QIAGEN Ingenuity Pathway Analysis (IPA): Biological Interpretation & Analysis of NGS data

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Agenda

Introduction to Ingenuity Pathway Analysis

Gaining biological insights through interpretation of omic data

- Identify pathways and biological mechanism
- Discover key regulators and targets
- Study impacted biological functions and diseases

Generating hypothesis without a dataset

- Build custom networks and in-silico predictions

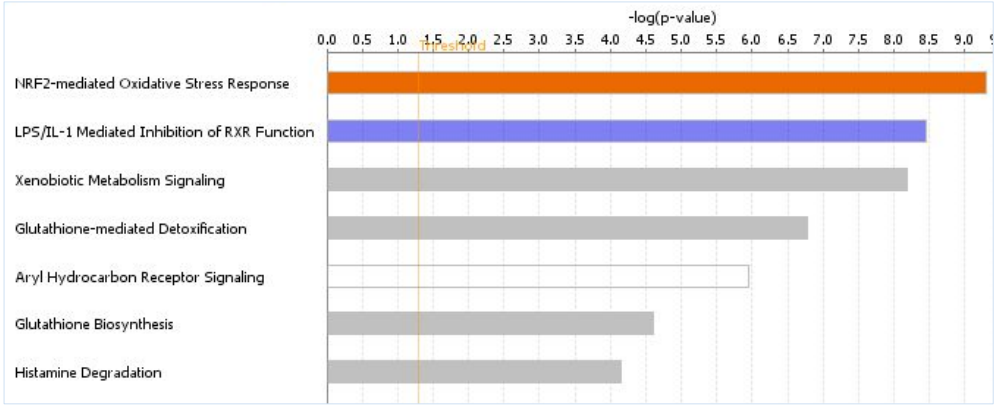
QIAGEN IPA

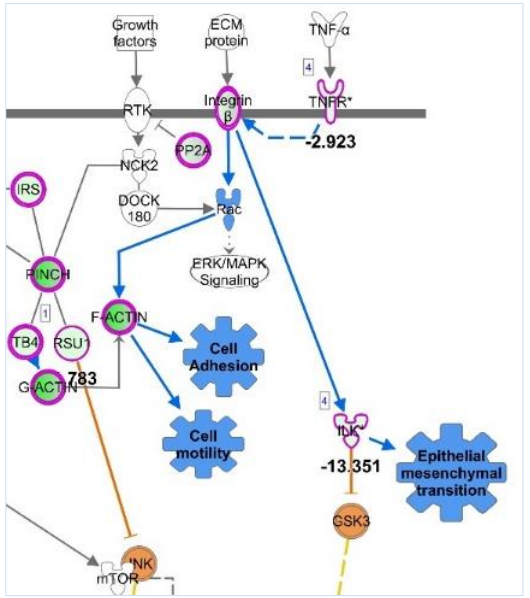
Perform analysis and interpretation of ‘omics data within the context of various biological systems

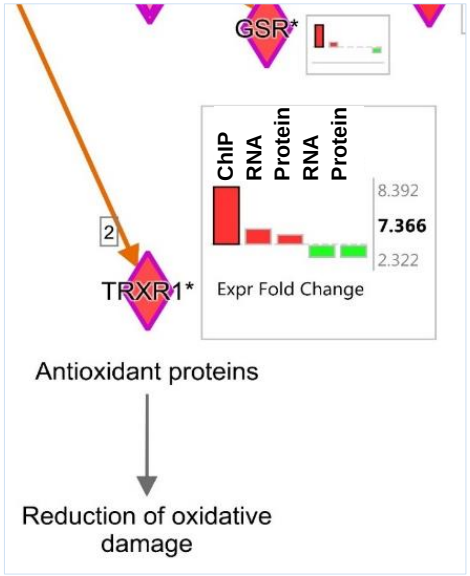
Study biological mechanisms underlying disease pathology, drug treatment or cellular functions

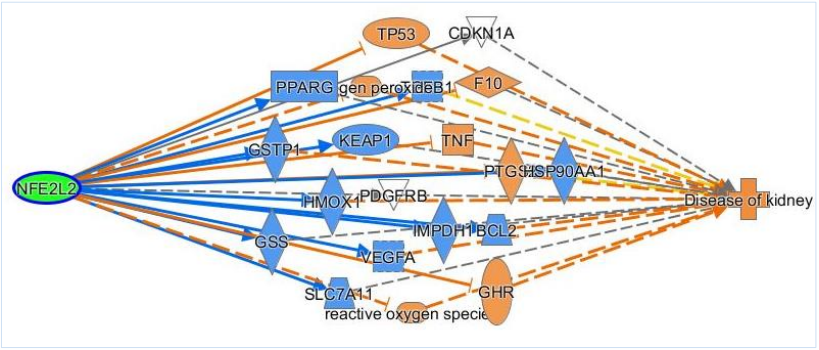
Identify biomarkers and key regulators associated with your experimental data

Investigate gene/disease interactions by generating custom networks

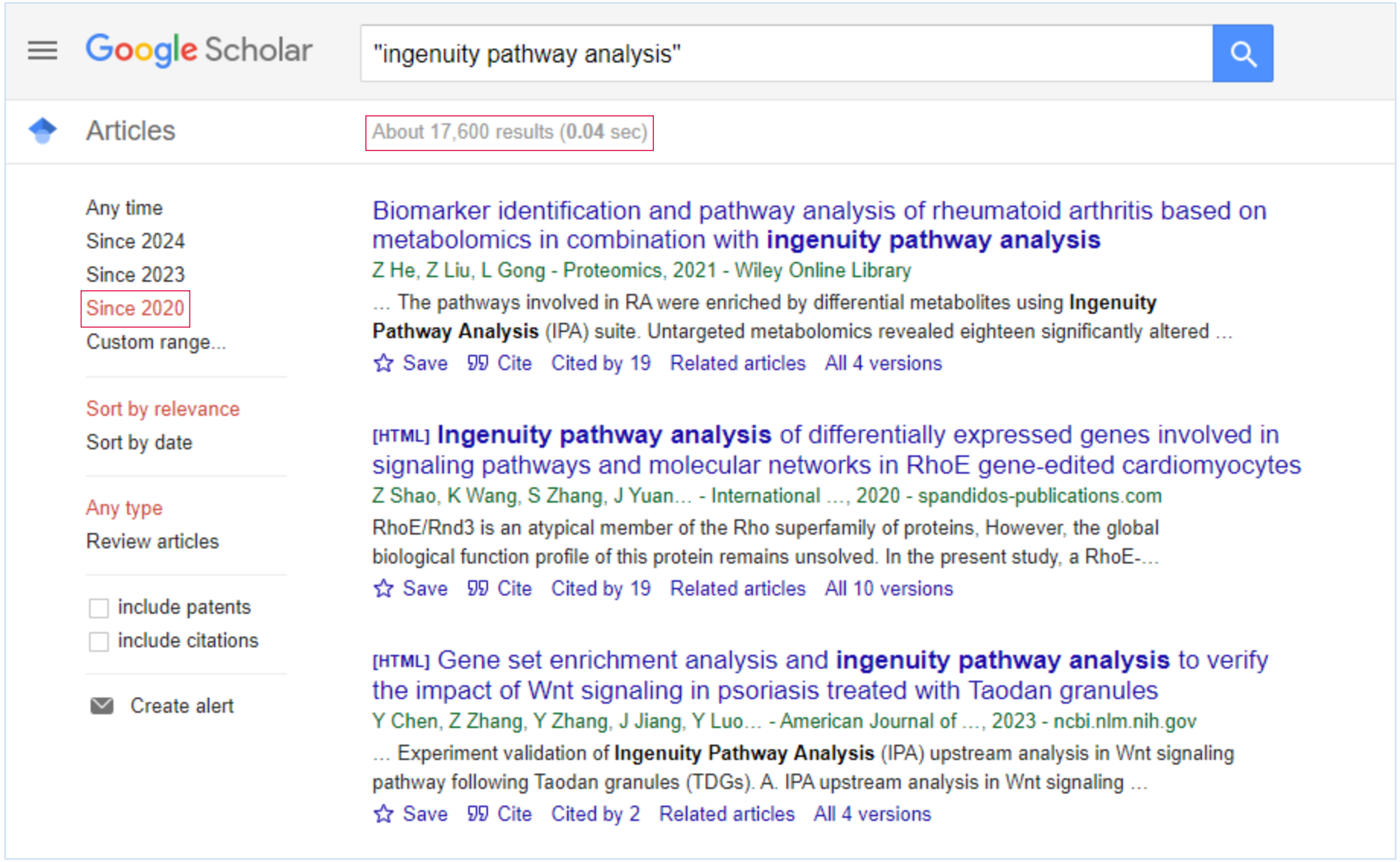








Studies using QIAGEN Ingenuity Pathway Analysis (IPA)



Studies using QIAGEN Ingenuity Pathway Analysis (IPA)

PLoS One. 2019 Jun 26;14(6):e0218674. doi: 10.1371/journal.pone.0218674. eCollection 2019.

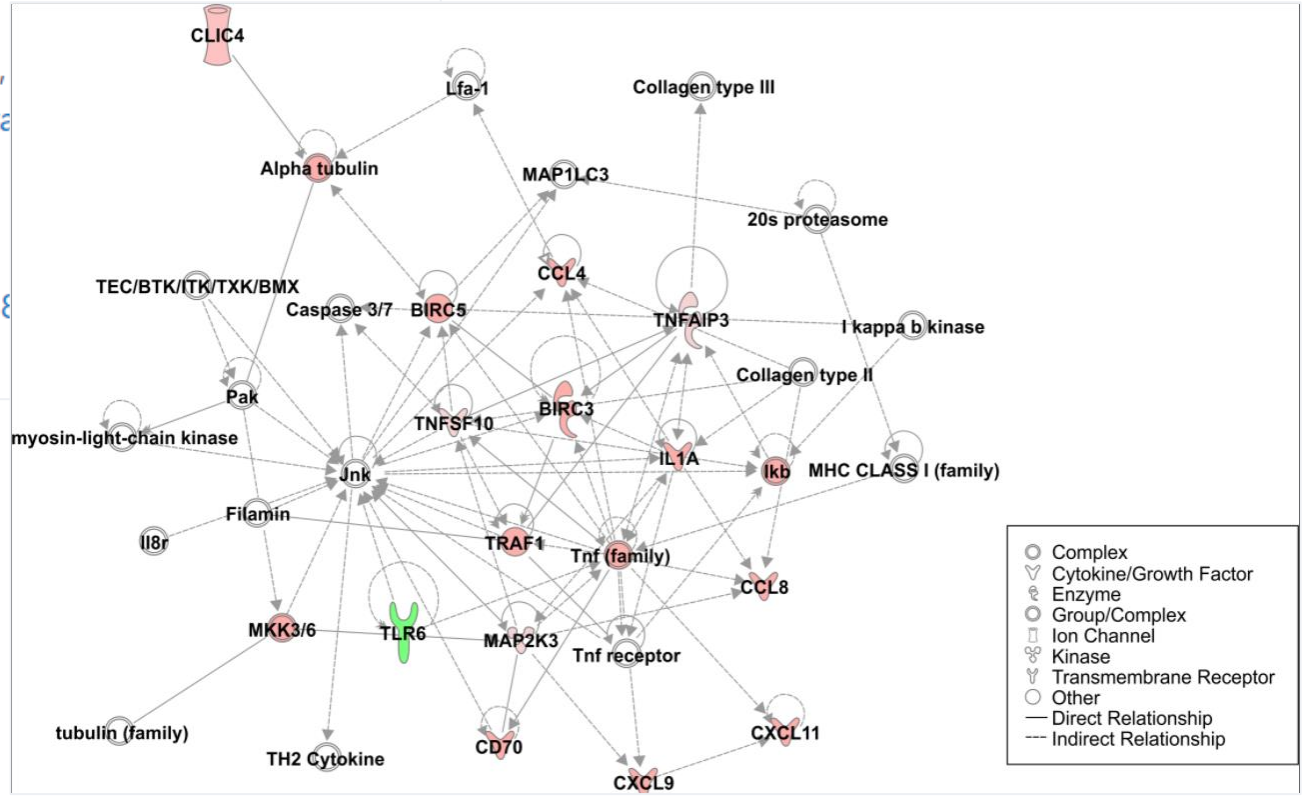
Tumor- and cytokine-primed human natural killer cells exhibit distinct phenotypic and transcriptional signatures

May Sabry [1], Agnieszka Zubiak [1], Simon P Hood [2], Poppy Simmonds [1], Helena Arellano-Ballestero [1], Eily Cournoyer [1], Meghavi Mashar [1], A Gra Mark W Lowdell [1 3]

Affiliations + expand

PMID: 31242243 PMCID: PMC6594622 DOI: 10.1371/journal.pone.021

Free PMC article



Studies using QIAGEN Ingenuity Pathway Analysis (IPA)

Sci Rep. 2021 Jul 6;11(1):13891. doi: 10.1038/s41598-021-93356-9.

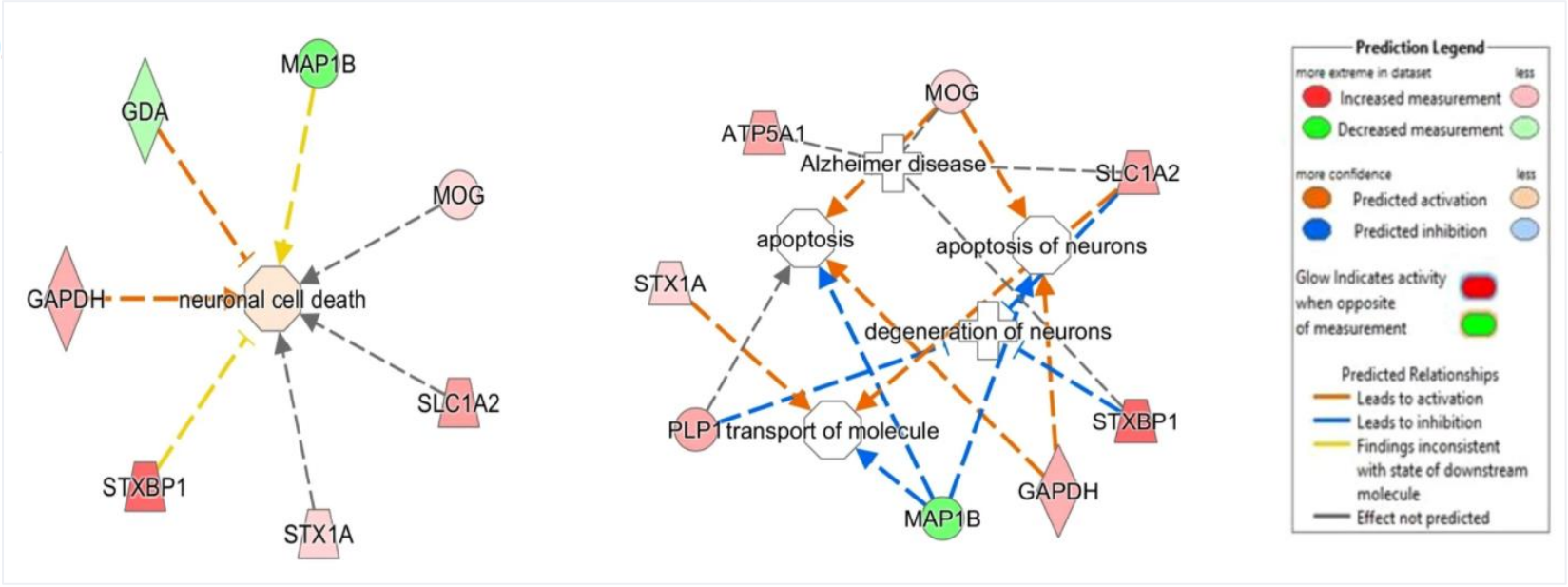
Characterization of functional protein complexes from Alzheimer's disease and healthy brain by mass spectrometry-based proteome analysis

Beena Hasan [1], Ayesha Khan [1], Christof Lenz [2 3], Abdul R Asif [2], Nikhat Ahmed [4]

Affiliations + expand

PMID: 34230543 PMCID: PMC8260596 DOI: 10

Free PMC article



Studies using QIAGEN Ingenuity Pathway Analysis (IPA)

Cells. 2020 Oct 29;9(11):2374. doi: 10.3390/cells9112374.

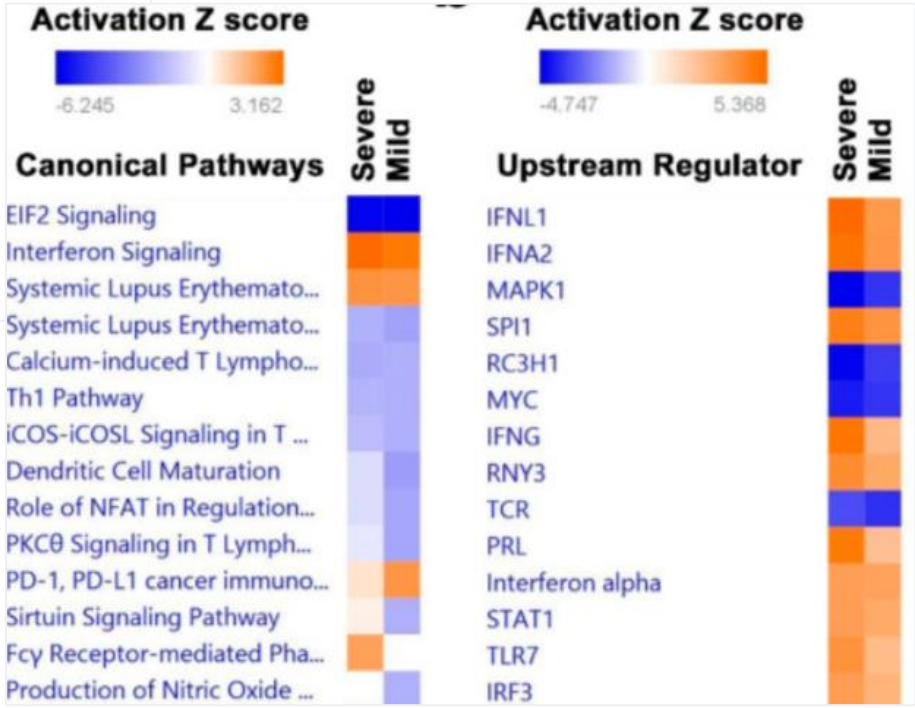
Single-Cell Transcriptome Analysis Highlights a Role for Neutrophils and Inflammatory Macrophages in the Pathogenesis of Severe COVID-19

Hibah Shaath [1,2], Radhakrishnan Vishnubalaji [1], Eyad Elkord [1,2], Nehad M Alajez [1,2]

Affiliations + expand

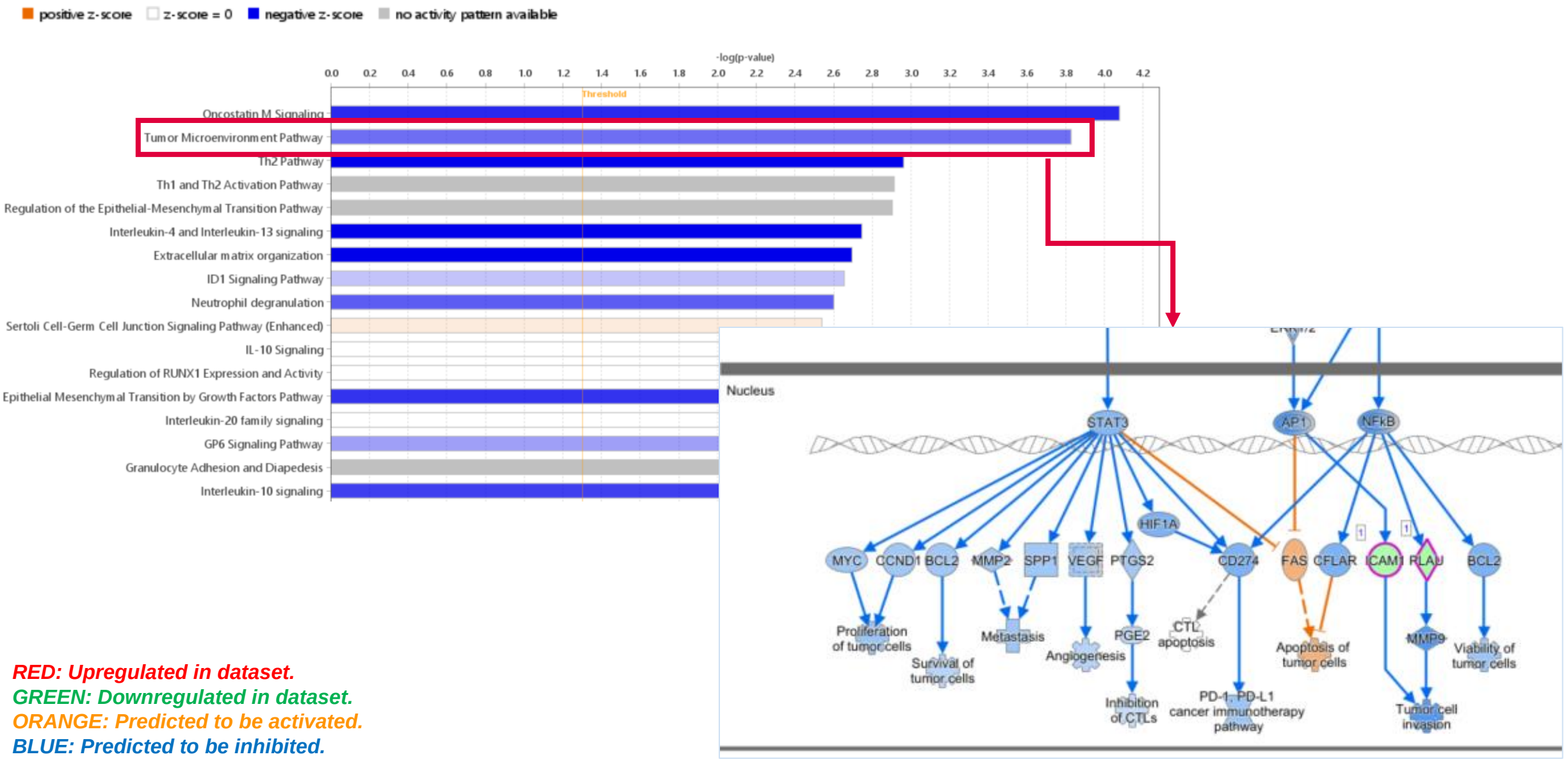
PMID: 33138195 PMCID: PMC7693119 DOI: 10.3390/cells9112374

Free PMC article



	A	B	C
1	**geneid**	**Log2FoldChange**	**p-value**
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
7920	CMTM2	0.4726	0.0001
7921	CMTM3	0.6099	0.000097742
7922	CMTM4	-0.815	1.5825E-07
7923	DYNC1LI2	-0.3924	7.2017E-10
7924	CCDC79	0.0023	0.9635
7925	NAE1	-0.2599	0.0098
7926	CA7	-1.8165	3.6214E-06
7927	PDP2	-0.6373	2.4407E-10
7928	CDH16	-0.0415	0.5431
7929	RRAD	0.2049	0.0106
7930	FAM96B	-0.1019	0.0571
7931	CES2	-1.1852	2.6332E-09
7932	CES3	-1.2535	1.0865E-07
7933	CES4A	0.0457	0.4449
7934	CBFB	0.8449	1.0268E-14
7935	C16orf70	-0.2996	1.1793E-07
7936	B3GNT9	0.3413	0.000032084
7937	BC007896	0.3413	0.000032084
7938	TRADD	0.0882	0.1007
7939	FBXL8	-0.073	0.2312
7940	HSF4	-0.2543	0.0015
7941	NOL3	-0.0595	0.2532
7942	KIAA0895L	-0.2385	0.001
7943	EXOC3L1	-0.2385	0.001
7944	E2F4	-0.0401	0.454
7945	ELMO3	-0.3649	0.0004
7946	LRRC29	-0.0481	0.5241
7947	TMEM208	0.2094	0.0005
7948	FHOD1	0.233	0.0024
7949	SLC9A5	-0.1668	0.0205
7950	PLEKHG4	-0.3191	2.1437E-06
7951	KCTD19	-0.095	0.062

Identify pathways and biological mechanisms



RED: Upregulated in dataset.
GREEN: Downregulated in dataset.
ORANGE: Predicted to be activated.
BLUE: Predicted to be inhibited.

Discover key regulators and targets

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

Upstream Regulators | Causal Networks

Add To My Pathway | Add To My List | Display as Network | Activity Plot | Customize Table | Mechanistic Networks

Upstream Regul..	Expr Log Ratio	Molecule Type	Predicted Activ...	Activation z-sc...	p-value of ...	Target Molecul...	Mechanistic Ne...
EGF	↑0.525	growth factor	Inhibited	-3.640	5.03E-07	↓ANPEP, ↓CCN1, ...all 30	117 (17)
IL3	↑3.619	cytokine	Inhibited	-2.708	1.97E-06	↓ADGRE5, ↓ATF5, ...all 19	99 (15)
AGT	↓-0.646	growth factor	Inhibited	-2.419	2.13E-06	↑ADD3, ↓AEBP1, ...all 34	109 (14)
LY294002		chemical drug	Activated	2.191	2.22E-06	↓ANPEP, ↑ART3, ...all 25	
ERBB3	↑2.227	kinase		0.565	2.23E-06	↑AMOTL2, ↓CCN1 ...all 11	
FGF2	↑0.896	growth factor	Inhibited	-3.939	2.50E-06	↓ANPEP, ↓CCN1, ...all 23	
ETS1	↓-0.866	transcription regulator		-1.854	2.58E-06	↓ANPEP, ↓EGR1, ...all 15	
CCR2	↓-5.853	G-protein coupled recept...	Inhibited	-2.236	2.62E-06	↓AEBP1, ↓C1QC, ...all 10	
N-[N-(3,5-difluorophenace		chemical - protease inhib...	Activated	2.668	2.68E-06	↓CXCL2, ↓DLL4, ...all 12	
TNF	↓-1.089	cytokine	Inhibited	-4.834	3.50E-06	↓AEBP1, ↑AKT3, ...all 59	
STAT3	↓-0.887	transcription regulator	Inhibited	-3.022	4.20E-06	↓CCND2, ↓CXCL2, ...all 30	
ALPHA CATENIN (family)		group	Activated	2.728	4.30E-06	↓CXCL2, ↑IGF2, ↓... ...all 11	
beta-estradiol		chemical - endogenous ...		-1.491	4.69E-06	↓ADAMTSL4, ↓A... ...all 75	
PD98059		chemical - kinase inhibitor	Activated	3.658	7.11E-06	↓ANPEP, ↑ARPP19 ...all 25	
HRAS	↓-0.184	enzyme		-0.084	7.12E-06	↓ADGRE5, ↑AM... ...all 28	
AKT (family)		group		-1.668	7.27E-06	↓CCND2, ↓DLL4, ...all 20	
TGFB1	↓-0.794	growth factor	Inhibited	-3.696	7.87E-06	↓ADRA1D, ↑AKT3, ...all 57	
TLR3	↓-0.697	transmembrane receptor	Inhibited	-3.396	8.10E-06	↑AKT3, ↓CXCL2, ...all 14	
estrogen		chemical drug		-1.084	9.88E-06	↑ART3, ↓CCN1, ...all 16	
PDGF-BB (complex)		complex	Inhibited	-2.441	1.33E-05	↑ADD3, ↓ADRA1D, ...all 18	
cycloheximide		chemical reagent		0.312	1.38E-05	↓CCN1, ↓CXCL2, ...all 19	
PDGF (complex)		complex		-1.085	1.63E-05	↓CCND2, ↓EGR1, ...all 9	
IL6	↓-2.805	cytokine	Inhibited	-4.212	1.81E-05	↓ADGRE5, ↓ANP... ...all 29	
ESTROGEN RECEPTOR (fan		group		0.898	1.90E-05	↑AKT3, ↓CA12, ...all 15	
SERPINE1	↓-1.921	other		-1.129	1.99E-05	↑CES1, ↓CXCL2, ...all 9	
Il3		cytokine		-1.673	2.08E-05	↓ANPEP, ↓ATF5, ...all 8	
IL1B	↓-1.082	cytokine	Inhibited	-4.529	2.30E-05	↑AKT3, ↓ATF5, ↓... ...all 37	
lysophosphatidic acid		chemical - other	Inhibited	-2.942	2.64E-05	↓CCN1, ↓CXCL2, ...all 9	

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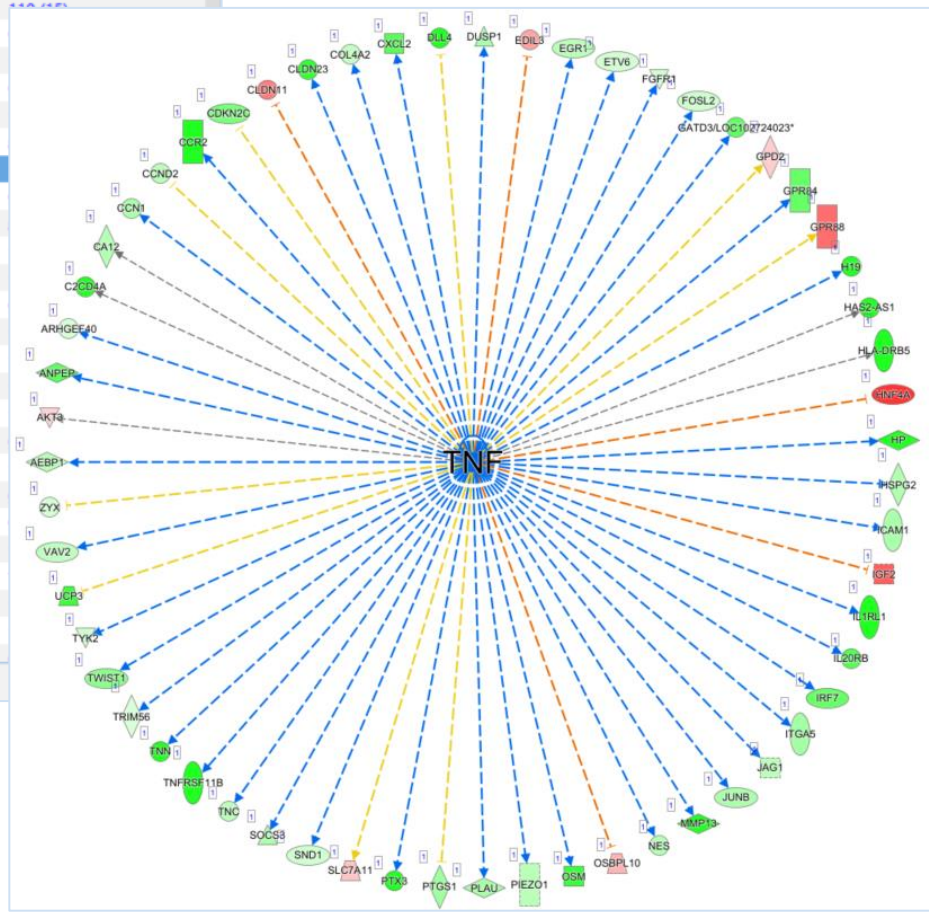

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Study enriched biological functions and diseases

ORANGE: Predicted to be activated.
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IPA is powered by the QIAGEN knowledge base

Manuscripts, clinical trials, and ‘omics data obtained from public and commercial sources

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

Over 20 years of expert literature curation

Ingenuity Pathway Analysis

Over 13.3 million research findings accessible by you in **seconds**

QIAGEN IPA Analysis Match and Land Explorer

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

Processing, curation and QA

QIAGEN OmicSoft Studio

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

204,000+ comparison

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

Curated Findings

Ingenuity Pathway Analysis

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

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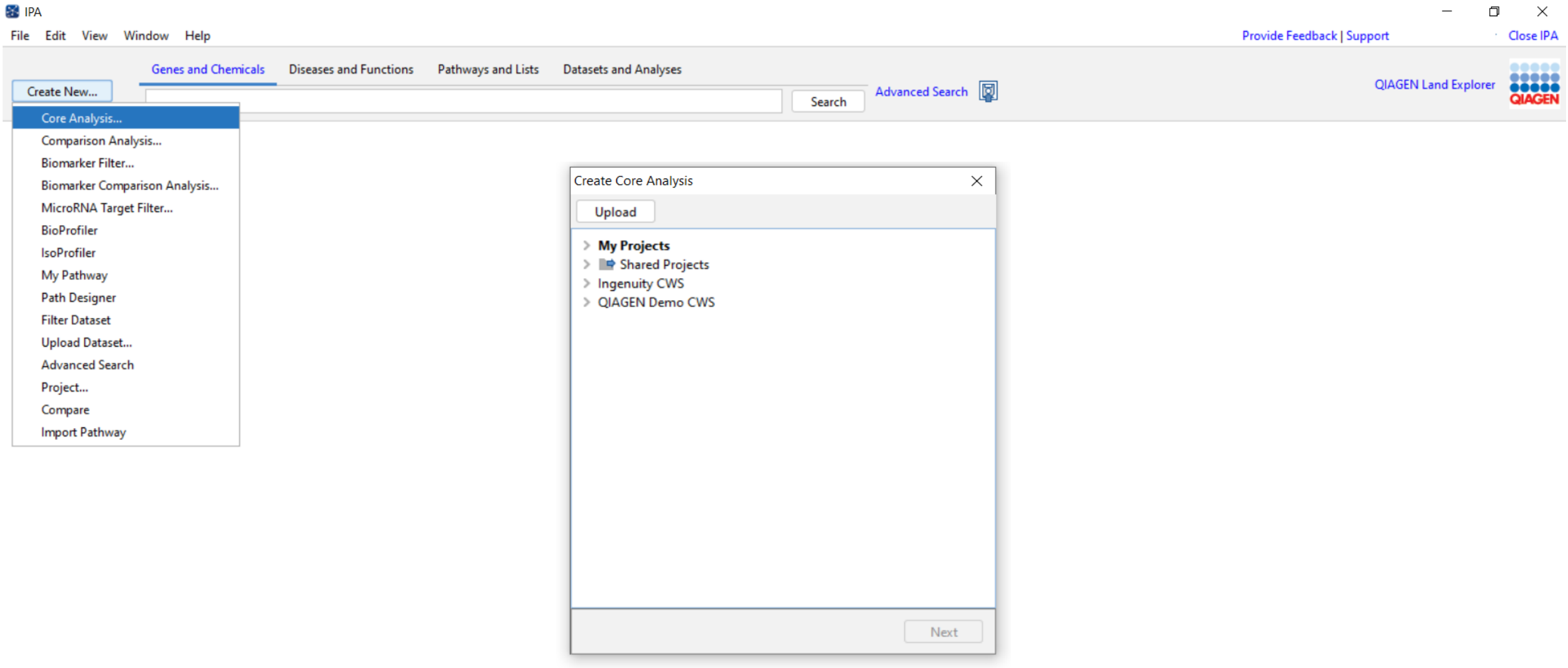
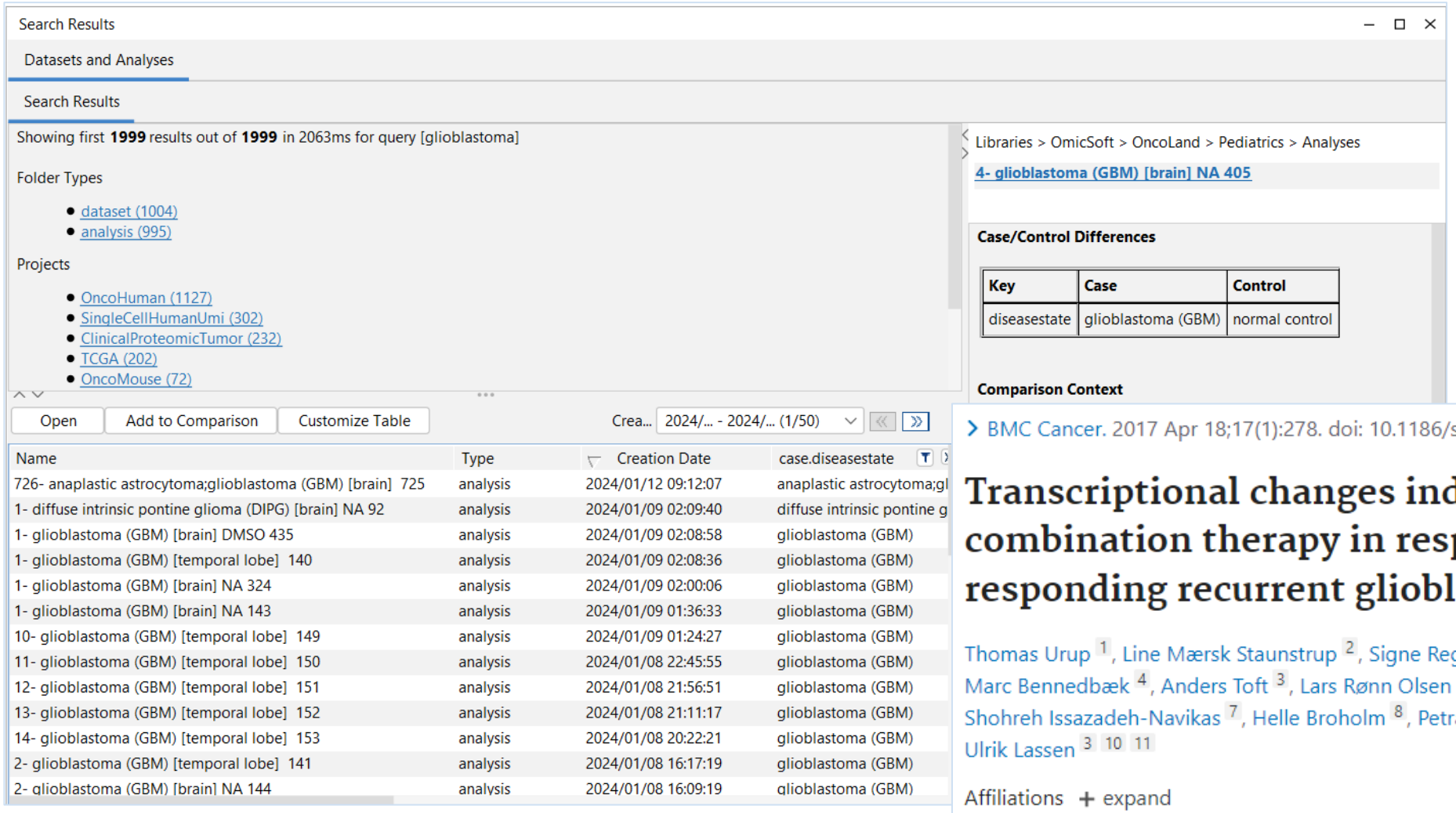
Uploading data to IPA



Public data core analysis search in QIAGEN IPA



Search terms:

- **Glioblastoma**
- **bevacizumab**
- **GSE79671**

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Use case

MAP2K3

Proteome profiling of immortalization-to-senescence transition of human breast epithelial cells identified **MAP2K3** as a senescence-promoting protein which is downregulated in human breast cancer.

Jia M, Souchelnytskyi N, Hellman U, O'Hare M, Jat PS, Souchelnytskyi S.

Proteomics Clin Appl. 2010 Nov;4(10-11):816-28. doi: 10.1002/prca.201000006.

PMID: 21137025

Genome-wide RNA interference screening reveals a COPI-**MAP2K3** pathway required for YAP regulation.

Kim YJ, Jung E, Shin E, Hong SH, Jeong HS, Hur G, Jeong HY, Lee SH, Lee JE, Kim GH, Kim J.

Proc Natl Acad Sci U S A. 2020 Aug 18;117(33):19994-20003. doi: 10.1073/pnas.1915387117. Epub 2020 Aug 3.

PMID: 32747557 Free PMC article.

Sulforaphene inhibits esophageal cancer progression via suppressing SCD and CDH3 expression, and activating the GADD45B-**MAP2K3**-p38-p53 feedback loop.

Han S, Wang Y, Ma J, Wang Z, Wang HD, Yuan Q.

Cell Death Dis. 2020 Sep 1;11(8):713. doi: 10.1038/s41419-020-02859-2.

PMID: 32873775 Free PMC article.

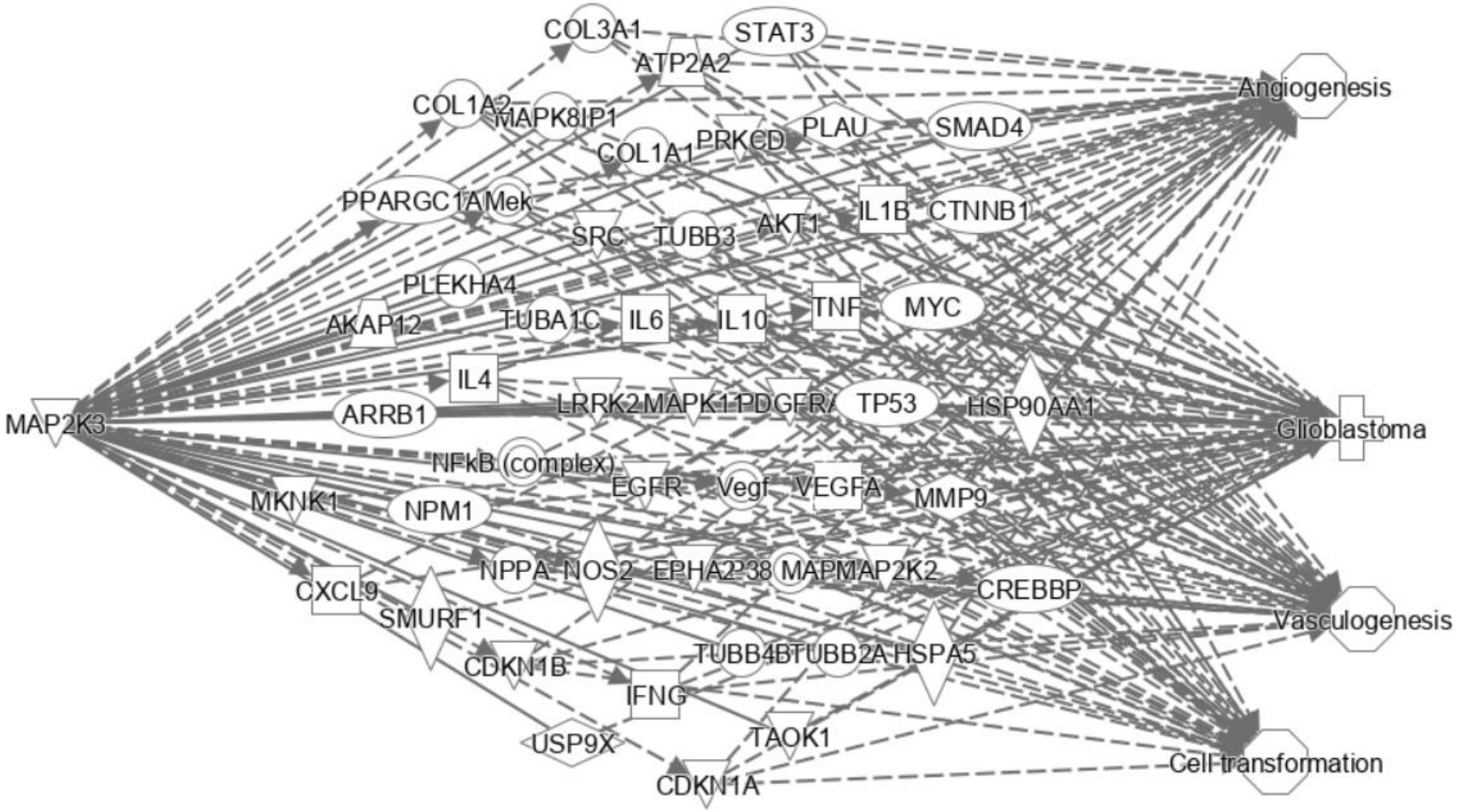
The miR-19b-3p-**MAP2K3**-STAT3 feedback loop regulates cell proliferation and invasion in esophageal squamous cell carcinoma.

Zhang Y, Lu W, Chen Y, Lin Y, Yang X, Wang H, Liu Z.

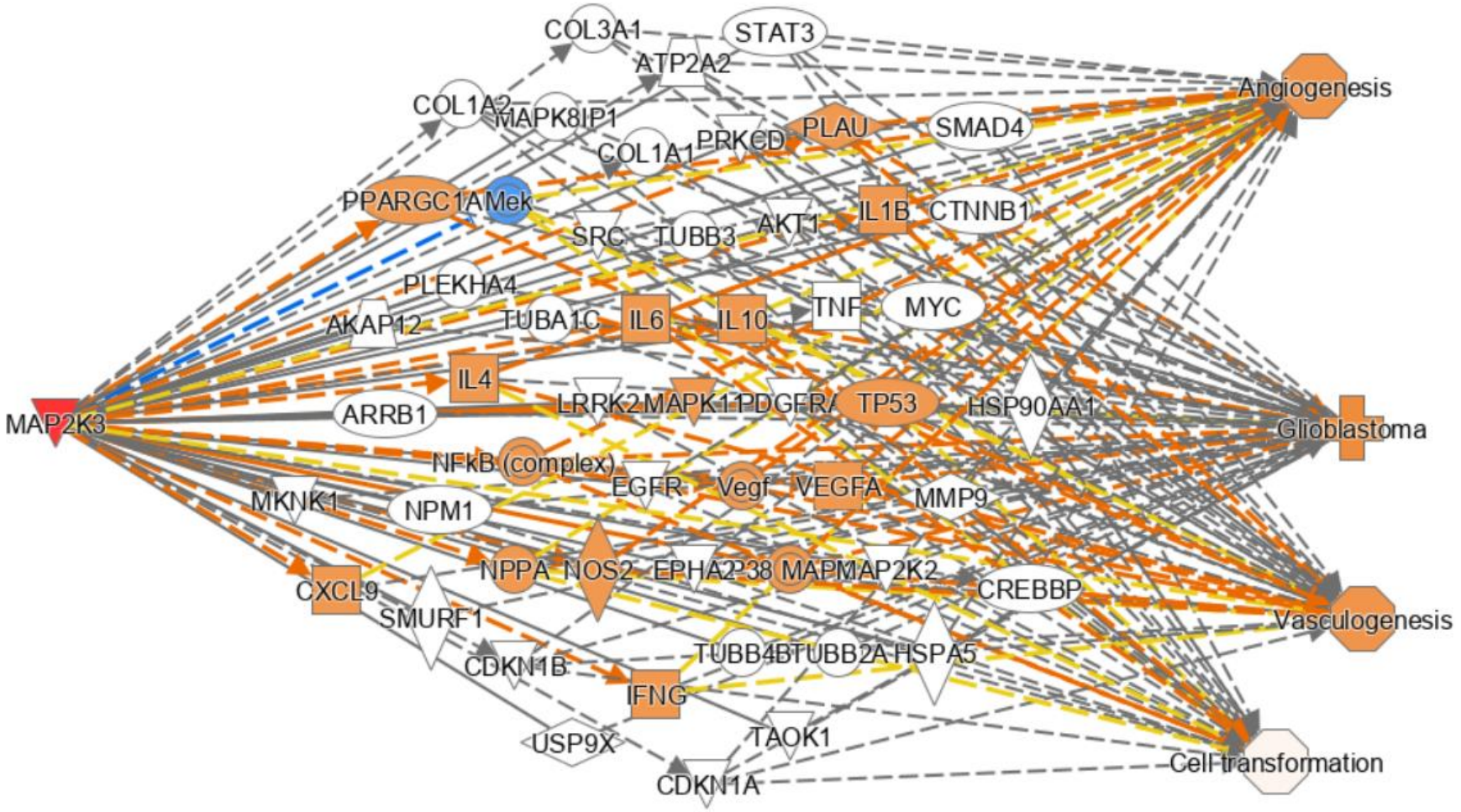
Mol Oncol. 2021 May;15(5):1566-1583. doi: 10.1002/1878-0261.12934. Epub 2021 Mar 14.

PMID: 33660414 Free PMC article.

Construct networks based on key biomarkers



Predict molecule activity



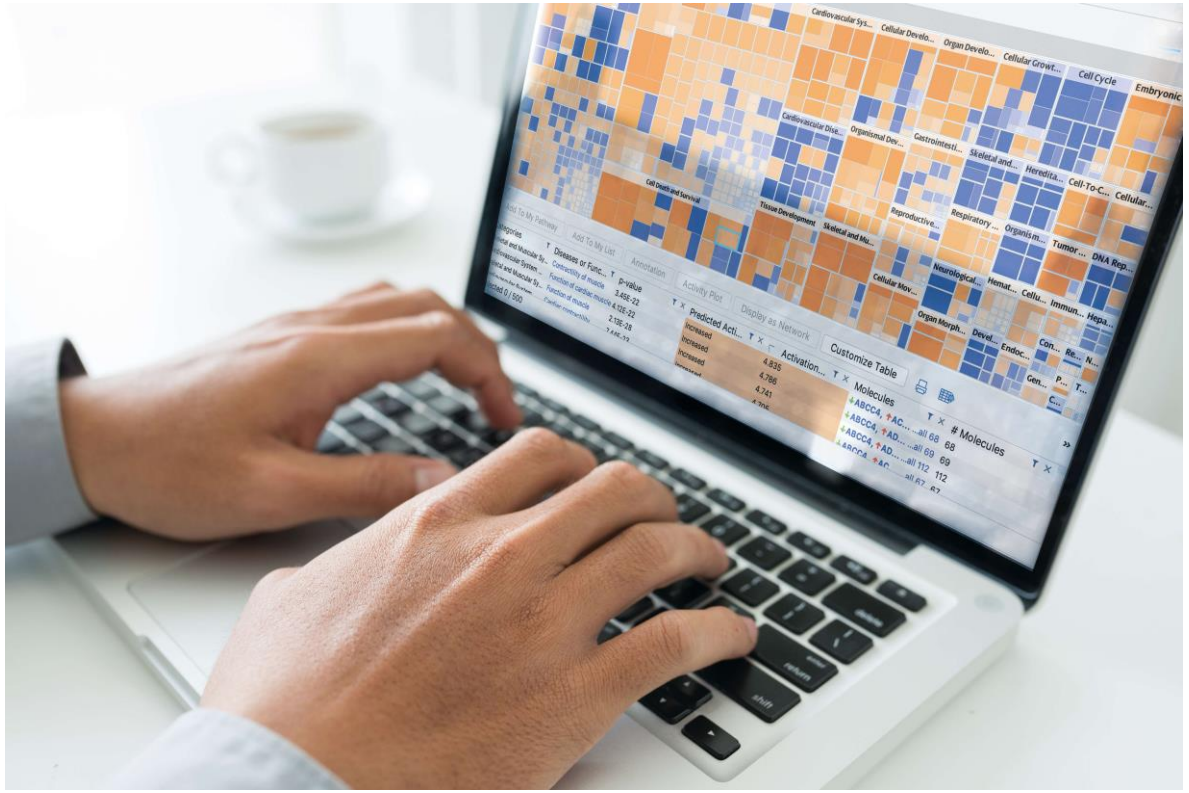
Summary

Biological interpretation of data using QIAGEN IPA

- Interrogate key pathways impacted by expression changes at varying levels of detail
- Identify predicted regulators driving the observed expression signature
- Compare biological findings with internal/public data to determine conserved/disparate biology
- Easily generate tables and figures based on the analysis

Utilizing QIAGEN IPA without a dataset

- Leverage QIAGEN Knowledgebase for literature findings
- Build networks in silico and predict activity



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Ingenuity Pathway Analysis trial:
https://qiagen.showpad.com/share/RC7IWOoVJnSsEd5w9LjiA

Software questions and support: ts-bioinformatics@qiagen.com
Additional feedback and training: devendra.mistry@qiagen.com