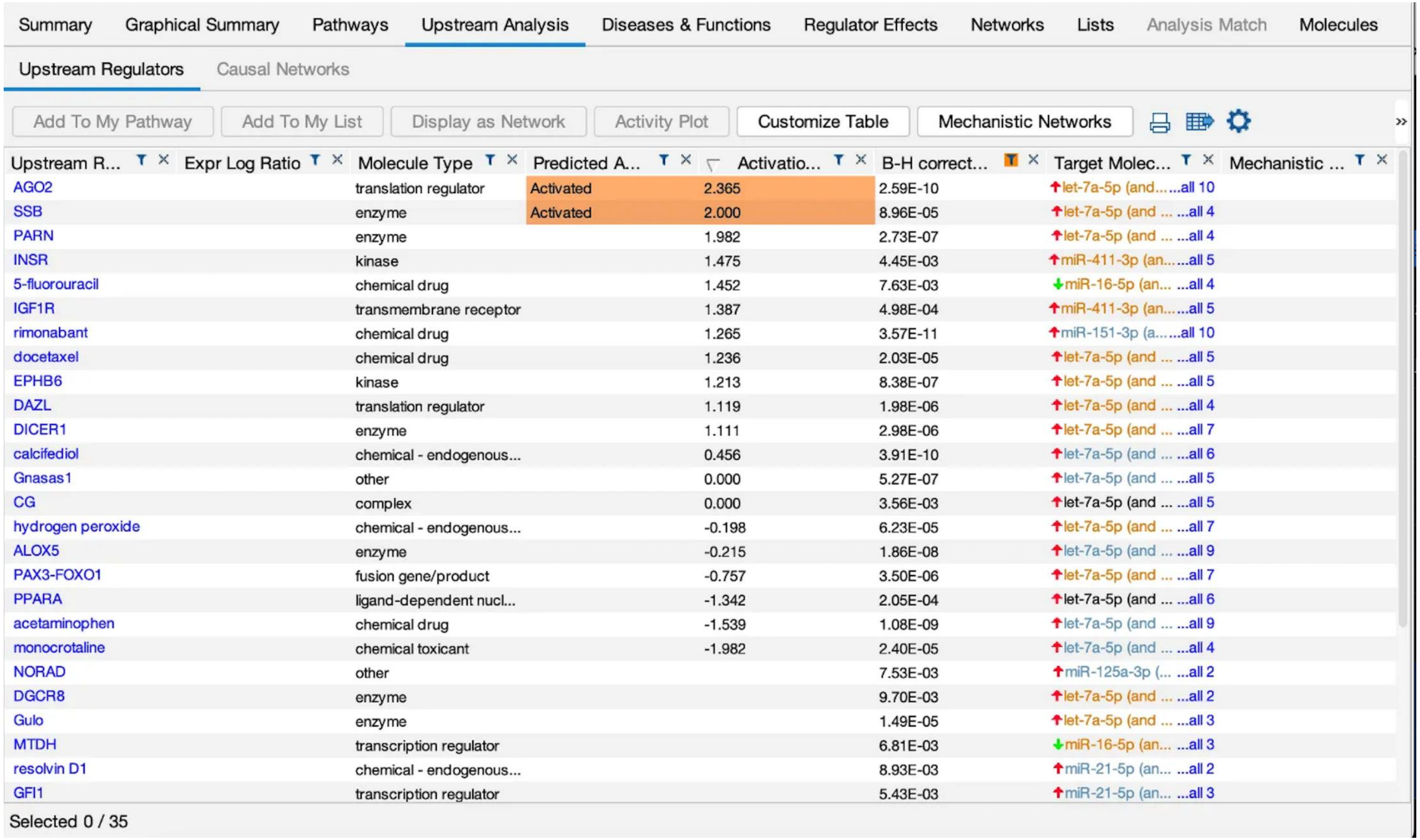


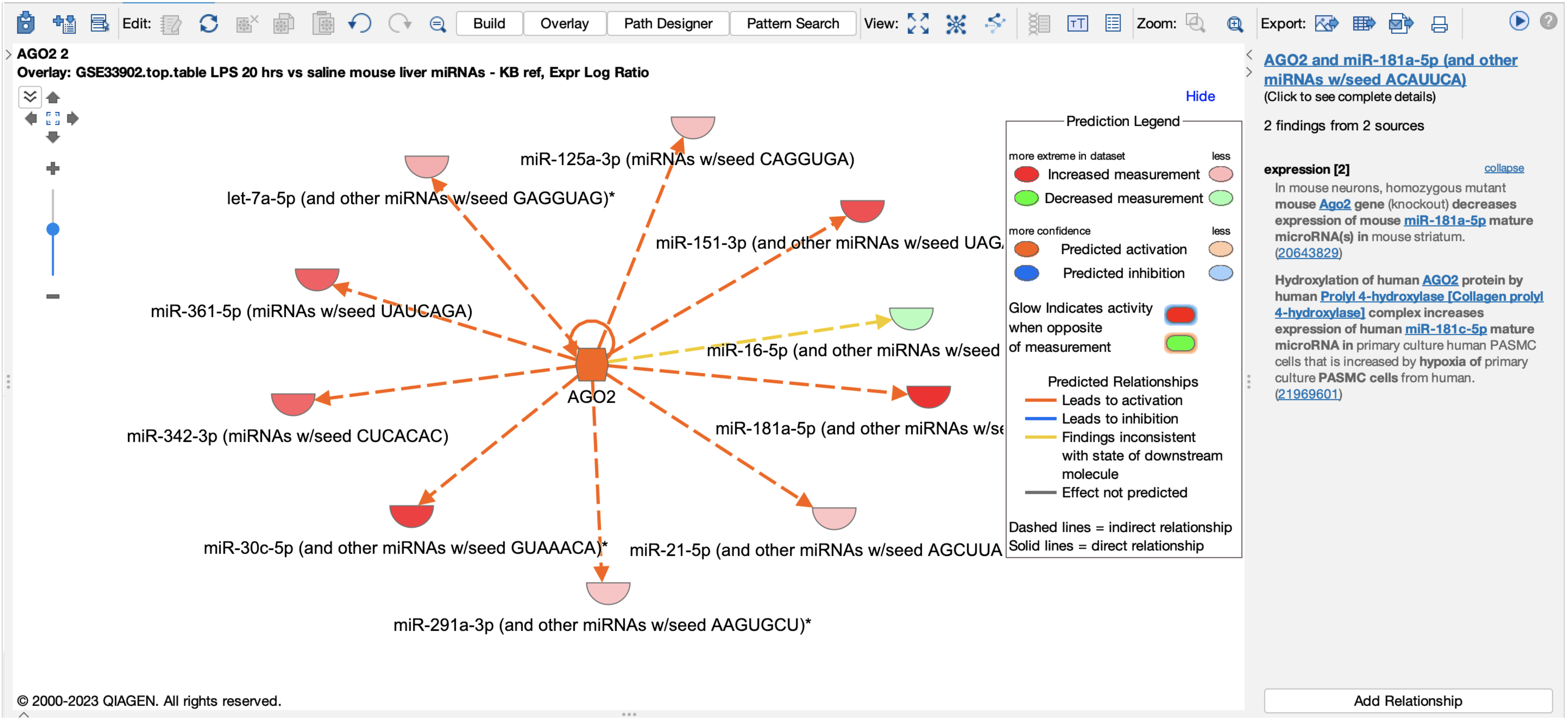
What's new in the IPA winter release (Dec 2023)



Upstream R...	Expr Log Ratio	Molecule Type	Predicted A...	Activatio...	B-H correct...	Target Molec...	Mechanistic ...
AGO2		translation regulator	Activated	2.365	2.59E-10	↑let-7a-5p (and... ...all 10	
SSB		enzyme	Activated	2.000	8.96E-05	↑let-7a-5p (and ... ...all 4	
PARN		enzyme		1.982	2.73E-07	↑let-7a-5p (and ... ...all 4	
INSR		kinase		1.475	4.45E-03	↑miR-411-3p (an... ...all 5	
5-fluorouracil		chemical drug		1.452	7.63E-03	↓miR-16-5p (an... ...all 4	
IGF1R		transmembrane receptor		1.387	4.98E-04	↑miR-411-3p (an... ...all 5	
rimonabant		chemical drug		1.265	3.57E-11	↑miR-151-3p (a... ...all 10	
docetaxel		chemical drug		1.236	2.03E-05	↑let-7a-5p (and ... ...all 5	
EPHB6		kinase		1.213	8.38E-07	↑let-7a-5p (and ... ...all 5	
DAZL		translation regulator		1.119	1.98E-06	↑let-7a-5p (and ... ...all 4	
DICER1		enzyme		1.111	2.98E-06	↑let-7a-5p (and ... ...all 7	
calcifediol		chemical - endogenous...		0.456	3.91E-10	↑let-7a-5p (and ... ...all 6	
Gnasas1		other		0.000	5.27E-07	↑let-7a-5p (and ... ...all 5	
CG		complex		0.000	3.56E-03	↑let-7a-5p (and ... ...all 5	
hydrogen peroxide		chemical - endogenous...		-0.198	6.23E-05	↑let-7a-5p (and ... ...all 7	
ALOX5		enzyme		-0.215	1.86E-08	↑let-7a-5p (and ... ...all 9	
PAX3-FOXO1		fusion gene/product		-0.757	3.50E-06	↑let-7a-5p (and ... ...all 7	
PPARA		ligand-dependent nucl...		-1.342	2.05E-04	↑let-7a-5p (and ... ...all 6	
acetaminophen		chemical drug		-1.539	1.08E-09	↑let-7a-5p (and ... ...all 9	
monocrotaline		chemical toxicant		-1.982	2.40E-05	↑let-7a-5p (and ... ...all 4	
NORAD		other			7.53E-03	↑miR-125a-3p (... ...all 2	
DGCR8		enzyme			9.70E-03	↑let-7a-5p (and ... ...all 2	
Gulo		enzyme			1.49E-05	↑let-7a-5p (and ... ...all 3	
MTDH		transcription regulator			6.81E-03	↓miR-16-5p (an... ...all 3	
resolvin D1		chemical - endogenous...			8.93E-03	↑miR-21-5p (an... ...all 2	
GFI1		transcription regulator			5.43E-03	↑miR-21-5p (an... ...all 3	

Selected 0 / 35

What's new in the IPA winter release (Dec 2023)



AGO2 2

Overlay: GSE33902.top.table LPS 20 hrs vs saline mouse liver miRNAs - KB ref, Expr Log Ratio

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AGO2 and miR-181a-5p (and other miRNAs w/seed ACAUUCA)
(Click to see complete details)

2 findings from 2 sources

expression [2] collapse

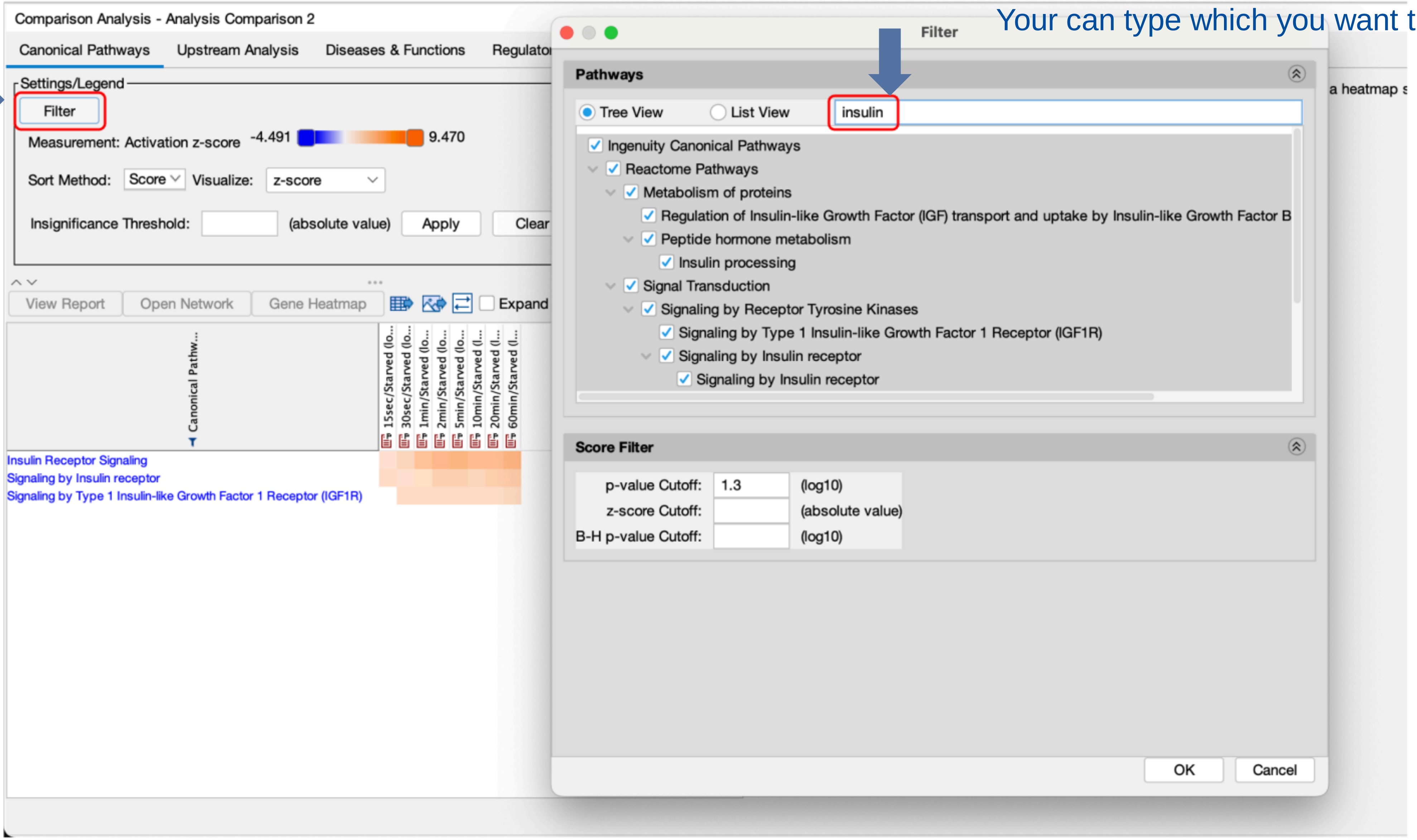
In mouse neurons, homozygous mutant **mouse Ago2 gene** (knockout) **decreases expression of mouse miR-181a-5p mature microRNA(s) in** mouse striatum. (20643829)

Hydroxylation of human AGO2 protein by human Prolyl 4-hydroxylase [Collagen prolyl 4-hydroxylase] complex increases expression of human miR-181c-5p mature microRNA in primary culture human PASMC cells that is increased by **hypoxia of** primary culture **PASMC cells** from human. (21969601)

What’s new in the IPA Spring release (Mar 2024)

Click filer

Your can type which you want to filter



Measurement: Activation z-score -4.491 9.470

Sort Method: Score Visualize: z-score

Insignificance Threshold: (absolute value)

Insulin Receptor Signaling

Signaling by Insulin receptor

Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)

Pathways

● Tree View ○ List View insulin

- ☑ Ingenuity Canonical Pathways
- ☑ Reactome Pathways
  - ☑ Metabolism of proteins
    - ☑ Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor B
    - ☑ Peptide hormone metabolism
      - ☑ Insulin processing
  - ☑ Signal Transduction
    - ☑ Signaling by Receptor Tyrosine Kinases
      - ☑ Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)
      - ☑ Signaling by Insulin receptor
        - ☑ Signaling by Insulin receptor

Score Filter

p-value Cutoff: 1.3 (log10)

z-score Cutoff: (absolute value)

B-H p-value Cutoff: (log10)

Summary IPA release pathway update(Before spring 2024)

After 2023 Dec

Explore eight new and two updated pathways

New Ingenuity signaling pathways

- BBSome Signaling Pathway
- Folate Signaling Pathway
- HEY1 Signaling Pathway
- IL-27 Signaling Pathway
- Sleep NREM Signaling Pathway
- Sleep REM Signaling Pathway
- UFMylation Signaling Pathway
- WNT/SHH Axonal Guidance Signaling Pathway

Existing pathways updated to include an activity pattern

- Eicosanoid Signaling Pathway
- Gap Junction Signaling Pathway

After 2024 Mar.

Canonical Pathways updates

New Ingenuity Signaling Pathways

- Cohesin Chromatin Regulation Pathway
- Hematoma Resolution Signaling Pathway
- Histone Modification Signaling Pathway
- Nuclear Cytoskeleton Signaling Pathway

Signaling pathways with Activity Pattern added, and content updated

- Cellular Effects of Sildenafil
- Ephrin A Signaling Pathway
- Hereditary Breast Cancer Signaling Pathway
- Parkinson’s Signaling Pathway

What's new in the IPA Spring release (Mar 2024)

Analysis Match: 54,489 new datasets for total of 204,146 datasets

Datasets and analyses of them will appear in IPA in late April 2024.

Land	Repository	Datasets Q4 2023	Datasets Q1 2024	Increase
DiseaseLand	HumanDisease	35,112	36,105	993
	MouseDisease	26,584	26,892	308
	RatDisease	9,287	9,287	
	LINCS	28,234	29,976	1,742
OncoLand	OncoHuman (Formerly OncoGEO)	21,373	22,219	846
	OncoMouse	1,054	1,054	
	TCGA	4,438	4,854	416
	MetastaticCancer	81	81	
	Hematology	4,267	4,267	
	Pediatrics	444	444	
	ENCODE RNA Binding	486	486	
	ClinicalProteomicTumor	254	628	374
Single Cell Land	SingleCellHuman	194	194	
	SingleCellHumanUmi	11,049	53,046	41,997
	SingleCellHumanUmiLite	603	603	
	SingleCellHumanHCL	1,469	1,469	
	SingleCellMouse	81	81	
	SingleCellMouseUmi	3,220	11,033	7,813
	SingleCellMouseUmiLite	115	115	
Normal Cells and Tissues	Human Tissues (GTEx)	1,312	1,312	

Comprehensive germline genomic profiles of children, adolescents and young adults with solid tumors

Hand on Case Study

Germline variants profile data

In a study of 1,507 C-AYA patients with solid tumors, 12% had pathogenic variants in known cancer-predisposing genes (KCPG), and 61% had such variants in non-KCPG genes like PRKN, SMARCAL1, and SMAD7. Pathway analysis pinpointed p53 as a key network. Drug-target analysis revealed that 1/3 of patients with germline P/LP variants had druggable alterations, with over half from non-KCPG genes, emphasizing the significance of considering candidate genes for targeted therapies.

Akhavanfard, S., Padmanabhan, R., Yehia, L. *et al.* Comprehensive germline genomic profiles of children, adolescents and young adults with solid tumors. *Nat Commun* **11**, 2206 (2020). https://doi.org/10.1038/s41467-020-16067-1

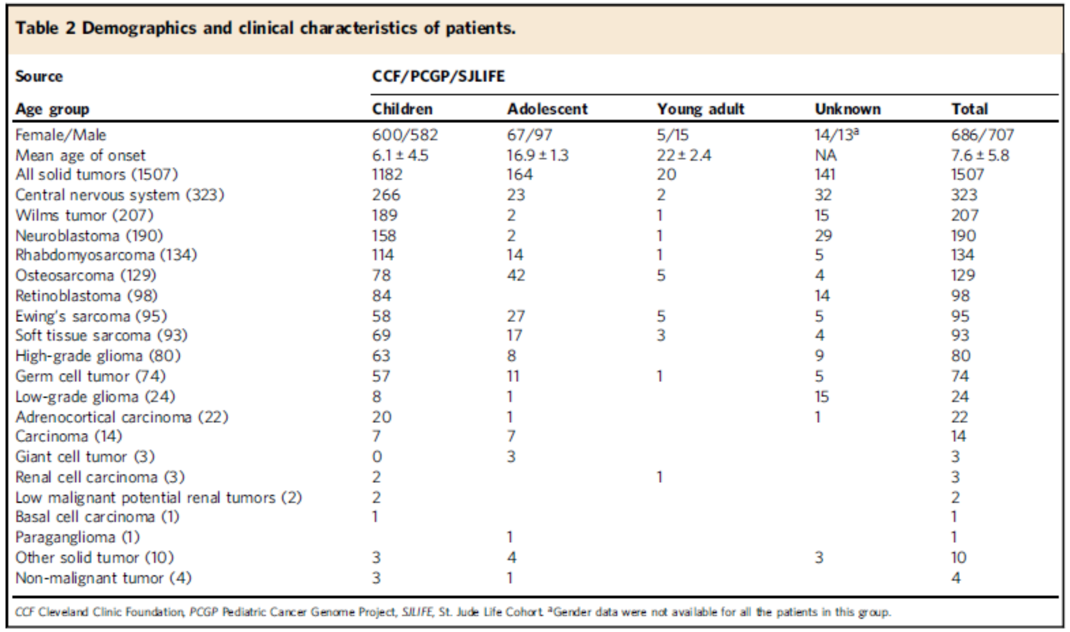
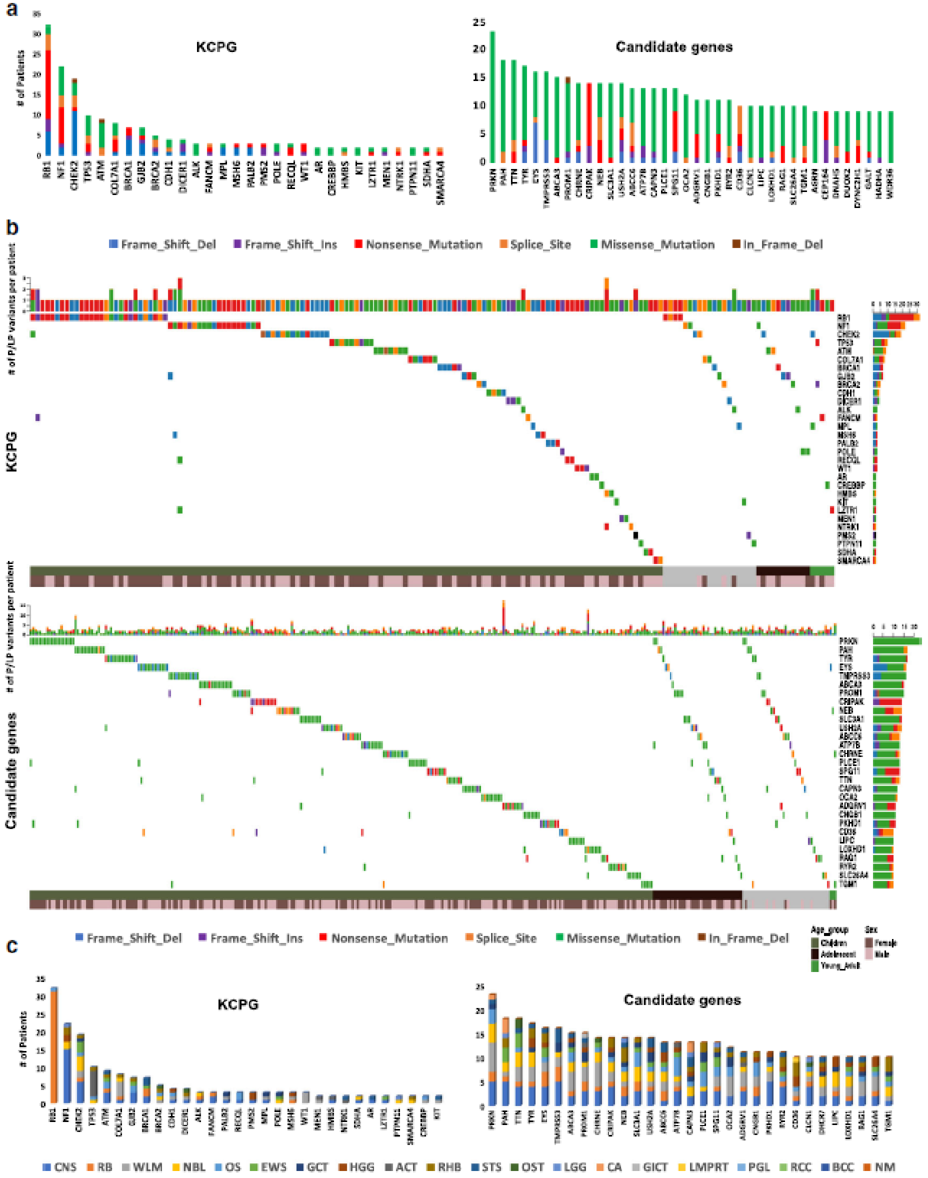


Table 2 Demographics and clinical characteristics of patients.

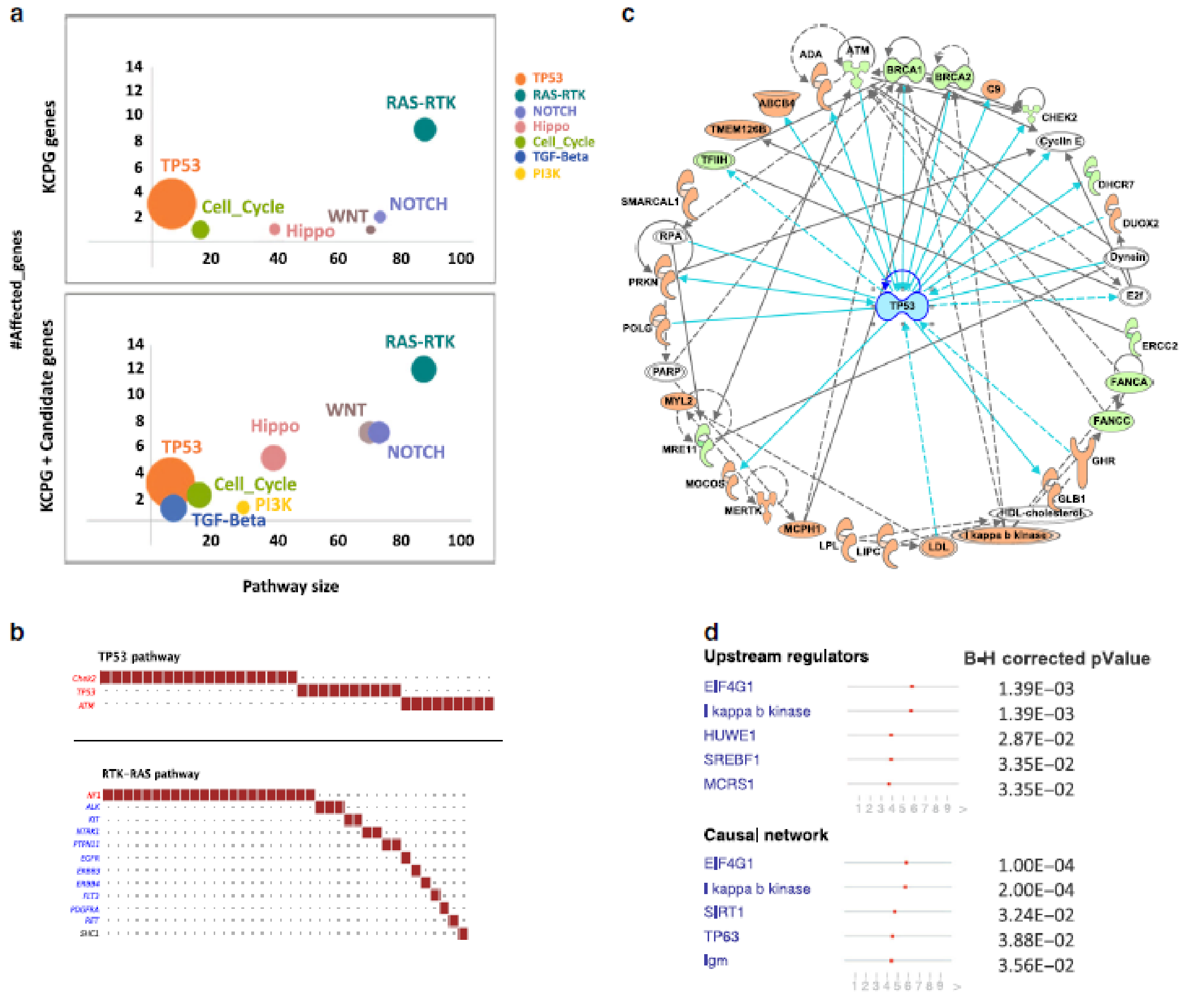
Source	**CCF/PCGP/SJLIFE**				
Age group	**Children**	**Adolescent**	**Young adult**	**Unknown**	**Total**
Female/Male	600/582	67/97	5/15	14/13ᵃ	686/707
Mean age of onset	6.1 ± 4.5	16.9 ± 1.3	22 ± 2.4	NA	7.6 ± 5.8
All solid tumors (1507)	1182	164	20	141	1507
Central nervous system (323)	266	23	2	32	323
Wilms tumor (207)	189	2	1	15	207
Neuroblastoma (190)	158	2	1	29	190
Rhabdomyosarcoma (134)	114	14	1	5	134
Osteosarcoma (129)	78	42	5	4	129
Retinoblastoma (98)	84			14	98
Ewing's sarcoma (95)	58	27	5	5	95
Soft tissue sarcoma (93)	69	17	3	4	93
High-grade glioma (80)	63	8		9	80
Germ cell tumor (74)	57	11	1	5	74
Low-grade glioma (24)	8	1		15	24
Adrenocortical carcinoma (22)	20	1		1	22
Carcinoma (14)	7	7			14
Giant cell tumor (3)	0	3			3
Renal cell carcinoma (3)	2		1		3
Low malignant potential renal tumors (2)	2				2
Basal cell carcinoma (1)	1				1
Paraganglioma (1)		1			1
Other solid tumor (10)	3	4		3	10
Non-malignant tumor (4)	3	1			4

CCF Cleveland Clinic Foundation, *PCGP* Pediatric Cancer Genome Project, *SJLIFE*, St. Jude Life Cohort ᵃGender data were not available for all the patients in this group.

Fig. 2 Distribution of germline pathogenic/likely pathogenic (P/LP) mutations in children, adolescents, and young adults (C-AYA) with solid tumors

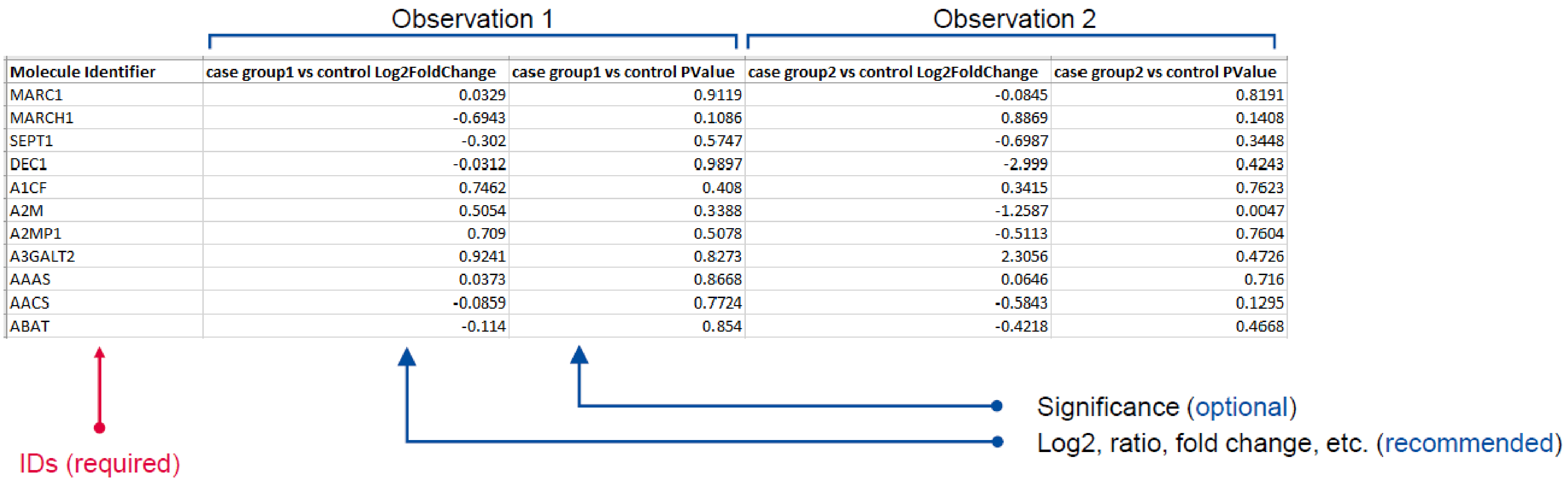


Pathway analysis results



ig. 4 Pathway analysis of altered genes with germline pathogenic/likely pathogenic (P/LP) variants in children, adolescents, and young adults C-AYA) with solid tumors. a Affected pathways based on altered genes with P/LP germline variants. Top panel: only known cancer-predisposing genes KCPG), lower panel: a combination of all KCPGs and candidate genes. Size of the circles increases as the fraction affected increases. **b** Genes mutated in P53 (top panel) and RAS-RTK (lower panel) pathways, and the number of patients affected in our cohort. Red font: tumor suppressor genes; blue font: ncogenes. **c** Top network, predicted by Ingenuity Pathway Analysis (IPA), based on all the KCPG (green color) and candidate genes (salmon color) with at east four P/LP variants in our C-AYA patients with solid tumors (right-tailed Fisher's exact test $P = 1 \times 10^{-42}$). **d** Eukaryotic Translation Initiation Factor 4 Gamma 1 (EIF4G1, B-H corrected $P = 1.39 \times 10^{-3}$) and I kappa b kinase (IκB kinase, B-H corrected $P = 1.39 \times 10^{-3}$) predicted to be the top upstream egulators/causal network based on our IPA analysis. Right-tailed Fisher's exact test was used, and Benjamini-Hochberg (B-H) P value correction erformed to reduce the false discovery rate (FDR).

Upload dataset format



Observation 1

Observation 2

Molecule Identifier	case group1 vs control Log2FoldChange	case group1 vs control PValue	case group2 vs control Log2FoldChange	case group2 vs control PValue
MARC1	0.0329	0.9119	-0.0845	0.8191
MARCH1	-0.6943	0.1086	0.8869	0.1408
SEPT1	-0.302	0.5747	-0.6987	0.3448
DEC1	-0.0312	0.9897	-2.999	0.4243
A1CF	0.7462	0.408	0.3415	0.7623
A2M	0.5054	0.3388	-1.2587	0.0047
A2MP1	0.709	0.5078	-0.5113	0.7604
A3GALT2	0.9241	0.8273	2.3056	0.4726
AAAS	0.0373	0.8668	0.0646	0.716
AACS	-0.0859	0.7724	-0.5843	0.1295
ABAT	-0.114	0.854	-0.4218	0.4668

IDs (required)

Significance (optional)

Log2, ratio, fold change, etc. (recommended)

Common identifier types

- RNA/scRNA-seq: Ensembl, Gene symbols (Entrez or Hugo
- Proteomics: UniProt, GenPept (Entrez or HUGO)
- Metabolomics: KEGG, CAS registry, HMDB, PubChem.

Accepted file formats

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

IDs are the only **required** column

Change values are needed
to calculate activity predictions

Supported Identifiers for Data Upload

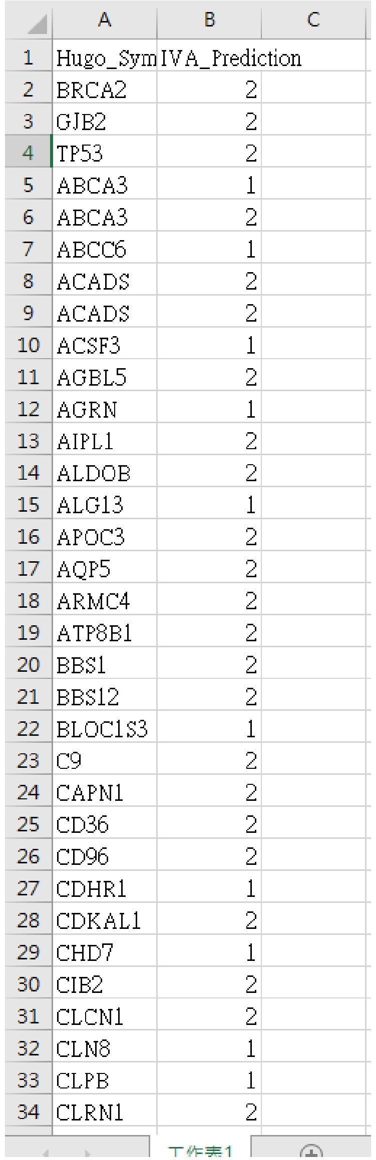
Get more complete mapping during dataset upload!

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

Variants upload format

Gene symbol

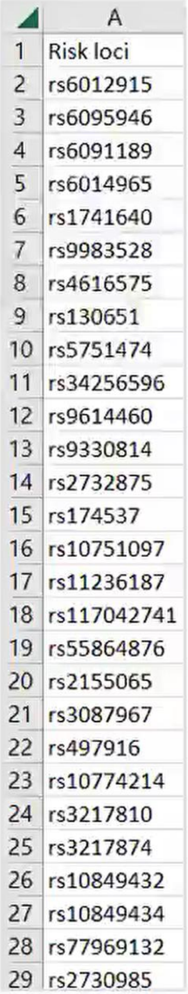
ACMG value



	A	B	C
1	Hugo_Sym	IVA_Prediction	
2	BRCA2	2	
3	GJB2	2	
4	TP53	2	
5	ABCA3	1	
6	ABCA3	2	
7	ABCC6	1	
8	ACADS	2	
9	ACADS	2	
10	ACSF3	1	
11	AGBL5	2	
12	AGRN	1	
13	AIPL1	2	
14	ALDOB	2	
15	ALG13	1	
16	APOC3	2	
17	AQP5	2	
18	ARMC4	2	
19	ATP8B1	2	
20	BBS1	2	
21	BBS12	2	
22	BLOC1S3	1	
23	C9	2	
24	CAPN1	2	
25	CD36	2	
26	CD96	2	
27	CDHR1	1	
28	CDKAL1	2	
29	CHD7	1	
30	CIB2	2	
31	CLCN1	2	
32	CLN8	1	
33	CLPB	1	
34	CLRN1	2	

Allowable values are:
- -2 benign
- -1 likely benign
- 0 uncertain significance
- 1 likely pathogenic
- 2 pathogenic

GWAS rs id

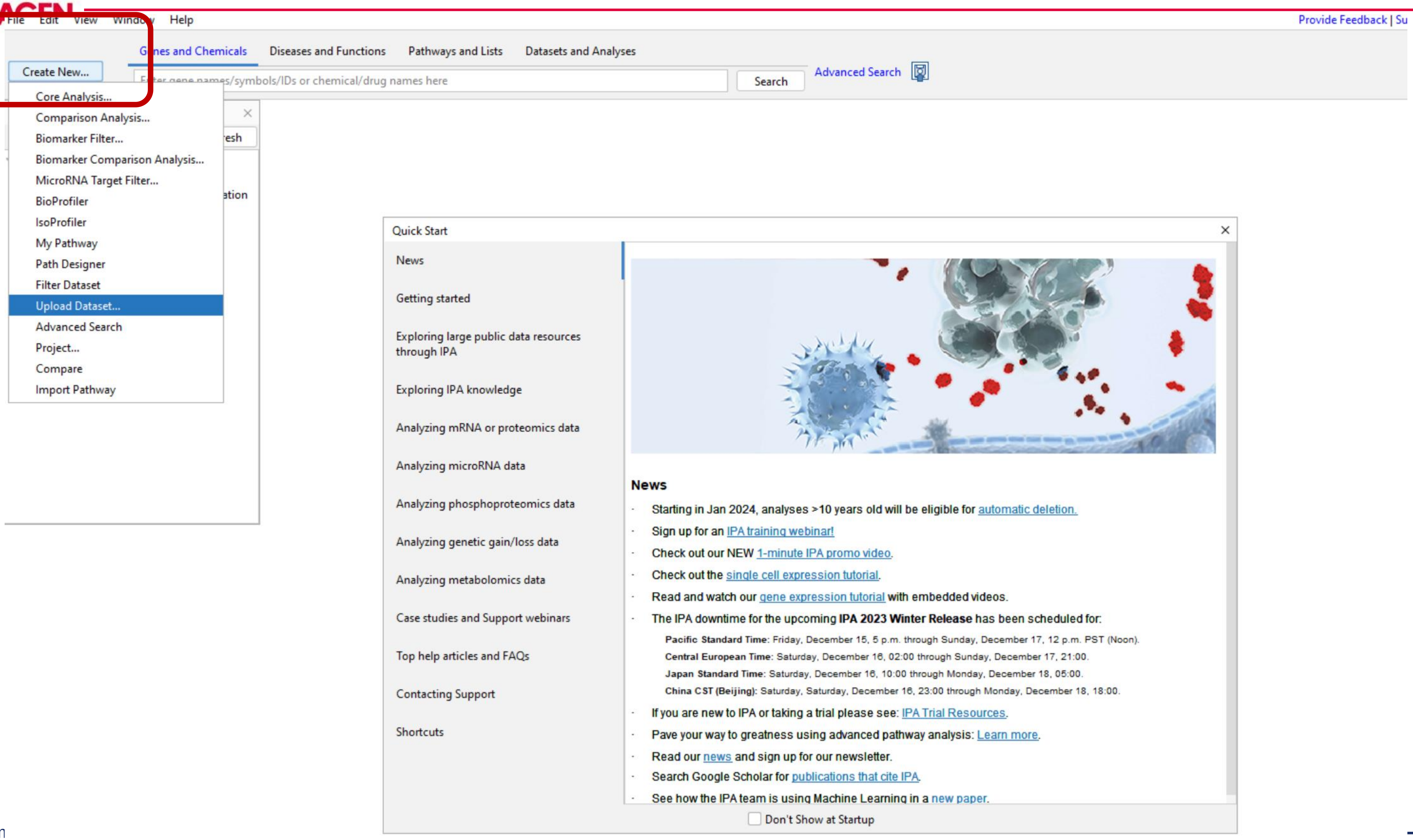


	A
1	Risk loci
2	rs6012915
3	rs6095946
4	rs6091189
5	rs6014965
6	rs1741640
7	rs9983528
8	rs4616575
9	rs130651
10	rs5751474
11	rs34256596
12	rs9614460
13	rs9330814
14	rs2732875
15	rs174537
16	rs10751097
17	rs11236187
18	rs117042741
19	rs55864876
20	rs2155065
21	rs3087967
22	rs497916
23	rs10774214
24	rs3217810
25	rs3217874
26	rs10849432
27	rs10849434
28	rs77969132
29	rs2730985

Multiple ID columns

	A	B
1	Risk loci	Mapped gene
2	rs6012915	LINC01271
3	rs6095946	COX6CP2
4	rs6091189	RIPOR3
5	rs6014965	BMP7
6	rs1741640	LAMA5
7	rs9983528	PCNT
8	rs4616575	ZNRF3
9	rs130651	PDGFB
10	rs5751474	SCUBE1
11	rs34256596	LINC01639
12	rs9614460	SMC1B
13	rs9330814	WNT7B
14	rs2732875	SHROOM2
15	rs174537	MYRF
16	rs10751097	ANO1
17	rs11236187	POLD3
18	rs117042741	XRRA1

Upload dataset



News

- Starting in Jan 2024, analyses >10 years old will be eligible for automatic deletion.
- Sign up for an IPA training webinar!
- Check out our NEW 1-minute IPA promo video.
- Check out the single cell expression tutorial.
- Read and watch our gene expression tutorial with embedded videos.
- The IPA downtime for the upcoming **IPA 2023 Winter Release** has been scheduled for:

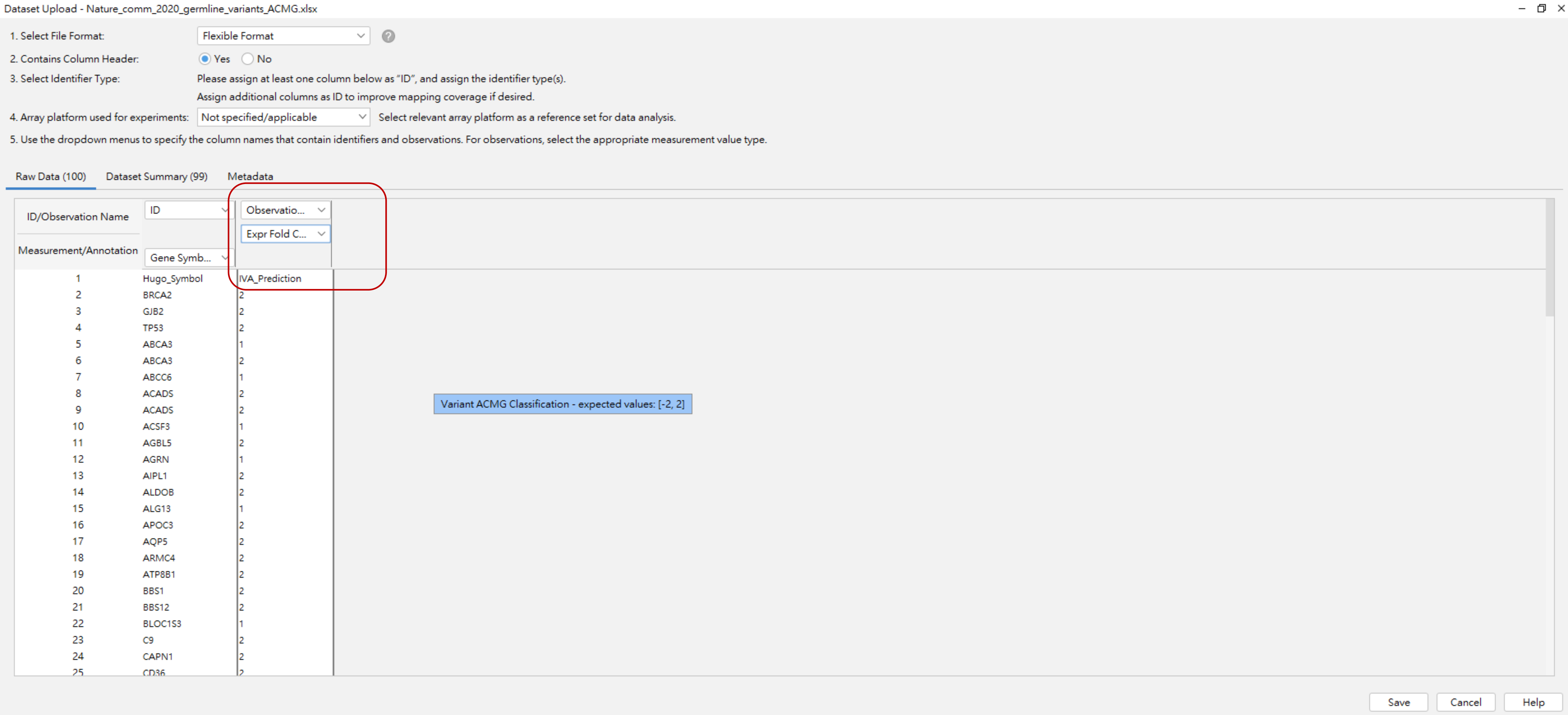
  Pacific Standard Time: Friday, December 15, 5 p.m. through Sunday, December 17, 12 p.m. PST (Noon).

  Central European Time: Saturday, December 16, 02:00 through Sunday, December 17, 21:00.

  Japan Standard Time: Saturday, December 16, 10:00 through Monday, December 18, 05:00.

  China CST (Beijing): Saturday, Saturday, December 16, 23:00 through Monday, December 18, 18:00.
- If you are new to IPA or taking a trial please see: IPA Trial Resources.
- Pave your way to greatness using advanced pathway analysis: Learn more.
- Read our news and sign up for our newsletter.
- Search Google Scholar for publications that cite IPA.
- See how the IPA team is using Machine Learning in a new paper.

Sam

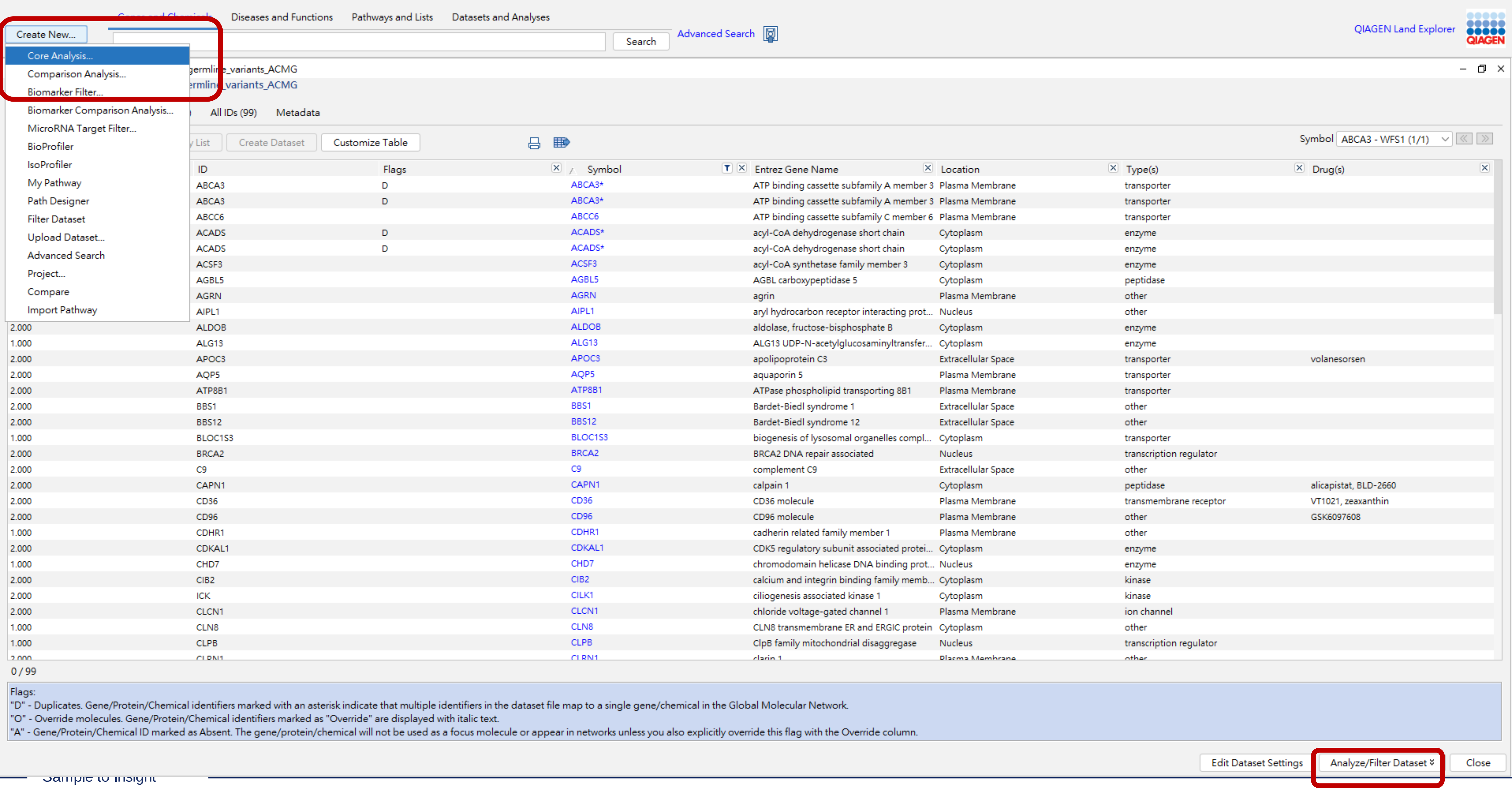


Dataset Upload - Nature_comm_2020_germline_variants_ACMG.xlsx

1. Select File Format: Flexible Format
2. Contains Column Header: ● Yes ○ No
3. Select Identifier Type: Please assign at least one column below as "ID", and assign the identifier type(s). Assign additional columns as ID to improve mapping coverage if desired.
4. Array platform used for experiments: Not specified/applicable Select relevant array platform as a reference set for data analysis.
5. Use the dropdown menus to specify the column names that contain identifiers and observations. For observations, select the appropriate measurement value type.

ID/Observation Name	ID	Observatio...
Measurement/Annotation	Gene Symb...	Expr Fold C...
1	Hugo_Symbol	IVA_Prediction
2	BRCA2	2
3	GJB2	2
4	TP53	2
5	ABCA3	1
6	ABCA3	2
7	ABCC6	1
8	ACADS	2
9	ACADS	2
10	ACSF3	1
11	AGBL5	2
12	AGRN	1
13	AIPL1	2
14	ALDOB	2
15	ALG13	1
16	APOC3	2
17	AQP5	2
18	ARMC4	2
19	ATP8B1	2
20	BBS1	2
21	BBS12	2
22	BLOC1S3	1
23	C9	2
24	CAPN1	2
25	CD36	2

Variant ACMG Classification - expected values: [-2, 2]

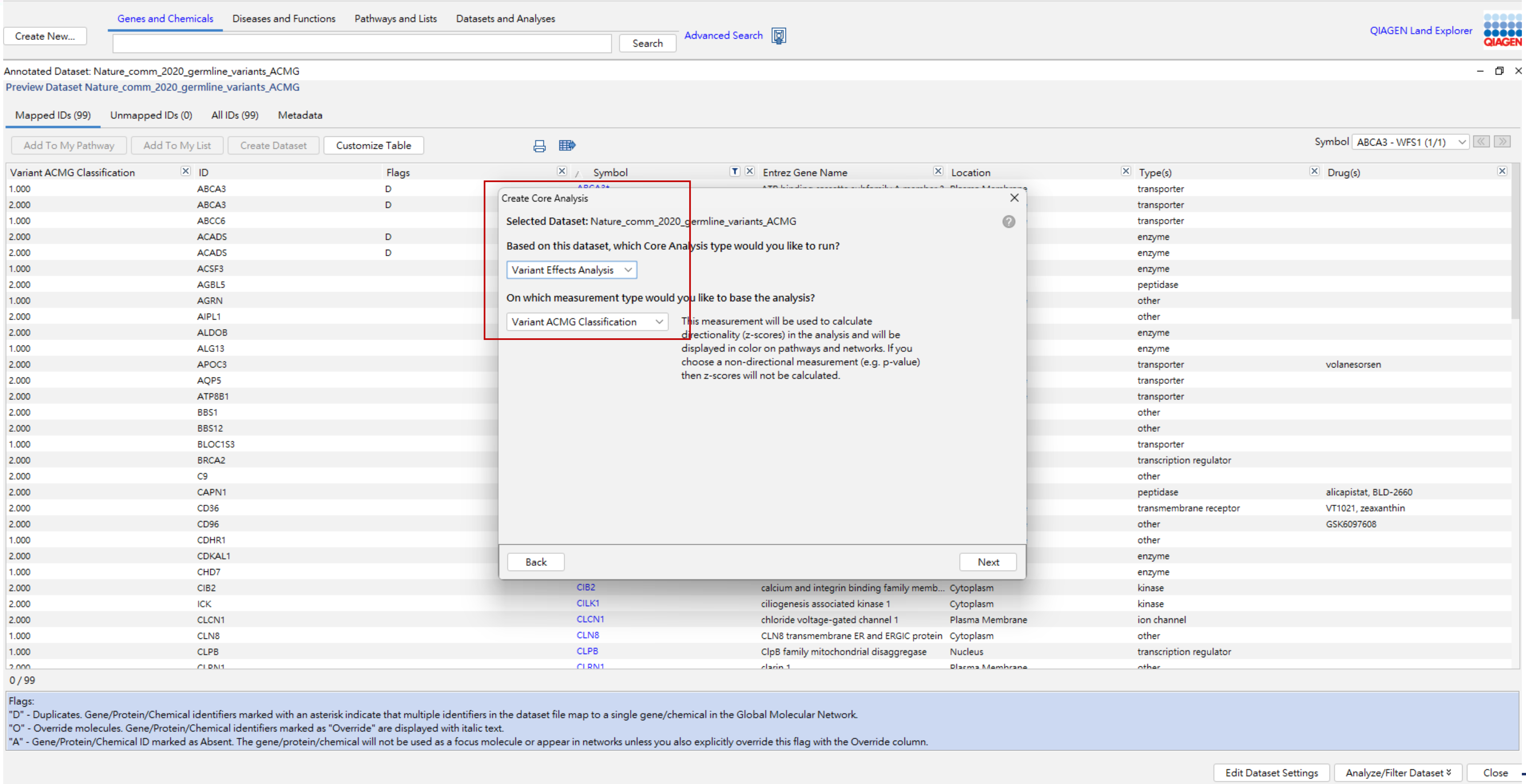


	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
	ABCA3	D	ABCA3*	ATP binding cassette subfamily A member 3	Plasma Membrane	transporter	
	ABCA3	D	ABCA3*	ATP binding cassette subfamily A member 3	Plasma Membrane	transporter	
	ABCC6		ABCC6	ATP binding cassette subfamily C member 6	Plasma Membrane	transporter	
	ACADS	D	ACADS*	acyl-CoA dehydrogenase short chain	Cytoplasm	enzyme	
	ACADS	D	ACADS*	acyl-CoA dehydrogenase short chain	Cytoplasm	enzyme	
	ACSF3		ACSF3	acyl-CoA synthetase family member 3	Cytoplasm	enzyme	
	AGBL5		AGBL5	AGBL carboxypeptidase 5	Cytoplasm	peptidase	
	AGRN		AGRN	agrin	Plasma Membrane	other	
	AIPL1		AIPL1	aryl hydrocarbon receptor interacting prot...	Nucleus	other	
2.000	ALDOB		ALDOB	aldolase, fructose-bisphosphate B	Cytoplasm	enzyme	
1.000	ALG13		ALG13	ALG13 UDP-N-acetylglucosaminyltransfer...	Cytoplasm	enzyme	
2.000	APOC3		APOC3	apolipoprotein C3	Extracellular Space	transporter	volanesorsen
2.000	AQP5		AQP5	aquaporin 5	Plasma Membrane	transporter	
2.000	ATP8B1		ATP8B1	ATPase phospholipid transporting 8B1	Plasma Membrane	transporter	
2.000	BBS1		BBS1	Bardet-Biedl syndrome 1	Extracellular Space	other	
2.000	BBS12		BBS12	Bardet-Biedl syndrome 12	Extracellular Space	other	
1.000	BLOC1S3		BLOC1S3	biogenesis of lysosomal organelles compl...	Cytoplasm	transporter	
2.000	BRCA2		BRCA2	BRCA2 DNA repair associated	Nucleus	transcription regulator	
2.000	C9		C9	complement C9	Extracellular Space	other	
2.000	CAPN1		CAPN1	calpain 1	Cytoplasm	peptidase	alicapistat, BLD-2660
2.000	CD36		CD36	CD36 molecule	Plasma Membrane	transmembrane receptor	VT1021, zeaxanthin
2.000	CD96		CD96	CD96 molecule	Plasma Membrane	other	GSK6097608
1.000	CDHR1		CDHR1	cadherin related family member 1	Plasma Membrane	other	
2.000	CDKAL1		CDKAL1	CDK5 regulatory subunit associated protei...	Cytoplasm	enzyme	
1.000	CHD7		CHD7	chromodomain helicase DNA binding prot...	Nucleus	enzyme	
2.000	CIB2		CIB2	calcium and integrin binding family memb...	Cytoplasm	kinase	
2.000	ICK		CILK1	ciliogenesis associated kinase 1	Cytoplasm	kinase	
2.000	CLCN1		CLCN1	chloride voltage-gated channel 1	Plasma Membrane	ion channel	
1.000	CLN8		CLN8	CLN8 transmembrane ER and ERGIC protein	Cytoplasm	other	
1.000	CLPB		CLPB	ClpB family mitochondrial disaggregase	Nucleus	transcription regulator	
2.000	CLRN1		CLRN1	clarin 1	Plasma Membrane	other	

0 / 99

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.

Upload dataset



Annotated Dataset: Nature_comm_2020_germline_variants_ACMG

Preview Dataset Nature_comm_2020_germline_variants_ACMG

Symbol: ABCA3 - WFS1 (1/1)

Variant ACMG Classification	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
1.000	ABCA3	D				transporter	
2.000	ABCA3	D				transporter	
1.000	ABCC6					transporter	
2.000	ACADS	D				enzyme	
2.000	ACADS	D				enzyme	
1.000	ACSF3					enzyme	
2.000	AGBL5					peptidase	
1.000	AGRN					other	
2.000	AIPL1					other	
2.000	ALDOB					enzyme	
1.000	ALG13					enzyme	
2.000	APOC3					transporter	volanesorsen
2.000	AQP5					transporter	
2.000	ATP8B1					transporter	
2.000	BBS1					other	
2.000	BBS12					other	
1.000	BLOC1S3					transporter	
2.000	BRCA2					transcription regulator	
2.000	C9					other	
2.000	CAPN1					peptidase	alicapistat, BLD-2660
2.000	CD36					transmembrane receptor	VT1021, zeaxanthin
2.000	CD96					other	GSK6097608
1.000	CDHR1					other	
2.000	CDKAL1					enzyme	
1.000	CHD7					enzyme	
2.000	CIB2		CIB2	calcium and integrin binding family memb...	Cytoplasm	kinase	
2.000	ICK		CILK1	ciliogenesis associated kinase 1	Cytoplasm	kinase	
2.000	CLCN1		CLCN1	chloride voltage-gated channel 1	Plasma Membrane	ion channel	
1.000	CLN8		CLN8	CLN8 transmembrane ER and ERGIC protein	Cytoplasm	other	
1.000	CLPB		CLPB	ClpB family mitochondrial disaggregase	Nucleus	transcription regulator	
2.000	CLRN1		CLRN1	clarin 1	Plasma Membrane	other	

0 / 99

Create Core Analysis

Selected Dataset: Nature_comm_2020_germline_variants_ACMG

Based on this dataset, which Core Analysis type would you like to run?

Variant Effects Analysis

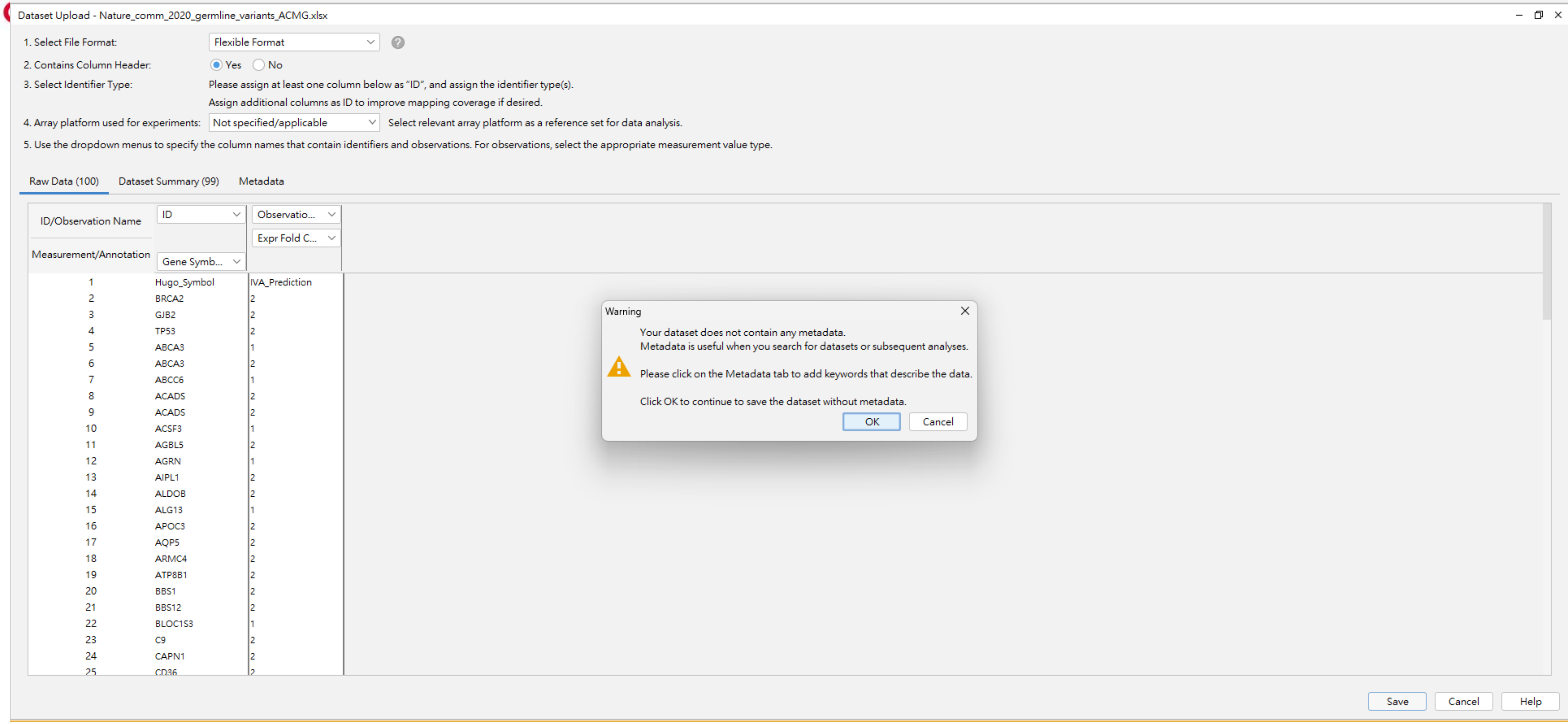
On which measurement type would you like to base the analysis?

Variant ACMG Classification

This measurement will be used to calculate directionality (z-scores) in the analysis and will be displayed in color on pathways and networks. If you choose a non-directional measurement (e.g. p-value) then z-scores will not be calculated.

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.

Upload dataset



Dataset Upload - Nature_comm_2020_germline_variants_ACMG.xlsx

1. Select File Format: Flexible Format
2. Contains Column Header: ● Yes ○ No
3. Select Identifier Type: Please assign at least one column below as "ID", and assign the identifier type(s). Assign additional columns as ID to improve mapping coverage if desired.
4. Array platform used for experiments: Not specified/applicable — Select relevant array platform as a reference set for data analysis.
5. Use the dropdown menus to specify the column names that contain identifiers and observations. For observations, select the appropriate measurement value type.

ID/Observation Name Measurement/Annotation	ID Gene Symb...	Observatio... Expr Fold C...
1	Hugo_Symbol	IVA_Prediction
2	BRCA2	2
3	GJB2	2
4	TP53	2
5	ABCA3	1
6	ABCA3	2
7	ABCC6	1
8	ACADS	2
9	ACADS	2
10	ACSF3	1
11	AGBL5	2
12	AGRN	1
13	AIPL1	2
14	ALDOB	2
15	ALG13	1
16	APOC3	2
17	AQP5	2
18	ARMC4	2
19	ATP8B1	2
20	BBS1	2
21	BBS12	2
22	BLOC1S3	1
23	C9	2
24	CAPN1	2
25	CD36	2

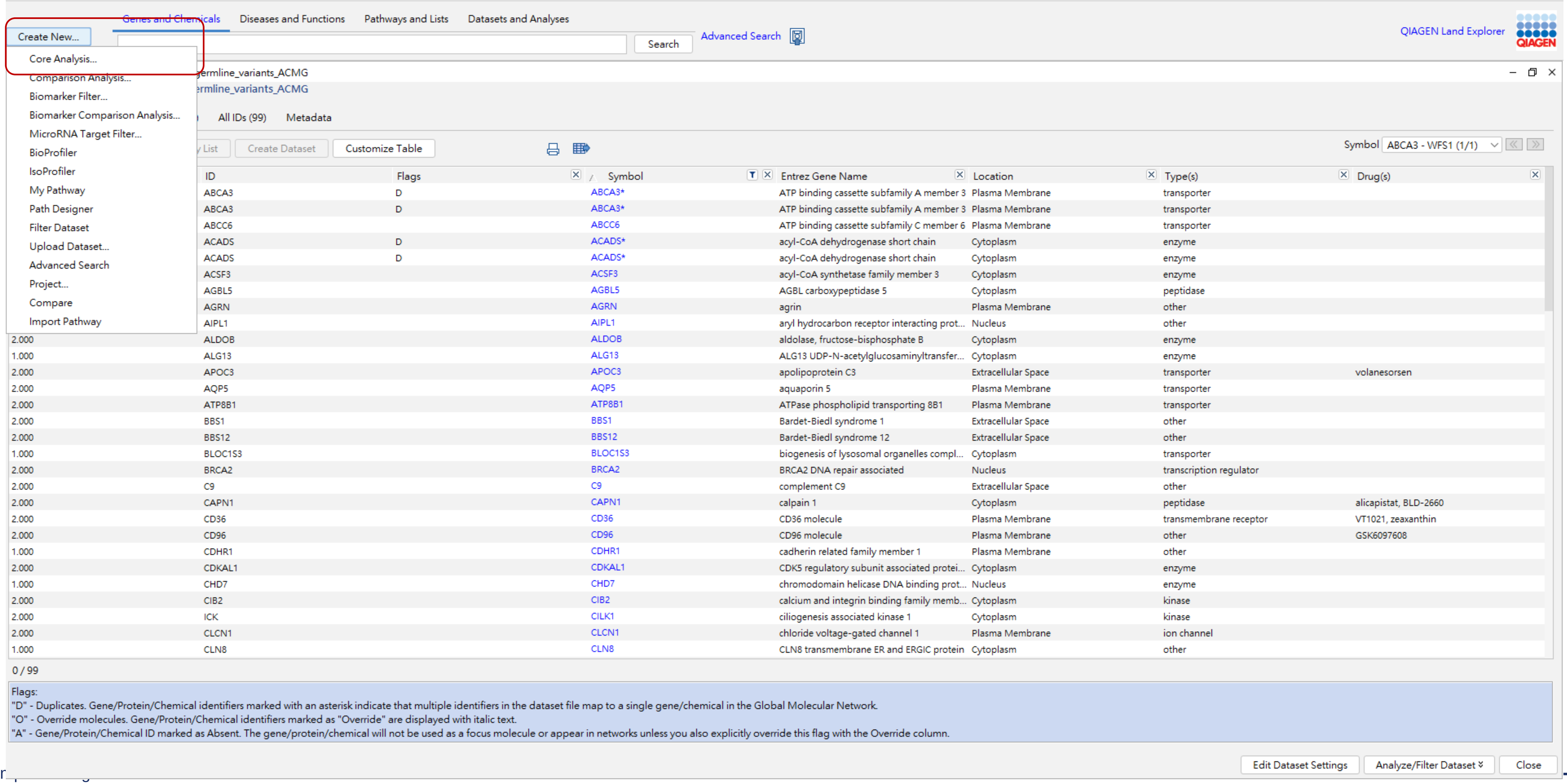
Warning

Your dataset does not contain any metadata.
Metadata is useful when you search for datasets or subsequent analyses.

Please click on the Metadata tab to add keywords that describe the data.

Click OK to continue to save the dataset without metadata.

Core analysis



	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
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	ABCA3	D	ABCA3*	ATP binding cassette subfamily A member 3	Plasma Membrane	transporter	
	ABCC6		ABCC6	ATP binding cassette subfamily C member 6	Plasma Membrane	transporter	
	ACADS	D	ACADS*	acyl-CoA dehydrogenase short chain	Cytoplasm	enzyme	
	ACADS	D	ACADS*	acyl-CoA dehydrogenase short chain	Cytoplasm	enzyme	
	ACSF3		ACSF3	acyl-CoA synthetase family member 3	Cytoplasm	enzyme	
	AGBL5		AGBL5	AGBL carboxypeptidase 5	Cytoplasm	peptidase	
	AGRN		AGRN	agrin	Plasma Membrane	other	
	AIPL1		AIPL1	aryl hydrocarbon receptor interacting prot...	Nucleus	other	
2.000	ALDOB		ALDOB	aldolase, fructose-bisphosphate B	Cytoplasm	enzyme	
1.000	ALG13		ALG13	ALG13 UDP-N-acetylglucosaminyltransfer...	Cytoplasm	enzyme	
2.000	APOC3		APOC3	apolipoprotein C3	Extracellular Space	transporter	volanesorsen
2.000	AQP5		AQP5	aquaporin 5	Plasma Membrane	transporter	
2.000	ATP8B1		ATP8B1	ATPase phospholipid transporting 8B1	Plasma Membrane	transporter	
2.000	BBS1		BBS1	Bardet-Biedl syndrome 1	Extracellular Space	other	
2.000	BBS12		BBS12	Bardet-Biedl syndrome 12	Extracellular Space	other	
1.000	BLOC1S3		BLOC1S3	biogenesis of lysosomal organelles compl...	Cytoplasm	transporter	
2.000	BRCA2		BRCA2	BRCA2 DNA repair associated	Nucleus	transcription regulator	
2.000	C9		C9	complement C9	Extracellular Space	other	
2.000	CAPN1		CAPN1	calpain 1	Cytoplasm	peptidase	alicapistat, BLD-2660
2.000	CD36		CD36	CD36 molecule	Plasma Membrane	transmembrane receptor	VT1021, zeaxanthin
2.000	CD96		CD96	CD96 molecule	Plasma Membrane	other	GSK6097608
1.000	CDHR1		CDHR1	cadherin related family member 1	Plasma Membrane	other	
2.000	CDKAL1		CDKAL1	CDK5 regulatory subunit associated protei...	Cytoplasm	enzyme	
1.000	CHD7		CHD7	chromodomain helicase DNA binding prot...	Nucleus	enzyme	
2.000	CIB2		CIB2	calcium and integrin binding family memb...	Cytoplasm	kinase	
2.000	ICK		CILK1	ciliogenesis associated kinase 1	Cytoplasm	kinase	
2.000	CLCN1		CLCN1	chloride voltage-gated channel 1	Plasma Membrane	ion channel	
1.000	CLN8		CLN8	CLN8 transmembrane ER and ERGIC protein	Cytoplasm	other	

0 / 99

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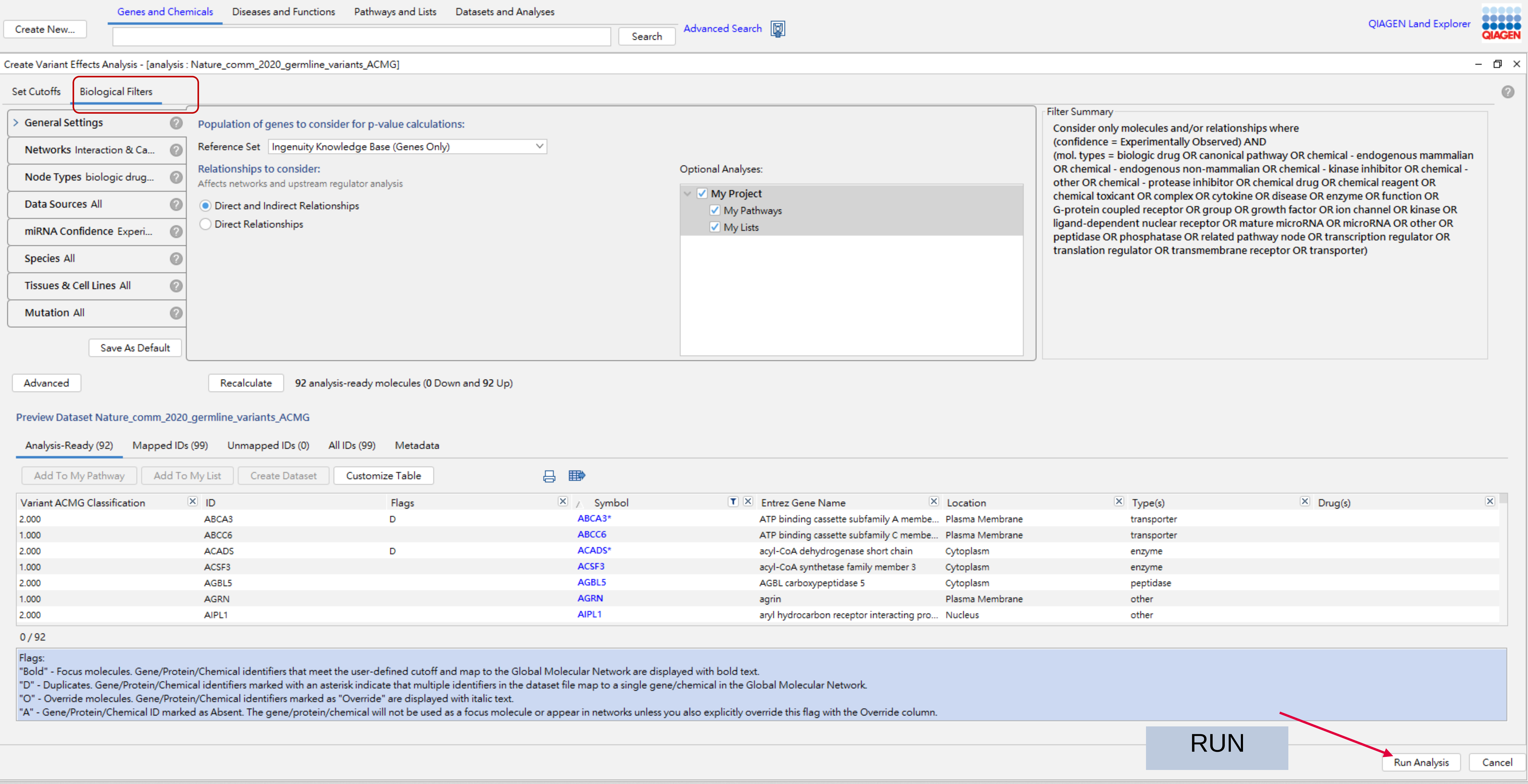
"A" - Gene/Protein/Chemical ID marked as Absent. The gene/protein/chemical will not be used as a focus molecule or appear in networks unless you also explicitly override this flag with the Override column.



Create Variant Effects Analysis - [analysis : Nature_comm_2020_germline_variants_ACMG]

General Settings

Networks Interaction & Ca...

Node Types biologic drug...

Data Sources All

miRNA Confidence Experi...

Species All

Tissues & Cell Lines All

Mutation All

Population of genes to consider for p-value calculations:

Reference Set: Ingenuity Knowledge Base (Genes Only)

Relationships to consider:

Affects networks and upstream regulator analysis

● Direct and Indirect Relationships

○ Direct Relationships

Optional Analyses:

- ☑ My Project
  - ☑ My Pathways
  - ☑ My Lists

Filter Summary

Consider only molecules and/or relationships where (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)

92 analysis-ready molecules (0 Down and 92 Up)

Preview Dataset Nature_comm_2020_germline_variants_ACMG

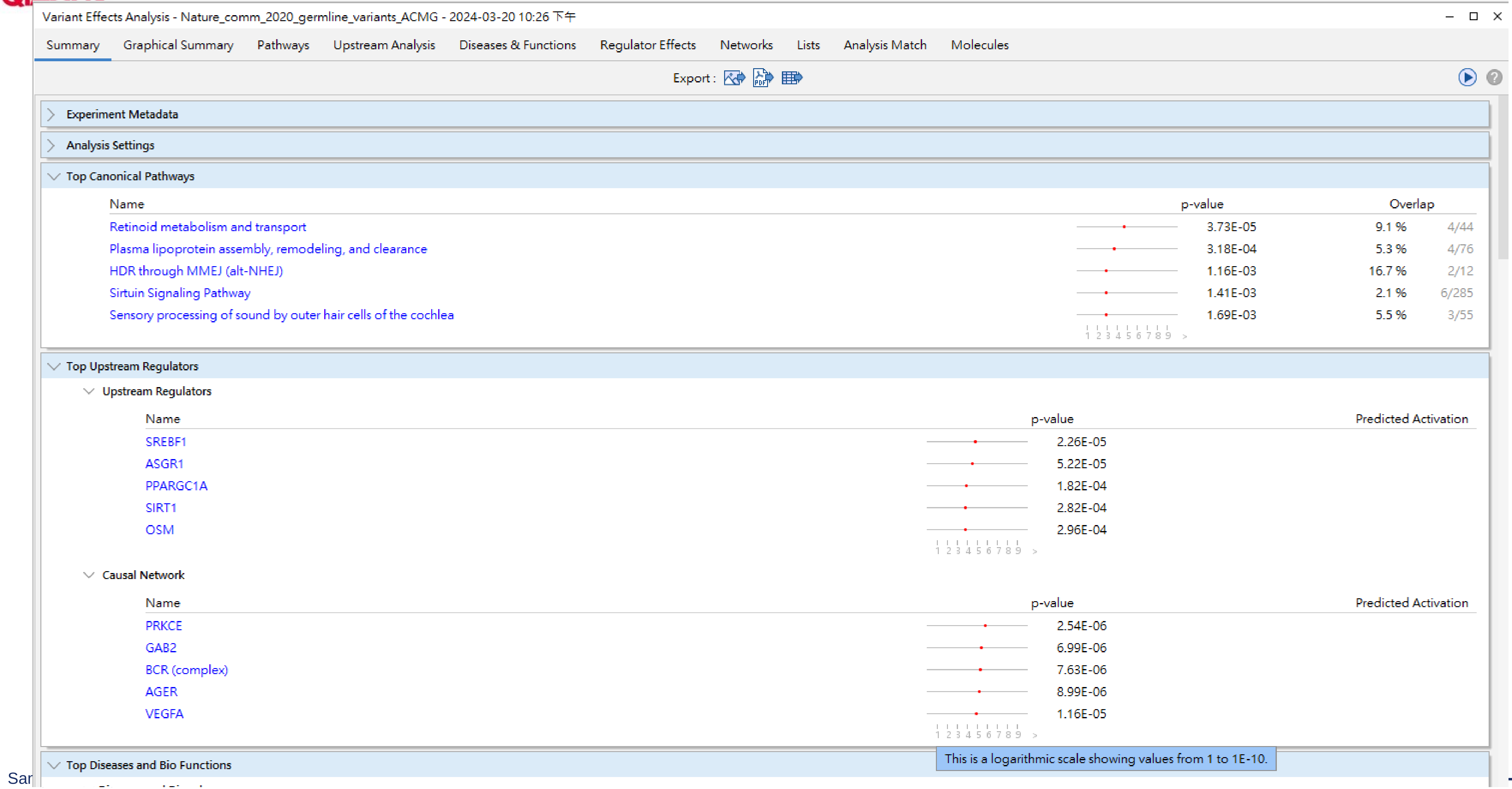
Variant ACMG Classification	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
2.000	ABCA3	D	ABCA3*	ATP binding cassette subfamily A membe...	Plasma Membrane	transporter	
1.000	ABCC6		ABCC6	ATP binding cassette subfamily C membe...	Plasma Membrane	transporter	
2.000	ACADS	D	ACADS*	acyl-CoA dehydrogenase short chain	Cytoplasm	enzyme	
1.000	ACSF3		ACSF3	acyl-CoA synthetase family member 3	Cytoplasm	enzyme	
2.000	AGBL5		AGBL5	AGBL carboxypeptidase 5	Cytoplasm	peptidase	
1.000	AGRN		AGRN	agrin	Plasma Membrane	other	
2.000	AIPL1		AIPL1	aryl hydrocarbon receptor interacting pro...	Nucleus	other	

0 / 92

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.
"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.

RUN

Core analysis report



Variant Effects Analysis - Nature_comm_2020_germline_variants_ACMG - 2024-03-20 10:26 下午

Experiment Metadata

Analysis Settings

Top Canonical Pathways

Name	p-value	Overlap	
Retinoid metabolism and transport	3.73E-05	9.1 %	4/44
Plasma lipoprotein assembly, remodeling, and clearance	3.18E-04	5.3 %	4/76
HDR through MMEJ (alt-NHEJ)	1.16E-03	16.7 %	2/12
Sirtuin Signaling Pathway	1.41E-03	2.1 %	6/285
Sensory processing of sound by outer hair cells of the cochlea	1.69E-03	5.5 %	3/55

Top Upstream Regulators

Upstream Regulators

Name	p-value	Predicted Activation
SREBF1	2.26E-05	
ASGR1	5.22E-05	
PPARGC1A	1.82E-04	
SIRT1	2.82E-04	
OSM	2.96E-04	

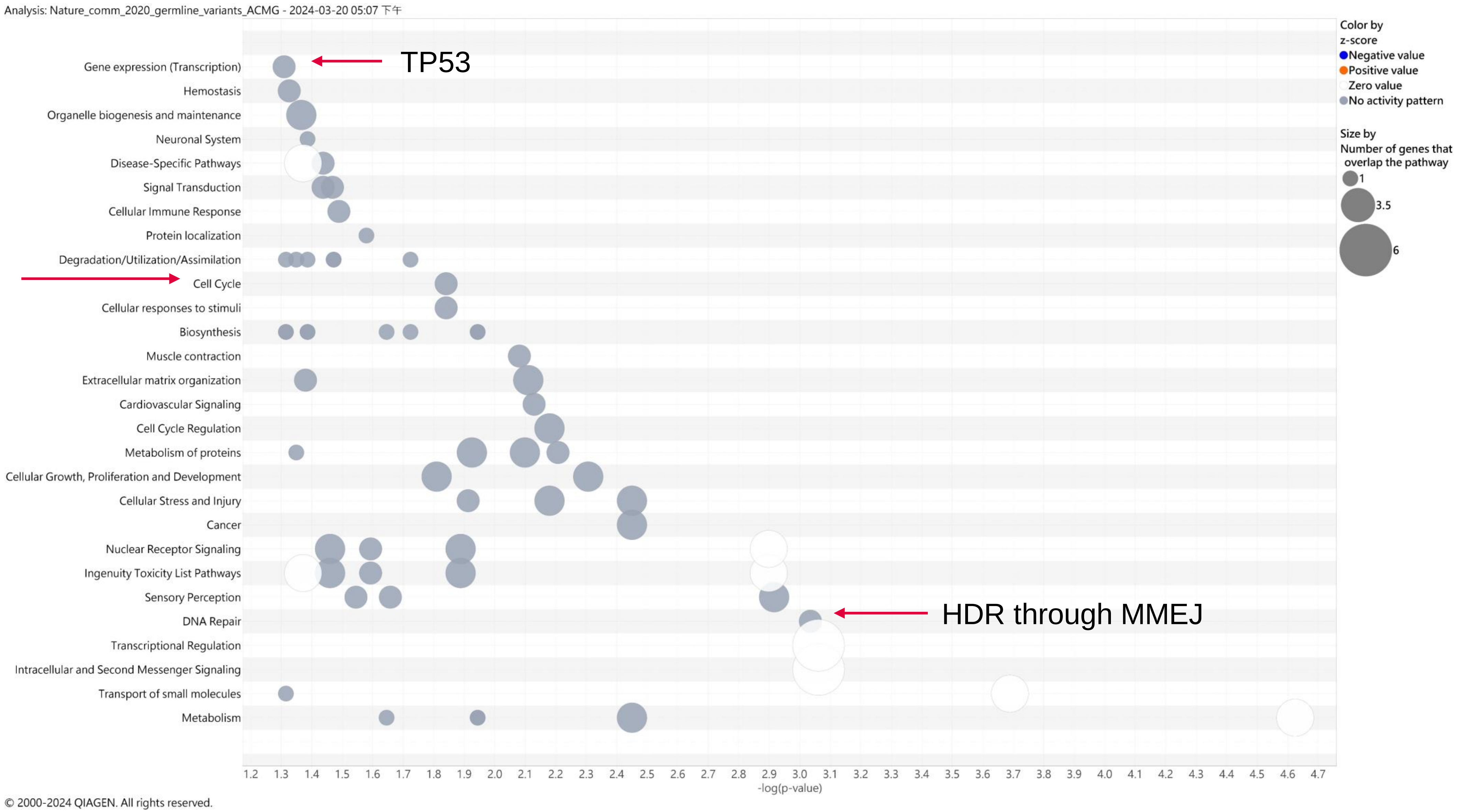
Causal Network

Name	p-value	Predicted Activation
PRKCE	2.54E-06	
GAB2	6.99E-06	
BCR (complex)	7.63E-06	
AGER	8.99E-06	
VEGFA	1.16E-05	

This is a logarithmic scale showing values from 1 to 1E-10.

Top Diseases and Bio Functions

Pathway bubble plot

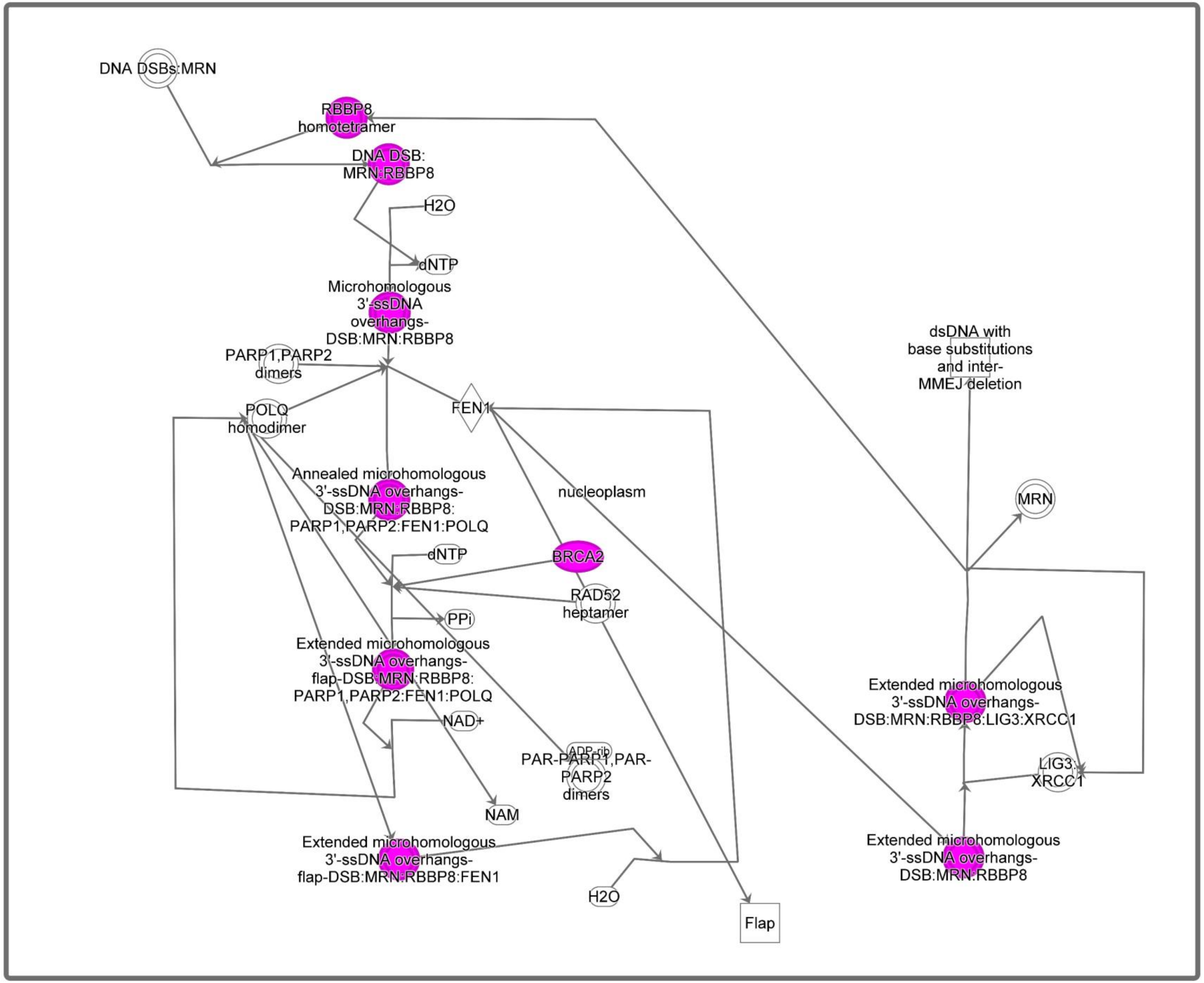


Analysis: Nature_comm_2020_germline_variants_ACMG - 2024-03-20 05:07 下午

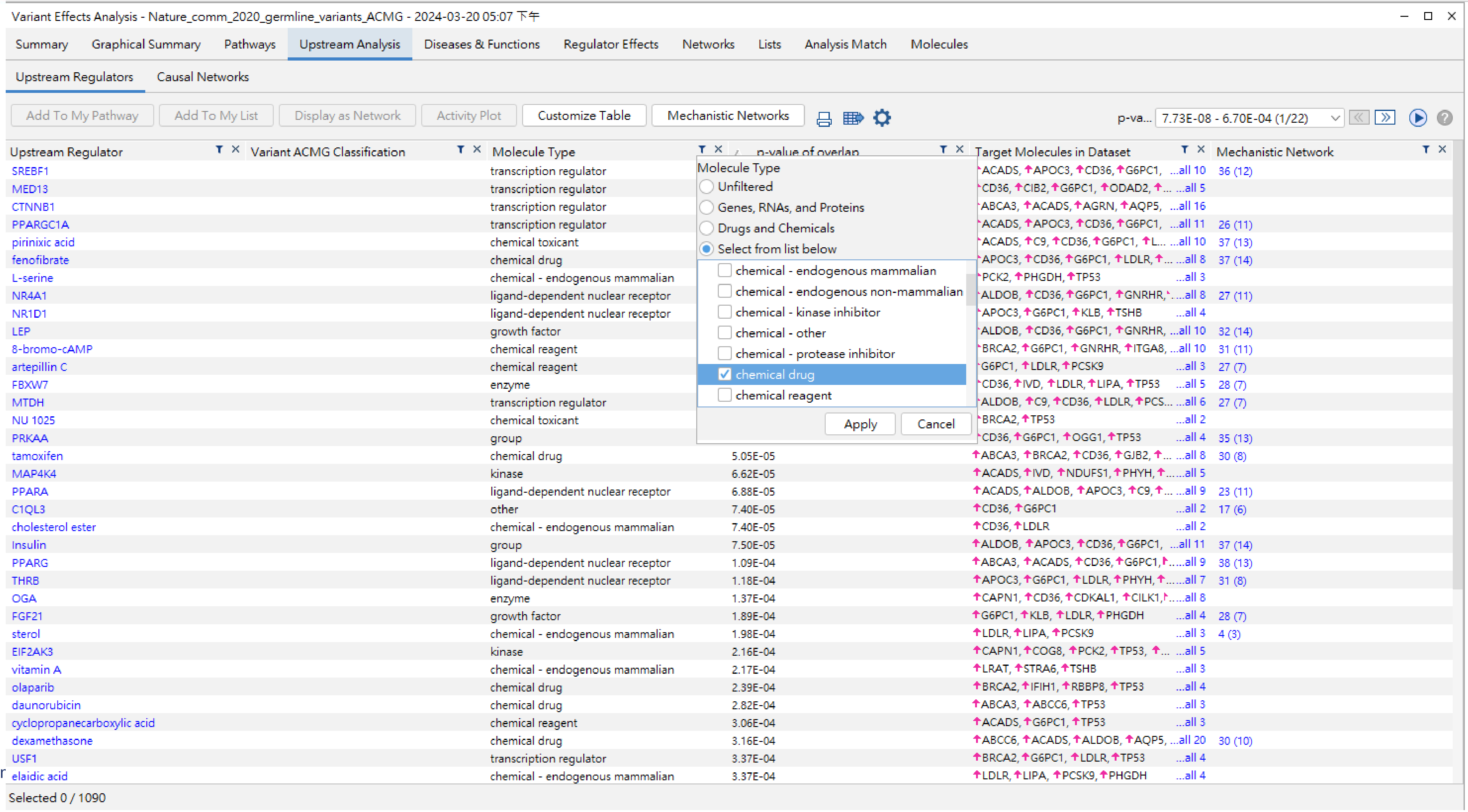
TP53

HDR through MMEJ

HDR through MMEJ (alt-NHEJ) : Nature_comm_2020_germline_variants_ACMG : Variant ACMG Classification



Upstream Analysis



Molecule Type
○ Unfiltered
○ Genes, RNAs, and Proteins
○ Drugs and Chemicals
● Select from list below
☐ chemical - endogenous mammalian
☐ chemical - endogenous non-mammalian
☐ chemical - kinase inhibitor
☐ chemical - other
☐ chemical - protease inhibitor
☑ chemical drug
☐ chemical reagent

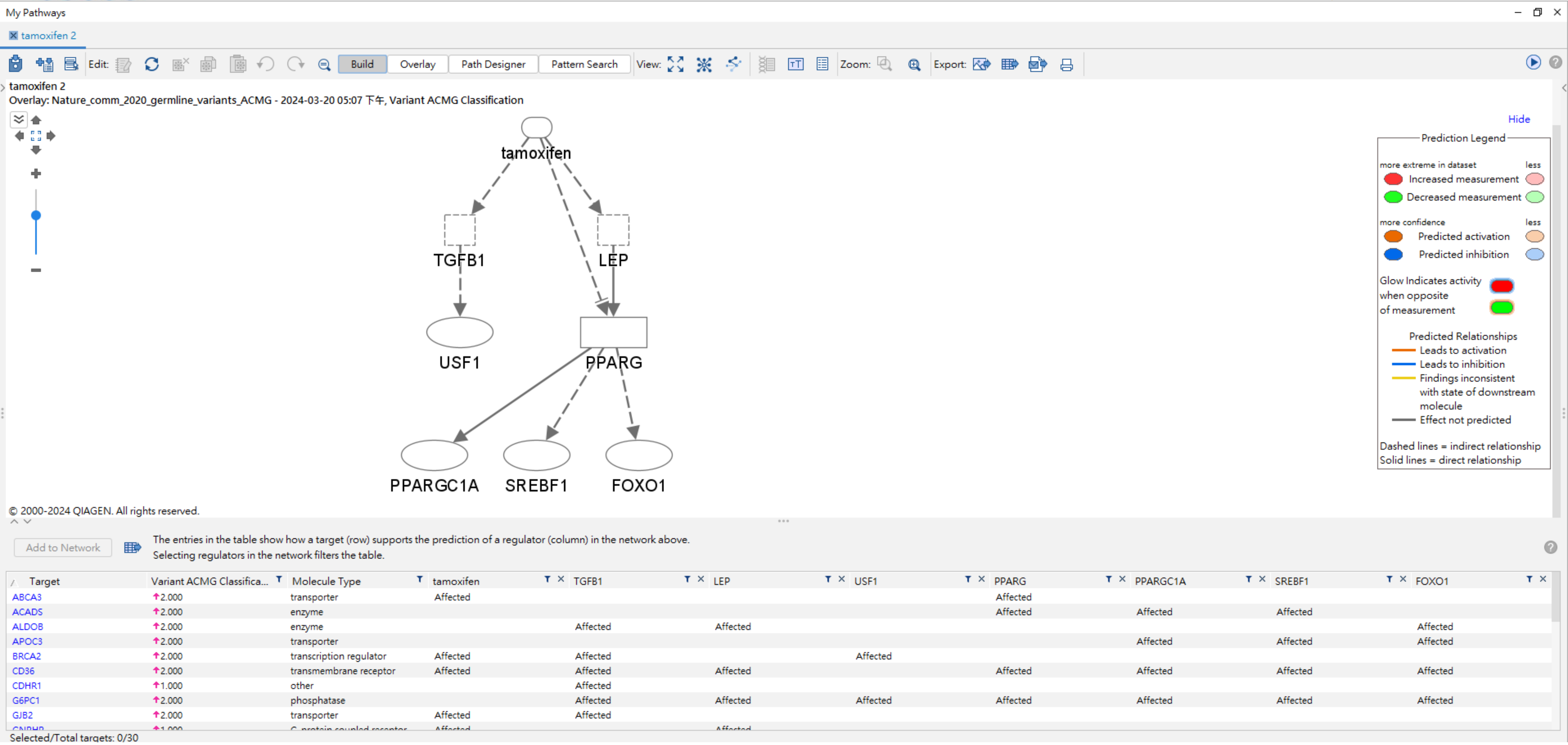
Apply | Cancel

Upstream Regulator	Variant ACMG Classification	Molecule Type	p-value of overlap	Target Molecules in Dataset		Mechanistic Network
SREBF1		transcription regulator		↑ACADS, ↑APOC3, ↑CD36, ↑G6PC1,	...all 10	36 (12)
MED13		transcription regulator		↑CD36, ↑CIB2, ↑G6PC1, ↑ODAD2, ↑...	...all 5	
CTNNB1		transcription regulator		↑ABCA3, ↑ACADS, ↑AGRN, ↑AQP5,	...all 16	
PPARGC1A		transcription regulator		↑ACADS, ↑APOC3, ↑CD36, ↑G6PC1,	...all 11	26 (11)
pirinixic acid		chemical toxicant		↑ACADS, ↑C9, ↑CD36, ↑G6PC1, ↑L...	...all 10	37 (13)
fenofibrate		chemical drug		↑APOC3, ↑CD36, ↑G6PC1, ↑LDLR, ↑...	...all 8	37 (14)
L-serine		chemical - endogenous mammalian		↑PCK2, ↑PHGDH, ↑TP53	...all 3	
NR4A1		ligand-dependent nuclear receptor		↑ALDOB, ↑CD36, ↑G6PC1, ↑GNRHR, ↑...	...all 8	27 (11)
NR1D1		ligand-dependent nuclear receptor		↑APOC3, ↑G6PC1, ↑KLB, ↑TSHB	...all 4	
LEP		growth factor		↑ALDOB, ↑CD36, ↑G6PC1, ↑GNRHR,	...all 10	32 (14)
8-bromo-cAMP		chemical reagent		↑BRCA2, ↑G6PC1, ↑GNRHR, ↑ITGA8,	...all 10	31 (11)
artepillin C		chemical reagent		↑G6PC1, ↑LDLR, ↑PCSK9	...all 3	27 (7)
FBXW7		enzyme		↑CD36, ↑IVD, ↑LDLR, ↑LIPA, ↑TP53	...all 5	28 (7)
MTDH		transcription regulator		↑ALDOB, ↑C9, ↑CD36, ↑LDLR, ↑PCS...	...all 6	27 (7)
NU 1025		chemical toxicant		↑BRCA2, ↑TP53	...all 2	
PRKAA		group		↑CD36, ↑G6PC1, ↑OGG1, ↑TP53	...all 4	35 (13)
tamoxifen		chemical drug	5.05E-05	↑ABCA3, ↑BRCA2, ↑CD36, ↑GJB2, ↑...	...all 8	30 (8)
MAP4K4		kinase	6.62E-05	↑ACADS, ↑IVD, ↑NDUFS1, ↑PHYH, ↑...	...all 5	
PPARA		ligand-dependent nuclear receptor	6.88E-05	↑ACADS, ↑ALDOB, ↑APOC3, ↑C9, ↑...	...all 9	23 (11)
C1QL3		other	7.40E-05	↑CD36, ↑G6PC1	...all 2	17 (6)
cholesterol ester		chemical - endogenous mammalian	7.40E-05	↑CD36, ↑LDLR	...all 2	
Insulin		group	7.50E-05	↑ALDOB, ↑APOC3, ↑CD36, ↑G6PC1,	...all 11	37 (14)
PPARG		ligand-dependent nuclear receptor	1.09E-04	↑ABCA3, ↑ACADS, ↑CD36, ↑G6PC1, ↑...	...all 9	38 (13)
THRB		ligand-dependent nuclear receptor	1.18E-04	↑APOC3, ↑G6PC1, ↑LDLR, ↑PHYH, ↑...	...all 7	31 (8)
OGA		enzyme	1.37E-04	↑CAPN1, ↑CD36, ↑CDKAL1, ↑CILK1, ↑...	...all 8	
FGF21		growth factor	1.89E-04	↑G6PC1, ↑KLB, ↑LDLR, ↑PHGDH	...all 4	28 (7)
sterol		chemical - endogenous mammalian	1.98E-04	↑LDLR, ↑LIPA, ↑PCSK9	...all 3	4 (3)
EIF2AK3		kinase	2.16E-04	↑CAPN1, ↑COG8, ↑PCK2, ↑TP53, ↑...	...all 5	
vitamin A		chemical - endogenous mammalian	2.17E-04	↑LRAT, ↑STRA6, ↑TSHB	...all 3	
olaparib		chemical drug	2.39E-04	↑BRCA2, ↑IFIH1, ↑RBBP8, ↑TP53	...all 4	
daunorubicin		chemical drug	2.82E-04	↑ABCA3, ↑ABCC6, ↑TP53	...all 3	
cyclopropanecarboxylic acid		chemical reagent	3.06E-04	↑ACADS, ↑G6PC1, ↑TP53	...all 3	
dexamethasone		chemical drug	3.16E-04	↑ABCC6, ↑ACADS, ↑ALDOB, ↑AQP5,	...all 20	30 (10)
USF1		transcription regulator	3.37E-04	↑BRCA2, ↑G6PC1, ↑LDLR, ↑TP53	...all 4	
elaidic acid		chemical - endogenous mammalian	3.37E-04	↑LDLR, ↑LIPA, ↑PCSK9, ↑PHGDH	...all 4	

Selected 0 / 1090

Sar

Chemical drug upstream



tamoxifen 2

Overlay: Nature_comm_2020_germline_variants_ACMG - 2024-03-20 05:07 下午, Variant ACMG Classification

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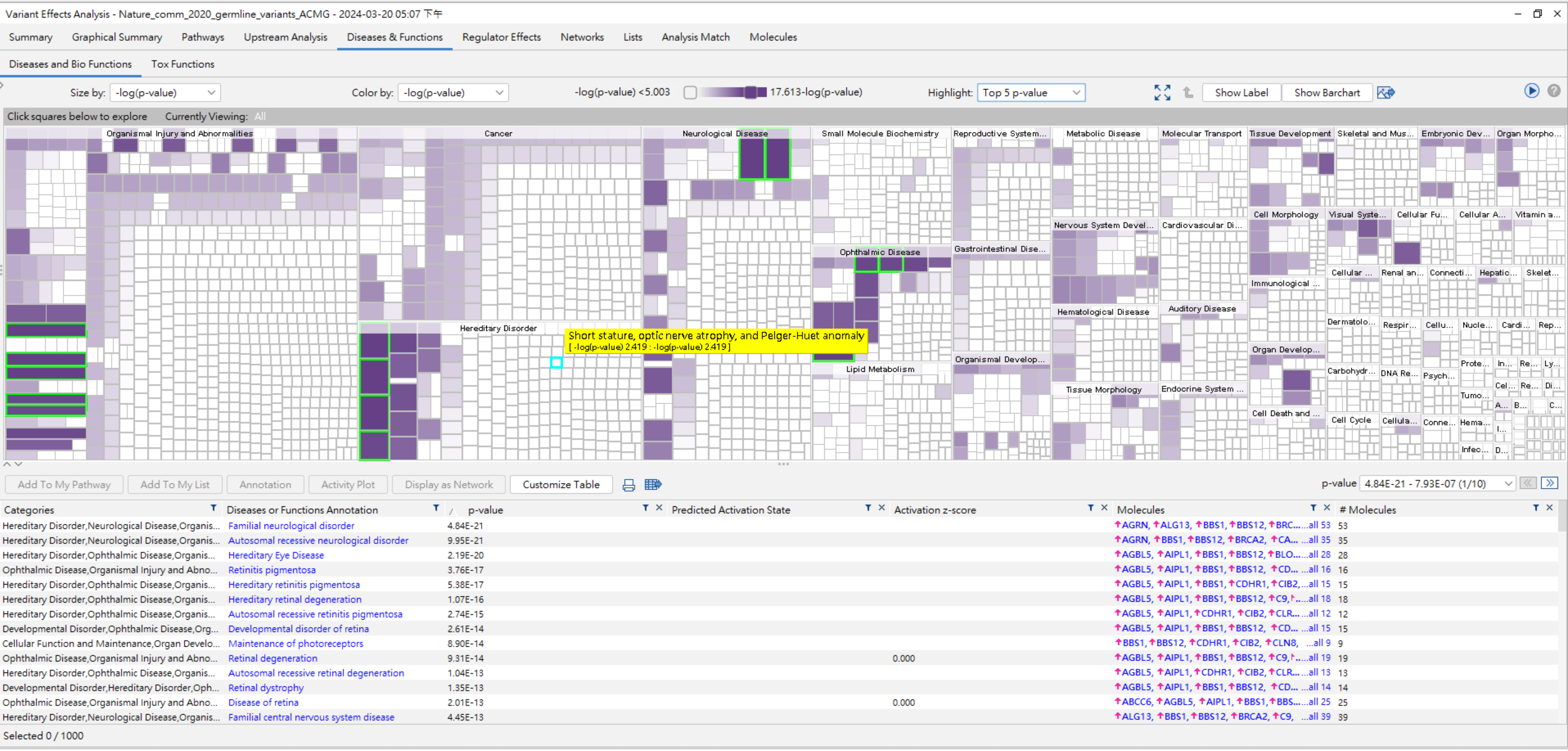
The entries in the table show how a target (row) supports the prediction of a regulator (column) in the network above.
Selecting regulators in the network filters the table.

Target	Variant ACMG Classifica...	Molecule Type	tamoxifen	TGFB1	LEP	USF1	PPARG	PPARGC1A	SREBF1	FOXO1
ABCA3	↑2.000	transporter	Affected				Affected			
ACADS	↑2.000	enzyme					Affected	Affected	Affected	
ALDOB	↑2.000	enzyme		Affected	Affected					Affected
APOC3	↑2.000	transporter						Affected	Affected	Affected
BRCA2	↑2.000	transcription regulator	Affected	Affected		Affected				
CD36	↑2.000	transmembrane receptor	Affected	Affected	Affected		Affected	Affected	Affected	Affected
CDHR1	↑1.000	other		Affected						
G6PC1	↑2.000	phosphatase		Affected	Affected	Affected	Affected	Affected	Affected	Affected
GJB2	↑2.000	transporter	Affected	Affected						

Selected/Total targets: 0/30

Disease & function



Variant Effects Analysis - Nature_comm_2020_germline_variants_ACMG - 2024-03-20 05:07 下午

Size by: -log(p-value)

Color by: -log(p-value)

-log(p-value) <5.003 17.613-log(p-value)

Highlight: Top 5 p-value

Currently Viewing: All

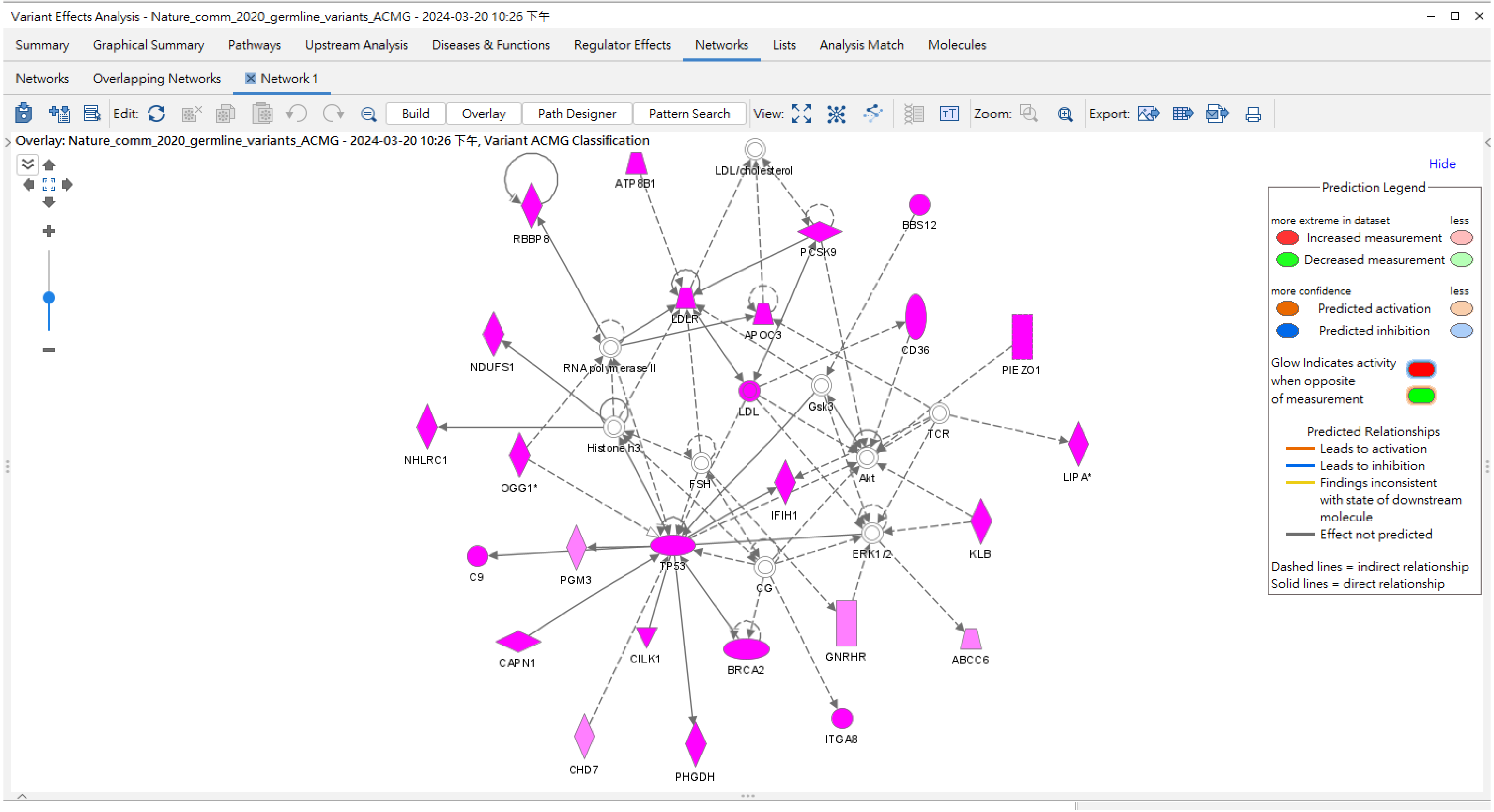
Short stature, optic nerve atrophy, and Pelger-Huet anomaly
[-log(p-value) 2.419 : -log(p-value) 2.419]

p-value 4.84E-21 - 7.93E-07 (1/10)

Categories	Diseases or Functions Annotation	p-value	Predicted Activation State	Activation z-score	Molecules	# Molecules
Hereditary Disorder,Neurological Disease,Organis...	Familial neurological disorder	4.84E-21			↑AGRN, ↑ALG13, ↑BBS1, ↑BBS12, ↑BRC... ...all 53	53
Hereditary Disorder,Neurological Disease,Organis...	Autosomal recessive neurological disorder	9.95E-21			↑AGRN, ↑BBS1, ↑BBS12, ↑BRCA2, ↑CA... ...all 35	35
Hereditary Disorder,Ophthalmic Disease,Organis...	Hereditary Eye Disease	2.19E-20			↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS12, ↑BLO... ...all 28	28
Ophthalmic Disease,Organismal Injury and Abno...	Retinitis pigmentosa	3.76E-17			↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS12, ↑CD... ...all 16	16
Hereditary Disorder,Ophthalmic Disease,Organis...	Hereditary retinitis pigmentosa	5.38E-17			↑AGBL5, ↑AIPL1, ↑BBS1, ↑CDHR1, ↑CIB2, ...all 15	15
Hereditary Disorder,Ophthalmic Disease,Organis...	Hereditary retinal degeneration	1.07E-16			↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS12, ↑C9, ...all 18	18
Hereditary Disorder,Ophthalmic Disease,Organis...	Autosomal recessive retinitis pigmentosa	2.74E-15			↑AGBL5, ↑AIPL1, ↑CDHR1, ↑CIB2, ↑CLR... ...all 12	12
Developmental Disorder,Ophthalmic Disease,Org...	Developmental disorder of retina	2.61E-14			↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS12, ↑CD... ...all 15	15
Cellular Function and Maintenance,Organ Develo...	Maintenance of photoreceptors	8.90E-14			↑BBS1, ↑BBS12, ↑CDHR1, ↑CIB2, ↑CLN8, ...all 9	9
Ophthalmic Disease,Organismal Injury and Abno...	Retinal degeneration	9.31E-14		0.000	↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS12, ↑C9, ...all 19	19
Hereditary Disorder,Ophthalmic Disease,Organis...	Autosomal recessive retinal degeneration	1.04E-13			↑AGBL5, ↑AIPL1, ↑CDHR1, ↑CIB2, ↑CLR... ...all 13	13
Developmental Disorder,Hereditary Disorder,Oph...	Retinal dystrophy	1.35E-13			↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS12, ↑CD... ...all 14	14
Ophthalmic Disease,Organismal Injury and Abno...	Disease of retina	2.01E-13		0.000	↑ABCC6, ↑AGBL5, ↑AIPL1, ↑BBS1, ↑BBS... ...all 25	25
Hereditary Disorder,Neurological Disease,Organis...	Familial central nervous system disease	4.45E-13			↑ALG13, ↑BBS1, ↑BBS12, ↑BRCA2, ↑C9, ...all 39	39

Selected 0 / 1000

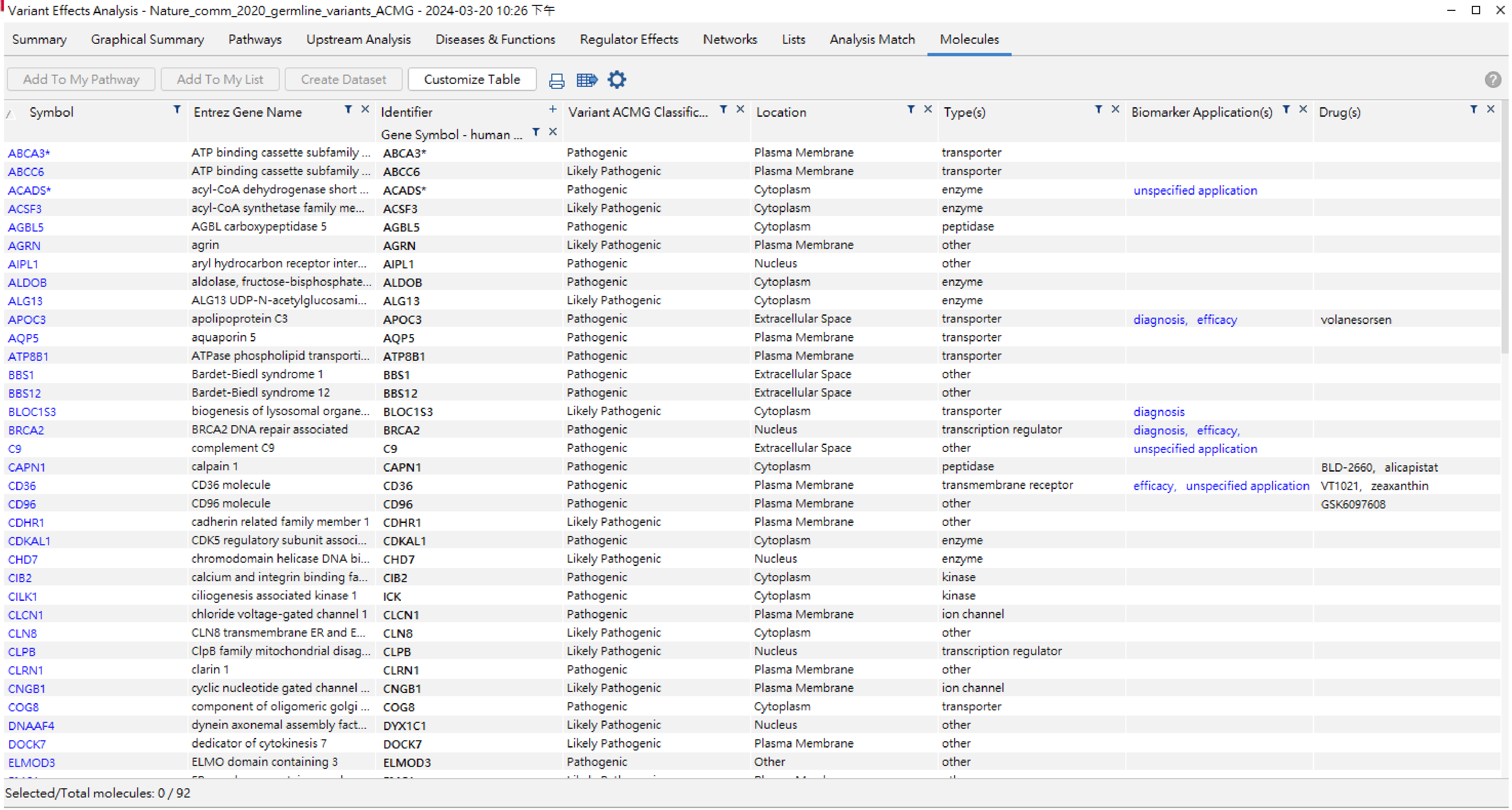
Network



Variant Effects Analysis - Nature_comm_2020_germline_variants_ACMG - 2024-03-20 10:26 下午

Overlay: Nature_comm_2020_germline_variants_ACMG - 2024-03-20 10:26 下午, Variant ACMG Classification

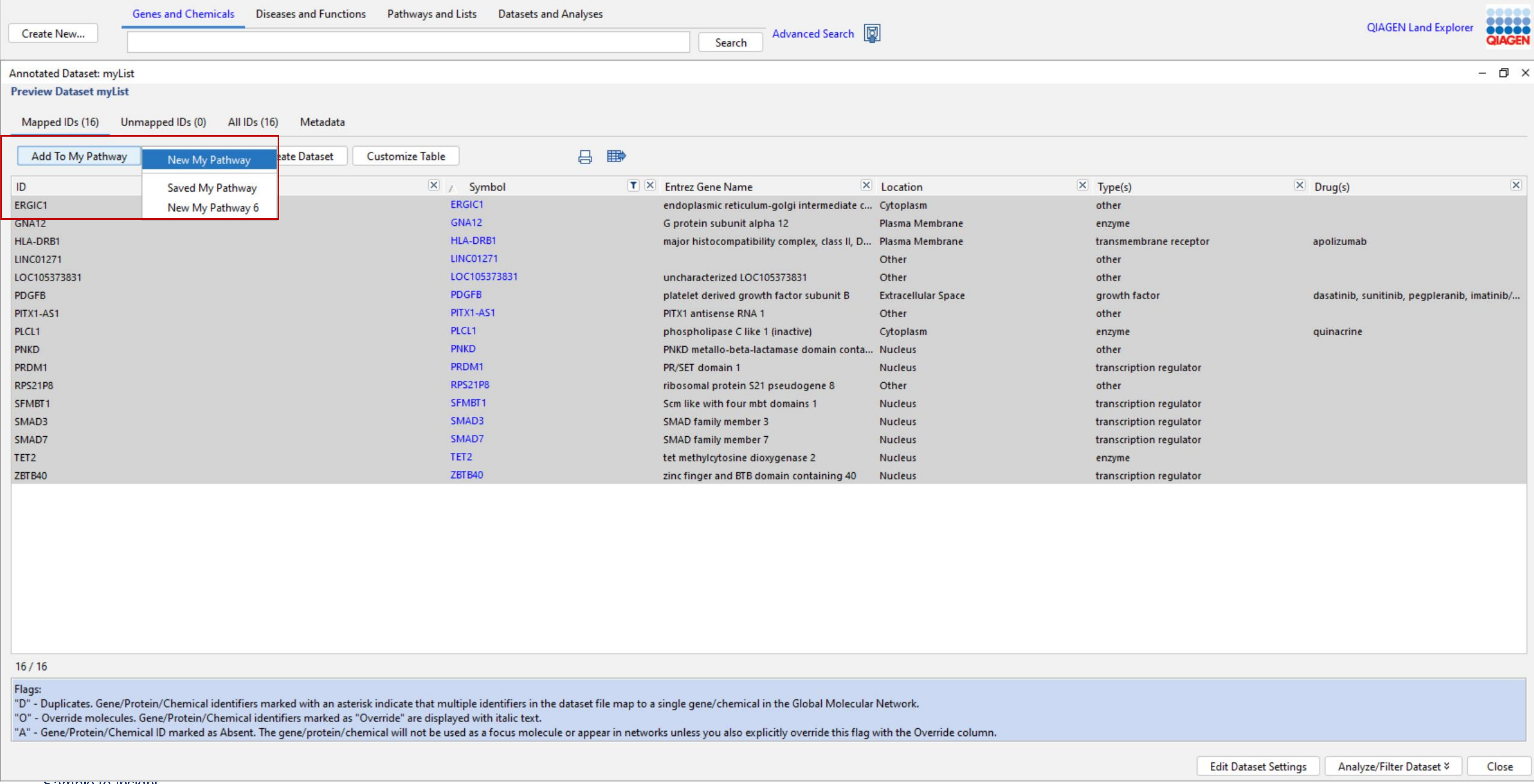
Molecular



Symbol	Entrez Gene Name	Identifier Gene Symbol - human ...	Variant ACMG Classific...	Location	Type(s)	Biomarker Application(s)	Drug(s)
ABCA3*	ATP binding cassette subfamily ...	ABCA3*	Pathogenic	Plasma Membrane	transporter		
ABCC6	ATP binding cassette subfamily ...	ABCC6	Likely Pathogenic	Plasma Membrane	transporter		
ACADS*	acyl-CoA dehydrogenase short ...	ACADS*	Pathogenic	Cytoplasm	enzyme	unspecified application	
ACSF3	acyl-CoA synthetase family me...	ACSF3	Likely Pathogenic	Cytoplasm	enzyme		
AGBL5	AGBL carboxypeptidase 5	AGBL5	Pathogenic	Cytoplasm	peptidase		
AGRN	agrin	AGRN	Likely Pathogenic	Plasma Membrane	other		
AIPL1	aryl hydrocarbon receptor inter...	AIPL1	Pathogenic	Nucleus	other		
ALDOB	aldolase, fructose-bisphosphate...	ALDOB	Pathogenic	Cytoplasm	enzyme		
ALG13	ALG13 UDP-N-acetylglucosami...	ALG13	Likely Pathogenic	Cytoplasm	enzyme		
APOC3	apolipoprotein C3	APOC3	Pathogenic	Extracellular Space	transporter	diagnosis, efficacy	volanesorsen
AQP5	aquaporin 5	AQP5	Pathogenic	Plasma Membrane	transporter		
ATP8B1	ATPase phospholipid transporti...	ATP8B1	Pathogenic	Plasma Membrane	transporter		
BBS1	Bardet-Biedl syndrome 1	BBS1	Pathogenic	Extracellular Space	other		
BBS12	Bardet-Biedl syndrome 12	BBS12	Pathogenic	Extracellular Space	other		
BLOC1S3	biogenesis of lysosomal organe...	BLOC1S3	Likely Pathogenic	Cytoplasm	transporter	diagnosis	
BRCA2	BRCA2 DNA repair associated	BRCA2	Pathogenic	Nucleus	transcription regulator	diagnosis, efficacy,	
C9	complement C9	C9	Pathogenic	Extracellular Space	other	unspecified application	
CAPN1	calpain 1	CAPN1	Pathogenic	Cytoplasm	peptidase		BLD-2660, alicapistat
CD36	CD36 molecule	CD36	Pathogenic	Plasma Membrane	transmembrane receptor	efficacy, unspecified application	VT1021, zeaxanthin
CD96	CD96 molecule	CD96	Pathogenic	Plasma Membrane	other		GSK6097608
CDHR1	cadherin related family member 1	CDHR1	Likely Pathogenic	Plasma Membrane	other		
CDKAL1	CDK5 regulatory subunit associ...	CDKAL1	Pathogenic	Cytoplasm	enzyme		
CHD7	chromodomain helicase DNA bi...	CHD7	Likely Pathogenic	Nucleus	enzyme		
CIB2	calcium and integrin binding fa...	CIB2	Pathogenic	Cytoplasm	kinase		
CILK1	ciliogenesis associated kinase 1	ICK	Pathogenic	Cytoplasm	kinase		
CLCN1	chloride voltage-gated channel 1	CLCN1	Pathogenic	Plasma Membrane	ion channel		
CLN8	CLN8 transmembrane ER and E...	CLN8	Likely Pathogenic	Cytoplasm	other		
CLPB	ClpB family mitochondrial disag...	CLPB	Likely Pathogenic	Nucleus	transcription regulator		
CLRN1	clarin 1	CLRN1	Pathogenic	Plasma Membrane	other		
CNGB1	cyclic nucleotide gated channel ...	CNGB1	Likely Pathogenic	Plasma Membrane	ion channel		
COG8	component of oligomeric golgi ...	COG8	Pathogenic	Cytoplasm	transporter		
DNAAF4	dynein axonemal assembly fact...	DYX1C1	Likely Pathogenic	Nucleus	other		
DOCK7	dedicator of cytokinesis 7	DOCK7	Likely Pathogenic	Plasma Membrane	other		
ELMOD3	ELMO domain containing 3	ELMOD3	Pathogenic	Other	other		

Selected/Total molecules: 0 / 92

Draw customer pathway



ID	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
ERGIC1	ERGIC1	endoplasmic reticulum-golgi intermediate c...	Cytoplasm	other	
GNA12	GNA12	G protein subunit alpha 12	Plasma Membrane	enzyme	
HLA-DRB1	HLA-DRB1	major histocompatibility complex, class II, D...	Plasma Membrane	transmembrane receptor	apolizumab
LINC01271	LINC01271		Other	other	
LOC105373831	LOC105373831	uncharacterized LOC105373831	Other	other	
PDGFB	PDGFB	platelet derived growth factor subunit B	Extracellular Space	growth factor	dasatinib, sunitinib, pegpleranib, imatinib/...
PITX1-AS1	PITX1-AS1	PITX1 antisense RNA 1	Other	other	
PLCL1	PLCL1	phospholipase C like 1 (inactive)	Cytoplasm	enzyme	quinacrine
PNKD	PNKD	PNKD metallo-beta-lactamase domain conta...	Nucleus	other	
PRDM1	PRDM1	PR/SET domain 1	Nucleus	transcription regulator	
RPS21P8	RPS21P8	ribosomal protein S21 pseudogene 8	Other	other	
SFMBT1	SFMBT1	Scm like with four mbt domains 1	Nucleus	transcription regulator	
SMAD3	SMAD3	SMAD family member 3	Nucleus	transcription regulator	
SMAD7	SMAD7	SMAD family member 7	Nucleus	transcription regulator	
TET2	TET2	tet methylcytosine dioxygenase 2	Nucleus	enzyme	
ZBTB40	ZBTB40	zinc finger and BTB domain containing 40	Nucleus	transcription regulator	

16 / 16

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.
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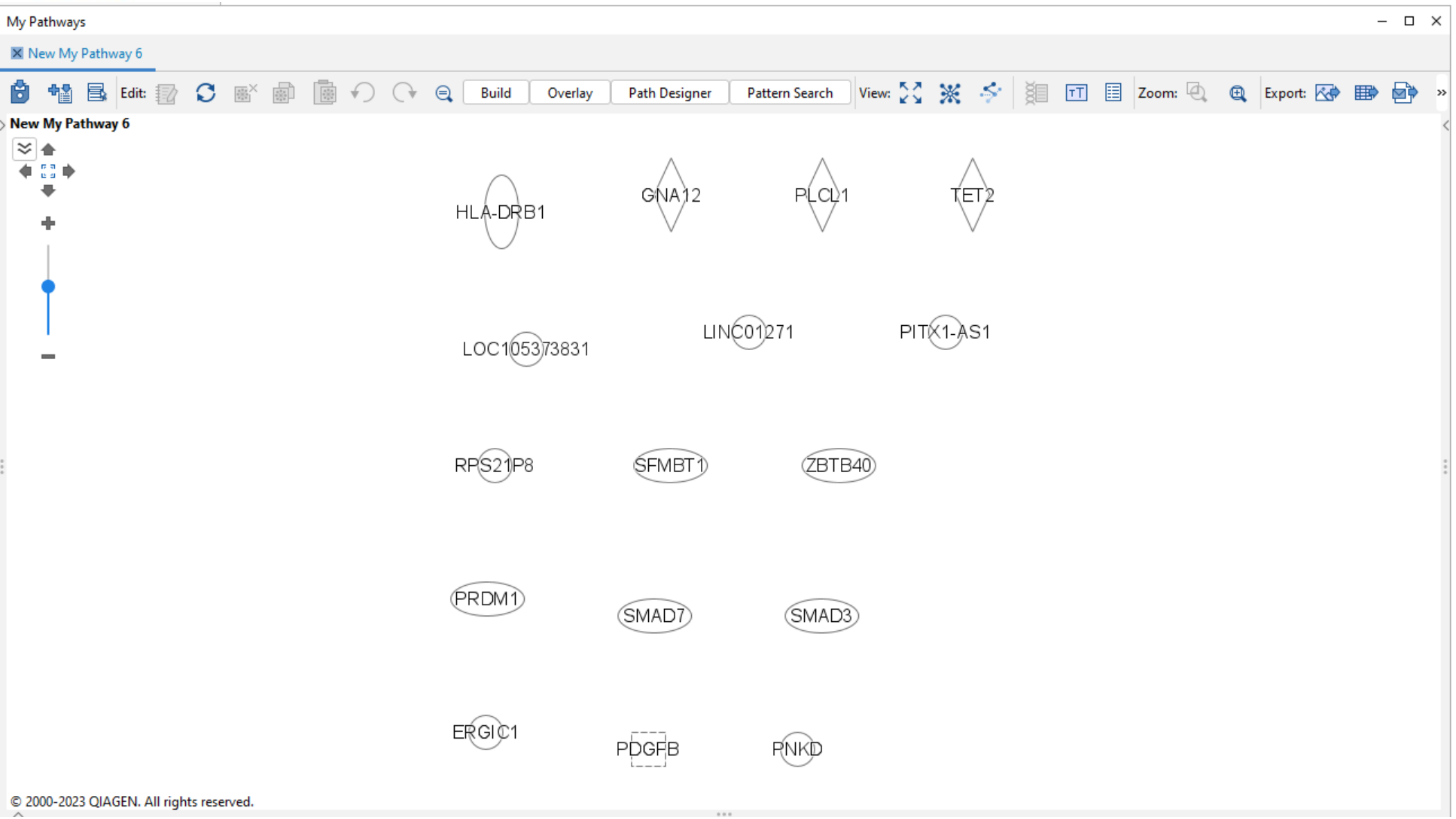
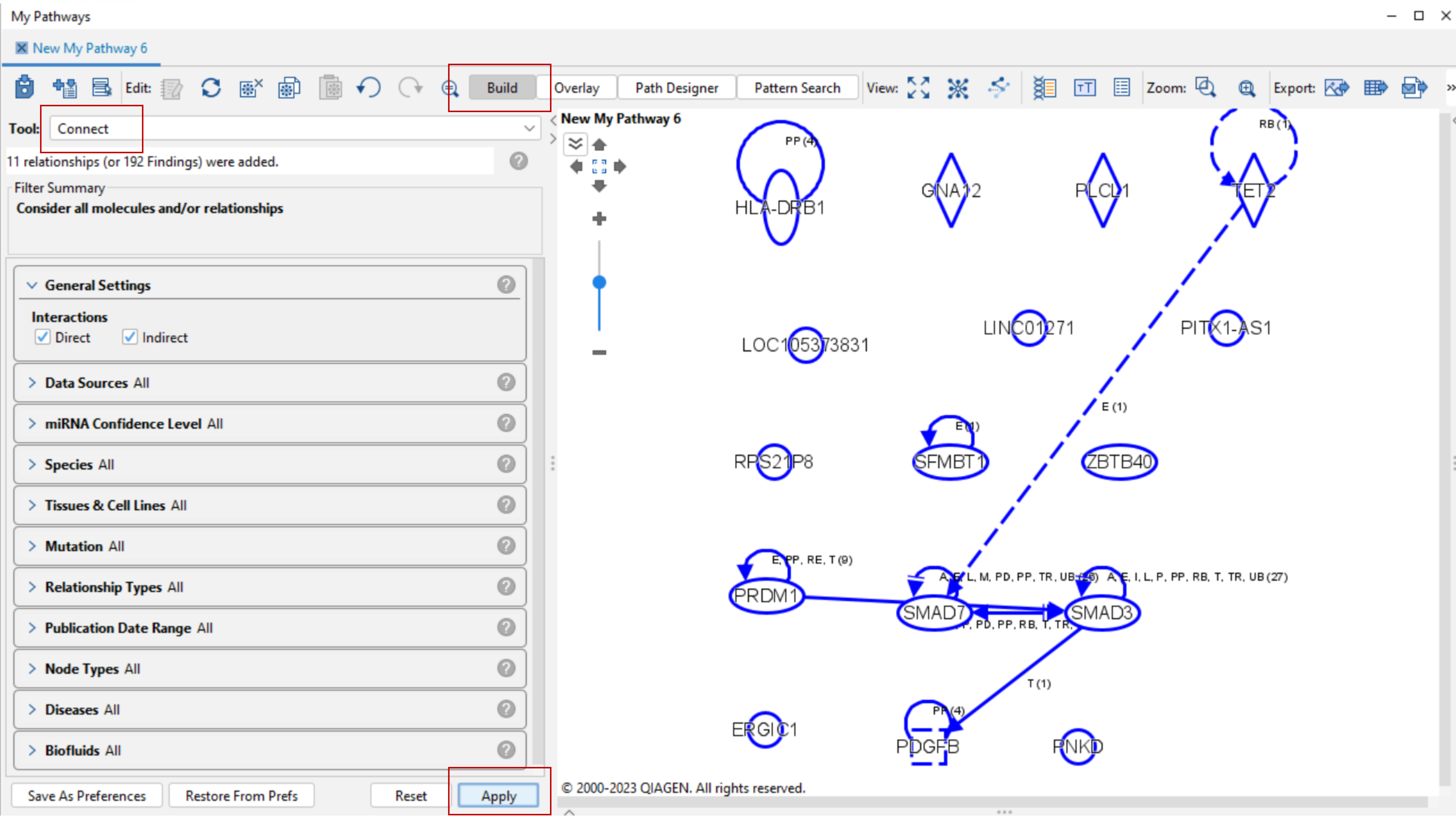
"A" - Gene/Protein/Chemical ID marked as Absent. The gene/protein/chemical will not be used as a focus molecule or appear in networks unless you also explicitly override this flag with the Override column.


My Pathways
New My Pathway 6
Edit:
Build
Overlay
Path Designer
Pattern Search
View:
Zoom:
Export:
New My Pathway 6
HLA-DRB1
GNA12
PLCL1
TET2
LOC105373831
LINC01271
PITX1-AS1
RPS21P8
SFMBT1
ZBTB40
PRDM1
SMAD7
SMAD3
ERGIC1
PDGFB
PNKD



Tool: Connect

11 relationships (or 192 Findings) were added.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☑ Direct ☑ Indirect

Data Sources All

miRNA Confidence Level All

Species All

Tissues & Cell Lines All

Mutation All

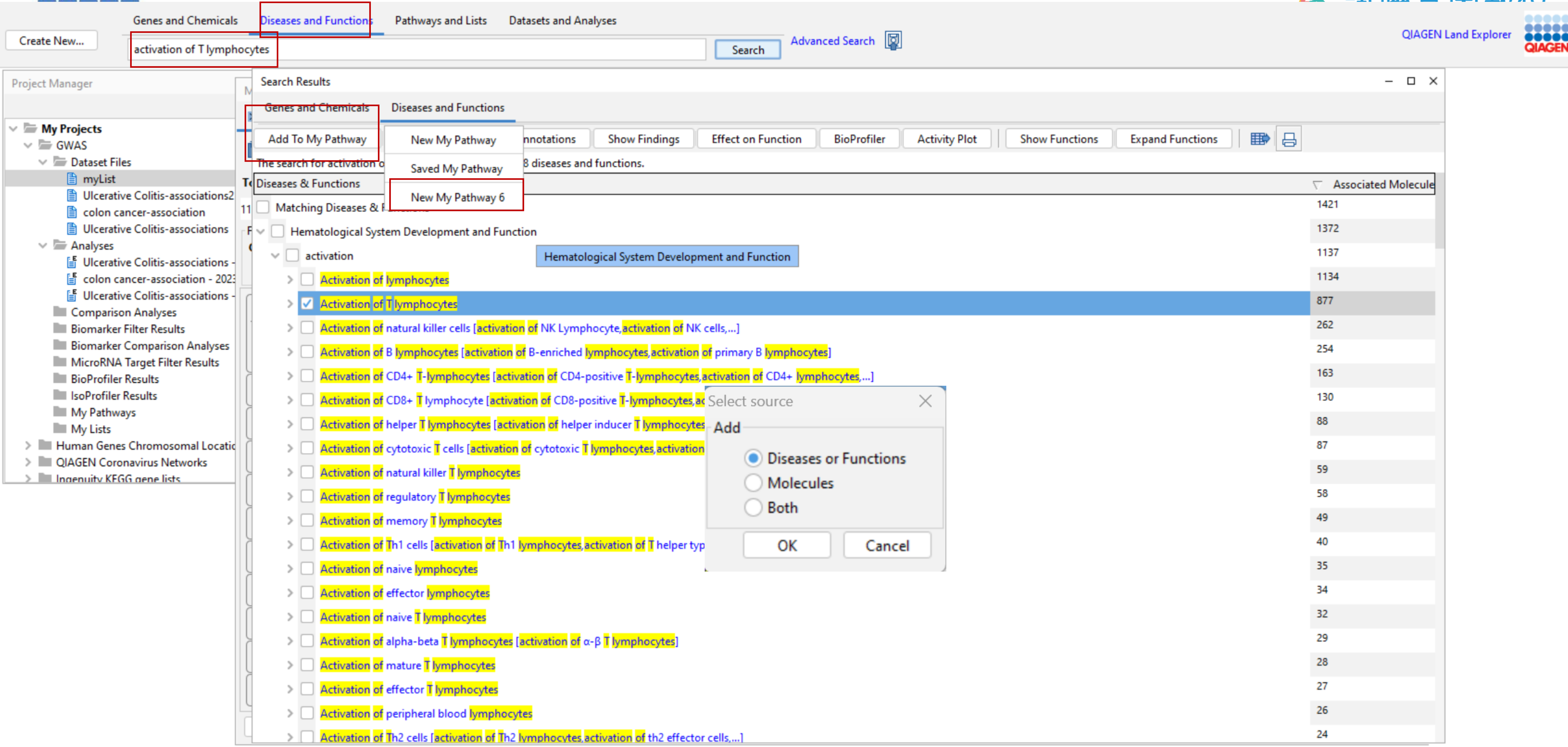
Relationship Types All

Publication Date Range All

Node Types All

Diseases All

Biofluids All



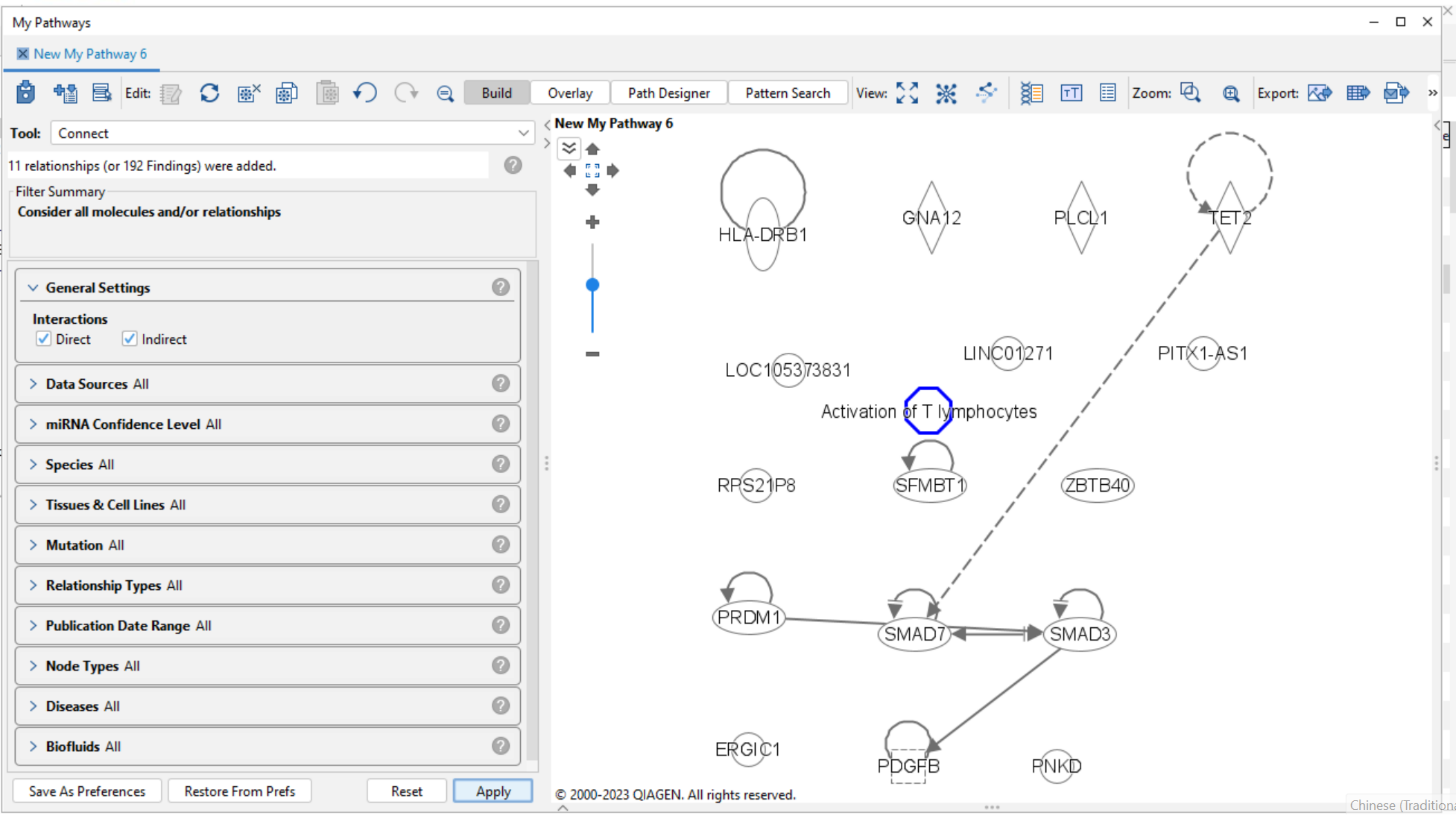
The search for activation o… 8 diseases and functions.

Diseases & Functions	Associated Molecule
☐ Matching Diseases & F…	1421
☐ Hematological System Development and Function	1372
☐ activation	1137
☐ Activation of lymphocytes	1134
☑ Activation of T lymphocytes	877
☐ Activation of natural killer cells [activation of NK Lymphocyte,activation of NK cells,...]	262
☐ Activation of B lymphocytes [activation of B-enriched lymphocytes,activation of primary B lymphocytes]	254
☐ Activation of CD4+ T-lymphocytes [activation of CD4-positive T-lymphocytes,activation of CD4+ lymphocytes,...]	163
☐ Activation of CD8+ T lymphocyte [activation of CD8-positive T-lymphocytes,ac	130
☐ Activation of helper T lymphocytes [activation of helper inducer T lymphocytes	88
☐ Activation of cytotoxic T cells [activation of cytotoxic T lymphocytes,activation	87
☐ Activation of natural killer T lymphocytes	59
☐ Activation of regulatory T lymphocytes	58
☐ Activation of memory T lymphocytes	49
☐ Activation of Th1 cells [activation of Th1 lymphocytes,activation of T helper typ	40
☐ Activation of naive lymphocytes	35
☐ Activation of effector lymphocytes	34
☐ Activation of naive T lymphocytes	32
☐ Activation of alpha-beta T lymphocytes [activation of α-β T lymphocytes]	29
☐ Activation of mature T lymphocytes	28
☐ Activation of effector T lymphocytes	27
☐ Activation of peripheral blood lymphocytes	26
☐ Activation of Th2 cells [activation of Th2 lymphocytes,activation of th2 effector cells,...]	24

Select source

Add

● Diseases or Functions
○ Molecules
○ Both



My Pathways

New My Pathway 6

Tool: Connect

11 relationships (or 192 Findings) were added.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☑ Direct ☑ Indirect

Data Sources All

miRNA Confidence Level All

Species All

Tissues & Cell Lines All

Mutation All

Relationship Types All

Publication Date Range All

Node Types All

Diseases All

Biofluids All

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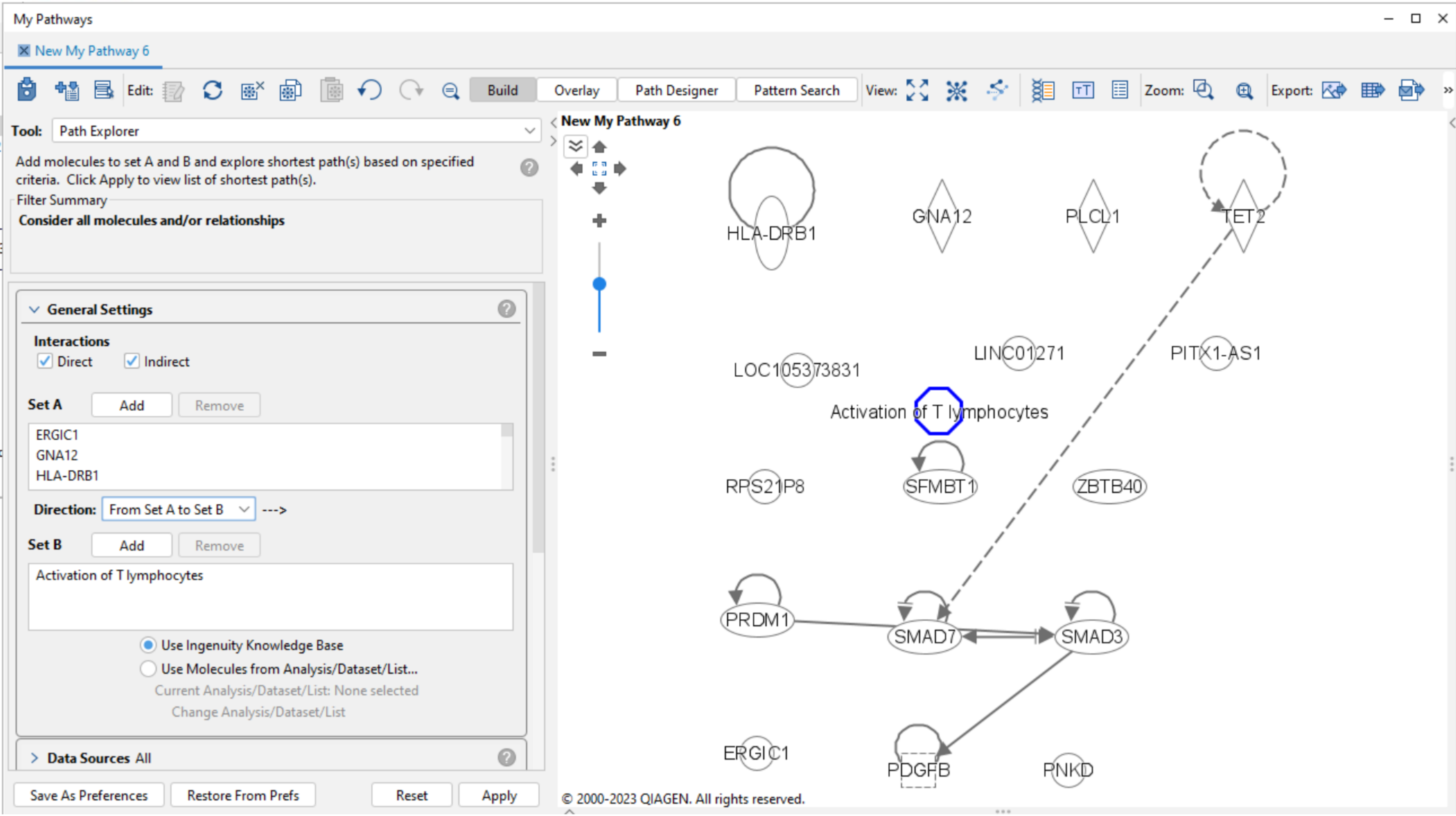

My Pathways

New My Pathway 6

Tool: Path Explorer

Add molecules to set A and B and explore shortest path(s) based on specified criteria. Click Apply to view list of shortest path(s).

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☑ Direct ☑ Indirect

Set A

ERGIC1
GNA12
HLA-DRB1

Direction: From Set A to Set B --->

Set B

Activation of T lymphocytes

● Use Ingenuity Knowledge Base
○ Use Molecules from Analysis/Dataset/List...

Current Analysis/Dataset/List: None selected

Change Analysis/Dataset/List

Data Sources All

New My Pathway 6

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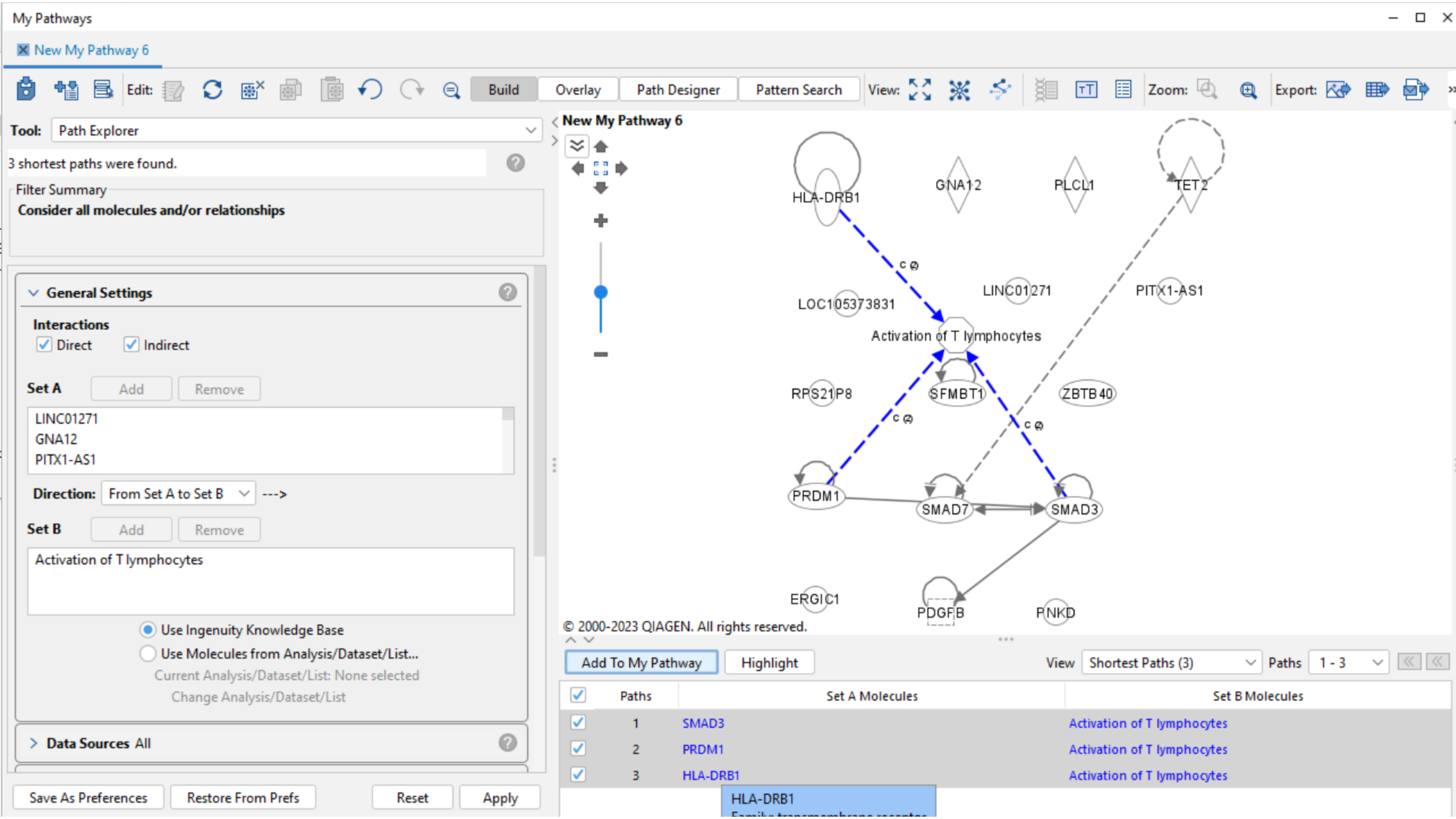

Tool: Path Explorer

3 shortest paths were found.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☑ Direct ☑ Indirect

Set A Add Remove

LINC01271
GNA12
PITX1-AS1

Direction: From Set A to Set B --->

Set B Add Remove

Activation of T lymphocytes

● Use Ingenuity Knowledge Base

○ Use Molecules from Analysis/Dataset/List...

Current Analysis/Dataset/List: None selected

Change Analysis/Dataset/List

Data Sources All

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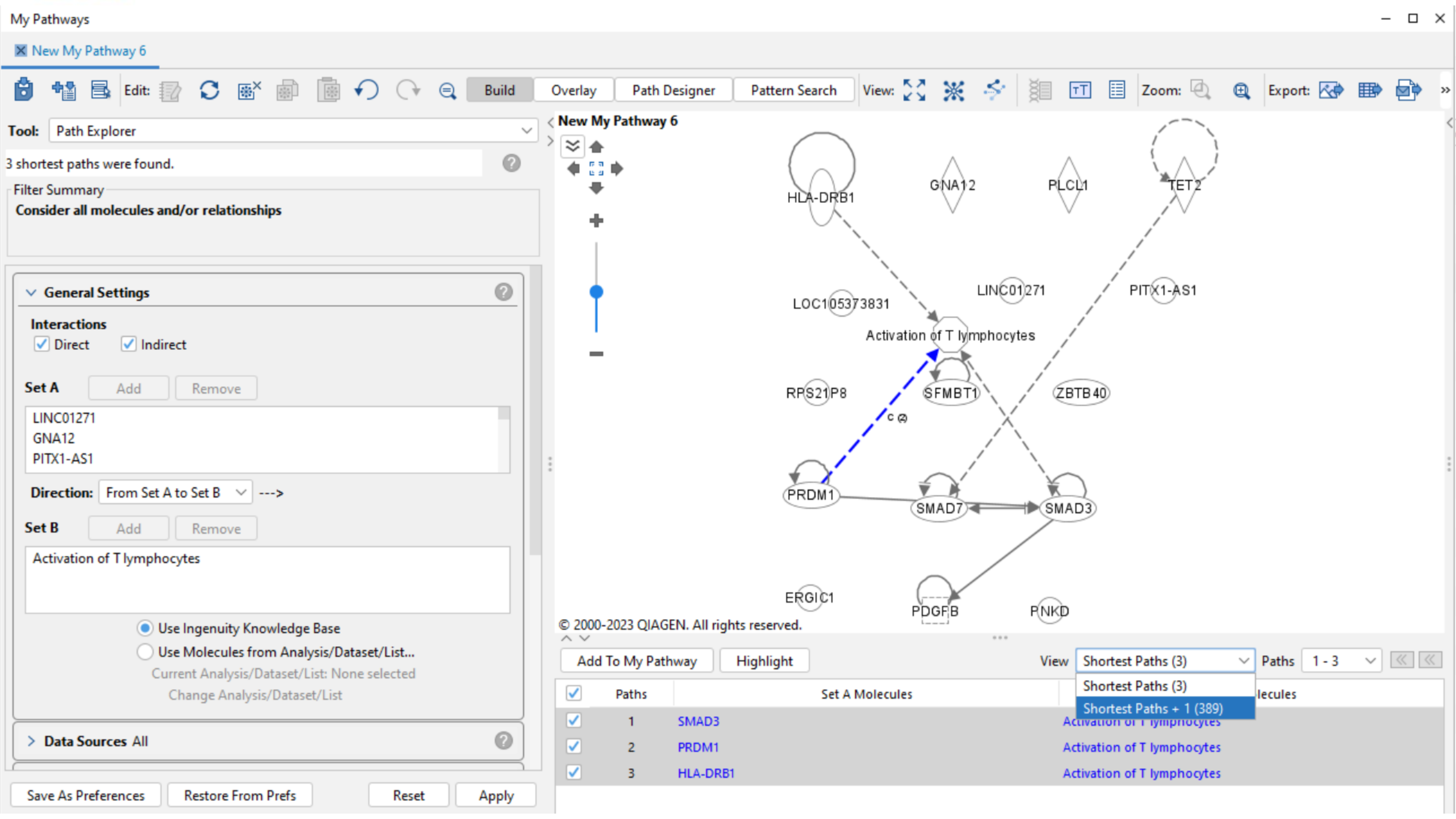
View Shortest Paths (3) Paths 1 - 3

☑	Paths	Set A Molecules	Set B Molecules
☑	1	SMAD3	Activation of T lymphocytes
☑	2	PRDM1	Activation of T lymphocytes
☑	3	HLA-DRB1	Activation of T lymphocytes

HLA-DRB1



Tool: Path Explorer

3 shortest paths were found.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☑ Direct ☑ Indirect

Set A Add Remove

LINC01271
GNA12
PITX1-AS1

Direction: From Set A to Set B --->

Set B Add Remove

Activation of T lymphocytes

● Use Ingenuity Knowledge Base

○ Use Molecules from Analysis/Dataset/List...

Current Analysis/Dataset/List: None selected

Change Analysis/Dataset/List

Data Sources All

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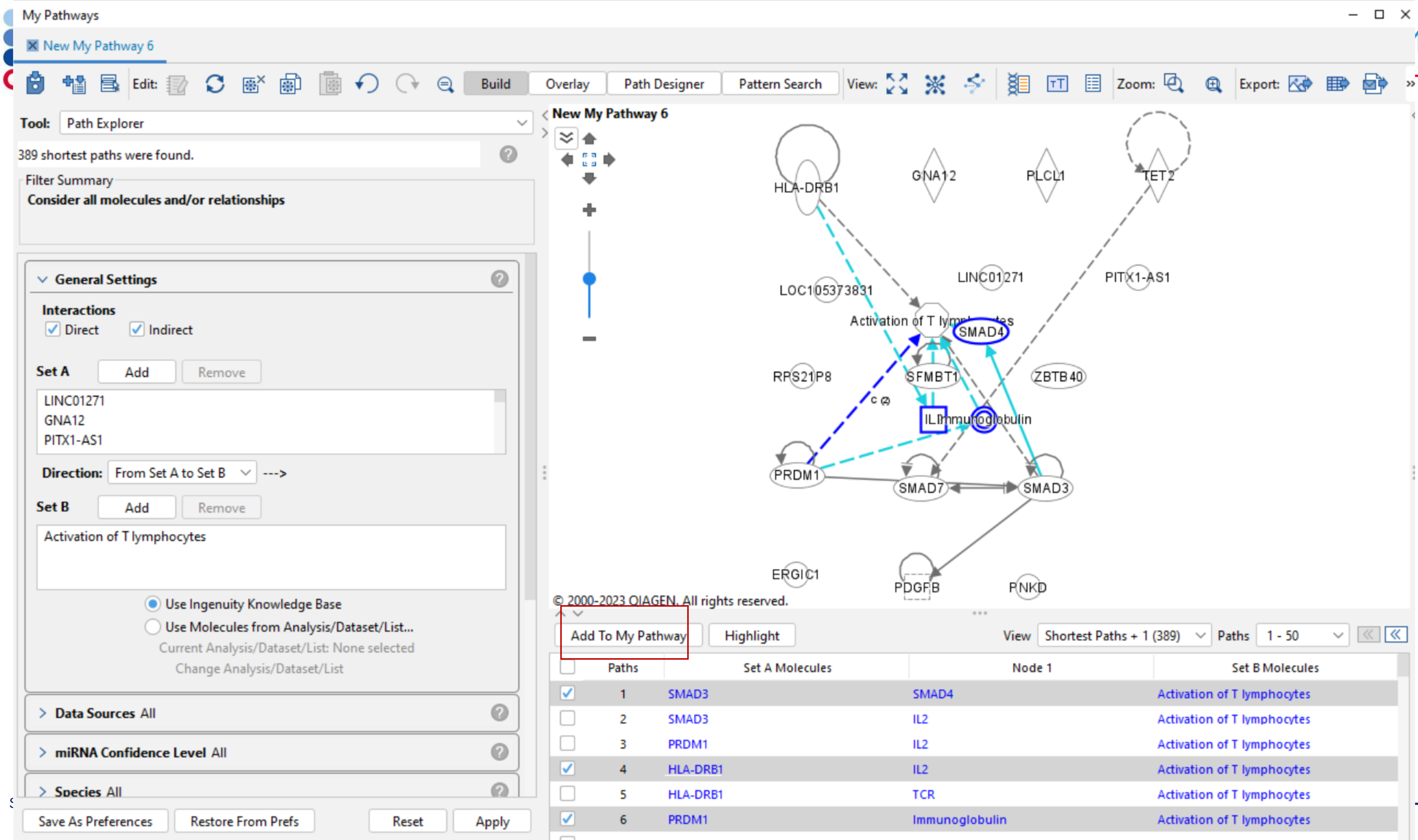
View: Shortest Paths (3) Paths: 1 - 3

☑	Paths	Set A Molecules	lecules
☑	1	SMAD3	Activation of T lymphocytes
☑	2	PRDM1	Activation of T lymphocytes
☑	3	HLA-DRB1	Activation of T lymphocytes



Tool: Path Explorer

389 shortest paths were found.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☑ Direct ☑ Indirect

Set A Add Remove

LINC01271
GNA12
PITX1-AS1

Direction: From Set A to Set B --->

Set B Add Remove

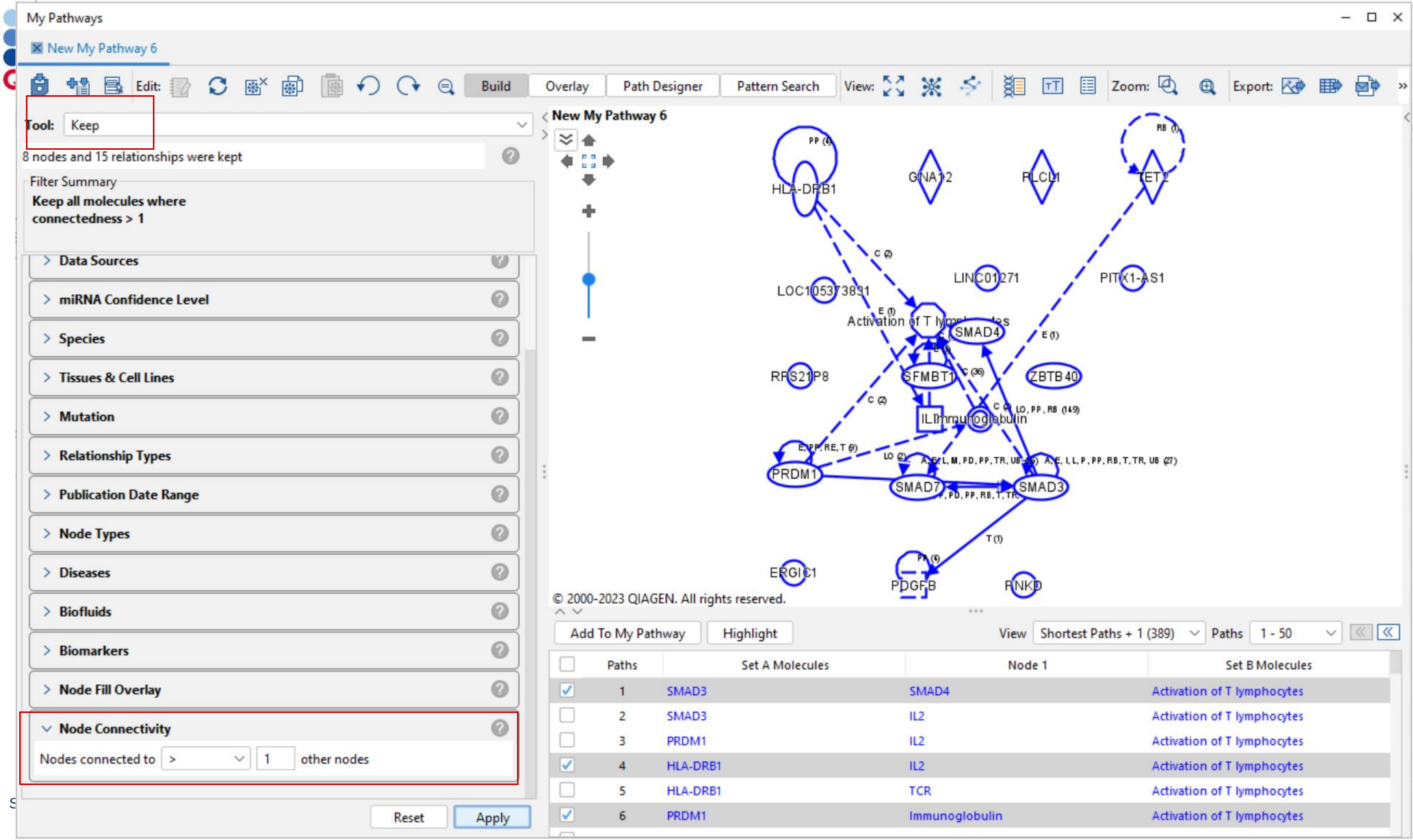
Activation of T lymphocytes

● Use Ingenuity Knowledge Base
○ Use Molecules from Analysis/Dataset/List...
Current Analysis/Dataset/List: None selected
Change Analysis/Dataset/List

> **Data Sources** All
> **miRNA Confidence Level** All
> **Species** All

View Shortest Paths + 1 (389) Paths 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes



My Pathways

New My Pathway 6

Tool: Keep

8 nodes and 15 relationships were kept

Filter Summary

Keep all molecules where connectedness > 1

Node Connectivity

Nodes connected to > 1 other nodes

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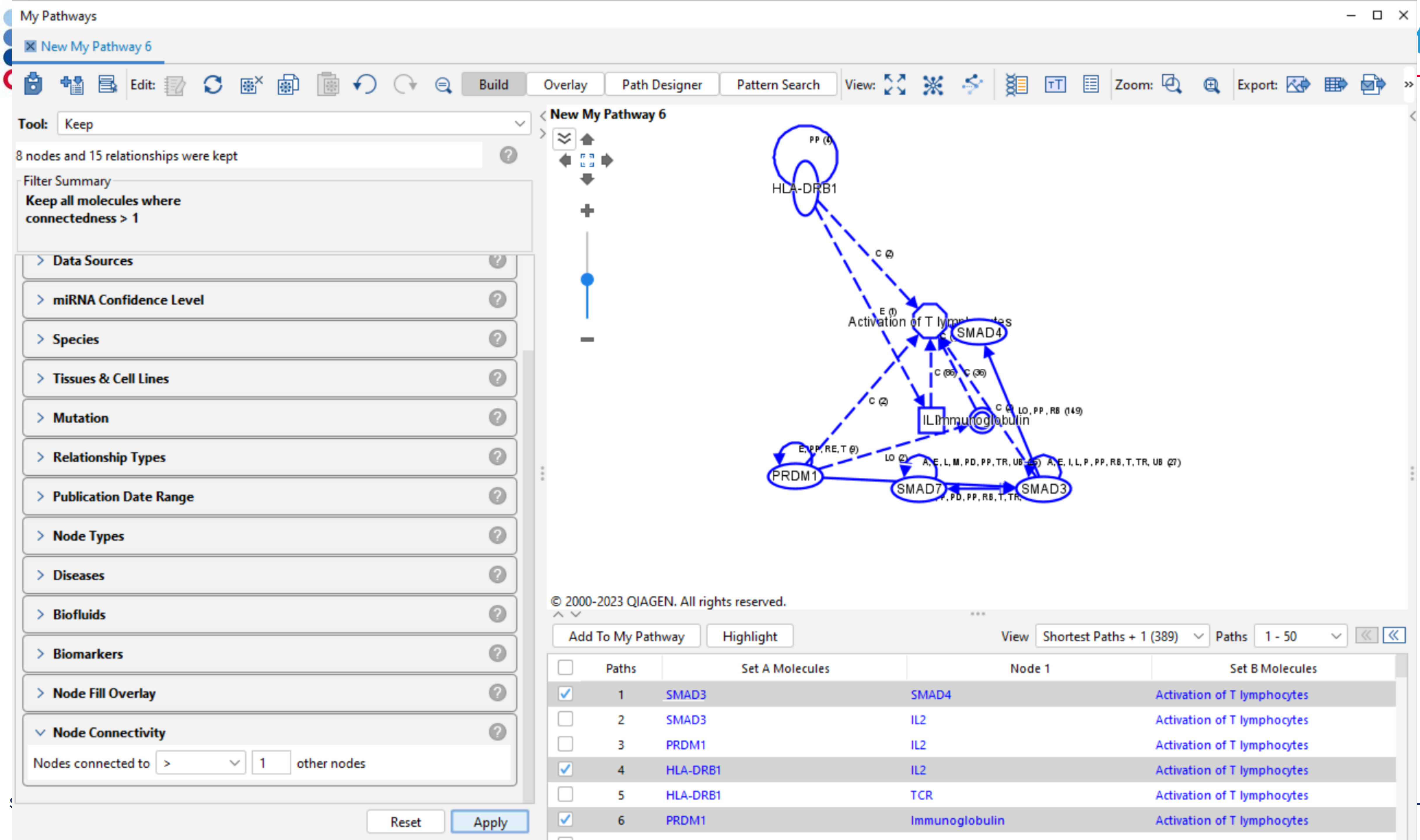
View: Shortest Paths + 1 (389)   Paths: 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

位



Tool: Keep

8 nodes and 15 relationships were kept

Filter Summary

Keep all molecules where connectedness > 1

Nodes connected to > 1 other nodes

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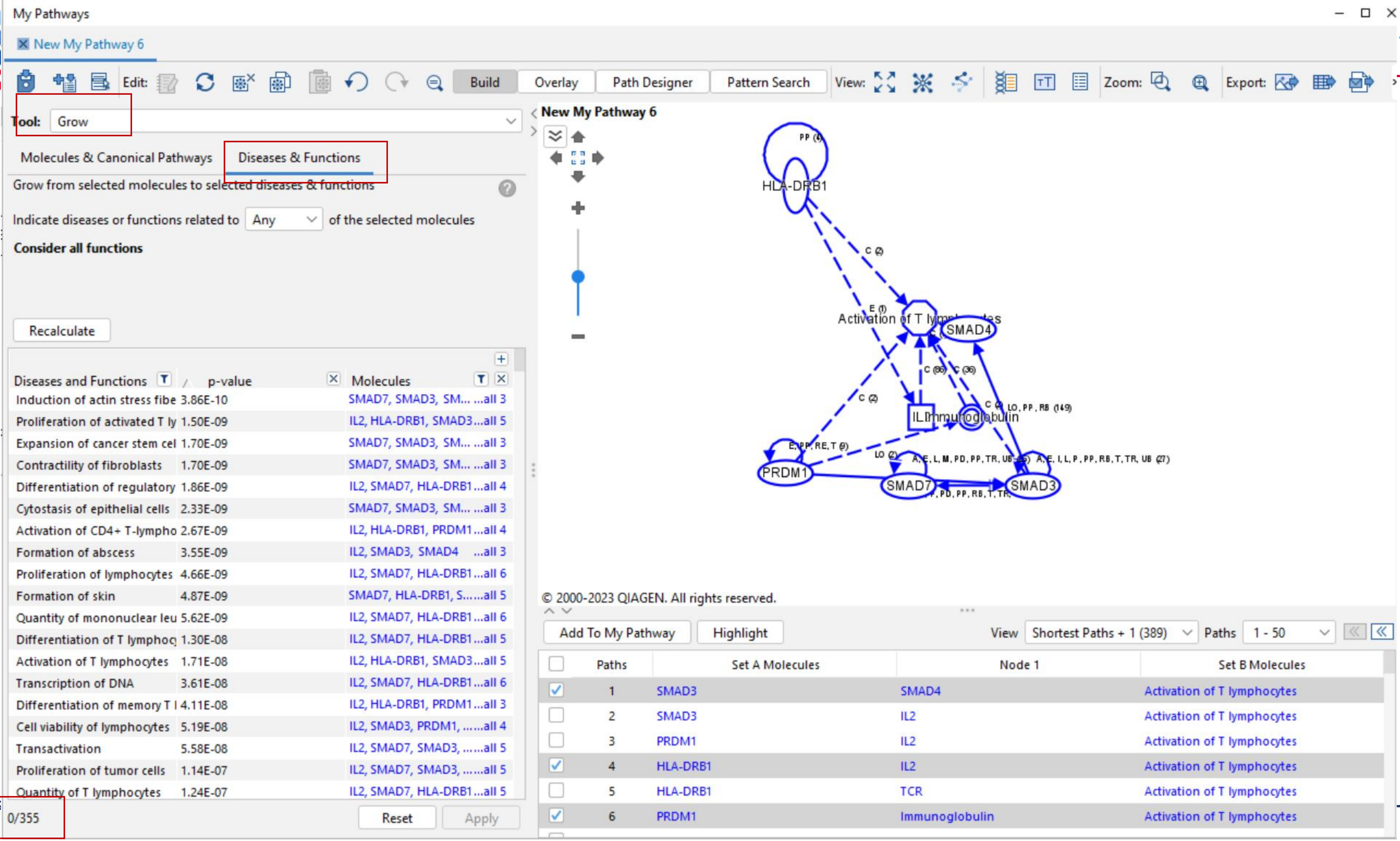
View: Shortest Paths + 1 (389) Paths: 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

位



Tool: Grow

Molecules & Canonical Pathways | Diseases & Functions

Grow from selected molecules to selected diseases & functions

Indicate diseases or functions related to Any of the selected molecules

Consider all functions

Recalculate

Diseases and Functions	p-value	Molecules
Induction of actin stress fibe	3.86E-10	SMAD7, SMAD3, SM... ...all 3
Proliferation of activated T ly	1.50E-09	IL2, HLA-DRB1, SMAD3...all 5
Expansion of cancer stem cel	1.70E-09	SMAD7, SMAD3, SM... ...all 3
Contractility of fibroblasts	1.70E-09	SMAD7, SMAD3, SM... ...all 3
Differentiation of regulatory	1.86E-09	IL2, SMAD7, HLA-DRB1...all 4
Cytostasis of epithelial cells	2.33E-09	SMAD7, SMAD3, SM... ...all 3
Activation of CD4+ T-lympho	2.67E-09	IL2, HLA-DRB1, PRDM1...all 4
Formation of abscess	3.55E-09	IL2, SMAD3, SMAD4 ...all 3
Proliferation of lymphocytes	4.66E-09	IL2, SMAD7, HLA-DRB1...all 6
Formation of skin	4.87E-09	SMAD7, HLA-DRB1, S... ...all 5
Quantity of mononuclear leu	5.62E-09	IL2, SMAD7, HLA-DRB1...all 6
Differentiation of T lymphoc	1.30E-08	IL2, SMAD7, HLA-DRB1...all 5
Activation of T lymphocytes	1.71E-08	IL2, HLA-DRB1, SMAD3...all 5
Transcription of DNA	3.61E-08	IL2, SMAD7, HLA-DRB1...all 6
Differentiation of memory T l	4.11E-08	IL2, HLA-DRB1, PRDM1...all 3
Cell viability of lymphocytes	5.19E-08	IL2, SMAD3, PRDM1, ...all 4
Transactivation	5.58E-08	IL2, SMAD7, SMAD3, ...all 5
Proliferation of tumor cells	1.14E-07	IL2, SMAD7, SMAD3, ...all 5
Quantity of T lymphocytes	1.24E-07	IL2, SMAD7, HLA-DRB1...all 5

S

0/355

Reset Apply

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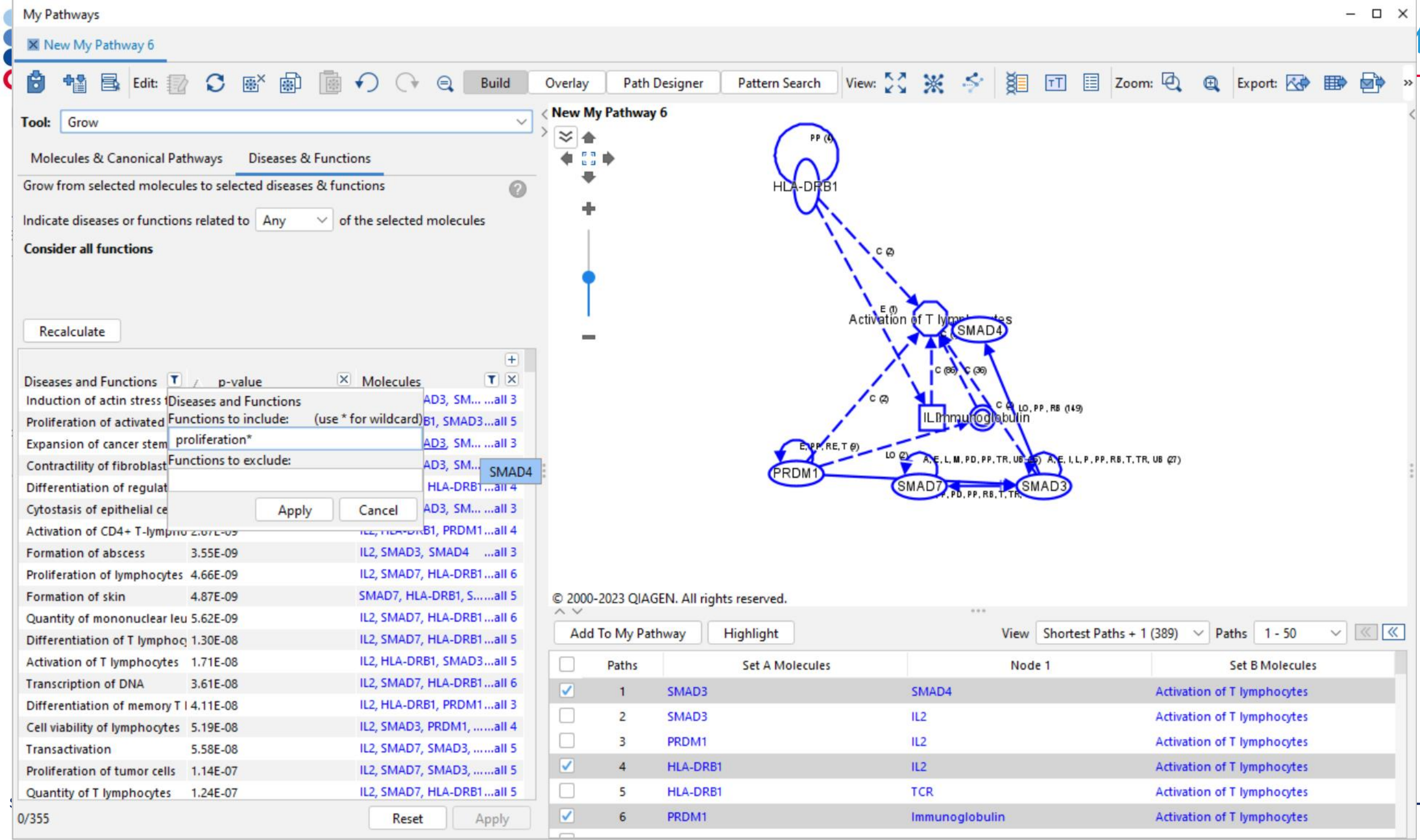
Add To My Pathway | Highlight

View: Shortest Paths + 1 (389) Paths 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes



Tool: Grow

Grow from selected molecules to selected diseases & functions

Indicate diseases or functions related to Any of the selected molecules

Consider all functions

Diseases and Functions	p-value	Molecules
Induction of actin stress f		AD3, SM... ...all 3
Proliferation of activated		B1, SMAD3...all 5
Expansion of cancer stem		AD3, SM... ...all 3
Contractility of fibroblast		AD3, SM...
Differentiation of regulat		HLA-DRB1...all 4
Cytostasis of epithelial ce		AD3, SM... ...all 3
Activation of CD4+ T-lympho	[illegible]	IL2, HLA-DRB1, PRDM1...all 4
Formation of abscess	3.55E-09	IL2, SMAD3, SMAD4 ...all 3
Proliferation of lymphocytes	4.66E-09	IL2, SMAD7, HLA-DRB1...all 6
Formation of skin	4.87E-09	SMAD7, HLA-DRB1, S... ...all 5
Quantity of mononuclear leu	5.62E-09	IL2, SMAD7, HLA-DRB1...all 6
Differentiation of T lymphoc	1.30E-08	IL2, SMAD7, HLA-DRB1...all 5
Activation of T lymphocytes	1.71E-08	IL2, HLA-DRB1, SMAD3...all 5
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Differentiation of memory T l	4.11E-08	IL2, HLA-DRB1, PRDM1...all 3
Cell viability of lymphocytes	5.19E-08	IL2, SMAD3, PRDM1, ...all 4
Transactivation	5.58E-08	IL2, SMAD7, SMAD3, ...all 5
Proliferation of tumor cells	1.14E-07	IL2, SMAD7, SMAD3, ...all 5
Quantity of T lymphocytes	1.24E-07	IL2, SMAD7, HLA-DRB1...all 5

Diseases and Functions

Functions to include: (use * for wildcard)

proliferation*

Functions to exclude:

New My Pathway 6

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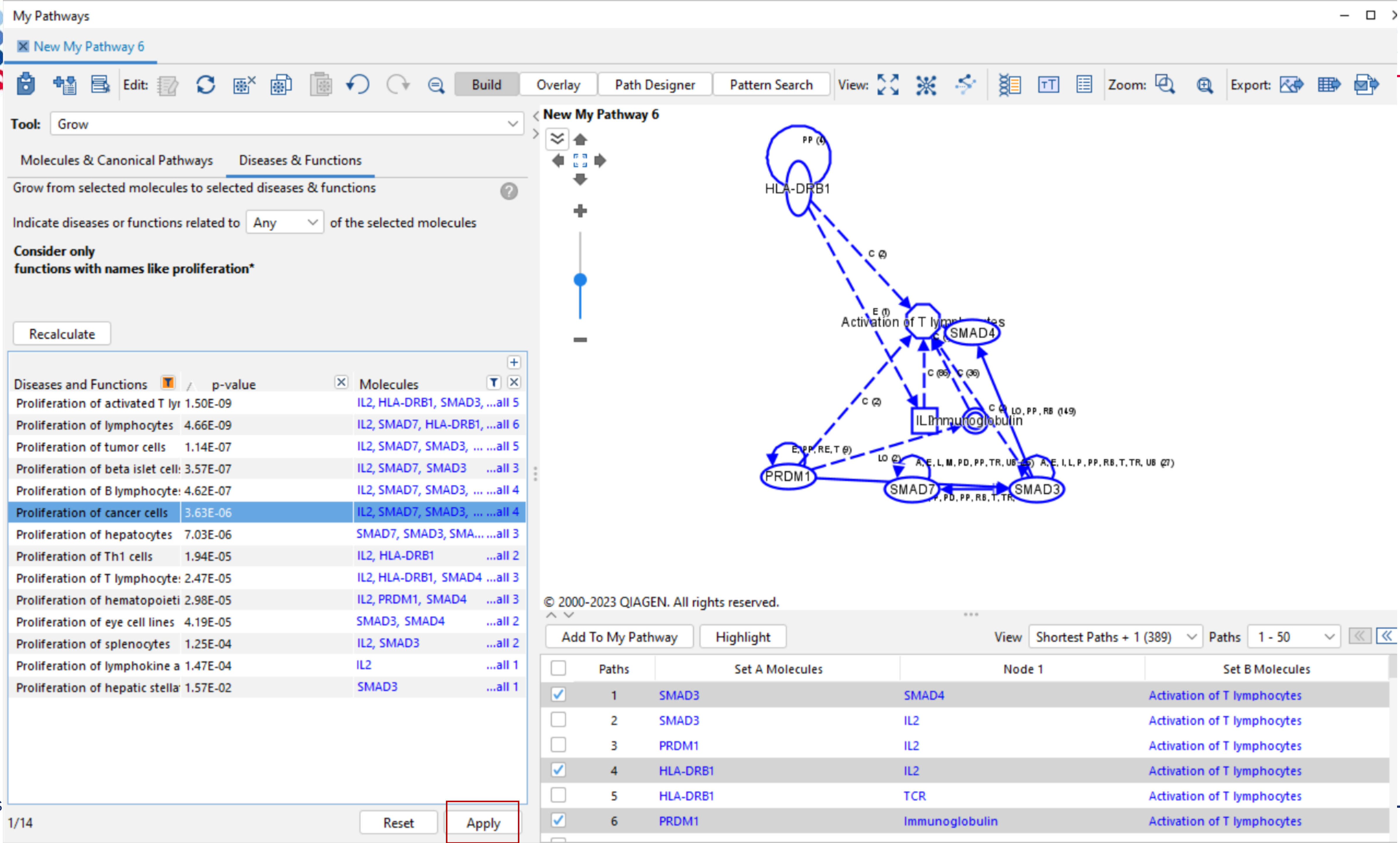
View: Shortest Paths + 1 (389) Paths: 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

位



Tool: Grow

Molecules & Canonical Pathways | Diseases & Functions

Grow from selected molecules to selected diseases & functions

Indicate diseases or functions related to Any of the selected molecules

Consider only
functions with names like proliferation*

Recalculate

Diseases and Functions	p-value	Molecules
Proliferation of activated T lyı	1.50E-09	IL2, HLA-DRB1, SMAD3, ...all 5
Proliferation of lymphocytes	4.66E-09	IL2, SMAD7, HLA-DRB1, ...all 6
Proliferation of tumor cells	1.14E-07	IL2, SMAD7, SMAD3, ...all 5
Proliferation of beta islet cell:	3.57E-07	IL2, SMAD7, SMAD3 ...all 3
Proliferation of B lymphocyte:	4.62E-07	IL2, SMAD7, SMAD3, ...all 4
Proliferation of cancer cells	3.63E-06	IL2, SMAD7, SMAD3, ...all 4
Proliferation of hepatocytes	7.03E-06	SMAD7, SMAD3, SMA... ...all 3
Proliferation of Th1 cells	1.94E-05	IL2, HLA-DRB1 ...all 2
Proliferation of T lymphocyte:	2.47E-05	IL2, HLA-DRB1, SMAD4 ...all 3
Proliferation of hematopoieti	2.98E-05	IL2, PRDM1, SMAD4 ...all 3
Proliferation of eye cell lines	4.19E-05	SMAD3, SMAD4 ...all 2
Proliferation of splenocytes	1.25E-04	IL2, SMAD3 ...all 2
Proliferation of lymphokine a	1.47E-04	IL2 ...all 1
Proliferation of hepatic stella	1.57E-02	SMAD3 ...all 1

1/14 Reset Apply

New My Pathway 6

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Add To My Pathway | Highlight | View: Shortest Paths + 1 (389) | Paths: 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

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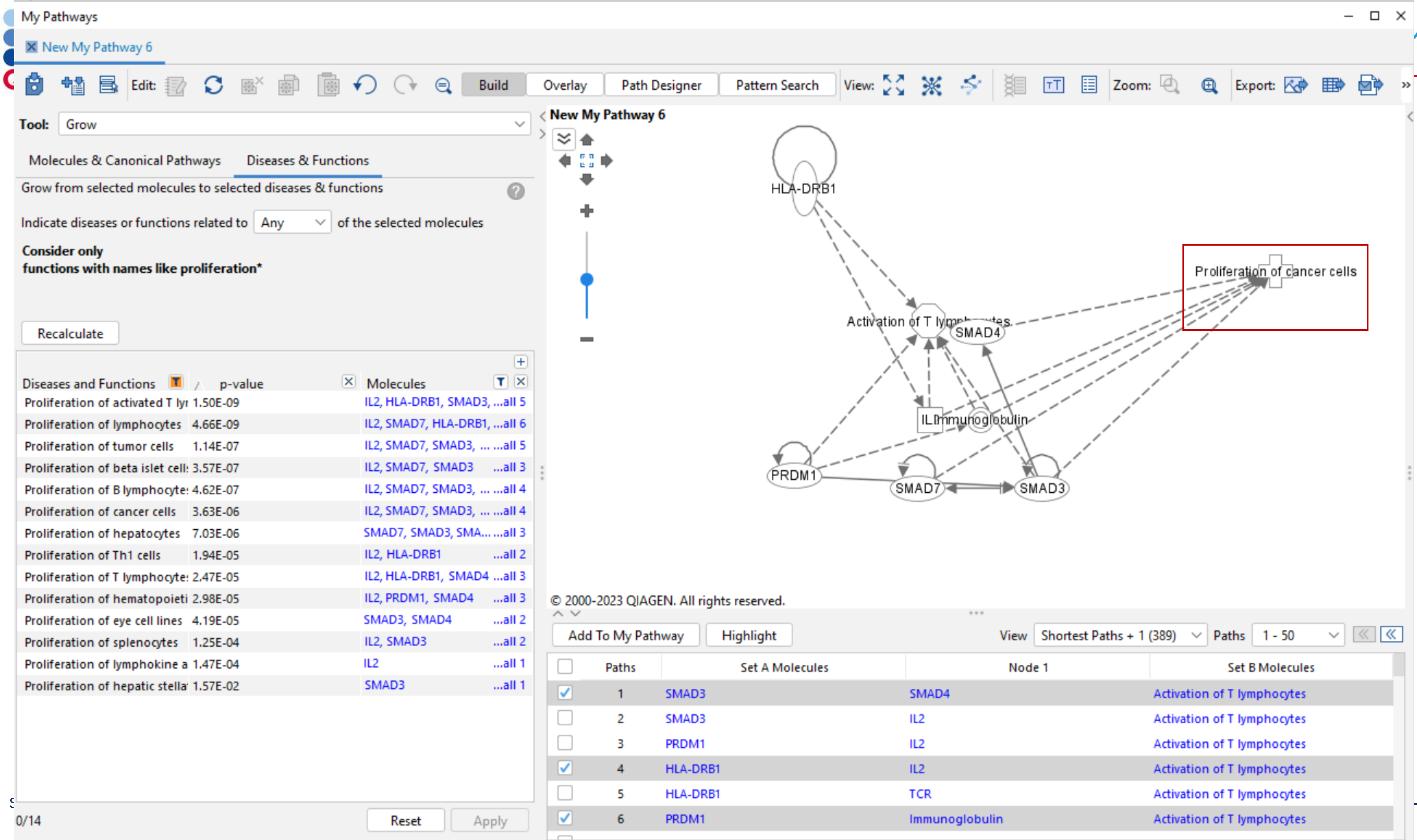
位



Tool: Grow

Molecules & Canonical Pathways | Diseases & Functions

Grow from selected molecules to selected diseases & functions

Indicate diseases or functions related to Any of the selected molecules

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Diseases and Functions	p-value	Molecules	
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Proliferation of tumor cells	1.14E-07	IL2, SMAD7, SMAD3, ...	...all 5
Proliferation of beta islet cell:	3.57E-07	IL2, SMAD7, SMAD3	...all 3
Proliferation of B lymphocyte:	4.62E-07	IL2, SMAD7, SMAD3, ...	...all 4
Proliferation of cancer cells	3.63E-06	IL2, SMAD7, SMAD3, ...	...all 4
Proliferation of hepatocytes	7.03E-06	SMAD7, SMAD3, SMA...	...all 3
Proliferation of Th1 cells	1.94E-05	IL2, HLA-DRB1	...all 2
Proliferation of T lymphocyte:	2.47E-05	IL2, HLA-DRB1, SMAD4	...all 3
Proliferation of hematopoieti	2.98E-05	IL2, PRDM1, SMAD4	...all 3
Proliferation of eye cell lines	4.19E-05	SMAD3, SMAD4	...all 2
Proliferation of splenocytes	1.25E-04	IL2, SMAD3	...all 2
Proliferation of lymphokine a	1.47E-04	IL2	...all 1
Proliferation of hepatic stella	1.57E-02	SMAD3	...all 1

0/14

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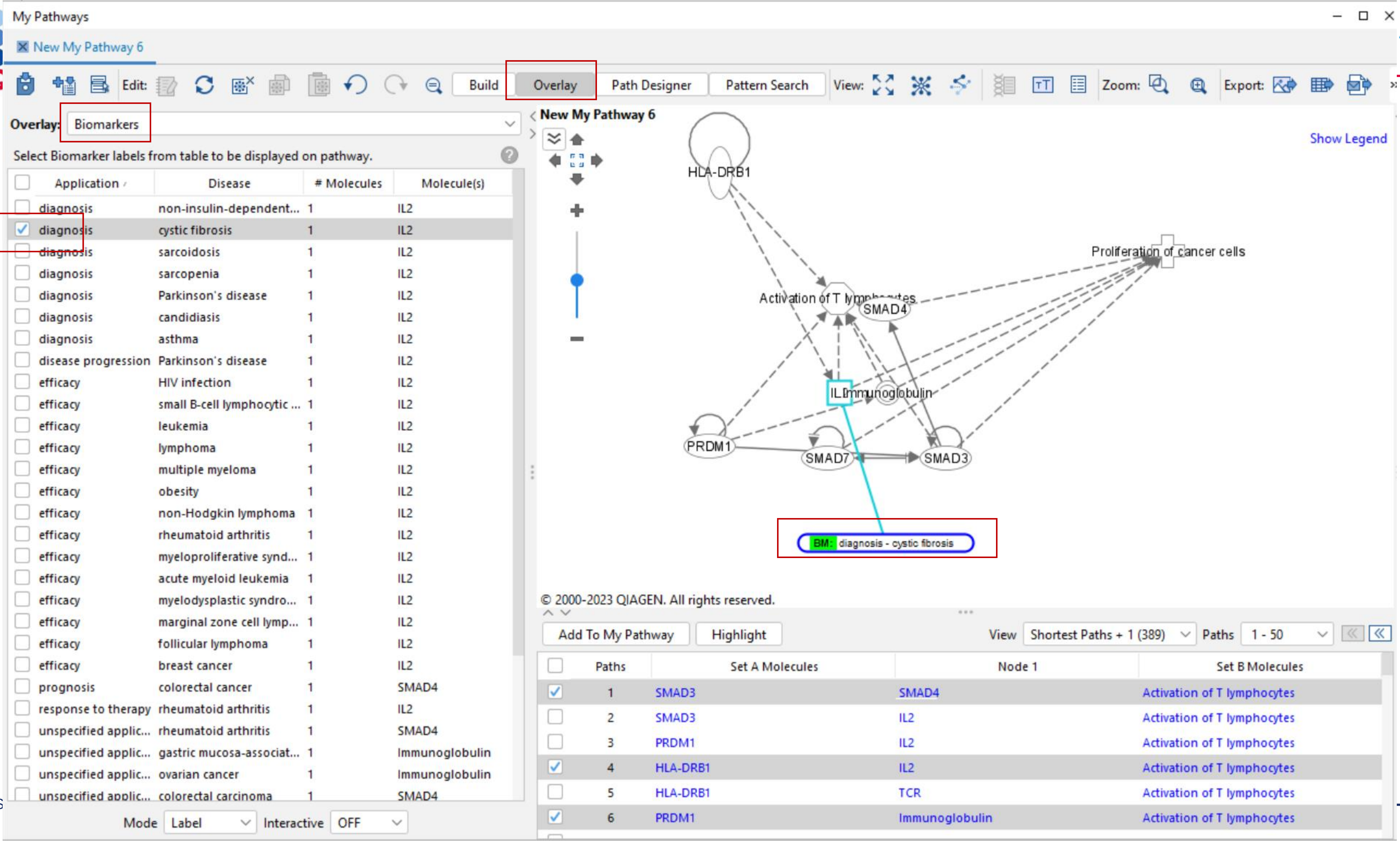
View Shortest Paths + 1 (389) Paths 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

位



Overlay: Biomarkers

Select Biomarker labels from table to be displayed on pathway.

☐	Application	Disease	# Molecules	Molecule(s)
☐	diagnosis	non-insulin-dependent...	1	IL2
☑	diagnosis	cystic fibrosis	1	IL2
☐	diagnosis	sarcoidosis	1	IL2
☐	diagnosis	sarcopenia	1	IL2
☐	diagnosis	Parkinson's disease	1	IL2
☐	diagnosis	candidiasis	1	IL2
☐	diagnosis	asthma	1	IL2
☐	disease progression	Parkinson's disease	1	IL2
☐	efficacy	HIV infection	1	IL2
☐	efficacy	small B-cell lymphocytic ...	1	IL2
☐	efficacy	leukemia	1	IL2
☐	efficacy	lymphoma	1	IL2
☐	efficacy	multiple myeloma	1	IL2
☐	efficacy	obesity	1	IL2
☐	efficacy	non-Hodgkin lymphoma	1	IL2
☐	efficacy	rheumatoid arthritis	1	IL2
☐	efficacy	myeloproliferative synd...	1	IL2
☐	efficacy	acute myeloid leukemia	1	IL2
☐	efficacy	myelodysplastic syndro...	1	IL2
☐	efficacy	marginal zone cell lymp...	1	IL2
☐	efficacy	follicular lymphoma	1	IL2
☐	efficacy	breast cancer	1	IL2
☐	prognosis	colorectal cancer	1	SMAD4
☐	response to therapy	rheumatoid arthritis	1	IL2
☐	unspecified applic...	rheumatoid arthritis	1	SMAD4
☐	unspecified applic...	gastric mucosa-associat...	1	Immunoglobulin
☐	unspecified applic...	ovarian cancer	1	Immunoglobulin
☐	unspecified applic...	colorectal carcinoma	1	SMAD4

Mode: Label Interactive: OFF

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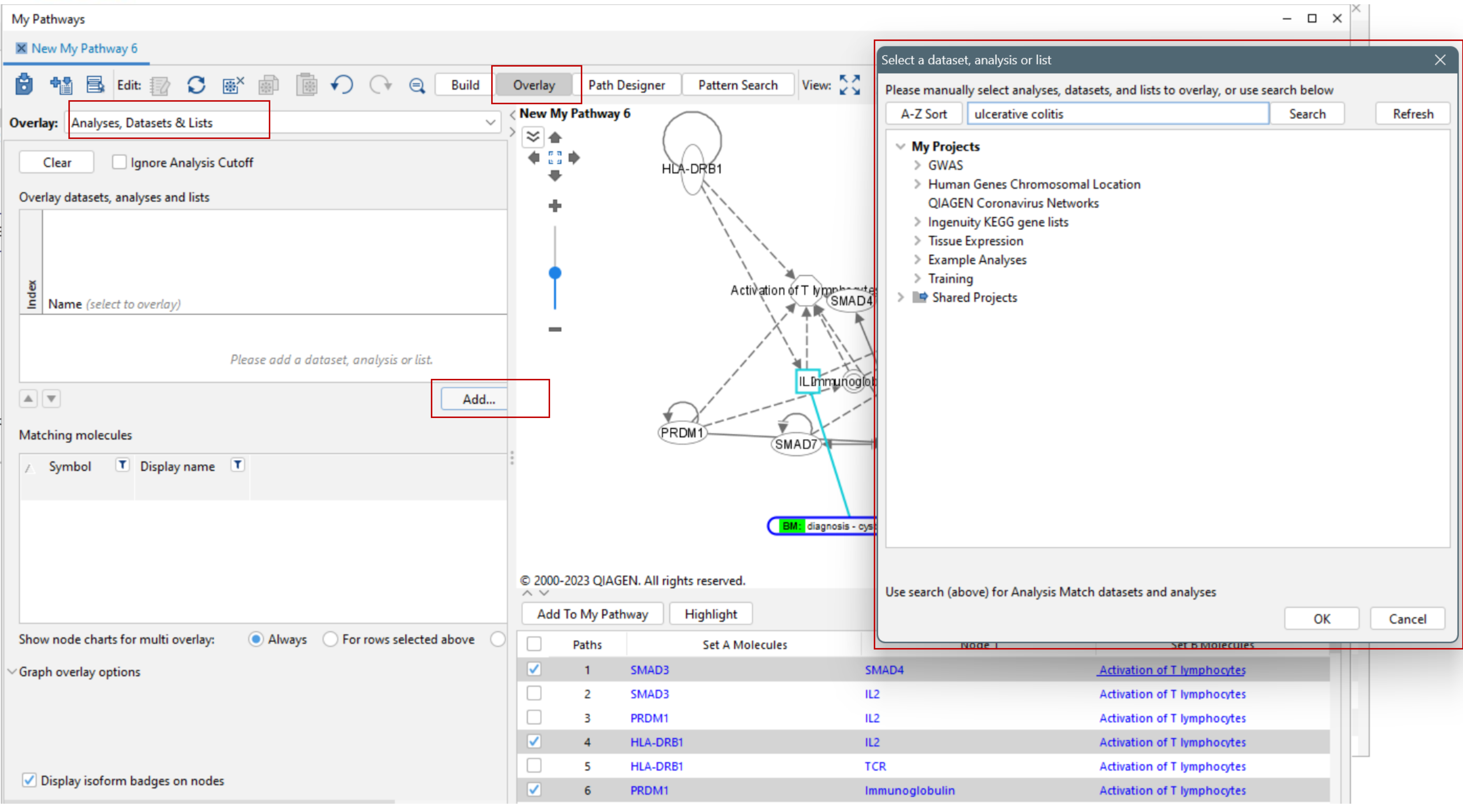
View: Shortest Paths + 1 (389) Paths: 1 - 50

☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes



Overlay: Analyses, Datasets & Lists

☐ Ignore Analysis Cutoff

Overlay datasets, analyses and lists

Name *(select to overlay)*

Please add a dataset, analysis or list.

Matching molecules

Symbol	Display name

Show node charts for multi overlay: ● Always ○ For rows selected above ○

Graph overlay options

☑ Display isoform badges on nodes

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☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

Select a dataset, analysis or list

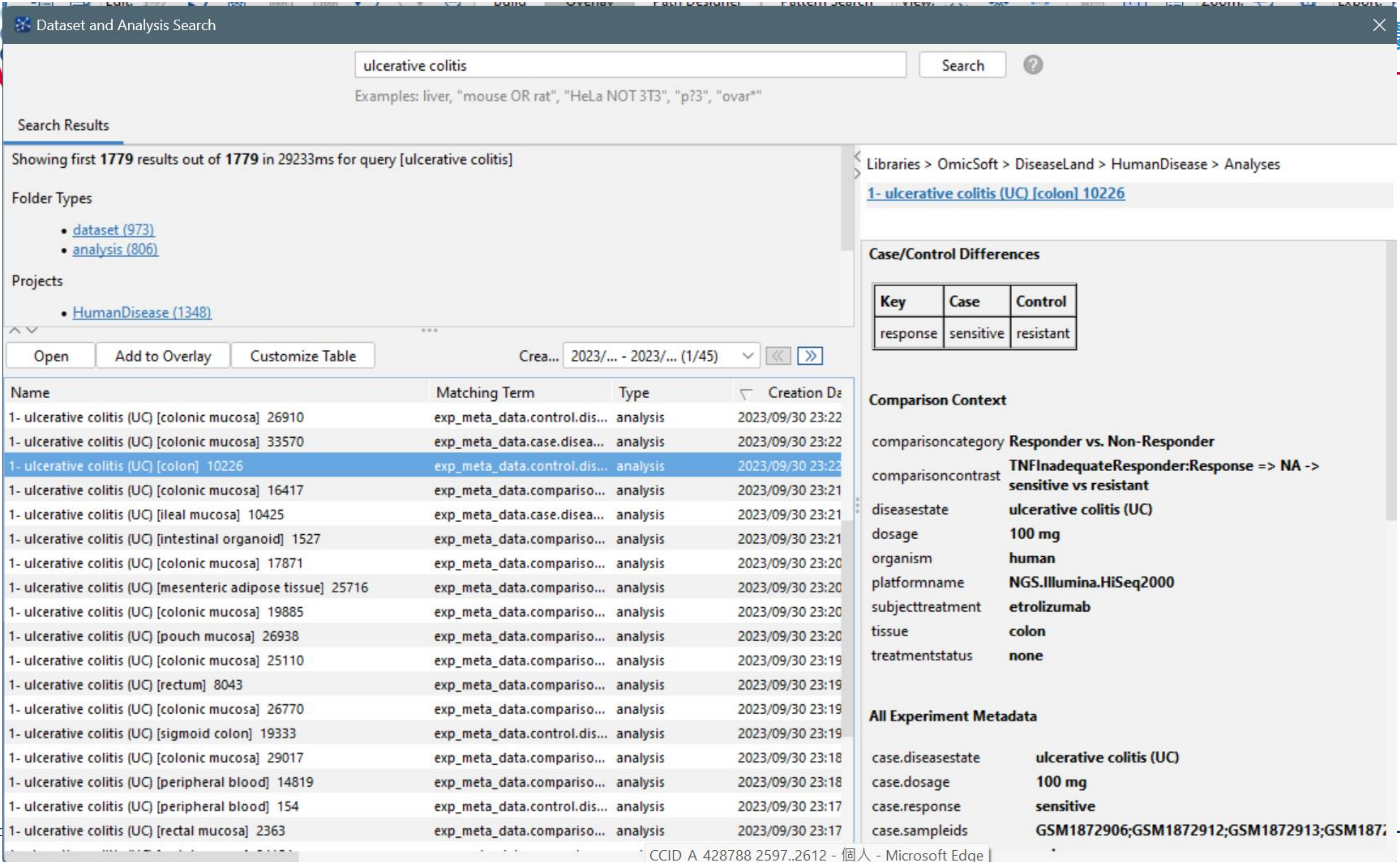
Please manually select analyses, datasets, and lists to overlay, or use search below

ulcerative colitis

- **My Projects**
  - GWAS
  - Human Genes Chromosomal Location
  - QIAGEN Coronavirus Networks
  - Ingenuity KEGG gene lists
  - Tissue Expression
  - Example Analyses
  - Training
- Shared Projects

Use search (above) for Analysis Match datasets and analyses

數位



Dataset and Analysis Search

ulcerative colitis

Search

Examples: liver, "mouse OR rat", "HeLa NOT 3T3", "p?3", "ovar*"

Search Results

Showing first **1779** results out of **1779** in 29233ms for query [ulcerative colitis]

Folder Types

- dataset (973)
- analysis (806)

Projects

- HumanDisease (1348)

Open | Add to Overlay | Customize Table | Crea... 2023/... - 2023/... (1/45)

Name	Matching Term	Type	Creation Da
1- ulcerative colitis (UC) [colonic mucosa] 26910	exp_meta_data.control.dis...	analysis	2023/09/30 23:22
1- ulcerative colitis (UC) [colonic mucosa] 33570	exp_meta_data.case.disea...	analysis	2023/09/30 23:22
1- ulcerative colitis (UC) [colon] 10226	exp_meta_data.control.dis...	analysis	2023/09/30 23:22
1- ulcerative colitis (UC) [colonic mucosa] 16417	exp_meta_data.compariso...	analysis	2023/09/30 23:21
1- ulcerative colitis (UC) [ileal mucosa] 10425	exp_meta_data.case.disea...	analysis	2023/09/30 23:21
1- ulcerative colitis (UC) [intestinal organoid] 1527	exp_meta_data.compariso...	analysis	2023/09/30 23:21
1- ulcerative colitis (UC) [colonic mucosa] 17871	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [mesenteric adipose tissue] 25716	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [colonic mucosa] 19885	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [pouch mucosa] 26938	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [colonic mucosa] 25110	exp_meta_data.compariso...	analysis	2023/09/30 23:19
1- ulcerative colitis (UC) [rectum] 8043	exp_meta_data.compariso...	analysis	2023/09/30 23:19
1- ulcerative colitis (UC) [colonic mucosa] 26770	exp_meta_data.compariso...	analysis	2023/09/30 23:19
1- ulcerative colitis (UC) [sigmoid colon] 19333	exp_meta_data.control.dis...	analysis	2023/09/30 23:19
1- ulcerative colitis (UC) [colonic mucosa] 29017	exp_meta_data.compariso...	analysis	2023/09/30 23:18
1- ulcerative colitis (UC) [peripheral blood] 14819	exp_meta_data.compariso...	analysis	2023/09/30 23:18
1- ulcerative colitis (UC) [peripheral blood] 154	exp_meta_data.control.dis...	analysis	2023/09/30 23:17
1- ulcerative colitis (UC) [rectal mucosa] 2363	exp_meta_data.compariso...	analysis	2023/09/30 23:17

Libraries > OmicSoft > DiseaseLand > HumanDisease > Analyses

1- ulcerative colitis (UC) [colon] 10226

Case/Control Differences

Key	Case	Control
response	sensitive	resistant

Comparison Context

comparisoncategory	**Responder vs. Non-Responder**
comparisoncontrast	**TNFInadequateResponder:Response => NA -> sensitive vs resistant**
diseasestate	**ulcerative colitis (UC)**
dosage	**100 mg**
organism	**human**
platformname	**NGS.Illumina.HiSeq2000**
subjecttreatment	**etrolizumab**
tissue	**colon**
treatmentstatus	**none**

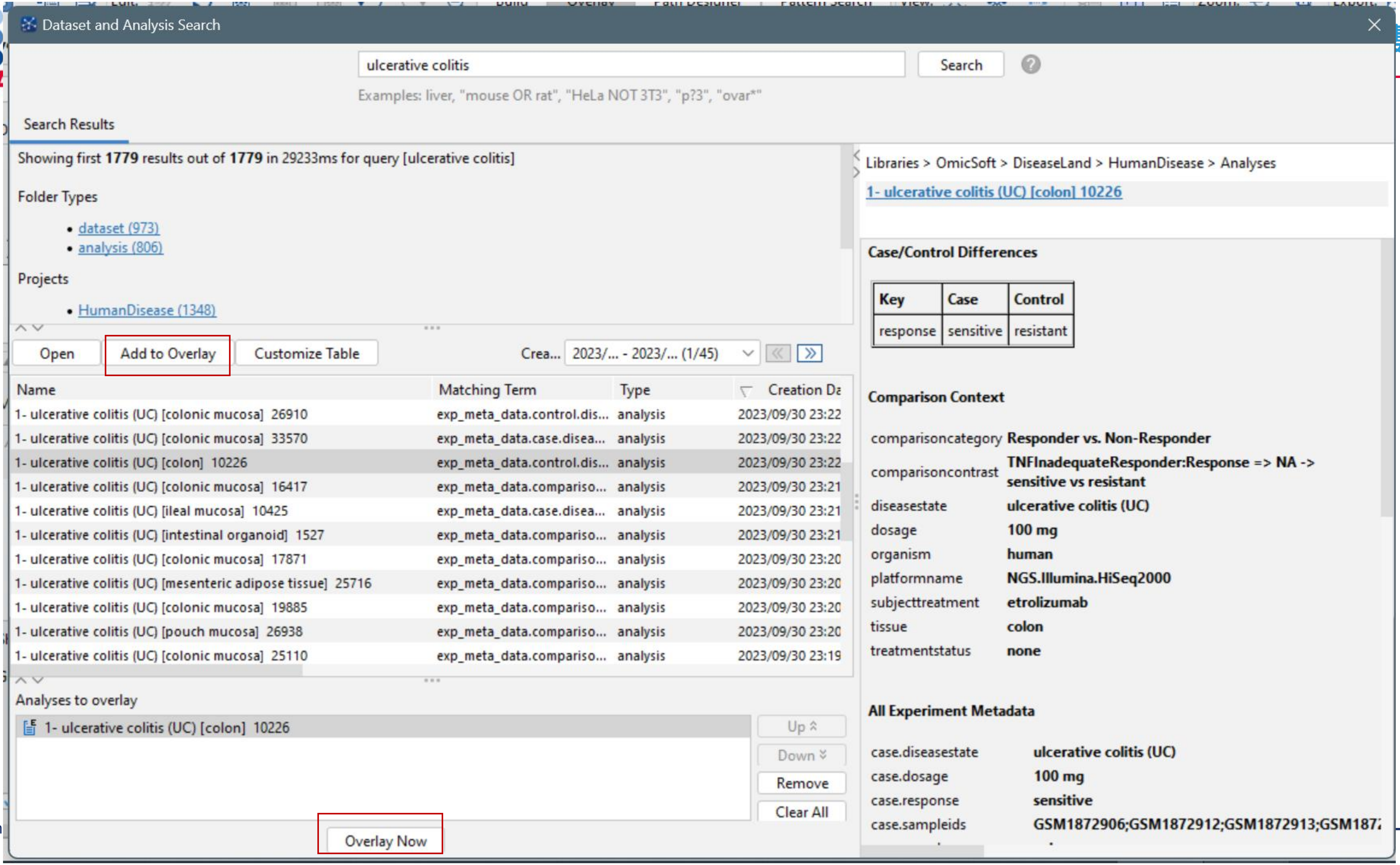
All Experiment Metadata

case.diseasestate	**ulcerative colitis (UC)**
case.dosage	**100 mg**
case.response	**sensitive**
case.sampleids	**GSM1872906;GSM1872912;GSM1872913;GSM187**

CCID_A_428788 2597..2612 - 個人 - Microsoft Edge

Samp

數位



Dataset and Analysis Search

ulcerative colitis

Examples: liver, "mouse OR rat", "HeLa NOT 3T3", "p?3", "ovar*"

Showing first **1779** results out of **1779** in 29233ms for query [ulcerative colitis]

Folder Types

- dataset (973)
- analysis (806)

Projects

- HumanDisease (1348)

Name	Matching Term	Type	Creation Da
1- ulcerative colitis (UC) [colonic mucosa] 26910	exp_meta_data.control.dis...	analysis	2023/09/30 23:22
1- ulcerative colitis (UC) [colonic mucosa] 33570	exp_meta_data.case.disea...	analysis	2023/09/30 23:22
1- ulcerative colitis (UC) [colon] 10226	exp_meta_data.control.dis...	analysis	2023/09/30 23:22
1- ulcerative colitis (UC) [colonic mucosa] 16417	exp_meta_data.compariso...	analysis	2023/09/30 23:21
1- ulcerative colitis (UC) [ileal mucosa] 10425	exp_meta_data.case.disea...	analysis	2023/09/30 23:21
1- ulcerative colitis (UC) [intestinal organoid] 1527	exp_meta_data.compariso...	analysis	2023/09/30 23:21
1- ulcerative colitis (UC) [colonic mucosa] 17871	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [mesenteric adipose tissue] 25716	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [colonic mucosa] 19885	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [pouch mucosa] 26938	exp_meta_data.compariso...	analysis	2023/09/30 23:20
1- ulcerative colitis (UC) [colonic mucosa] 25110	exp_meta_data.compariso...	analysis	2023/09/30 23:19

Analyses to overlay

- 1- ulcerative colitis (UC) [colon] 10226

Libraries > OmicSoft > DiseaseLand > HumanDisease > Analyses

1- ulcerative colitis (UC) [colon] 10226

Case/Control Differences

Key	Case	Control
response	sensitive	resistant

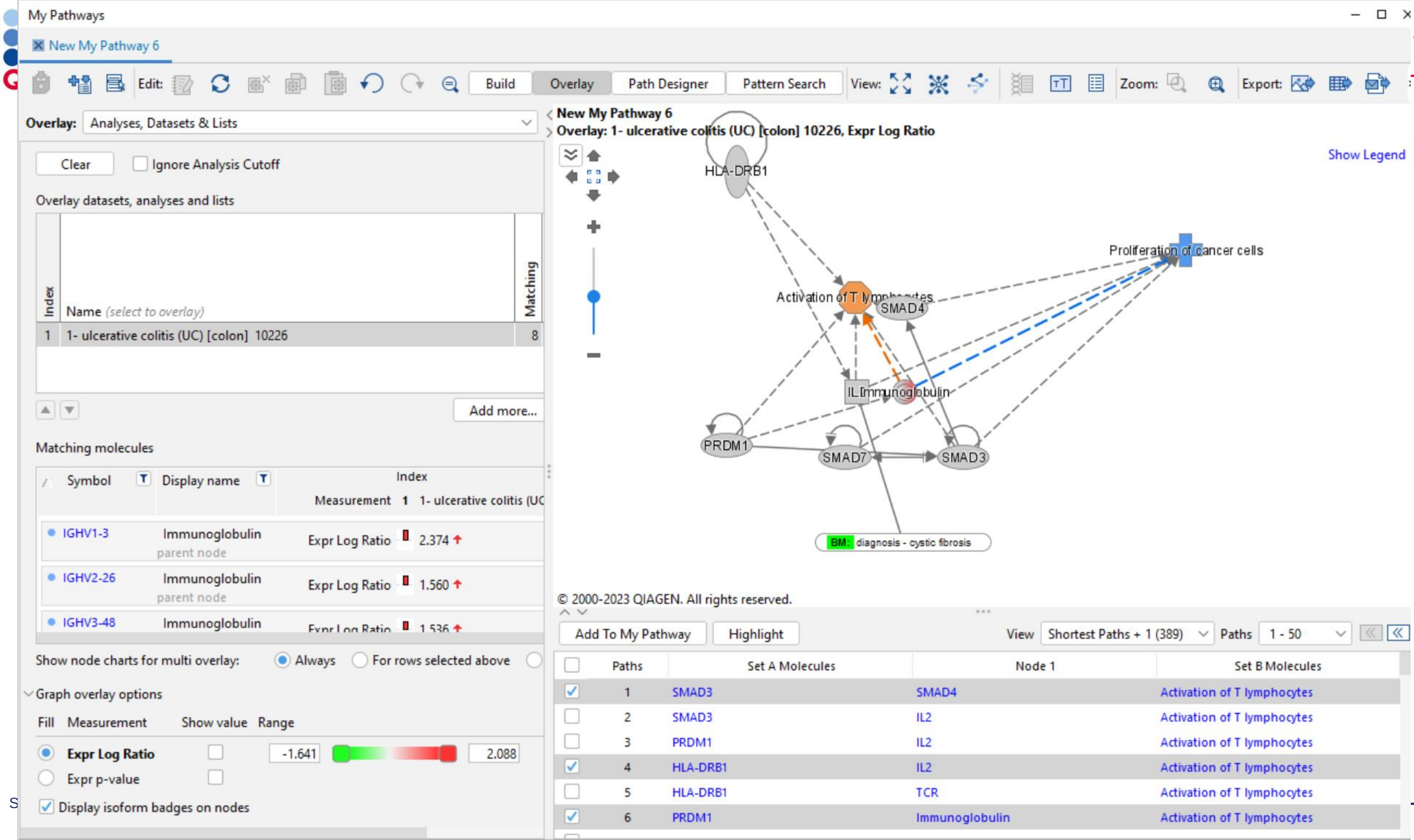
Comparison Context

comparisoncategory	**Responder vs. Non-Responder**
comparisoncontrast	**TNFInadequateResponder:Response => NA -> sensitive vs resistant**
diseasestate	**ulcerative colitis (UC)**
dosage	**100 mg**
organism	**human**
platformname	**NGS.Illumina.HiSeq2000**
subjecttreatment	**etrolizumab**
tissue	**colon**
treatmentstatus	**none**

All Experiment Metadata

case.diseasestate	**ulcerative colitis (UC)**
case.dosage	**100 mg**
case.response	**sensitive**
case.sampleids	**GSM1872906;GSM1872912;GSM1872913;GSM187**

位



Overlay: Analyses, Datasets & Lists

☐ Ignore Analysis Cutoff

Overlay datasets, analyses and lists

Index	Name (select to overlay)	Matching
1	1- ulcerative colitis (UC) [colon] 10226	8

Matching molecules

Symbol	Display name	Measurement	1 1- ulcerative colitis (UC
IGHV1-3	Immunoglobulin parent node	Expr Log Ratio	2.374 ↑
IGHV2-26	Immunoglobulin parent node	Expr Log Ratio	1.560 ↑
IGHV3-48	Immunoglobulin	Expr Log Ratio	1.536 ↑

Show node charts for multi overlay: ● Always ○ For rows selected above ○

Graph overlay options

Fill	Measurement	Show value	Range
●	**Expr Log Ratio**	☐	-1.641 to 2.088
○	Expr p-value	☐	

☑ Display isoform badges on nodes

New My Pathway 6
Overlay: 1- ulcerative colitis (UC) [colon] 10226, Expr Log Ratio

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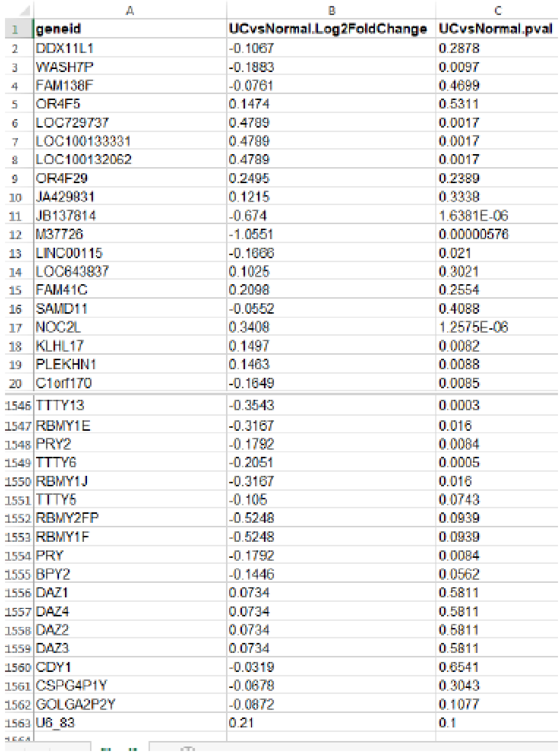
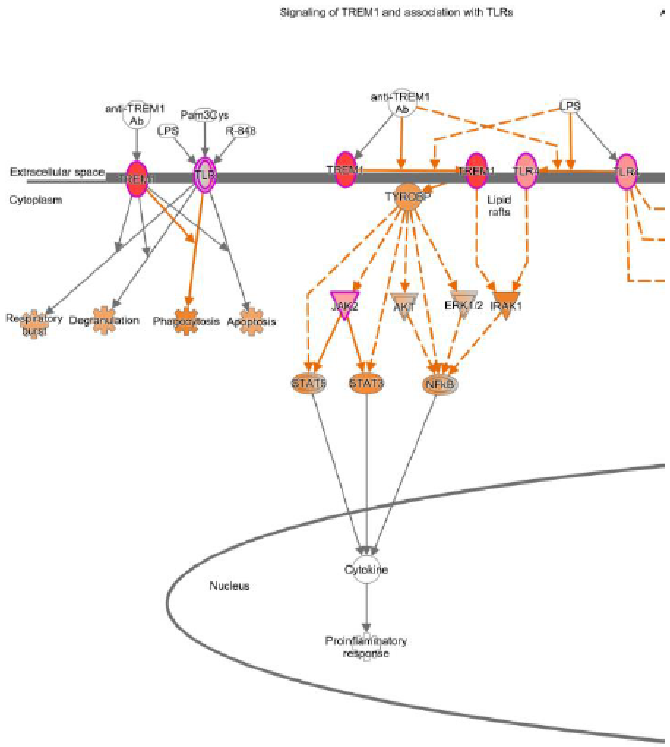
View: Shortest Paths + 1 (389) Paths: 1 - 50

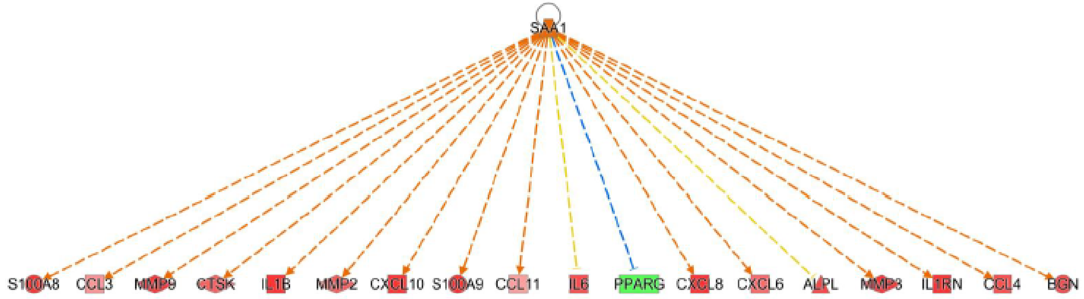
☐	Paths	Set A Molecules	Node 1	Set B Molecules
☑	1	SMAD3	SMAD4	Activation of T lymphocytes
☐	2	SMAD3	IL2	Activation of T lymphocytes
☐	3	PRDM1	IL2	Activation of T lymphocytes
☑	4	HLA-DRB1	IL2	Activation of T lymphocytes
☐	5	HLA-DRB1	TCR	Activation of T lymphocytes
☑	6	PRDM1	Immunoglobulin	Activation of T lymphocytes

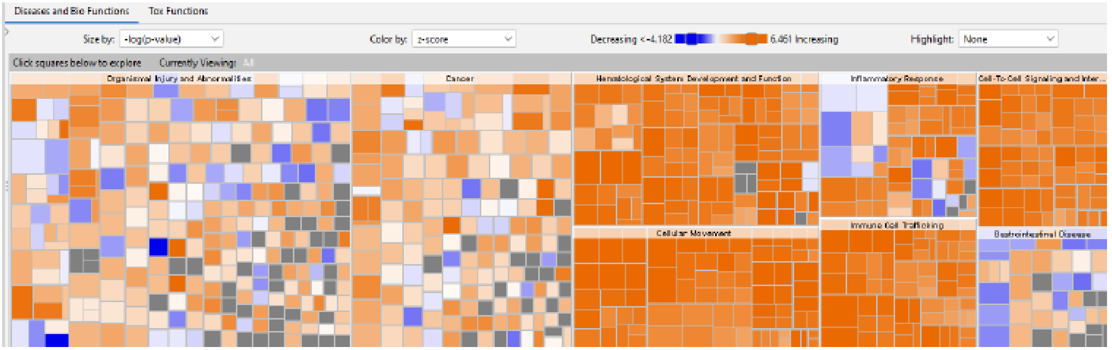
Summary: Evaluating your’s omics data using IPA



	A	B	C
1	**geneid**	**UCvsNormal.Log2FoldChange**	**UCvsNormal.pval**
2	DDX11L1	-0.1067	0.2878
3	WASH7P	-0.1883	0.0097
4	FAM138F	-0.0761	0.4699
5	OR4F5	0.1474	0.5311
6	LOC729737	0.4789	0.0017
7	LOC100133331	0.4789	0.0017
8	LOC100132062	0.4789	0.0017
9	OR4F29	0.2495	0.2389
10	JA429831	0.1215	0.3338
11	JB137814	-0.674	1.6381E-06
12	M37726	-1.0551	0.00000576
13	LINC00115	-0.1666	0.021
14	LOC643837	0.1025	0.3021
15	FAM41C	0.2098	0.2554
16	SAMD11	-0.0552	0.4088
17	NOC2L	0.3408	1.2575E-06
18	KLHL17	0.1497	0.0082
19	PLEKHN1	0.1463	0.0088
20	C1orf170	-0.1649	0.0085
1546	TTTY13	-0.3543	0.0003
1547	RBMY1E	-0.3167	0.016
1548	PRY2	-0.1792	0.0084
1549	TTTY6	-0.2051	0.0005
1550	RBMY1J	-0.3167	0.016
1551	TTTY5	-0.105	0.0743
1552	RBMY2FP	-0.5248	0.0939
1553	RBMY1F	-0.5248	0.0939
1554	PRY	-0.1792	0.0084
1555	BPY2	-0.1446	0.0562
1556	DAZ1	0.0734	0.5811
1557	DAZ4	0.0734	0.5811
1558	DAZ2	0.0734	0.5811
1559	DAZ3	0.0734	0.5811
1560	CDY1	-0.0319	0.6541
1561	CSPG4P1Y	-0.0678	0.3043
1562	GOLGA2P2Y	-0.0872	0.1077
1563	U6_83	0.21	0.1





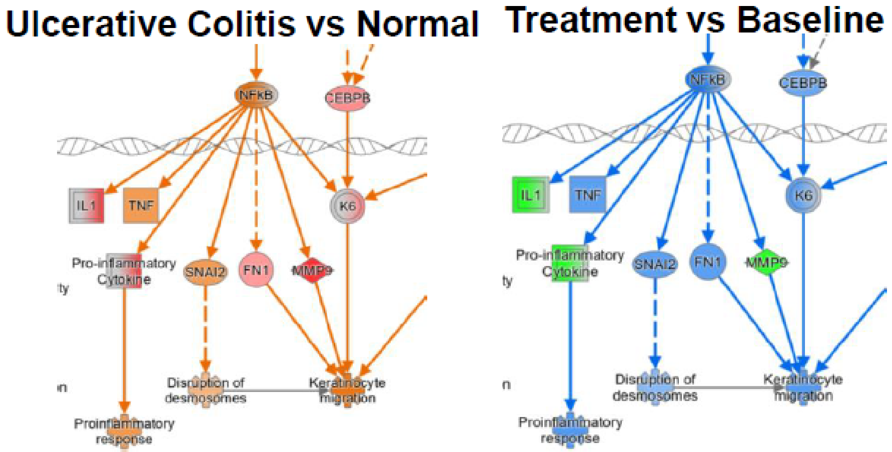


Size by: -log(p-value)

Color by: z-score

Decreasing <-4.182 — 6.461 Increasing

Highlight: None



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

After-Class Questionnaire

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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