IPA 系統生物學分析軟體暨資料庫

洪千琇 **Chien**
Product Specialist

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Copyright and Disclaimer

Basic training course

A. **Introduction and Getting Started in IPA**
     IPA介紹與啟動IPA

B. **Searching and Accessing the Knowledge Base**
     利用IPA進行搜尋

C. **Building and Editing a Pathway for Publication**
     使用IPA進行分子模型建構並繪製訊息傳遞路徑

Advanced training course

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

C. Comparison Analysis
     比較分析結果的差異

IPA是 All-in-one, web-based 的分析軟體與資料庫，幫助研究人員分析手上分子生物學實驗後的資料，可以快速提供研究人員更多的證據與文獻去解釋複雜的實驗背景與實驗成因並建構可以延伸的假設。

INTERPRET BIOLOGICAL MEANING

Generate Data
- mRNA
- miRNA
- Protein
- SNP
- Metabolite

Perform Basic Statistics
- Background Correction
- Normalization
- p-value
- SNP call

Query Ingenuity® Knowledge Base
- Accurate data
- Detailed structure
- Millions of findings
- Up-to-date

Analyze Affected Biology
- Diseases
- Functions
- Networks
- Pathways

Visualize Data in Context
- Exploration
- Navigation
- Interaction
- Discovery

IPA 的應用:

- 生物標記開發研究

- 藥物活性機轉研究

- 藥物毒性機制研究

- 疾病發生機制研究

IPA 支援的實驗平台與技術:

- 基因表現實驗:
  qPCR analysis
  Microarray
  RNA-Seq (NGS)
  microRNA
  mRNA

- 蛋白質體實驗
- 代謝體實驗
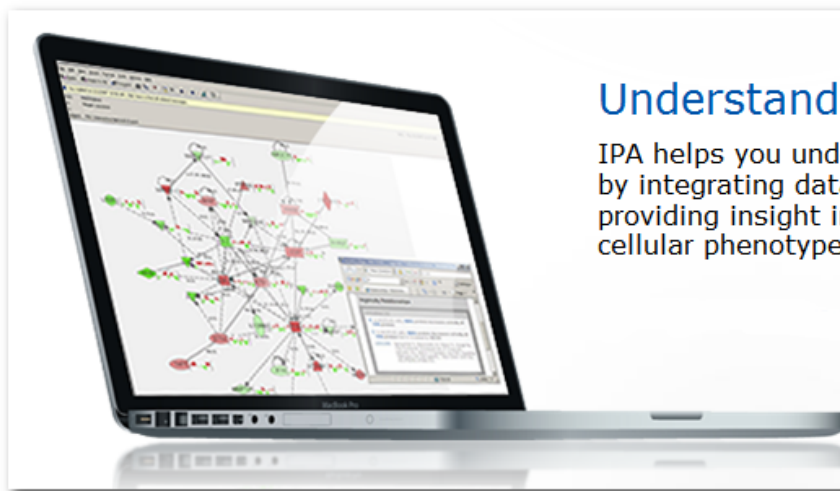
Understand Complex 'Omics Data

IPA helps you understand complex 'omics data at multiple levels by integrating data from a variety of experimental platforms and providing insight into the molecular and chemical interactions, cellular phenotypes, and disease processes of your system.

>10,000 publications that used IPA -- and growing!
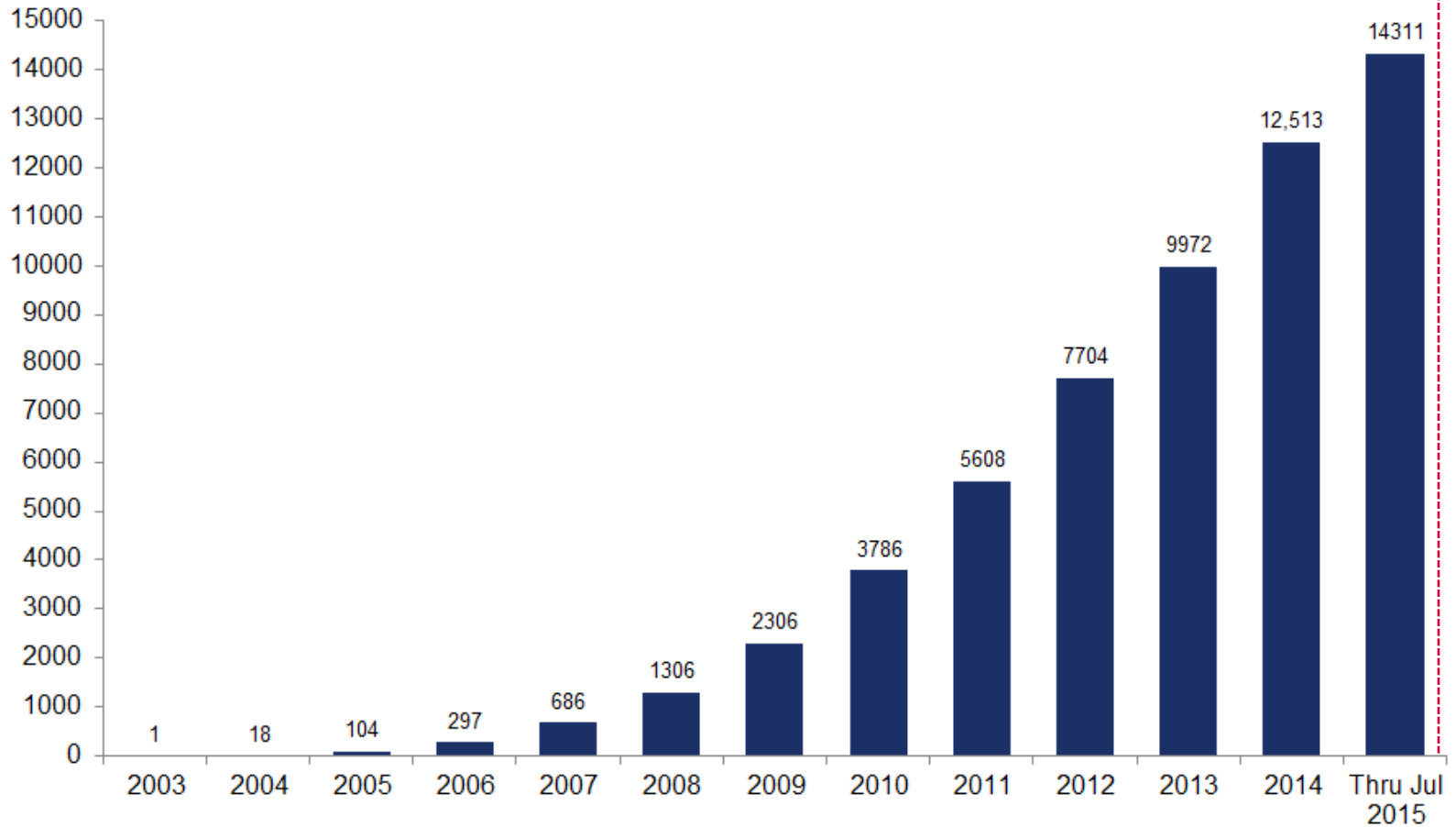
>10,000 publications that used IPA -- and growing!

Discovery

nature
LETTERS — Genomic analysis of increased host immune and cell death responses induced by 1918 influenza virus

Biomarkers

nature medicine
Classification and prediction of clinical Alzheimer's diagnosis based on plasma signaling proteins

Toxicology

TOXICOLOGICAL SCIENCES
Correlation between protein accumulation profiles and conventional toxicological findings using a model antiandrogenic compound, flutamide.

Mechanism of Action

Proceedings of the National Academy of Sciences of the United States of America — PNAS
MYC inhibition induces metabolic changes leading to accumulation of lipid droplets in tumor cells

Disease Models

Cell PRESS
An iPSC Line from Human Pancreatic Ductal Adenocarcinoma Undergoes Early to Invasive Stages of Pancreatic Cancer Progression

Pharmacogenomics

NEUROBIOLOGY of AGING
Pharmacogenomics in Alzheimer's disease: a genome-wide association study of response to cholinesterase inhibitors

Gene Expression

Metabolomics

Proteomics

Genotyping

Epigenetics

miRNA

Ingenuity Expert Findings

創源生技 GGA
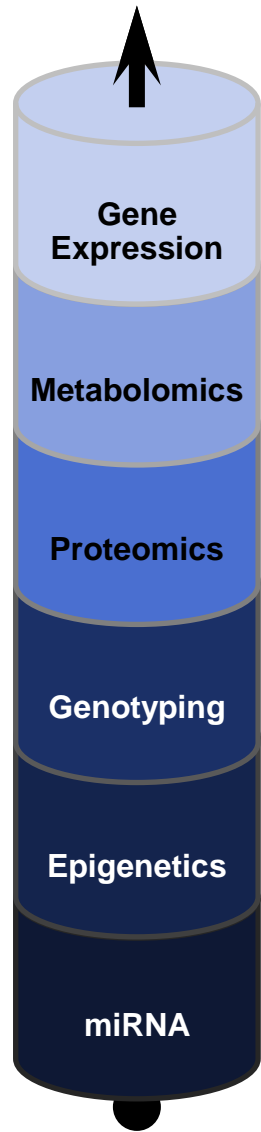
From full text, contextual detail, experimentally demonstrated

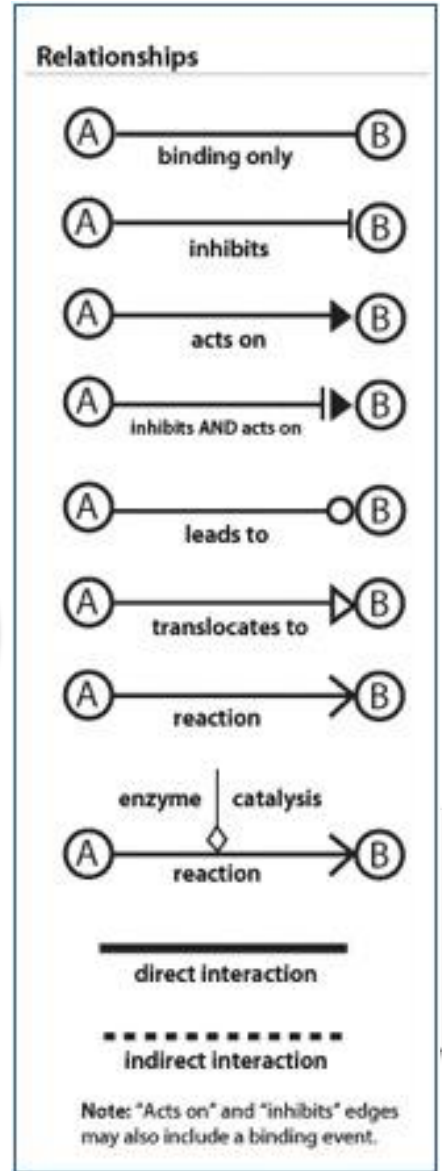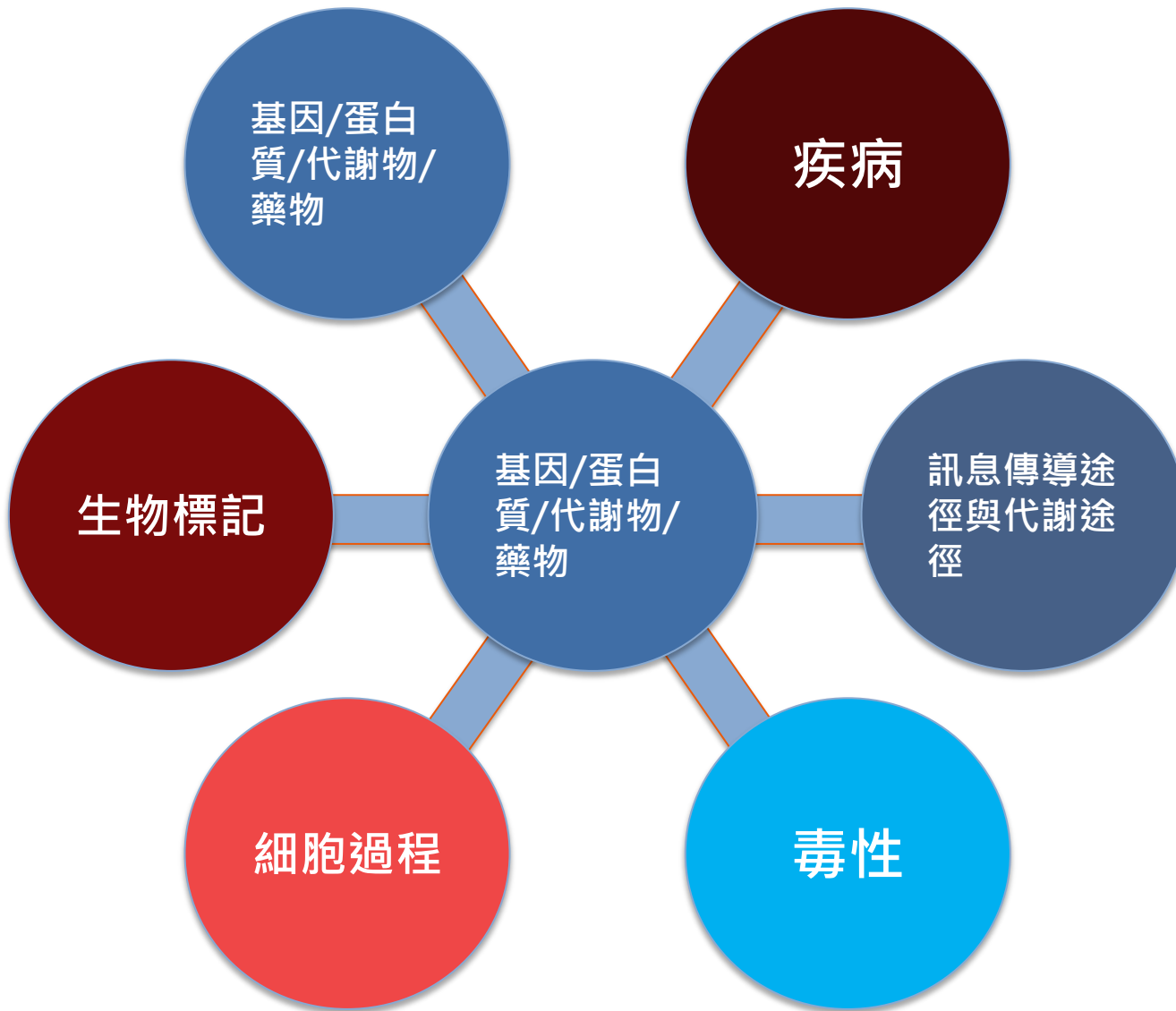| Original sentence from publication	Ingenuity Expert Findings
nNOS overexpression mice showed reduced myocardial contractility.	Transgenic nNOS in myocardium from mouse heart decreases the contractility of myocardium in left ventricle from mouse heart.
Francisella organisms efficiently induce IL-1beta processing and release.	Francisella tularensis subsp. novicida U112 increases (in a time-dependent manner) release of human IL1B protein from human monocytes.

► **Contextual details**: Manual curation process captures relevant details

► **Experimentally demonstrated:** Findings are from full text articles – includes tables and figures

► **Structured:** Supports computation and answering in-depth biological questions in the relevant context

► **High quality:** QC'd to ensure accuracy

► **Timely information:** Weekly updates so up to date information is captured

五百多萬筆以上IPA Finding，包含各種生物分子的關係建構

zygosity   gene   disease/phenotype

In mouse, homozygous mutant **mouse Abcb4 gene** (knockout) **increases** chronic **cholestasis in** mouse.

Experiment Type: bilirubin quantification assay, in vitro phosphatase assay

22982378   Hochrath K, Krawczyk M, Goebel R, Langhirt M, Rathkolb B, Micklich K, Rozman J, Horsch M, Beckers J, Klingenspor M, Fuchs H, Gailus-Durner V, Wolf E, Acalovschi M, Volmer DA, Hrabě de Angelis M, Lammert F. The hepatic phosphatidylcholine transporter ABCB4 as modulator of glucose homeostasis. FASEB J. 2012 Dec;26(12):5081-91. Epub 2012 Sep 14.

Source: Ingenuity Expert Findings

mutation type   direct of the effect on disease/phenotype
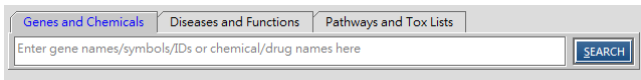
cholestasis

ABCB4

IPA Finding均由博士級人員由數千種期刊與第三方資料庫萃取而得，融合下列資訊

- Species
- Synonyms
- Experimental method
- Site of post-translational modification

- Direction of change
- Tissue context
- Cell line context
- Original source

Entry Points in IPA

創源生技
GGA

Biological Questions

Search

Experiment Data
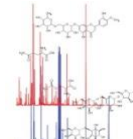
Expression arrays   **Mass spec**
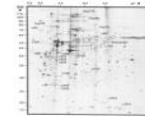
Protein arrays   **2D Gel electrophoresis**

Custom Pathway
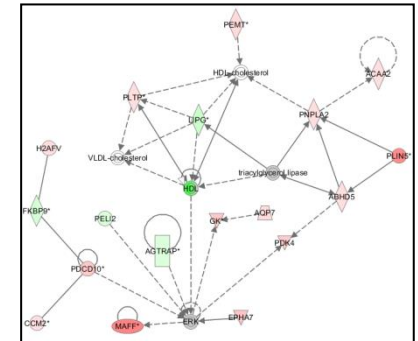
Networks

Core   **IPA-Biomarker**

IPA-Tox   **IPA-Metabolomics**

Bio/Tox Functions
Diseases/Disorders
Canonical Pathways
Upstream regulators
Mechanistic/Casual Network
Interaction Network

CP: Actin Cytoskeleton Signaling   **CP:** Axonal Guidance Signaling

CP: RhoA Signaling
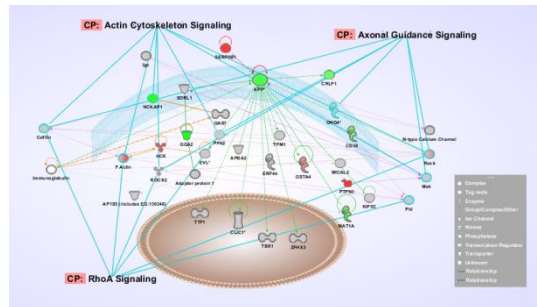
Communicate & Collaborate

QIAGEN

創源生技
GGA

Gene View, Chem View, and Disease/Function View

Human and Mouse Isoform Views

Canonical Pathways

Upstream Analysis

Diseases and Biological Functions

Regulator Effects

Comparison Analysis

Interaction Networks, Build and Overlay tools

BioProfiler

IsoProfiler (Beta)

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New IPA Client Installer

- Easier access

- Faster launch

- Can launch without a browser or Java plugin

https://www.ingenuity.com/products/login
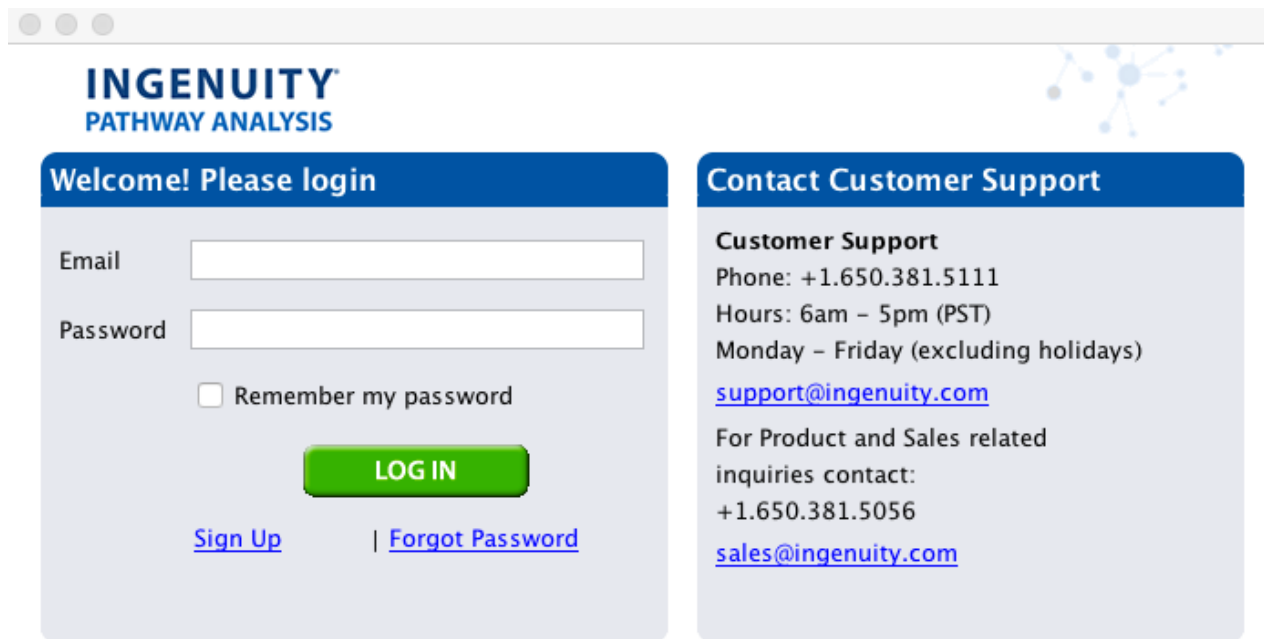
Ingenuity Platform: 15-years, massive investment

Highest-quality interpretation of genomics and sequencing data
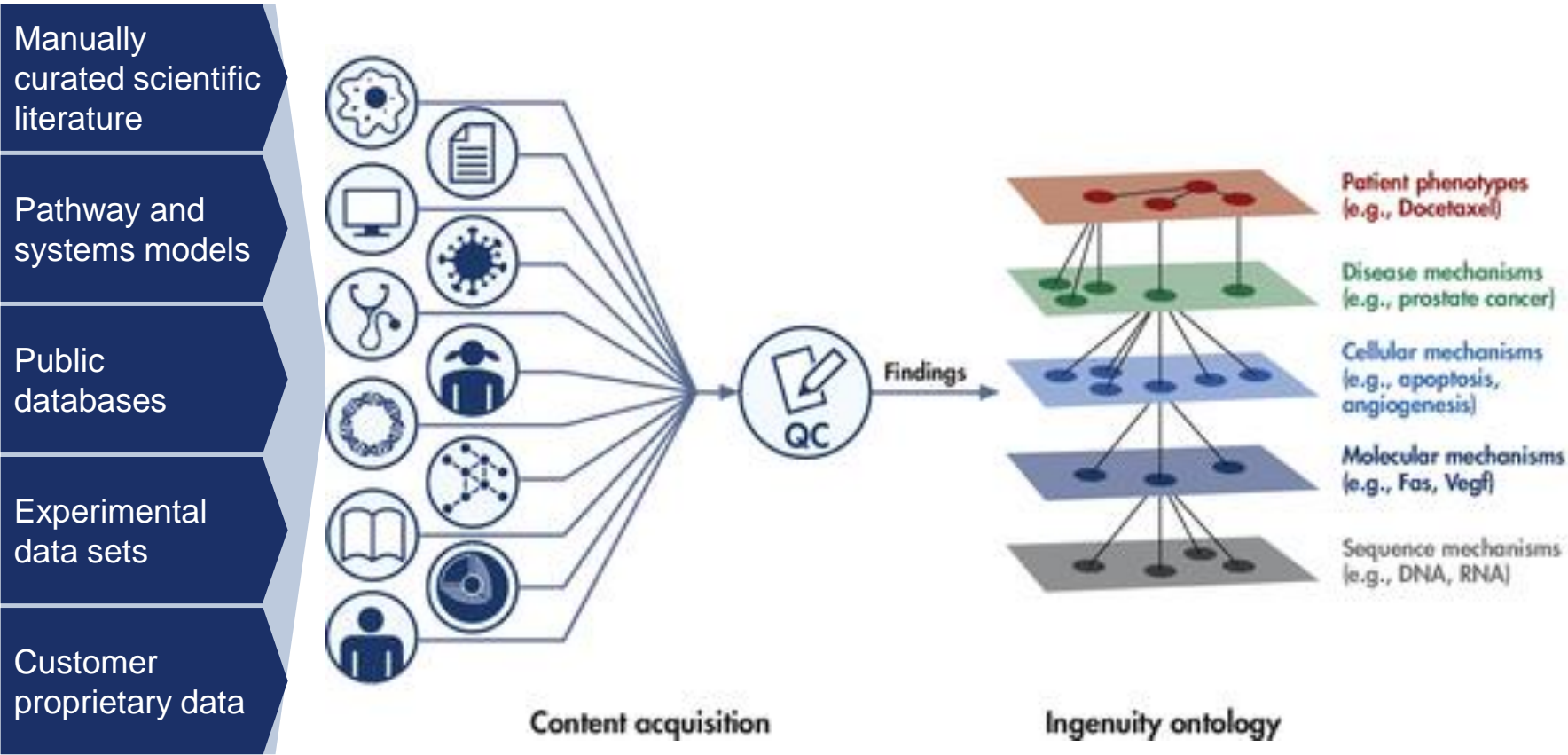
Manually curated scientific literature

Pathway and systems models

Public databases

Experimental data sets

Customer proprietary data

Findings

QC

Patient phenotypes (e.g., Docetaxel)

Disease mechanisms (e.g., prostate cancer)

Cellular mechanisms (e.g., apoptosis, angiogenesis)

Molecular mechanisms (e.g., Fas, Vegf)

Sequence mechanisms (e.g., DNA, RNA)

Content acquisition

Ingenuity ontology

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- Searching Basics
- **Gene/chemical search and results**
- **Function/Disease search and results**
- **Pathway/Tox list search and results**
- Advanced search: Limiting results to a molecule type, family or subcellular location
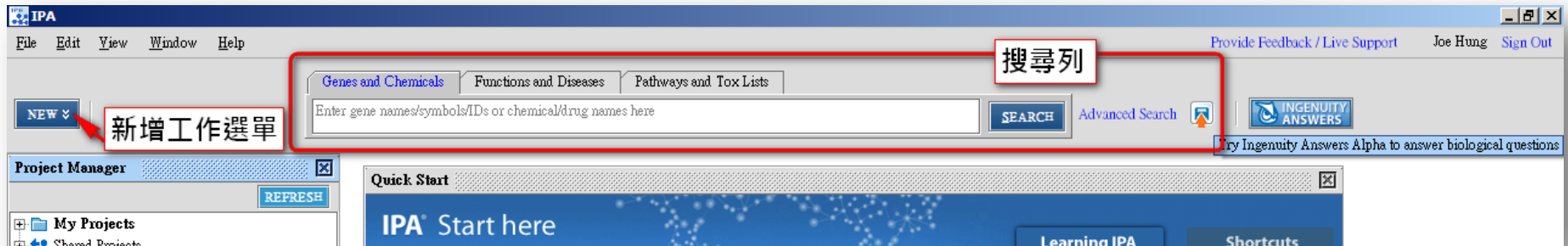
- **Finding:**
  - A single piece of evidence from a literature source or database in the **Ingenuity Knowledge Base**
  - Includes context of the fact such as experiment type, species, tissue/cell location, etc.

- **Canonical Pathway (Signaling and Metabolic)**
  - Are generated prior to data input, based on the literature
  - Do NOT change upon data input
  - Do have directionality

Live Demo

Build and Grow Networks of Molecules
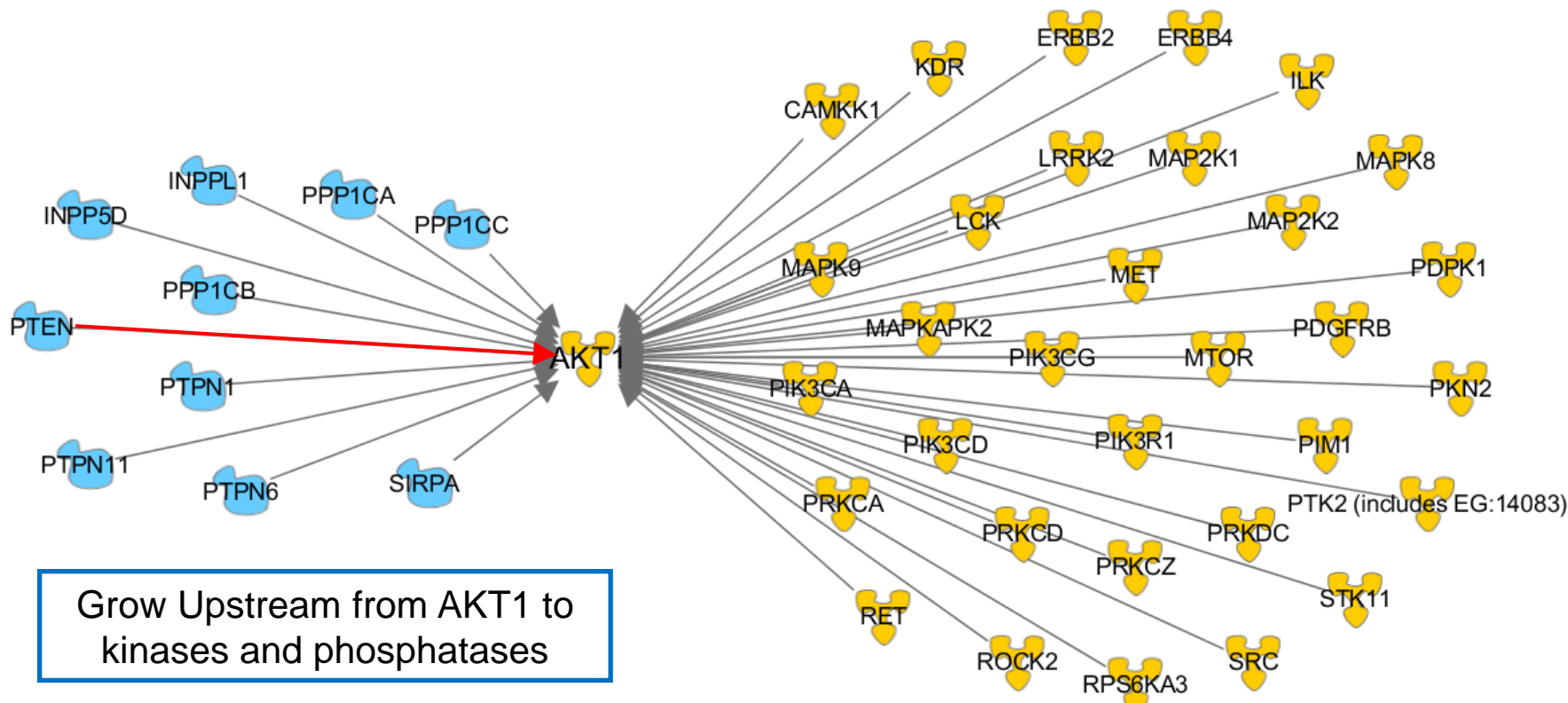
Grow Upstream from AKT1 to kinases and phosphatases

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

Introduction to Pathway Building

Key Terminology

Adding Molecules to a New Pathway

General pathway navigating

Using the Build Tools

Understanding the legend

Using the Overlay tools

Saving work for future analyses

How to build pathway

Networks:
- Generated de novo based upon input data
- Do NOT have directionality

Canonical Pathways (Signaling and Metabolic):
- Are pre-built and generated prior to data input, based on the literature
- Do NOT change upon data input
- Do have directionality (proceed "from A to Z")

My Pathways and **Path Designer Pathways**:
- Custom built pathways manually created based on user input

Relationship Type:
- An interaction between two molecules in IPA (seen as a line)
- Direct (physical contact) and Indirect (do NOT require physical contact)

Live Demo

- Calculates the "Shortest Path" between 2 molecules or 2 sets of molecules

- If 2 molecules/sets don't have specific connections in IPA, Path Explorer will find how many and which molecules can be added to this pathway to create the shortest path
  - Shortest Path (n)
  - Shortest Path + 1 (n+1)
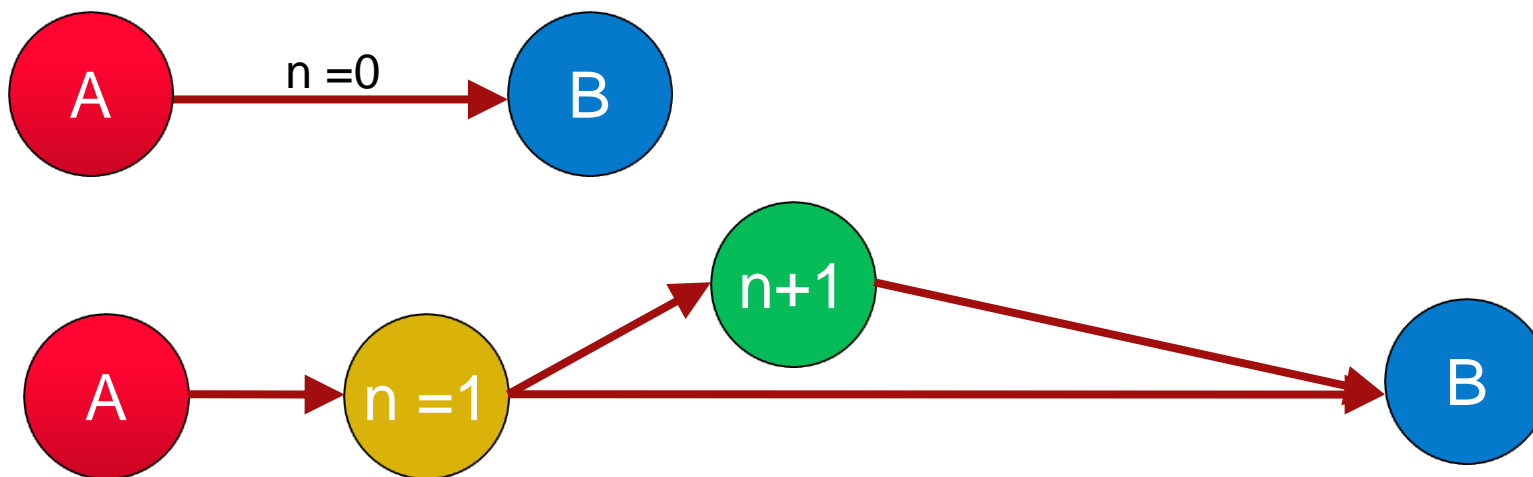
Advanced training course

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IPA分析結果介紹

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比較分析結果的差異

D. Q & A

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Supported Identifiers for Data Upload

Vendor IDs	Gene	Protein	Transcript	microRNA	SNP	Chemical
Affymetrix	Entrez Gene (LocusLink)	GenPept	Ensembl	miRBase (mature)	Affy SNP IDs	CAS Registry Number
Agilent	GenBank	International Protein Index (IPI)	RefSeq	miRBase (stemloop)	dbSNP	HMDB
Life Tech (ABI)	Symbol-human (HUGO/ HGNC, EG)	UniProt/ Swiss-Prot Accession	UCSC (hg18)			KEGG
Codelink	Symbol-mouse (EG)		UCSC (hg19)			PubChem CID
Illumina	Symbol- rat (EG)					
Ingenuity	GI Number					
	UniGene					

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

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

Identify functions, diseases, and canonical pathways associated with your data
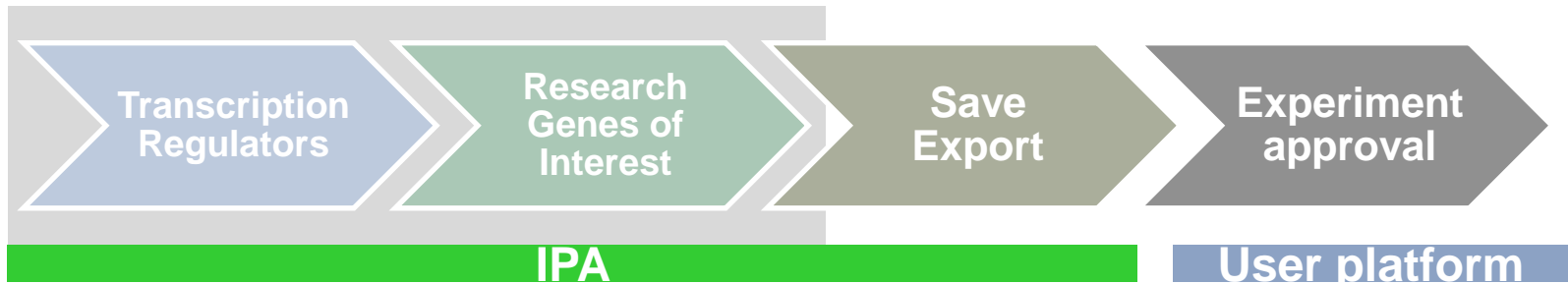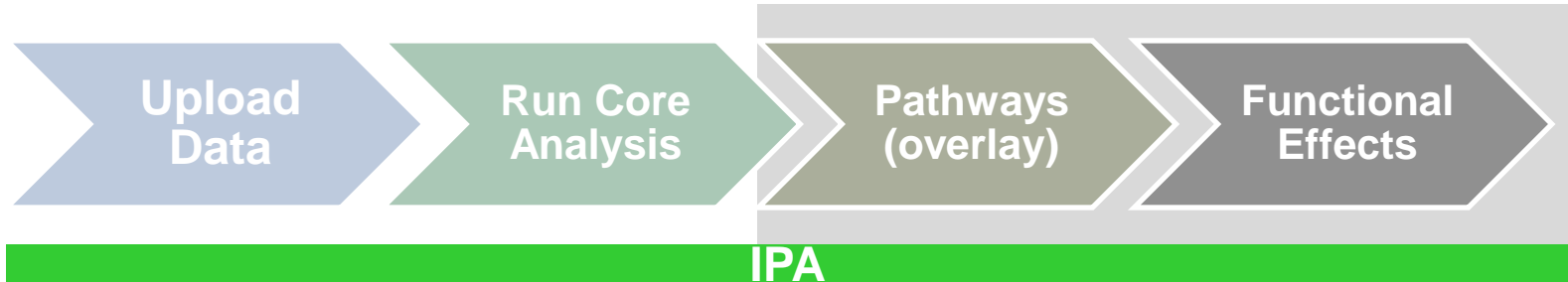
General Analysis Workflow in IPA

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

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 (	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 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	1-10-11-10	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	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

■ **重複性實驗的數值平均、p-value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。

Live Demo

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B.　Functional Interpretation in IPA
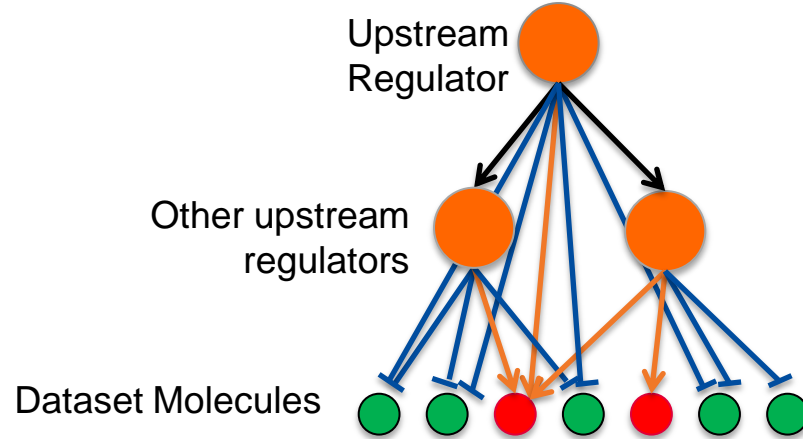　　　IPA分析結果介紹
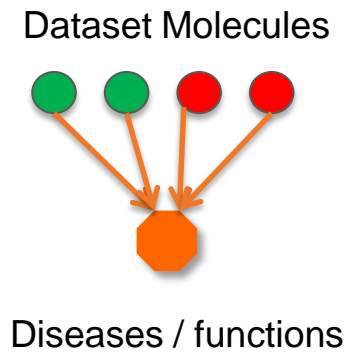
C.　Comparison Analysis
　　　比較分析結果的差異

D.　Q & A

Network types in IPA

Upstream Analysis

Dataset Molecules
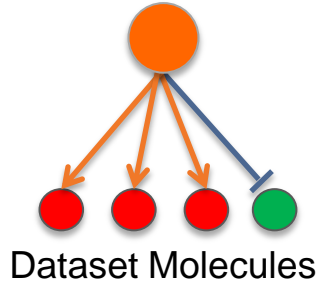
Mechanistic Network of Upstream Regulators

Upstream Regulator

Other upstream regulators

Dataset Molecules

Function Analysis

Dataset Molecules

Diseases / functions

Regulator Effect Network

Any

Diseases / functions

Interaction Network

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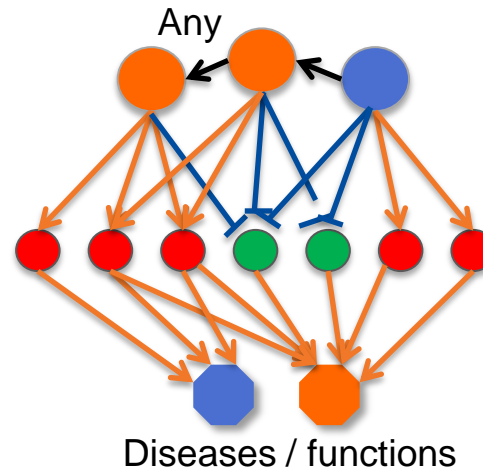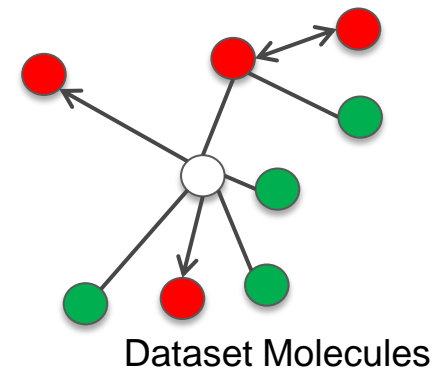
Functions analysis: 呈現因為分子變化而受影響的生物功能、疾病與毒性學結果。

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

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
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

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
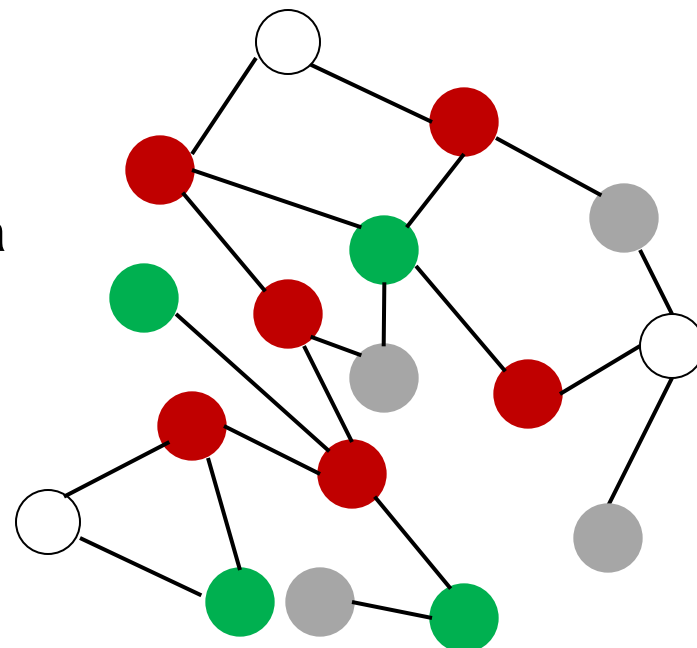
Molecules per Network	Networks per Analysis
35 ▼	25 ▼
35	10
70	25
140	50

Single Experiment
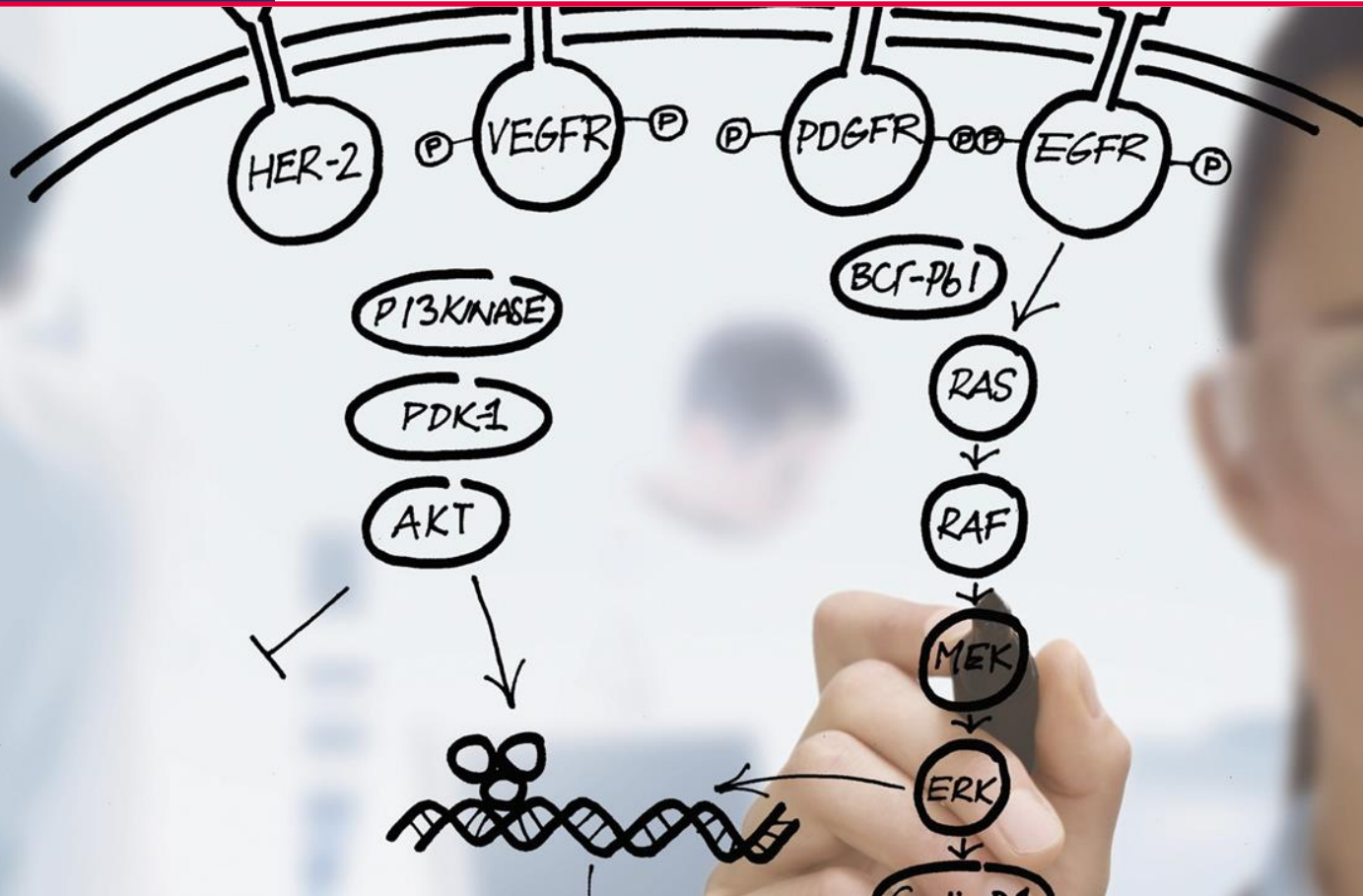
- Time Course
- Dose Response

Multi Experiment

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

Set Analysis

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

Q&A

歡迎與我們聯絡

Office: +886-2-2795-1777#3014

Fax: +886-2-2793-8009 EXT 1022

My E-mail: Chienhung@gga.asia

MSC Support: **msc-support@gga.asia**