IPA 系統生物學分析軟體暨資料庫
進階操作課程

KMU
2017 Oct

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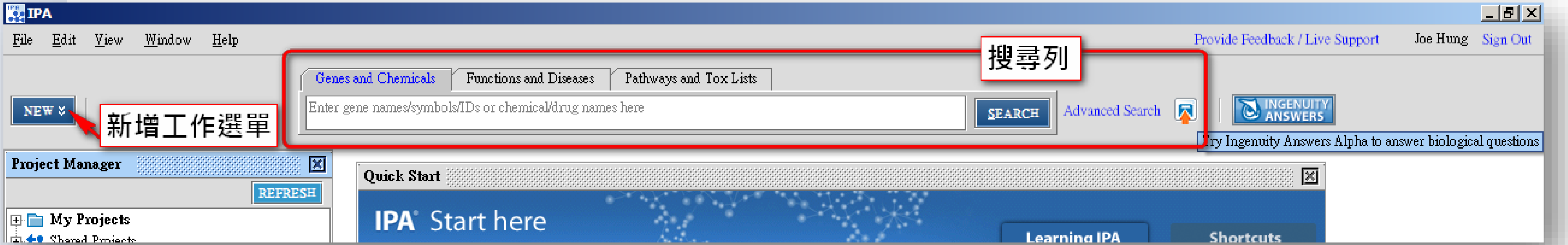
Senior Deputy Manager and IPA certified analyst

Review for Introductory Training course

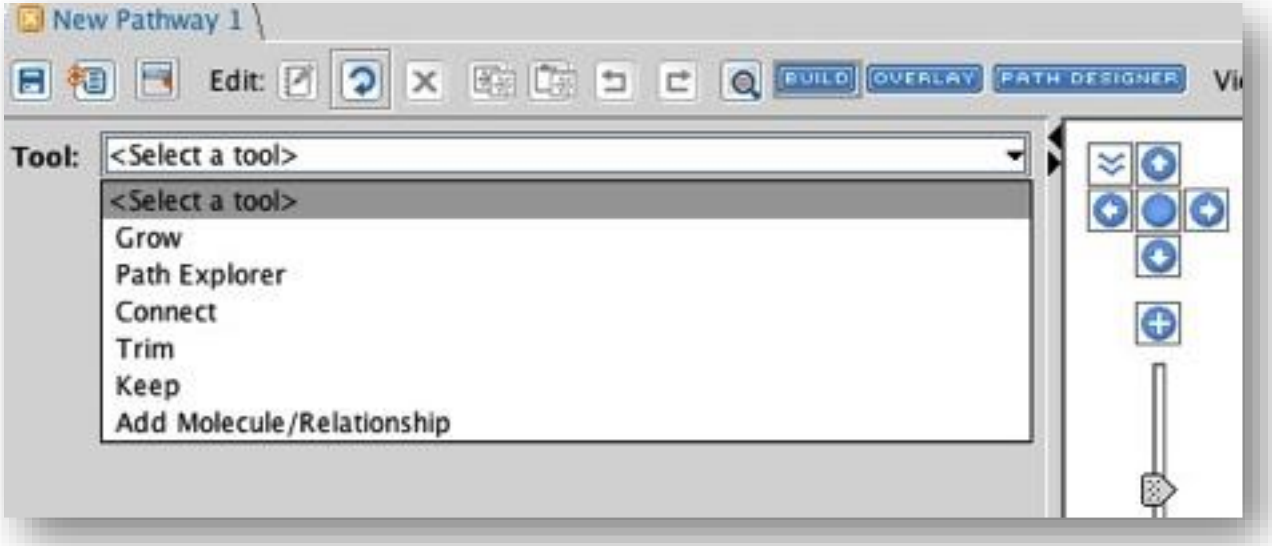
- 利用IPA進行搜尋
- 使用IPA進行分子模型建構
- 繪製訊息傳遞路徑

Searching

- Searching Basics
- 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



Build Tools 的功能

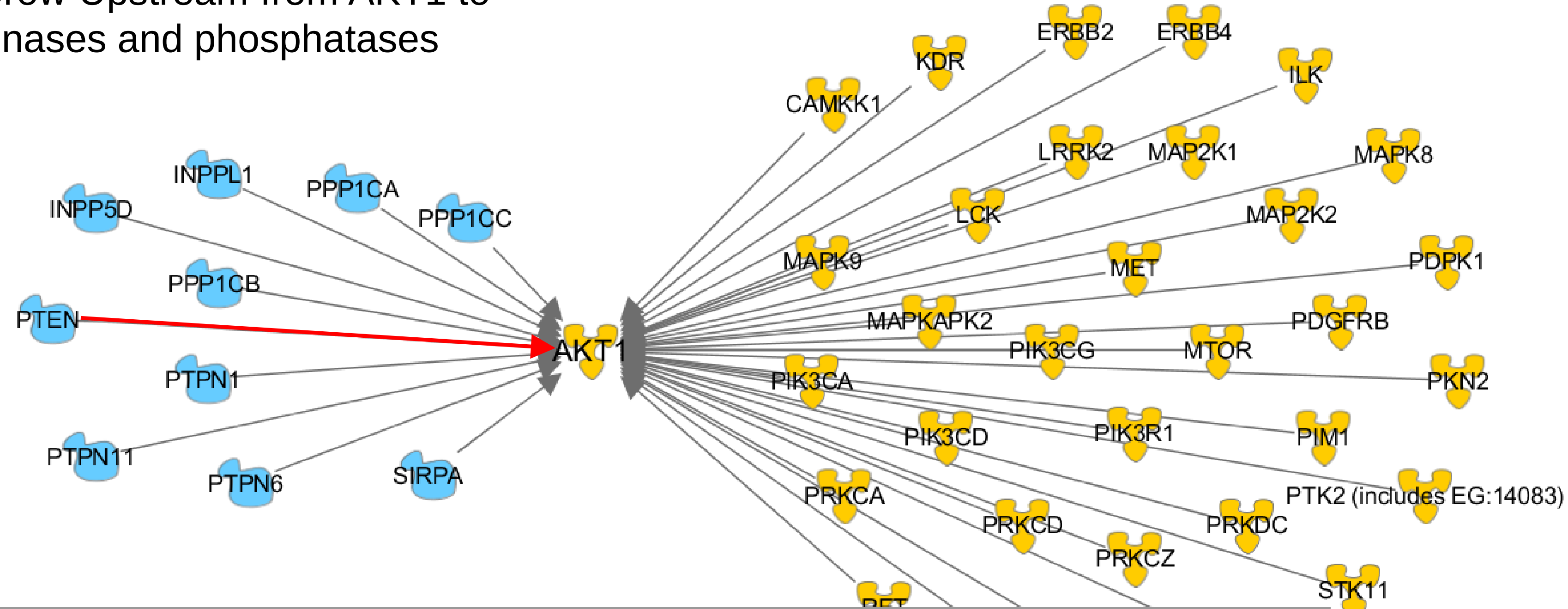


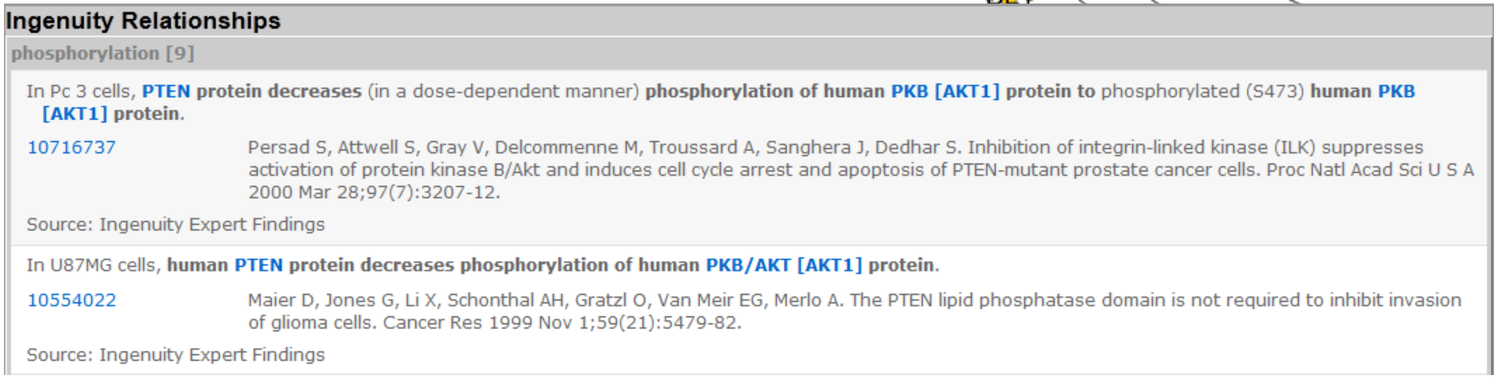
Build Tools包含下列數個建構pathway圖型的工具:

- 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

Build and Grow Networks of Molecules

Grow Upstream from AKT1 to kinases and phosphatases





Ingenuity Relationships

phosphorylation [9]

In Pc 3 cells, **PTEN protein decreases** (in a dose-dependent manner) **phosphorylation of human PKB [AKT1] protein to** phosphorylated (S473) **human PKB [AKT1] protein.**

10716737 Persad S, Attwell S, Gray V, Delcommenne M, Troussard A, Sanghera J, Dedhar S. Inhibition of integrin-linked kinase (ILK) suppresses activation of protein kinase B/Akt and induces cell cycle arrest and apoptosis of PTEN-mutant prostate cancer cells. Proc Natl Acad Sci U S A 2000 Mar 28;97(7):3207-12.

Source: Ingenuity Expert Findings

In U87MG cells, **human PTEN protein decreases phosphorylation of human PKB/AKT [AKT1] protein.**

10554022 Maier D, Jones G, Li X, Schonthal AH, Gratzl O, Van Meir EG, Merlo A. The PTEN lipid phosphatase domain is not required to inhibit invasion of glioma cells. Cancer Res 1999 Nov 1;59(21):5479-82.

Source: Ingenuity Expert Findings

大綱

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. **Comparison Analyses**
比較分析結果的差異

D. **Q&A**

大綱

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IPA的資料上傳與分析功能介紹

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

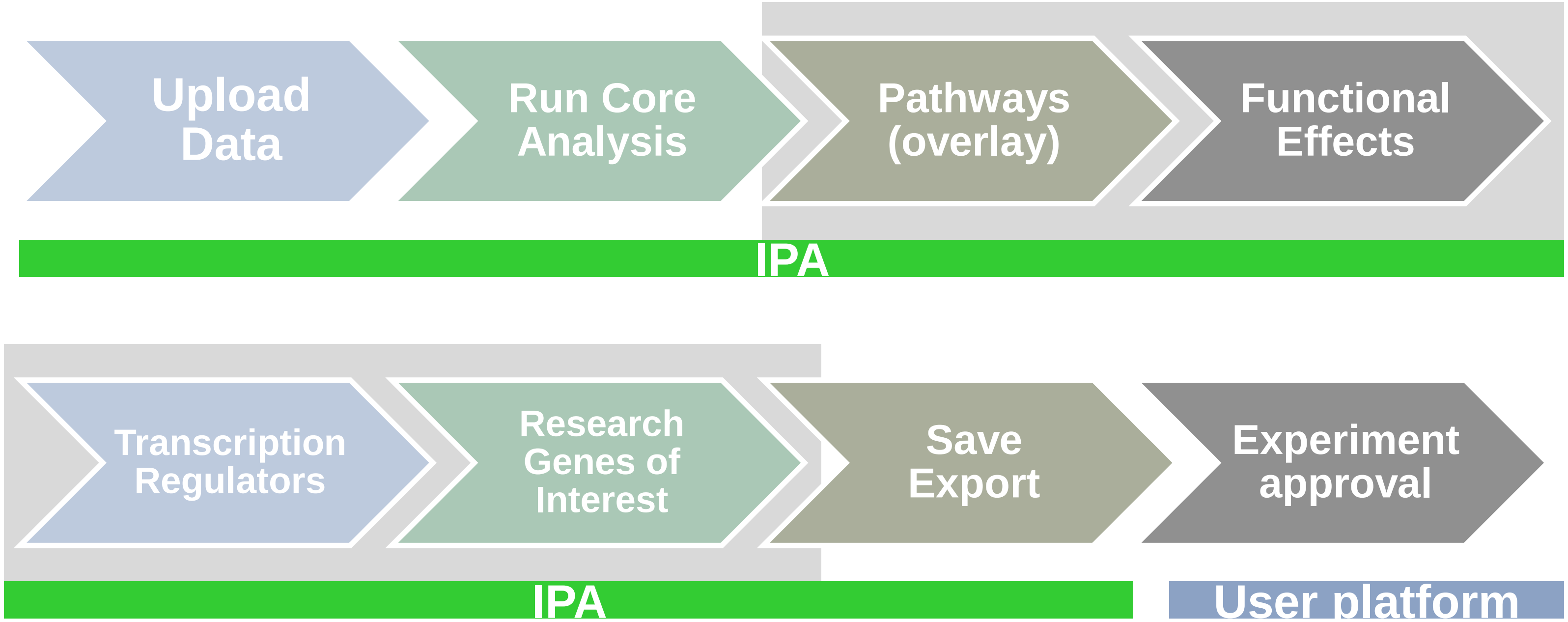
分析功能種類:

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

IPA Data Analysis Workflow



Upload Data

Run Core Analysis

Pathways (overlay)

Functional Effects

IPA

Transcription Regulators

Research Genes of Interest

Save Export

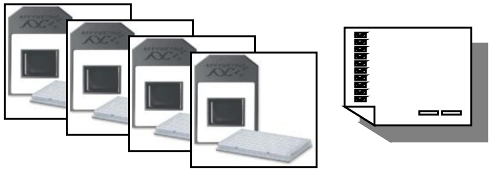
Experiment approval

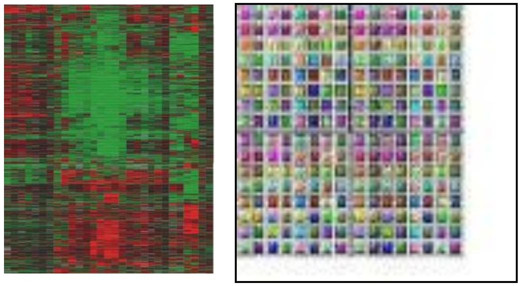
IPA

User platform

General Analysis Workflow in IPA

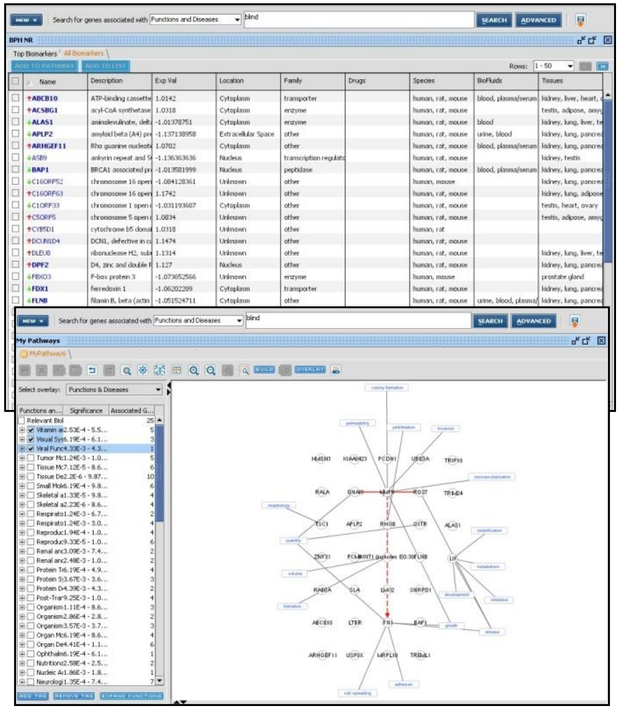
Workflow for Dataset Analysis





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

IPA



Identify functions, diseases, and canonical pathways associated with your data

Key Terminology

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

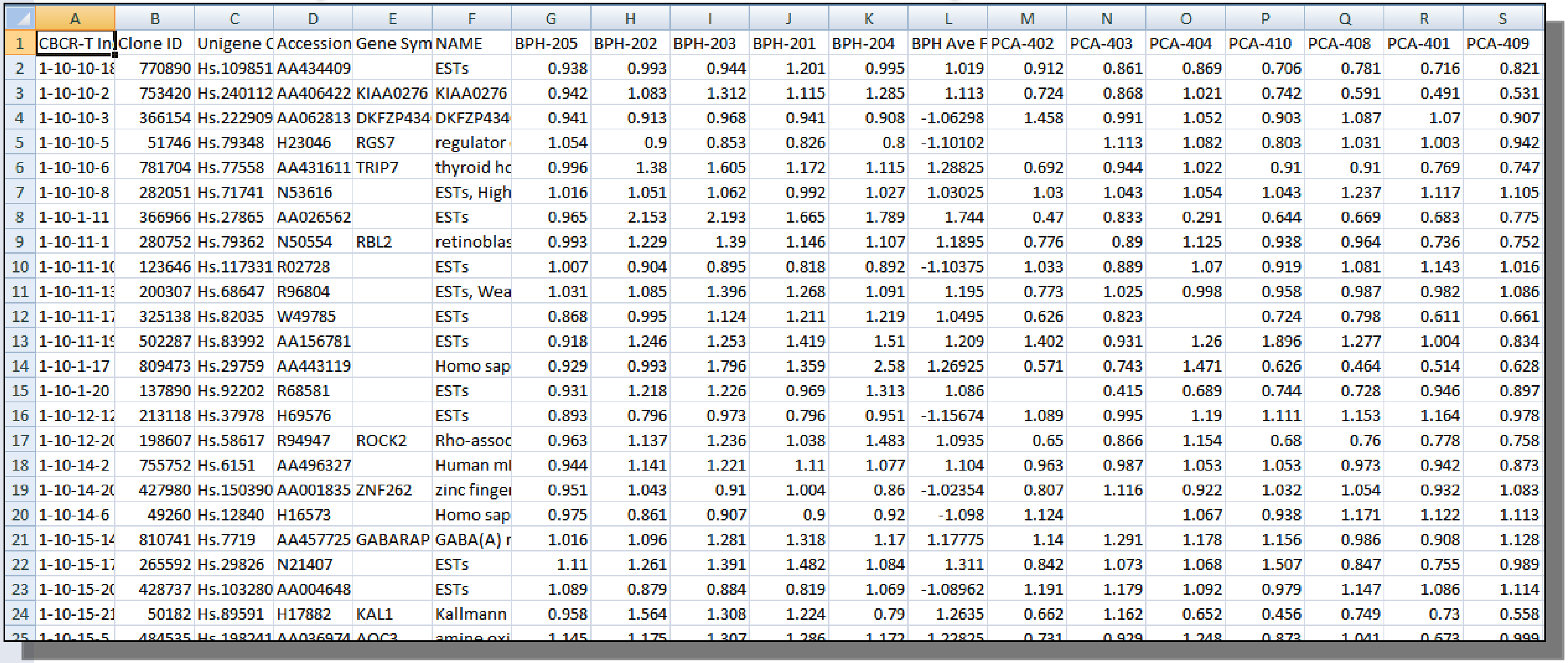
準備IPA分析用的Dataset

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	1-10-10-1	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 hc	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	1-10-11-1	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	1-10-11-1	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	1-10-11-1	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	1-10-11-1	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	1-10-12-1	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	1-10-12-2	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	1-10-14-2	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	1-10-15-1	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	1-10-15-1	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	1-10-15-2	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	1-10-15-2	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

準備IPA分析用的Dataset

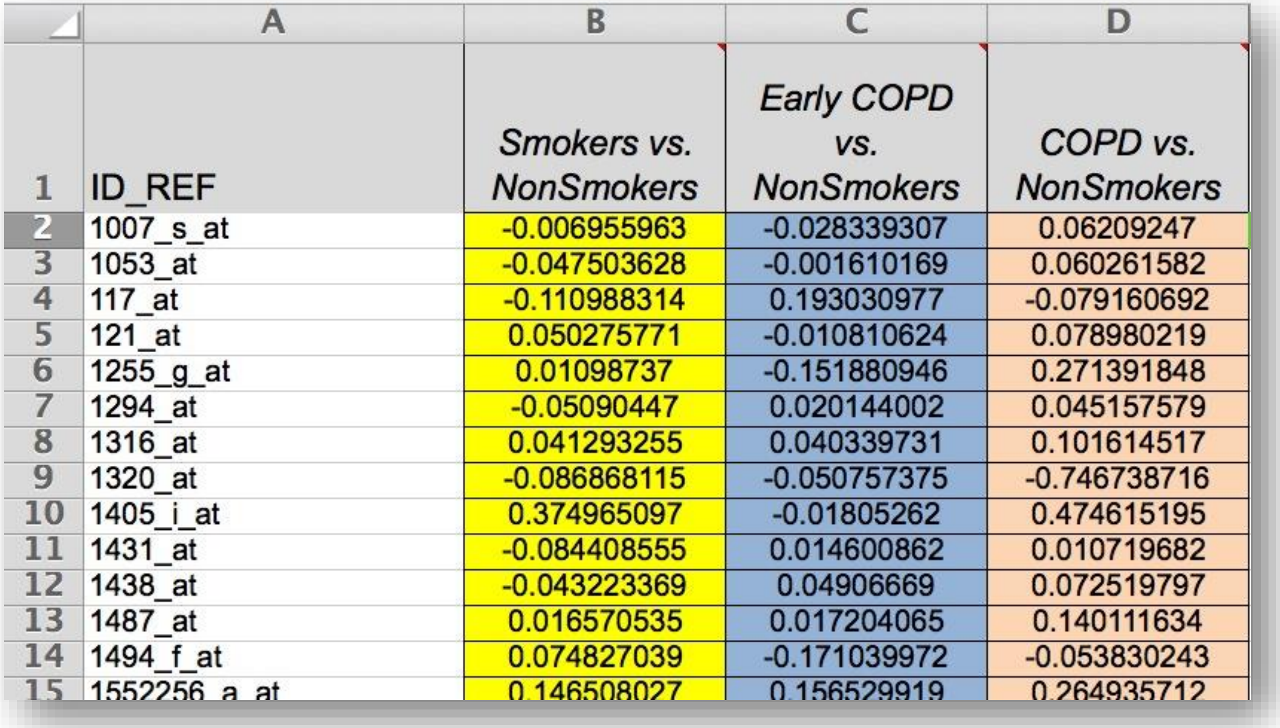
- 重複性實驗的數值平均、p-vlaue或fold-change等統計計算，要先在IPA分析之前完成。

- 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。

分析用的Dataset的範例格式

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



	A	B	C	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

IPA®

Live Demo

大綱

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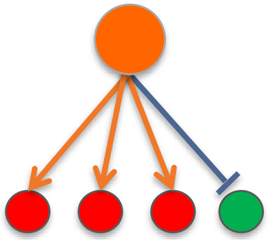
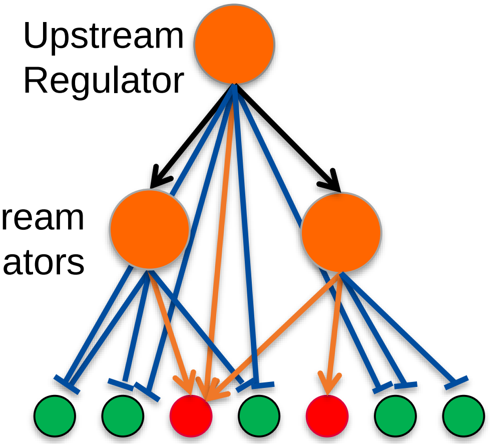
Network types in IPA

Upstream Analysis



Dataset Molecules

Mechanistic Network of Upstream Regulators



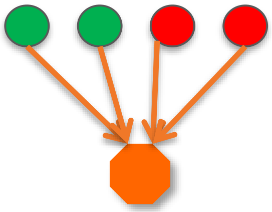
Upstream Regulator

Other upstream regulators

Dataset Molecules

Function Analysis

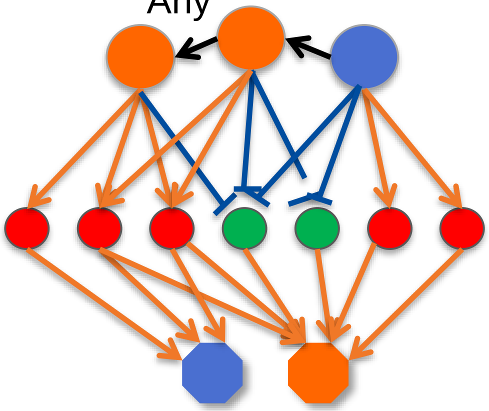
Dataset Molecules



Diseases / functions

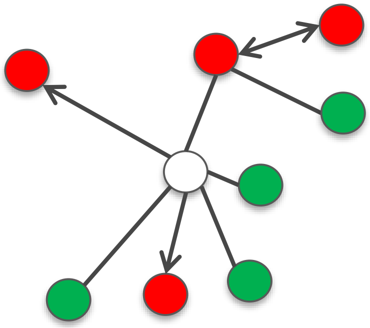
Regulator Effect Network

Any



Diseases / functions

Interaction Network



Dataset Molecules

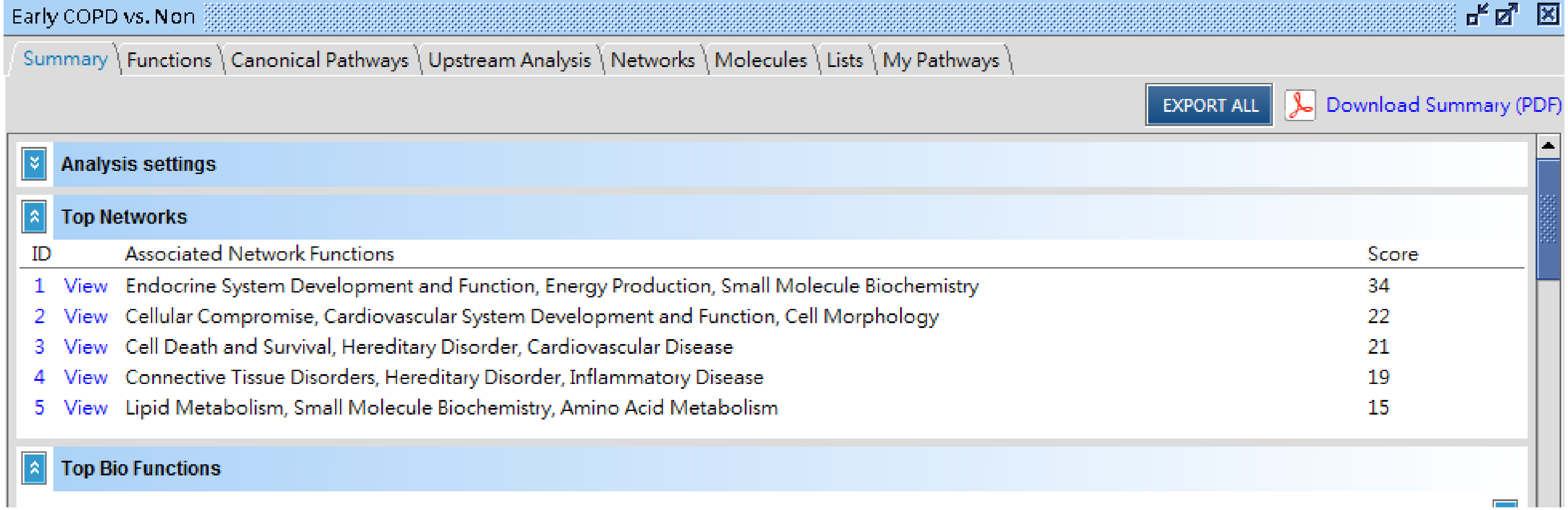
IPA 分析結果

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。



Analysis settings

Top Networks

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
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

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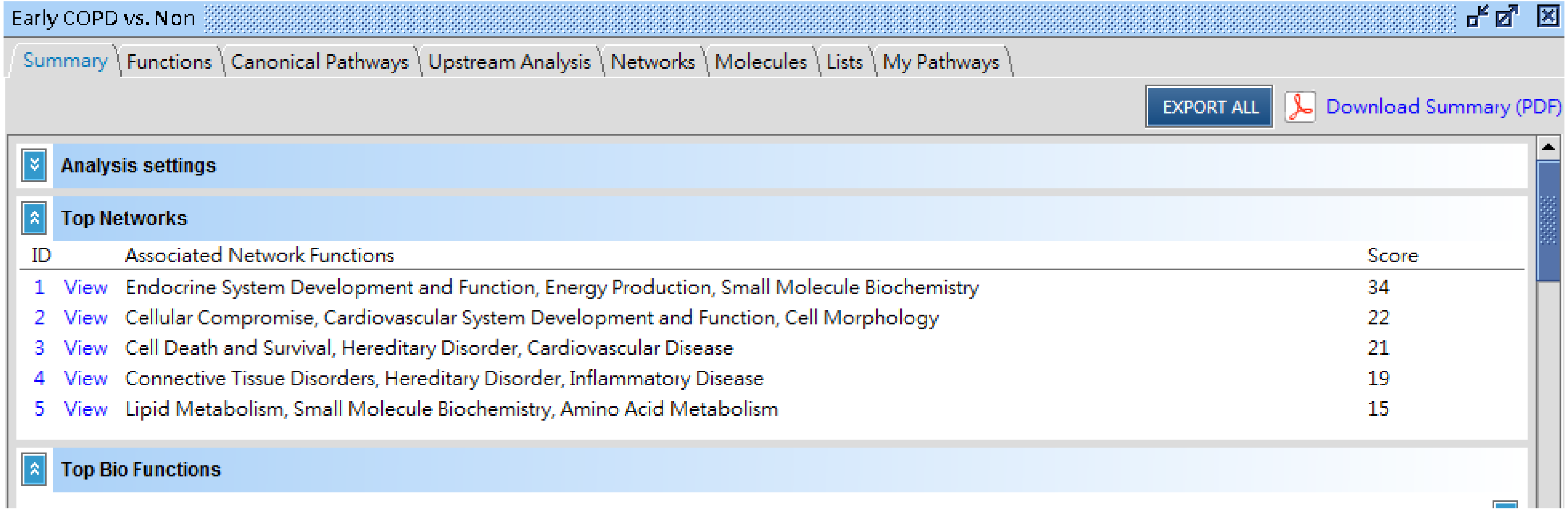

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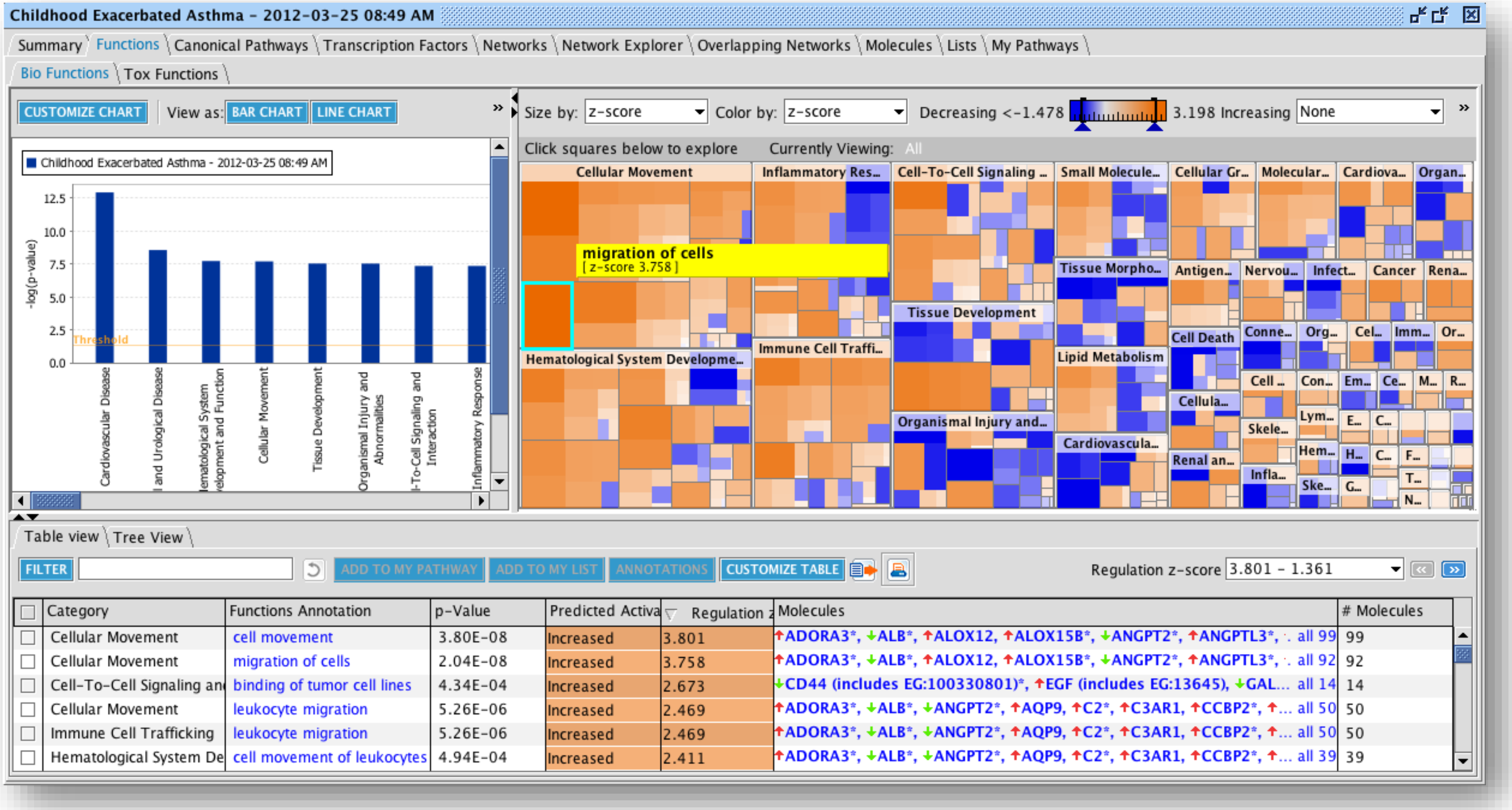
Interpret Downstream Biological Functions



Size by: z-score
Color by: z-score
Regulation z-score 3.801 - 1.361

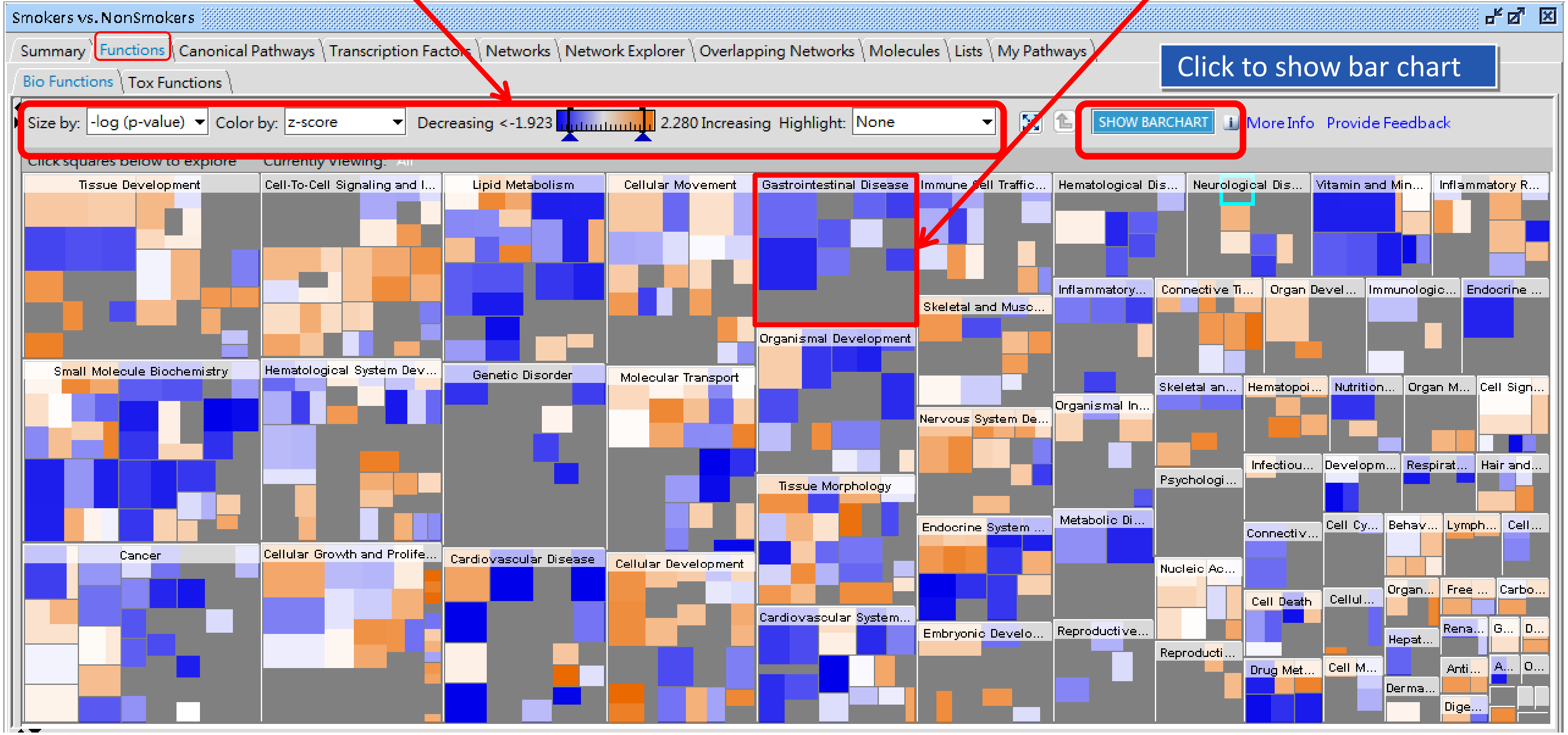
☐	Category	Functions Annotation	p-Value	Predicted Activa	Regulation z	Molecules	# Molecules
☐	Cellular Movement	cell movement	3.80E-08	Increased	3.801	↑ADORA3*, ↓ALB*, ↑ALOX12, ↑ALOX15B*, ↓ANGPT2*, ↑ANGPTL3*, . all 99	99
☐	Cellular Movement	migration of cells	2.04E-08	Increased	3.758	↑ADORA3*, ↓ALB*, ↑ALOX12, ↑ALOX15B*, ↓ANGPT2*, ↑ANGPTL3*, . all 92	92
☐	Cell-To-Cell Signaling an	binding of tumor cell lines	4.34E-04	Increased	2.673	↓CD44 (includes EG:100330801)*, ↑EGF (includes EG:13645), ↓GAL... all 14	14
☐	Cellular Movement	leukocyte migration	5.26E-06	Increased	2.469	↑ADORA3*, ↓ALB*, ↓ANGPT2*, ↑AQP9, ↑C2*, ↑C3AR1, ↑CCBP2*, ↑... all 50	50
☐	Immune Cell Trafficking	leukocyte migration	5.26E-06	Increased	2.469	↑ADORA3*, ↓ALB*, ↓ANGPT2*, ↑AQP9, ↑C2*, ↑C3AR1, ↑CCBP2*, ↑... all 50	50
☐	Hematological System De	cell movement of leukocytes	4.94E-04	Increased	2.411	↑ADORA3*, ↓ALB*, ↓ANGPT2*, ↑AQP9, ↑C2*, ↑C3AR1, ↑CCBP2*, ↑... all 39	39

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

Downstream Effects Analysis介紹

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: **Mid-level functional category (level 2)** 與 **Specific functions (level 3)**



Size by: -log (p-value) Color by: z-score Decreasing <-1.923 2.280 Increasing Highlight: None

Click squares below to explore Currently Viewing: All

Click to show bar chart

IPA 分析結果

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

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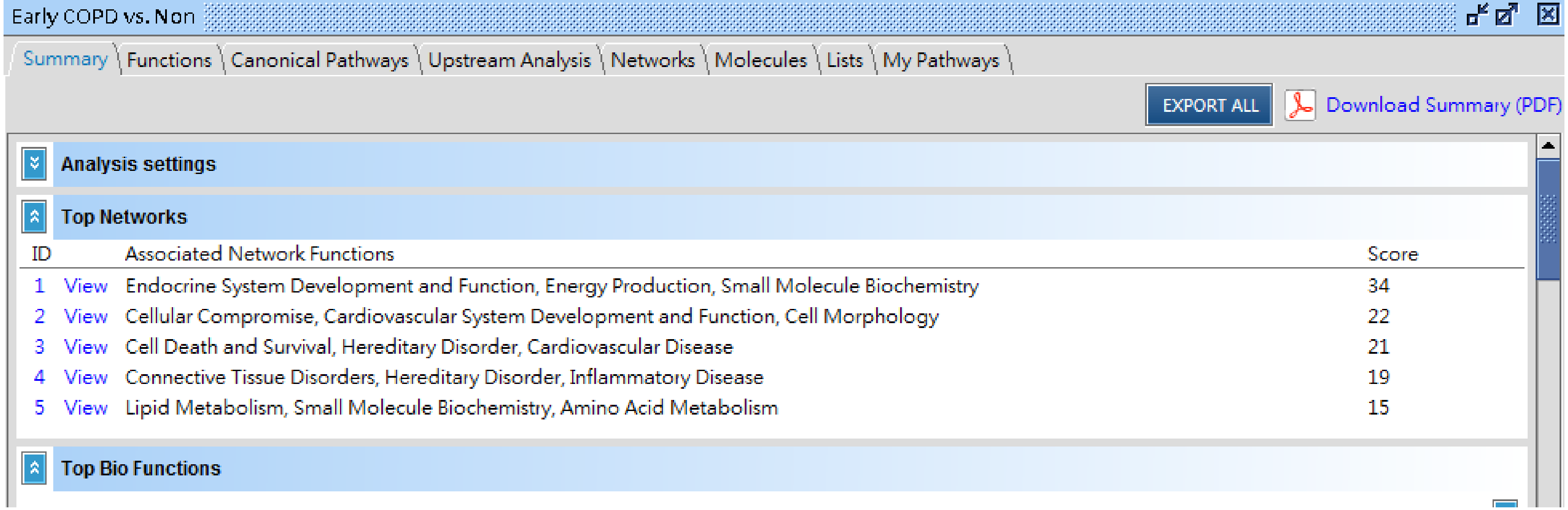
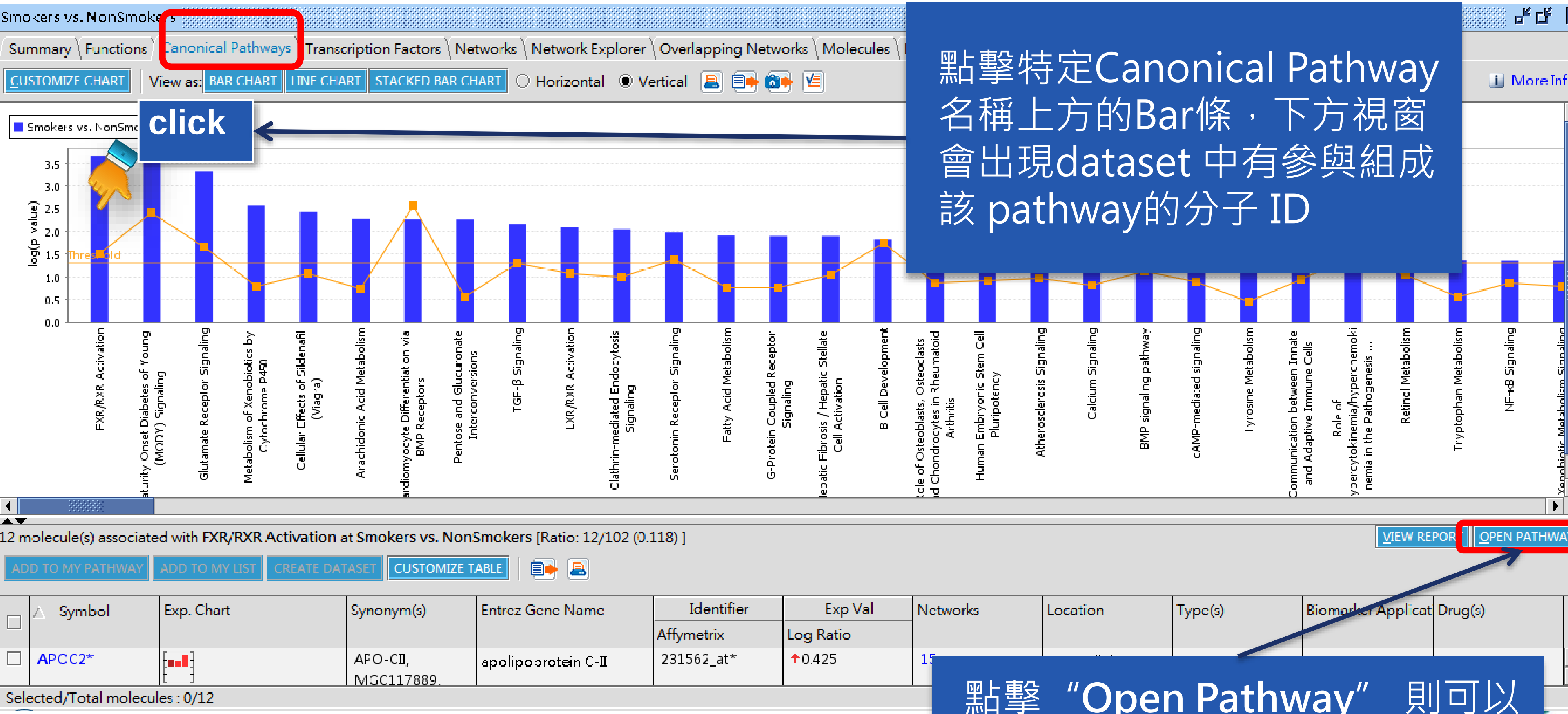


ID		Associated Network Functions	Score
1	View	Endocrine System Development and Function, Energy Production, Small Molecule Biochemistry	34
2	View	Cellular Compromise, Cardiovascular System Development and Function, Cell Morphology	22
3	View	Cell Death and Survival, Hereditary Disorder, Cardiovascular Disease	21
4	View	Connective Tissue Disorders, Hereditary Disorder, Inflammatory Disease	19
5	View	Lipid Metabolism, Small Molecule Biochemistry, Amino Acid Metabolism	15

Canonical Pathway Analysis

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



12 molecule(s) associated with **FXR/RXR Activation** at **Smokers vs. NonSmokers** [Ratio: 12/102 (0.118)]

☐	Symbol	Exp. Chart	Synonym(s)	Entrez Gene Name	Identifier Affymetrix	Exp Val Log Ratio	Networks	Location	Type(s)	Biomarker Applicat	Drug(s)
☐	APOC2*		APO-CII, MGC117889,	apolipoprotein C-II	231562_at*	↑0.425	15				

Selected/Total molecules : 0/12

點擊特定Canonical Pathway名稱上方的Bar條，下方視窗會出現dataset 中有參與組成該 pathway的分子 ID

點擊“Open Pathway” 則可以展開那個Canonical Pathway，實驗資料中的分子會用顏色提示。

IPA 分析結果

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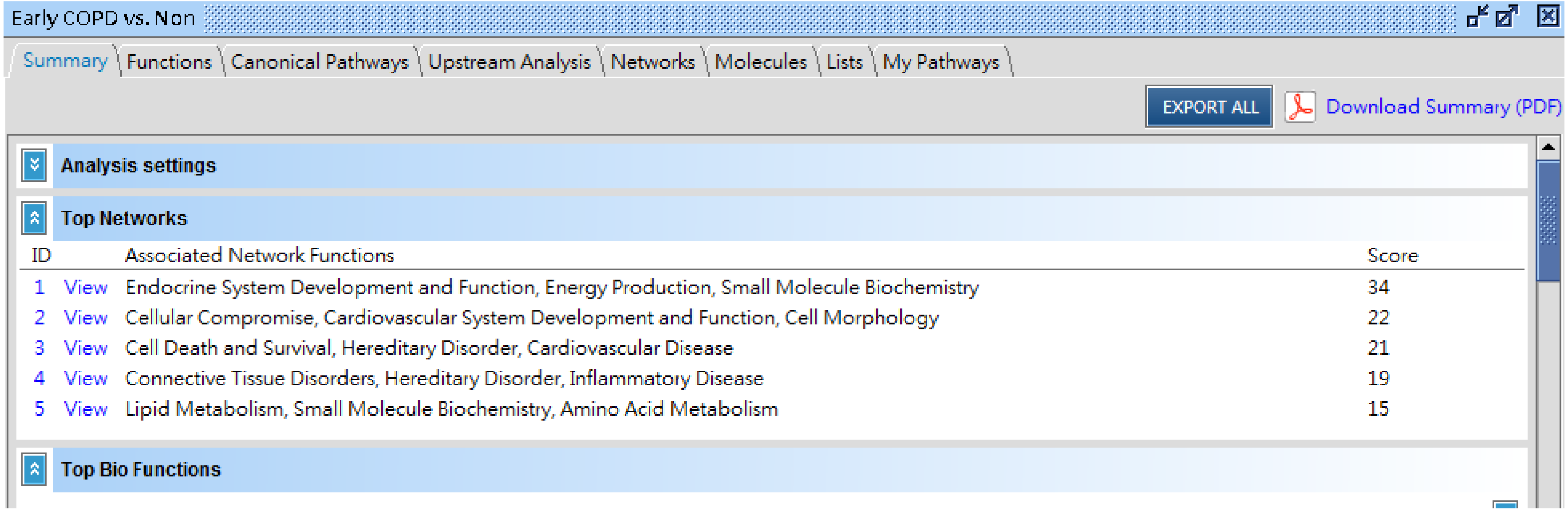

Top Networks

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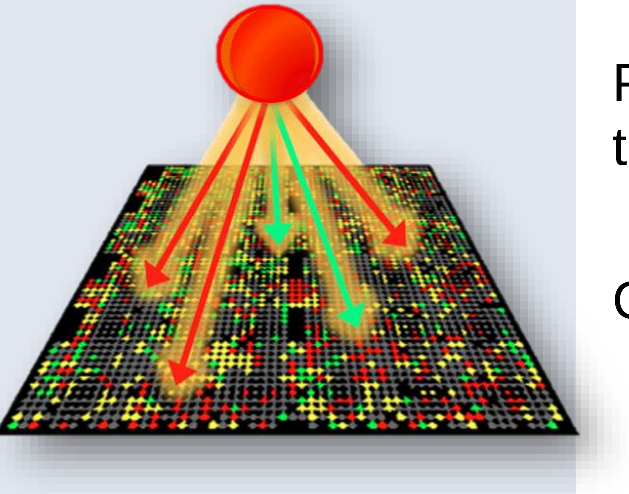
Upstream Regulator Analysis: *How does it work?*



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

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

Calculates two complementary statistical measures:

- ☐ Activation z-score
- ☐ Overlap p-value

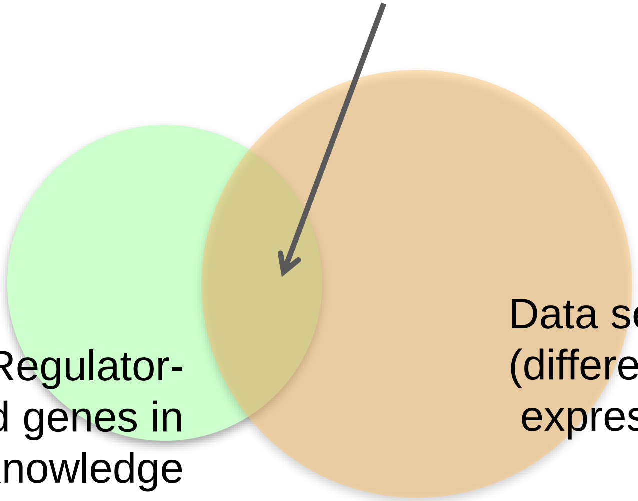
Upstream Regulator Analysis: *How does it work?*

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

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

TR → target edge types considered:
- Expression
- Transcription
- Protein-DNA binding

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

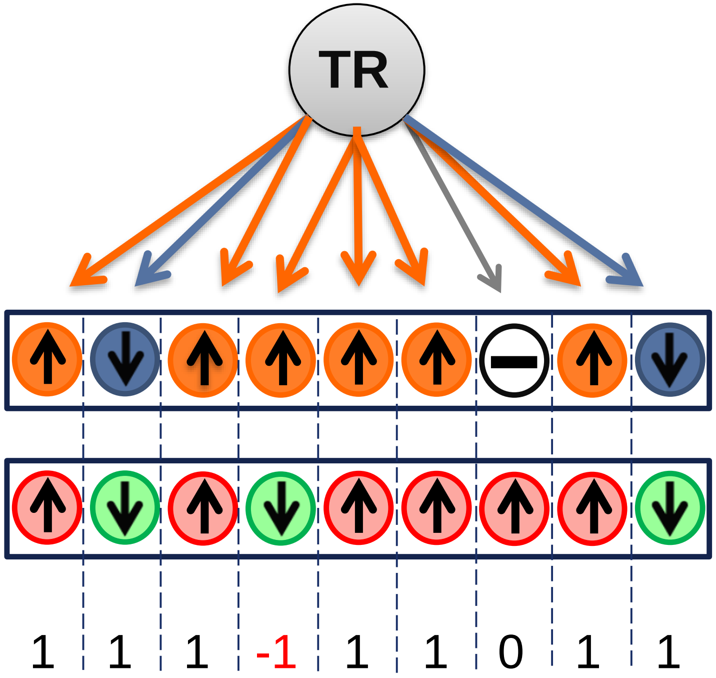


Upstream Regulator-regulated genes in Ingenuity Knowledge Base

Data set (differentially-expressed genes)

Upstream Analysis Activation z–score

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



N = 8 genes

TR effect on downstream genes
(Literature)

Differential gene expression
(Uploaded Data)

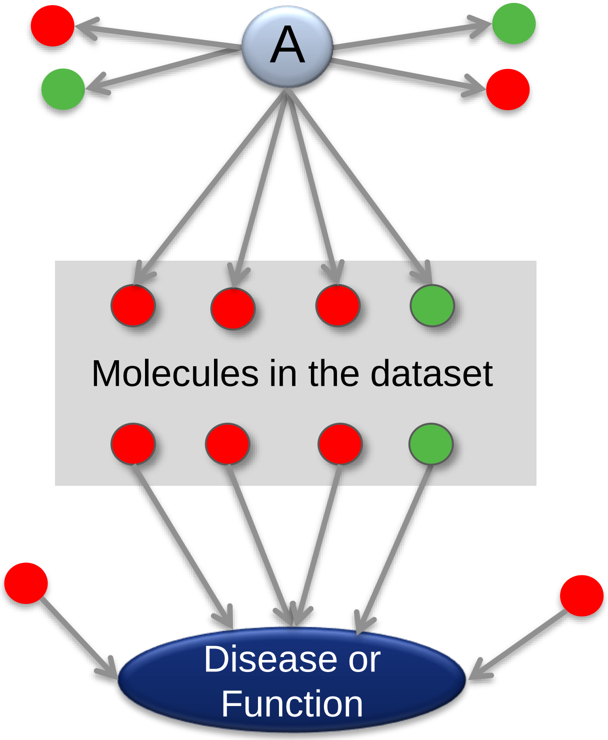
z-score > 2 or < -2 is considered significant

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

Concept of “Regulator Effects” - Spring 2014

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

Upstream Regulators



A

Molecules in the dataset

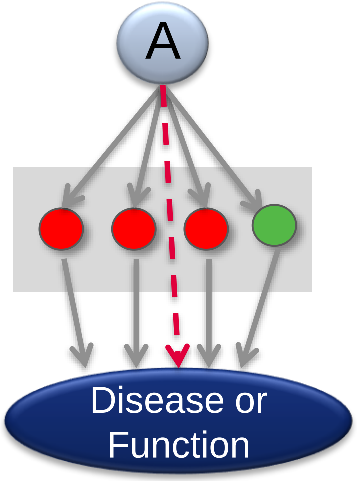
Disease or Function

Downstream Effects Analysis

Algorithm

First iteration

Simplest Regulator Effects result



A

Disease or Function

Displays a relationship between the regulator and disease/function if it exists

Causally consistent networks score higher

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

IPA 分析結果

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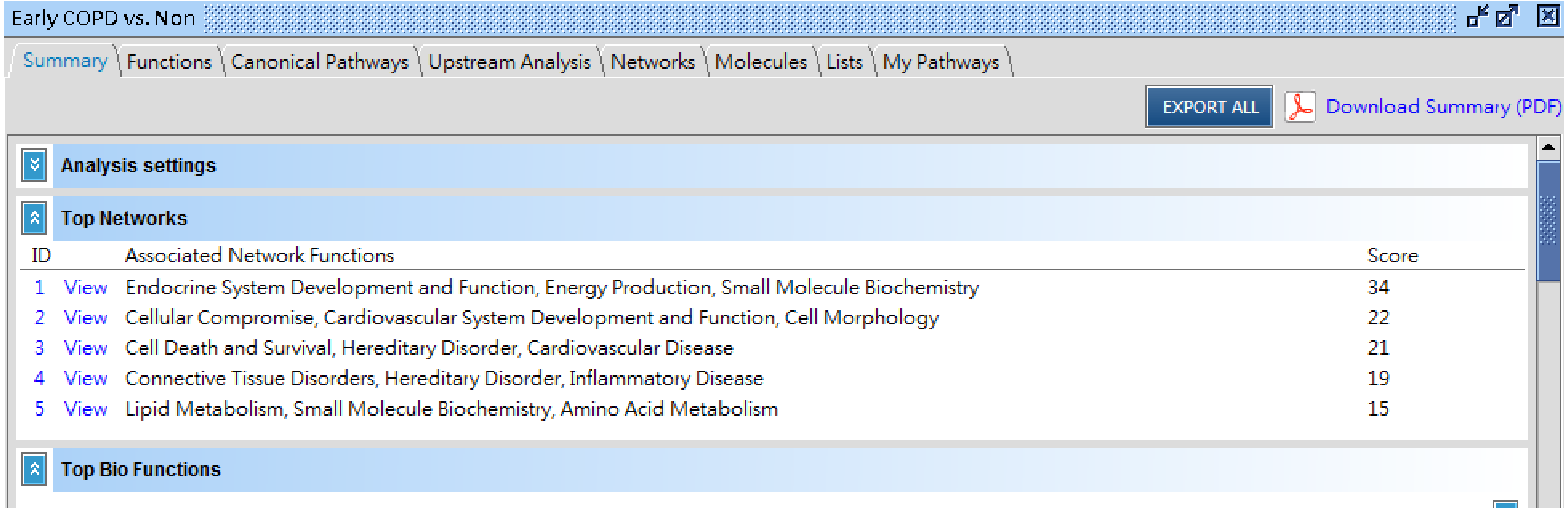

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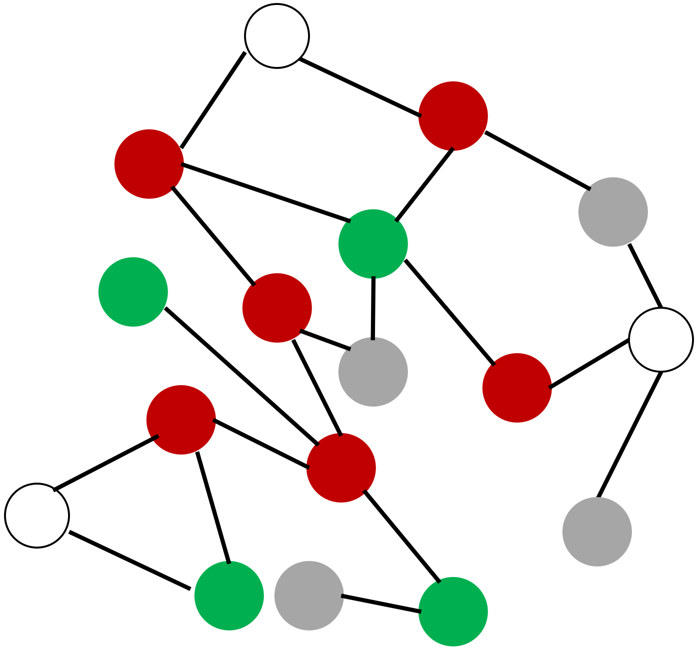
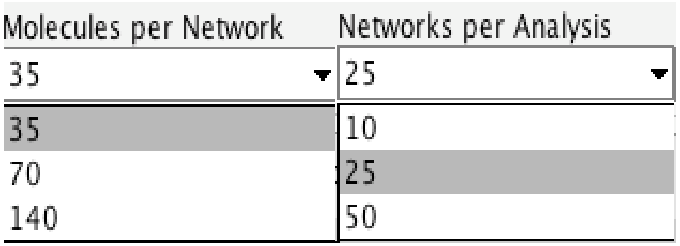
Top Bio Functions

How Networks Are Generated

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
35
35
70
140

Networks per Analysis
25
10
25
50

IPA®

Live Demo

大綱

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. **Comparison Analyses**
比較分析結果的差異

D. Q&A

Single Experiment

- Time Course
- Dose Response

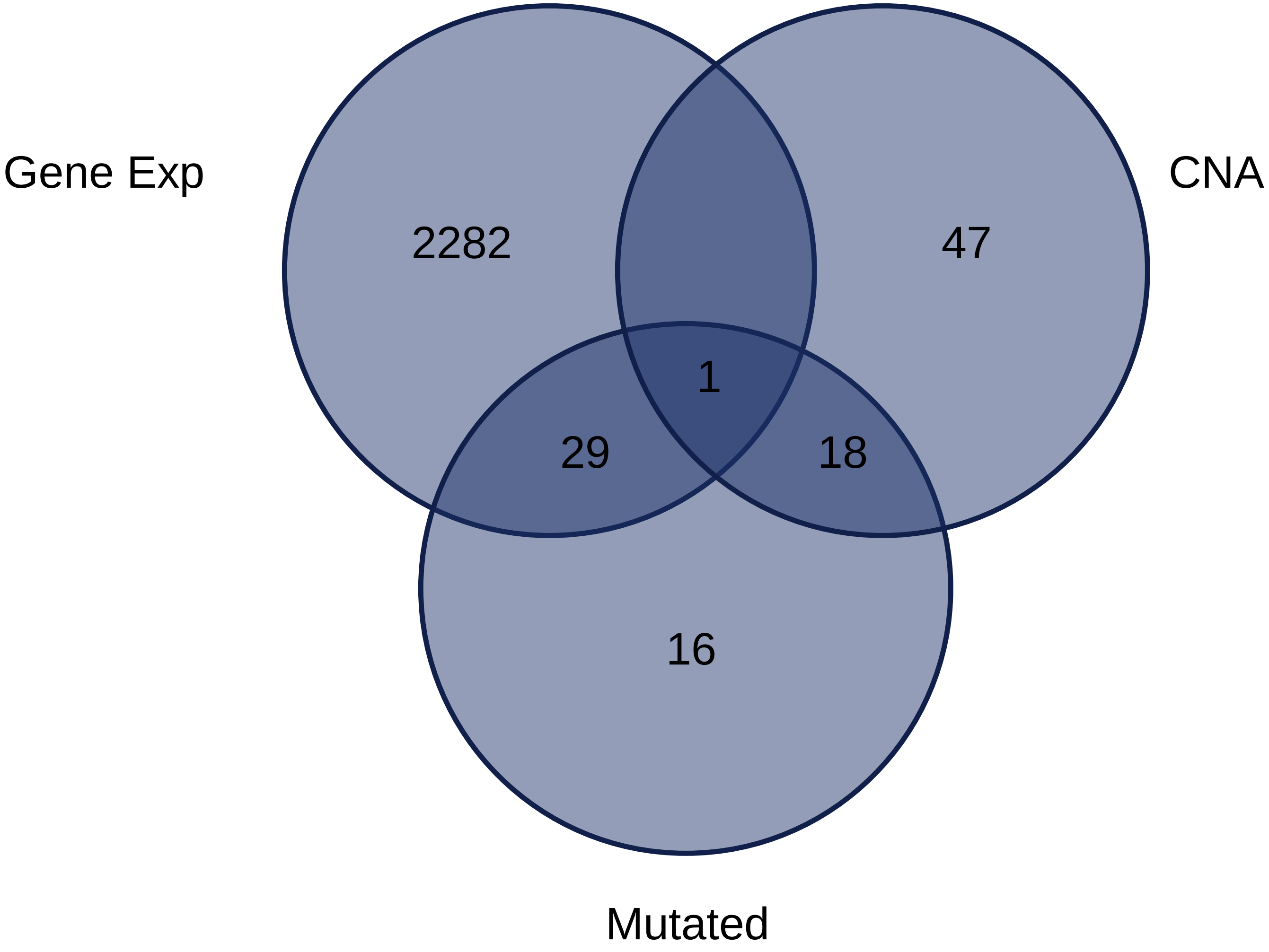
Multi Experiment

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

Set Analysis

- Exploring Common Molecules across one or more experiment (s)

Genes Overlap



Bringing together multiple types of genomic data

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

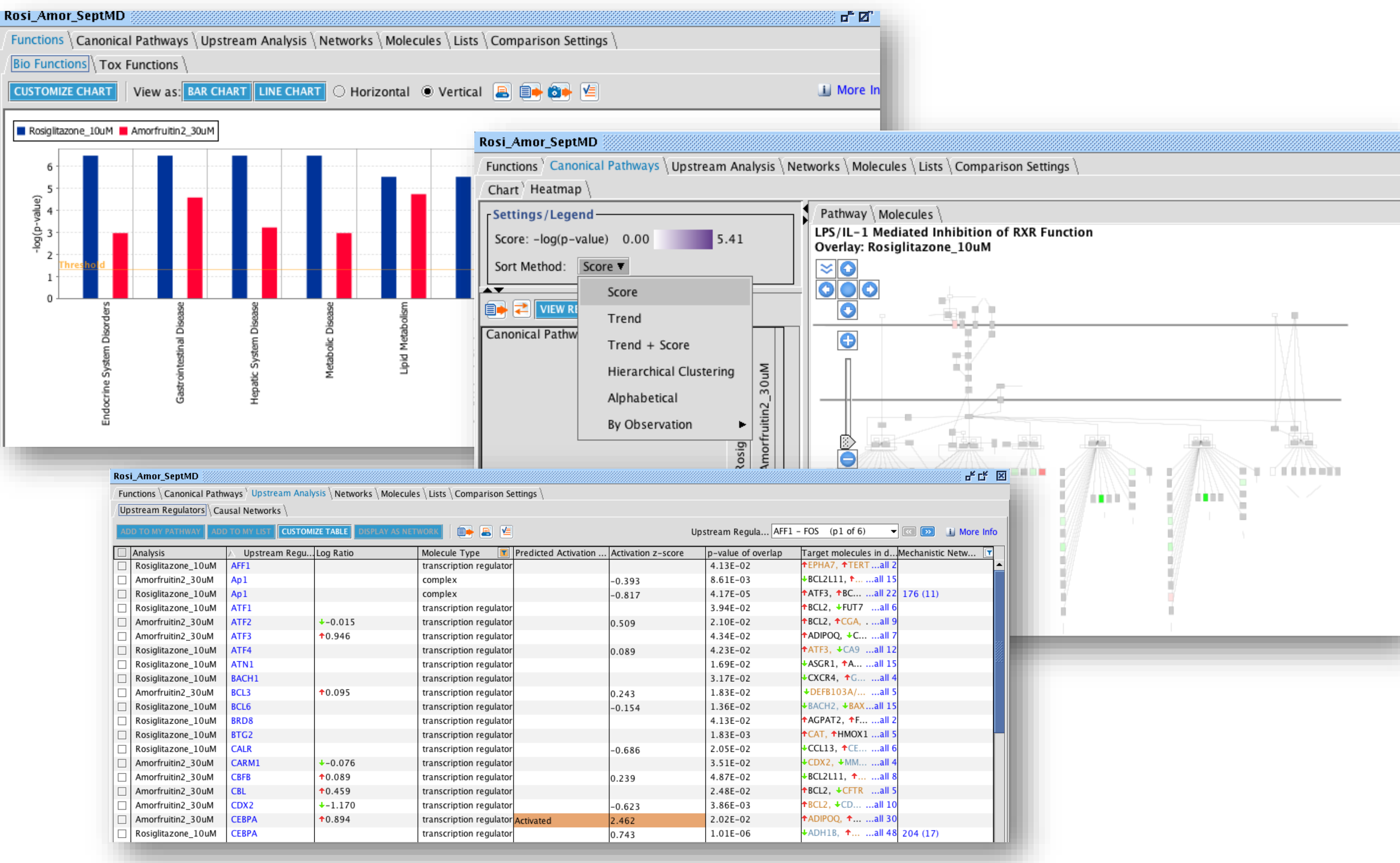
Multi Experiment

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

Set Analysis

- Exploring Common Molecules across one or more experiment (s)

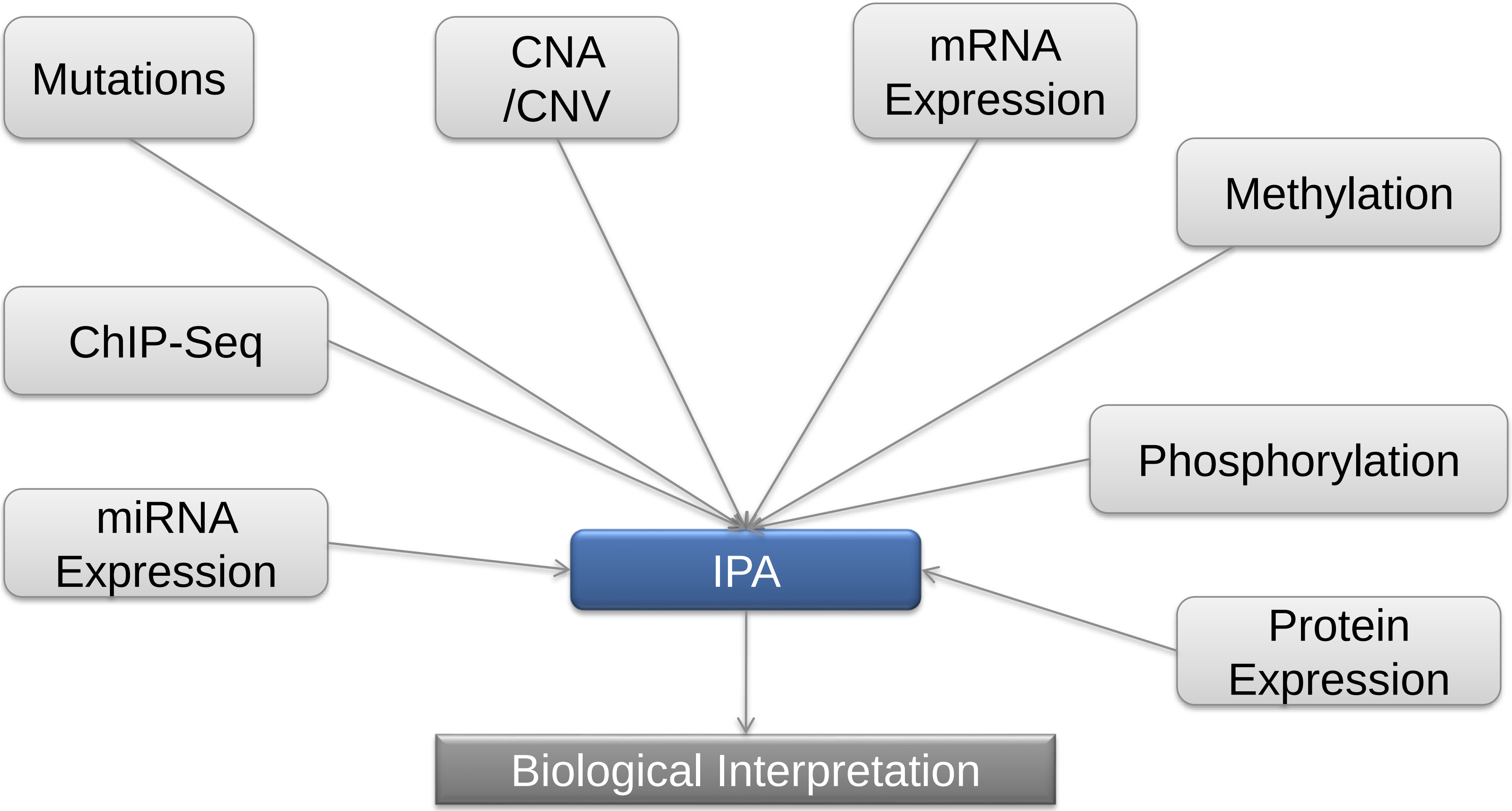
Core Comparison Analysis



Upstream Regula... AFF1 - FOS (p1 of 6)

☐	Analysis	Upstream Regu...	Log Ratio	Molecule Type	Predicted Activation ...	Activation z-score	p-value of overlap	Target molecules in d...	Mechanistic Netw...
☐	Rosiglitazone_10uM	AFF1		transcription regulator			4.13E-02	↑EPHA7, ↑TERT ...all 2	
☐	Amorfruitin2_30uM	Ap1		complex		-0.393	8.61E-03	↓BCL2L11, ↑... ...all 15	
☐	Rosiglitazone_10uM	Ap1		complex		-0.817	4.17E-05	↑ATF3, ↑BC... ...all 22	176 (11)
☐	Rosiglitazone_10uM	ATF1		transcription regulator			3.94E-02	↑BCL2, ↓FUT7 ...all 6	
☐	Amorfruitin2_30uM	ATF2	↓-0.015	transcription regulator		0.509	2.10E-02	↑BCL2, ↑CGA, ...all 9	
☐	Amorfruitin2_30uM	ATF3	↑0.946	transcription regulator			4.34E-02	↑ADIPOQ, ↓C... ...all 7	
☐	Rosiglitazone_10uM	ATF4		transcription regulator		0.089	4.23E-02	↑ATF3, ↓CA9 ...all 12	
☐	Rosiglitazone_10uM	ATN1		transcription regulator			1.69E-02	↓ASGR1, ↑A... ...all 15	
☐	Rosiglitazone_10uM	BACH1		transcription regulator			3.17E-02	↓CXCR4, ↑G... ...all 4	
☐	Amorfruitin2_30uM	BCL3	↑0.095	transcription regulator		0.243	1.83E-02	↓DEFB103A/... ...all 5	
☐	Rosiglitazone_10uM	BCL6		transcription regulator		-0.154	1.36E-02	↓BACH2, ↓BAX...all 15	
☐	Rosiglitazone_10uM	BRD8		transcription regulator			4.13E-02	↑AGPAT2, ↑F... ...all 2	
☐	Rosiglitazone_10uM	BTG2		transcription regulator			1.83E-03	↑CAT, ↑HMOX1 ...all 5	
☐	Rosiglitazone_10uM	CALR		transcription regulator		-0.686	2.05E-02	↓CCL13, ↑CE... ...all 6	
☐	Amorfruitin2_30uM	CARM1	↓-0.076	transcription regulator			3.51E-02	↓CDX2, ↓MM... ...all 4	
☐	Amorfruitin2_30uM	CBFB	↑0.089	transcription regulator		0.239	4.87E-02	↓BCL2L11, ↑... ...all 8	
☐	Amorfruitin2_30uM	CBL	↑0.459	transcription regulator			2.48E-02	↑BCL2, ↓CFTR ...all 5	
☐	Amorfruitin2_30uM	CDX2	↓-1.170	transcription regulator		-0.623	3.86E-03	↑BCL2, ↓CD... ...all 10	
☐	Amorfruitin2_30uM	CEBPA	↑0.894	transcription regulator	Activated	2.462	2.02E-02	↑ADIPOQ, ↑... ...all 30	
☐	Rosiglitazone_10uM	CEBPA		transcription regulator		0.743	1.01E-06	↓ADH1B, ↑... ...all 48	204 (17)

IPA: A Point of Data Integration



Mutations

CNA /CNV

mRNA Expression

Methylation

ChIP-Seq

Phosphorylation

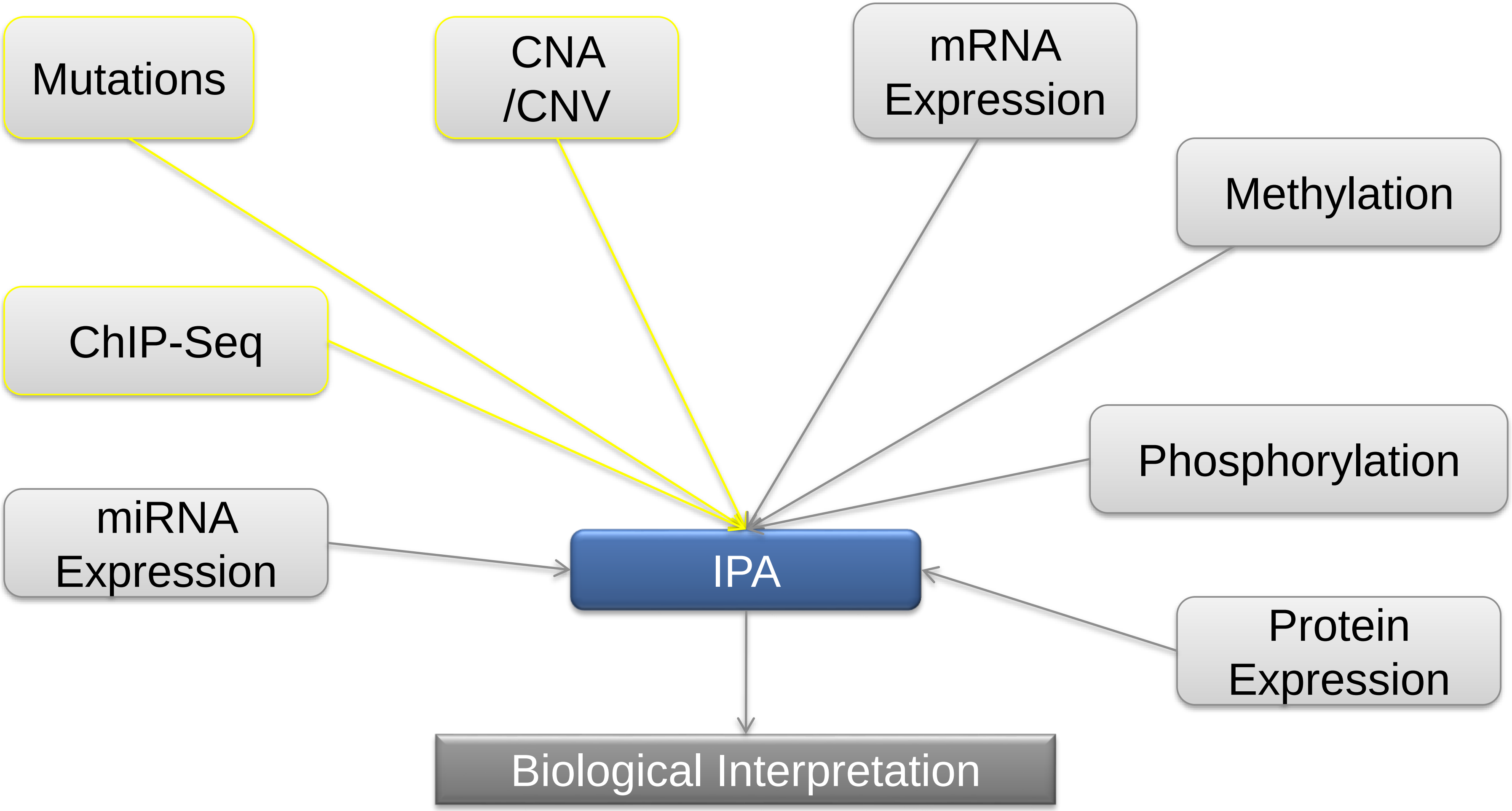
miRNA Expression

IPA

Protein Expression

Biological Interpretation

IPA: A Point of Data Integration



Mutations

CNA /CNV

mRNA Expression

Methylation

ChIP-Seq

Phosphorylation

miRNA Expression

IPA

Protein Expression

Biological Interpretation

Example of Core Analysis with 3-Data Types

	Mutations	CNAs	mRNAs
File Name	GBM paper mutation data	GBM paper CNA	GBM vs Norm Expression
ID	Gene Symbol	Gene Symbol	Gene Symbol
Observation 1	frequency of non-silent mutation across samples Pct. Sample/Other	frequency of CNA across samples [Pct/Other], increase or decrease in copy number [Amp/Other], and [q-value/p-value]	Log2 ratio change, p-value
Core Analysis	Frequency of mutation ≥ 2%	p-value < 0.05	Log ratio ≥ |1.5|

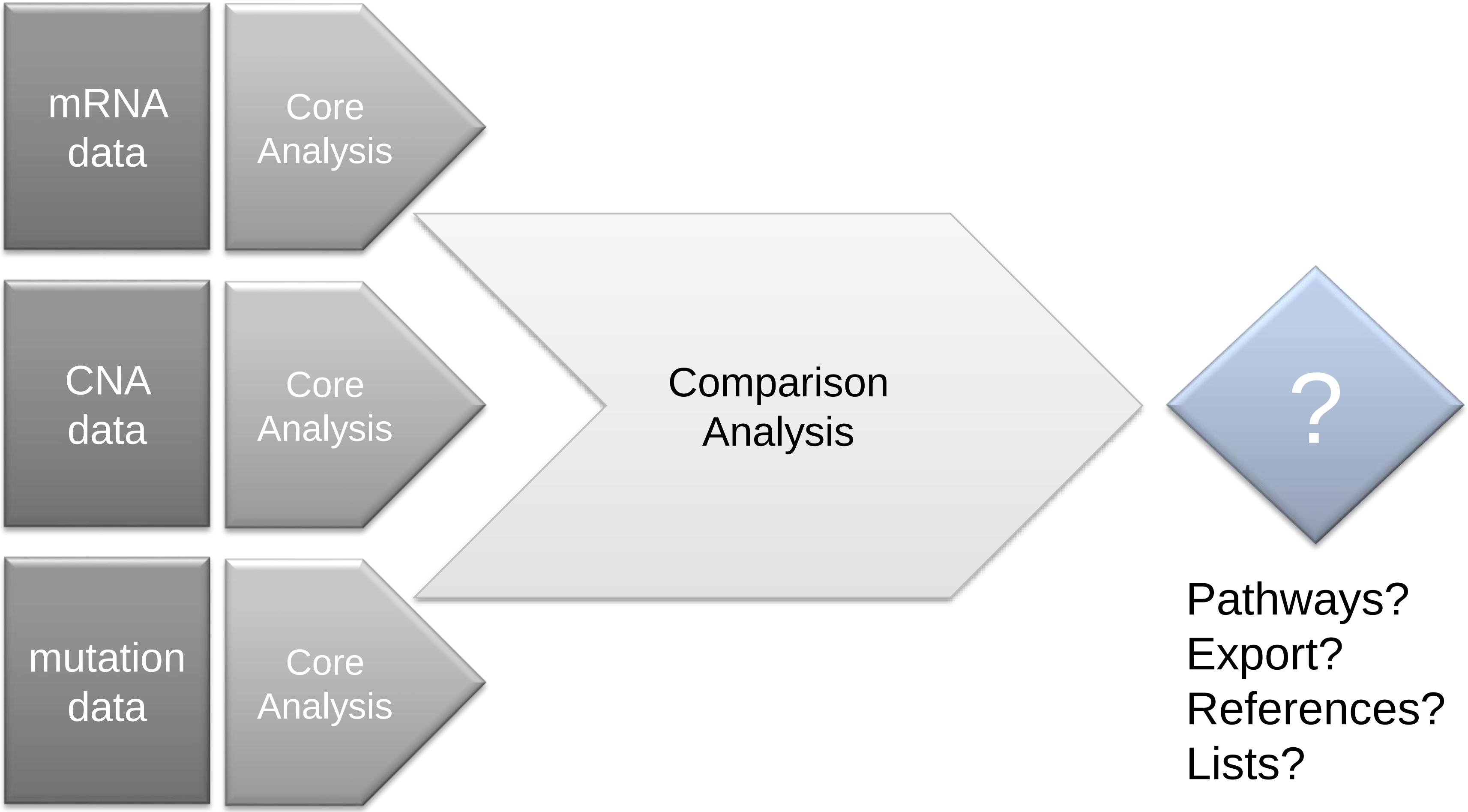
Keep in mind

To set the same Reference Set across the 3 core analyses

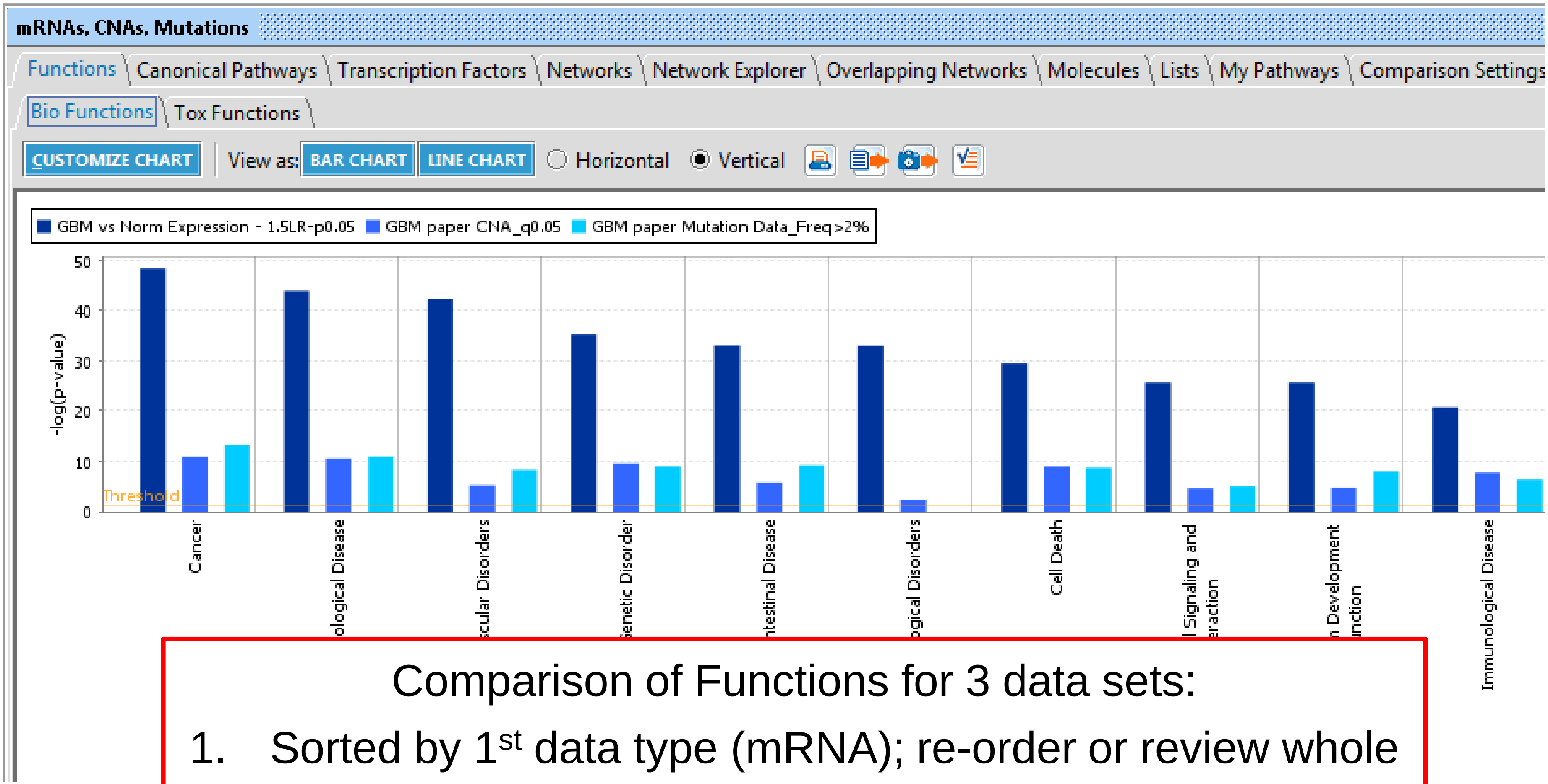
To check the Expression value type used for coloring the nodes

What do you want out of this comparison?

Review your workflow – What are your goals?



Pathways?
Export?
References?
Lists?



Comparison of Functions for 3 data sets:

1. Sorted by 1st data type (mRNA); re-order or review whole table for Functions significant for other data types
2. Look for Functions common to mRNA, CNA, mutations from glioblastoma
3. Table may be customized or exported

Single Experiment

- Time Course
- Dose Response

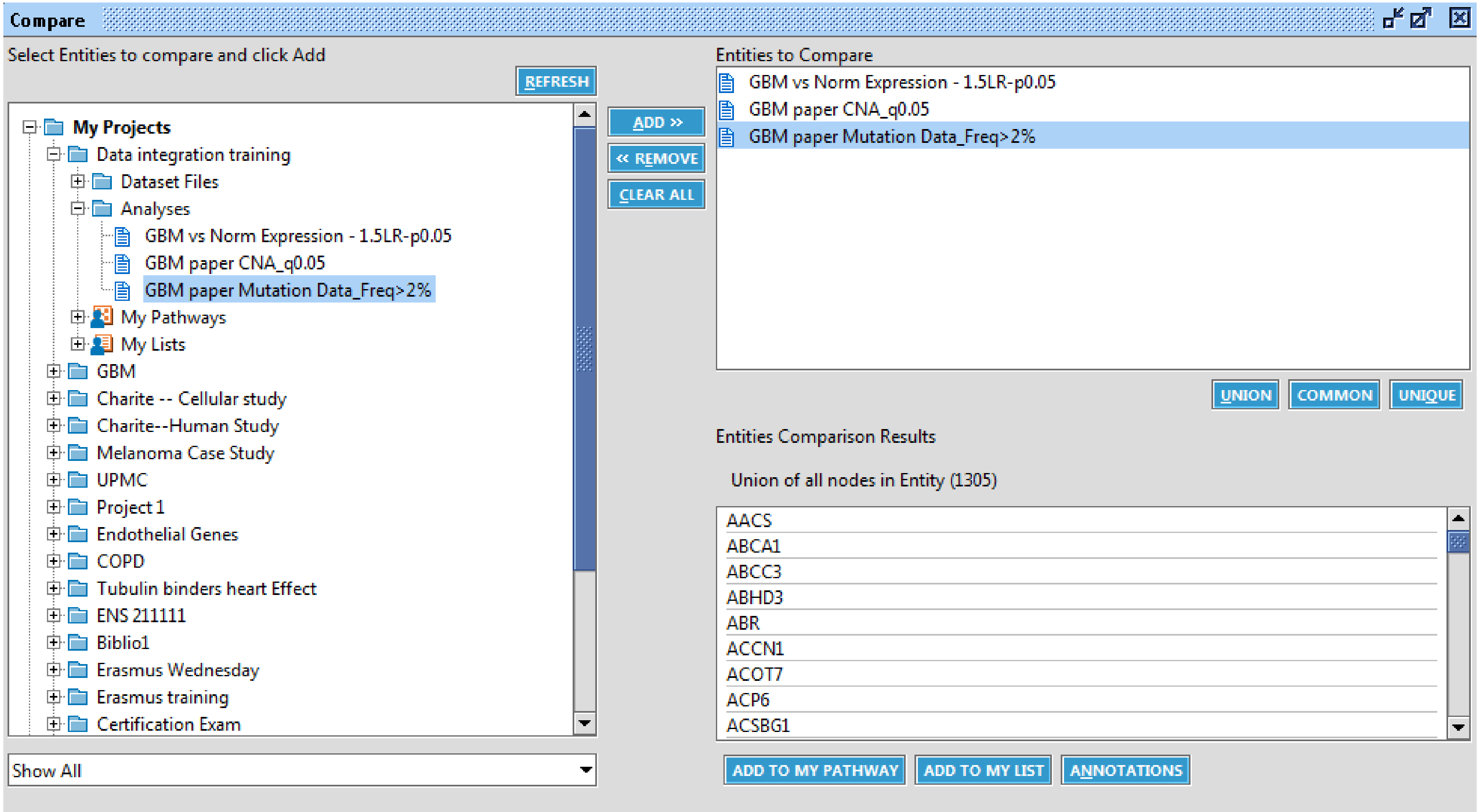
Multi Experiment

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

Set Analysis

- Exploring Common Molecules across one or more experiment (s)

Compare Tool



Select Entities to compare and click Add

- My Projects
  - Data integration training
    - Dataset Files
    - Analyses
      - GBM vs Norm Expression - 1.5LR-p0.05
      - GBM paper CNA_q0.05
      - GBM paper Mutation Data_Freq>2%
    - My Pathways
    - My Lists
  - GBM
  - Charite -- Cellular study
  - Charite--Human Study
  - Melanoma Case Study
  - UPMC
  - Project 1
  - Endothelial Genes
  - COPD
  - Tubulin binders heart Effect
  - ENS 211111
  - Biblio1
  - Erasmus Wednesday
  - Erasmus training
  - Certification Exam

Show All

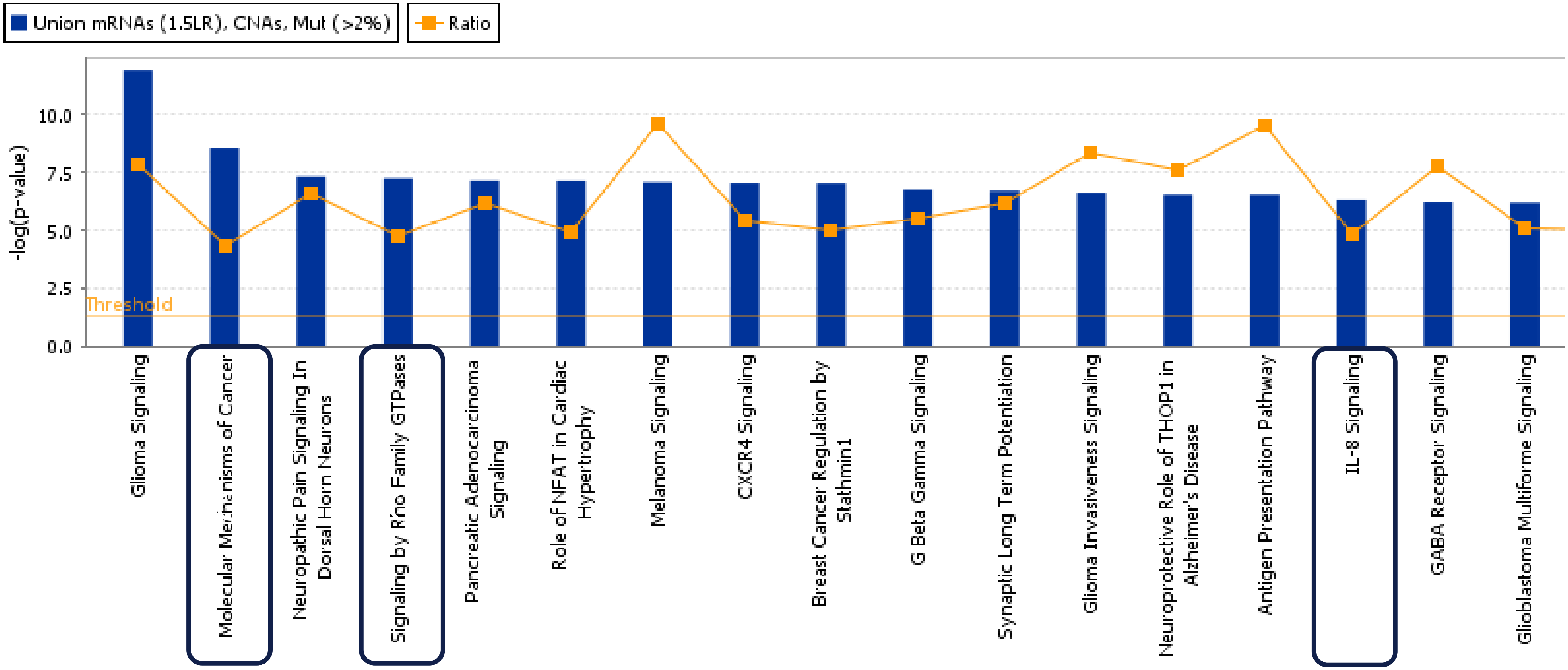
Entities to Compare

- GBM vs Norm Expression - 1.5LR-p0.05
- GBM paper CNA_q0.05
- GBM paper Mutation Data_Freq>2%

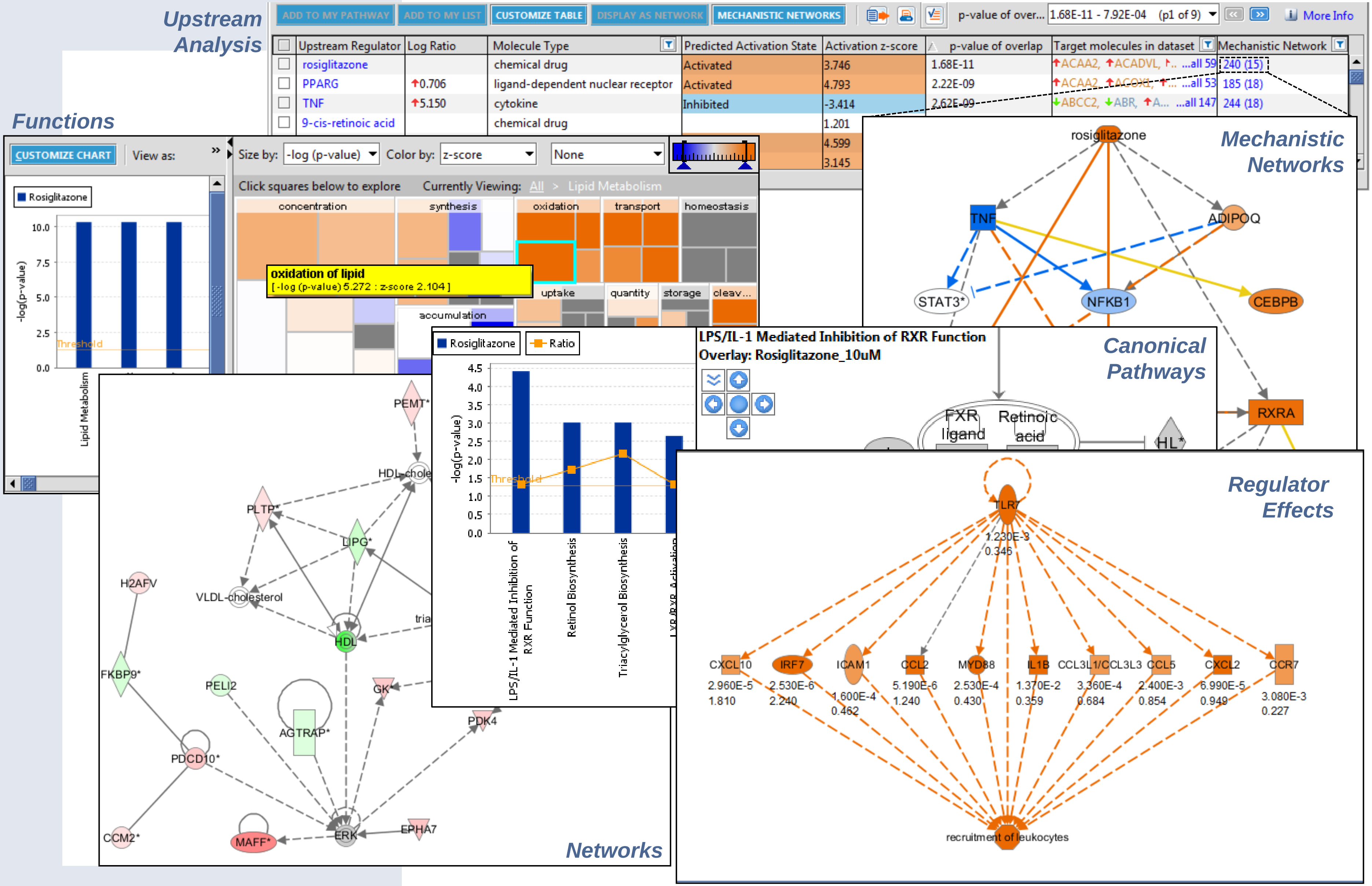
Entities Comparison Results

Union of all nodes in Entity (1305)

AACS
ABCA1
ABCC3
ABHD3
ABR
ACCN1
ACOT7
ACP6
ACSBG1


Union mRNAs (1.5LR), CNAs, Mut (>2%)
Ratio
-log(p-value)
10.0
7.5
5.0
2.5
0.0
Threshold
Glioma Signaling
Molecular Mechanisms of Cancer
Neuropathic Pain Signaling In Dorsal Horn Neurons
Signaling by Rho Family GTPases
Pancreatic Adenocarcinoma Signaling
Role of NFAT in Cardiac Hypertrophy
Melanoma Signaling
CXCR4 Signaling
Breast Cancer Regulation by Stathmin1
G Beta Gamma Signaling
Synaptic Long Term Potentiation
Glioma Invasiveness Signaling
Neuroprotective Role of THOP1 in Alzheimer's Disease
Antigen Presentation Pathway
IL-8 Signaling
GABA Receptor Signaling
Glioblastoma Multiforme Signaling

IPA Core Analysis:



Upstream Analysis

ADD TO MY PATHWAY | ADD TO MY LIST | CUSTOMIZE TABLE | DISPLAY AS NETWORK | MECHANISTIC NETWORKS

p-value of over... 1.68E-11 - 7.92E-04 (p1 of 9)

☐	Upstream Regulator	Log Ratio	Molecule Type	Predicted Activation State	Activation z-score	p-value of overlap	Target molecules in dataset	Mechanistic Network
☐	rosiglitazone		chemical drug	Activated	3.746	1.68E-11	↑ACAA2, ↑ACADVL, ↑.. ...all 59	240 (15)
☐	PPARG	↑0.706	ligand-dependent nuclear receptor	Activated	4.793	2.22E-09	↑ACAA2, ↑ACOX1, ↑... ...all 53	185 (18)
☐	TNF	↑5.150	cytokine	Inhibited	-3.414	2.62E-09	↓ABCC2, ↓ABR, ↑A... ...all 147	244 (18)
☐	9-cis-retinoic acid		chemical drug		1.201			
					4.599			
					3.145			

Functions

Size by: -log (p-value) Color by: z-score None

Click squares below to explore Currently Viewing: All > Lipid Metabolism

oxidation of lipid
[-log (p-value) 5.272 : z-score 2.104]

Mechanistic Networks

Canonical Pathways

LPS/IL-1 Mediated Inhibition of RXR Function
Overlay: Rosiglitazone_10uM

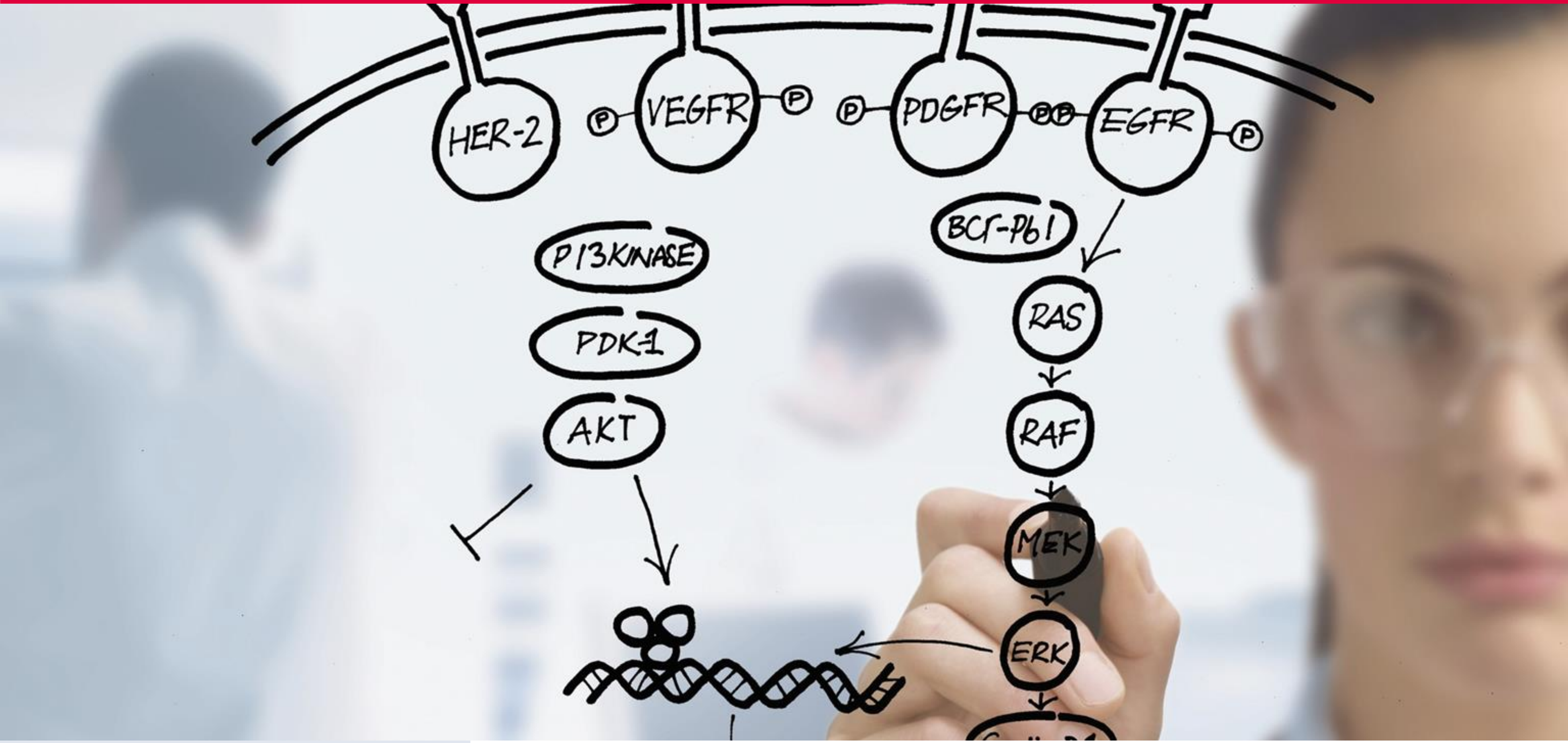
Networks

Regulator Effects

IPA®

Live Demo

Q&A



歡迎與我們聯絡

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GGA

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