

## 2018 IPA 系統生物學分析軟體暨資料庫 基礎操作課程

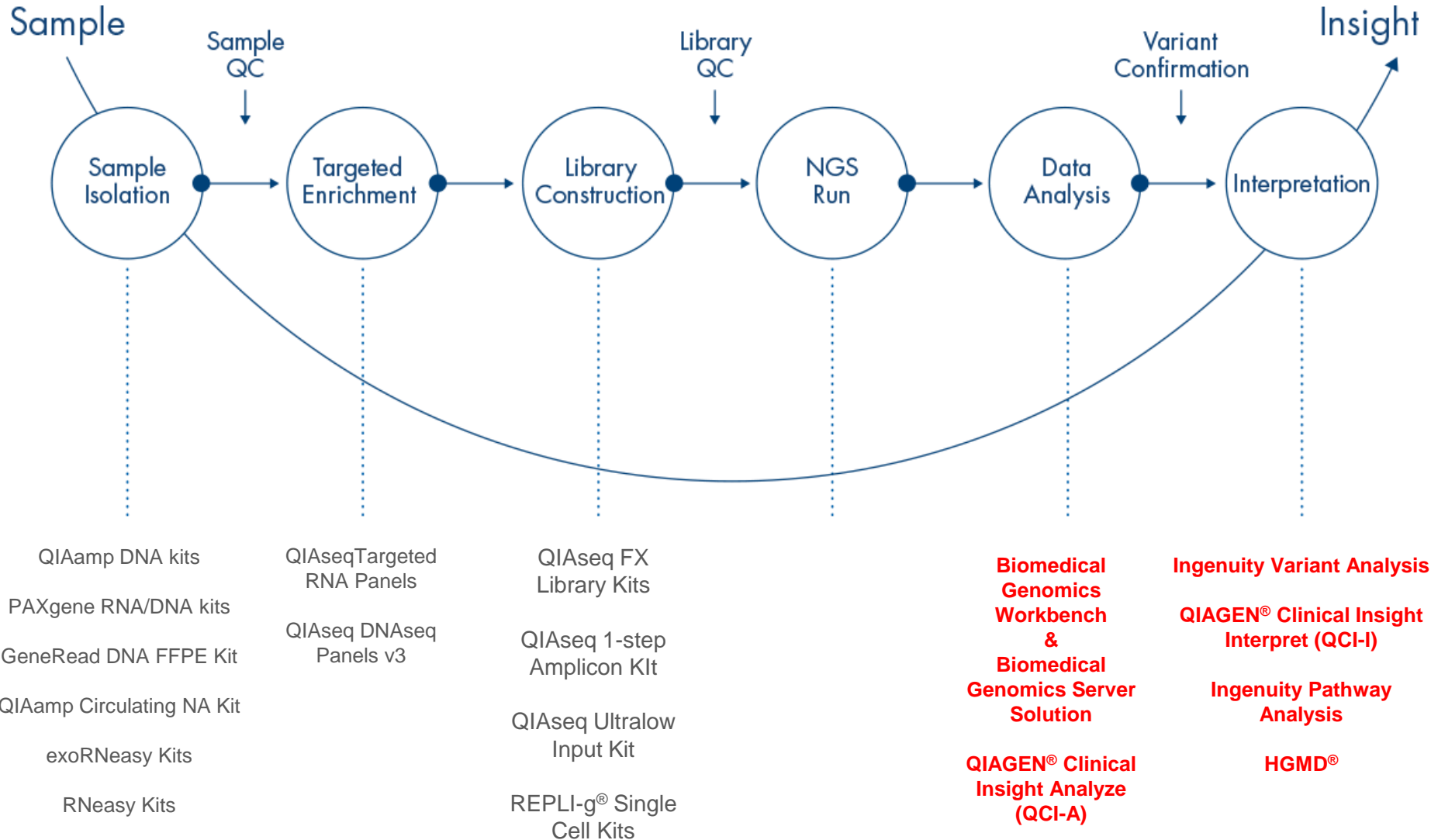
Clair 蔡宜庭

Specialist

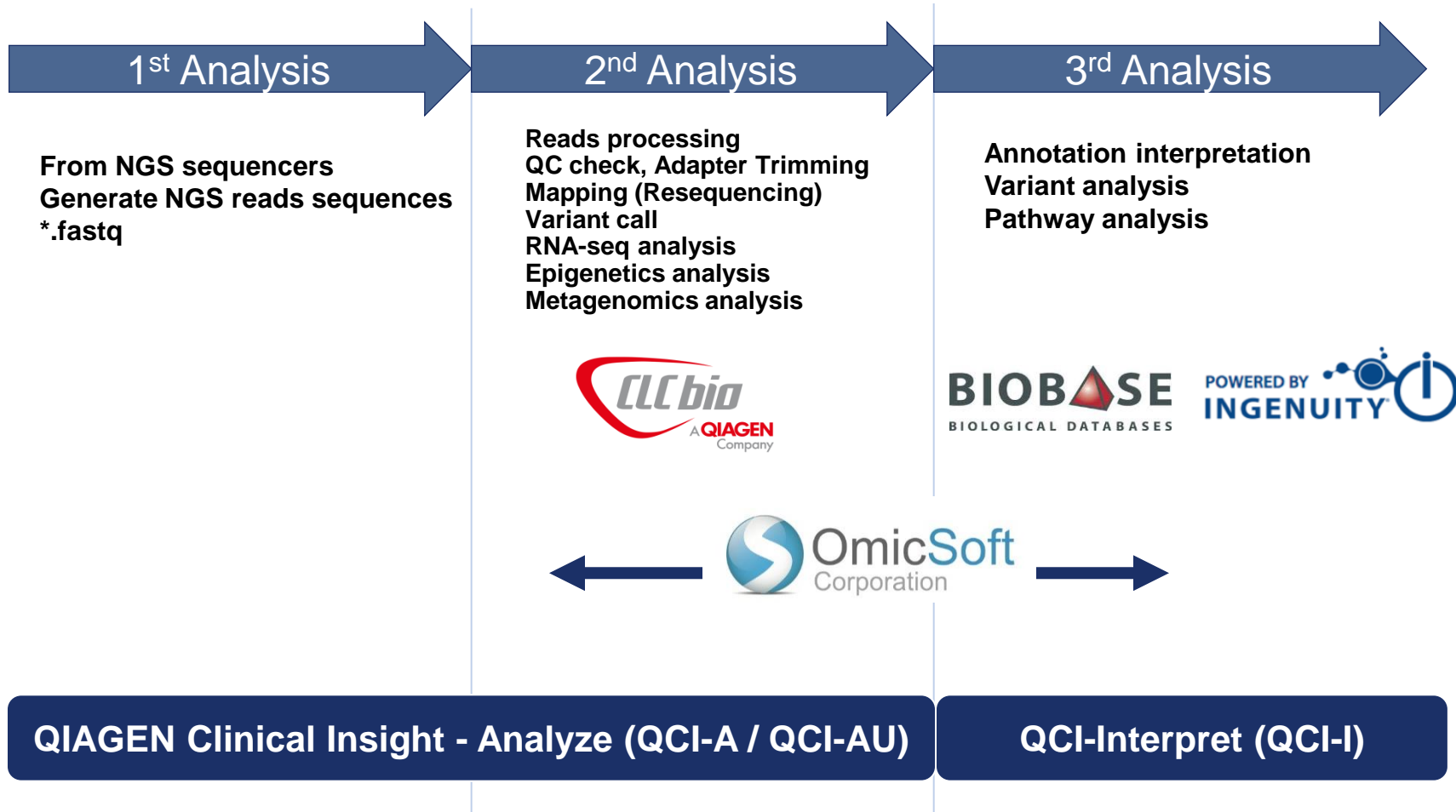
National Yang Ming University

## **Copyright © 2018 GGA Corp. All rights reserved.**

- This presentation and/or any related documents contains statements regarding our plans or expectations for future features, enhancements or functionalities of current or future products (collectively "Enhancements"). Our plans or expectations are subject to change at any time at our discretion. Accordingly, GGA Corp. is making no representation, undertaking no commitment or legal obligation to create, develop or license any product or Enhancements.
- The presentation, documents or any related statements are not intended to, nor shall, create any legal obligation upon GGA Corp., and shall not be relied upon in purchasing any product. Any such obligation shall only result from a written agreement executed by both parties.
- In addition, information disclosed in this presentation and related documents, whether oral or written, is confidential or proprietary information of GGA Corp.. It shall be used only for the purpose of furthering our business relationship, and shall not be disclosed to third parties.



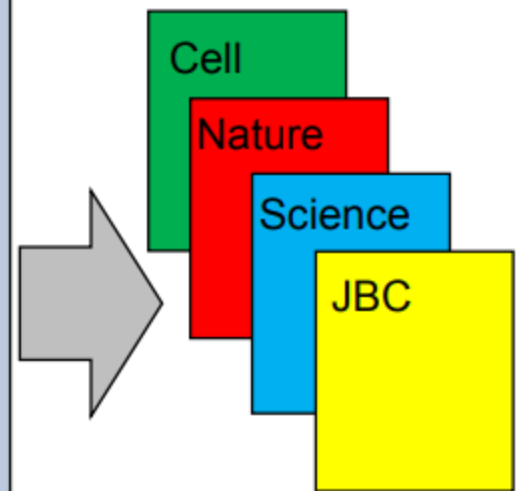
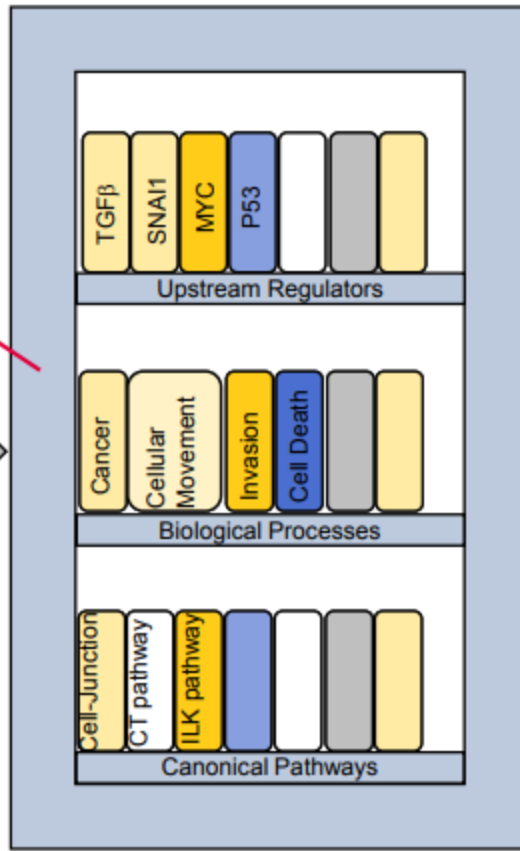
## By NGS Data analysis workflow



ID	A	B	C	D
	Log2Ratio	p-value	Intensity	RPM/FPKM
1				
2	NM_138768	0.14	8.68E-01	2921.85
3	NM_016380	-0.99	2.24E-01	1649.26
4	NM_138932	-0.02	9.83E-01	1.87
5	NM_014876	-0.02	9.86E-01	1.77
6	NM_138933	0.02	9.79E-01	1.93
7	NM_200914	-4.79	1.03E-01	229.75
8	NM_026871	-0.67	6.17E-01	213.76
9	NM_144878	-5.96	1.38E-01	670.64
10	NM_001808438	-1.97	3.47E-01	3.91
11	NM_017426	-1.99	5.02E-01	8196.83
12	NM_016161	2.02	5.97E-02	149.86
13	NM_016965	-0.27	6.68E-01	13330.34



WorkBench  
IPA  
IVA/HGMD/QCI



## A. Expression Application – Ingenuity Pathway Analysis

1. What's New in IPA 2017 Winter Release
2. Getting Start with IPA

IPA介紹與啟動IPA

## B. Searching and Accessing the Knowledge Base

1. Introduction for Search Tools
2. My List

利用IPA進行搜尋

## C. Building and Editing a Pathway for Publication

1. My Pathway
2. Path Designer

使用IPA進行分子模型建構並繪製訊息傳遞路徑

## D. Q & A



## A. Expression Application – Ingenuity Pathway Analysis

1. What's New in IPA 2017 Winter Release
2. Getting Start with IPA

IPA介紹與啟動IPA

## B. Searching and Accessing the Knowledge Base

1. Introduction for Search Tools
2. My List

利用IPA進行搜尋

## C. Building and Editing a Pathway for Publication

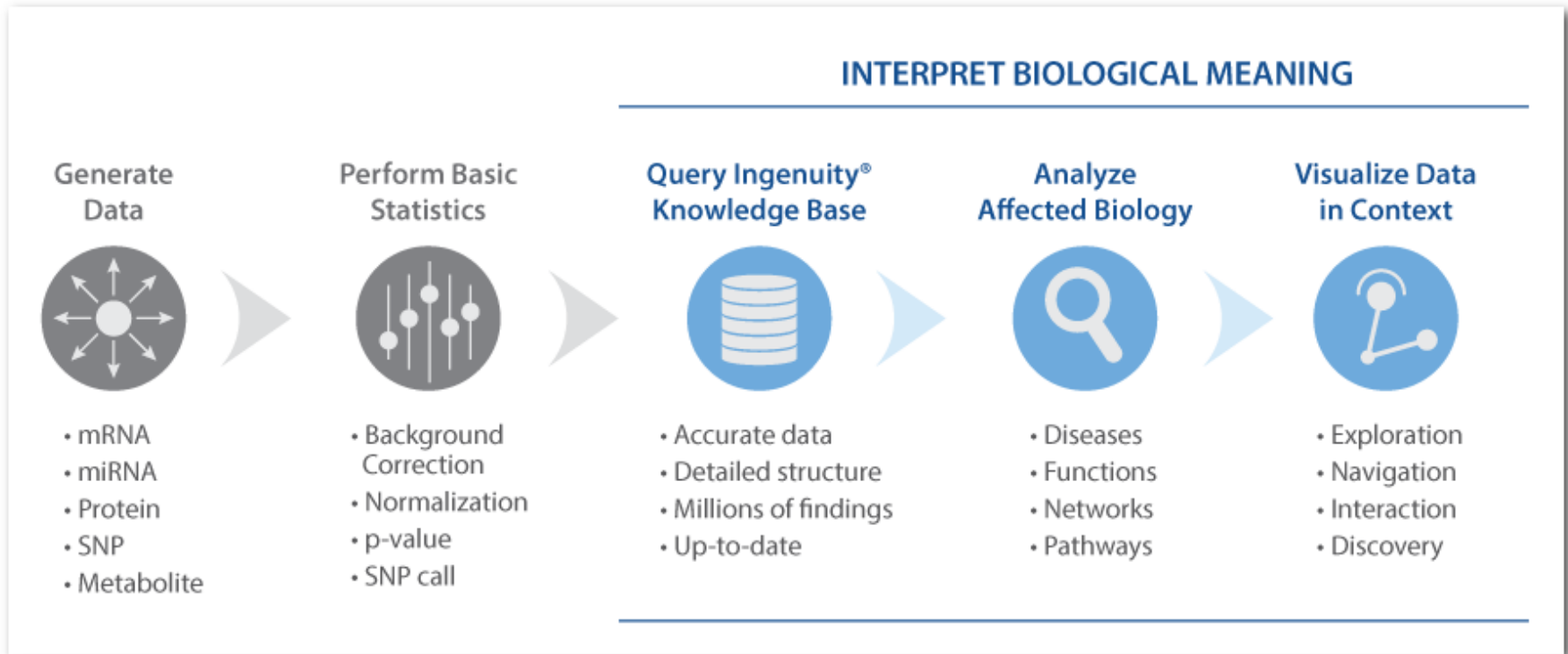
1. My Pathway
2. Path Designer

使用IPA進行分子模型建構並繪製訊息傳遞路徑

## D. Q & A



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。





## IPA 支援的物種(orthologous):

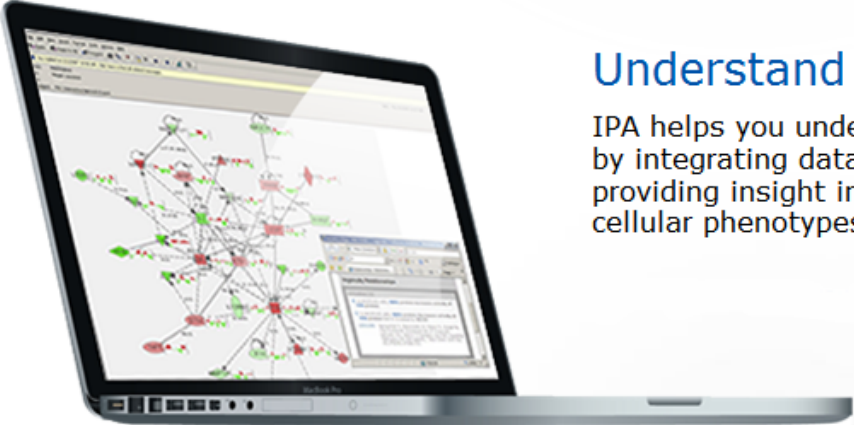
Arabidopsis thaliana  
 Bos taurus (bovine)  
 Caenorhabditis elegans  
 Gallus gallus (chicken)  
 Pan troglodytes (chimpanzee)  
 Danio rerio (zebrafish)  
 Canis lupus familiaris (canine)  
 Drosophila melanogaster  
 Macaca mulatta (Rhesus Monkey)  
 Saccharomyces cerevisiae  
 Schizosaccharomyces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

## IPA 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
  - PhosphoProteomics<sup>New</sup>
- 代謝體實驗

## 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



### 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.

>14,000 publications that used IPA -- and growing!

Format: Summary ▾ Sort by: Best Match ▾ Per page: 20 ▾

Send to ▾

Filters: [Manage Filters](#)

## Search results

Items: 1 to 20 of 1707

<< First < Prev Page  of 86 Next > Last >>

- [Causal analysis approaches in Ingenuity Pathway Analysis.](#)  
1. Krämer A, Green J, Pollard J Jr, Tugendreich S.  
Bioinformatics. 2014 Feb 15;30(4):523-30. doi: 10.1093/bioinformatics/btt703. Epub 2013 Dec 13.  
PMID: 24336805 [Free PMC Article](#)  
[Similar articles](#)
- [Genome-wide analysis of genetic variations assisted by Ingenuity Pathway Analysis to comprehensively investigate potential genetic targets associated with the progression of hepatocellular carcinoma.](#)  
2. Yu F, Shen XY, Fan L, Yu ZC.  
Eur Rev Med Pharmacol Sci. 2014;18(15):2102-8.  
PMID: 25070813 [Free Article](#)  
[Similar articles](#)
- [Potential predictive plasma biomarkers for cervical cancer by 2D-DIGE proteomics and Ingenuity Pathway Analysis.](#)  
3. Guo X, Hao Y, Kamilijiang M, Hasimu A, Yuan J, Wu G, Reyimu H, Kadeer N, Abudula A.  
Tumour Biol. 2015 Mar;36(3):1711-20. doi: 10.1007/s13277-014-2772-5. Epub 2014 Nov 27.  
PMID: 25427637  
[Similar articles](#)
- [Gene set enrichment analysis and ingenuity pathway analysis of metastatic clear cell renal cell carcinoma cell line.](#)  
4. Khan MI, Dębski KJ, Dabrowski M, Czarnecka AM, Szczylik C.  
Am J Physiol Renal Physiol. 2016 Aug 1;311(2):F424-36. doi: 10.1152/ajprenal.00138.2016. Epub 2016 Jun 8.  
PMID: 27279483  
[Similar articles](#)

## Results by year



[Download](#)

## Related searches

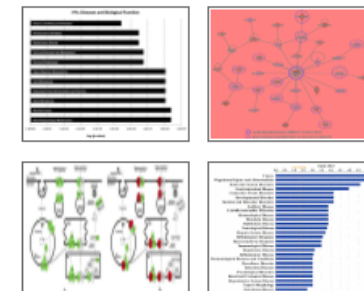
[ingenuity pathway analysis gene](#)

[ingenuity pathway analysis mima](#)

[ingenuity pathway analysis network](#)

[ingenuity pathway analysis proteomics](#)

## PMC Images search for *ingenuity pathway analysis*



>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**

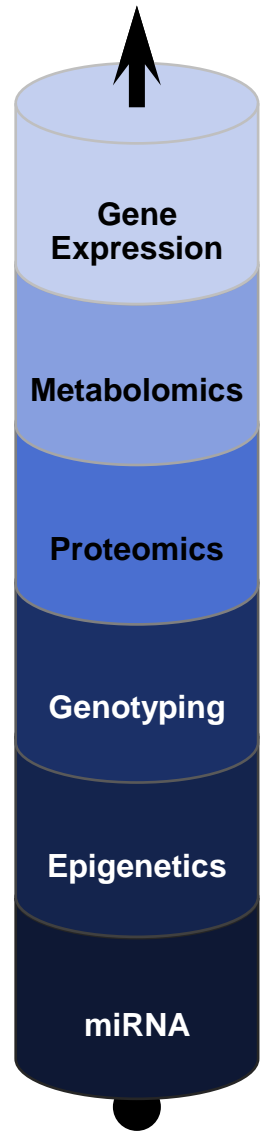
Proceedings of the National Academy of Sciences of the United States of America **PNAS**  
MYC inhibition induces metabolic changes leading to accumulation of lipid droplets in tumor cells

**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



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

RESEARCH ARTICLE

## A Multi-Omics Approach Identifies Key Hubs Associated with Cell Type-Specific Responses of Airway Epithelial Cells to Staphylococcal Alpha-Toxin

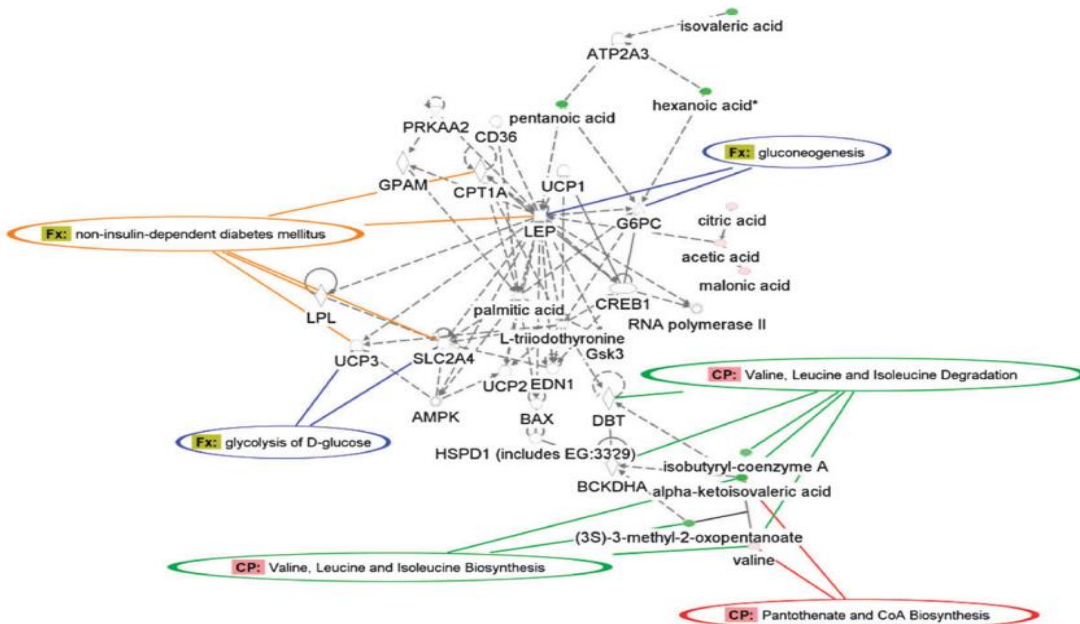
Erik Ric  
Jan-Pe

Integ  
disco

Susan C  
Terence

Received  
First pub  
DOI: 10

Sample tr



Multi Experiment

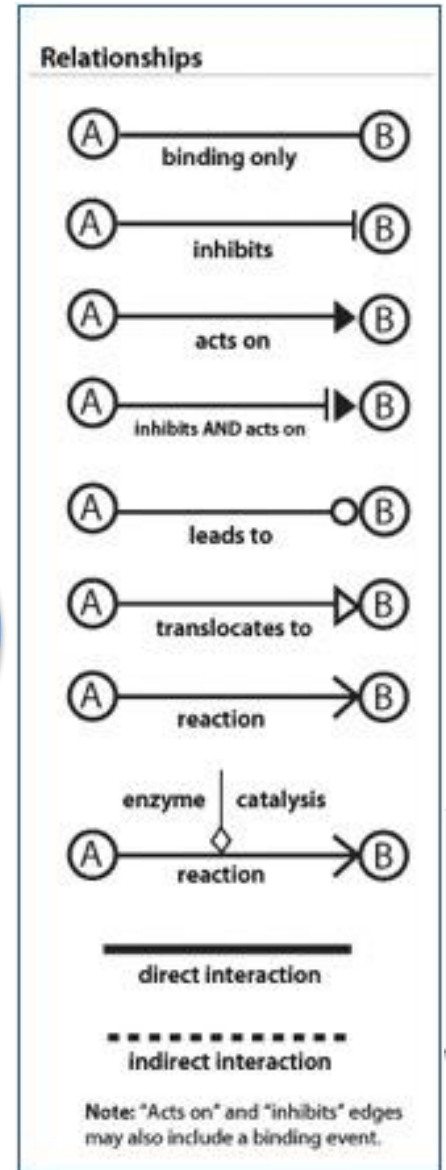
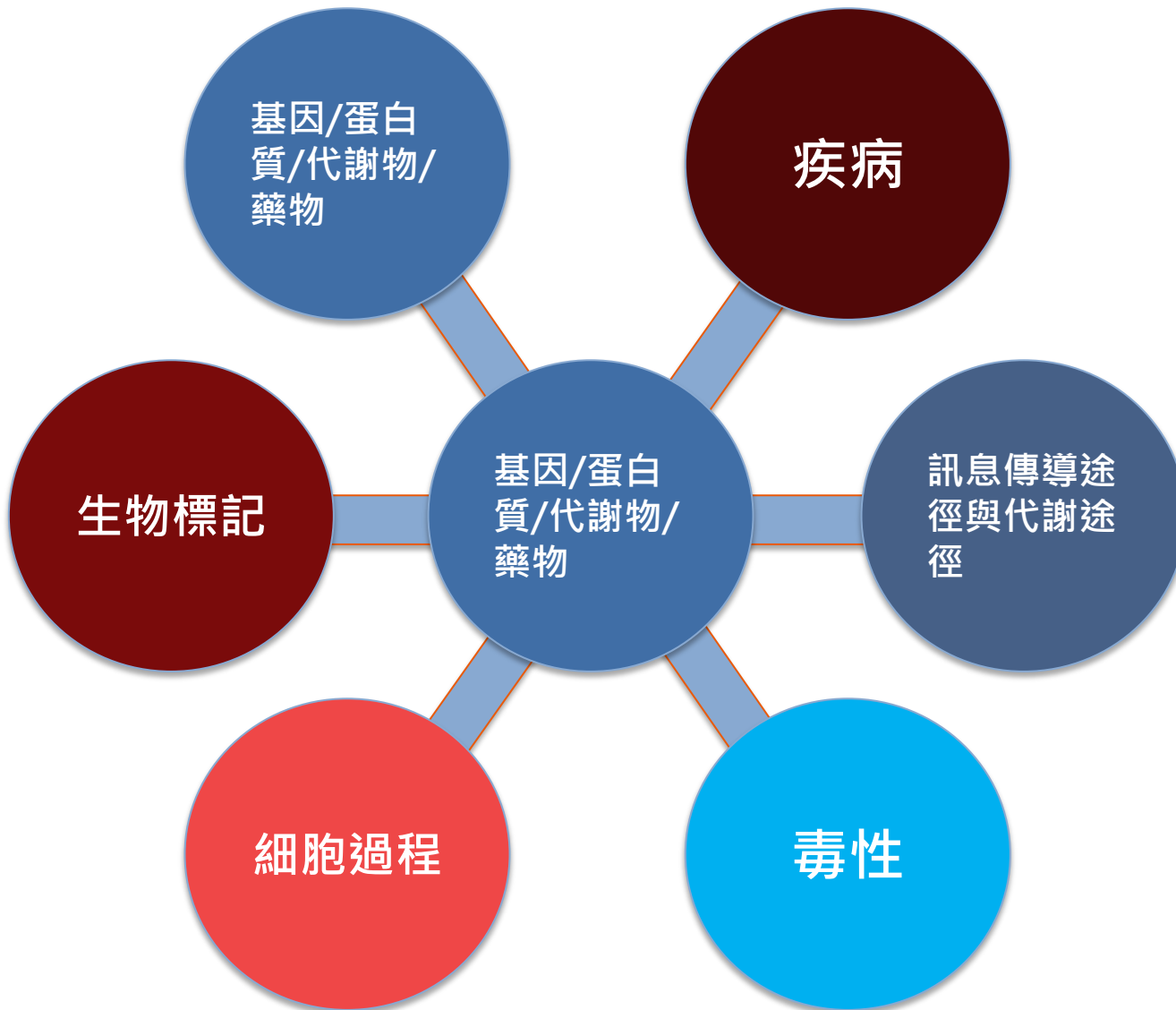
Phosphorylation

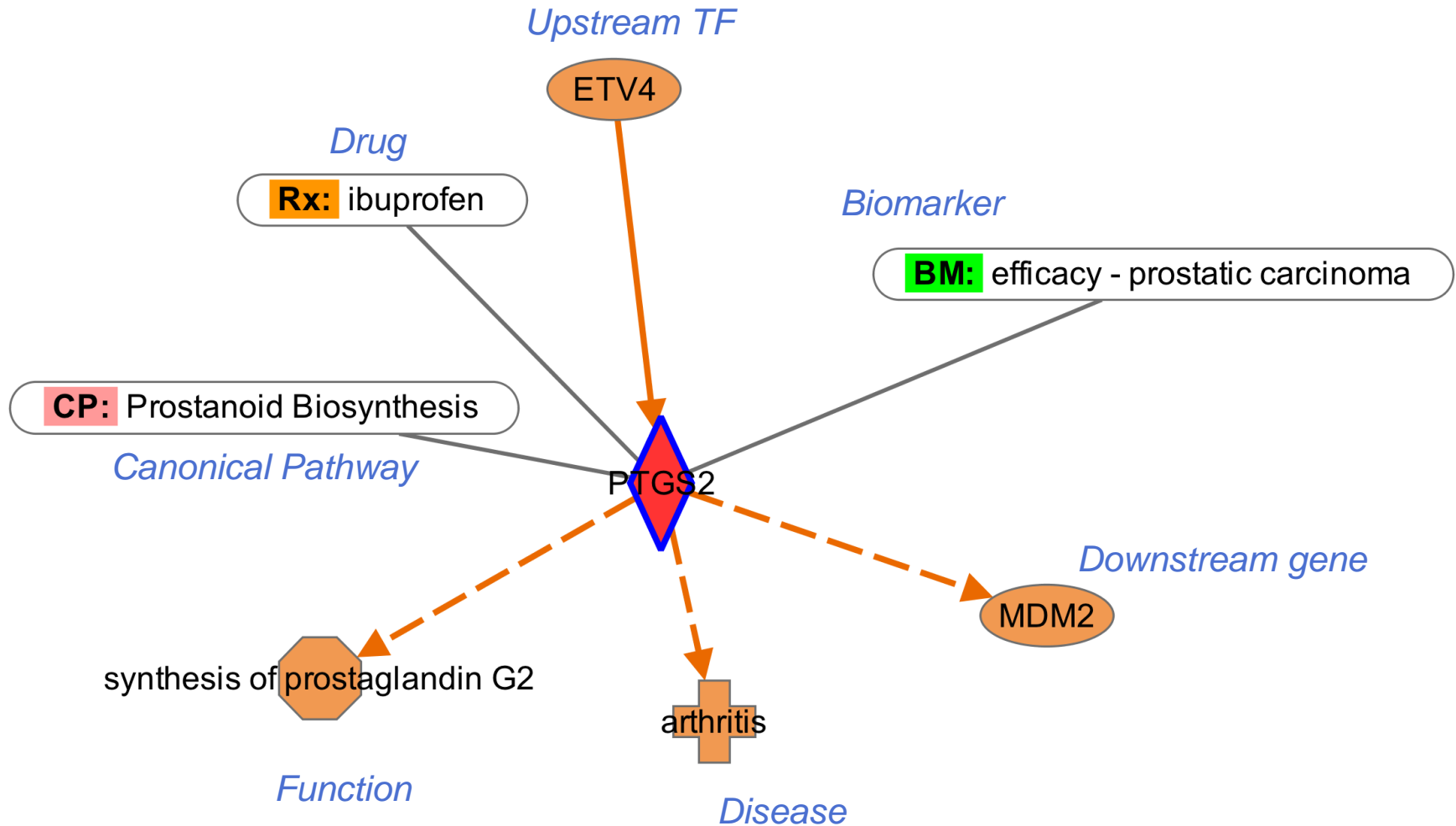
Protein Expression

mRNA Expression

miRNA Expression

IPA analysis





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

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



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



# How IPA content is different: context and direction of effect

In 129S1/Sv \* 129X1/SvJ \* Swiss Webster mouse, mutant **mouse Pex2 gene** (allele Pex2<sup>tm1Plf/Pex2<sup>tm1Plf</sup></sup>) (homozygous knockout) **increases cholestasis in mouse**.  
 12746876 Faust PL. Abnormal cerebellar histogenesis in PEX2 Zellweger mice reflects multiple neuronal defects induced by peroxisome deficiency. J Comp Neurol. 2003 Jun 30;461(3):394-413.  
 MGI allele: 2180128  
 MGI phenotype: 0000610  
 Source: Mouse Genome Database (MGD)

disease/ phenotype

strain

gene

zygosity

Direction of effect on disease / phenotype

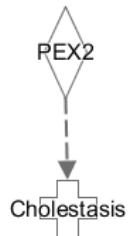
species

mutation type

This structure provides **rich contextual detail**

and powers the algorithms for **causal analysis in IPA**

Activity of the molecule in this finding (decreased)



Gene View Summaries

Human & Mouse Isoform Views

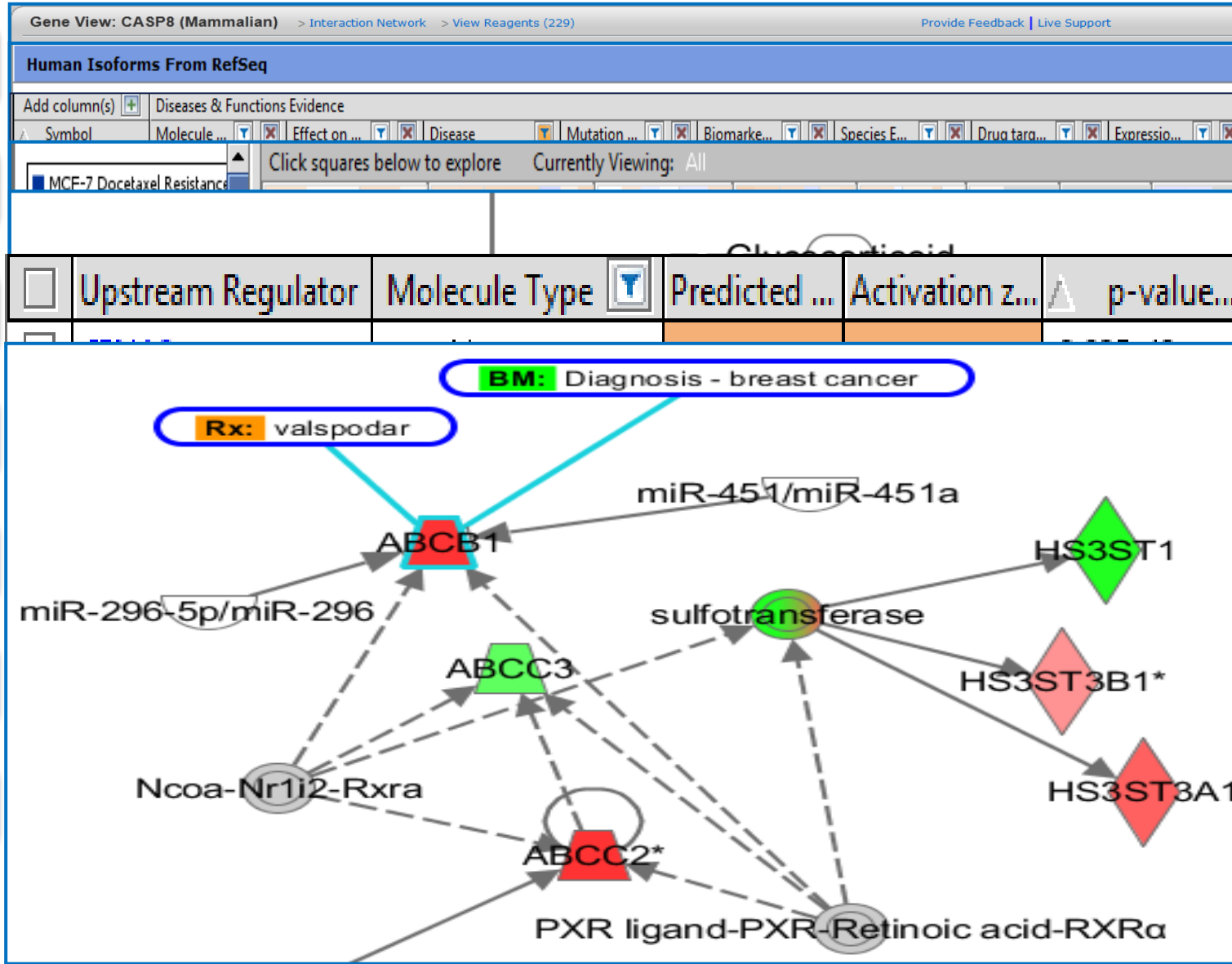
BioProfiler

Diseases & Bio Functions

Canonical Pathways

Upstream Regulator Analysis

Build & Overlay and Interactions



IsoProfiler

Multi-omics  
Overlay

Phosphorylation  
Analysis

Comparison  
Analysis

Analysis Match\*  
w/ OmicSoft Lands

ISOProfiler: Universe – Human isoforms from RefSeq with Exp Fold Change and Exp Intensity/RPKM/FPKM/Counts

Symbol: A1BG – AARD (p1 of 756)

My Pathways: NONO-2 1

Phosphorylation Analysis – 1min

Canonical Pathways: Upstream Analysis | Diseases & Functions | Regulator Effects | Networks | Lists | My Pathways | Molecules | Ins1 1

Chart: Heatmap

Settings/Legend: FILTER

Pathway: Molecules

Cardiomyocyte Differentiation via BMP Receptors  
Overlay: ESC vs. CM (cardiomyocytes) Fold Change

Expression Analysis – Mock vs. WNV-TE Ensembl Jan2015 |FC|>1 p<0.05 RPKM>10 in o – 2017-08-08 04:29 PM

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

VIEW AS HEATMAP | VIEW COMPARISON | CUSTOMIZE TABLE

z-score overall... | 71.83891386274442 – 57.4973960... (p1 of 23)

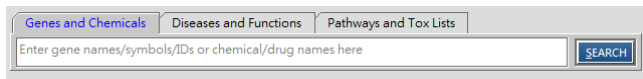
Analysis Name	Project	ca...	comparisoncontrast	CP...	...	...	...	...	...
GSE48210_GPL6246_test4-type 1 diabetes mellitus[spleen]ant – 2017-08-1	MouseDisease	spleen	CellType:CellDescription:SamplingTime[hours] ...	85.63	76.16	63.48	62.08	71.84	
GSE53166_GPL6244_test2-NA[peripheral blood]NS1-deleted PR8 – 2017-08	HumanDisease	periphera...	Treatment => NS1-deleted PR8 virus vs none	77.46	83.67	69.11	54.96	71.30	
GSE18686_GPL6947_test2-NA[peripheral blood]IFN gamma;lipop – 2017-08	HumanDisease	periphera...	Treatment => IFN gamma;lipopolysaccharide ...	68.31	81.85	64.65	66.93	70.43	
GSE45251_GPL4133_test1-normal control[pulmonary airway]TNF – 2017-08	HumanDisease	pulmonar...	Treatment => TNF alpha vs none	73.03	84.26	58.59	60.38	69.07	
GSE18686_GPL6947_test1-NA[peripheral blood]IFN gamma – 2017-08-10	HumanDisease	periphera...	Treatment => IFN gamma vs lipopolysacchari...	57.74	82.46	72.28	60.38	68.21	
GSE61141_GPL11154_test1-asthma[tracheal epithelium]Infecti – 2017-08-1	HumanDisease	tracheal e...	DiseaseState:Infection => asthma -> HRV16 ...	68.31	82.46	66.91	54.01	67.92	
GSE31022_GPL6887_test3-influenza A[lung]NA – 2017-08-11 05:12 PM	MouseDisease	lung	SamplingTime[dpj] => 3 vs baseline	77.46	74.83	57.30	61.24	67.71	
GSE61141_GPL11154_test2-normal control[tracheal epithelium – 2017-08-1	HumanDisease	tracheal e...	DiseaseState:Infection => normal control -> ...	68.31	84.26	65.79	52.04	67.60	
GSE49709_GPL10558_test1-normal control[peripheral blood]li – 2017-08-1	HumanDisease	periphera...	Treatment:PreTreatment => fluticasone (Flowe...	73.03	84.26	58.59	53.03	67.23	
GSE52405_GPL11002_test14-influenza A[lung]SubjectInfection – 2017-08-1	MouseDisease	lung	SubjectInfection:SamplingTime[dpj]:AnimalStra...	68.31	78.10	62.29	58.63	66.84	
GSE42606_GPL10558_test2-normal control[peripheral blood]C_ – 2017-08-	HumanDisease	periphera...	Treatment:TreatTime[hours] => 24 -> C. alb...	68.31	83.07	59.85	55.90	66.78	
GSE44595_GPL7202_test9-influenza A[lung]NA – 2017-08-11 06:34 PM	MouseDisease	lung	SamplingTime[dpj]:SubjectInfection => 5 -> i...	68.31	79.37	62.29	54.96	66.24	
GSE42638_GPL6887_test3-influenza A[lung]NA – 2017-08-11 06:16 PM	MouseDisease	lung	SubjectTreatment:SamplingTime => 2 days -...	68.31	78.74	59.85	56.83	65.93	
GSE72008_GPL10787_test1-influenza A[lung]SubjectInfection_ – 2017-08-14	MouseDisease	lung	SubjectInfection:SamplingTime[dpj] => 1 -> i...	63.25	79.37	68.02	53.03	65.92	
GSE68945_GPL11202_test6-influenza A[lung]SubjectInfection_ – 2017-08-14	MouseDisease	lung	SubjectInfection:SamplingTime[dpj] => 2 -> i...	63.25	78.10	70.18	52.04	65.89	
GSE49709_GPL10558_test2-normal control[peripheral blood]li – 2017-08-1	HumanDisease	periphera...	Treatment:PreTreatment => none -> lipopol...	63.25	78.74	66.91	54.01	65.73	
GSE31022_GPL6887_test5-influenza A[lung]NA – 2017-08-11 05:12 PM	MouseDisease	lung	SamplingTime[dpj] => 5 vs baseline	68.31	73.48	62.29	58.63	65.68	
GSE53166_GPL6244_test1-NA[peripheral blood]lipopolysacchar – 2017-08-	HumanDisease	periphera...	Treatment => lipopolysaccharide (LPS) vs none	73.03	81.24	51.83	55.90	65.50	
GSE64798_GPL8833_test2-influenza A[lung]NA – 2017-08-14 08:05 PM	MouseDisease	lung	SamplingTime[dpj]:AnimalStrain => 129S1/Sv...	63.25	76.16	64.65	57.74	65.45	
GSE49706_GPL10558_test3-normal control[peripheral blood]IF – 2017-08-1	HumanDisease	periphera...	Treatment => IFN gamma vs none	68.31	72.11	72.28	48.95	65.41	
GSE53454_GPL16311_test15-normal control[pancreatic islets] – 2017-08-12	HumanDisease	pancreati...	Treatment:TreatTime[hours] => 72 -> IL-1 b...	57.74	79.37	68.02	55.90	65.26	
GSE13168_GPL96_test14-normal control[airway smooth muscle] – 2017-08-	HumanDisease	airway sm...	Transfection:Treatment => PKI-GFP -> IL-1 ...	77.46	81.24	51.83	50.00	65.13	
GSE48757_GPL570_test1-normal control[foreskin]IFN alpha;IF – 2017-08-12	HumanDisease	foreskin	Treatment => IFN alpha;IFN gamma;IL-1 beta...	63.25	80.62	65.79	50.00	64.91	
GSE68945_GPL11202_test9-influenza A[lung]SubjectInfection_ – 2017-08-14	MouseDisease	lung	SubjectInfection:SamplingTime[dpj] => 4 -> i...	57.74	76.16	66.91	58.63	64.86	
GSE52405_GPL11002_test29-viral infectious disease[lung]Sub – 2017-08-14	MouseDisease	lung	SubjectInfection:SamplingTime[dpj]:AnimalStra...	68.31	78.10	55.99	56.83	64.81	
GSE72008_GPL10787_test1-influenza A[lung]SubjectInfection_ – 2017-08-	MouseDisease	lung	Treatment:TreatTime[hours] => 24 -> C. alb...	63.25	79.37	68.02	53.03	65.92	

Selected/Total match analyses : 0 / 4560

\*Q4 2017

## Biological Questions

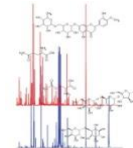
### Search



### Experiment Data



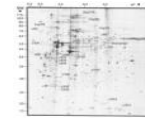
Expression arrays



Mass spec

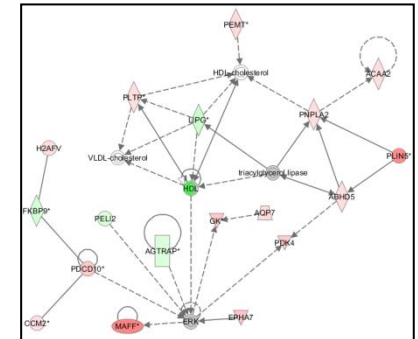


Protein arrays



2D Gel electrophoresis

### Custom Pathway



Networks



Core



IPA-Biomarker

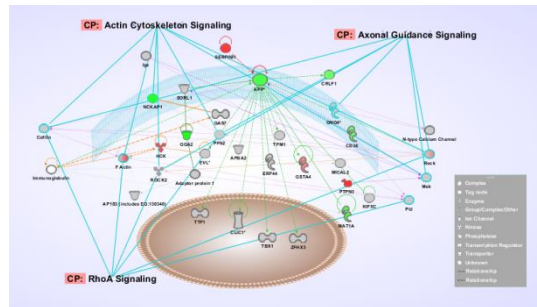


IPA-Tox



IPA-Metabolomics

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



Communicate & Collaborate

## Basic Module

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

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

## Advanced Analytics (AA)

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

[https://www.qiagenbioinformatics.com/files/flyers/IPA\\_Advanced\\_Analytics\\_WEB.pdf](https://www.qiagenbioinformatics.com/files/flyers/IPA_Advanced_Analytics_WEB.pdf)

## Content Updates Time Line

### Summer Release (June 2017)

- IsoProfiler with new GTEx human tissue expression data.
- Easily navigate to each of your open windows in IPA
- ~120,000 new findings (bringing total to greater than 6 million findings)
- New Canonical Pathway: Osteoarthritis Pathway

### Winter Release (2017 December)

- Enhancements to Analysis Match—updated additional analyses from OmicSoft
- Focus on the most important z-scores in the heat map by setting a threshold
- Entering metadata for a dataset—help you quickly find and search those datasets
- New criteria to select, highlight or trimming nodes on networks and pathways
- New findings, including 120,000 (bringing total to over 6.3 million findings)
- New Canonical Pathways—Opioid Signaling Pathway

### Spring Release (March 2018)

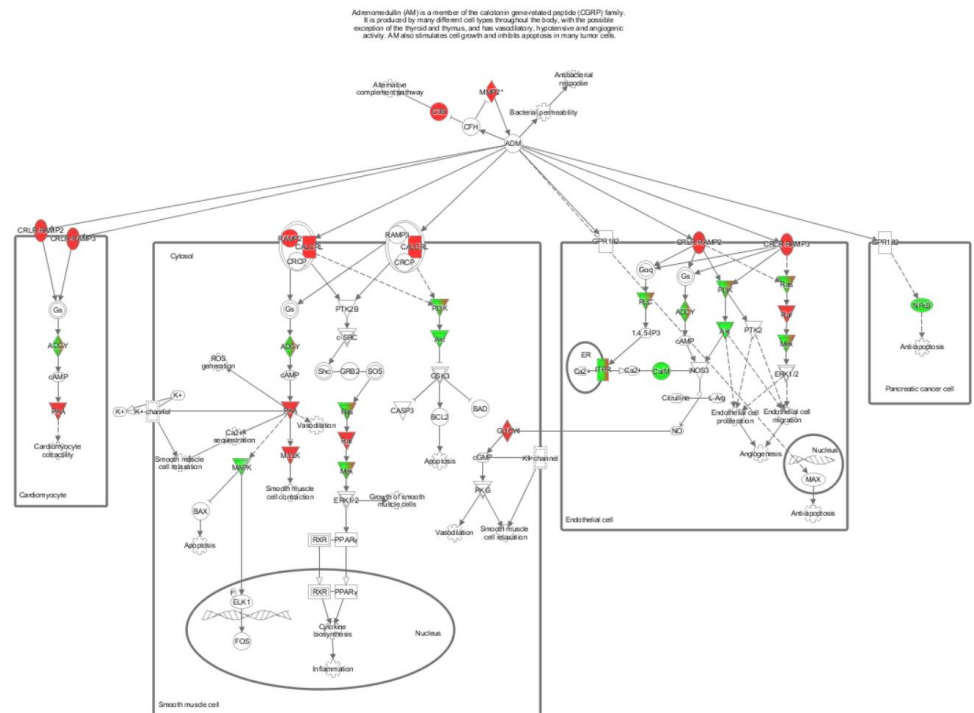
- Predict Activity of Metabolic Pathways
- New Datasets for Analysis Match
- 130,000 new findings (bringing total to over 6.4 million findings)
- New Canonical Pathways
  - Adrenomedullin signaling pathway, Iron homeostasis signaling pathway

## Content Updates

- Predict Activity of Metabolic Pathways
- New Datasets for Analysis Match
- Content Updates
- New Canonical Pathways
  - Adrenomedullin signaling pathway
  - Iron homeostasis signaling pathway

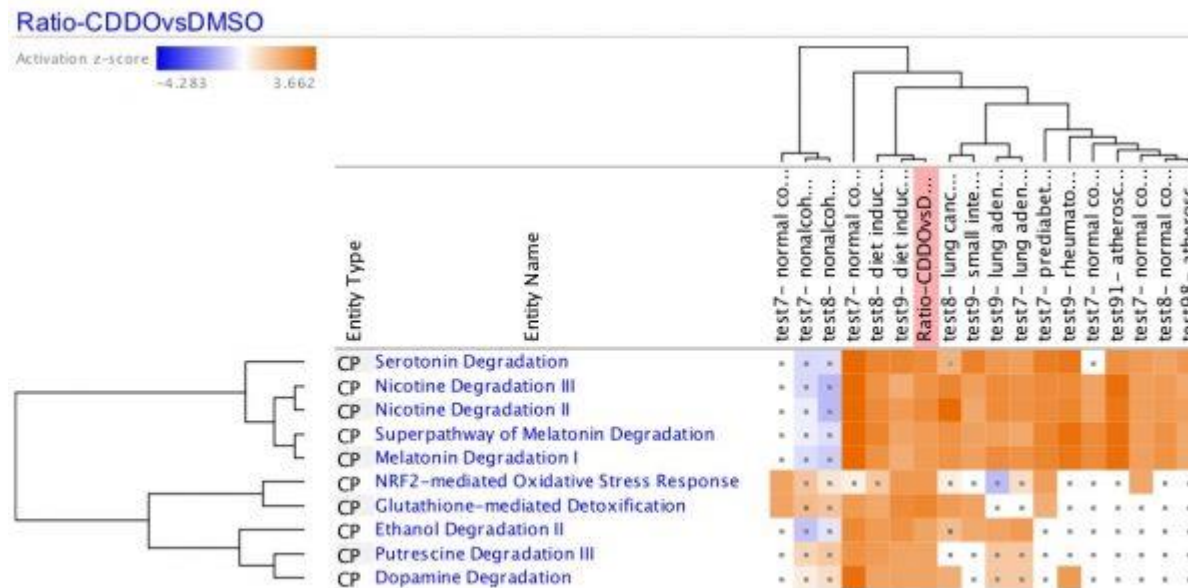
~130,000 new findings (bringing total to over 6.4 million findings), including:

- ~40,000 new Expert findings
- ~62,000 new mutation-to-disease findings from ClinVar
- ~14,000 new cancer mutation disease association findings from COSMIC
- ~1,800 drug-to-disease findings from ClinicalTrials.gov
- ~1,700 new disease-to-target findings from ClinicalTrials.gov
- ~2,000 new functional annotations from Gene Ontology
- ~11,500 new protein-protein interactions from the BioGRID database
- ~1,000 new protein-protein interactions from the IntAct database
- ~600 new mouse knockout-to-phenotype findings from MGD (JAX Labs)



## Content Updates

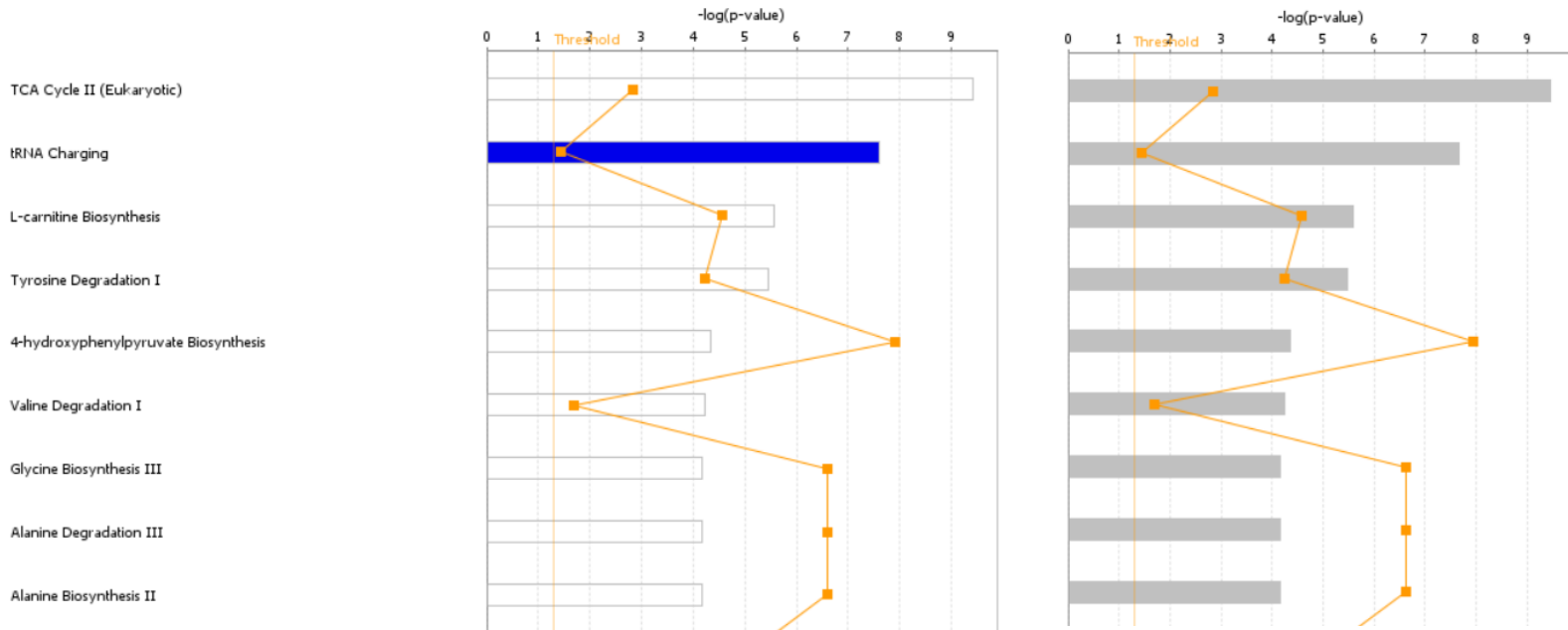
- Predict Activity of Metabolic Pathways
- New Datasets for Analysis Match
- Content Updates
- New Canonical Pathways
  - Adrenomedullin signaling pathway
  - Iron homeostasis signaling pathway





## Content Updates

- Predict Activity of Metabolic Pathways
- New Datasets for Analysis Match
- Content Updates
- New Canonical Pathways
  - Adrenomedullin signaling pathway
  - Iron homeostasis signaling pathway



2018 Spring Release

Before

## Content Updates

- Predict Activity of Metabolic Pathways
- **New Datasets for Analysis Match**
- Content Updates
- New Canonical Pathways
  - Adrenomedullin signaling pathway
  - Iron homeostasis signaling pathway

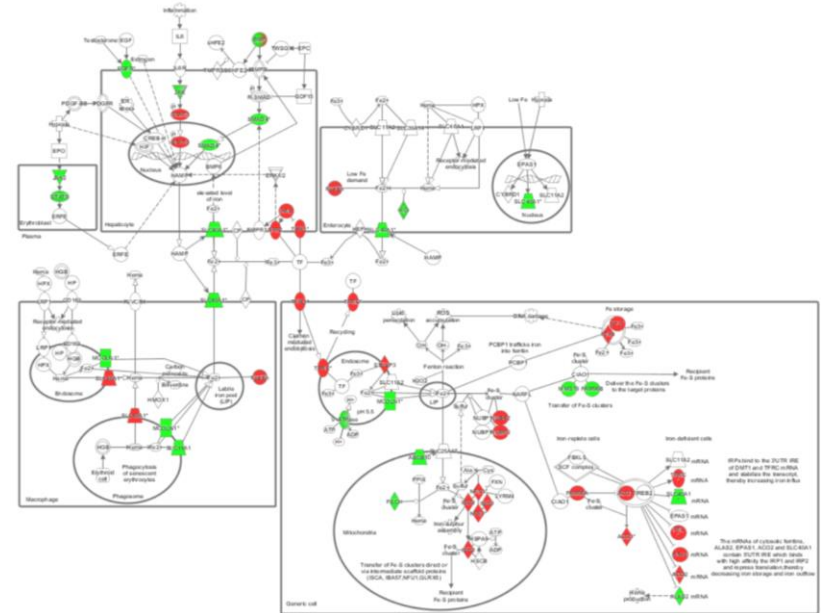
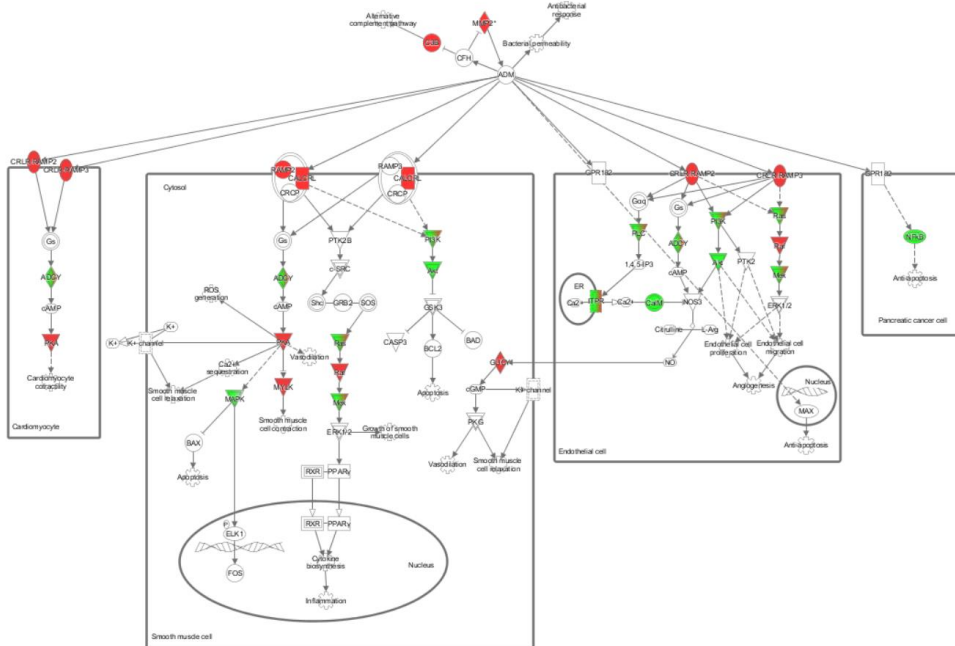
Land	Repository	Q4 2017 (December)	Q1 2018 (March)	Increase
DiseaseLand	HumanDisease	3239	3762	523
	MouseDisease	2516	2798	282
	Hematology	108	108	0
	<b>RatDisease (New)</b>	0	124	124
OncoLand	OncoGEO	1028	1169	141
	TCGA	24	24	0
	MetastaticCancer	53	53	0
	<b>Pediatrics (New)</b>	0	127	127

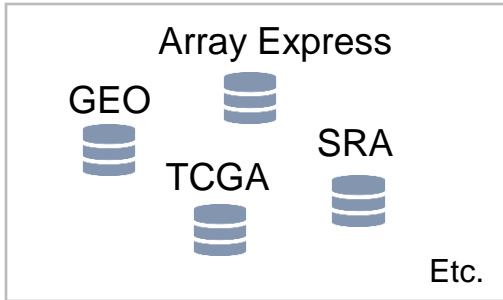
There are 1,100+ new datasets for Analysis Match in this release, bringing the total available in IPA to >8,000. This includes two new repositories, RatDisease (under DiseaseLand) and Pediatrics (under OncoLand). Table 1 compares the repositories and their respective sizes in this release versus the prior one.

## Content Updates

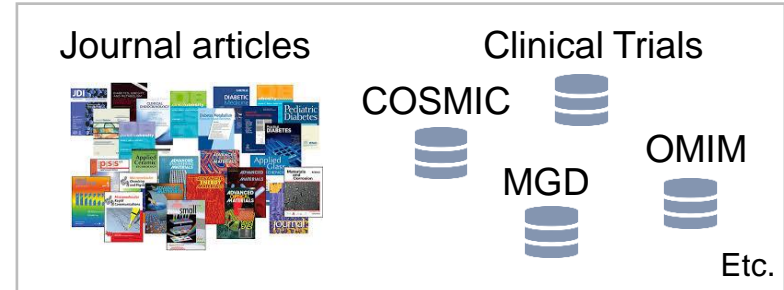
- Predict Activity of Metabolic Pathways
- New Datasets for Analysis Match
- Content Updates
- **New Canonical Pathways**
  - Adrenomedullin signaling pathway
  - Iron homeostasis signaling pathway

Adrenomedullin (AM) is a member of the calcitonin gene-related peptide (CGRP) family. It is produced by many different cell types throughout the body, with the possible exception of the thyroid and thymus, and has vasodilatory, hypotensive and angiogenic activity. AM also stimulates cell growth and inhibits apoptosis in many tumor cells.





Curation, Processing, & QA



Curation & QA

**Datasets integrated into  
OmicSoft Lands**



OncoLand  
DiseaseLand

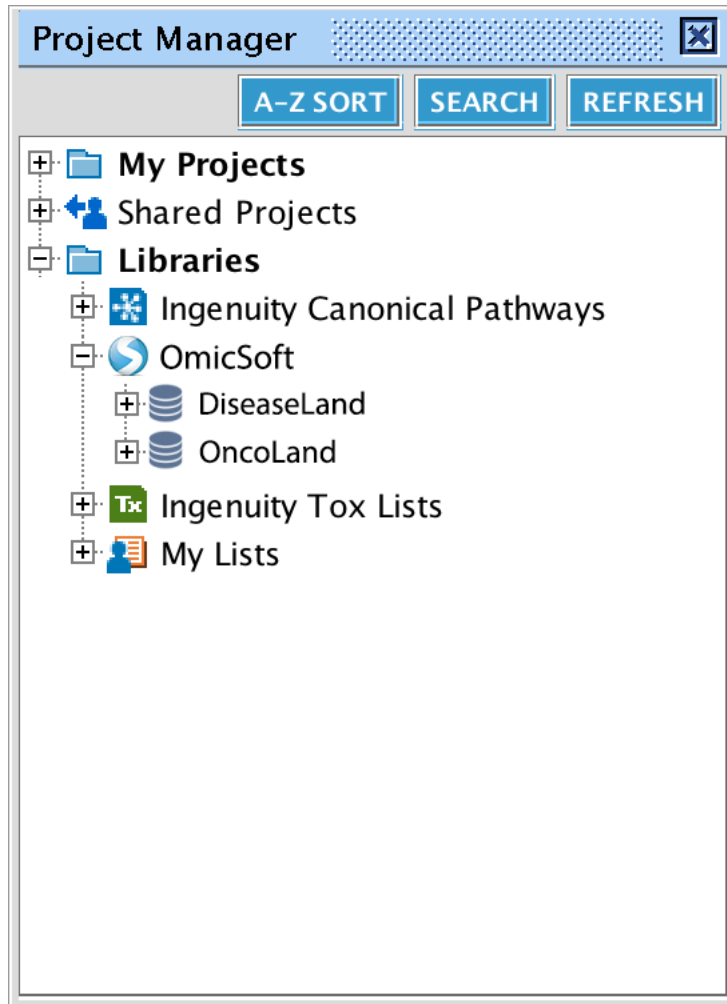
6000+  
Expression  
comparison  
datasets

**Curated  
Findings**

**INGENUITY<sup>®</sup>  
PATHWAY ANALYSIS**



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



- DiseaseLand
  - HumanDisease (2,929)
  - MouseDisease (2,257)
- OncoLand
  - OncoGEO (986)
  - TCGA (25)
  - Hematology (68)

Total datasets for release: 6000+

## Human DiseaseLand

- 350 diseases
- 185 tissues of origin
- 48 expression platforms (primarily array), >450 RNA-seq studies

## Mouse DiseaseLand

- 194 diseases
- 145 tissues of origin
- 39 expression platforms (primarily array), >500 RNA-seq studies

## OncoGEO

- 98 cancers
- 49 tissues of origin
- 27 expression platforms (primarily array), >160 RNA-seq studies

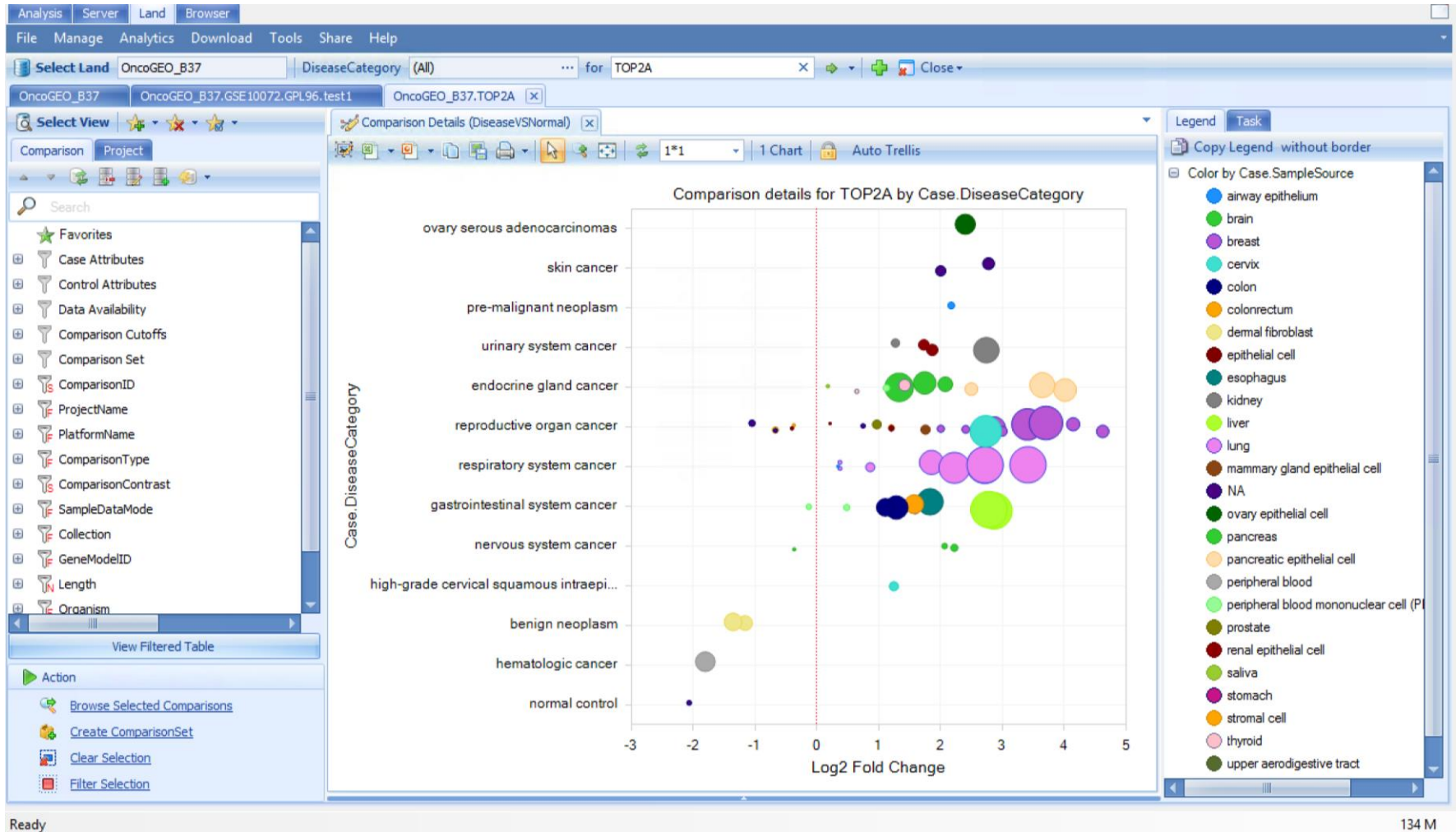
## TCGA

- 23 cancers (23 tissues)

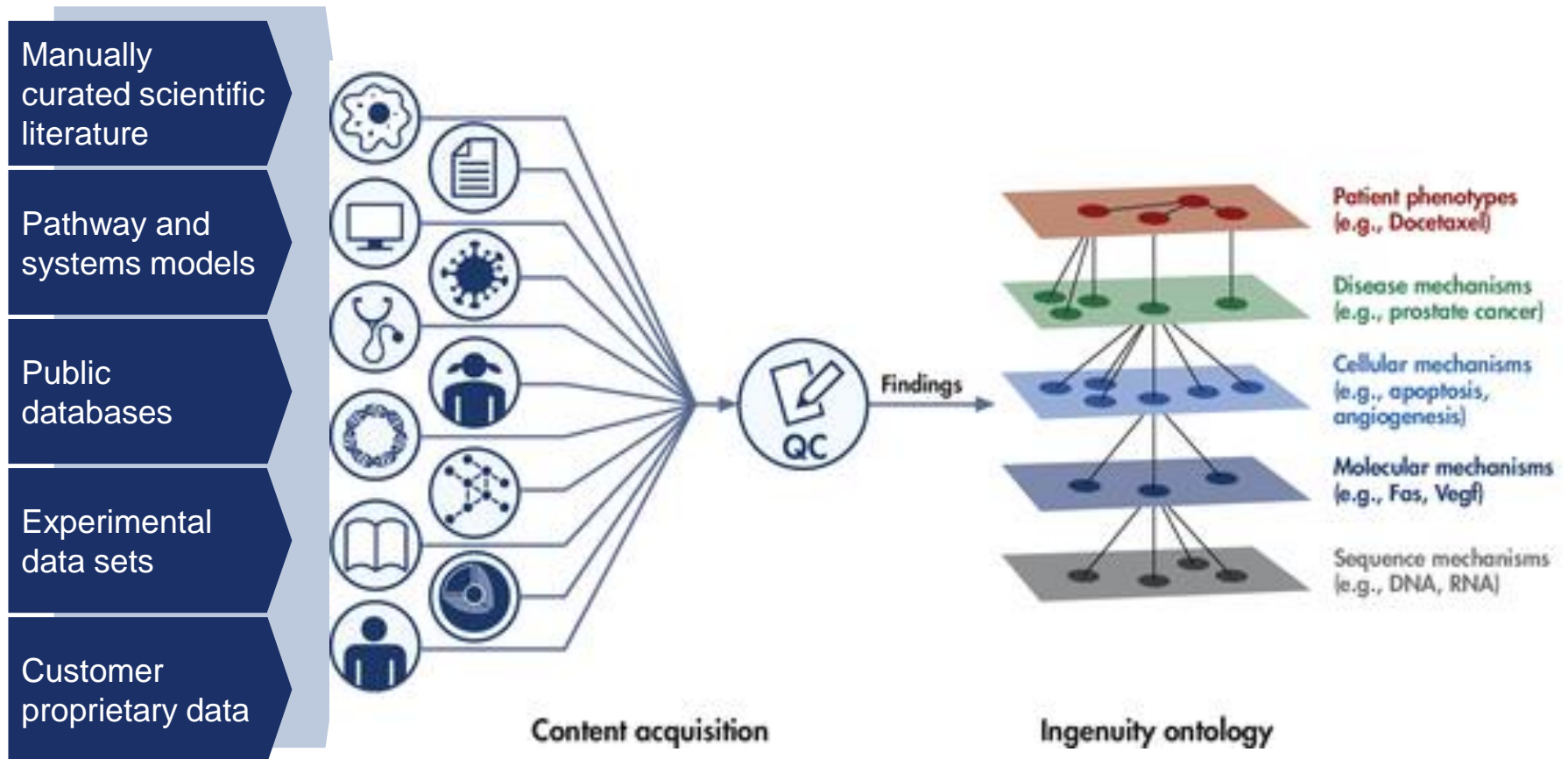
## Hematology

- 7 tissues of origin
- 16 diseases

## Visualizing an individual gene across comparisons



Highest-quality interpretation of genomics and sequencing data





## A. Expression Application – Ingenuity Pathway Analysis

1. What's New in IPA 2017 Winter Release
2. Getting Start with IPA

IPA介紹與啟動IPA

## B. Searching and Accessing the Knowledge Base

1. Introduction for Search Tools
2. My List

利用IPA進行搜尋

## C. Building and Editing a Pathway for Publication

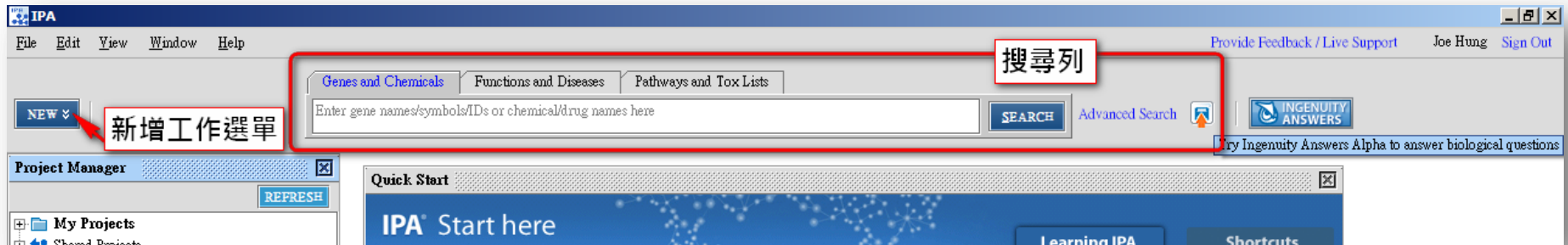
1. My Pathway
2. Path Designer

使用IPA進行分子模型建構並繪製訊息傳遞路徑

## D. Q & A



- 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



The screenshot shows the IPA software interface. A red box highlights the search bar area, which contains the text 'Enter gene names/symbols/IDs or chemical/drug names here' and a 'SEARCH' button. The label '搜尋列' (Search Bar) is placed over this area. To the left, a 'NEW' button is labeled '新增工作選單' (New Work Menu). The interface also shows a 'Project Manager' section with 'My Projects' and 'Shared Projects' options, and a 'Quick Start' section with 'IPA Start here' and 'Learning IPA' buttons.

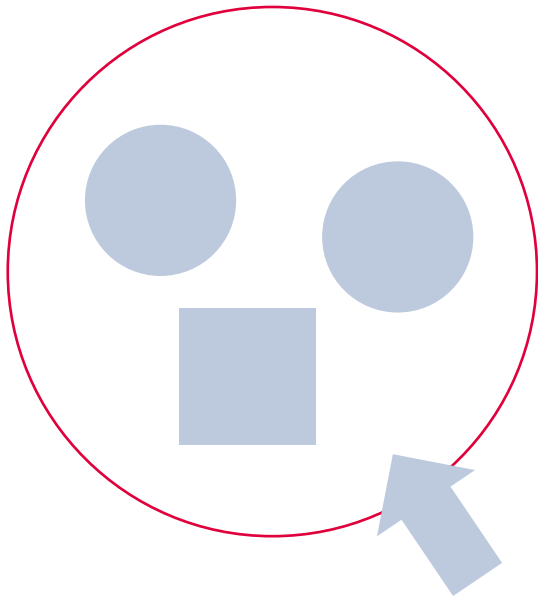
- **Finding:**

- 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.

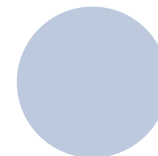
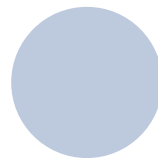
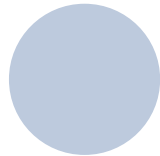
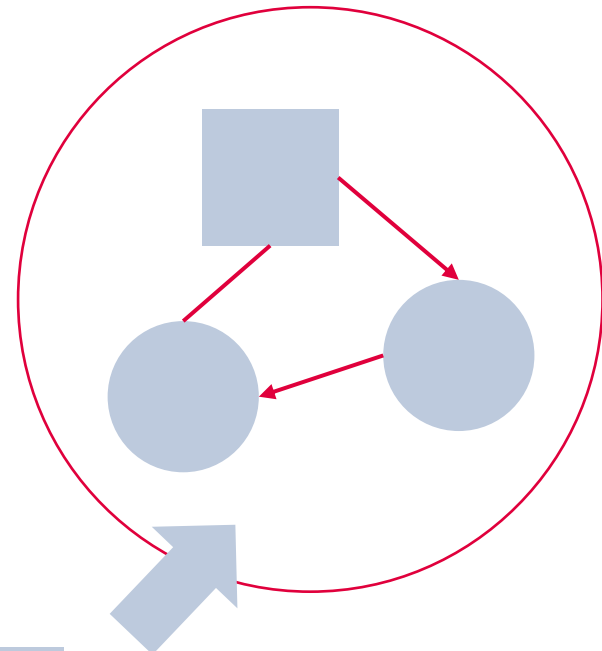
- **Canonical Pathway (Signaling and Metabolic)**

- Are generated prior to data input, based on the literature
- Do NOT change upon data input
- Do have directionality

Set of Genes and Chemicals associated with Disease/Function (without relationship information)



Set of Genes and Chemicals associated with Disease/Function (with relationship information)



Chemical

Gene

# Live Demo

## BioProfiler

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									
<a href="#">ADD TO MY PATHWAY</a> <a href="#">ADD TO MY LIST</a> <a href="#">DISPLAY AS NETWORK</a> <a href="#">CREATE DATASET</a> <a href="#">LIMIT TO DATASET</a> <a href="#">Genentech BMC T...</a>									
Molecule						Disease or Function 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...
▶ ADAMDEC1	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	↑0.375	1.01E-03	3.34E-03	decreased a...	affects,decreases,i...	Abnormal morp... all 64	frameshift,h...
▶ ANAPC5	other	200098_s_at	↑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	↑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...

## When will I use 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**

ADD TO MY PATHWAY | ADD TO MY LIST | DISPLAY AS NETWORK

Molecule	Add column(s)	Disease or Function Evidence
Symbol	Molecule Type	Effect on Dise...
(6R)-tetrahydrobiopt...	chemical drug	decreases
▶ABAT	enzyme	affects
acamprosate	chemical drug	decreases
ACHE	enzyme	affects
▶ADRA1A	G-protein coupled r	affects
▶ADRA1B	G-protein coupled r	affects
▶ADRA1D	G-protein coupled r	affects
▶ADRA2A	G-protein coupled r	affects
▶ADRA2B	G-protein coupled r	affects
▶ADRA2C	G-protein coupled r	affects
▶ALDH5A1	enzyme	affects
▶aripiprazole	chemical drug	increased activity

**Add Column(s) to section**

- Symbol
- Molecule Type
- Disease Count
- Synonym(s)
- Entrez Gene Name
- Tissue/Cell Line
- Location

Apply Cancel

pterin - val... (p1 of 1) << >> More Info

Causal or Corr.	Add Column(s) to section
causal	<input checked="" type="checkbox"/> Molecule Activity
correlation	<input checked="" type="checkbox"/> Effect on Disease or Function
causal	<input checked="" type="checkbox"/> Disease or Function
correlation	<input checked="" type="checkbox"/> Mutation evidence
correlation	<input checked="" type="checkbox"/> Biomarker Application Evidence
correlation	<input checked="" type="checkbox"/> Species Evidence
correlation	<input checked="" type="checkbox"/> Drug target evidence
correlation	<input checked="" type="checkbox"/> Expression evidence
correlation	<input checked="" type="checkbox"/> Causal or Correlated
causal	<input type="checkbox"/> Tissue/Cell Line
causal	<input checked="" type="checkbox"/> Findings
causal	
correlation	
causal	

Apply Cancel

1. What **disease** is **BCR (the kinase)** associated with? Please list one of them.
2. How many categorized literature findings are in Ingenuity knowledge base on BCR (the kinase)?
3. Search for genes associated with the function antigen presentation in IPA. How many genes are associated with the function **activation of antigen presenting cells**?
4. Find the common genes between Diabetes mellitus and Alzheimer disease



1. What **disease** is **BCR (the kinase)** associated with? Please list one of them.

Chronic myeloid leukemia, adenocarcinoma, epithelial cancer, hyperactive behavior, leukemogenesis, hemangioblastoma, capillary hemangioma, squamous-cell carcinoma, melanoma, melanoma cancer, gliosis, edema, squamous cell cancer, weight loss, bipolar disorder, acute lymphocytic leukemia, sepsis, T-cell leukemia, ectopia, B-cell leukemia, Philadelphia-positive acute lymphoblastic leukemia, acute myeloid leukemia, carcinoma, hypertrophy, productive infection by HIV-1, tumorigenesis, Parkinson's disease, serous ovarian carcinoma, serous ovarian adenocarcinoma

2. How many categorized literature findings are in Ingenuity knowledge base on BCR (the kinase)?

1,569

3. Search for genes associated with the function antigen presentation in IPA. How many genes are associated with the function **activation of antigen presenting cells**?

671

4. Find the common genes between Diabetes mellitus and Alzheimer disease

## A. Expression Application – Ingenuity Pathway Analysis

1. What's New in IPA 2017 Winter Release
2. Getting Start with IPA

IPA介紹與啟動IPA

## B. Searching and Accessing the Knowledge Base

1. Introduction for Search Tools
2. My List

利用IPA進行搜尋

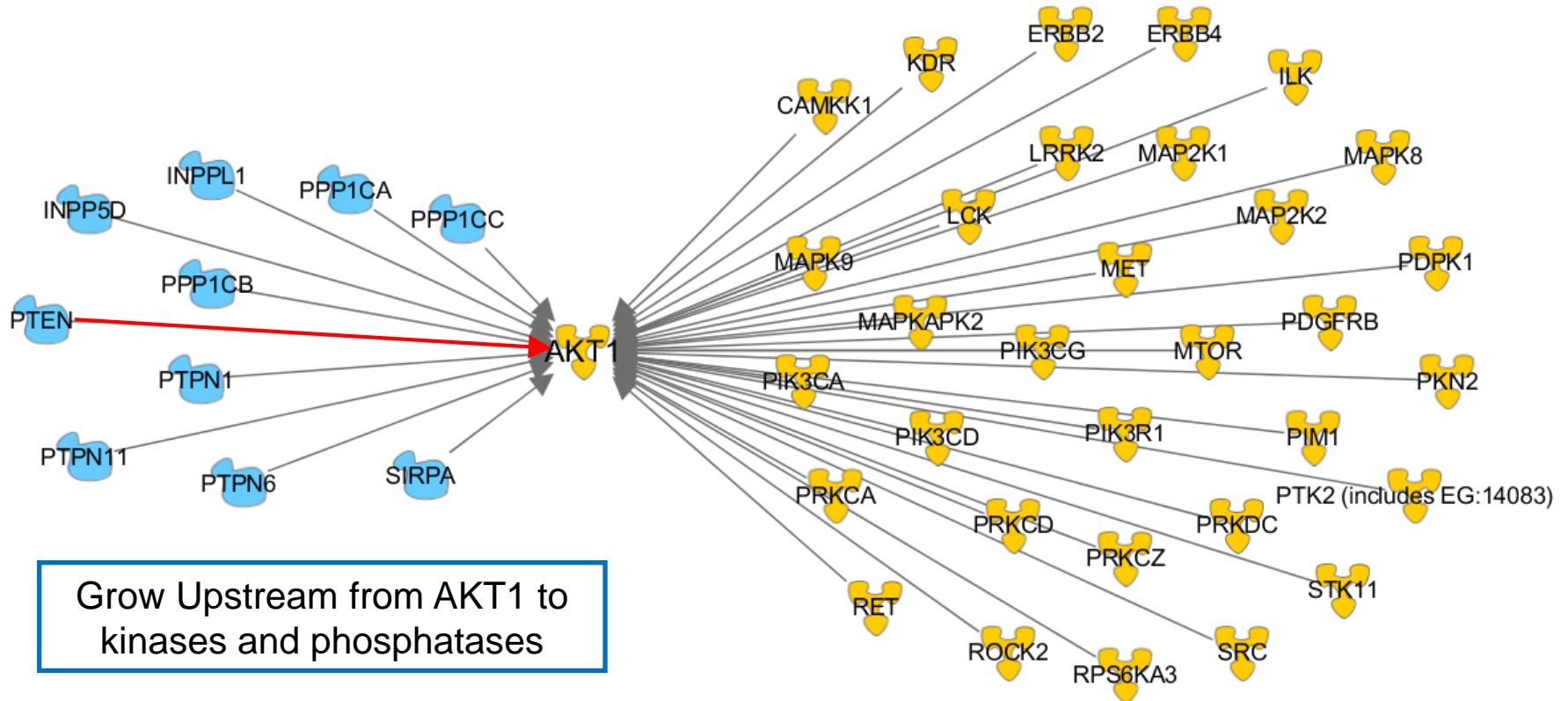
## C. Building and Editing a Pathway for Publication

1. My Pathway
2. Path Designer

使用IPA進行分子模型建構並繪製訊息傳遞路徑

## D. Q & A





Ingenuity Relationships	
phosphorylation [9]	
In Pc 3 cells, <b>PTEN protein decreases</b> (in a dose-dependent manner) <b>phosphorylation of human PKB [AKT1] protein to phosphorylated (S473) human PKB [AKT1] protein.</b>	
<a href="#">10716737</a>	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, <b>human PTEN protein decreases phosphorylation of human PKB/AKT [AKT1] protein.</b>	
<a href="#">10554022</a>	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 have directionality (proceed “from A to Z”)

## My Pathways and Path Designer Pathways:

- Custom built pathways manually created based on user input

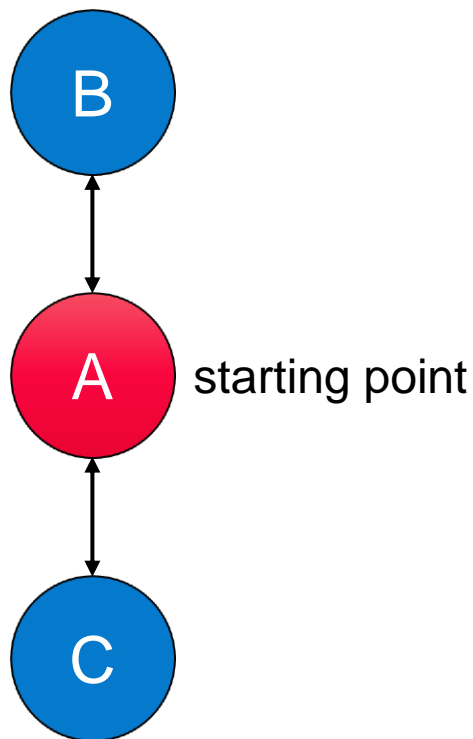
## Relationship Type:

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

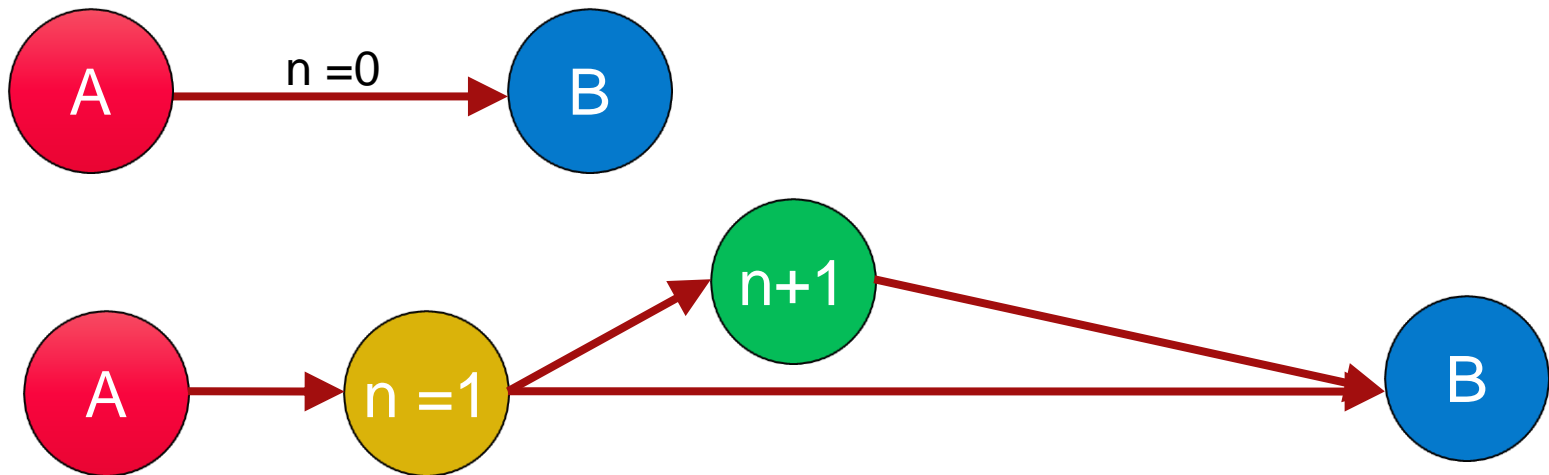
## Node

- Single molecule in Network such as Gene, Chemicals, Disease, and Pathway

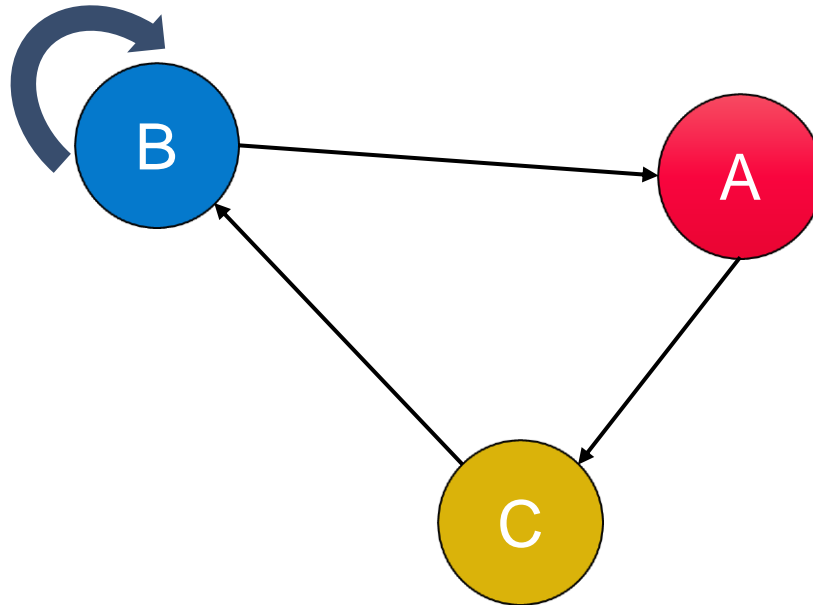
- Using one molecule of interest as a starting point, the Grow feature allows you to find (and add) other molecules of interest to a pathway. You can also grow to functions and diseases.



- 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)

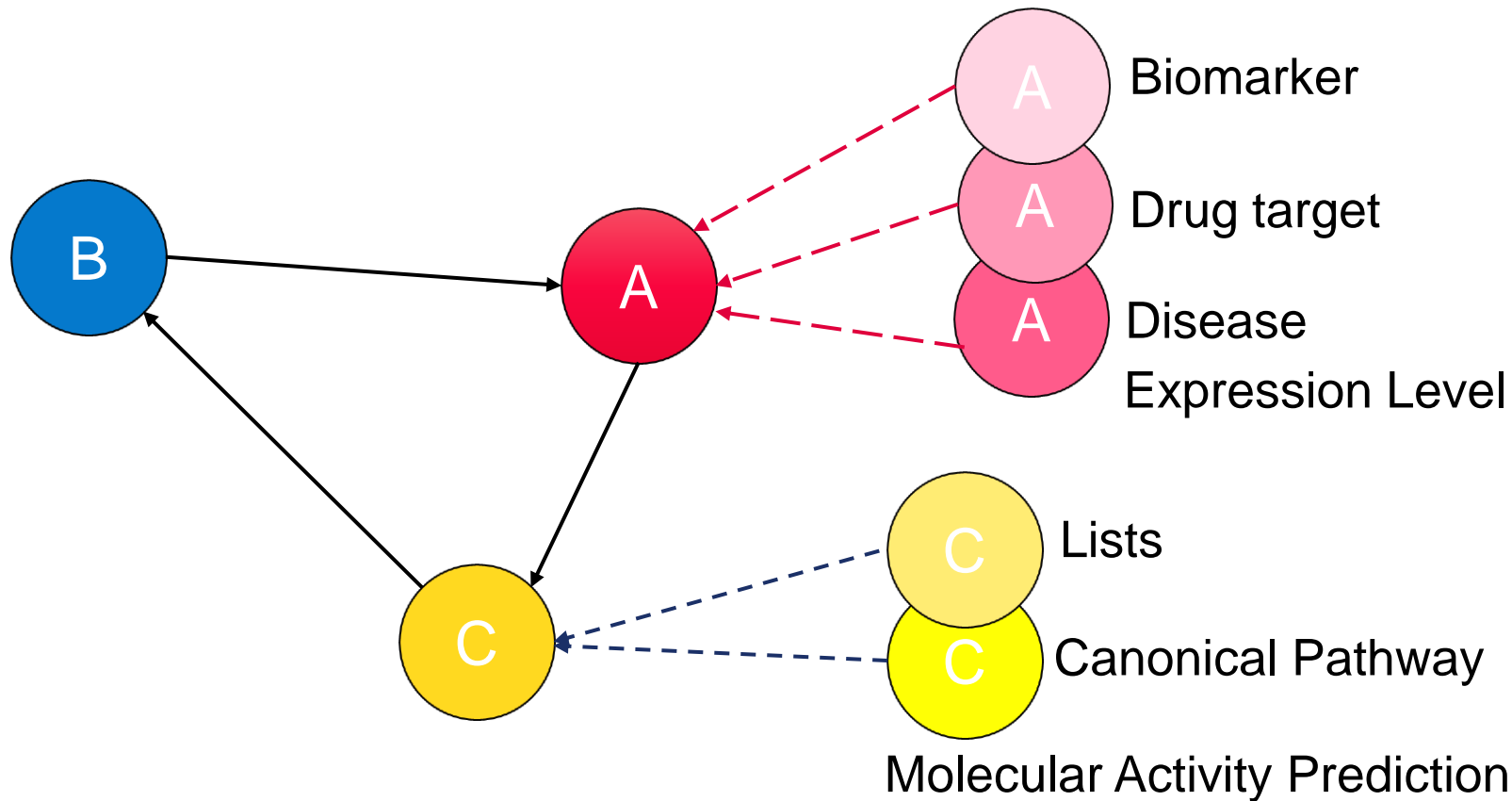


- Connect allows you to see specific molecular interactions between nodes or groups of nodes.

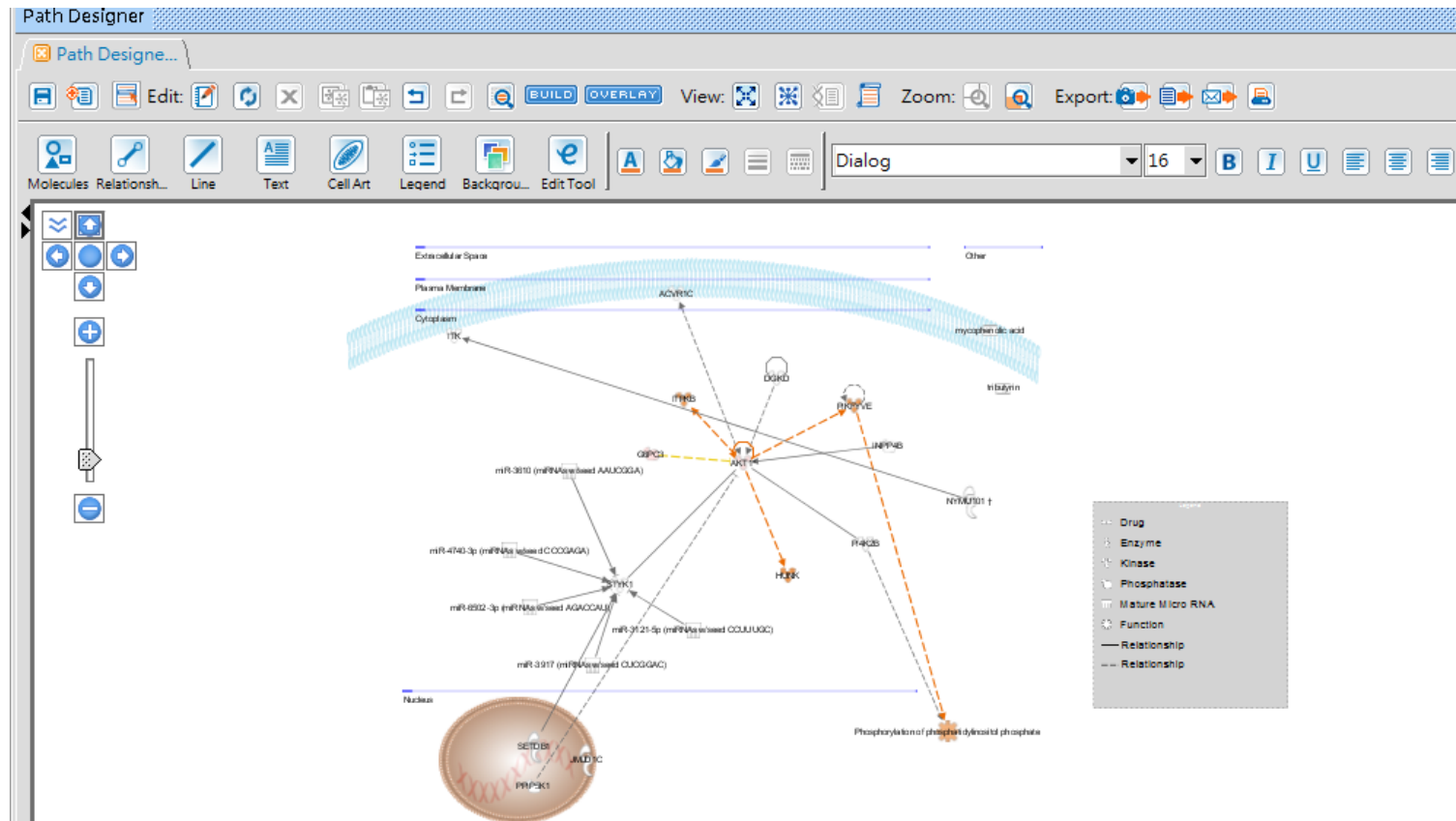




- Overlay tools allows you to compare and contrast different kinds of information within networks



- Use Path Designer to transform your networks and pathways in IPA into publication quality pathway graphics rich with color, customized text and fonts, biological icons, organelles, and custom backdrops.



1. Search for the following genes in IPA and add them to a pathway:  
**A2M, APOE, APP, HFE2, LRP1, PSEN1, PSEN2, SLC40A1, TRF2**
2. What are the connections between these molecules that occur in nervous system tissues and CNS cell lines?
3. Are these molecules involved in any Canonical Pathways?
4. Add at least one organelle or other cellular structure to your pathway and move the molecules on your pathway to the appropriate location.

## A. Expression Application – Ingenuity Pathway Analysis

1. What's New in IPA 2017 Winter Release
2. Getting Start with IPA

IPA介紹與啟動IPA

## B. Searching and Accessing the Knowledge Base

1. Introduction for Search Tools
2. My List

利用IPA進行搜尋

## C. Building and Editing a Pathway for Publication

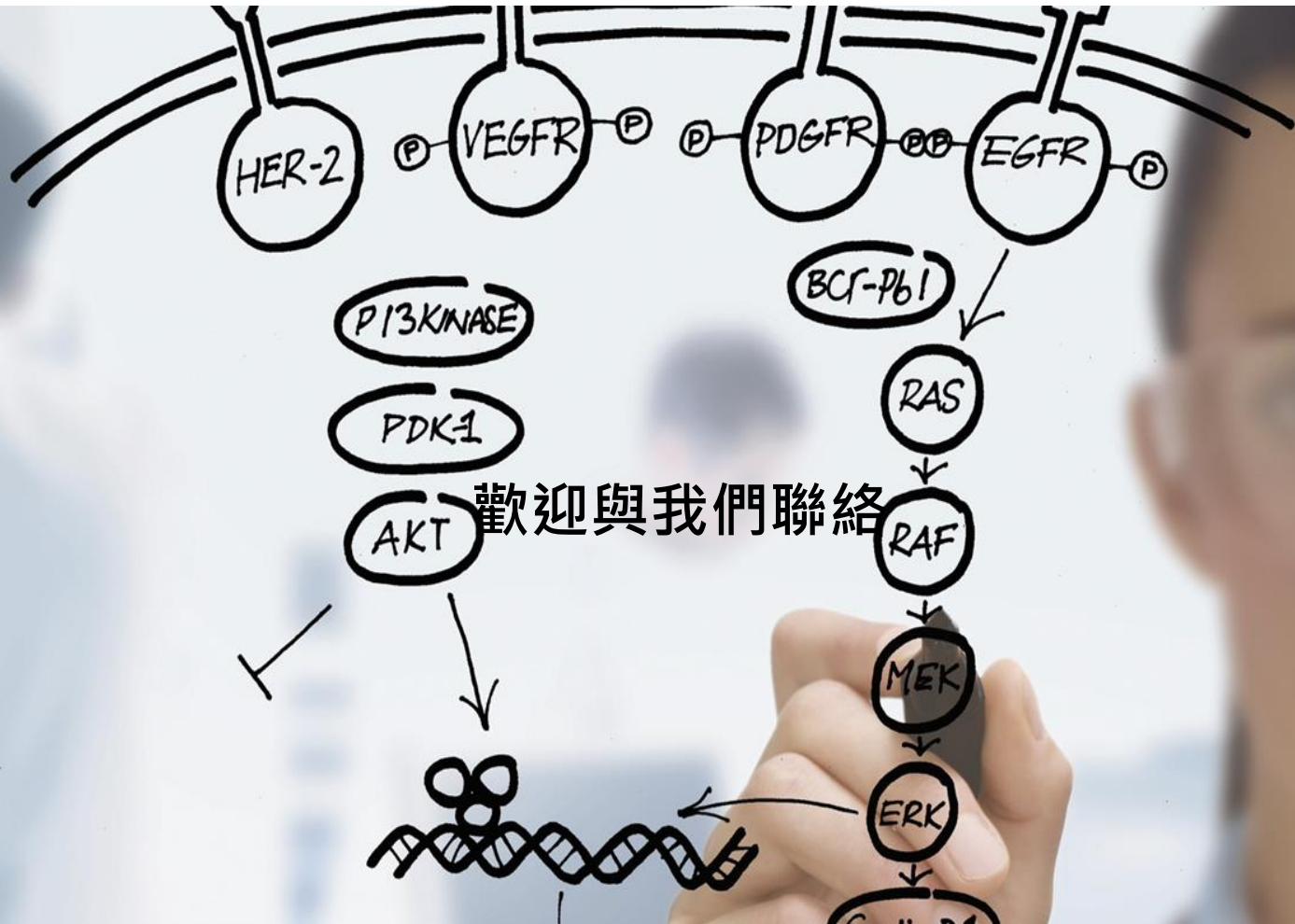
1. My Pathway
2. Path Designer

使用IPA進行分子模型建構並繪製訊息傳遞路徑

## D. Q & A



# Q&A



Office: +886-2-2795-1777#3027

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

My E-mail: [clairtsai@gga.asia](mailto:clairtsai@gga.asia)

MSC Support: [msc-support@gga.asia](mailto:msc-support@gga.asia)