





## **Dataset analysis using QIAGEN IPA**

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# *Dataset:* https://reurl.cc/9V2Ogj

## Client: (IPA Login)







- 1. What's New in the IPA
- 2. Data Upload and How to Run a Core Analysis Upload experiment data
- 3. Functional Interpretation in IPA Introduction for Analysis Tools
- 4. Comparison Analyses
- 5. Q&A





Select cells and tissues to be displayed on	pathway.		· · · · ·			Contraction of the second
Cells and Tissues	p-value	# Molecules Molecules				
Relevant Cells and Tissues		26 ALB, OBLB, CCL3, CD	1244, CUIC 🥠	GT: natural ki	ter cells	
V C physiological system	4.87E-25 - 1ED	26 ALB, OBLB, COL3, COS	244, CLIC	10.3		
🛛 🖓 🖂 immune system	4,87E-25 - 1E0	25 CBLB, CCL3, CD244, C	CUCILET	11 11		
V C leukocytes	4.87E-25 - 1ED	26 CBLB, CCL3, CD244, C	CLICS, ET		0013 00044	
V I mononuclear laukocytes	4.876-25 - 1.126-1	24 CBLB, CCL3, CD244, C	CLICA, ET	Corp.	The sease	
- jymphocytes	4.876-25 - 1.796-3	24 CBLB, CDL3, CD244, C	CLICA, ET			
T lymphocytes	4.876-25	21 CBLB, CD244, ETS1, F	ASLG, PY			
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<ul> <li>Z type 1 innate lymphol</li> </ul>	d 2.04E-20 - 2.04E-20	16 C0244, CLIC3, ET51, F	FABLO, FY	STATE	N I AN AN	
Vinstural killer cells	2.04E-20	18 CD244, CLIC3, ETS1, F	FABLE, FY		A A A A A A A A A A A A A A A A A A A	
> B lymphocytes	1.79E-3 - 1.79E-3	6 COL3, KLRC4-KLRKUP	KLRK1, P.	witter / market	TWA	
in monocytes	1.12E-1	3 CD244, HLA-A, SLAMF	7	STATES -	NY2 FLY	
> phagocytes	1.126-1 - 160	25 CBLB, CCL3, CD244, C	CLIDA, ET			
> antigen presenting cells	3.17E-1 - 1ED	22 CBLB, CCL3, CD244, C	CLICS, ET	84,98/	fallen	
Impeloid leukocytes	1.126-1 - 160	5 CCL3, CD244, HLA-A, H	HSPATA/		GENO CIDENS	
hematolymphoid system	4.87E-25 - 1ED	25 CBLB, CCL3, CD244, C	CUG3, EY		Shines -	
Classifive system	1.40E-1 - 1E0	5 ALB. COL3, CD244, HL	LA A. 1LS2	SHERA	Willie - /	
> endocrine system	1.49E-1 - 1ED	4 HLA-A, 1L32, RASA2, ST	TATA	1.5	HAR	
Combourinary system	\$-27E-1 - 1E0	7 COLS, CLICS, FYN, HSI	PA1AHS	RASA2	ALL	
> neuromuscular system	160 - 160	6 CBLB, FVN, HSPASA/H	HSPA1B,		ALL	
> physiological system component	1.49E-1 - 1ED	13 ALR, CIBLIS, COLA, COL	244, GLIC	arritht an	HSPATAHSPATB*	
kelatomuscular system	100 - 100	1 HSPATA/HSPATE				
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## QIAGEN IPA 近期更新內容介紹



THE HUMAN PROTEIN ATLAS

#### 1. Identify potential cell types based on the set of genes on networks and pathways

### Overlay :Cell and Tissues



Figure 1. Enrichment of natural killer enriched genes on a network.



## 2. Causally score My Pathways in Core Analysis





Figure 3. A custom My Pathway with nodes assigned by the user as activated (red) or green (inhibited).



## 2. Causally score My Pathways in Core Analysis



Figure 4. Causally scoring a My Pathway.



### 3. Set the "User Dataset" as the reference set when uploading a dataset

1.	Select File Format:		Flexi	ole Format	× 0	
2.	Contains Column Header	:	• Ye	s 🔵 No		
3.	Select Identifier Type:		Please	e assign at least one	column below as "	ID", and assig
			Assigr	additional columns	as ID to improve m	napping cover
4.	Array platform used for e	xperiments:	Not s	pecified/applicable	✓ Select	relevant array
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			Cod	eLink	>	
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	2	ENSMUSG0000	00051	0.8708015979022331	1.0	0.9077575903
	3	ENSMUSG0000	00025	4.504633100231221	8.57456910629013E.	. 4.4210170566
	4	ENSMUSG0000	00033	6.221800613621819	1.184319746802913	. 7.3009378079
	5	ENSMUSG0000	00025	1.682341354813838	3.202336768888141	. 1.4496821829

Figure 5. Setting the reference set to User Dataset reference during dataset upload.





## 1. What's New in the IPA

- 2. Data Upload and How to Run a Core Analysis Upload experiment data
- 3. Functional Interpretation in IPA Introduction for Analysis Tools
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Ingenuity Pathways Analysis的分析的結果回傳

- 與實驗資料相關的生物功能或是疾病分析
- 所影響的Signaling Pathway與Metabolic Pathway以及裡面的組成分子
- 受影響的Transcription regulator的種類以及相關基因與蛋白

■ 實驗資料中的分子關係如何形成的網路

分析功能種類:

IPA-Core Analysis: 分析mRNA, miRNA或是protein的實驗資料

IPA-Tox Analysis: 分析後得到毒性學相關結果

IPA-Metabolomics Analysis: 主要用於分析代謝體(Metabolomics)實驗相關資料







Formatting transcriptomics data before uploading to IPK 2005 2005



Observation 1

**Observation 2** 

#### Common identifier types

CIAGEN

- Arrays from Affymetrix, Illumina, etc.
- Gene symbols (Entrez or HUGO)
- Ensembl, RefSeq, UCSC, etc.

#### Accepted file formats

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

IDs are the only required column

**Change measurements** are needed for IPA to make activity predictions



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

**Observation 1** 

- Ratio, fold change, etc. (recommended)
- Significance (optional)

#### Common protein IDs

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

UniProt ID conversion tool:

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

Phosphorylation changes (ratio, fold change, etc.) and sites are supported, but these columns must be assigned



	Multiple	ID colun	nns		Ratio, fold ch	ange, etc. (	recommend	ed)
		Ţ			(optional)	Ī	Significar	nce (optional)
	A .	P	C	D	1 ♥	* 	G	Ц
	Pubchem	Kegg	HMDB	CAS	E Metabolites	Fold change	P value	P value adjust
1	rubenem	ILE BB		UN3	metabolites	r old change	-value	-value_aujust
2					(2 or 3)-decenoate (10:1n7 or n8)	1.212936133	4.44028E-05	0.000585189
3	6443013	C14762	HMDB0004667	29623-28-7	13-HODE + 9-HODE	0.584109411	0.003698077	0.016919182
4	10111	C02294	HMDB01522	471-29-4	1-methylguanidine	1.219937764	0.015399637	0.049446834
5	5462190	C15606	HMDB0012134	746507-19-7	2,3-dihydroxy-5-methylthio-4-pentenoate (DMTPA)*	1.566518315	0.002802172	0.013670263
6	80283	C02356	HMDB00452	1492-24-6	2-aminobutyrate	0.633800292	0.011016709	0.038805594
7	10796774		HMDB00317	488-15-3	2-hydroxy-3-methylvalerate	0.997343835	0.006172648	0.024774766
8	11427		HMDB37115	120-91-2	2-hydroxy-4-(methylthio)butanoic acid	1.294720456	0.000305912	0.002622524

#### **Observation 1**

#### Common metabolite IDs

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

Metabolite ID conversion tools:

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





		Observatio	on 1	Observation	12
		 [			
	A	В	С	D	E
1	geneid	UCvsNormal.Log2FoldChange	UCvsNormal.pval	52wksVedolizumabvsBaseline.Log2FoldChange	52wksVedolizumabvsBaseline.pval
2	DDX11L1	-0.1067	0.2878	0.1183	0.1624
3	WASH7P	-0.1883	0.0097	0.3063	0.0006
4	FAM138F	-0.0761	0.4699	0.2466	0.0191
5	OR4F5	0.1474	0.5311	0.1713	0.2913
6	LOC729737	0.4789	0.0017	0.029	0.8331
7	LOC100133331	0.4789	0.0017	0.029	0.8331
8	LOC100132062	0.4789	0.0017	0.029	0.8331
9	OR4F29	0.2495	0.2389	0.2181	0.1887
10	JA429831	 0.1215	0.3338	0.2556	0.0004
10	JA420001	0.1215	0.0000	0.2000	0.0004

## Analyte identifier REQUIRED to explore enrichment

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

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

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

#### Change values needed to calculate activity predictions

Change value examples: fold changes, ratios, etc.

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

#### Accepted file formats:

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

Multiple comparisons or observations may be uploaded in one file





## Pathway or gene activity predicted by IPA

Inhibited

Activated

## Actual measurement of gene expression in your dataset

**Downregulated** 

Upregulated







Diseases / functions

Diseases / functions

**Dataset Molecules** 





Dataset: https://reurl.cc/9V20gj

use the browser version of IPA: (如果您有登入錯誤或是網路連線問題) https://analysis.ingenuity.com/pa/







# Live Demo Data Upload





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Diseases / functions

Diseases / functions

**Dataset Molecules** 





**Graphical Summary:** This feature selects and connects a subset of the most significant entities predicted in the analysis, including the relationship between molecules, functions, diseases and pathways.

Pathways: List the Signaling Pathway and Metabolic Pathway affected by the experiment

**Upstream Analysis:** List the upstream molecules related to the changed molecules in the data, and predict whether they are activated or inhibited according to the research literature.

**Diseases & Function:** Present biological functions, diseases and toxicological results affected by molecular changes

**Regulator Effects:** Hypothesize the effects of activation or inhibition of upstream regulators on downstream molecules

**Networks:** Present the network relationship between molecules in the experimental data. And the Build Tool and Overlay Tool can be used to extend and expand knowledge. The above analysis results are important basis for explaining the phenomena observed in the experiment.

Summary	Graphical Summary	Pathways	Upstream Analysis	Diseases & Functions	Regulator Effects	Networks	Lists	Analysis Match	Molecules		
				Export : 🐼							۷
> Experime	ent Metadata										
> Analysis	Settings										
✓ Top Cane	onical Pathways										
	Name							p-value		Overla	ар
	EIF2 Signaling							• 4.75E-36		32.1 %	72/224
	Regulation of eIF4 and p	o70S6K Signal	ing					• 5.64E-16		23.5 %	42/179
	ILK Signaling							• 9.78E-16		22.2 %	44/198





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Summary	Graphical Summary	Pathways	Upstream Analysis	Diseases & Functions	Regulator Effects	Networks	Lists	Analysis Match	Molecules		
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> Experime	ent Metadata										
> Analysis	Settings										
✓ Top Cane	onical Pathways										
1	Name							p-value		Overla	ар
	EIF2 Signaling							• 4.75E-36		32.1 %	72/224
	Regulation of eIF4 and p	o70S6K Signal	ing					• 5.64E-16		23.5 %	42/179
	ILK Signaling							• 9.78E-16		22.2 %	44/198





The Graphical Summary can include entities such as canonical pathways, upstream regulators, diseases, and biological functions. The algorithm that constructs the summary uses machine learning techniques to prioritize and connect entities that are in some cases not yet connected by findings in the QIAGEN Knowledge Graph.







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				Export : 🐼							
> Experime	ent Metadata										
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✓ Top Cane	onical Pathways										
1	Name							p-value		Overla	ар
1	EIF2 Signaling							• 4.75E-36		32.1 %	72/224
	Regulation of eIF4 and p	70S6K Signal	ing					• 5.64E-16		23.5 %	42/179
I	ILK Signaling							• 9.78E-16		22.2 %	44/198





- The affected Signaling Pathway and Metabolic Pathway are arranged in a bar chart according to their significance
- Click the Bar above the name of a specific Canonical Pathway, and the lower window will display the molecular IDs that participate in the composition of the pathway in the dataset
- Click "Open Pathway" to expand the Canonical Pathway, and the molecules in the experimental data will be indicated by colors.

Summary Graphic	cal Summary	Pathways	Upstre	eam Ana	lysis D	Disease	s & Func	tions	Regu	lator Effec	cts	Network	List	s A	nalysis M	atch	Molecu	ules												
Canonical Pathways	My Pathway	ys																												
Chart Overlappin	g																													
Customize Chart	Vertical Bar (	Chart	~	8	<b>1</b>	¢																							►	0
positive z-score 🛛 z-	-score = 0 <mark>=</mark> ne	egative z-score	e 🗏 no act	ivity patte	rn availabl	e																								
35 30 (a) 25 25 20 5 7 10 5 7 10 5 7 10 5 7 10 10 5 7 10 10 10 10 10 10 10 10 10 10 10 10 10	Signaling ILK Signaling -	mTOR Signaling - Fibrosis Idiopathic aling Pathway	avirus Pathogenesis Pathway	h Receptor Signaling -	c Fibrosis Signaling	n Signaling Pathway -	cocyte Extravasation Signaling	signaling	iondrial Dysfunction -	ertoli Cell Junction . Signaling	IGF-1 Signaling -	idiated Endocytosis Signaling	's Disease Signaling	Integrin Signaling -	c Fibrosis / Hepatic ate Cell Activation	IL-8 Signaling	HIF1a Signaling -	RHOGDI Signaling	quitination Pathway -	Rho Family GTPases -	mediated Oxidative	oli Cell-Sertoli Cell unction Signaling	deling of Epithelial herens Junctions	2 Signaling Pathway -	IL-6 Signaling -	Signaling In Cancer ills Pathway	ive Phosphorylation -	of Nitric Oxide and Oxygen Species in acrophages	coskeleton Signaling -	ERK/MAPK Signaling
legulation		Pulmona	Coror	Estroge	Hepal	Sirtu	Leu	Glu	Mitor	erm Cell-		.lathrin-m	Iuntingto		Hepal Stel				<sup>1</sup> rotein Ul	d guileng	NRF2	Ser	Ren A	BA		VISP-RON C	Oxida	Production Reactive	Actin C)	
72 molecule(s associat	ted with EIF2 S	ignaling [Ra	tio: 72/22	4 (0.321)	)] [z-score	e: 1.234	4] [p-valu	ue: <mark>4.75</mark>	E-36]														A	ctivity Pla	ot	View Re	port	Open	Pathway	7
Add To My Pathwa	y Add To	o My List	Create	Dataset	Cu	stomize	e Table		8	C Ex	pand																			
/ Symbol	Entrez Gene	Name ×	Identifier	ALICSC /	+ M	leasure	ment	×	Everle	tenritu/PD	+	Add/Ren	nove co	lumn(s	) Expect	ted	>	K Locati	on		× тур	e(s)		× Bion	narker.	Applica	×D	rug(s)		×
ACTA2*	actin alpha 2	2, smooth mu	ENST0000	0022478	4* <b>•</b>	-130.77	6	e	2711.14	49	N	20.731	ensity/R	P D				Cytopla	asm		othe	er		effica	scy	al	11			











Click "Open Pathway" to expand the Canonical Pathway, and the molecules in the experimental data will be indicated by colors.







#### Click on the View Report button to display the Canonical Pathway report.

Ing	enuity	Pathw	vay A	analysis 🖕	$\times$		C	anonical Path	way
Report I Report V Content	Date: 2022- Version: Version: 81	I0-18 I348237 (Re	lease Dat	e: 2022-09-15)			Prov	vide Feedback   Contact Support 🗾 Downlo	ad Report (PDF)
Cano	nical Pathway:	Tumor Mi	croenvir	onment Pathwa	y				
	Description:	The tumor micr network, the pr only manages t tumor progress	oenvironmen o-tumorigeni o escape fror ion.31500650	t (TME) comprises cance c immune response, me n the host immune syste	er cells, the cytokine enviro diated by diverse immuno: em, but it effectively benef	onment, extracellular matrix, suppressive cell signaling mole its from infiltrating cells by m	immune cell ecules, plays odifying the	subsets and other components. In this c s a pivotal role in driving immune evasion ir functions to create the microenvironme	omplex . The tumor not nt favorable for
		The majority of st impact on cancer intermediate meta	romal cells with progression the abolites and im	hin the TME are specific fibr prough remodeling the ECM mune suppressive cytokine	oblasts with a myofibroblastic , inducing angiogenesis, recru s.28382138	phenotype and are distinguished iting inflammatory cells, and direct	d as cancer-as	sociated fibroblasts (CAFs). These CAFs have g cancer cell proliferation via the secretion of g	a significant rowth factors,
		Myeloid-derived s suppressive facto enzyme responsil promote MDSC a	suppressor cell ors, such as arg ole for the cata occumulation.3	s (MDSCs) are a heterogene jinase and inducible nitric o bolism of tryptophan, which 1430935	eous population of immature r kide synthase (NOS2), thus re leads to inhibition of T cell p	nyeloid cells, which are expanded ducing lymphocyte functions. MD oliferation and induces T cell apo	d in pathologic ISCs also sho ptosis. Local	al conditions and up-regulate expression of im w high expression of indolearnine 2,3-dioxyger hypoxia has been identified as another key reg	mune lase (IDO), an ulator that can
		and TNF-a) which inflammation. TAM	erived cytokine stimulate tum As also produc	es, such as IL-4, IL-13, CSF or progression and in parall e vascular endothelial grow	el inhibit lymphocyte function th factor (VEGF), which stimul	ated macrophage (IAM) differenti s through the secretion of IL-10, a ate tumor angiogenesis, promotir	ation. These s and also contr ag its invasive	secrete multiple key proinflammatory cytokines ibute to the expansion of Th17 cells, which ind ness and metastatic potential.31500650	(e.g. IL-16, IL-6, uce local
		Tumor-associated the blood circulat production.31430	I neutrophils (T ion into the TM 1935	ANs) are associated with ag IE is stimulated by tumor-de	gressive cancer phenotypes, rived CXCL8. TANs mainly su	facilitate angiogenesis, promote r ppress anti-tumor immunity via in	nutagenesis a iteracting with	nd suppresse the immune system. The migrati CD8+ T cells, inducing their apoptosis througi	on of TANs from n nitric oxide
Sigr	naling Pathway Categories:	Cancer							
Т	op Functions & Diseases:	Cell-To-Cell Signa	aling and Intera	ction; Cellular Growth and I	Proliferation; Lymphoid Tissue	Structure and Development			
	Molecules: show all	Accumulation of a cytotoxic T cells, CSPG4, CTLA4, 0 of Th17 cells, EG	ATP, Accumula Apoptosis of T CXCL12, CXCL F, Epithelial-me	tion of myeloid-derived sup h1 cells, Apoptosis of tumo 8, CXCR4, D-glucose, Deve senchymal transition, ERK	pressor cells, Adaptive immur r cells, ARG1, BAD, BCL2, CC alopment of regulatory T lymp I/2, FAS, FASLG, fatty acid, F	ne response of CD8+ T lymphocyt CL2, CCND1, CD274, CD44, Cell v hocytes, Differentiation of M2 mar af, FN1, Foxo, glutamine, glutathi	te, Akt, Angio viability of tun crophages, Di one, HGF, HIF	genesis, Ap1, Apoptosis of CD8+ T lymphocyte for cells, CFLAR, collagen type i (family), CSF1 fferentiation of myeloid-derived suppressor cel 1A, Hypoxia of tumor, ICAM1, IDO, Iaf, IL10	, Apoptosis of , CSF2, CSF3, Is, Differentiation
									Back to top >>
Drug Sum	mary - Overview	of drugs targeting	molecules in (	Canonical Pathway					
Showing 3	of 1028 row(s) of I	Drug data. (Show )	4JI)						
(-)-gossypol	Drug Nam	ie	BCL2	Targets	Actions     Actions	Brand Names	÷	adrenal cortex carcinoma/Phase 2	1
1-(3-(1,4-dihy	droimidazo[4,5-c]	pyrazol-5-yl)-4-	RAF1		inhibitor			adult Burkitt lymphoma/Phase 1 adult diffuse large-cell lymphoma/Phase 1	
(trifluorometh 131I-chloroto	yl)phenyl)urea	H-Imidazoi-T-yi)-a	MMP2		binder			astrocytoma/Phase 1/Phase 2	
								brain tumor/Phase 1/Phase 2 glioblastoma/Phase 1/Phase 2	
Target Info	ormation - Over	riew of known drug	g targets in Car	nonical Pathway					Back to top >>
Showing 3	of 112 row(s) of Ta	arget data. (Show)	AJI)						
Target (Gene Symbol)	Entrez Gene Name	Location +	Туре 🗢			Drug(s)		٠	Species \$
Akt		Cytoplasm	group	afuresertib, Akt inhibitor X	, AT13148, HTBPI, ipatasertib	, MSC2363318A, ONC-201, SR-1	3668, TAS-11	7, TAS0612	Human, Mouse, Bat
AKT1	AKT serine/threonine kinase 1	Cytoplasm	kinase	A-443654, AKT inhibitor X MPT0E028, perifosine, tric	II, archexin, BAY1125976, ca iribine, triciribine phosphate,	oivasertib, CCT129524, enzastaur uprosertib, vevorisertib	rin, GSK69069	33, ipatasertib, LY2780301, miransertib, MK220	6, Human, Mouse, Rat
AKT2	AKT serine/threonine	Cytoplasm	kinase	AKT inhibitor XIII, BAY112	5976, CCT128930, CCT12952	4, enzastaurin, GSK690693, tricir	ibine, triciribir	ne phosphate	Human, Mouse, Rat





**Graphical Summary:** This feature selects and connects a subset of the most significant entities predicted in the analysis, including the relationship between molecules, functions, diseases and pathways.

Pathways: List the Signaling Pathway and Metabolic Pathway affected by the experiment

# **Upstream Analysis:** List the upstream molecules related to the changed molecules in the data, and predict whether they are activated or inhibited according to the research literature.

**Diseases & Function:** Present biological functions, diseases and toxicological results affected by molecular changes

**Regulator Effects:** Hypothesize the effects of activation or inhibition of upstream regulators on downstream molecules

**Networks:** Present the network relationship between molecules in the experimental data. And the Build Tool and Overlay Tool can be used to extend and expand knowledge. The above analysis results are important basis for explaining the phenomena observed in the experiment.

Summary	Graphical Summary	Pathways	Upstream Analysis	Diseases & Functions	Regulator Effects	Networks	Lists	Analysis Match	Molecules		
				Export : 🐼							•
> Experime	ent Metadata										
> Analysis	Settings										
$\checkmark$ Top Can	onical Pathways										
	Name							p-value		Overla	ар
	EIF2 Signaling							• 4.75E-36	3	32.1 %	72/224
	Regulation of eIF4 and p	o70S6K Signal	ing					• 5.64E-16	2	23.5 %	42/179
	ILK Signaling							• 9.78E-16	2	22.2 %	44/198





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

Predict activation or inhibition of regulator to explain the changes in gene expression in your dataset.

Calculates two complementary statistical measures:

- Activation z-score
- Overlap p-value

## Upstream Analysis







Can we predict the activation state (activated/inhibited) of a potential regulator from expression data?

Approach: Two complementary statistical measures: Activation z-score and Overlap p-value

TR  $\rightarrow$  target edge types considered:

- Expression
- Transcription
- Protein-DNA binding

Evaluate the perturbed genes in the dataset that are known targets of a particular regulator

Upstream Regulatorregulated genes in Ingenuity Knowledge Base Data set (differentiallyexpressed genes)







and your expression data







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

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

← Differential Gene Expression (Uploaded Data)

- ← Predicted activation state of TF/UR:
  - 1 = Consistent with activation of UR
  - -1 = Consistent with inhibition of UR

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

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

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

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

Sample to Insight





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	Name							p-value		Overla	ар
	EIF2 Signaling							• 4.75E-36		32.1 %	72/224
	Regulation of eIF4 and p	o70S6K Signal	ing					• 5.64E-16		23.5 %	42/179
	ILK Signaling							• 9.78E-16		22.2 %	44/198







Identify over-represented biological functions and predict how those functions are increased or decreased in the experiment










- Powerful functionality enables you to understand causal connections between molecules and diseases.
- Interactive visual exploration of causality between molecules and disease, function, or phenotypes from a network or My Pathway.







provides details associated with the disease or biological function such as molecules associated with that disease or function, known drug targets, drugs known to target those molecules, and more.

### Ingenuity Pathway Analysis

Provide Feedback | Contact Support

Back to top >>

**Disease or Function** 

#### Disease or Function: Cell movement of leukocytes

Synonyms: immune cell movement, innate immune cell movement, leukocyte movement, white blood cell movement, cell movement of immune cell, cell movement of immune cells, cell movement of immune cells, cell movement of innate immune cells, cell movement of leukocyte, cell movement of white blood cell, cell movement of white blood cells, movement of leukocyte, cell movement of innate immune cells, movement of immune cells, movement of immune cells, movement of immune cells, movement of innate immune cells, movement of immune cells, movement of innate immune cells, movement of leukocytes, cell movement of innate immune cells, movement of innate immune cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of innate immune cells, movement of leucocytes cells, movement of leucocytes cells, movement cells, movement

Molecules: (+)-butaclamol, (2R\*,4S\*)-N-(1-benzoyl-2-methyl-1,2,3,4-tetrahydroquinolin-4-yl)-N-phenylcyclopropanecarboxamide, (S,R)-3-(4-hydroxyphenyl)-4,5-dihydro-5-isoxazole acetic acid, methyl ester, (Z,E)-5-(4-ethylbenzylidine)-2show all thioxothiazolidin-4-one, (±)-4-DOI, 1,1-diethyl-2-hydroxy-2-nitrosohydrazine, 1,10-phenanthroline, 1,2-dimethylhydrazine, 1-(palmitoyl)-2-(5-keto-6-octene-dioyl) phosphatidylcholine, 1-chloro-2,4-dinitrobenzene, 1-methyl-4-phenyl-1,2,3,6tetrahydropyridine, 1-naphthylisothiocyanate, 1-o-hexadecyl-2-o-methyl-rac-glycerol, 1-palmitoyl-2-oleoylphosphatidylserine, 10-Cl-BBQ, 11,12-epoxyeicosatetraenoic acid, 12-hydroxy=17, 18-epoxyeicosatetraenoic acid, 12-hydroxy=0, 17, 18-epoxyeicosatetraenoic acid, 12-hydroxy=0, 13, 14-dihydro-15ketoprostaglandin D2, 15-deoxy-delta-12,14 -PGJ 2, 15-epi-lipoxin A4, 15-hydroxyeicosatetraenoic acid, 15-LOX, 15S-methyl-prostaglandin d2, 16,16-dimethylprostaglandin E2, 17-epi-resolvin D1, 17-octadecynoic acid, 2'-fucosyllactose, 2'3-cyclic guanosine monophosphate, 2,4-dinitrofluorobenzene, 2,4-O-di-sulfated iduronic acid, 2-(4-acetoxyphenyl)-2-chloro-N-methylethylamine, 2-(p-hydroxynilino)-4-(p-chlorophenyl) thiazole, 2arachidonoylglycerol, 2-mercaptoacetate, 2610528A11Rik, 27-hydroxycloesterol, 3'-O-(4-benzoyl)benzoyladenosine 5'-triphosphate, 3,4-dinloroisocoumarin, 3-aminobenzamide, 3-deoxy-2-octulosonic acid, 2'-hydroxy-2-nitro-14, 2-hydroxy-17,18-epoxyeicosatetraenoic acid, 2-fu-octoxyphenyl)-2-chloro-N-methylethylamine, 2-(p-hydroxynonenal, 4-methylydroxycloesterol, 3'-O-(4-benzoyl)benzoyladenosine 5'-triphosphate, 3,4-dinloro-15kydroxydodecanoic acid, 3M-052, 4-hydroxynonenal, 4-methyl umbelliferone-8-carbaldehyde

Ontology







**Graphical Summary:** This feature selects and connects a subset of the most significant entities predicted in the analysis, including the relationship between molecules, functions, diseases and pathways.

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> Experime	ent Metadata										
> Analysis	Settings										
🗸 Top Can	onical Pathways										
	Name							p-value		Overla	ар
	EIF2 Signaling							• 4.75E-36	:	32.1 %	72/224
	Regulation of eIF4 and p	70S6K Signal	ing					• 5.64E-16	:	23.5 %	42/179
	ILK Signaling							• 9.78E-16	:	22.2 %	44/198







**Downstream Effects Analysis** 

Sample to Insight ·





Click on the Network ID or Display As Network button to open a Regulator Effects network.







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Pathways: List the Signaling Pathway and Metabolic Pathway affected by the experiment

**Upstream Analysis:** List the upstream molecules related to the changed molecules in the data, and predict whether they are activated or inhibited according to the research literature.

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✓ Top Can	onical Pathways										
	Name							p-value		Overla	ар
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	ILK Signaling							• 9.78E-16		22.2 %	44/198





- 1. Focus molecules are "seeds"
- 2. Focus molecules with the most interactions to other focus molecules are then connected together to form a network
- 3. Non-focus molecules from the dataset are then added
- 4. Molecules from the Ingenuity's Knowledge Base are added
- 5. Resulting Networks are scored and then sorted based on the score



Molecules per Network	Networks per Analysis
35	<b>▼</b> 25 <b>▼</b>
35	10
70	25
140	50



Purpose:

- To show as many interactions between user-specified molecules in a given dataset and how they might work together at the molecular level
- Why are Ingenuity networks biologically interesting?
  - Highly-interconnected networks are likely to represent significant biological function
  - Networks involve molecules you don't see in your data set. This allows genes you have assayed to be linked to metabolites and chemicals that you could not have assayed for, to imply a regulation network that is meaningful.





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.

Expression Analysis - CDDO vs DMSO ge	enes											100
Summary Graphical Summary Pat	hways Upstrear	n Analysis Diseas	es & Functions Reg	ulator Effects	Networks	Lists Ana	lysis Match Molecule	s				
Evaluate Metadata View As Heatr	map View Cor	nparison Custo	mize Table 🛛 д 🏢	•					z-sc 37.3	32 - 16.28 (1/44	8) ~	« » (
Analysis Namo	Project T X				com T X		com T X webl					×
32- normal control [lund] NA 12384	MouseDisesse	normal control	king	NA T	Treatment ve	Genotype:Ge	GSE109776 GP https://www	UF (	52 52	37.59	59.16	37 32
28- bronchitis:emphysema [lung] NA 12379	MouseDisease	honchitis:em	lung	NA	Treatment vs	Genotype:Ge	GSE109776 GP https://www	N.D	55 71	45.44	44 72	36.47
- chronic obstructive pulmonary disease (COPD)		chronic obstr	lung	NA	Treatment vs	SubjectTreat	GSE87292 GPL https://www	ND 5	51 21	46.63	44.72	35.64
1- normal control [nasal epithelium] NA 11786	MouseDisease	normal control	nasal epithelium	NA	Treatment vs	SubjectTreat	E-MTAB-3150.4 http://www	eb	50.85	40.38	44.72	33.99
8- normal control [peripheral blood] NA 4945	MouseDisease	normal control	peripheral blo	NA	Treatment1 v	SubjectTreat	GSE131914.GP https://www	vn 4	43.55	19.78	59.16	30.62
- alcoholic fatty liver [liver] NA 17035	MouseDisease	alcoholic fatty	liver	NA I	Disease vs. N.	DiseaseState	GSE40334.GPL http://www	nc	42.11	27.86	44.72	28.67
47- normal control [stomach] 946	SingleCellMouseUm	i normal control	stomach		CellType1 vs	pithelial cell v	GSE108097 UN https://www	N.D 4	42.11	23.31	44.72	27.54
- skin disease [skin] NA 16522	MouseDisease	skin disease	skin	NA	Disease vs. N [	DiseaseState	GSE35160.GPL https://www	vn f	50.17	48.90		27 27
- normal control [lung] NA 16447	MouseDisease	normal control	luna	NA	Treatment vs	SubjectTreat	GSE33512.GPL https://www	w.n	57.24	51.08		27.08
7- colorectal cancer [colon] NA 409	OncoMouse	colorectal can	colon	NA	Other Compa	SubjectTreat	GSE109520.GP https://www	w.n	37.14		70.71	26.96
3- normal control [nasal epithelium] NA 11777	MouseDisease	normal control	nasal epithelium	NA	Treatment vs S	SubjectTreat	E-MTAB-3150.4 http://www	eb	50.17	44.23		26.10
0888- pancreas adenocarcinoma (PAAD) [pancr	er LINCS	pancreas ade KEAP	1 pancreas	KEAP1 overe	Treatment vs	Freatment =>	GSE70138.GPL https://www	N.D 5	54.14	48.90		25.76
5- normal control [nasa] epithelium] NA 11779	MouseDisease	normal control	nasal epithelium	NA	Treatment vs	SubjectTreat	E-MTAB-3150.4 http://www	eh f	60.17	40.38		25 14
- ovarian cancer (ovary) NA 8121	OncoHuman	ovarian cancer	ovary	NA I	Disease1 vs F	ExperimentGr	GSE30274.GPL https://www	vn S	27.85	27.58	44 72	25.04
- normal control [peripheral blood] NA 18008	MouseDisease	normal control	nerinheral blo	NA	Treatment1 v [	Dosage:Samp	GSE52403.GPL http://www	nc s	37 14	17.38	44 72	24.81
- normal control [lung] NA 19305	MouseDisease	normal control	lung	NA	Treatment vs.	Senotype:Su	GSE65124.GPL http://www	nc f	81.59	37.59		24 79
9- normal control liejunum] NA 16270	MouseDisease	normal control	ieiunum	NA	Tissue1 vs Ti	SamplingTime	GSE32513 GPL http://www	nc	32 16	20.85	44 72	24.43
- atherosclerosis:hyperlipidemia [liver] NA 19373	MouseDisease	atherosclerosi	liver	NA (	Other Compa	AnimalStrain	GSE66568 GPL https://www	vn 4	19 52	46.63		24.04
7- normal control (nasal epithelium) NA 11781	MouseDisease	normal control	nasal enithelium	NA	Treatment vs	SubjectTreat	E-MTAB-3150.4 http://www	eh F	52 52	41.96		23.62
21- small intestine carcinoid neuroendocrine tum	or OncoHuman	small intestine	small intestine	luminespib	Treatment vs.	IreatTime:Ex	GSE96760.GPL https://www	vn.	24.81	23.31	44.72	23.21
62- normal control [liver] 561	SingleCellMouseLlm	i normal control	liver	idinino opio	CellType1 vs	enatocyte vs	GSE108097 UN https://www	vn s	30.64	17.03	44 72	23.10
- disease control [liver] NA 952	OncoMouse	disease control	liver	NA (	Other Compa	ExperimentGr	GSE79084 GPL https://www	ND 5	55 71	36.12		22.96
- type 1 diabetes mellitus (liver) NA 16835	MouseDisease	type 1 diabet	liver	NA	Treatment vs	ExperimentGr	GSE38138 GPL https://www	wn d	17 34	44.23		22.89
- diet induced obesity (hypothalamus) NA 779	MouseDisease	diet induced	hypothalamus	NA	Treatment1 v	SubjectTreat	GSE102415 GP https://www	ND 1	17.62	23.31	50.00	22.00
- normal control [large airway epithelium] NA 225	27 HumanDisease	normal control	large airway e	NA (	Other Compa	TissueRegion:	GSE5056 GPI 8 http://www	nc 4	17 34	42.99	00.00	22.58
- emphysema [lung] NA 20909	MouseDisease	emphysema	lung un way e	NA	Treatment vs	FreatTime:Su	GSE8790.GPL1: http://www	nc	49.13	40.38		22.38
emphysema [lung] NA 7610	MouseDisease	emphysema	lung	NA	Treatment vs.	SubjectTreat	GSE76205 GPL https://www	ND 5	54 14	34 58		22.18
- alcoholic fatty liver [liver] NA 18043	MouseDisease	alcoholic fatty	liver	NA T	Treatment vs	Senotype:Su	GSE52644 GPL http://www	nc (	47 77	40.38		22.10
- normal control (liver) NA 2696	BatDisease	normal control	liver	NA	Treatment vs	SubjectTreat	GSE122184.GP https://www	v.n	52 52	34.58		21.78
- nonalcoholic steatohepatitis (NASH) [liver] NA 1	87 MouseDisease	nonalcoholic s	liver	NA	Treatment vs.	Senotype:Su	GSE61534.GPL https://www	ND F	52 52	34.58		21.78
63- normal control [kidney] NA 7126	RatDisease	normal control	kidnev	NA	Treatment1 v	ExperimentGr	GSE57811.GPL https://www	vn s	21.44	20.85	44.72	21.75
186- normal control [liver] NA 4243	RatDisease	normal control	liver	NA	Treatment vs	ExperimentGr	GSE57815.GPL https://www	vn 4	15.96	40.38		21 58
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5- normal control [liver] NA 6176	MouseDisease	normal control	liver	NA	CellType1 vs	ExperimentGr	GSE145820 GP https://www	ND	34 74	00.02	50.00	21 19
1- normal control [heart left ventricle] NA 16761	MouseDisease	normal control	heart left wort	NA A	Other Compa	Sender:Genet	GSE37597 GPL https://www	w.n	15.40	39.01	00.00	21.19
25- Ebola hemorrhadic fever [spleen] NA 4045	MouseDisease	Ebola homorr	near ten vent	NA	Other Compa	Sender Genot	GSE130629 GP https://www	w.n	20.20	00.01	44.72	21.12
Looia nemormagio rever (spieeri) INA 4045	MouseDisease	Ebola nemorr	SDIEEL		ouler comba I		COL 10023.GF HubS://WW	William Control of Con	39.39		44.72	21.03







DiseaseLandHumanDisease MouseDisease RatDisease •LINCS OncoLand Hematology Metastatic Cancer OncoHuman (Formerly OncoGEO) Pediatrics •TCGA OncoMouse ENCODE RNA Binding SingleCellLand SingleCellHuman SingleCellHumanUmi SingleCellHumanUmiLite SingleCellHumanHCL SingleCellMouse SingleCellMouseUmi SingleCellMouseUmiLite Normal Cells and Tissues •Human Tissues (GTEx)

Total datasets for release: 121,000 +





#### How OmicSoft datasets were analyzed in IPA

Example of Omicsoft Dataset







My Analysis

Match?	<ul> <li>a +</li> <li>b +</li> <li>c +</li> <li>d +</li> <li>e +</li> </ul>
	(g) - (b) + (c) + (c) + (c) + (c) (c) (c) (c) (c) (c) (c) (c) (c) (c)

Query Upstream Regulator signature Scoring against Upstream Regulator signature from another analysis

Another analysis

- Z = <u>matches mismatches</u> Square root of all matches
- z-score is a measure of the match between two patterns
- Assumes the pattern is created from two sets of entities where the sign of the matching entities is random

$$= (8-1)/\sqrt{9} = 2.33$$
 (raw z-score)

Yes, it matches (because z>2)





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







# Live Demo





- 1. What's New in the IPA Winter Release (December 2022)
- 2. Data Upload and How to Run a Core Analysis Upload experiment data
- 3. Functional Interpretation in IPA Introduction for Analysis Tools
- 4. Comparison Analyses
- 5. Q&A





#### Single Experiment

- Time Course
- Dose Response

#### Multi Experiment

- System biology
- Combining SNP, CNA, mRNA, microRNA, proteomics, etc.

#### Set Analysis

 Exploring Common Molecules across one or more experiment (s)

Multi-omics analysis of the liver in response to instant 



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Create Comparison Analysis					
lect analyses for side-by-side comparison. Click View	Comparison t	o view comparison results.			
Create Comparison Analysis					
Select Analyses       A-Z Sort         My Projects       Training Project         Image: Claudin View of the state	Add >>	<ul> <li>Ib Compare</li> <li>Ib Low Dose 6 hr</li> <li>Ib High Dose 6 hr</li> <li>Ib Low Dose 24 hr</li> <li>Ib High Dose 48 hr</li> </ul>		Move	Up * Down *
			« Remove	]	
			View Comp	aricon	Cance







Comparison Analysis - Prostrate Cancer	My Heatmaps
Canonical Pathways Upstream Analysis Diseases & Functions Regulator E	Role of NFAT in Regulation of the Immune Response
Canonical Pathways Upstream Analysis Diseases & Functions Regulator E Settings/Legend Filter More Info Measurement: Activation z-score -2.646 Sort Method: Score Visualize: z-score Insignificance Threshold: 2 (absolute value) Apply Now Report Edit Network Gene Heatmap View Report Edit Network Gene Heatmap Regulation Of The Epithelial Mese Gaq Signaling Th1 Pathway HMGB1 Signaling CXCR4 Signaling Th2 Pathway Xenobiotic Metabolism General Si XR/RXR Activation La Signaling HOTAIR Regulatory Pathway	Role of NFAT in Regulation of the Immune Response  Settings/Legend  More Info Measurement: Expr Fold Change -5.932 2.426 Sort Method: Expression  Edit Network  Figure  Figure Figure Figure  Figure Fi

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Sample to Insight













#### Comparison analysis heat map for Diseases and Functions





Sample to Insight

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Canonical Pathways Upstream Analysis	Diseases & Function	ns Regulator Effects	Lists	My Pathways	Molecules	Netw
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Edit Network Gene Heatmap		V Cancer, Ga	strointesti	nal Disease, Inflan	nmatory D	
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Liver tumor Gastrointestinal tract cancer	_	Cancer, He	matologic	al Disease, Immu	nological [	1
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		Score Filter			۲	
		p-value Cutoff:	1.3	(log10)		
		z-score Cutoff:		(absolute valu	ue)	
		B-H p-value Cutoff:		(log10)		
				ОК	Cancel	ved.
	L					

QIAGEN

Filter





#### Single Experiment

- Time Course
- Dose Response

#### Multi Experiment

- System biology
- Combining SNP, CNA, mRNA, microRNA, proteomics, etc

### Set Analysis

 Exploring Common Molecules across one or more experiment (s)









- The **Union** operator will display a list of the total population of molecules present in all off the entities (the sum of the molecules).

- The **Common** operator will display the intersection of molecules. In order to appear on this list, a molecule would have to be present on each of the individual entities used in the General Comparison.

- The **Unique** operator will display only the molecules that are present on individual entities. Use the pull-down menu to choose the entity for which you would like to display the results.

compare			- 0
elect Entities to compare and click Add	Refresh	Entities to Compare	More Inf
<ul> <li>✓ My Projects</li> <li>✓ 2020-3</li> <li>✓ Dataset Files</li> <li>✓ Dataset Files</li> <li>✓ Dataset Files</li> <li>✓ Descent f</li></ul>	A «« F CI 10718 :ules SE11352 ytes GSE47948 D 25816343 2017-04-10 SRP	dd » emove enove ear All	Union Common Unique

創源生技 GGA





## To view the molecule details or to create a new dataset from these, click on the **'Annotations'** button.

Select Entities to compare and click Add       Refresh       Initias to Compare       More In <ul> <li>My Projects</li> <li>2020-3</li> <li>Dataset Files</li> <li>Wigh Dose 24 hr</li> <li>High Dose 24 hr</li> <li>High Dose 24 hr</li> <li>Low Dose 6 hr</li> <li>Low D</li></ul>	Compare			>
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Mo	Molecule Annotations – D ×										
A	Add To My Pathway 🛛 Add To My List 🔹 Create Dataset Customize Table 🔄 🌐 🖨										
	Symbol	Expr. Chart	△ Entrez Gene Name	Identifier Affymetrix	Measurement Expr Fold Change	Location	Type(s)	Biomarker Applica	Drug(s)		
	Anp32a		acidic (leucine-rich) nucle	1371986_at	<b>↓</b> -2.379	Nucleus	other				
	ACO2	[ - ]	aconitase 2	1367589_at	<b>↓</b> -2.026	Cytoplasm	enzyme				
✓	ADH5		alcohol dehydrogenase 5	1371470_at	<b>↓</b> -2.747	Cytoplasm	enzyme				
	AKR1D1	[]	aldo-keto reductase famil	1398310_at	<b>↓</b> -2.215	Cytoplasm	enzyme		azelaic acid		
	AQP9	[]	aquaporin 9	1368621_at	<b>↓</b> -2.856	Plasma Membrane	transporter				
	ARNTL	[ - ]	aryl hydrocarbon receptor	1370510_a_at	<b>†</b> 2.653	Nucleus	transcription re				
✓	ASRGL1		asparaginase and isoaspa	1387966_at	<b>↓</b> -2.527	Cytoplasm	enzyme				
	ACKR3	[-]	atypical chemokine recept	1367940_at	<b>†</b> 5.610	Plasma Membrane	G-protein coupl				
	Cald1	[ _ ]	caldesmon 1	1371969_at	<b>↓</b> -2.208	Plasma Membrane	other				
<b>V</b>	CLIP2		CAP-Gly domain containin	1368571_at	<b>†</b> 2.295	Cytoplasm	transcription re				
<b>V</b>	CPT2		carnitine palmitoyltransfe	1386927_at	÷-5.226	Cytoplasm	enzyme	unspecified applie	perhexiline		
	СТН	[ - ]	cystathionine gamma-lyase	1367838_at	<b>↓</b> -13.240	Cytoplasm	enzyme				
	CYP2F1		cytochrome P450 family 2	1368608_at	<b>↓</b> -4.498	Cytoplasm	enzyme				
	DGAT2	[ _ ]	diacylglycerol O-acyltransf	1371615_at	<b>↓</b> -2.656	Cytoplasm	enzyme				
	DDIT3		DNA damage inducible tr	1369590_a_at	<b>↑</b> 3.956	Nucleus	transcription re				
Sele	cted/ lotal molecul	es: 5/00									





# Live Demo





#### Pusheen.com



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: 周儀柔 資深業務專員 <u>GraceChou@gga.asia</u> 02-2795 1777 #3019 黃柔諭 產品專員 <u>ZoeHuang@gga.asia</u> 02-2795 1777 #3028







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



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

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







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

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

← Differential Gene Expression (Uploaded Data)

- ← Predicted activation state of TF/UR:
  - 1 = Consistent with activation of UR
  - -1 = Consistent with inhibition of UR

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

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

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

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