



2018 IPA 系統生物學分析軟體暨資料庫

進階操作課程



National Yang Ming University

Sample to Insight





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Review for Introductory Training course

- □ IPA介紹
- 利用IPA進行搜尋
- □ 使用IPA進行分子模型建構並繪製訊息傳遞路徑



Searching

Searching Basics

Review

- Gene/chemical search and results
- Function/Disease search and results
- Drug target search and results
- Advanced search: Limiting results to a molecule type, family or subcellular location

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	Genes and Chemicals Functions and Diseases Pathways and Tox Lists	
№₩♥	Enter gene names/symbols/IDs or chemical/drug names here	
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Build Tools 的功能

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	Grow	0
	Path Explorer	
	Connect	G
	Trim	п
	Keep	
	Add Molecule/Relationship	

Build Tools包含下列數個建構pathway圖型的工具:

- Grow: 依照使用者的篩選以及參數設定,找出與Pathway圖型目標分子下有關係的其他分子
- Path Explorer: 此工具可以找出兩群分子的最短關係途徑
- □ Connect: 依照使用者的條件設定, 迅速將Pathway圖型內的各分子關係找出並連結
- □ Trim: 依照使用者的條件設定,移除Pathway圖型的分子
- □ Keep: 依照使用者的條件設定,保留符合條件的Pathway圖型內的分子
- Add Molecule/Relationship: 讓使用者加入自行訂定名稱以及相關註解的資訊到Pathway 圖型裡面,但此資訊只限定在使用者自己的帳號內可使用

Sample to Insight



Build and Grow Networks of Molecules



QIAGEN

Review



Why are we using IPA?







Unique Tools for Biological Analysis and Interpretation









Uncover causality — the next level of pathway analysis

This set of capabilities includes Causal Network Analysis, BioProfiler, IsoProfiler, Relationship Export, and Phosphoproteomics Analysis, all designed to help you understand causal connections between diseases, genes, and networks of upstream regulators.

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RioProfiler	test1- normal control [lung] H_ influenzae (heat	ki MouseDise	normal cont	. lung	Treatment	PreTreatm	64.89	74.83	76.01	62.22	69.49	1.49E-05	1.56E-67	1.23E-85	1.35E-34	69.35
DIOFICILIEI	test2- experimental autoimmune encephalomye	lit MouseDise	experiment	lumbar spi	Disease vs	DiseaseStat	64.89	76.16	62.36	74.05	69.37	3.9E-05	1.43E-71	2.76E-48	2.34E-53	75.98
	test1- experimental autoimmune encephalomye	lit MouseDise	experiment	lumbar spi	Disease vs	DiseaseStat	56.20	76.16	68.31	74.05	68.68	7.79E-04	1.43E-71	1E-62	6.79E-56	76.55
	test1- normal control [pulmonary airway] TNF al	p HumanDise	. normal cont	pulmonary	Treatment	Treatment	51.30	73.48	80.28	67.20	68.07	8.59E-04	1.32E-63	9.65E-101	9.1E-43	72.55
	test4- bacterial pneumonia [lung] NA	MouseDise	bacterial p	lung	Disease vs	DiseaseStat	45.88	74.16	71.49	75.13	66.67	1.2E-02	1.48E-65	4.25E-72	2.19E-60	75.96
	test4- atopic dermatitis [skin] NA	HumanDise	. atopic der	skin	Disease vs	SamplePat	56.20	72.80	67.49	68.39	66.22	5.87E-05	1.11E-61	9.47E-62	1.05E-44	74.11
	test8- dysbiosis [ileum] NA	MouseDise	dysbiosis	ileum	Treatment	Tissue:Sam	60.70	71.41	61.46	70.71	66.07	2.67E-06	6.5E-58	3.04E-47	1.83E-49	75.41
Relationshin	test1- viral infectious disease [hippocampus] NA	MouseDise	viral infecti	hippocampus	Disease vs	DiseaseStat	56.20	76.81	56.76	74.05	65.96	2.81E-05	1.24E-73	4.23E-37	1.99E-54	70.46
Relationship	test2- crohn's disease (CD) [colon] NA	MouseDise	crohn's dis	colon	Treatment	Genotype:S	51.30	72.80	70.71	68.39	65.80	4.95E-04	1.11E-61	1.43E-69	3.23E-47	74.90
E and a set	test3- pulmonary fibrosis [lung] NA	MouseDise	pulmonary	lung	Treatment	SubjectTre	45.88	72.80	74.54	69.56	65.70	5.69E-03	1.11E-61	7.8E-81	3.06E-49	75.38
EXDOIT	test3- normal control [lung] lipopolysaccharide ((LF Mouse Dise	normal cont	. lung	Treatment	PreTreatm	51.30	75.50	74.54	60.91	65.56	2.14E-03	1.54E-69	7.8E-81	3.44E-33	67.57
	test1- neuronopathic Gaucher disease (nGD) [th	al MouseDise	neuronopat	. thalamus	Disease vs	DiseaseStat	60.70	77.46	54.77	68.39	65.33	4.25E-05	1.01E-75	8.38E-34	1.23E-39	63.18
	test8- normal control [skin] NA	HumanDise	. normal cont	. skin	Treatment	TreatmentS	56.20	70.71	71.49	62.22	65.15	1.11E-04	4.55E-56	1.46E-71	5.16E-35	69.12
	test2- normal control [peripheral blood] lipopol	ys HumanDise	. normal cont	. peripheral	Treatment	Molecule:T	51.30	71.41	73.03	64.76	65.13	2.14E-03	6.5E-58	3.82E-76	1.68E-38	70.22
	test2- bacterial pneumonia;influenza A [lung] N/	A MouseDise	bacterial p	lung	Treatment	SubjectInfe	45.88	74.83	67.49	71.84	65.01	8.45E-03	1.56E-67	1.39E-60	1.21E-50	76.00
	test11- viral infectious disease [lung] NA	MouseDise	viral infecti	lung	Treatment	SubjectInfe	51.30	74.83	58.69	75.13	64.99	1.39E-03	1.56E-67	8.93E-42	3.32E-56	71.95
loo Drofilor	test1- kidney disease [kidney] NA	HumanDise	. kidney dise	. kidney	Disease vs	DiseaseOn	51.30	71.41	64.12	72.96	64.95	4.95E-04	6.5E-58	1.77E-52	3.96E-56	76.65
ISOPIOIIIEI	test3- bacterial pneumonia [lung] NA	MouseDise	bacterial p	lung	Disease vs	DiseaseStat	45.88	72.80	69.12	71.84	64.91	8.45E-03	1.11E-61	6.78E-65	2.21E-52	76.04
	test4- cerebral malaria [brain] NA	MouseDise	cerebral m	brain	Treatment	SamplingTi	51.30	76.16	62.36	69.56	64.84	1.39E-03	1.43E-71	1.8E-48	1.57E-44	72.20
	test2 - NA [adipose tissue] TNF alpha	MouseDise	NA	adipose tis	Treatment	TreatTime:	51.30	74.16	73.79	59.57	64.70	1.23E-04	1.48E-65	1.78E-78	3.42E-31	67.19
	test14- rheumatoid arthritis (RA) [synovial mem	brHumanDise	. rheumatoid	synovial me	. Treatment	DiseaseStat	56.20	72.11	72.26	58.20	64.69	1.96E-04	8.75E-60	7.7E-74	5.35E-30	66.49
	test4- normal control [bronchoalveolar lavage] K	MouseDise	normal cont	. bronchoalv	Treatment	Treatment	45.88	72.11	69.92	70.71	64.66	1.63E-02	8.75E-60	2.43E-67	6.54E-47	73.99
	test14- normal control [pancreatic islets] IL-1 b	et HumanDise	. normal cont	. pancreatic i	. Treatment	Treatment:	56.20	70.71	70.71	60.91	64.63	1.11E-04	4.55E-56	2.59E-69	7.95E-34	68.53
a sub-sub-ta-sub-ta-	test21- normal control [lung] lipopolysaccharide	MouseDise	normal cont	. lung	Treatment	PreTreatm	45.88	72.11	76.74	63.50	64.56	2.16E-02	8.75E-60	4.42E-88	5.1E-38	69.48
nosphoproteomics	test2 - NA [synovial tissue] TNF	HumanDise	. NA	synovial tis	Treatment	Treatment	51.30	74.16	71.49	60.91	64.47	1.39E-03	1.48E-65	1.46E-71	3.25E-32	67.17
	test1- melanoma [skin] NA	MouseDise	melanoma	skin	Other Com	Genotype[h	45.88	67.82	71.49	71.84	64.26	5.69E-03	6.04E-49	7.9E-72	6.42E-51	75.23
Analysis	test14- NA (peripheral blood) anti-CD28 antibo	d HumanDise	. NA	peripheral	Treatment	Treatment	56.20	70.00	73.03	56.80	64.01	5.87E-05	3E-54	3.82E-76	2.38E-26	64.93
	test11- normal control [pancreatic islets] IL-1 b	et HumanDise	. normal cont	. pancreatic i	. Treatment	Treatment:	56.20	71.41	67.49	60.91	64.00	2.81E-05	6.5E-58	1.39E-60	1.31E-33	68.72
	test8- lung cancer [lung] NA	MouseDise	lung cancer	lung	Treatment	SubjectTre	-45.88	-72.80	-76.01	-63.50	-64.55	1.63E-02	1.11E-61	1.23E-85	2.62E-37	69.18
	test2- normal control [endothelium] Transfection	n_HumanDise	. normal cont	. endothelium	Treatment	Transfectio	-56.20	-70.71	-74.54	-62.22	-65.91	2.81E-05	4.55E-56	7.8E-81	6.68E-36	69.86
	Itest7- lung cancer [lung] NA	MouseDise	lung cancer	llung	Treatment	SubjectTre	-51.30	1-74.83	-74.54	-64.76	-66.36	2.14E-03	1.56E-67	[7.8E-81	4.56E-38	170.01





Basic Module

- Canonical Pathway
- Isoform View
- Disease View
- Gene and Chem View
- Path Designer
- Interactive Disease and Functions Nodes
- Biomarker filter
- Molecule Activity Predictor (MAP)
- Mechanistic Network
- Upstream regulator Analysis
- Downstream Effects Analysis
- Regulator Effects
- Network Analysis
- Comparison Analysis
- MicroRNA Target Filter
- Tox Lists and Tox Functions

Advanced Analytics (AA)

- Causal Network Analysis
- BioProfiler
- Relationship Export
- IsoProfiler
- PhosphoProteomics Analysis
- Analysis Match (Pay extra)

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

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



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A. Data Upload and How to Run a Core Analysis

- 1. Upload experiment data
- 2. Data process with IPA Core Analysis
 - 上傳實驗資料並使用IPA分析功能
- **B.** Functional Interpretation in IPA
 - □ Hands-on Exercises
 - 1. Introduction for Analysis Tools
 - Interpret the data output information IPA分析結果介紹

C. Multi-Omics Analysis using IPA

Integrate and compare genomics, transcriptomics, proteomics and metabolomics data to see the big picture on your focus research 比較分析結果的差異

D. Case study

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E. Q&A





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







General Analysis Workflow in IPA





IPA

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	+FEND3	F-bax protein 3	-1.073652566	Uningen	enzyme		human, mouse		prostate g	land
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Identify functions, diseases, and canonical pathways associated with your data





Genomic, exon, miRNA, SNP, protein arrays; Any molecule lists; Other proteomic & metabolomic assays



Observation:

An experimental condition such as a time point, disease subtype, or compound concentration

Expression Value:

Numerical value indicating level of expression, significance, or other assay result for a specific identifier (gene, RNA, protein, or chemical)

Reference Set:

The set of molecules used as the universe of molecules when calculating the statistical relevance of biological functions and pathways with respect to a dataset file. The set of molecules are the user's dataset or molecules in Ingenuity's Knowledge Base (genes, endogenous chemicals, or both).

Focus Molecule:

Molecules that are from uploaded list, pass filters are applied, and are available for generating networks





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2	1-10-10-2	366154	Hs 222000	AA400422	DKE7D/12/	DKE7D424	0.942	1.083	1.512	0.9/1	1.285	-1 06299	1 //59	0.008	1.021	0.742	1 097	1 0.491	0.331
4	1-10-10-5	51746	Hs 793/8	H23046	RGS7	regulator	1 054	0.913	0.508	0.541	0.508	-1 10102	1.430	1 112	1.052	0.903	1 021	1.07	0.507
6	1-10-10-5	781704	Hs 77558	ΔΔ431611	TRIP7	thyroid be	0.996	1.38	1.605	1.172	1 115	1.28825	0.692	0.944	1.002	0.803	0.91	0.769	0.542
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	1.022	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 ml	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	Hc 1982/11	A A 036974	AOC3	amine ovi	1 1/15	1 175	1 307	1 286	1 172	1 22825	0 731	0 929	1 2/18	0 873	1.041	0.673	0 999

QIAGEN





■ 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。





這表格為標準IPA分析用資料表格範例,裡面的數值類型是 Log Ratio 這組實驗資料裡面有三個Observation:

- Observation 1 : Smokers vs. NonSmokers
- Observation 2 : Early COPD vs. NonSmokers
- Observation 3 : COPD vs. NonSmokers

	А	В	С	D
1	ID_REF	Smokers vs. NonSmokers	Early COPD vs. NonSmokers	COPD vs. NonSmokers
2	1007_s_at	-0.006955963	-0.028339307	0.06209247
3	1053_at	-0.047503628	-0.001610169	0.060261582
4	117_at	-0.110988314	0.193030977	-0.079160692
5	121_at	0.050275771	-0.010810624	0.078980219
6	1255_g_at	0.01098737	-0.151880946	0.271391848
7	1294_at	-0.05090447	0.020144002	0.045157579
8	1316_at	0.041293255	0.040339731	0.101614517
9	1320_at	-0.086868115	-0.050757375	-0.746738716
10	1405_i_at	0.374965097	-0.01805262	0.474615195
11	1431_at	-0.084408555	0.014600862	0.010719682
12	1438_at	-0.043223369	0.04906669	0.072519797
13	1487_at	0.016570535	0.017204065	0.140111634
14	1494_f_at	0.074827039	-0.171039972	-0.053830243
15	1552256 a at	0.146508027	0.156529919	0.264935712

*不同observation的 重複實驗數值已經在 先前經過平均才放入 此表格





Live Demo

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p-value of

overlap

z-score



- Null hypothesis: No overlap between molecules from dataset and disease/function/upstream regulator/pathway.
- Calculate using the right-tailed Fisher's Exact Test.
- Significant p-value ≤ 0.05

Note: Benjamini-Hochberg correction for multiple testing can be implemented in some cases





Predicts Activation or Inhibition

• Correlation between what is known (IPA Knowledge Base) and

your expression data

Sample to Insight



Functions analysis: 呈現因為分子變化而受影響的生物功能、疾病與毒性學結果 Canonical Pathways:列出受實驗影響的Signaling Pathway與Metabolic Pathway Upstream Analysis:列出與資料中變動分子有關的Upstream molecules,以及根據研究 文獻預測它們是否是被啟動或是被抑制。

Networks:呈現實驗資料中的分子間的網路關係。並且可以利用Build Tool與Overlay Tool進行延伸與知識的拓展,以上各分析結果都是用來解釋實驗觀察到的現象的重要依據。

Early COPD vs. Non	
$\fbox{\label{eq:summary}{\scales}} Summary \bar{\scales} Functions \bar{\scales} Canonical Pathways \bar{\scales} Upstream Analysis \bar{\scales} Networks \bar{\scales} Molecutered \bar{\scales} Molecutered \bar{\scales} Molecutered \bar{\scales} Networks \bar{\scales} Molecutered \bar{\scales} Networks \bar{\scales} Netw$	les \ Lists \ My Pathways \
	EXPORT ALL Download Summary (PDF)
Analysis settings	
Top Networks	
ID Associated Network Functions	Score
1 View Endocrine System Development and Function, Energy Production, Small	Nolecule Biochemistry 34
2 View Cellular Compromise, Cardiovascular System Development and Function,	Cell Morphology 22
3 View Cell Death and Survival, Hereditary Disorder, Cardiovascular Disease	21
4 View Connective Tissue Disorders, Hereditary Disorder, Inflammatory Disease	19
5 View Lipid Metabolism, Small Molecule Biochemistry, Amino Acid Metabolism	15
Top Bio Functions	

IPA 分析結果



Sample to Insight



Functions analysis: 呈現因為分子變化而受影響的生物功能、疾病與毒性學結果

Canonical Pathways:列出受實驗影響的Signaling Pathway與Metabolic Pathway Upstream Analysis:列出與資料中變動分子有關的Upstream molecules,以及根據研究 文獻預測它們是否是被啟動或是被抑制。

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Early COPD vs	. Non	r ^e 2 [¶] ⊠
Summary F	unctions \ Canonical Pathways \ Upstream Analysis \ Networks \ Molecules \ Lists \ My Pathways \	
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Analysis	settings	A
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ID As	ssociated Network Functions	Score
1 View Er	ndocrine System Development and Function, Energy Production, Small Molecule Biochemistry	34
2 View C	ellular Compromise, Cardiovascular System Development and Function, Cell Morphology	22
3 View C	ell Death and Survival, Hereditary Disorder, Cardiovascular Disease	21
4 View C	onnective Tissue Disorders, Hereditary Disorder, Inflammatory Disease	19
5 View Li	pid Metabolism, Small Molecule Biochemistry, Amino Acid Metabolism	15
Top Bio F	unctions	

IPA 分析結果







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





方塊代表受實驗影響的生物功能與疾病,顏色可以用[Color by]指定是z-score, -log (p-value), 或是 # of genes上色。如果是用z-score上色的話,藍色區塊是預測被減低的功能,橘色則是此功能會增加。是根據實驗資料做出的演算。

每個矩形可以經由點擊進入下一層分區: Midlevel functional category (level 2) 與 Specific functions (level 3)



Sample to Insight

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Functions analysis: 呈現因為分子變化而受影響的生物功能、疾病與毒性學結果

Canonical Pathways:列出受實驗影響的Signaling Pathway與Metabolic Pathway

Upstream Analysis: 列出與資料中變動分子有關的Upstream molecules,以及根據研究 文獻預測它們是否是被啟動或是被抑制。

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Early	у СОРЕ	vs. Non	с ^к Ф. 🗙
Sur	mmary	Functions \ Canonical Pathways \ Upstream Analysis \ Networks \ Molecules \ Lists \ My Pathways \	
			EXPORT ALL 🔎 Download Summary (PDF)
	Analy	sis settings	
*	Top N	etworks	
ID		Associated Network Functions	Score
1	View	Endocrine System Development and Function, Energy Production, Small Molecule Biochemistry	34
2	View	Cellular Compromise, Cardiovascular System Development and Function, Cell Morphology	22
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4	View	Connective Tissue Disorders, Hereditary Disorder, Inflammatory Disease	19
5	View	Lipid Metabolism, Small Molecule Biochemistry, Amino Acid Metabolism	15
*	Тор В	o Functions	

IPA 分析結果





Canonical Pathways結果標籤: 受影響的Signaling Pathway與Metabolic Pathway依照顯著性用條狀圖排列





Functions analysis: 呈現因為分子變化而受影響的生物功能、疾病與毒性學結果 Canonical Pathways: 列出受實驗影響的Signaling Pathway與Metabolic Pathway Upstream Analysis: 列出與資料中變動分子有關的Upstream molecules,以及根據研究 文獻預測它們是否是被啟動或是被抑制。

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Early	/ СОРБ	9 vs. Non	r⊠. ⊼
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			EXPORT ALL Sownload Summary (PDF
	Analy	sis settings	· · · · · · · · · · · · · · · · · · ·
8	Top N	etworks	
ID		Associated Network Functions	Score
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5	View	Lipid Metabolism, Small Molecule Biochemistry, Amino Acid Metabolism	15
8	Тор В	io Functions	

IPA 分析結果





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



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







Statistical measure of correlation between the transcription regulator (TR) and resulting gene expression





TR effect on downstream genes (Literature)

Differential gene expression (Uploaded Data)

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

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







Hypotheses for how activated or inhibited upstream regulators cause downstream effects on biology



Downstream Effects Analysis

Causally consistent networks score higher

The algorithm runs iteratively to merge additional regulators with diseases and functions

Sample to Insight



Functions analysis: 呈現因為分子變化而受影響的生物功能、疾病與毒性學結果 Canonical Pathways:列出受實驗影響的Signaling Pathway與Metabolic Pathway Upstream Analysis:列出與資料中變動分子有關的Upstream molecules,以及根據研究 文獻預測它們是否是被啟動或是被抑制。

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Early COPD vs. Non		ь б <u>л</u> х
Summary \ Functions \ Canonical Pathways \ Upstream Analysis	Networks Molecules Lists My Pathways	
		EXPORT ALL Download Summary (PDF)
Analysis settings		
Top Networks		
ID Associated Network Functions		Score
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4 View Connective Tissue Disorders, Hereditary Disorder, Int	flammatory Disease	19
5 View Lipid Metabolism, Small Molecule Biochemistry, Am	ino Acid Metabolism	15
Top Bio Functions		

IPA 分析結果





- 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 -	25 •
35	10
70	25
140	50





Live Demo



The enhanced Causal Network Analysis (CNA) provides a comprehensive approach to identifying upstream molecules that control the expression of the genes in your datasets. You can now, in a single click, visualize the diseases and functions you are scoring against, understand the effect of the master regulator on that disease or function, and drill-down to the evidence supporting those relationships. In addition, increase the predictive power by allowing intervening molecules or functions, up to three steps or 'hops', to connect a hypothesis to the scoring criteria.



Causal analysis approaches in Ingenuity Pathway Analysis. 2014 Bioinformatics

Causal Network


How to Create Causal networks?

Causal Network

The option to build causal networks is available in IPA on the Create Analysis page. Select the check box for Causal network under General Settings > Networks to include Casual Analysis in your analysis results.

General Settings	Generate the	e following Networks (inc	reases analysis ti	me)		
Networks Interaction & Causa	Interaction	on networks				
Node Types	? Inclue	de endogenous chemicals	Molecules p	per network N	letworks per analysis	
Data Sources All	Genes ar	e always included	35 🔻	2	5 🔻	
Confidence Experimentally Ob	Causal net	tworks aster regulators for relation	ships to diseases	, functions, genes,	or chemicals (max 50)	
Species All	? ✓ Score	using causal paths only				
Tissues & Cell Lines All	? different	tiation of cardiomyocytes				ADD
Mutation All	?			Add functions and	d genes/chemicals	
ADVANCED SAVE AS DEFAULTS				Genes and Chemic Differentiation of ca	ardiomyocytes andiomyocytes anterentiation of cardion ar System Development a	DIS SEARCH
Click on Add to be or genes and che your causal netwo	egin searchin micals that yo orks.	g for specific functic ou may wish to scor	n, disease e against	differentiat	tion tiation of cardiomyocytes differentiation of cardiom lopment tion	iyocytes





Mechanism of scoring path types



The effect of the upstream node on the downstream node:

- **Increases:** The upstream node *increases* the activity of the downstream node
- **Deceases:** The upstream *decreases* the activity of the downstream node
- *Affects: The upstream node neither increases nor decreases the activity of the downstream node

The position of the master regulator node relative to the entity being scored:

- **Upstream:** The master regulator is upstream (acts on) of the entity being scored
- **Downstream:** The master regulator is downstream (is acted upon) by the entity being scored
- ***Both:** The master regulator is neither upstream nor downstream of the entity being scored



Result

Master Regulator and Networks

Specific function, disease or genes and chemicals that you wish to score against your causal networks.

+ Add/Remove column(s)							CNR1 🛨 Diabet		Diabetes mellit	Diabetes mellitus [diabetes] 🗄 🛛 Inst		insulin 🕂		letween M 🛨		
Master 🔳	Expr 🝸 🗶	Mol 🍸 🗶	Participating regulators	T X	Depth 🝸 🗵	😾 Pre 🕱	Acti 🝸	🗶 p-va 🍸 🗶	Length I 🗵	Path 🝸 🗶	Length I 🗵	Path 🝸 🗶	Length I 🗵	Path 👅 🗵	Incr 🝸 🔀	Decr 🝸 🗵
ICMT		enzyme	ICMT	all 1	1	Activated	2.000	1.31E-08	3 18	DU(3),	211	DU(1)	3 1 2 3	DD(2),		
G6PC		phosphatase	↑D-glucose, G6PC	all 2	2	Activated	2.000	9.99E-03	2112	DD(6),	3 1 5 1	DU(23),	111	DD(1)	GCall 9	7alpall 8
afatinib		chemical drug	əfatinib	all 1	1		-1.667	8.47E-16	211	DU(1)	213	DU(2),	213	IU(3)		
UCP2		transporter	UCP2	all 1	1		-1.633	6.82E-13	217	DD(4),	111	IU(1)	111	DD(1)	sirolall 1	PLIall 5
propylthiourad		chemical drug	propylthiouracil	all 1	1		-1.134	8.83E-13	211	IU(1)	213	DU(3)	211	IU(1)		
sirolimus		chemical drug	sirolimus	all 1	1		-1.265	3.23E-09	212	DU(2)	111	IU(1)	111	IU(1)		
methimazole		chemical drug	methimazole	all 1	1		-1.342	2.62E-08	212	DU(1),	211	DU(1)	212	DU(1),		
probenecid		chemical drug	CASP1, DIO2, PANX1,	all 7	3		0.816	1.23E-06	315	DU(5)	3177	DU(36),	317	DU(2),		
HTT		transcription	HTT	all 1	1		-0.447	2.05E-06	1 1	IU(1)	111	DU(1)	217	DD(2),		sirolall 2



Sample to Insight



BioProfiler allows you to make novel discoveries by providing you the ability to filter the fine-grained relationships between molecules (genes, RNAs, proteins, and chemicals) and diseases or functions.

BioProfiler									
ADD TO MY PA	THWAY ADD T	O MY LIST DISPI	AY AS NETWORK	CREATE DATA	SET 🖪 手	LIMIT TO DATAS	Genentech BMC	: <u>T</u>	
Molecule				+ Add/Rem	ove column(s)	Disease or Fu	nction Evidence		
🛆 Sym 🝸	Mole 🍸 🗵	ID ×	Expr 🝸 🗙	Expr 🝸 🗵	Expr 🍸 🗵	Mole 🝸 🗵	Effect on D 🍸 🗵	Disease or Function	Muta 🝸 🛙
ABCB9	transporter	214209_s_at	† 1.072	3.59E-04	1.30E-03	increased ac	affects,increases	Adenosquamous all 6	heterozygou
ABHD17A	enzyme	221267_s_at	↓ -0.602	3.44E-04	1.26E-03	unknown ch	affects	Acute myeloid leu all 4	heterozygou
ABI2	other	225112_at	† 0.091	3.92E-01	6.19E-01	decreased a	affects,decreases,i	Abnormal morp all 25	heterozygou
ACAT2	enzyme	209608_s_at	↓ -0.787	1.12E-02	2.92E-02	decreased a	affects,decreases,i	Absorption of ch all 23	homozygou.
►ACTN4	transcription	200601_at	† 1.464	8.88E-16	2.48E-14	decreased a	affects,decreases,i	Abnormal morp all 81	dominant,he
ADAM28	peptidase	205997_at	† 1.646	9.07E-01	1.00E00	decreased a	affects,decreases,i	Adhesion of end all 19	frameshift,h
ADAMDEC	peptidase	206134_at	† 1.399	1.00E00	1.00E00	increased ac	affects	Adenosquamous all 8	heterozygou
ADAP2	other	222876_s_at	† 1.021	9.60E-01	1.00E00	increased ac	affects	Advanced stage all 4	heterozygou
ADGRE5	G-protein co	202910_s_at	† 1.182	1.80E-06	1.05E-05	decreased a	affects,decreases,i	Accumulation of all 36	homozygou.
ADGRL1	G-protein co	203488_at	† 1.334	1.11E-13	2.18E-12	decreased a	affects,decreases,i	Abnormal functi all 10	homozygou.
ADNP2	other	203321_s_at	+-0.466	3.03E-03	8.99E-03	increased ac	affects,decreases,i	Cell death all 7	heterozygou
AGPAT4	enzyme	228667_at	+-1.675	2.74E-06	1.52E-05	decreased a	affects	Abnormal quantit all 8	heterozygou
AK3	kinase	224655_at	+-1.323	2.52E-05	1.14E-04	decreased a	affects,decreases	Cell viability of m all 6	frameshift,wi
AKAP11	other	203156_at	+-1.330	2.72E-09	2.65E-08	decreased a	affects,decreases,i	Abnormal morp all 24	heterozygou
AKAP8	other	203847_s_at	† 0.630	5.05E-09	4.71E-08	decreased a	affects,increases	Cleft palate synd all 11	heterozygou
AKAP8L	other	218064_s_at	† 1.058	6.40E-12	9.58E-11	decreased a	affects,decreases,i	Activation of DN all 17	heterozygou
ALG5	enzyme	218203_at	+-0.653	3.14E-08	2.47E-07	increased ac	affects	Adenosquamous all 8	heterozygou
ALS2	other	226291_at	1 0.375	1.01E-03	3.34E-03	decreased a	affects,decreases,i	Abnormal morp all 64	frameshift,h
ANAPC5	other	200098_s_at	1 0.471	1.72E-04	6.74E-04	decreased a	affects	Liver carcinoma all 6	missense,sile.
ANKRD33B	other	231963_at	† 2.676	2.66E-15	6.59E-14	unknown ch	affects	Cutaneous melan all 3	frameshift,h
ANP32E	other	221505_at	1 0.544	2.78E-04	1.04E-03	unknown ch	affects	Endometrioid en all 3	missense,no.
AP2B1	transporter	200612_s_at	↓ -1.040	1.15E-04	4.66E-04	decreased a	affects,decreases,i	Activation of RNA all 7	nonsense,un
AP3D1	transporter	206592_s_at	+-0.410	1.04E-04	4.25E-04	decreased a	affects,decreases,i	Acidification of all 23	frameshift,h

BioProfiler





- Targets of toxicity: Which genes when [decreased] in activity [increase][liver cholestasis]? What types of [genetic] evidence support this?
- Target discovery: What [heterozygous knockouts] in [mouse] can [decrease] [asthma]?
- Which drugs or which targets have been in late stage clinical trials or approved to decrease [diabetes]?
- Biomarker research: Which genes are potential [diagnosis OR prognosis] biomarkers of [breast cancer] and are [upregulated] in breast cancer?

BioProfiler					t د ا
ADD TO MY PATHWAY ADD	TO MY LIST DISPLAY AS N	etwork		opterin - val (<u>(p1 of 1)</u> ▼ (C) → More Info
Molecule	Add column(s)	E Desease or Function Evi	dence		Add column(s) 🖽
△ Symbol	Molecule Type	Add Column(s) to section	Effect on Dise 🝸 💌	Causal or Corr	Add Column(s) to section
(6R)-tetrahydrobiopt ABAT	chemical drug enzyme	Symbol	decreases affects	causal correlation	Molecule Activity
acamprosate	chemical drug	Molecule Type	decreases	causal	Effect on Disease or Function
ACHE	enzyme	Disease Count	affects	correlation	Disease or Function
ADRA1A	G-protein coupled r	Svnonvm(s)	affects	correlation	Mutation evidence
ADRA1B	G-protein coupled r		affects	correlation	Biomarker Application Eviden
ADRA1D	G-protein coupled r		affects	correlation	
ADRA2A	G-protein coupled r	. Tissue/Cell Line	affects	correlation	Species Evidence
ADRA2B	G-protein coupled r	Location	affects	correlation	Drug target evidence
ADRA2C	G-protein coupled r		affects	correlation	Expression evidence
ALDH5A1	enzyme	Apply Cancel	affects	correlation	Causal or Correlated
aripiprazole	chemical drug	increased activity	decreases	causal	
	-	1		causal	Tissue/Cell Line
				causal	Findings
				causal	Apply Conce
				correlation	Apply Cance
				causal	11



• Type: Transporter

BioProfiler

- Location: Cytoplasm
- Tissue: Adipose, Liver
- Disease: Abnormal Conduction by Nerves
- Effect: Decrease

Type: Transporter

- Location: Cytoplasm
- Tissue: Liver, Lung
- Disease: Abnormal Conduction by Nerves
- Effect: Increase

HBZ

- Type: Growth Factor
- Location: Extracellular Space
- Tissue: Adrenal
- Disease: Abnormal Conduction by Nerves
- Effect: Decrease

- Whitehkigten of Theoremsense temperature
 fexportises of Aimeo?mal
 conclustion, by Prerves?
 - ABCD2, ARTN







The new Relationship Export capability in IPA enables you to export the structural information contained within IPA networks or pathways for visualization in other tools such as Cytoscape. The export format contains relationships modeled as triples: Node A --> Relationship -->Node B





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Cytoscape



IsoProfiler displays and enables filtering on transcripts & isoforms in your RNA-seq dataset(s)

Your data must be mapped using **RefSeq**, **Ensembl**, or **UCSC** identifiers. You cannot use gene names or gene-level IDs to map your dataset for IsoProfiler, you must use **transcript** IDs. Furthermore, for IsoProfiler your dataset must consist of a single source for your dataset-- i.e. only Ensembl, or only RefSeq. **You cannot mix sources**.



IsoProfiler

OIAGEN



Once IsoProfiler launches, it will display results such as in this example

Dataset Chooser

QIAGEN

IsoProfiler

Genes and their isoforms from the dataset

✓ Datasets	ADD TO	MY PATHWA	Y ADD TO MY LIST ISOP	OFILER FINDINGS CREATE	DAT/	ASET C	USTOMIZE TABLE									lore Info
	Sym.	. Mole ×	Gene-level Disease or Functio	n	X	Gen 🗵	Expression Patterns	s X	Ma 🗵	Tra 🗵	Ra 🗵	Isoform-spec	X Isoform-spec	ific Disease	or Functi	on 🗵
Index aureau p-velue Felas Disc	ABCB1	transporter	Abnormal morphology of CD	3-positive alpha-beta intraall :	235	432	GTEx 4 2 1 -	× 2122-	↓-5.244	2	9.801	3	Acute myeloi	l leukemia,	Breast ca.	all 16
1 HCC EM pool Tumor vs_Normal 2016-09-30 √√√√	CEACAM	1 transporter	Abnormal morphology of cold	n, Accumulation of triacyall	1.38	208	GTEx 9 15 - 8 - 1	14487-	↓ -47.085	2	50.309		7 Apoptosis of	colorectal c	ancer cell	all 5
	FKBP8	other	Abnormal morphology of brai	n,Abnormal morphology oal	63	107	OO GTEx 3 1 116-	11-111	↓ -17.076	2	20.332		1 Apoptosis of (pithelial ce	ll lines,Aj)all 2
Add more Remove selected	RTN4	other	Acute brain infarction, Acute co	oronary syndrome, Adenoall	117	222		•••	↓ -3.560	2	6.192	1	8 Acute corona	y syndrom	e,Angina.	all 14
riters T					, i											
✓ Expr Fold Change ×																
-1.000	Selected ro	ws1/4														
	A I	soform Tracks											+ Add/Remove	column(s)	G C	ARTS
✓ Expression Patterns ×		ranscript	Protein 🗙	Schematic 🗵	🗴	X	APPRIS ×	Biotype	K X	Isoform-sp	ecific Disea	se or Function		× I ×	All t	Tiss
Transcripts are both up and down regulated in the dataset	1 F.	(BP8-209	FKBP8 isoform 1	······	413	1781	PRINCIPAL:3	protein-coding	TSL:5	Apoptosis o	f epithelial	cell lines,Apopto	sas of eye call	2 1	6.054	3 tissues
○ Gene has > ▼ 1 transcript(s) in the dataset	2 F	(BP8-213	FKBP8 isoform 1		413	1849	PRINCIPAL:3	protein-coding	TSL:1	Apoptosis o	f epithelial	cell lines,Apopto	sis of eye call	2 1	64.073	1 tissue
Switch in the highest intensity isoform for the gene	3 F.	(BP8-201	FKBP8 isoform 2	······	412	1710	ALTERNATIVE:1	protein-coding	TSL:1						57.872	1 tissue
Describe the intensity column(s) in the dataset	4 F.	KBP8-206	FKBP8 isoform 2	••••••••••••••••••••••••••••••••••••••	412	1756	ALTERNATIVE:1	protein-coding	TSL:2						8.451	1 tissue
One intensity column that is the max intensity of expr't vs control [fold change only]	5 F.	(BP8-208	FKBP8-208		256	966		protein-coding	TSL:3						0.091	6 tissues
 One intensity column that is the avg intensity of expr't vs control [fold 	6 F	GBP8-202	FKBP8-202	·····	248	1292		protein-coding	TSL:1						0.094	
change only]	7 F	KBP8-210	FKBP8-210		203	1140		protein-coding	TSL:2						3.697	1 tissue
 Two intensity columns (expr't and control) 	8 F.	KBP8-204	FKBP8-204		181	612		protein-coding	TSL:3						0.350	1 tissue
\sim Isoform-specific Disease or Function count $~~\times~$	9 F.	KBP8-203	FKBP8-203	-	166	593		protein-coding	TSL:4						0.000	
Has at least 1 isoform(s) involved in at least 1	10 F	KBP8-207	FKBP8-207	·····	162	574		protein-coding	TSL:3						0.077	1 tissue
disease (s) or function(s)	11 F	KBP8-211	FKBP8-211		116	1548		protein-coding	TSL:5						0.171	1 tissue
	12 F	(BP8-212	FKBP8-212		102	460		protein-coding	TSL:2						1.408	1 tissue
	13 F	KBP8-214	FKBP8-214	1	22	220		protein-coding	TSL:2						0.000	
	14 F	(BP8-205				439		retained intron	TSL:3						0.463	
Suna (Analy)								1								
Apply					39999	%.										
Isoform filters				Isoform	de	eta	ils on	the se	elec	ctec	d ge	ene				



If your dataset is based on human expression data, additional functionality appears in IsoProfiler to help you explore tissue expression information from the **GTEx consortium**, which profiled **51 tissues** from multiple human tissue donors by RNA-seq.



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Find out how to understand your **Phosphoproteomics** Analysis and about the multiple ways of relating the molecules in your dataset to the body of information in the Ingenuity Knowledge Base.

Halos indicate the protein's activity when it is opposite of the direction of phosphorylation



CFL1 has *increased* phosphorylation in dataset but prediction of *decreased* protein activity



GSK3B has *decreased* phosphorylation in dataset but prediction of *increased* protein activity





Gene expression data: FST causes the up-or-down-regulation of target genes



PLG, CD36, CPS1 are *up-regulated* by *activated* PST

FN1 is down-regulated by activated PST

Phosphorylation data:

LEP causes the up-or-down phosphorylation of target proteins



AKT1, IRS2 are *activated* by *increased* phosphorylation from *activated* LEP

EIF2A's activity is *inhibited* by *decreased* phosphorylation from *activated* LEP

ACACA has *increased* phosphorylation from activated LEP

The blue halo indicates that phosphorylation cause *inhibition* of ACACA's activity



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 - 4 hr lung															- 5 2
Summary Canonical Pathways Upstream Analys	is \ Diseases &	& Functions \ R	egulator Effects	Lists \ Moleo	cules Analysi	s Match \									_
VIEW AS HEATMAP VIEW COMPARISON CUSTOMIZE T															I More Info
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Analysis Name	Proj 🏋 🗵	case 🍸 🗶	case 🍸 🗵	com 🍸 🗵	com 🝸 🗵	СР (🍸 🗵	UR (🍸 🗵	CN (🝸 👗	DE (🝸 🤅	🗸 🗷 🗵	СР 🍸 🗵	UR 🍸 🗵			p-v 🍸 🗶
test1- normal control [lung] H_ influenzae (heat ki	MouseDise	normal cont	lung	Treatment	PreTreatm	64.89	74.83	76.0	62.22	69.49	1.49E-05	1.56E-67		4	69.35
test2- experimental autoimmune encephalomyelit	MouseDise	experiment	lumbar spi	Disease vs	DiseaseStat	64.89	76.16	62.35	74.05	69.37	3.9E-05	1.43E-71	4	\$3	75.98
test1- experimental autoimmune encephalomyelit	MouseDise	experiment	lumbar spi	Disease vs	DiseaseStat	56.20	76.16	68.3.	74.05	68.68	7.79E-04	1.43E-71	1E-0		76.55
test1- normal control [pulmonary airway] TNF alp	HumanDise	normal cont	pulmonary	Treatment	Treatment	51.30	73.48	80.20	67.20	68.07	8.59E-04	1.32E-63	9.65E-101	9.1E-4	72.55
test4- bacterial pneumonia [lung] NA	MouseDise	bacterial p	lung	Disease vs	DiseaseStat	45.88	74.16	71.49	75.13	66.67	1.2E-02	1.48E-65	4.25E-72	2.19E-60	75.96
test4- atopic dermatitis [skin] NA	HumanDise	atopic der	skin	Disease vs	SamplePat	56.20	72.80	67.49	68.39	66.22	5.87E-05	1.11E-61	9.47E-62	1.05E-44	74.11
test8– dysbiosis [ileum] NA	MouseDise	dysbiosis	ileum	Treatment	Tissue:Sam	60.70	71.41	61.46	70.71	66.07	2.67E-06	6.5E-58	3.04E-47	1.83E-49	75.41
test1- viril infectious diseas [hippocampus] NA	MouseDise	viral infecti	ist enpus	Disease vs	DiseaseStat	56.20	76.81	56.7	74.05	65.96	2.81E-05	1.24E-73	4.23E	1.99E-54	70.46
test2- crohi s disease (02) colon] NA	MouseDise	crohn's di		eatment	Genotype:S	51.30	72.80	70.7.	68.39	65.80	4.95E-04	1.11E-61		1 Mar	74.90
test3- pumpnary fibrosis [lung] NA	MouseDise	pulmon	\sim of	reatment	SubjectTre	45.88	72.80	74.5	69.50	65.70	5.69E-03	1.11E-61		6 19	75.38
test3- no mai control (lung) lip polysaccharide (Li	MouseDise	normal		reatment	PreTreatm	51.30	75.50	74.5	60.91	65.56	2.14E-03	1.54E-69	ry_	3	67.57
test1- neurono <u>pathic Gauch</u> er lisease (nGD) [tha	MouseDise	neurond	σ	isease vs	DiseaseStat	p0.70	.46	54.7	68.39	65.33	4.25E-05	1.01E-75	ΙΟ	9	63.18
test8- no mal control [skin] NA	HumanDise	normal co		Treatment	TreatmentS	56.20	70.71	71.4)	62.22	65.15	1.11E-04	4.55E-56		35	69.12
test2- no mal control [periphe al blood] lipopolys	HumanDise	normal cont.		atment	Molecule: T	51.30	71.41	73.08	64.76	65.13	2.14E-03	6.5E-58	3.82		70.22
test2- batterial pneumonia;influenza A [lung] NA	MouseDise	bacterial p	lung	nent	Subject of e.	Mark	74. B	67.4	71.84	65.01	8.45E-03	1.56E-67	1.39E-60	1.21E-	76.00
test11- viral infectious disease [lung] NA	MouseDise	viral infecti	lung	Treatment	SubjectInfe	51.30	74.83	58.69	75.13	64.99	1.39E-03	1.56E-67	8.93E-42	3.32E-56	71.95
test1- kidney disease [kidney] NA	HumanDise	kidney dise	kidney	Disease vs	DiseaseOn	51.30	71.41	64.12	72.96	64.95	4.95E-04	6.5E-58	1.77E-52	3.96E-56	76.65
test3 - Dactesial province (lung) NA	MouseDise	bacteria .r	l malvei	Sease vs	DiseaseStat	45.88	72.80	69.12	71.84	64.91	8.45E-03	1.11E-61	6.78E-65	2.21E-52	76.04
test4- cerebral malaria (brail) NA	MouseDise	cerebral m	ical y OI	Freatment	SamplingTi	51.30	76.16	62.36	60.56	64.84	1.39E-03	1.43E-71	1.8E-48	1,57E-44	72.20
test2- 14 [adipose tissue] TNF alpha	MouseDise	NA fro	adipose tis	Treatment	TreatTime:	51.30	74.16	73.7	59.57	64.70	1.23E-04	1.48E-65	1.7	<u>_</u> 0-	67.19
test14-rbe matomatic RA) [synovial membr	HumanDise	rheumatoid	synovial ye	Treatment	DiseaseStat	56.20	72.11	72.2	58.20	64.69	1.96E-04	8.75E-60		0	66.49
test4- normal control [bronchoalveolar lavage] K_	MouseDise	normal cont	bronchoalv	Treatment	Treatment	45.88	72.11	69.9	70.71	64.66	1.63E-02	8.75E-60	HQ .		73.99
test14- normal control [pancreatic islets] IL-1 bet	HumanDise	norma	taset	Treatment	Treatment:	56.20	70.71	70.7	60.91	64.63	1.11E-04	4.332 36		- 1 A	68.53
test21- normal control [lung] lipopolysaccharide (MouseDise	normal cont	lung	Treatment	PreTreatm	45.88	72.11	76.7	63.50	64.56	2.16E-02	8.75E-60			69.48
test2- NA [synovial tissue] TNF	HumanDise	NA	synovial tis	Treatment	Treatment	51.30	74.16	71.49	60.91	64.47	1.39E-03	1.48E-65	1.4	\checkmark	67.17
test1- melanoma [skin] NA	MouseDise	melanoma	skin	Other Com	Genotype[h	45.88	67.82	71.4	71.84	64.26	5.69E-03	6.04E-49	7.9E-72	6.42E-	75.23
test14- NA [peripheral blood] anti-CD28 antibod	HumanDise	NA	peripheral	Treatment	Treatment	56.20	70.00	73.03	56.88	64.01	5.87E-05	3E-54	3.82E-76	2.38E-26	64.93
test11- normal control [pancreatic islets] IL-1 bet	HumanDise	normal cont	pancreatic i	Treatment	Treatment:	56.20	71.41	67.49	60.91	64.00	2.81E-05	6.5E-58	1.39E-60	1.31E-33	68.72
test8- lung cancer [lung] NA	MouseDise	lung cancer	lung	Treatment	SubjectTre	-45.88	-72.80	-76.0	nrar	-64.55	1.63E-02	1.11A6h	àłłyëi	e ⁶² fro	69-1 8
test2- normal control [endothelium] Transfection_	HumanDise	normal cont	endothelium	Treatment	Transfectio	-56.20	-70.71	-74.5	162.22	-65.91	2.81E-05	4.55E36		9.68EJ3	69.86
test7- lung cancer [lung] NA	MouseDise	lung cancer	lung	Treatment	SubjectTre	-51.30	-74.83	-74.5	-64.76	-66.36	2.14E-03	1.56E-67	7.8E-81	4.56E-38	70.01
test9- lung cancer [lung] NA	MouseDise	lung cancer	lung	Treatment	SubjectTre	-51.30	-72.80	-71.4	liase	-55.58	3.15E-03	1.100	164710	atas	ets.
Selected/Total match analyses : 0 / 32															

Analysis Match



- A. Data Upload and How to Run a Core Analysis 上傳實驗資料並使用IPA分析功能
- B. Functional Interpretation in IPA IPA分析結果介紹 Hands-on Exercises

C. <u>Multi-Omics</u> Analysis using IPA

Integrate and compare genomics, transcriptomics, proteomics and metabolomics data to see the big picture on your focus research 比較分析結果的差異



大綱











Research AIM:

To attain a systems biology understanding of your research by bringing multiple types of genomic data together (SNP, CNA, mRNA, microRNA, proteomics, etc.).

Challenge:

- Data types measured different molecular status in experiment
- □ Too much data, some data types may have extra 'noise'(i.e. arrays)
- □ Venn Diagram-type comparison excludes 'A affects B' information

Solution:

- Identify phenotypes, disease associations, and pathways that are common themes for multiple data types using Comparison Analysis
- Interactive pathways overlay multiple data types and find genes up or down-stream that change in the various data types.
- Pathway tools find regulatory connections between molecules of interest and the various data types
- microRNA Target Filter can link microRNAs and targets from miRNA and target data sets

How do you integrate multiple data types now?





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)

















Review your workflow – What are your goals?







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)



IPA Analysis of Metabolomics Data Including Cross-Platform Integration with Transcriptomics Data from a Diabetic Mouse Model

Integration of metabolomics and transcriptomics data to aid biomarker discovery in type 2 diabetes

Susan C. Connor, \dagger^{*a} Michael K. Hansen, \ddagger^{b} Adam Corner, ^c Randall F. Smith^d and Terence E. Ryan \ddagger^{b}

Received 15th July 2009, Accepted 4th December 2009 First published as an Advance Article on the web 23rd March 2010 DOI: 10.1039/b914182k

Case study 1









Goal:

Case study

- providing novel biomarkers of T2D and drug efficacy
 Challenge:
- difficult to determine the precise pathophysiology in individual T2D patients

Solution:

 Integrate metabolomics of study data from other platforms, such as transcriptomics, thus linking known metabolites and genes to relevant biochemical pathways.

Outcome:

 These biomarkers may be useful by identifying patient populations that share common disease and may respond better to a particular class of anti-diabetic drugs.





Input dataset

- Observation 1 : urinary NMR-based metabolomics data •
- Observation 2 : liver transcriptomic data •
- Observation 3 : adipose transcriptomic data •
- Observation 4 : muscle transcriptomic data •

metabolomics data

transcriptomic data

ID	Symbol	Fold Chang	p-value	ID	Fold Change	p-value	ID	Fold Chang	p-value	ID	Fold Change	p-value
C00671	(3S)-3-methyl-2-oxopentanoate	-1.344	0.00E+00	C00671	-1.344	0.00E+00	C05270	-1.49	0.00E+00	C00671	-1.344	0.00E+00
C01089	(R)-3-hydroxybutyric acid	-1.311	0.00E+00	C01089	-1.311	0.00E+00	C00888	-1.49	0.00E+00	C01089	-1.311	0.00E+00
C05984	2-hydroxybutyric acid	-1.344	0.00E+00	1418083_a	t -2	3.83E-02	C00026	2.031	0.00E+00	1452730_at	2	2.60E-03
C00322	2-oxoadipic acid	2		1433936_a	t -2	2.86E-03	C00233	-1.371	0.00E+00	1436187_at	-2	2.94E-12
C00026	2-oxoglutaric acid	2.031	0.00E+00	1434484_a	t 2	1.86E-02	C00141	-1.559	0.00E+00	1424722_at	-2	3.67E-02
C01468	4-cresol	1.64	0.00E+00	1453238_s	_at 2	8.93E-05	C01089	-1.311	0.00E+00	1456546_at	-2	1.13E-02
C00642	4-hydroxyphenylacetic acid	1.002	0.00E+00	1435137_s	_at 2	3.06E-06	C11457	-1.838	0.00E+00	1455692_x_	-2	1.11E-02
C00033	acetic acid	1.226	1.83E-02	1427932_s	_at 2	9.77E-08	C02642	-1.072	0.00E+00	1448038_at	-2	4.14E-04
C02571	acetyl-L-carnitine	-1.011	0.00E+00	1430989_a	_at -2	3.71E-02	C02571	-1.011	0.00E+00	1451588_at	-2	6.20E-27
C00212	adenosine	-1.066	0.00E+00	1448038_a	t -2	3.91E-02	C00212	-1.066	0.00E+00	1424365_at	2	1.04E-04
C01551	allantoin	1.081	0.00E+00	1424365_a	t -2	2.54E-07	C00041	1.119	0.00E+00	1436339_at	2	2.61E-12
C00233	alpha-ketoisocaproic acid	-1.371	0.00E+00	C05984	-1.344	0.00E+00	C01551	1.081	0.00E+00	C05984	-1.344	0.00E+00
C00141	alpha-ketoisovaleric acid	-1.559	0.00E+00	C00322	2	0.00E+00	C05984	-1.344	0.00E+00	C00322	2	
C00417	cis-aconitic acid	1.208	0.00E+00	C00026	2.031	0.00E+00	C01585	-1.49	0.00E+00	C00026	2.031	0.00E+00
C00158	citric acid	1.262	0.00E+00	1429115_a	t -2	4.59E-02	C00803	-1.49	0.00E+00	1435524_at	-2	7.42E-06
C00327	citrulline	2		1435522 a	_at2	1.86E-08	C00671	-1.344	0.00E+00	1452170_at	2	6.82E-08
C00300	creatine	-1.33	0.00E+00	1428083 a	t -2	1.06E-09	C00417	1.208	0.00E+00	1424968_at	-2	1.94E-06
C00791	creatinine	-1.281	6.00E-06	1455207 a	t -2	2.75E-04	C00158	1.262	0.00E+00	1433530_at	-2	1.46E-03
C00879	D-galactaric acid	2.896	0.00E+00	1420269 a	t 2	5.55E-05	C00300	-1.33	0.00E+00	1428500_at	-2	4.00E-05
C00124	D-galactose	3.183	0.00E+00	1423357 a	t -2	2.68E-03	C00543	-1.12	0.00E+00	1439962_at	-2	5.34E-05
C00031	D-glucose	10.945	0.00E+00	1453207 a	t -2	4.41E-03	C00346	1.248	0.00E+00	1435522_a_	2	2.54E-03
Somo	le te lecight											

Sample to insign



Network describing lipid metabolism, small molecule biochemistry and transport

Sample to Insight







Gluconeogenesis pathway mapping metabolomics and transcriptomics results



Result:

Case study

- Several biomarkers (e.g., BCAAs, nicotinamide metabolites, pantothenic acid) have not previously been suggested as possible biomarkers for diabetes.
- metabolomics highlighted at least <u>24 distinct pathways</u> that distinguish diabetic and control mice. The pathways most affected were amino acid, amino group metabolism and the urea cycle. Also affected were fatty acid biosynthesis, degradation and transport, DNA and protein synthesis changes in urinary protein, MUP and NAG, energy metabolism, and steroid hormone synthesis.





Live Demo

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RESEARCH ARTICLE

- A Multi-Omics Approach Identifies Key Hubs Associated with Cell Type-Specific Responses of Airway Epithelial Cells to Staphylococcal Alpha-Toxin
- Erik Richter¹, Manuela Harms¹, Katharina Ventz¹, Philipp Gierok², Ravi Kumar Chilukoti³, Jan-Peter Hildebrandt⁴, Jörg Mostertz¹, Falko Hochgräfe¹*







Transcriptomics



Hla-susceptible 16HBE14o-



Sample to Insight



Goal:

- Better understanding of Hla-induced cellular programs Challenge:
- Diverse cellular reactions of Hla-treatment, difficult to defined cell-specific responses

Solution:

- Integrate phosphoproteomics and transcriptomics data, thus linking known metabolites and genes to revealed a substantial impact on phosphorylation-dependent signaling and the interaction between gene expression
 Outcome:
- Revealed a substantial in both cell models and highlights alterations in signaling pathways associated with contacts





Input dataset

- Observation 1 : S9 alpha-toxin treatment phosphoproteomics data
- Observation 2 : S9 alpha-toxin treatment transcriptomic data

Phosphoprot	eomics	lata 🕂	t	ranscrip	tomic data
First Hit ID	Phosp Alpha	Affy	ID	Gene Name	Exp Fold Change [S9 vs. HLA:
Q9UNL2	5.0485912	805	55952	NR4A2	7.99979
P49207	5.0406868	795	75779	FOS	6.99416
095747	3.5411981	813	31803	IL6	4.07129
Q14573	3.5139138	811	15831	DUSP1	3.85729
Q9NZQ3	3.2174572	810	08370	EGR1	3.82366
P04792	3.2136851	809	95680	IL8	3.33594
Q13085	3.1679433	793	38390	ADM	3.31279
Q9Y580	3.1565325	806	69676	ADAMTS1	3.18191
P04792	3.155894	816	53002	KLF4	2.84788
P46779	3.0451337	802	29693	FOSB	2.75585
P57678	3.0223869	790	09610	ATF3	2.73689
Q8NC51	3.0177892	808	83594	PTX3	2.68894
P17858	2.9980667	814	48304	TRIB1	2.68555
A6ND36	2.7129297	795	55589	NR4A1	2.66317
Q96N67	2.6753043	812	29677	SGK1	2.61712
094874	2.6740569	814	48317	MYC	2.52871
P29966	2.6586675	796	65335	DUSP6	2.44648
Q9NS69	2.6523421	815	56848	NR4A3	2.33387
Q8ND04	2.5458685	792	26677		2.3149
Q14573	2.4490019	803	30128	PPP1R15A	2.19422
Q8NDI1	2.444508	810	00994	CXCL2	2.1804

Sample to Insight



Result:

Case study

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- metabolomics highlighted at least <u>24 distinct pathways</u> that distinguish diabetic and control mice. The pathways most affected were amino acid, amino group metabolism and the urea cycle. Also affected were fatty acid biosynthesis, degradation and transport, DNA and protein synthesis changes in urinary protein, MUP and NAG, energy metabolism, and steroid hormone synthesis.





Live Demo

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Sample to Insight