QIAGEN IPA 系統生物學分析軟體



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

Ingenuity Pathway Analysis

Leo Hung 洪慈懋
創源生技 產品專員
Office: 02-2795-1777#5034 E-mail: LeoHung@gga.asia



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

CEO: Christopher Tsai, Ph.D. 蔡政憲 博士

Established: Nov. 2008

Main Product & Service Areas:

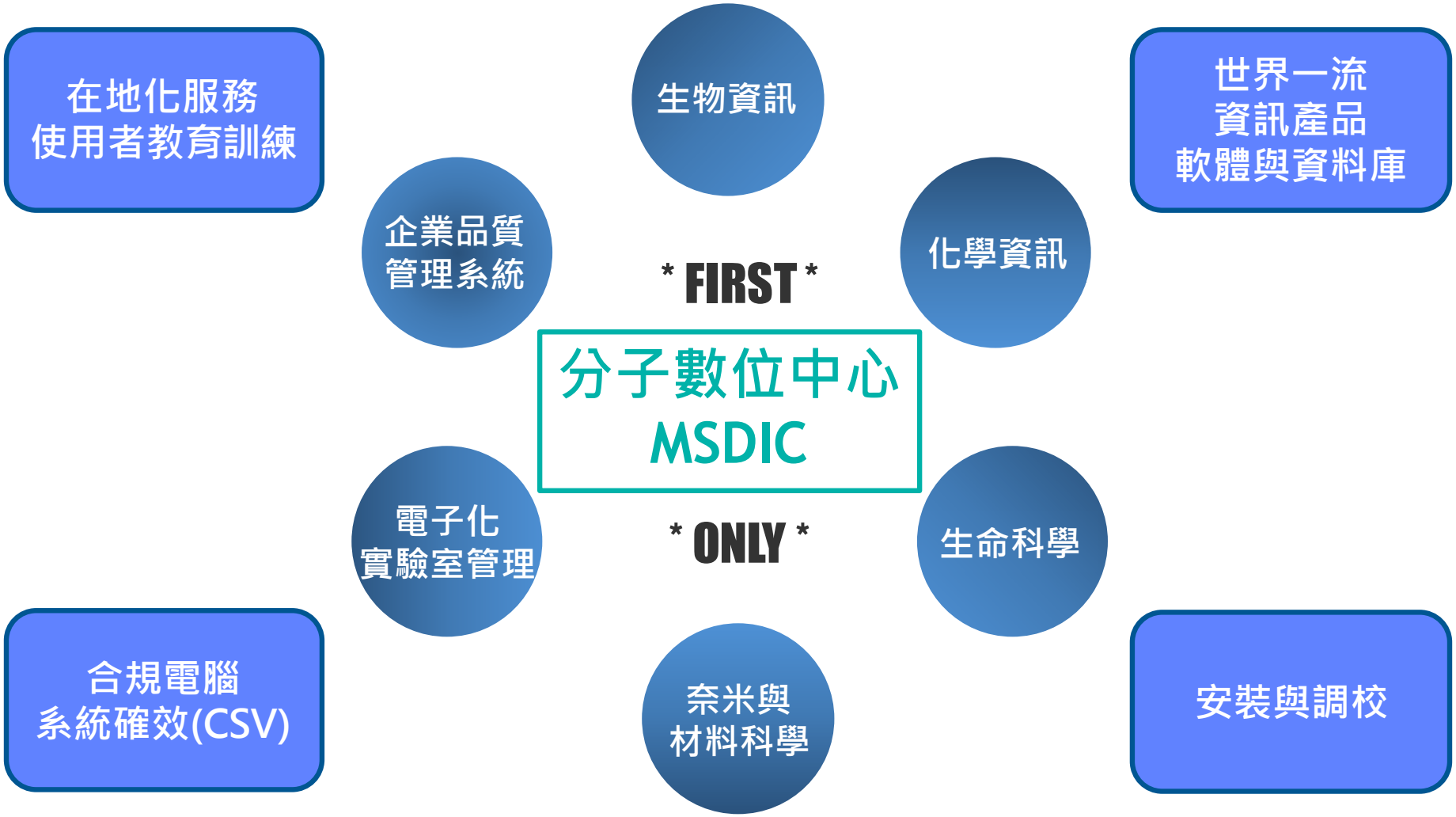
- Genetic Testing & Molecular Diagnosis
- **Scientific Informatics & Bio IT**

IPO Date: September 17, 2012

Stock Ticker: 4160 (Taiwan OTC)

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Molecular Science and digital innovation center

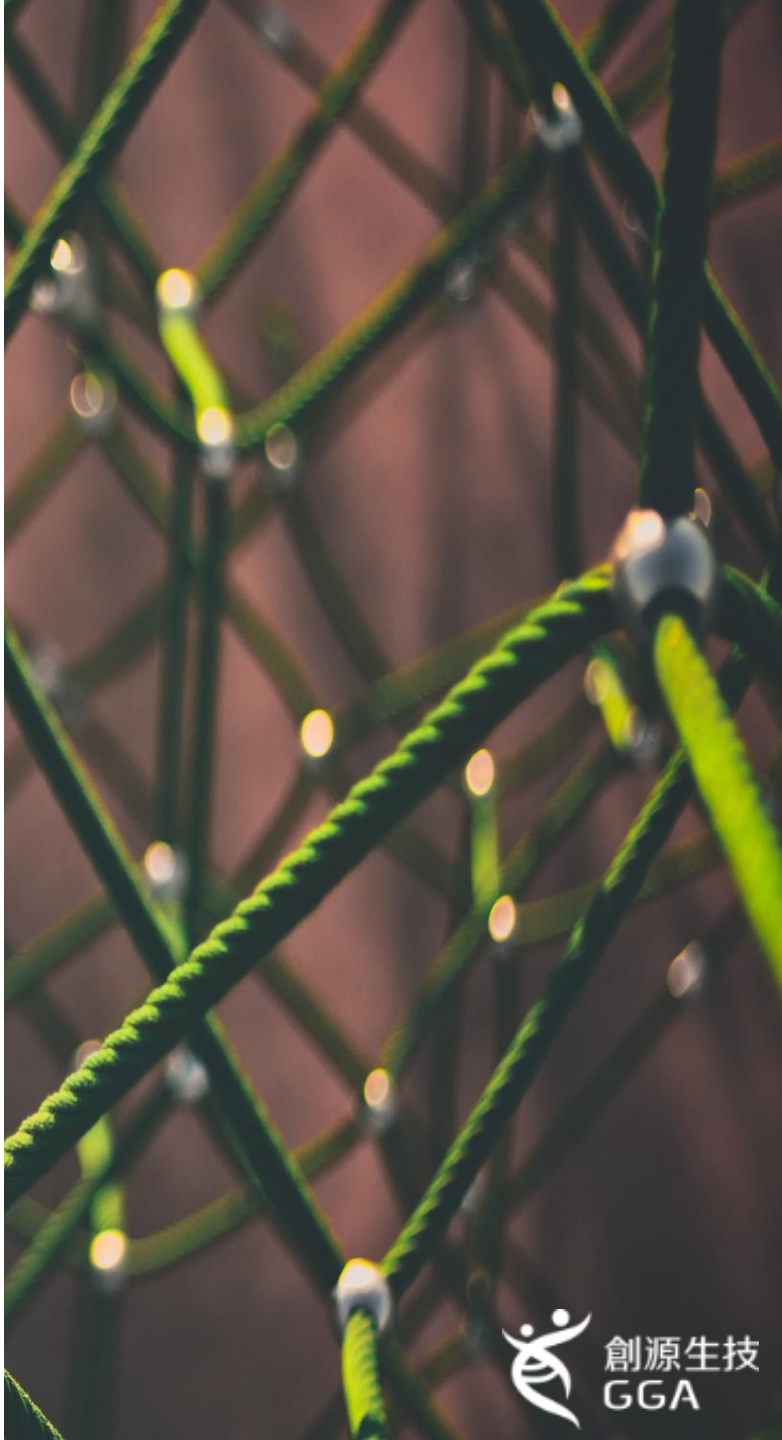


https://www.gga.asia/tc/msdic/index.html

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Our Vision

用科學的知識與技術，提昇台灣產業科技創新能量。





分子數位中心

Be Your Partner

我們是由物理、化工、生物、統計、資訊等超過十位不同領域的專家組成，具備多年產業經驗。

10+

我們服務全台灣超過四十所大專院校，每年舉辦超過100場以上教育訓練課程。

100+

我們擁有包含化學、材料、生物領域，超過百萬筆資料數據，並有實際處理分析案例。

1M+

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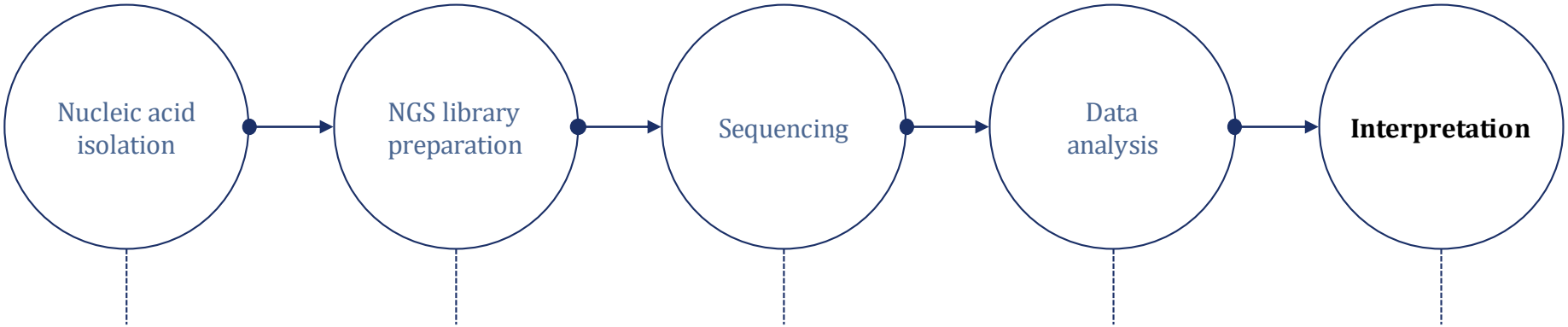
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QIAGEN Bioinformatics Solution



- QIAcube Connect
- QIAsymphony
- EZ1 Advanced XL

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

- QIAseq RNA
- QIAseq DNA

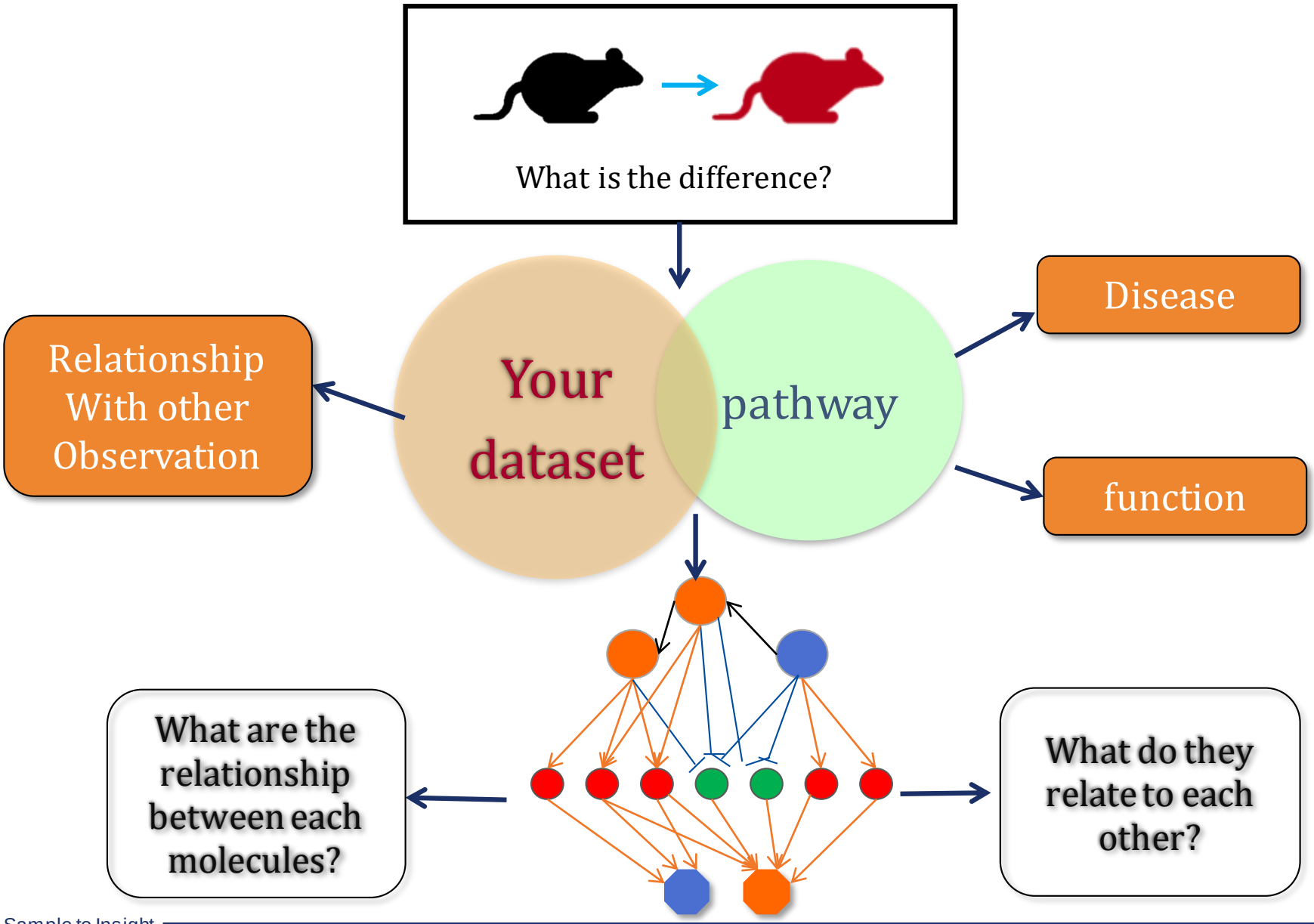
- Illumina and Thermo Fisher sequencers
- Pacific BioSciences (PacBio) single-molecule real-time sequencing (SMRT) *
- Oxford Nanopore Technologies nanopore-based platform *

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

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

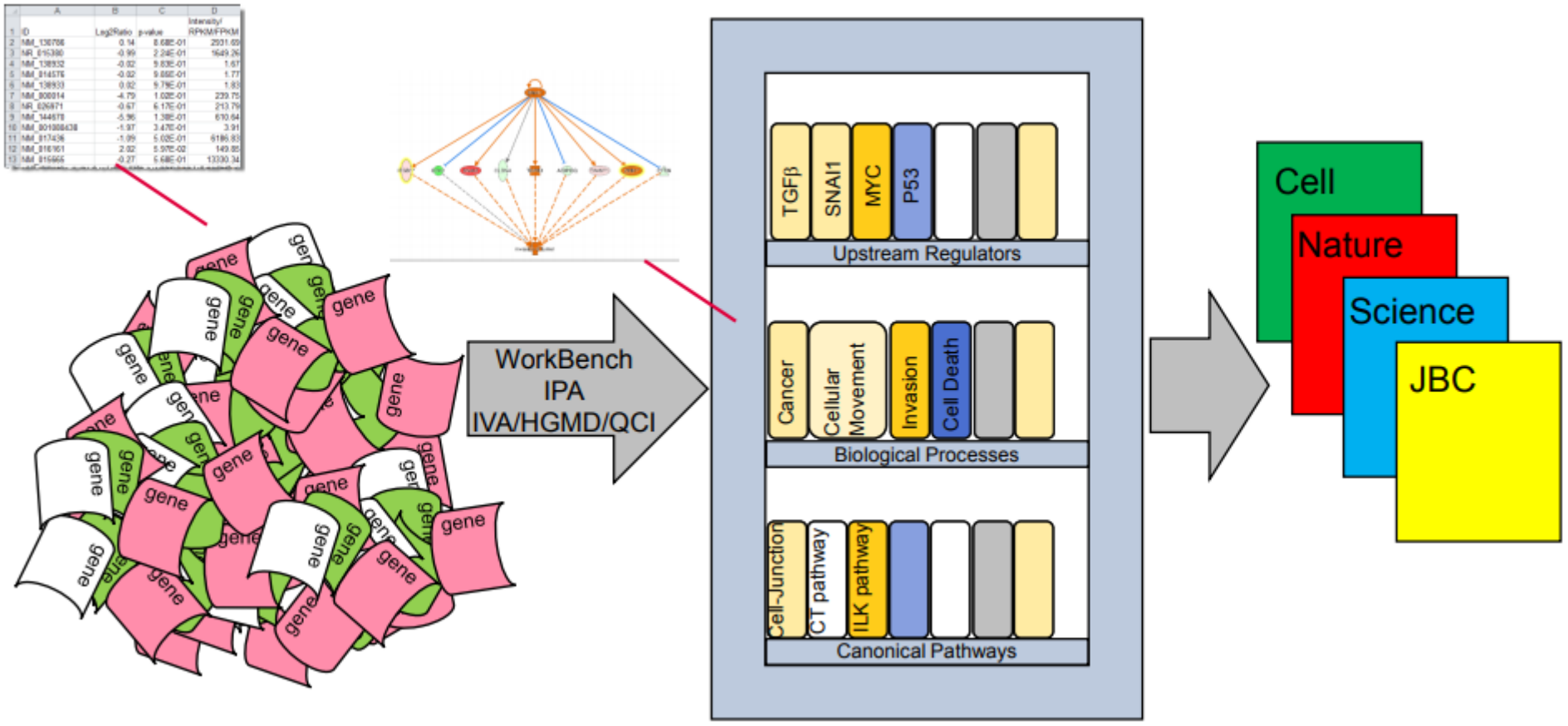
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Why are we using IPA?



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What can QIAGEN bioinformatics products do for you?



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IPA Supported

IPA orthologous :

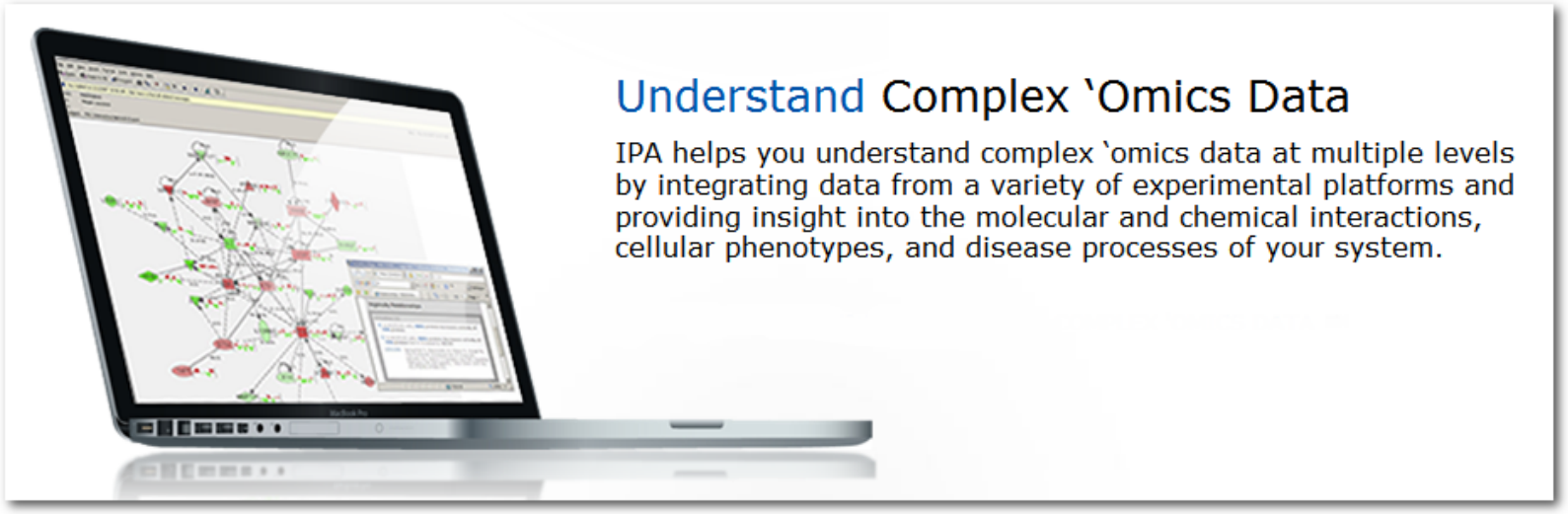
- Arabidopsis thaliana
- Bos taurus (bovine)
- Caenorhabditis elegans
- Gallus gallus (chicken)
- Pan troglodytes (chimpanzee)
- Danio rerio (zebrafish)
- Canis lupus familiaris (canine)
- Drosophila melanogaster
- Macaca mulatta (Rhesus Monkey)
- Saccharomyces cerevisiae
- Schizosaccharomyces pombe

IPA supported platform :

- **Gene expression:**
  - qPCR analysis
  - Microarray
  - RNA-Seq (NGS)
  - MicroRNA
  - mRNA
- **Proteomics**
  - PhosphoProteomics[New]
- Metabolomics

IPA application:

- Biomarker finding
- Toxicity Functions
- Diseases regulation



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Supported Identifiers for Data Upload

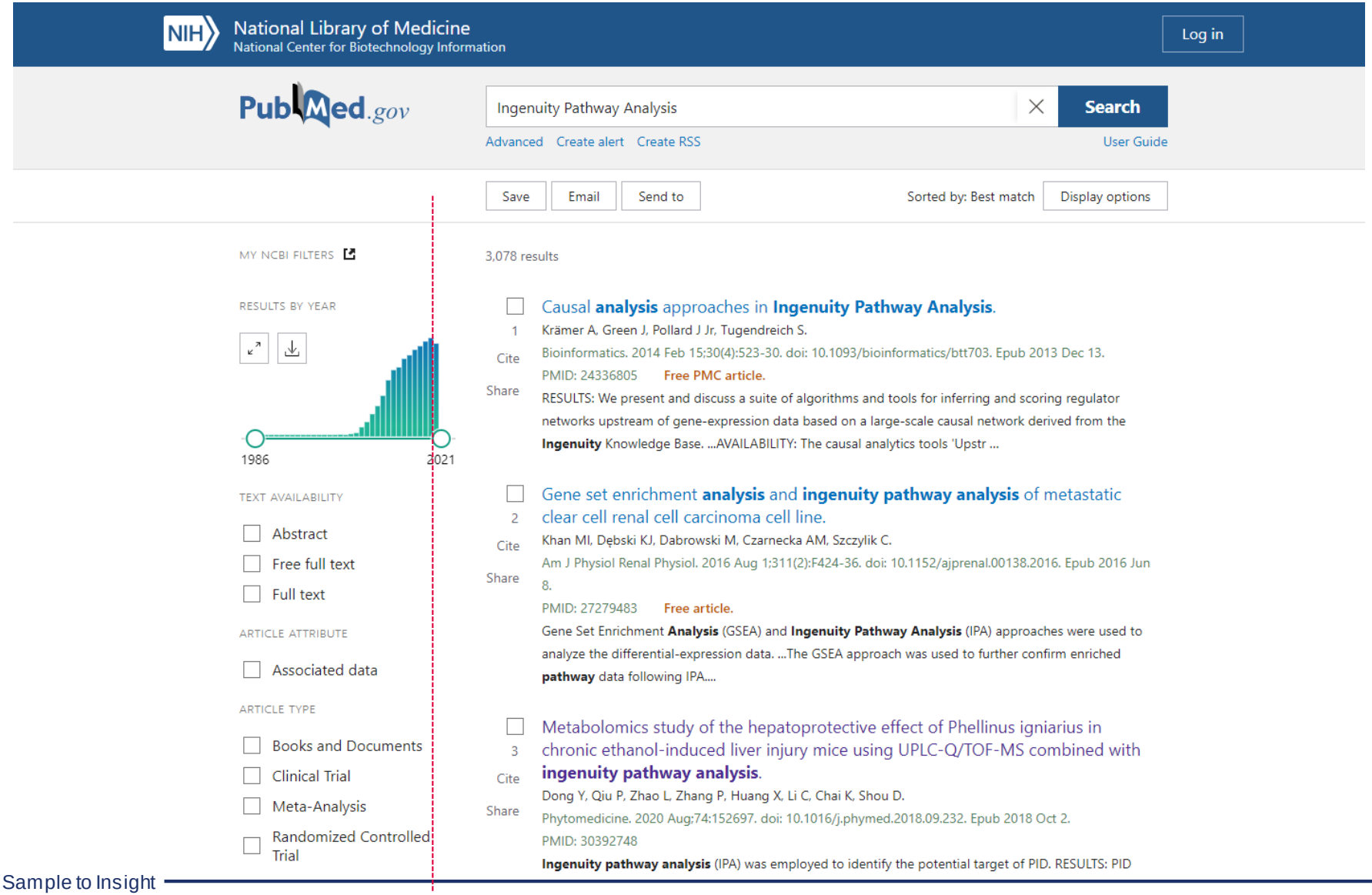
Get more complete mapping during dataset upload!

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					

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Peer-reviewed publications citing Ingenuity apps

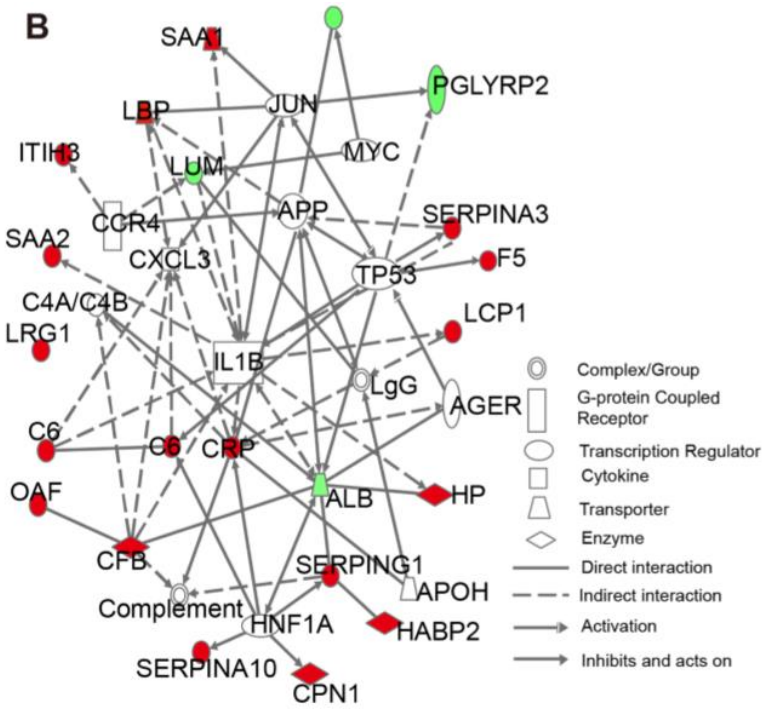
>45,800 publications that used IPA and growing! (Search Google Scholar for publications that cite IPA.)

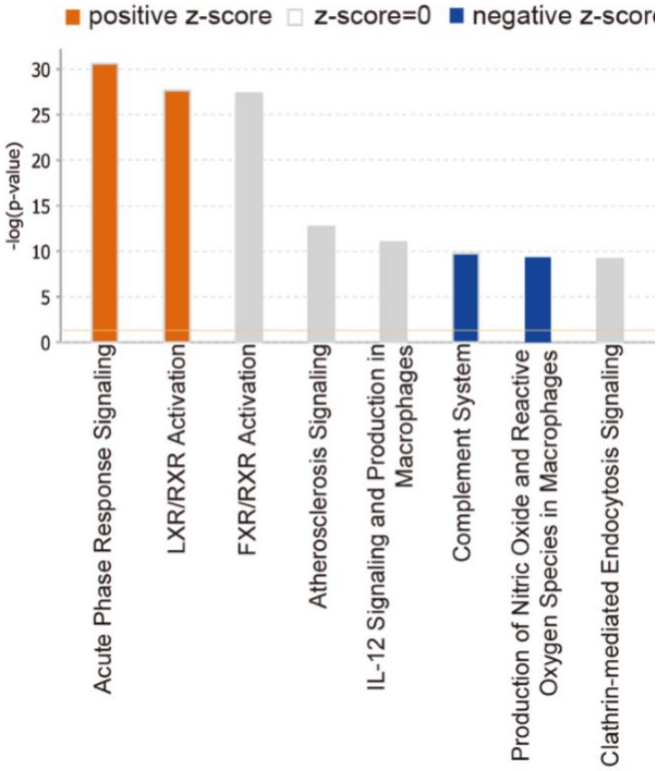


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IPA was cited in paper to study severe COVID-19

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





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

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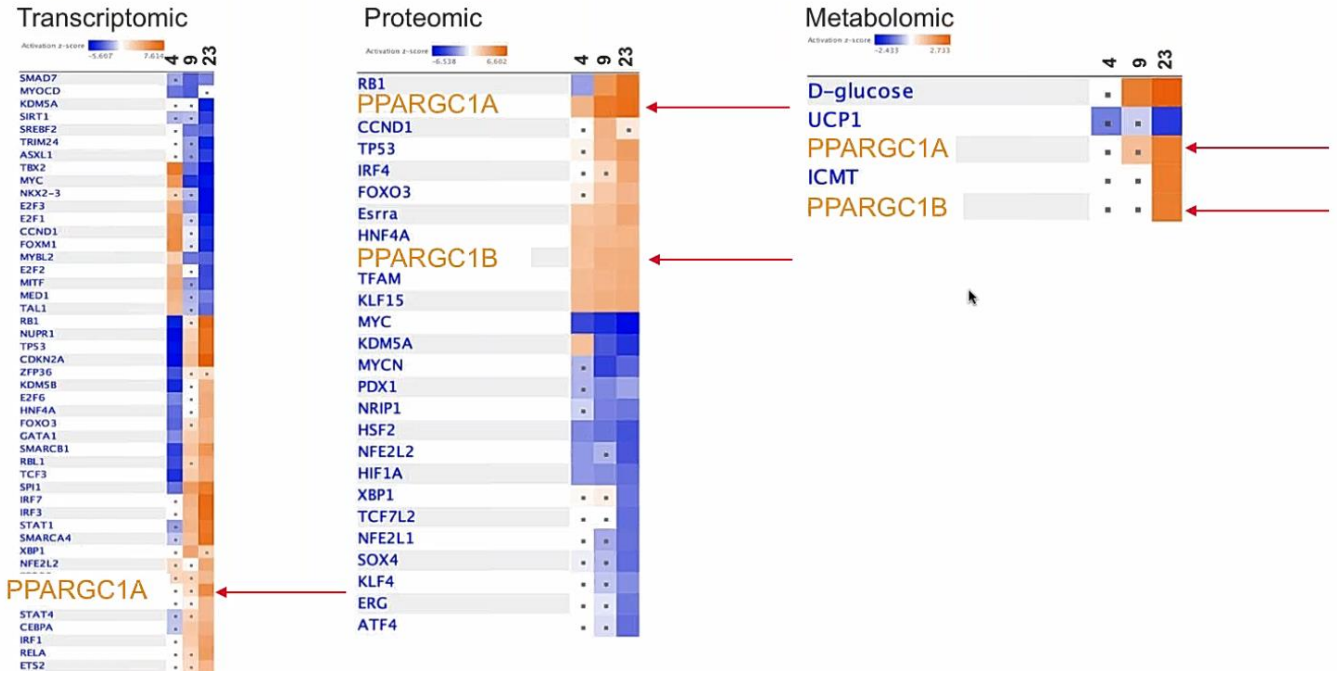
Multi-Omics Analysis using IPA

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

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

Multi-omics analysis indicate similar transcriptional drivers

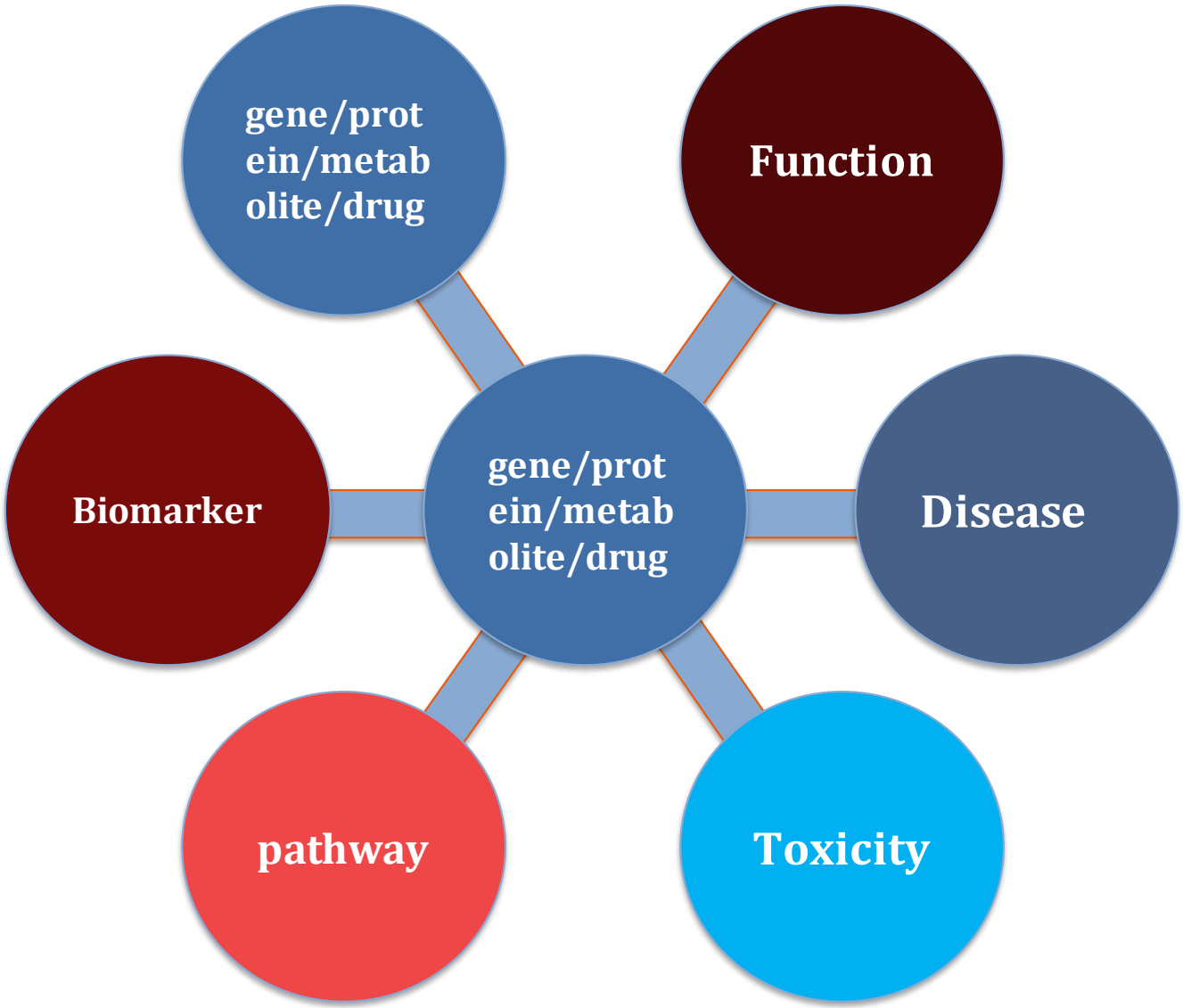
Upstream Analysis of transcriptomic, proteomic, and metabolomic data show induction of fatty oxidation regulation by PPARG coactivators.

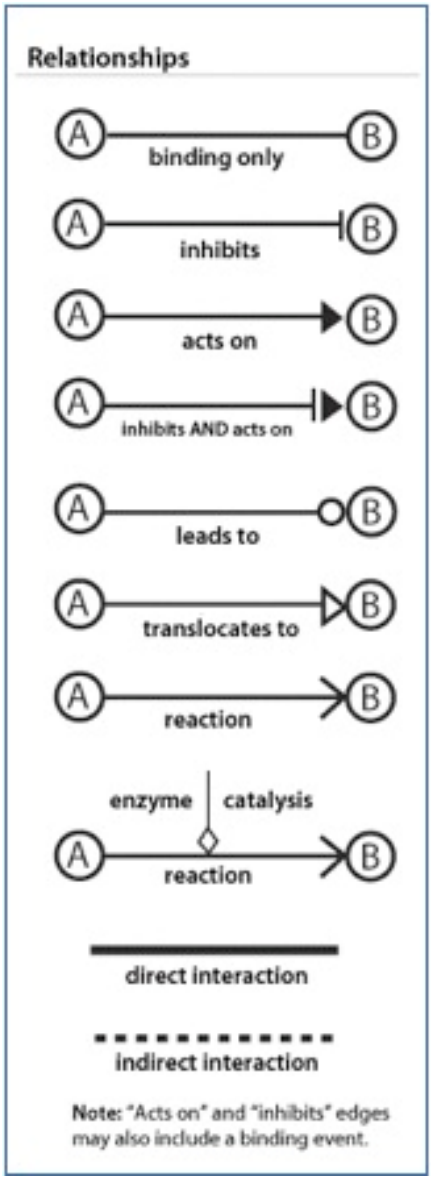


https://go.qiagen.com/IPA-multi-omics-analysis-webinar

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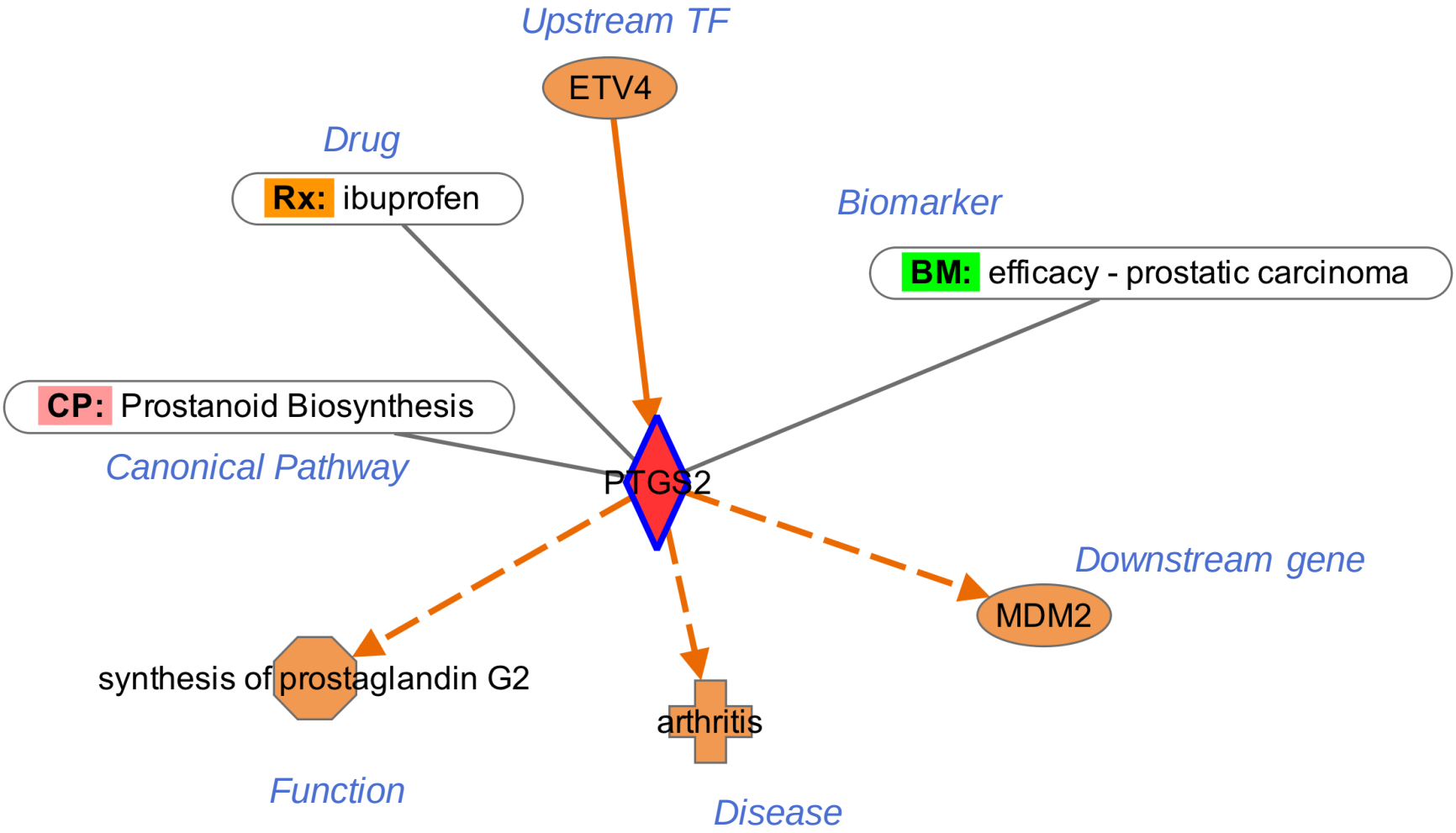
用IPA來發掘實驗資料中各類型關係





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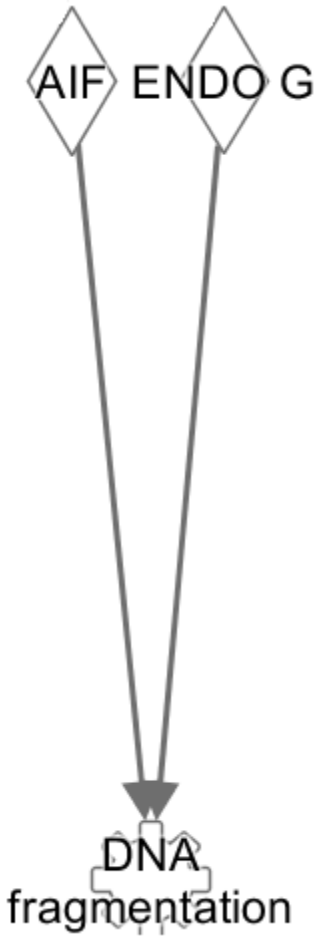
Capturing molecular information from the literature



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

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How IPA content is different: context and direction of effect



IPA Relationships: ENDO G|DNA fragmentation

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

EndNote ▼ EXPORT REFERENCES

Ingenuity Relationships

causation [16]

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

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

Source: Ingenuity Expert Findings

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

Experiment Type: agarose gel electrophoresis

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

Source: Ingenuity Expert Findings

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

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

Source: Ingenuity Expert Findings

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

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

Source: Ingenuity Expert Findings

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

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

Source: Ingenuity Expert Findings

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Third Party Database

- **Synonyms, Protein Family, Domains**
  - GO, Entrez Gene, Pfam
- **Tissue and Biofluid Expression & Location**
  - GNF, Plasma Proteome
- **Molecular Interactions**
  - BIND, DIP, MIPS, IntAct, Biogrid[New], MINT, Cognia, etc.
- **miRNA/mRNA target databases**
  - TarBase, TargetScan, miRecords
- **Gene to Disease Associations**
  - OMIM, GWAS databases
- **Metabolomics**
  - HumanCyc[New]
- **Clinical Trial information**
  - ClinicalTrials.gov

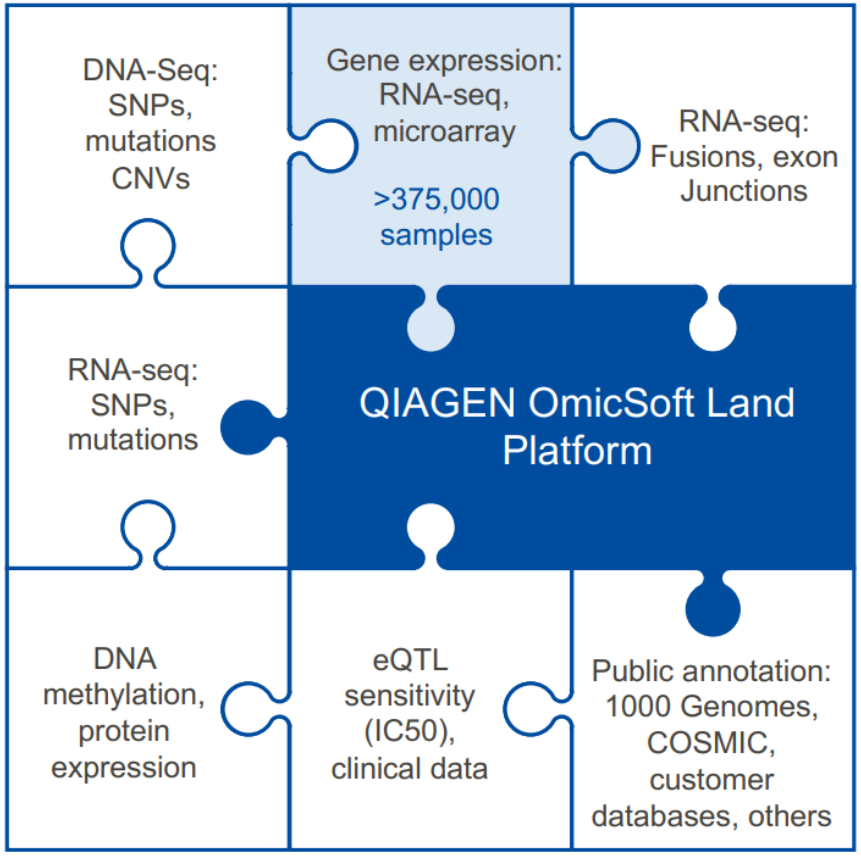


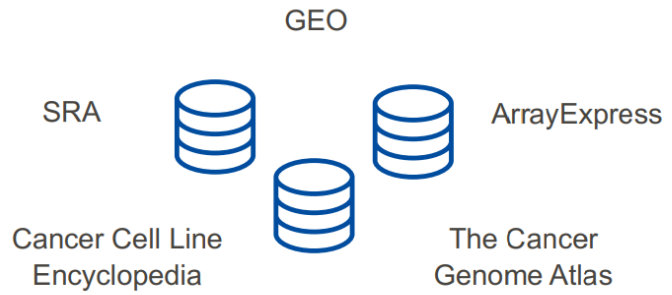
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OmicSoft Lands and findings in QIAGEN IPA

- More than 7.8 -> **8.4 million** findings from literature source or database.
- More than 96,000 -> **102,000 comparison datasets** from QIAGEN OmicSoft Lands.

Lands provide expression data to QIAGEN IPA





Land	Repository	Datasets Q2 2021	Datasets Q3 2021	Increase
DiseaseLand	HumanDisease	20,506	22,605	2,099
	MouseDisease	16,795	18,684	1,889
	RatDisease	7,809	7,809	
	LINCS	28,234	28,234	
OncoLand	OncoGEO	9,254	10,852	1,598
	OncoMouse	1,054	1,054	
	TCGA	4,789	4,789	
	MetastaticCancer	81	81	
	Hematology	3,455	3,819	364
	Pediatrics	444	444	
Single Cell Land	HumanSingleCellCluster	207	207	
	HumanSingleCellClusterUMI	548	548	
	MouseSingleCellCluster	465	465	
	MouseSingleCellClusterUMI	751	751	
	HumanSingleCellHCL	1,476	1,476	
	HumanSingleCellType	73	73	
	MouseSingleCellType	75	75	
	HumanSingleCellTypeUMI	278	278	
	MouseSingleCellTypeUMI	184	184	
Normal Cells and Tissues	Human Tissues (GTEx)		52	52

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Newly revised Land Explorer links

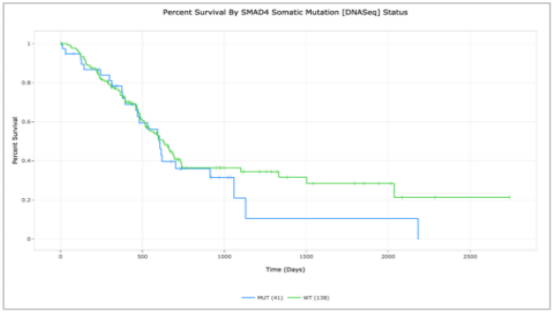
OmicSoft Land Explorer: Sample-level experimental data					
Data Type / Data Source	**Normal Tissue**	**Cell Lines**	**Oncology Consortia**	**Oncology Studies**	**Disease Studies**
RNA-seq expression:	Solid tissue (GTEx), Solid tissue (HPA), Blueprint	Cancer cell lines (CCLE)	TCGA, TARGET, BeatAML, ICGC, CGCI, CCLE+GTEx+TCGA	General oncology, Hematology, Metastasis, Pediatrics, Mouse studies	Human disease, Mouse disease, Rat disease
Microarray expression:	Solid tissue (GTEx)	Cancer cell lines (CCLE), GSK cell lines, NCI cell lines, Pfizer cell lines	TCGA, TARGET, expO, METABRIC, CCLE+GTEx	General oncology, Hematology, Metastasis, Pediatrics, Mouse studies	Human disease, Mouse disease, Rat disease
Differential regulation:		Treated cells (LINCS)	TCGA	General oncology, Hematology, Metastasis, Pediatrics, Mouse studies	Human disease, Mouse disease, Rat disease
Alteration frequency:		Cancer cell lines (CCLE), NCI cell lines	TCGA, TRACERx, BeatAML, ICGC, TARGET, METABRIC	General oncology, Hematology, Metastasis, Pediatrics	
Survival by expression:			TCGA, BeatAML, TARGET, CGCI	General oncology, Clinical outcomes, Hematology	



Expression in Rat, Mouse, and Human Disease



Mutation frequency



Survival plots



Cell line expression



Tumor expression



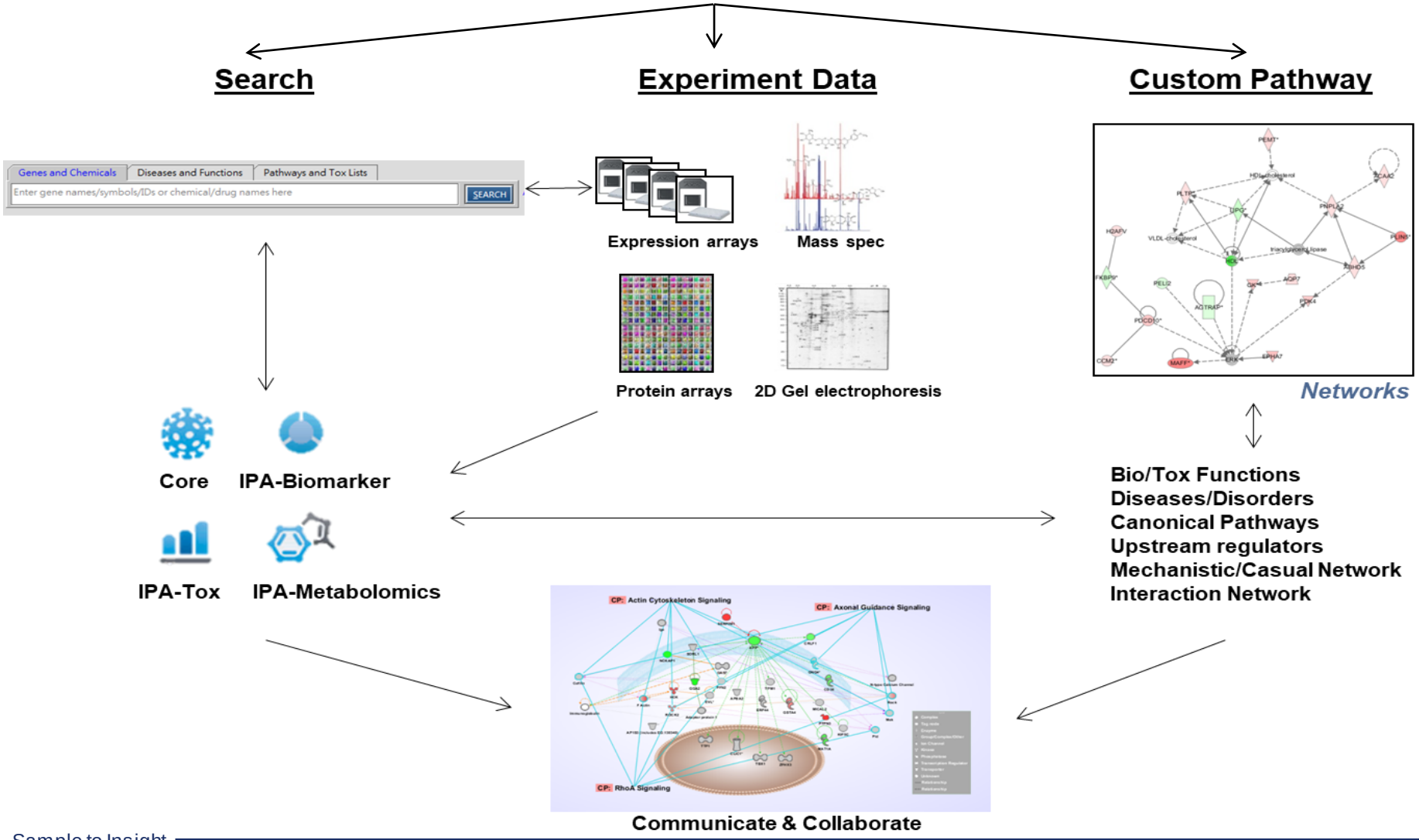
Hematopoietic expression (BluePrint)

Blueprint, CCLE, GTEx, HumanDisease, MouseDisease, OncoHuman, OncoMouse, TCGA, TARGET

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Entry Points in IPA

1) What does the data reveal about the underlying biology in the sampled cells or tissues?
2) What relevance does that biological information have with respect to other biological samples?



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Agenda

1. Learn how to search database in IPA
2. Draw the relationship between 3 nodes (Gene/Disease/Pathway)
3. Upload dataset to IPA and Create core analysis
4. Realize the meaning of the IPA analysis result

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Live Demo

Case Study: Investigating the tumor microenvironment

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Explore key target molecules and disease indications

Construct networks based on key targets and predict molecule activity

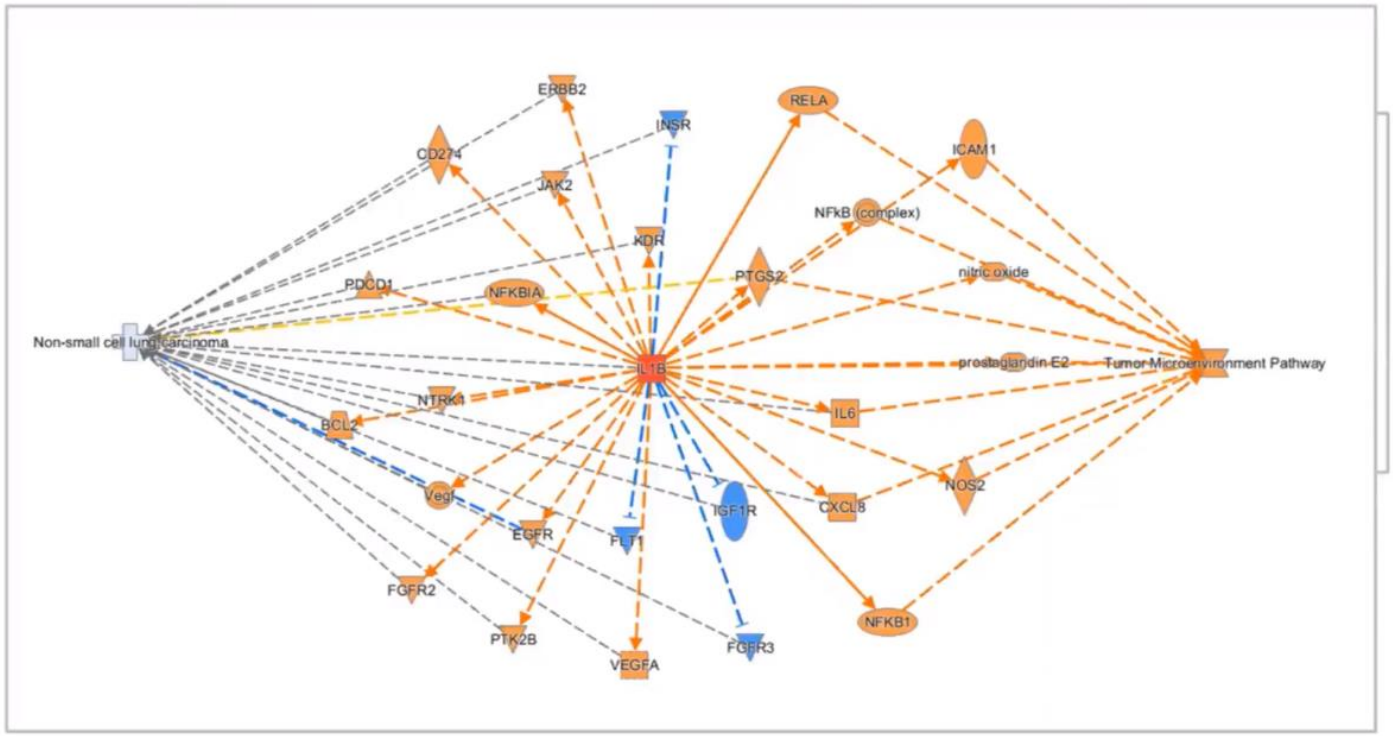
Review > Curr Pharm Des. 2017;23(32):4893-4905. doi: 10.2174/1381612823666170613080919.

Targeting the Tumor Microenvironment by Intervention in Interleukin-1 Biology

Elena Voronov [1], Ron N Apte [1]

Affiliations + expand

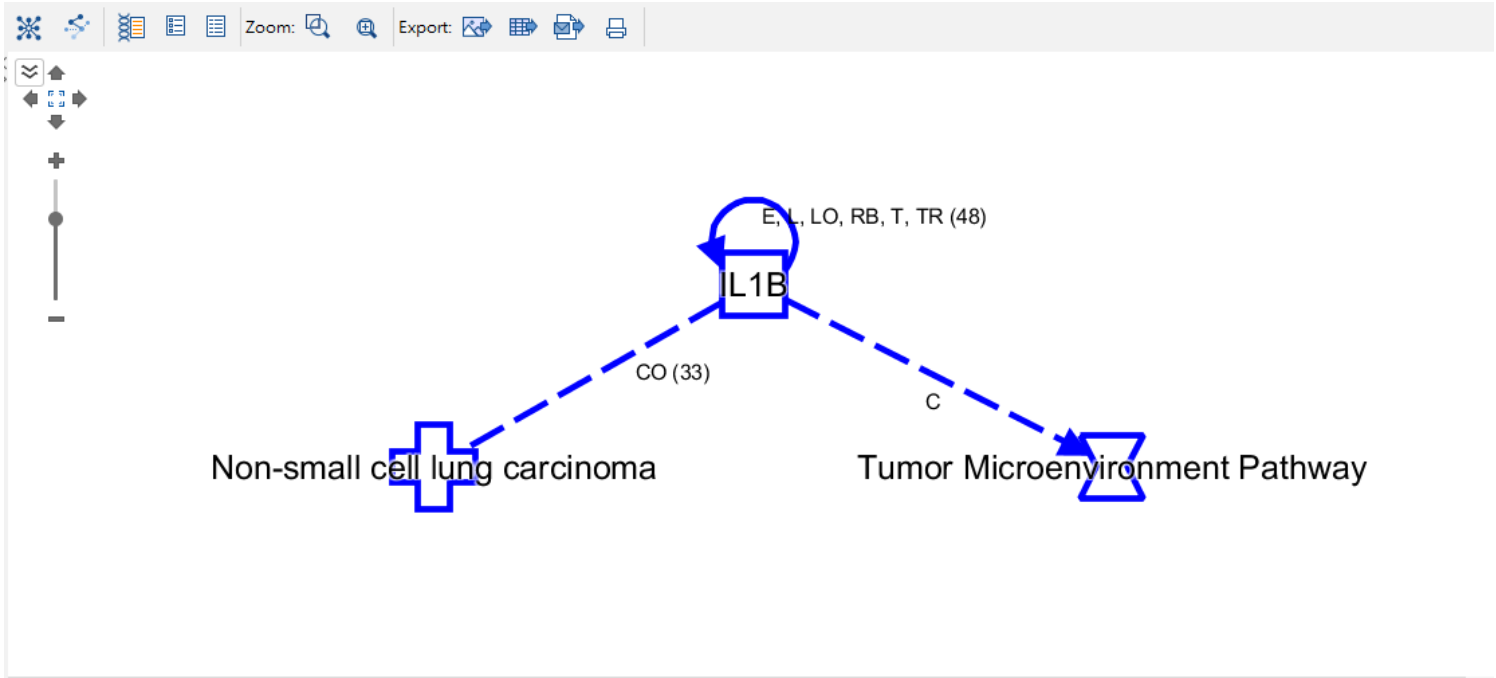
PMID: 28606052 DOI: 10.21



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Build networks linking molecules to the TME and disease endpoints

- Search: IL1B、Non-small cell lung carcinoma、Tumor Microenvironment Pathway
- Path Explore: activation、causation、inhibition



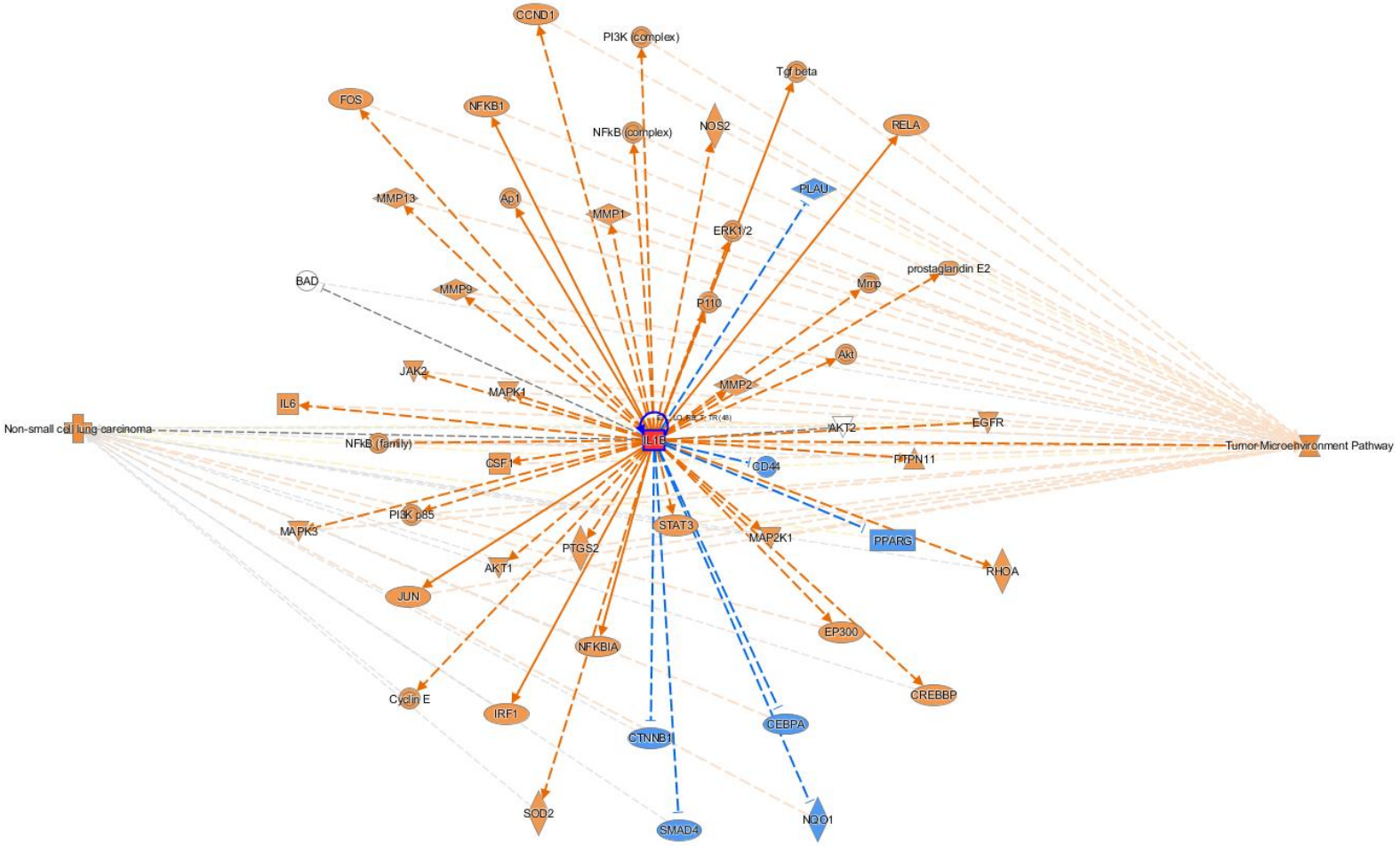
Add To My Pathway | Highlight | View: Shortest Paths + 1 (54) | Paths: 1 - 50

Paths	Set A Molecules	Node 1	Set B Molecules
1	IL1B	NFkB (complex)	Tumor Microenvironment Pathway
2	IL1B	EGFR	Non-small cell lung carcinoma
3	IL1B	NFKB1	Tumor Microenvironment Pathway
4	IL1B	ERK1/2	Tumor Microenvironment Pathway
5	IL1B	Ap1	Tumor Microenvironment Pathway
6	IL1B	MAPK1	Tumor Microenvironment Pathway
7	IL1B	RELA	Tumor Microenvironment Pathway

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Predict molecule activity of IL1B

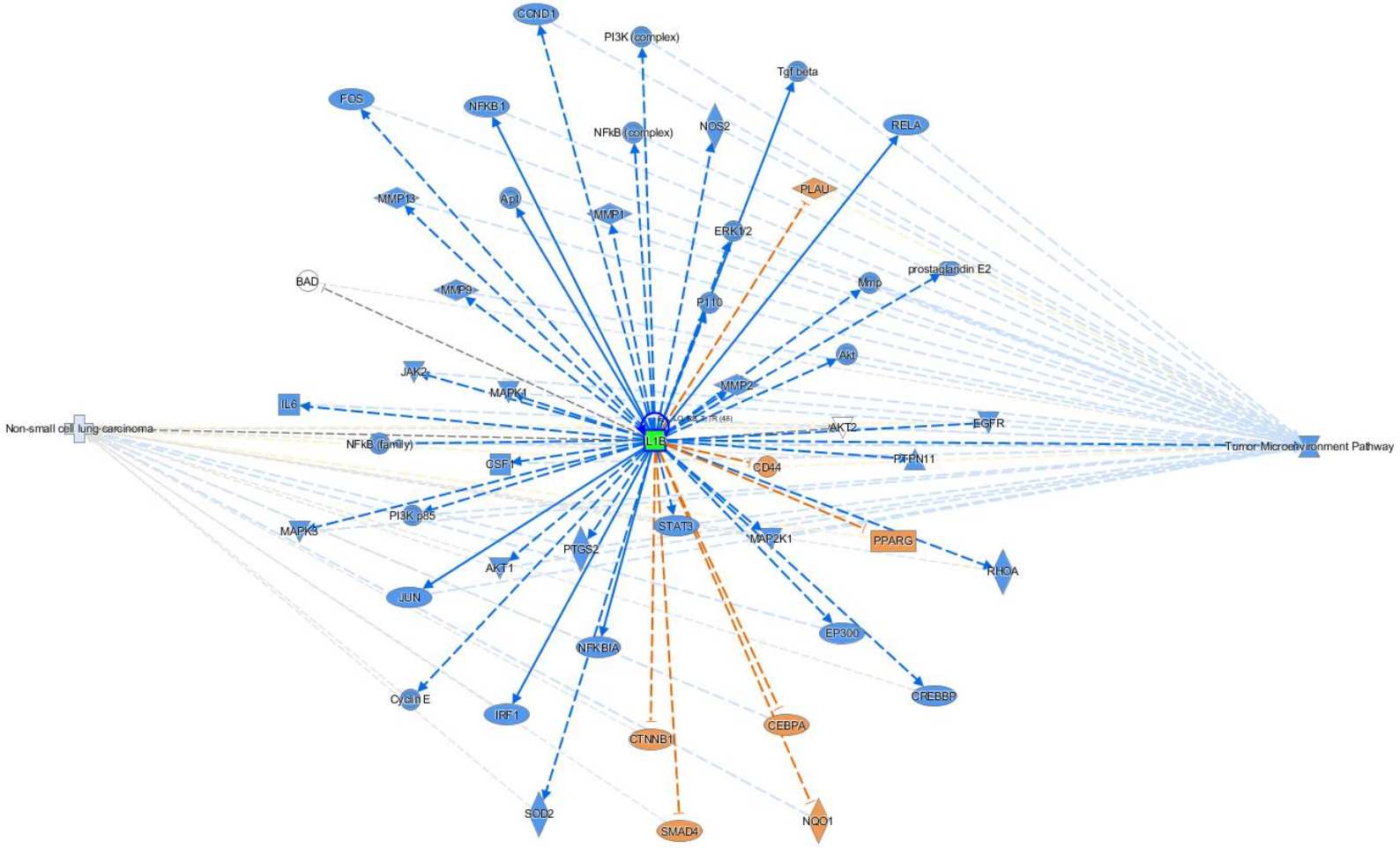
- MAP: IL1B Increased
- Lead to Tumor Microenvironment Pathway activation
- Correlation Non-small cell lung carcinoma activation



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Predict molecule activity of IL1B

- MAP: IL1B Decreased
- Lead to Tumor Microenvironment Pathway inhibition
- Correlation Non-small cell lung carcinoma inhibition



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Profile key immune molecules in the context of cancer

- Search: Non-small cell lung carcinoma
- BioProfiler: Cytokine

BioProfiler

Add To My Pathway | Add To My List | Display as Network | Create Dataset | Limit to Dataset

Molecule		Disease or Function Evidence						
Symbol	Molecule Type	Molecule Activity	Effect on Disease ...	Disease or Function	Mutation evidence	Biomarker Applic...	Species Evidence
AIMP1	cytokine	unknown change in activity	affects	Lung squamous cell c... all 1	unclassified mutation	not applicable	Human
▶CXCL2	cytokine	decreased activity	affects	Lung adenocarcinoma all 2	wild type	not applicable	Human
CXCL8	cytokine	increased activity	affects	Non-small cell lung carc all 1	wild type	efficacy	Human
IFNA10	cytokine	unknown change in activity	affects	Lung squamous cell c... all 1	missense	not applicable	Human
IFNA8	cytokine	unknown change in activity	affects	Lung adenocarcinoma all 1	missense	not applicable	Human
▶IFNG	cytokine	decreased activity,increase...	affects,increases	Lung adenocarcinoma all 2	homozygous,knockout,wil...	not applicable	Human,Mouse
▶IL10	cytokine	increased activity,unknown...	affects	Lung adenocarcinoma all 2	heterozygous,nonsense,wil...	not applicable	Human
IL1A	cytokine	increased activity	affects	Non-small cell lung carc all 1	wild type	efficacy	Human
▶IL1B	cytokine	increased activity	affects	Advanced non-small... all 24	wild type	not applicable	Human
IL36G	cytokine	unknown change in activity	affects	Lung adenocarcinoma all 1	missense	not applicable	Human
IL5	cytokine	unknown change in activity	affects	Lung adenocarcinoma all 1	unclassified mutation	not applicable	Human
▶IL6	cytokine	increased activity,unknown...	affects	Lung adenocarcinoma all 3	unclassified mutation,wild ...	efficacy,not applicable	Human
NAMPT	cytokine	unknown change in activity	affects	Adenocarcinoma in ri... all 1	missense	not applicable	Human
PF4V1	cytokine	unknown change in activity	affects	Lung adenocarcinoma all 1	missense	not applicable	Human
SCG2	cytokine	unknown change in activity	affects	Adenocarcinoma in ri... all 1	missense	not applicable	Human
▶SPP1	cytokine	increased activity,unknown...	affects	Lung adenocarcinoma all 2	missense,wild type	not applicable	Human,Mouse
▶TIMP1	cytokine	increased activity	affects	Lung squamous cell c... all 2	wild type	unspecified application	Human
▶TNF	cytokine	decreased activity	affects	Advanced non-small c... all 3	wild type	not applicable	Human
TNFSF11	cytokine	increased activity	affects	ALK rearrangement n... all 4	wild type	not applicable	Human
TNFSF13	cytokine	increased activity	affects	Non-small cell lung carc all 1	wild type	not applicable	Human
WNT2	cytokine	increased activity	affects	Non-small cell lung carc all 1	wild type	not applicable	Human
WNT7A	cytokine	increased activity	decreases	Development of non-... all 1	wild type	not applicable	Uncategorized

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Live Demo

Data Upload

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Data Upload Workflow

- ID、Observation
- Annotated Dataset

Dataset Preparation

- Create Core Analysis
  - Expression type
  - Measurement type
- Create Expression Analysis
  - Criteria
  - Cutoffs

Analyze Dataset

- Summary
- Diseases/Disorders
- Canonical Pathways
- Upstream regulators
- Interaction Network

Expression Analysis

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準備IPA分析用的Dataset

必須有一欄放入ID

Replicates

Average

Other observations (Comparison)

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

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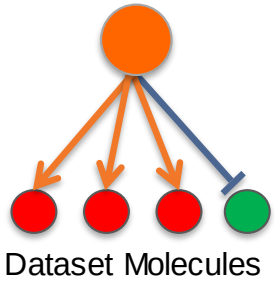
準備IPA分析用的Dataset

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

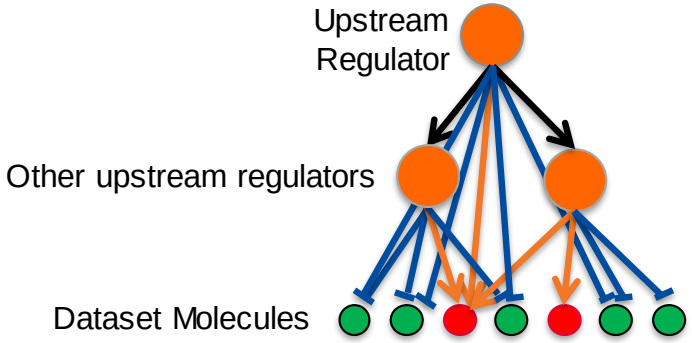
- 將實驗資料用 Excel 表格檔案儲存，檔案裡面只能有一個Sheet存在。
  - Excel Sheet當中必須要有一欄是列出**分子的ID** (如Gene Symbol, Refseq number, Uniprot number, HMDB等常用命名皆支援)
  - 每個Excel Sheet 最多可以放入 **20個 observations** (即20個實驗變因的資料欄的意思)
  - 每個Observation可以有3個不同的表現值種類 (ex. p-Value，fold-change等)
  - **表格欄位最上方只能有一個Head row (首行)**
  - 資料上傳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

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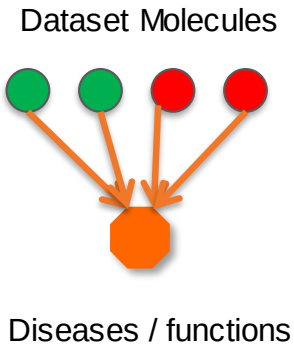
Upstream Analysis



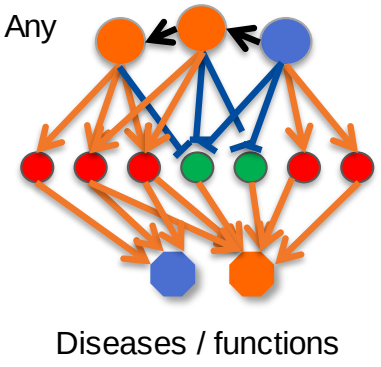
Mechanistic Network of Upstream Regulators



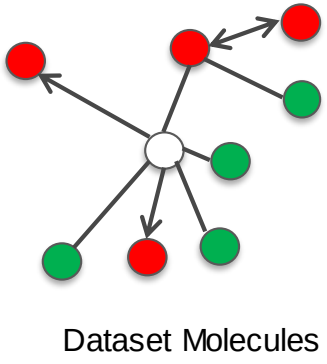
Function Analysis



Regulator Effect Network



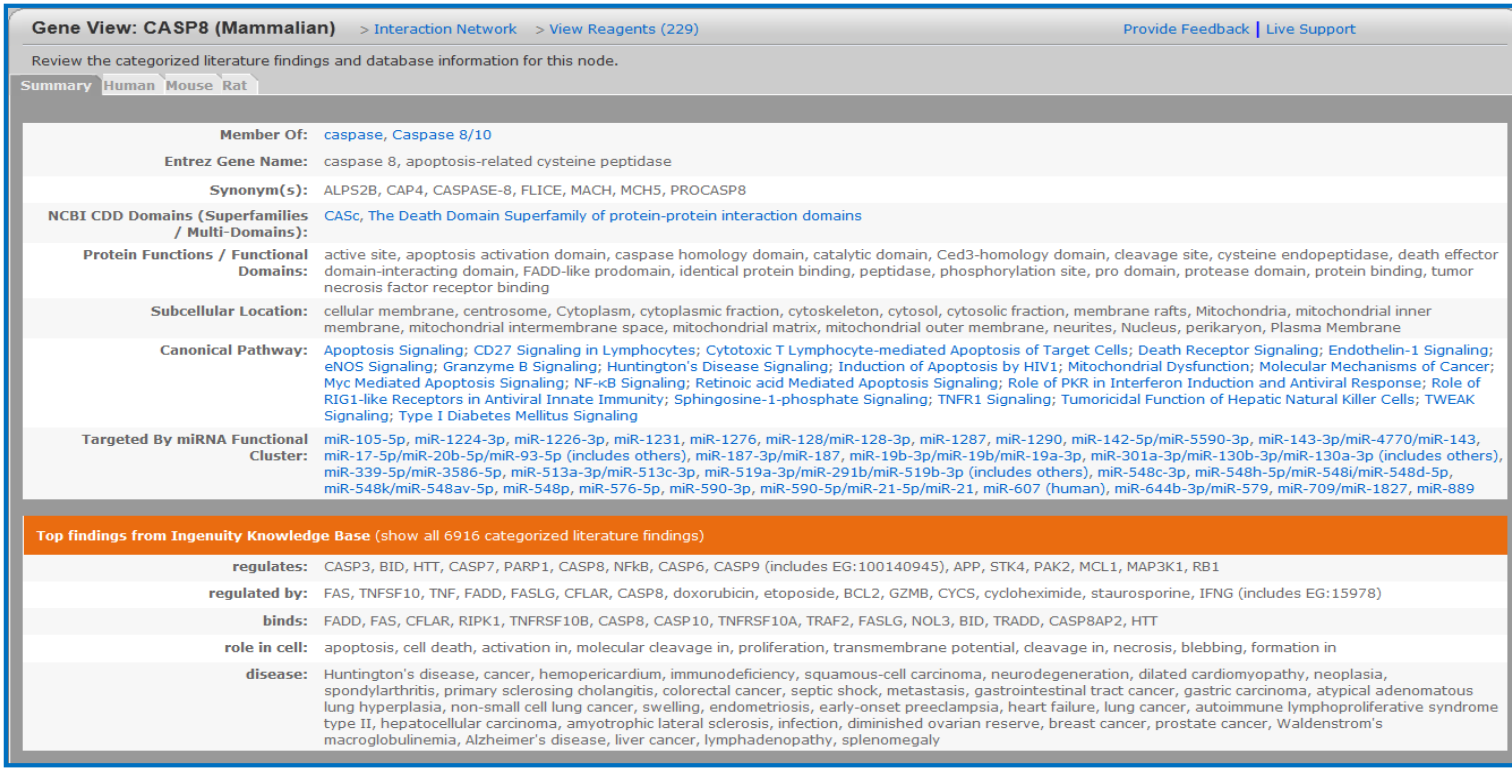
Interaction Network



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Gene View: CASP8 (Mammalian) > Interaction Network > View Reagents (229) Provide Feedback | Live Support

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

Summary | Human | Mouse | Rat

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

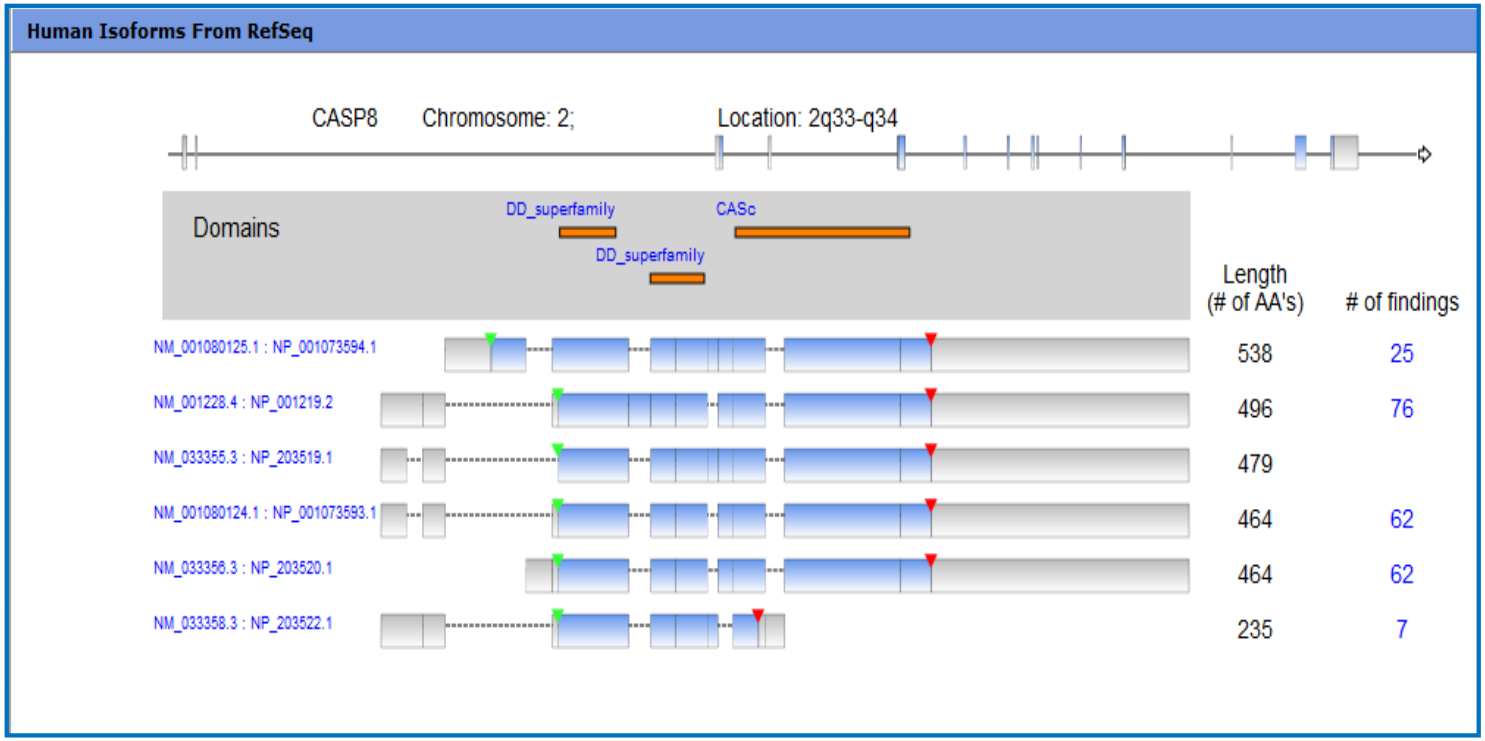
Top findings from Ingenuity Knowledge Base (show all 6916 categorized literature findings)

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

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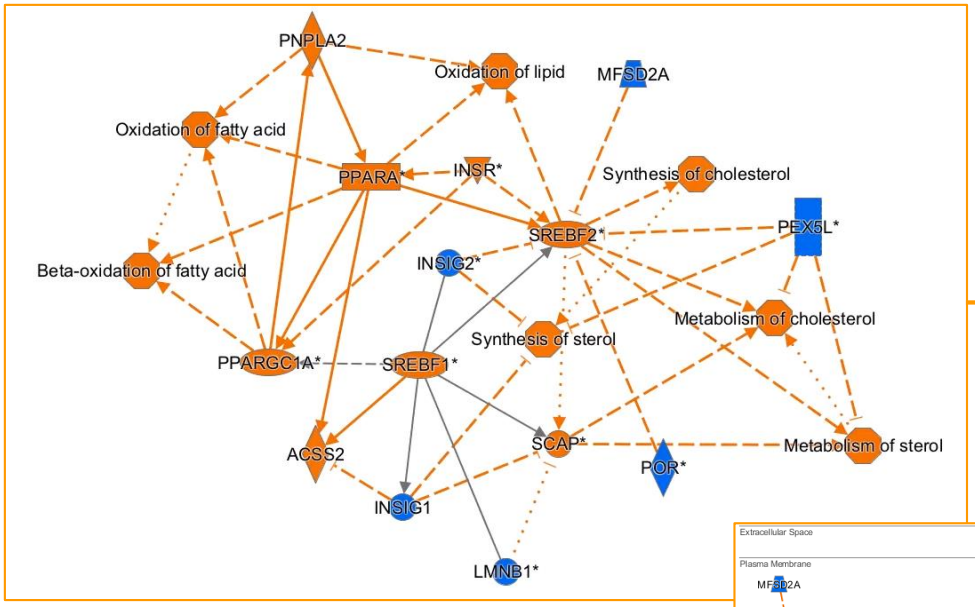
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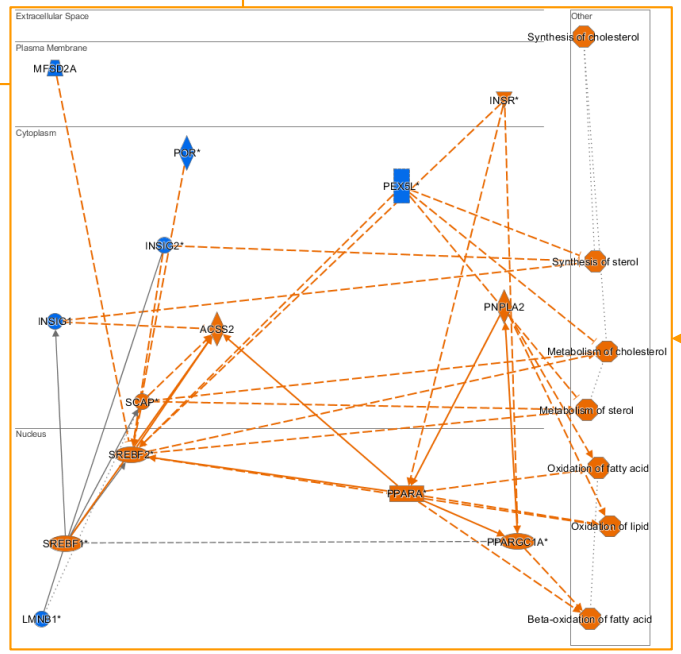
Add column(s)	Diseases & Functions Evidence							
Symbol	Molecule ...	Effect on ...	Disease	Mutation ...	Biomarke...	Species E...	Drug targ...	Expressio...
2,3,4,7,8-pentachlo...	increased activity	increases	hepatic steatosis	wild type	not applicable	Rat	not applicable	not applicable
3,4,5,3',4'-pentachl...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

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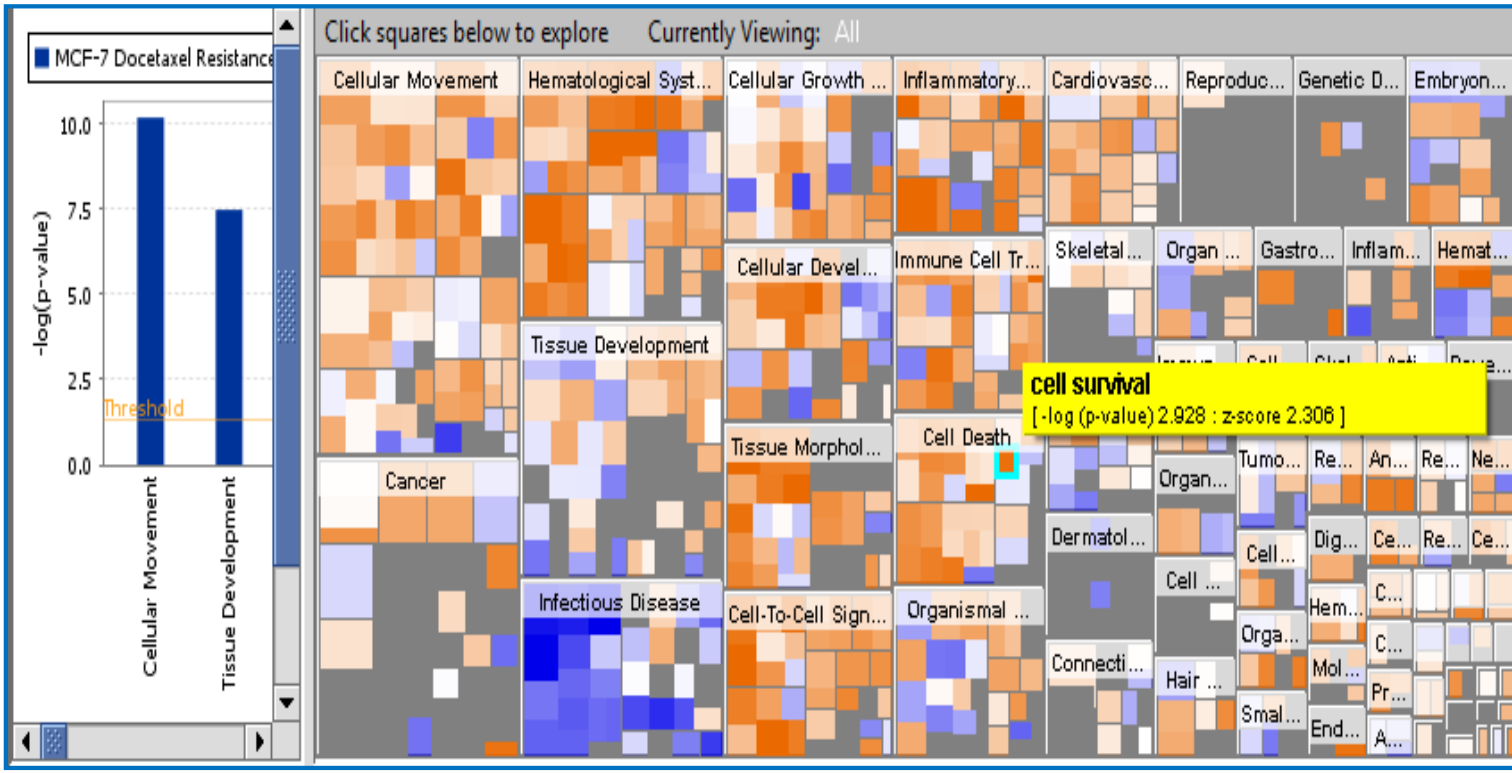




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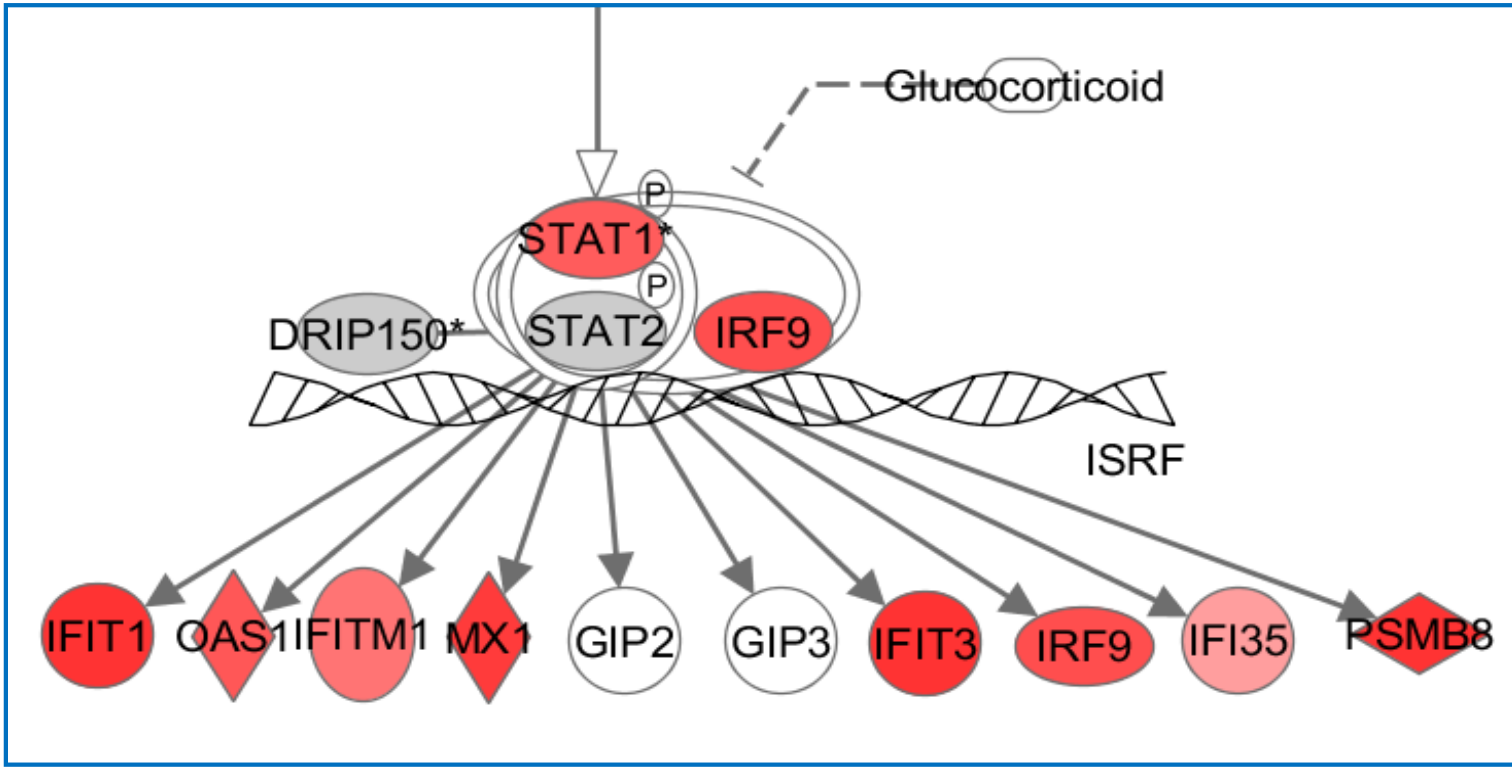
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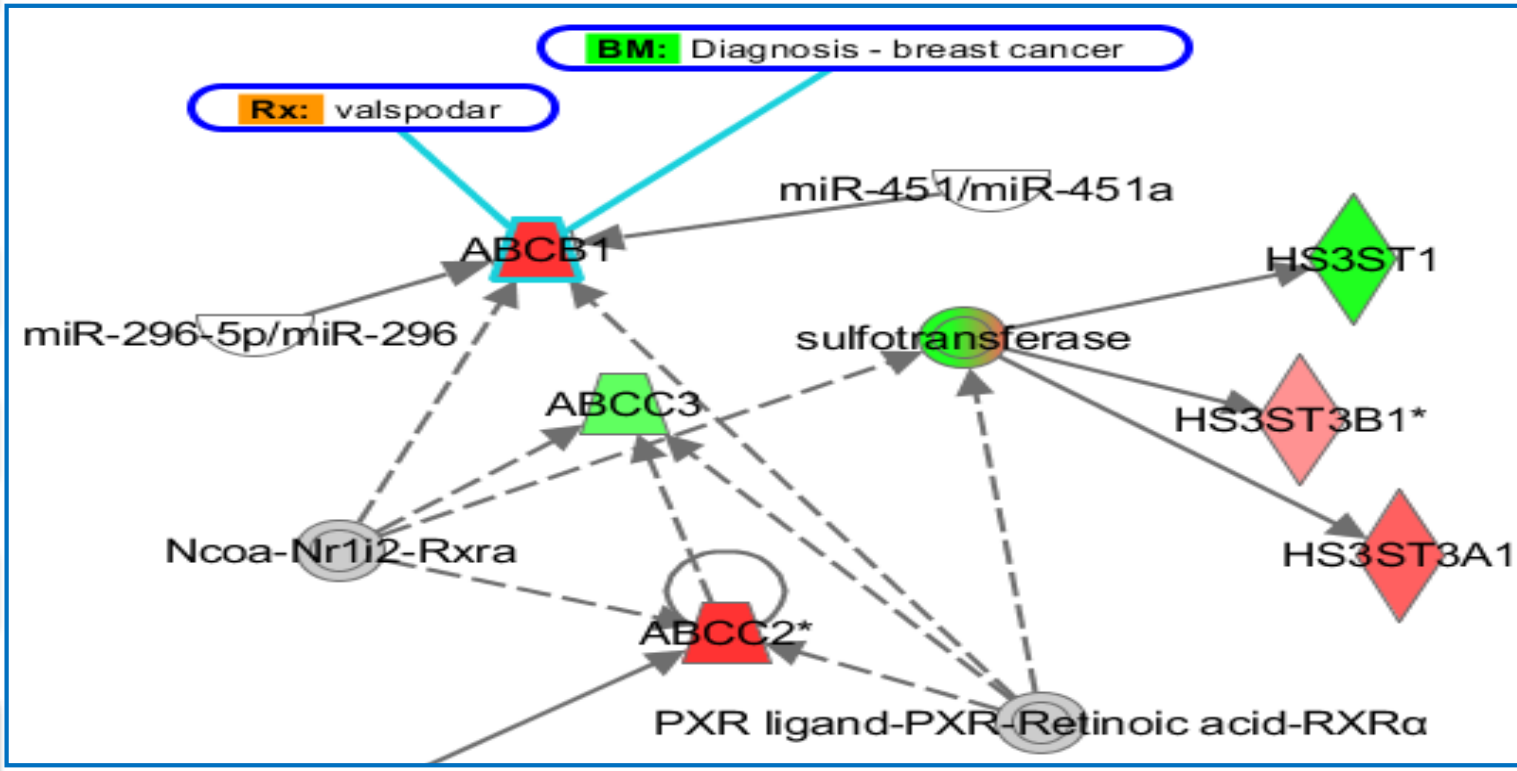
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Upstream Regulator	Molecule Type	Predicted ...	Activation z...	p-value...
IFNA2	cytokine	Activated	7.729	3.83E-42
MAPK1	kinase	Inhibited	-6.204	4.47E-36
IRF7	other	Activated	6.513	8.22E-34
IFNG (includes EG:15	cytokine	Activated	8.418	1.96E-31
IL1RN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

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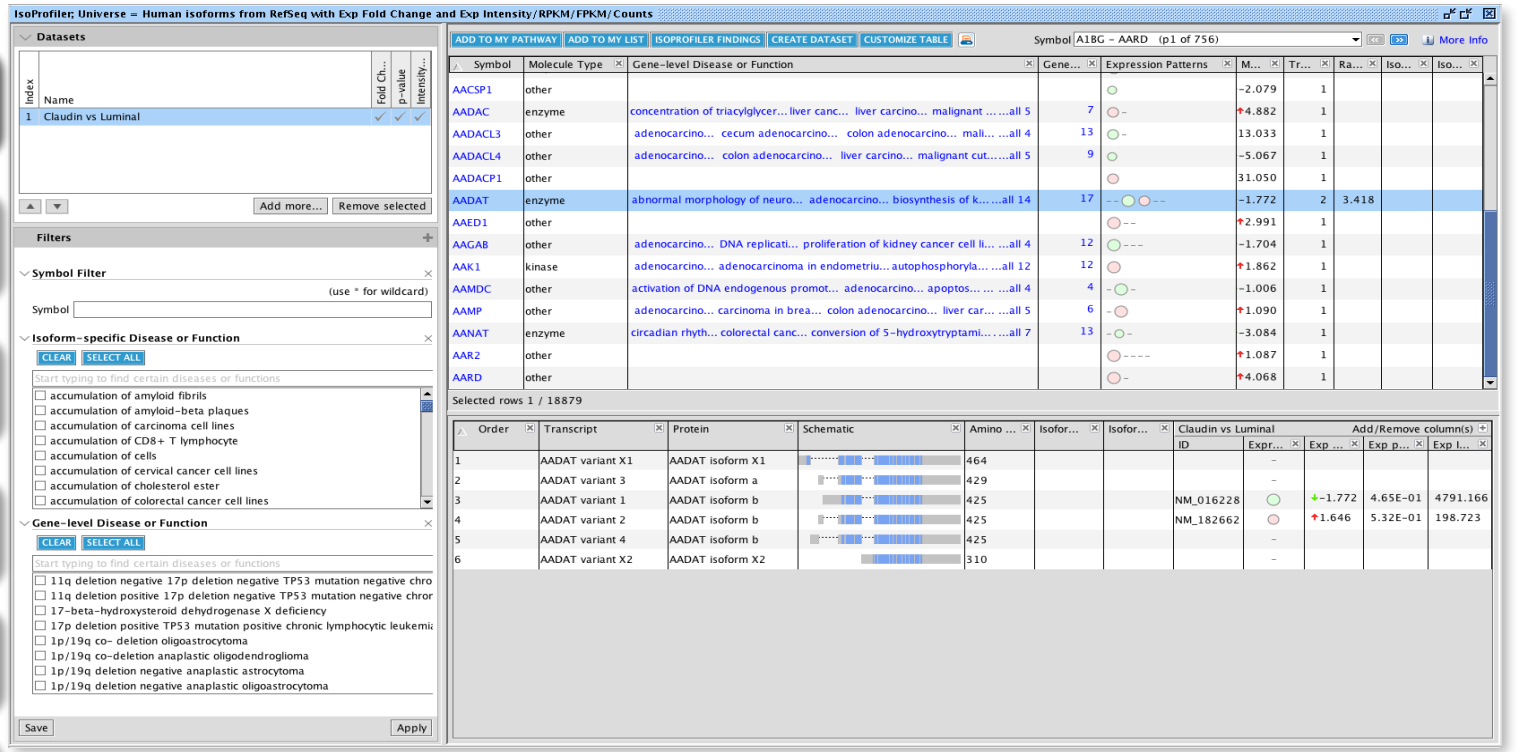
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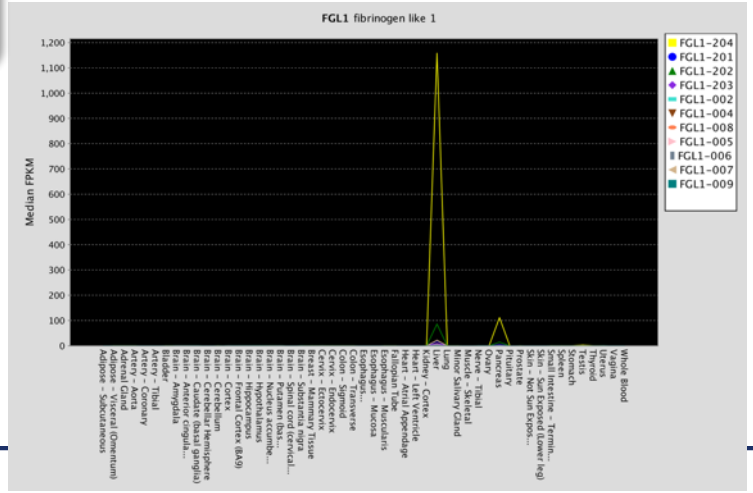


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Unique Tools for Biological Analysis and Interpretation (advanced)

- IsoProfiler
- Multi-omics Overlay
- Phosphorylation Analysis
- Comparison Analysis
- Activity Plot
- Analysis Match w/ OmicSoft Lands

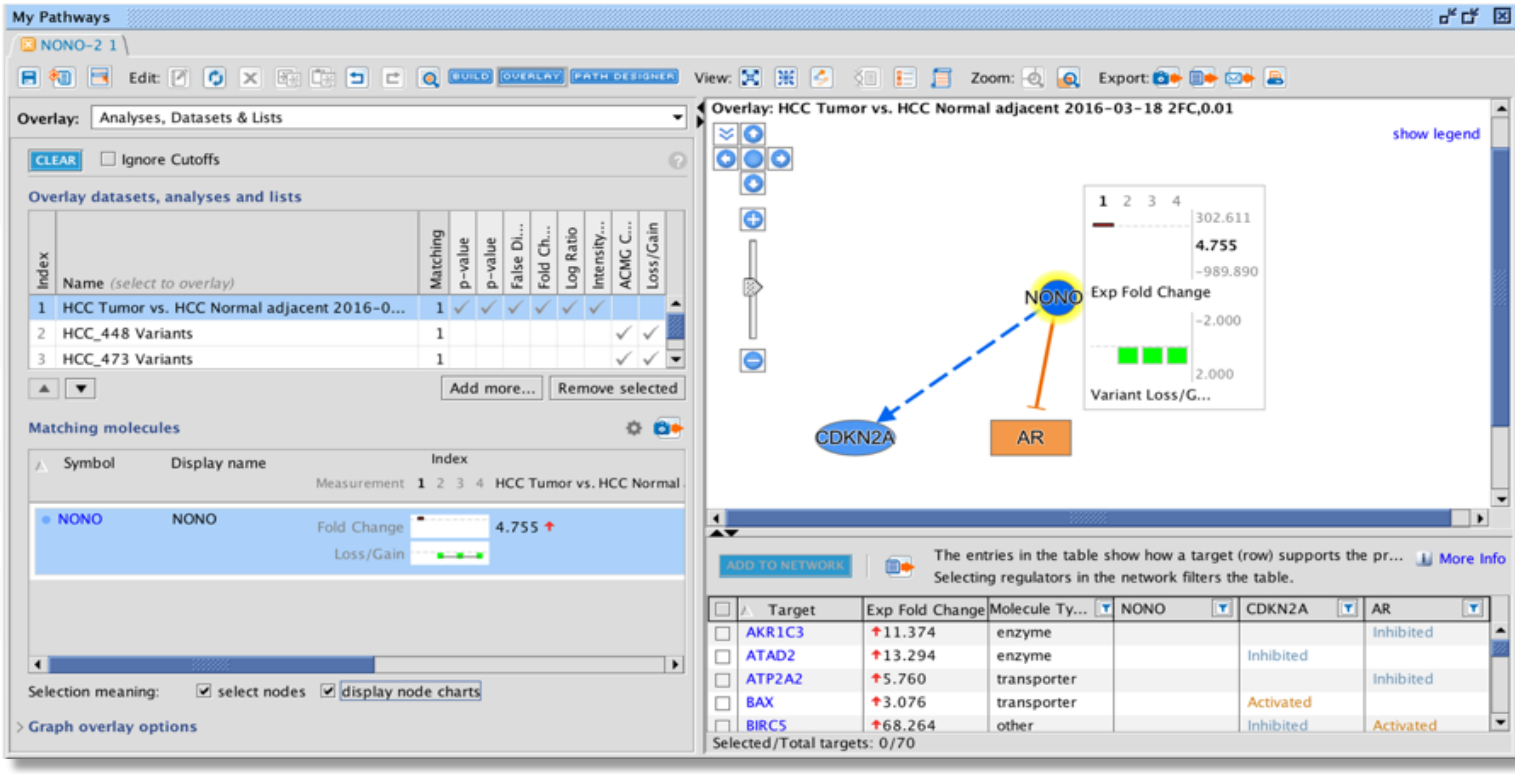




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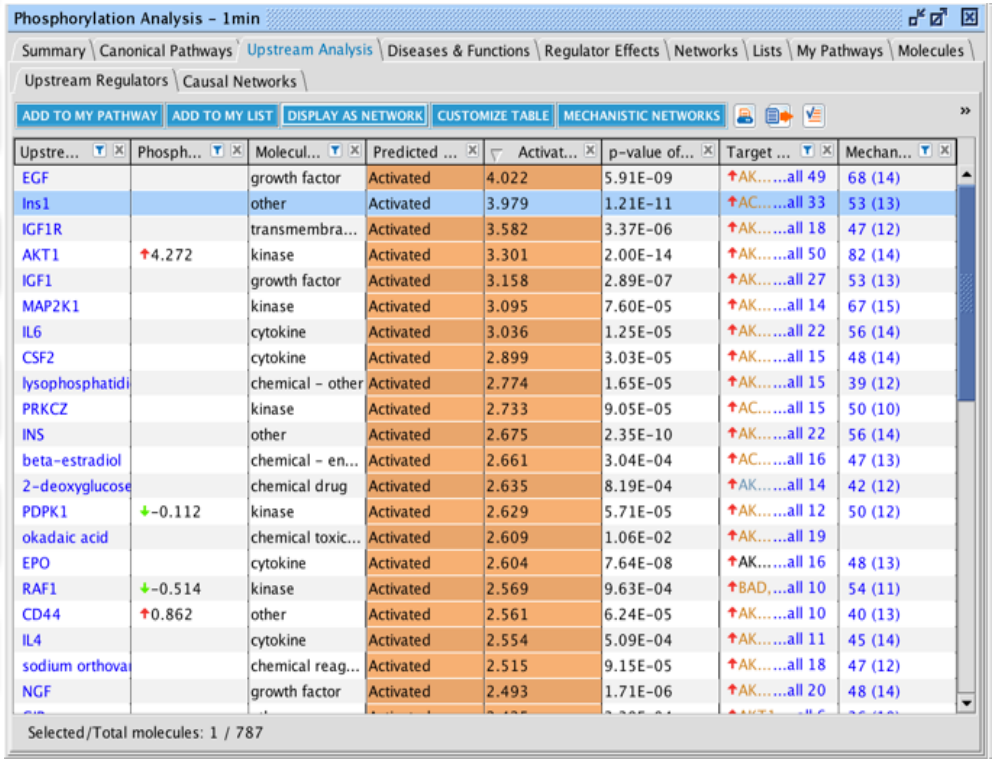
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- Phosphorylation Analysis
- Comparison Analysis
- Activity Plot
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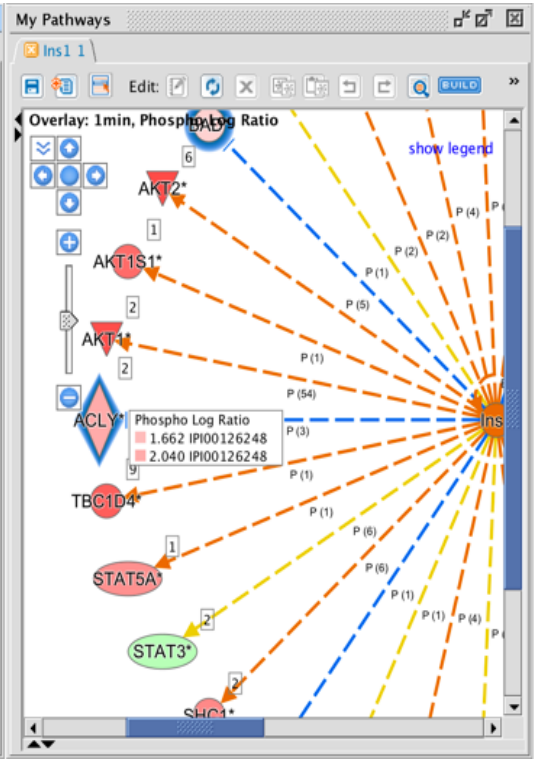


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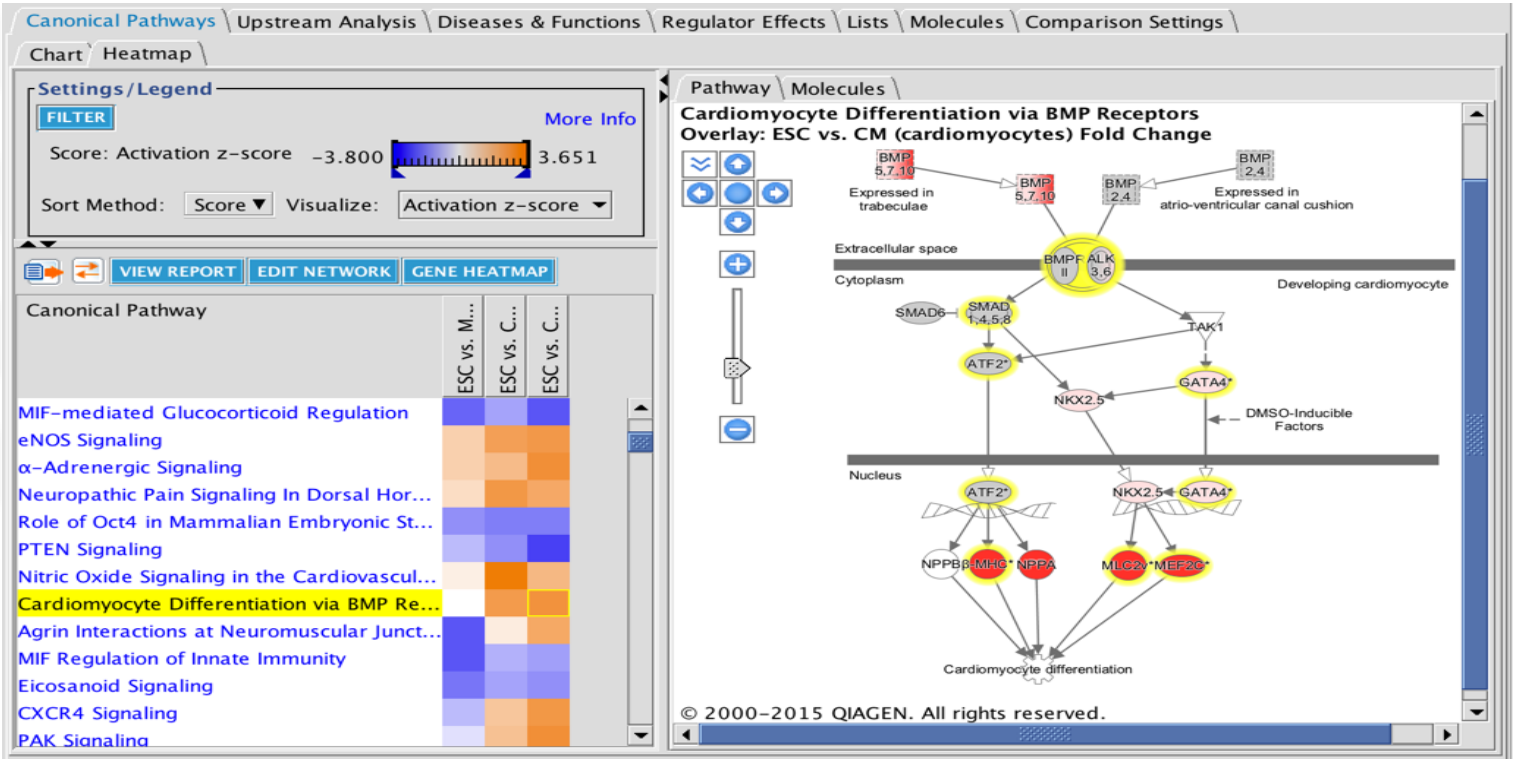




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Unique Tools for Biological Analysis and Interpretation (advanced)

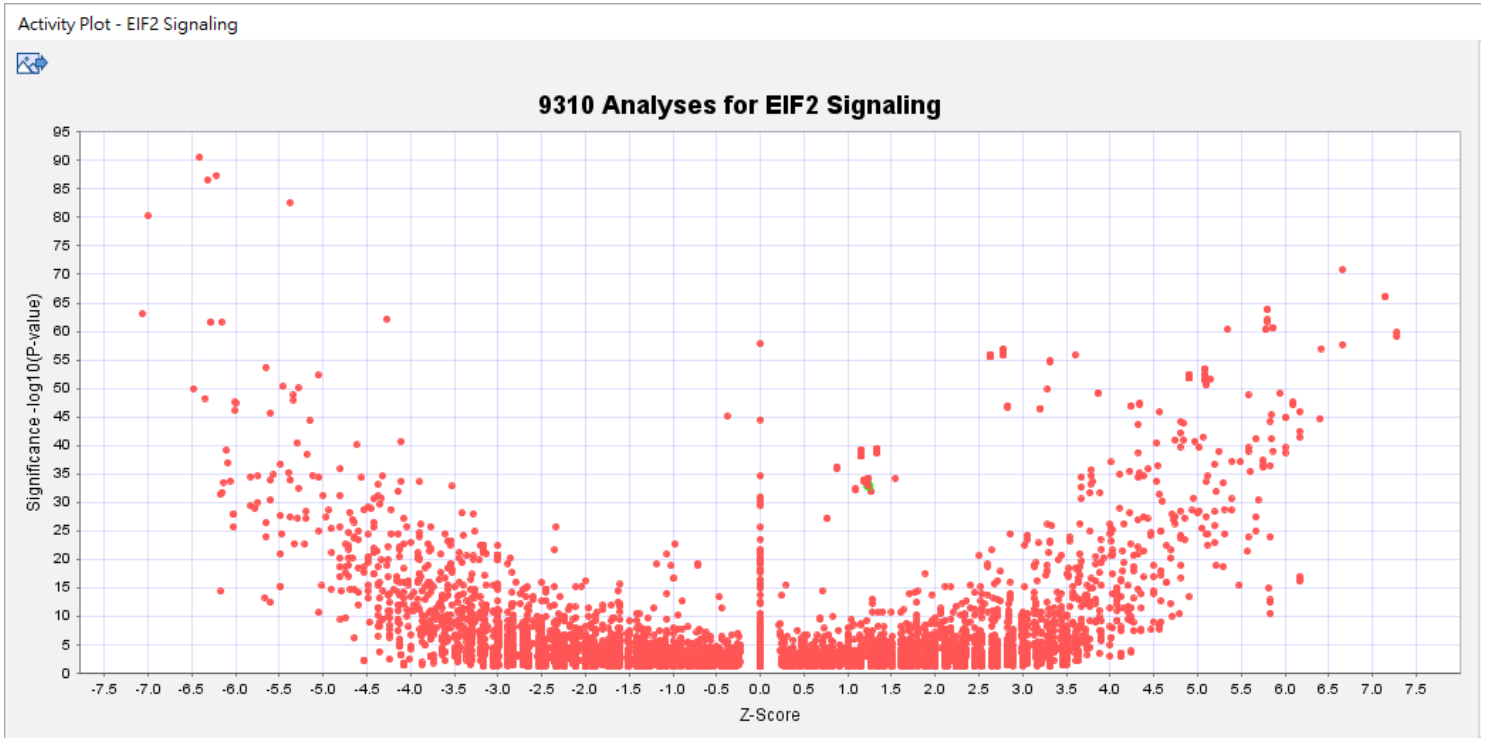
- IsoProfiler
- Multi-omics Overlay
- Phosphorylation Analysis
- Comparison Analysis
- Activity Plot
- Analysis Match w/ OmicSoft Lands



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Unique Tools for Biological Analysis and Interpretation (advanced)

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- Analysis Match* w/ OmicSoft Lands

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

Evaluate Metadata | View As Heatmap | View Comparison | Customize Table | z-sc... 44.48 - 24.62 (1/249)

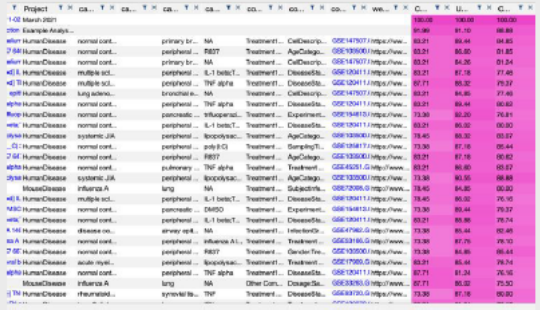
Analysis Name	Project	case.dis...	case.tiss...	compar...	compar...	CP (z-sc...	UR (z-s...	CN (z-s...	DE (z-sc...	z-s...
1- prostate cancer [prostate] NA 76	MetastaticCancer	prostate cancer	prostate	Disease vs. Nor...	LandSampleTy...	55.90	37.55	26.73	57.74	44.48
343- normal control [heart] NA 996	RatDisease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

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New Pattern Search with QIAGEN OmicSoft

➢ Analysis Match, Activity Plot, and Pattern Search: How do they differ?

Analysis Match

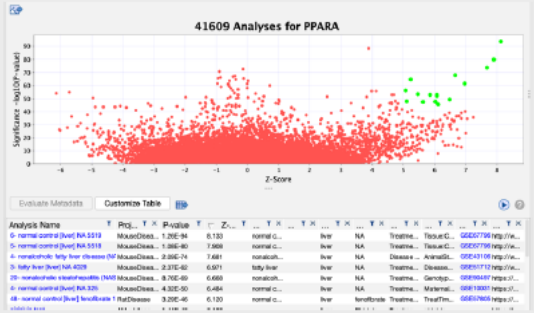


Which analyses have similar or dissimilar biology compared to mine?

- Automatically find similar and anti-similar analyses as compared to yours
- How: Matches the signatures of predicted entities (upstream regulators, canonical pathways etc.) in your analysis to signatures from other analyses.

- Core analysis

Activity Plot

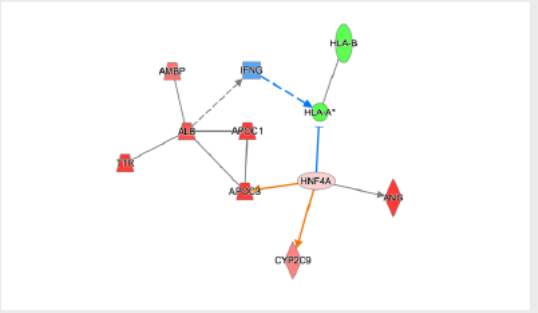


In which analyses is a biological entity of interest significantly impacted?

- Discover analyses that activate or inhibit a particular entity (an upstream regulator like PPARA, or a Canonical Pathway)
- How: Matches all the targets of the entity (from the Knowledge Base) against the analyses

- Canonical Pathway
- Upstream regulator

Pattern Search (New)



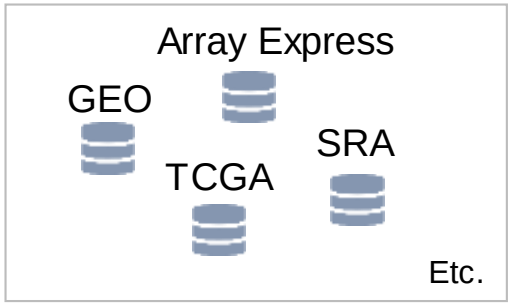
Is this pattern of activity seen among a massive collection of expression data?

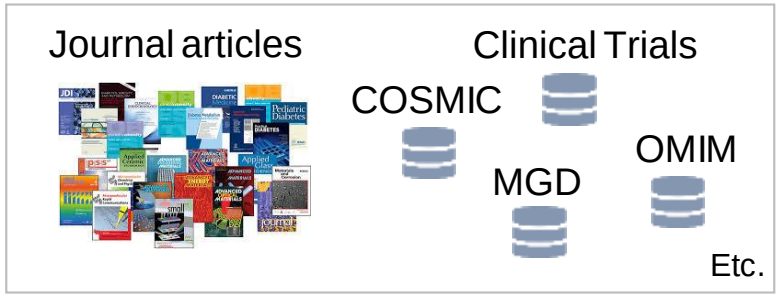
- Any network or pathway with genes and a pattern can be the "query"
- How: Find all OmicSoft analyses that match or anti-match any molecular pattern you choose (from a network or pathway)

- Canonical Pathway (expression)
- Networks (expression)

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Unprecedented discovery, together





Curation, Processing, & QA

Curation & QA

Datasets integrated into OmicSoft Lands

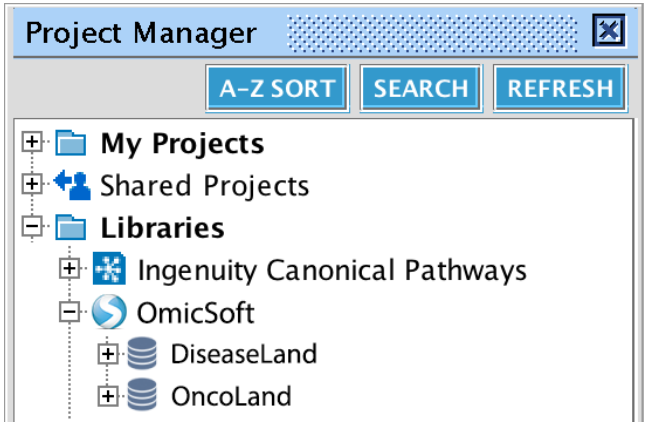
Curated Findings

OmicSoft Array Suite

OncoLand
DiseaseLand
SingleCellLand

96,000+ Expression comparison datasets

INGENUITY PATHWAY ANALYSIS





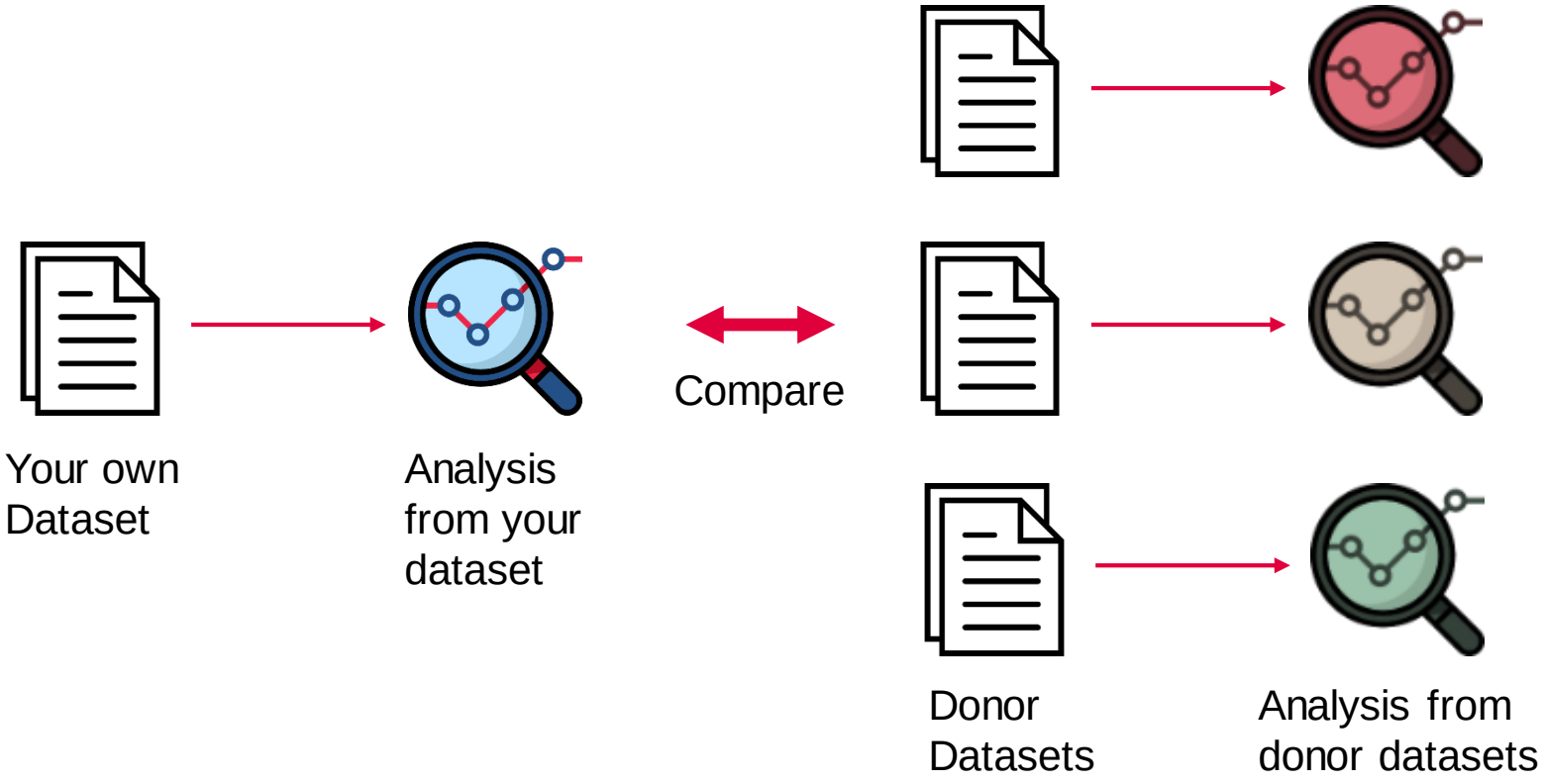
- Biological analyses of each dataset
- Compare your analysis to all OmicSoft analyses

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Analysis Match

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

並自 **DiseaseLand & OncoLand** 再添加大約**28,000**個分析組，總數將超過**90,000**個



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Analysis Match Database

>102,000 datasets available in Analysis Match and Activity Plot and Pattern Search

Land	Repository	Datasets Q2 2021	Datasets Q3 2021	Increase
DiseaseLand	HumanDisease	20,506	22,605	2,099
	MouseDisease	16,795	18,684	1,889
	RatDisease	7,809	7,809	
	LINCS	28,234	28,234	
OncoLand	OncoGEO	9,254	10,852	1,598
	OncoMouse	1,054	1,054	
	TCGA	4,789	4,789	
	MetastaticCancer	81	81	
	Hematology	3,455	3,819	364
	Pediatrics	444	444	
Single Cell Land	HumanSingleCellCluster	207	207	
	HumanSingleCellClusterUMI	548	548	
	MouseSingleCellCluster	465	465	
	MouseSingleCellClusterUMI	751	751	
	HumanSingleCellHCL	1,476	1,476	
	HumanSingleCellType	73	73	
	MouseSingleCellType	75	75	
	HumanSingleCellTypeUMI	278	278	
	MouseSingleCellTypeUMI	184	184	
Normal Cells and Tissues	Human Tissues (GTEx)		52	52

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Basic Module and Advanced module on IPA

Basic Module

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

Advanced Analytics (AA)

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

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

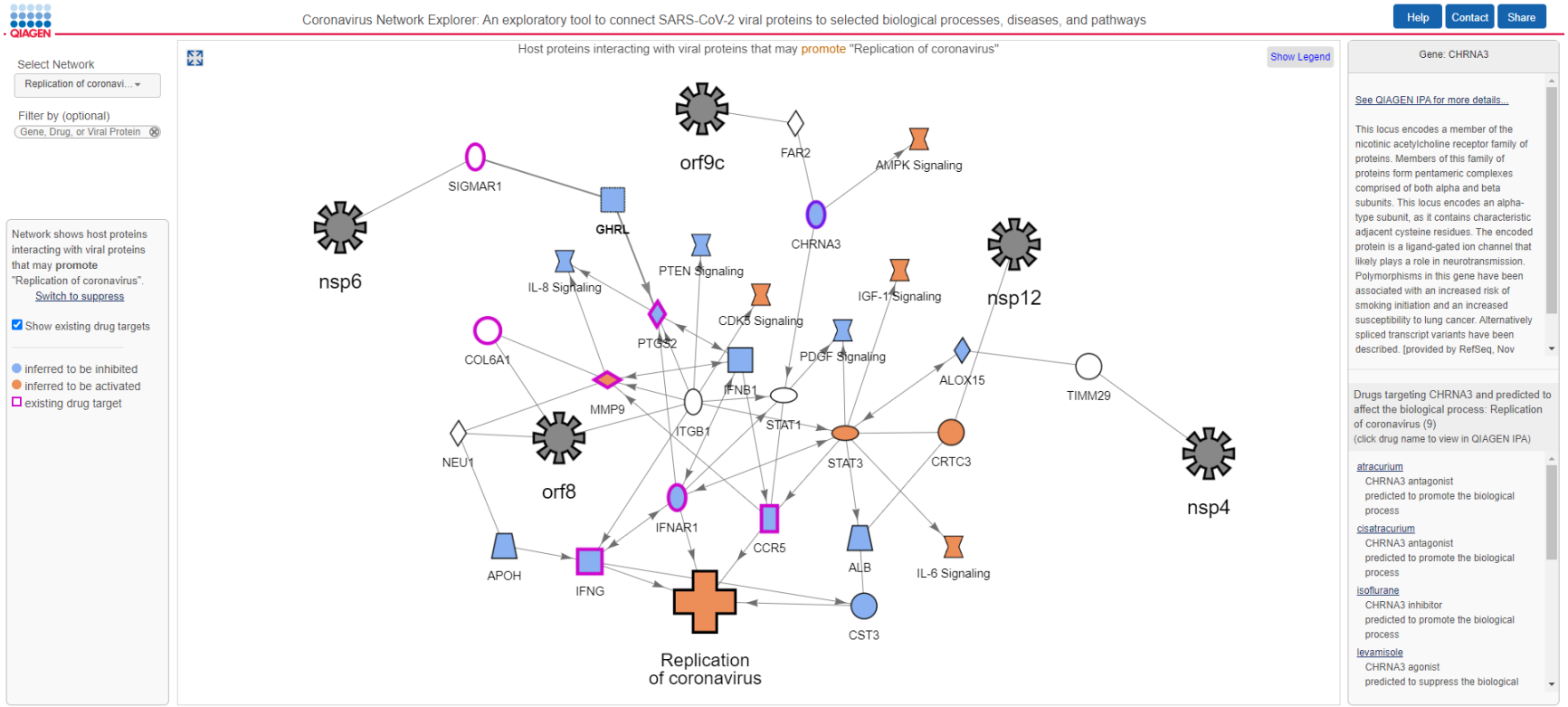
https://www.qiagenbioinformatics.com/products/features/

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

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The Coronavirus Network Explorer

- A web portal with 70 networks depicting how SARS-CoV-2 might affect its host cells and tissues.
- Coronavirus Network Explorer is free and available to everyone.
- This approach is applicable to other areas of research too, including drug repurposing.



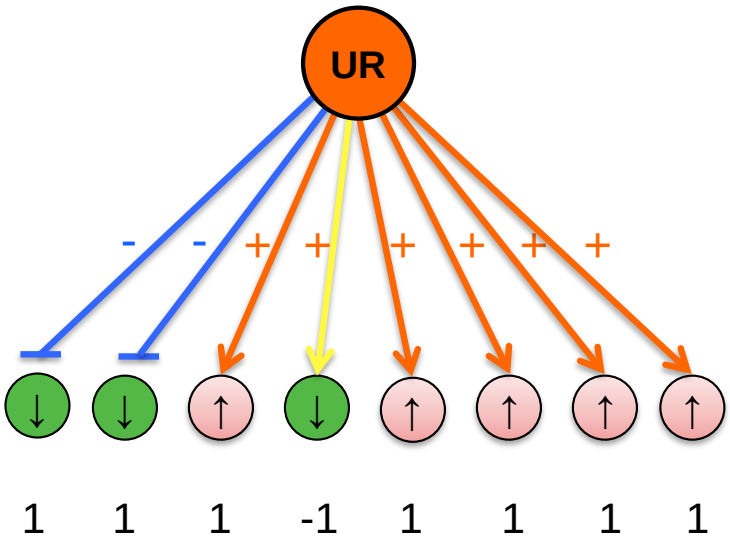
https://digitalinsights.qiagen.com/coronavirus-network-explorer/

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Q&A

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Predicting upstream regulators of a dataset



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

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

← Differential Gene Expression (Uploaded Data)

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

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

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

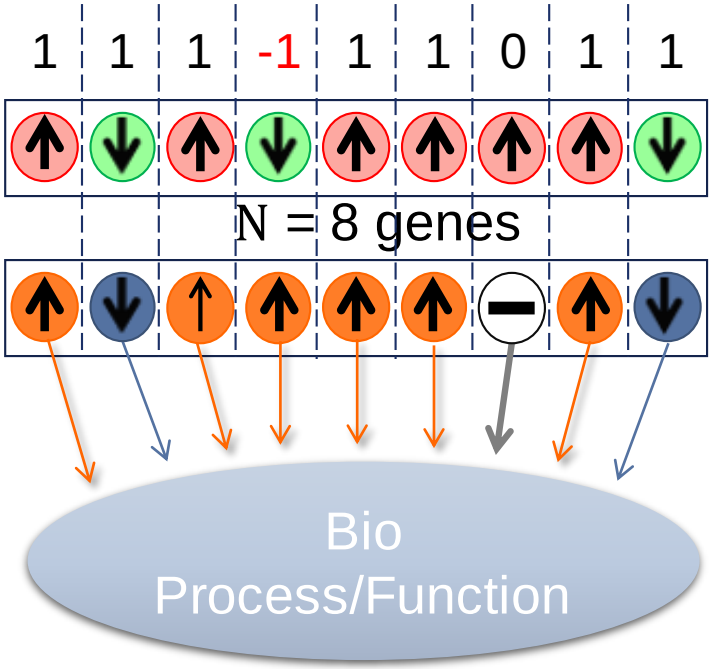
- z-score is a statistical measure of the match between expected relationship direction and observed gene expression
- z-score > 2 or < -2 is considered significant

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

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Downstream Effect Activation z–score

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



Differential gene expression
(Uploaded Data)

Effect genes have on a process or function
(Literature)

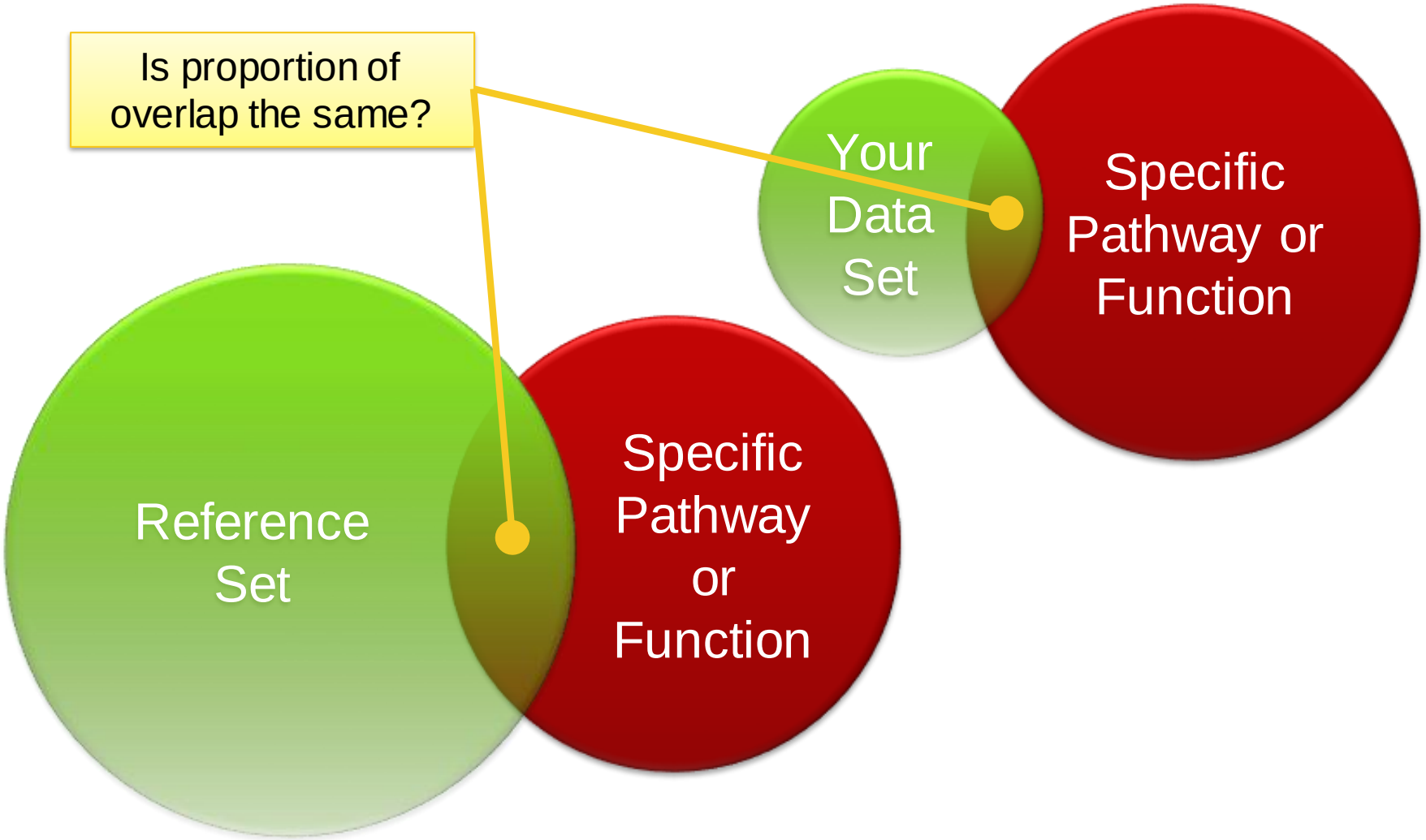
$$z = \frac{x}{\sigma_x} = \frac{\sum_i x_i}{\sqrt{N}} = \frac{N_+ - N_-}{\sqrt{N}}$$

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

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

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Determining Significance of Your Data to IPA



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Important note: Statistics in Biology

The Fisher's Exact Test

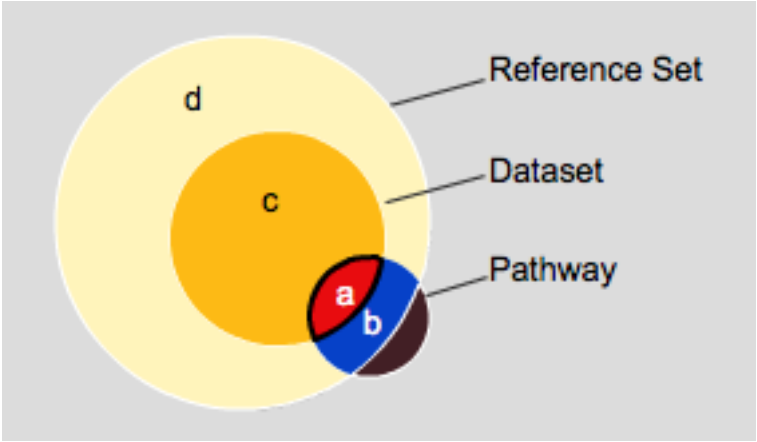
Given a list of differentially expressed genes in a dataset, what is the probability that the overlap with the set of genes on a particular pathway is by random chance?

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

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

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

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



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

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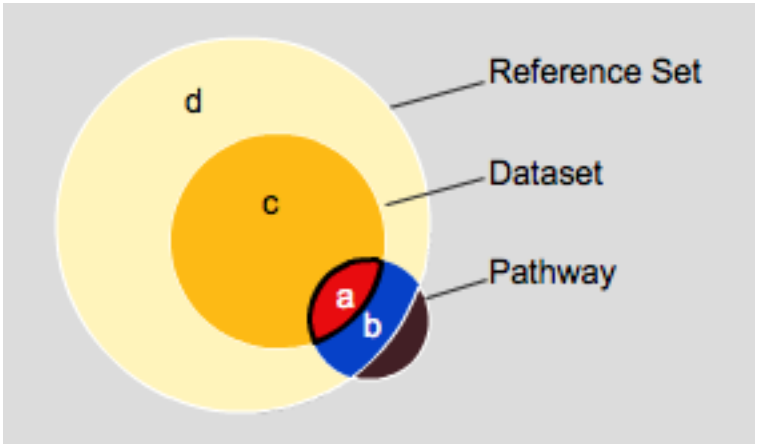
Statistics in Biology: Fisher's Exact, continued

If you had this situation:

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

What is the significance of that overlap?

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



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

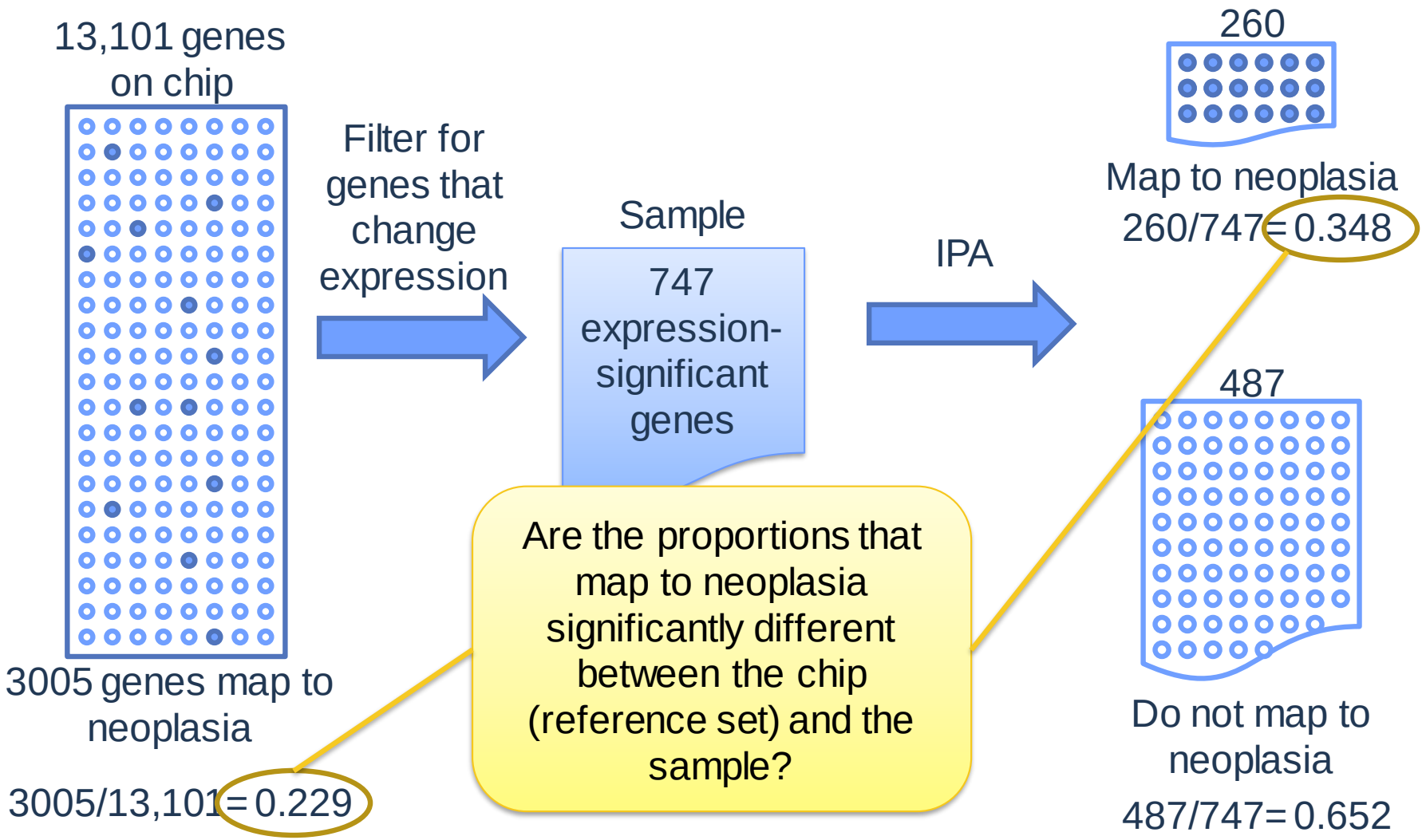
$$p = \frac{(5+76)!\,(281+11715)!\,(5+281)!}{(76+11715)!\,(5+76+281+11715)!\,5!\,76!\,281!\,11715!}$$

$$= 0.043$$

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

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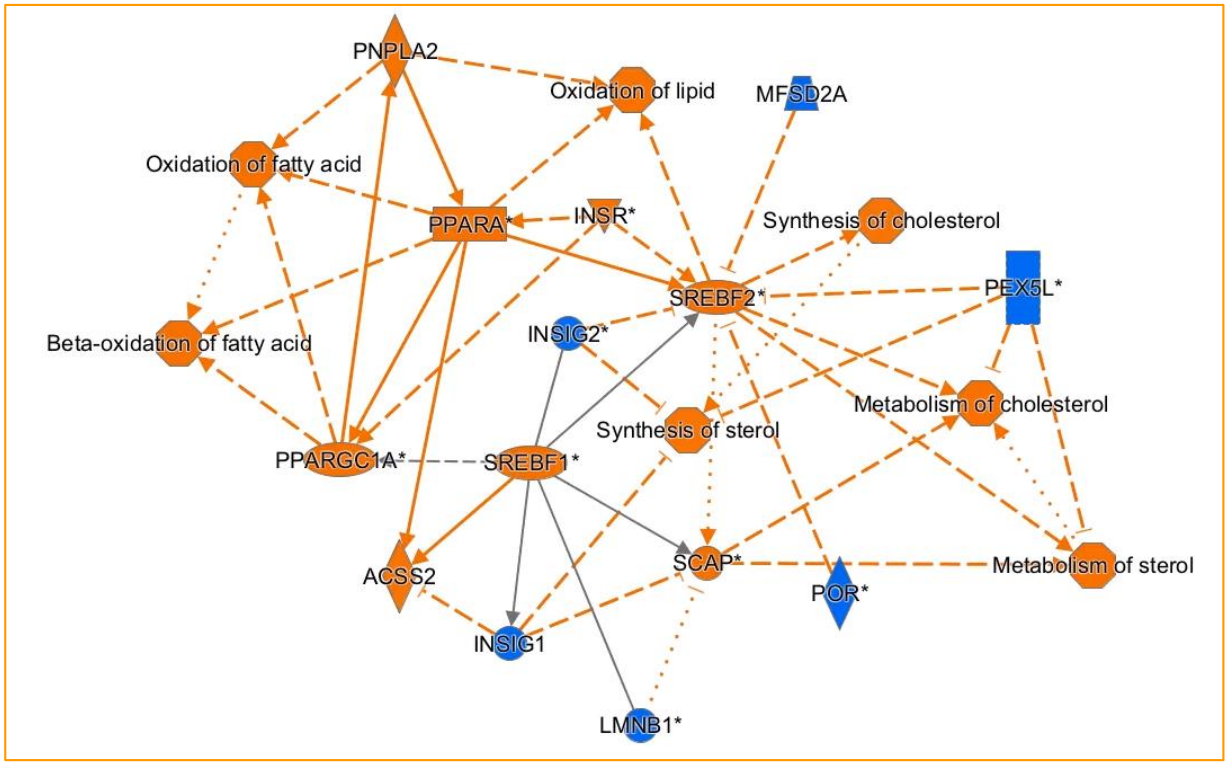
Mapping Colorectal Cancer Expression Data to the Function "Neoplasia"



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Graphical Summary

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



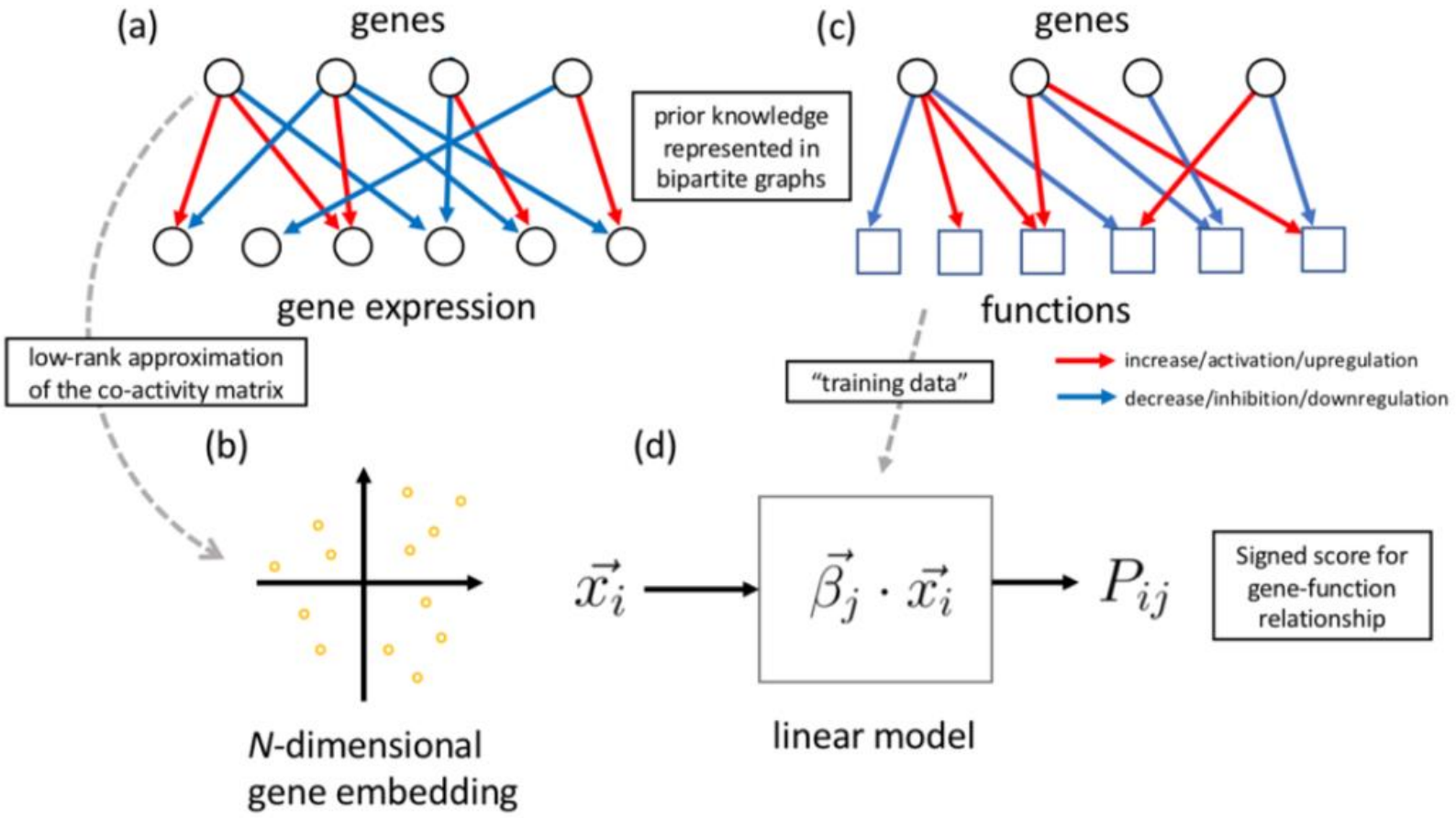
Criteria for selection

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

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

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Graphical Content-based machine learning



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

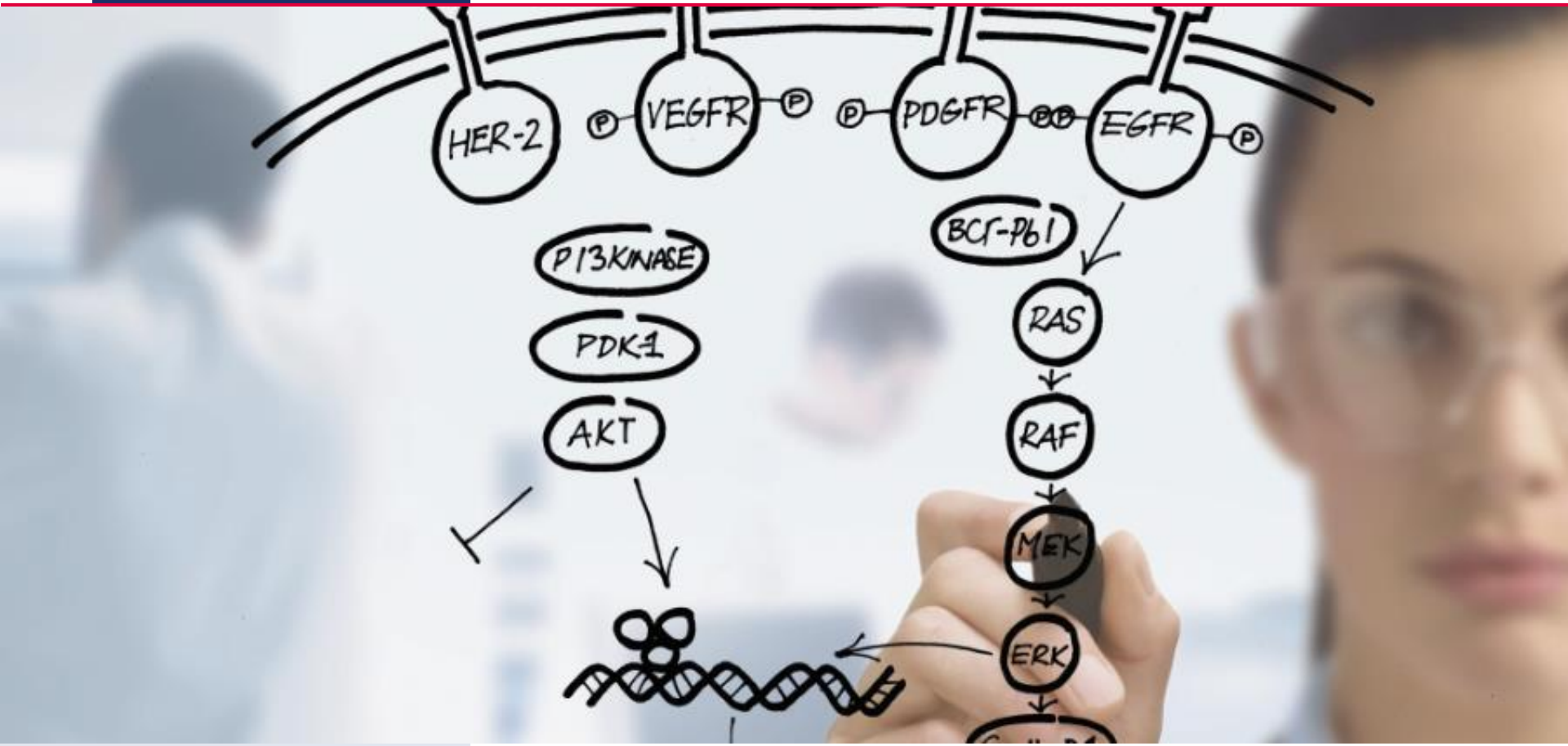
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Calculating the Fisher's Exact Test

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

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

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



歡迎與我們聯絡

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