

IPA 系統生物學分析軟體暨資料庫
基礎操作課程

KMU
2017 Oct

Gene 陳冠文
Senior Deputy Manager and IPA certified analyst

Copyright and Disclaimer

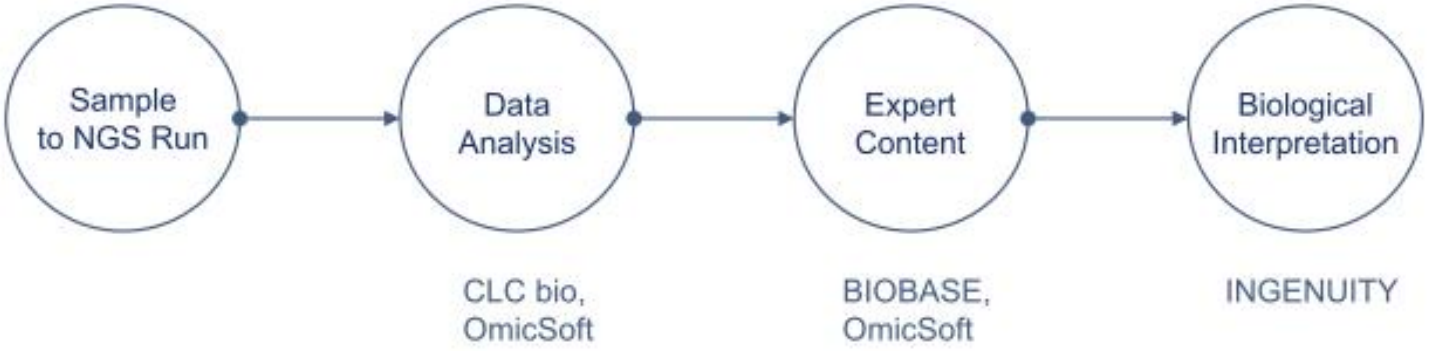
Copyright © 2017 GGA Corp. All rights reserved.

- 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.

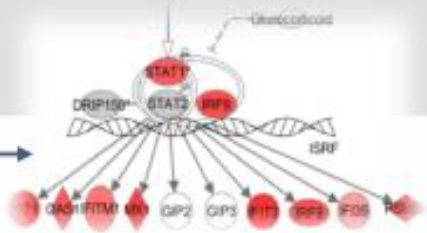
- In addition, information disclosed in this presentation and related documents, whether oral or written, is confidential or proprietary information of GGA Corp.. It shall be used only for the purpose of furthering our business relationship, and shall not be disclosed to third parties.

QIAGEN Bioinformatics Solution



Qiagen Products	CLC Main Workbench	HGMD	Ingenuity Variant Analysis
Various Providers	CLC Genomics Workbench (CLC Microbial Genomics Module, CLC Genome Finishing Module)	ANNOVAR	Ingenuity Pathway Analysis (IPA)
	CLC Genomics Server (CLC Genomics Cloud Engine, CLC Assembly Cell)	INOVA Genomes	QIAGEN Clinical Insight - Interpret
	OmicSoft ArraySuite	OmicSoft OncoLand	
	CLC Biomedical Genomics Workbench	OmicSoft DiseaseLand	
	QIAGEN Clinical Insight – Analyze	OmicSoft GeneticsLand	





*Custom Solutions / Analysis Services also available

大綱

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

D. Q & A

Copyright©2017 GGA Corp. All rights reserved.

大綱

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

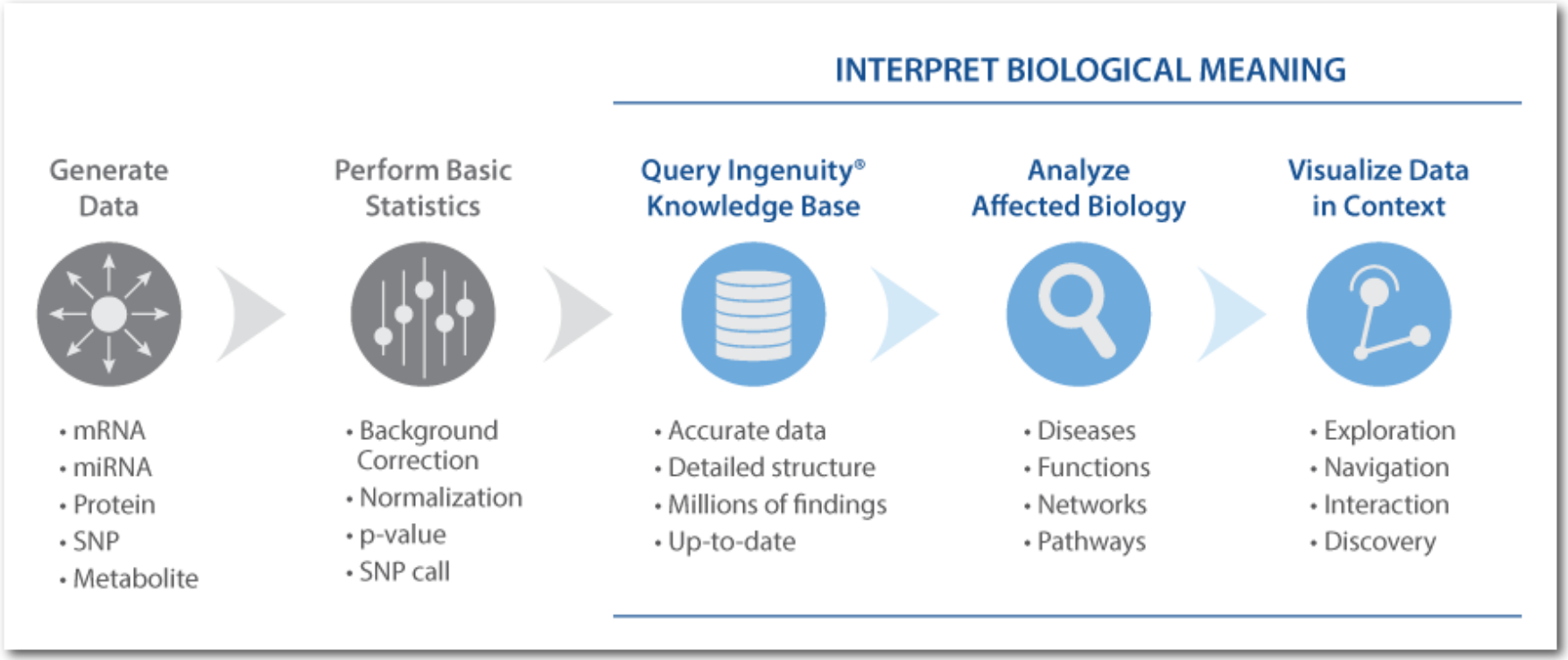
使用IPA進行分子模型建構並繪製訊息傳遞路徑

D. Q & A

Copyright©2017 GGA Corp. All rights reserved.

IPA

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。



Copyright©2017 GGA Corp. All rights reserved.

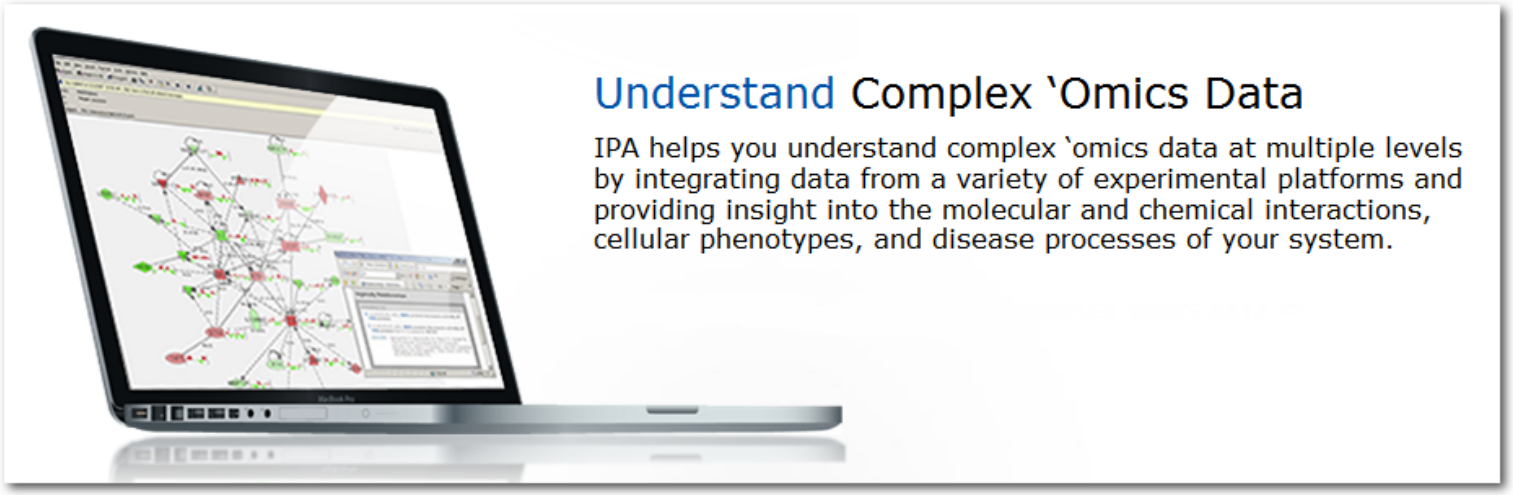
IPA

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
  - PhosphoProteomics
- 代謝體實驗



Copyright©2017 GGA Corp. All rights reserved.

Peer-reviewed publications citing Ingenuity apps

>10,000 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 1 of 86 Next > Last >>

1. Causal **analysis** approaches in **Ingenuity Pathway Analysis**.
   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

2. Genome-wide **analysis** of genetic variations assisted by **Ingenuity Pathway Analysis** to comprehensively investigate potential genetic targets associated with the progression of hepatocellular carcinoma.
   Yu F, Shen XY, Fan L, Yu ZC.
   Eur Rev Med Pharmacol Sci. 2014;18(15):2102-8.
   PMID: 25070813 **Free Article**
   Similar articles

3. Potential predictive plasma biomarkers for cervical cancer by 2D-DIGE proteomics and **Ingenuity Pathway Analysis**.
   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

4. Gene set enrichment **analysis** and **ingenuity pathway analysis** of metastatic clear cell renal cell carcinoma cell line.
   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

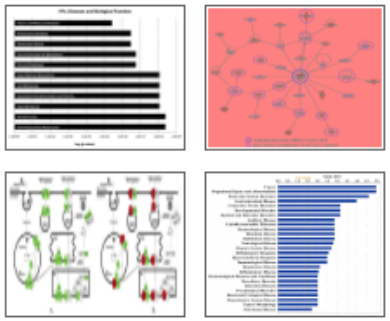
Results by year

Download

Related searches

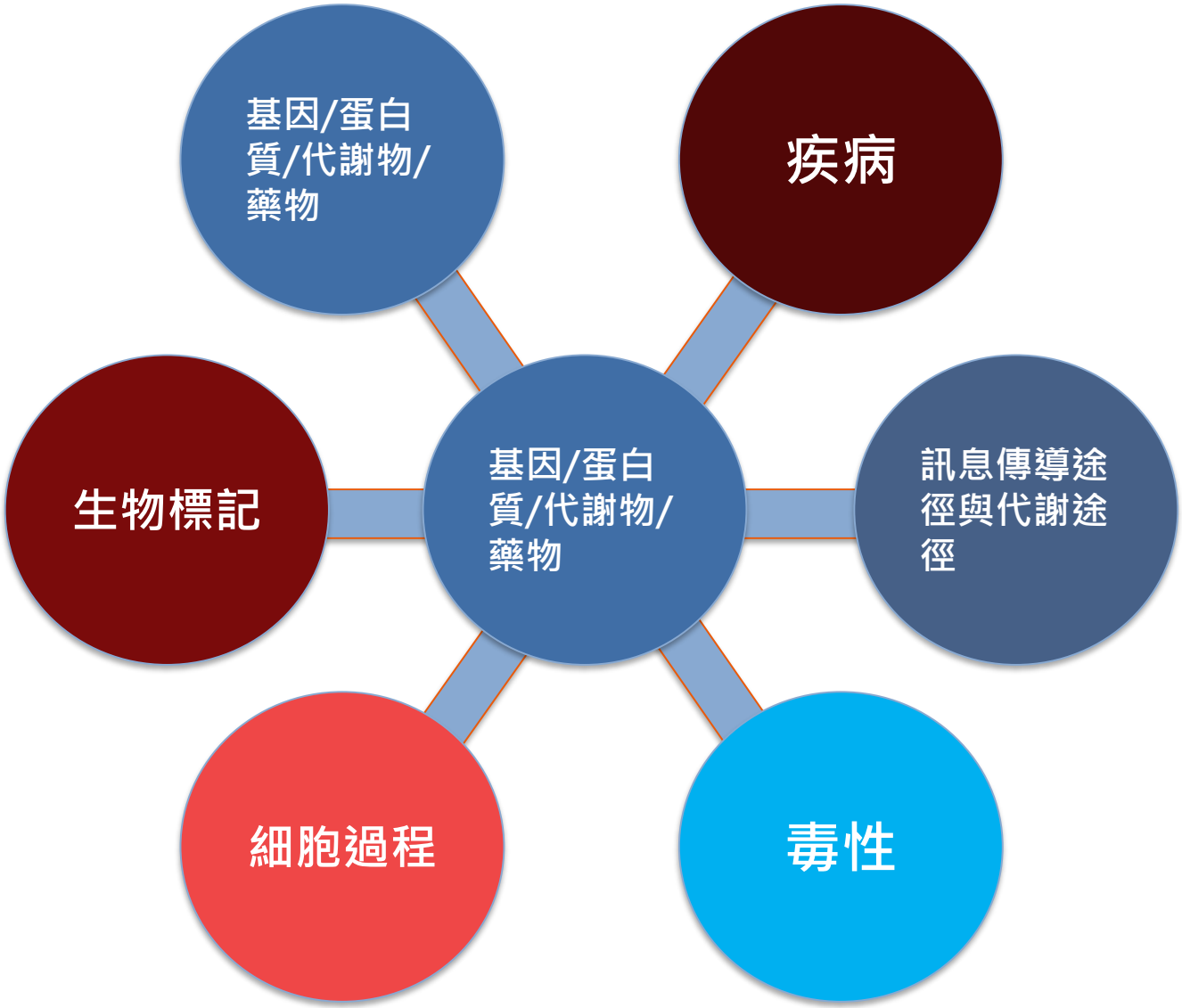
ingenuity pathway analysis gene
ingenuity pathway analysis mirna
ingenuity pathway analysis network
ingenuity pathway analysis proteomics

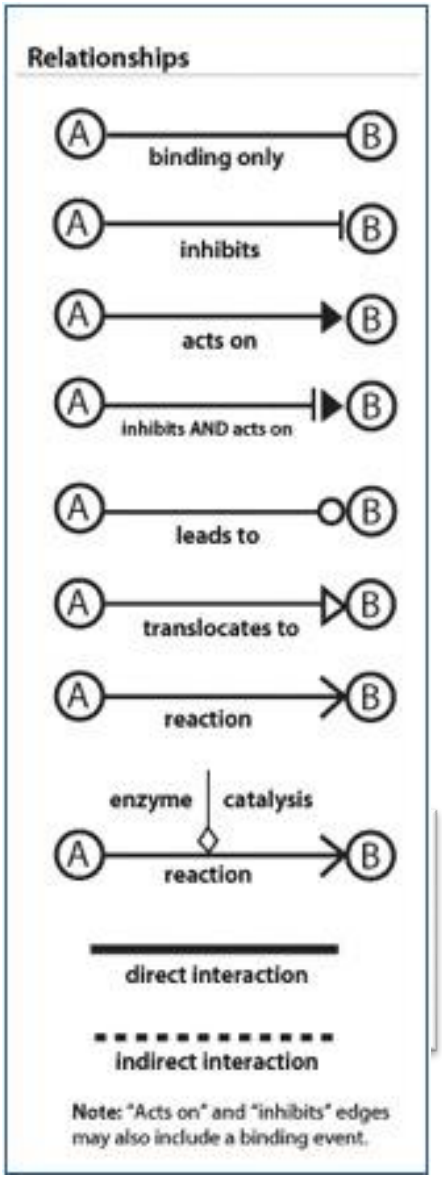
PMC Images search for *ingenuity pathway analysis*



Copyright©2017 GGA Corp. All rights reserved.

用IPA來發掘實驗資料中各類型關係





Copyright©2017 GGA Corp. All rights reserved.

Third Party Database

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



Copyright©2016 GGA Corp. All rights reserved.

Ingenuity Expert Findings

From full text, contextual detail, experimentally demonstrated

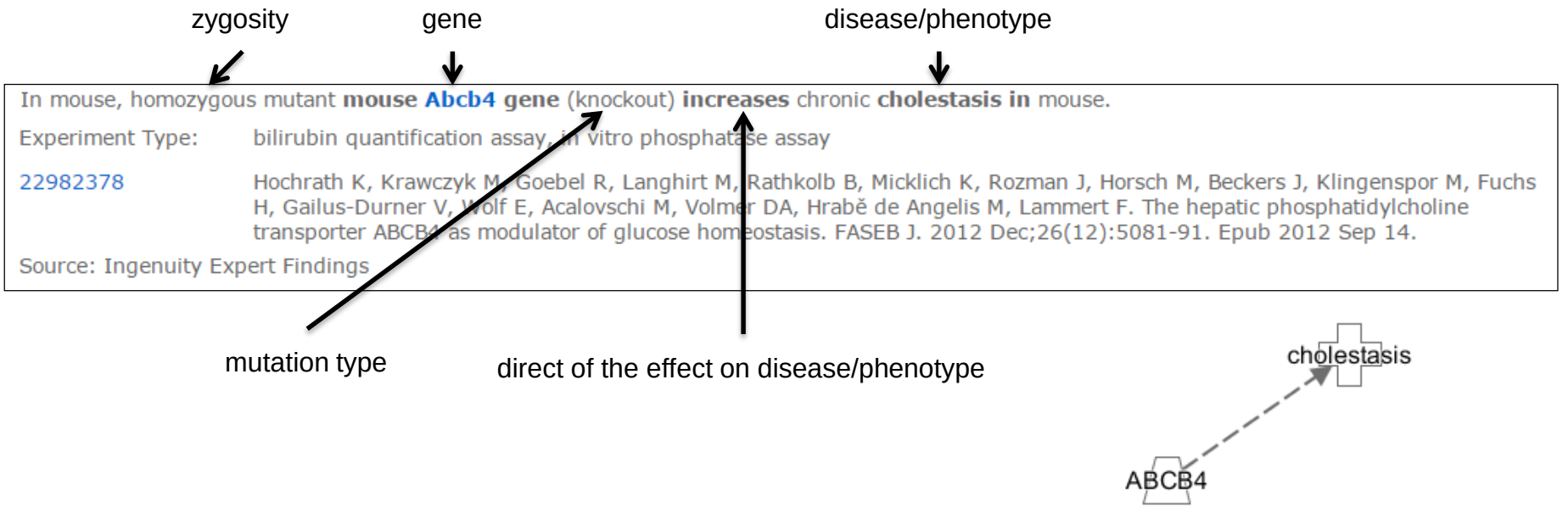
Original sentence from publication	Ingenuity Expert Findings
nNOS overexpression mice showed reduced myocardial contractility.	Transgenic nNOS in myocardium from mouse heart decreases the contractility of myocardium in left ventricle from mouse heart.
Francisella organisms efficiently induce IL-1beta 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

Copyright©2017 GGA Corp. All rights reserved.

What are Findings

五百多萬筆以上IPA Finding，包含各種生物分子的關係建構



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

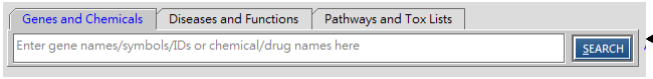
- Species
- Synonyms
- Experimental method
- Site of post-translational modification
- Direction of change
- Tissue context
- Cell line context
- Original source

Copyright©2017 GGA Corp. All rights reserved.

Entry Points in IPA

Biological Questions

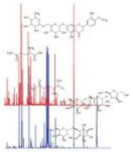
Search



Experiment Data



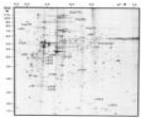
Expression arrays



Mass spec

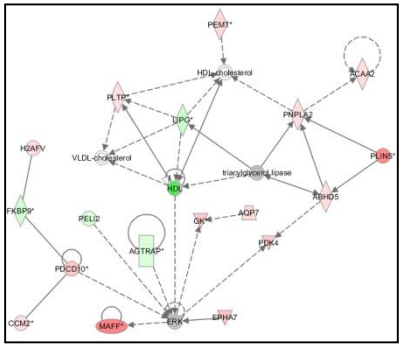


Protein arrays



2D Gel electrophoresis

Custom Pathway



Networks

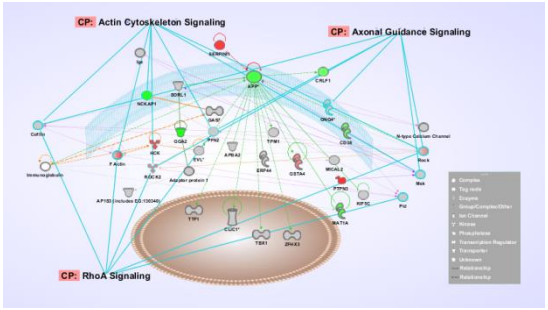
Core

IPA-Biomarker

IPA-Tox

IPA-Metabolomics

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

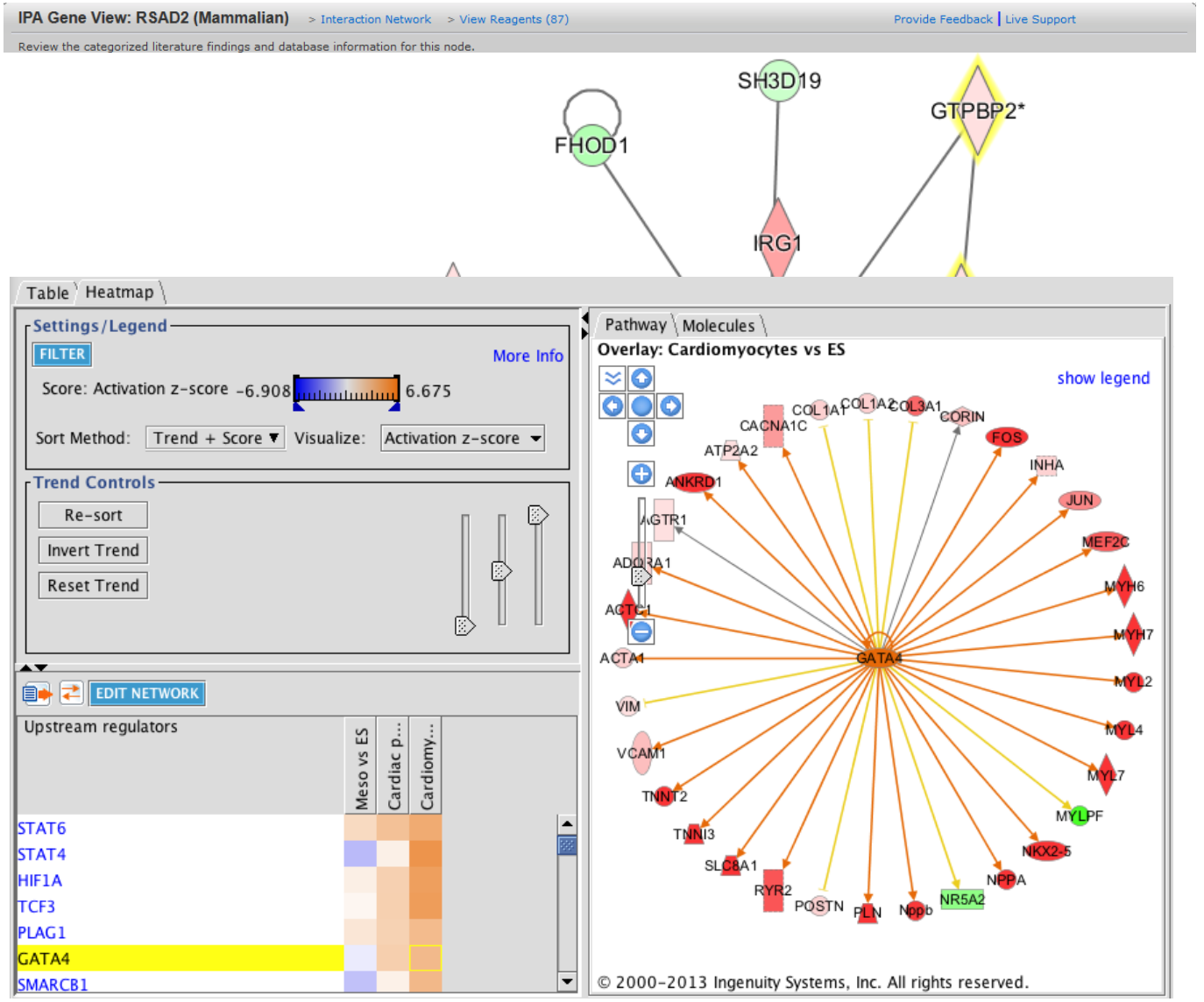


Communicate & Collaborate

Copyright©2017 GGA Corp. All rights reserved.

IPA: Unique Tools for Biological Analyses and Interpretation

- 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

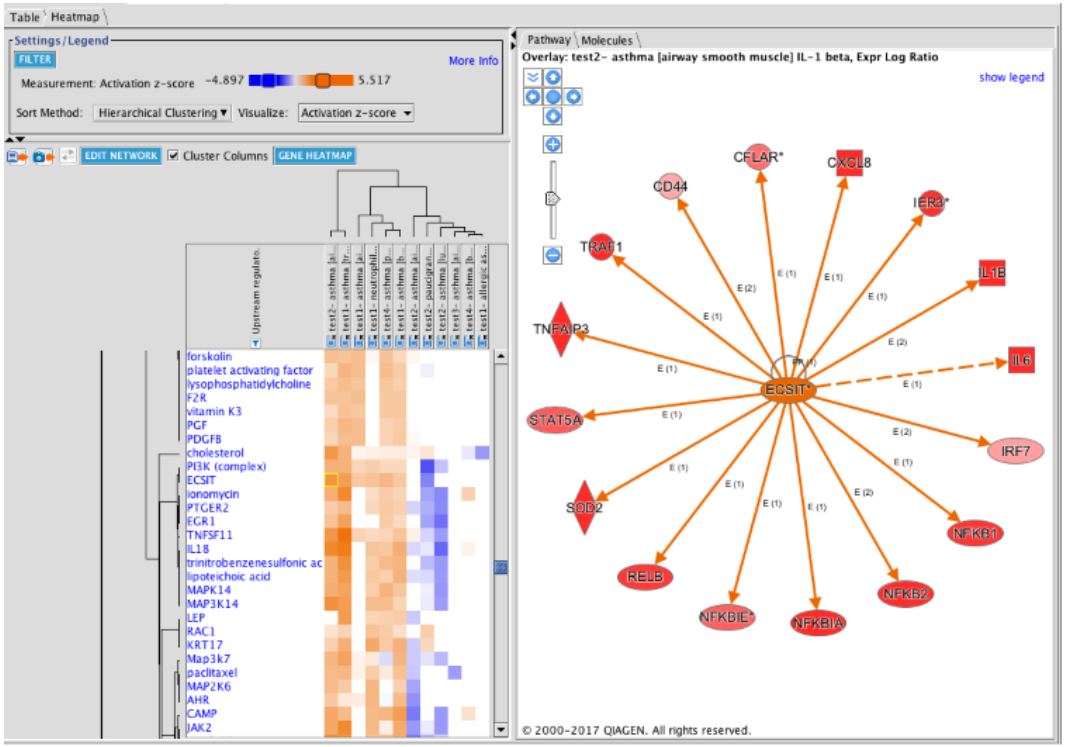


Copyright©2017 GGA Corp. All rights reserved.

What's new in the IPA Fall Release

Content Updates

- Dendrograms in the Comparison Analysis heatmap
- Export of chemical IDs from networks and pathways
- Four new Canonical Pathways
- Support for Clariom arrays from Affymetrix
- New findings, including 56,000 from the BioPlex 2.0 protein-protein interaction database

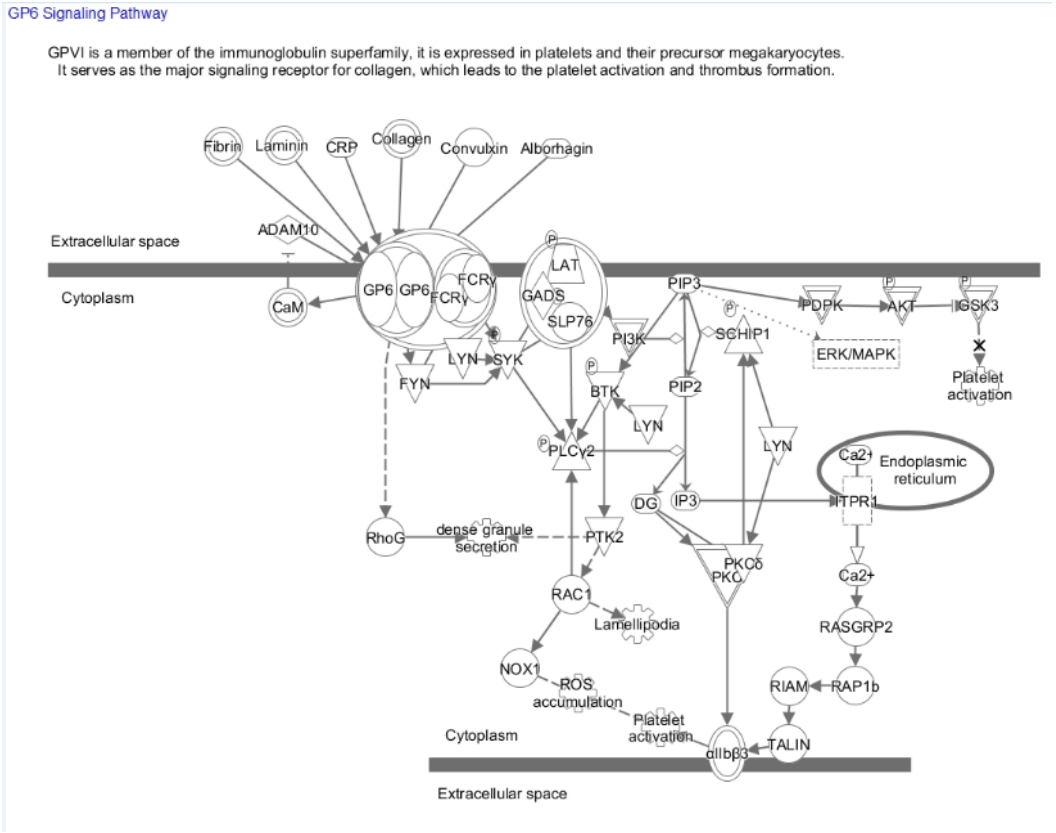


Dendrograms in the Comparison Analysis heatmap

Copyright©2017 GGA Corp. All rights reserved.

Content Updates

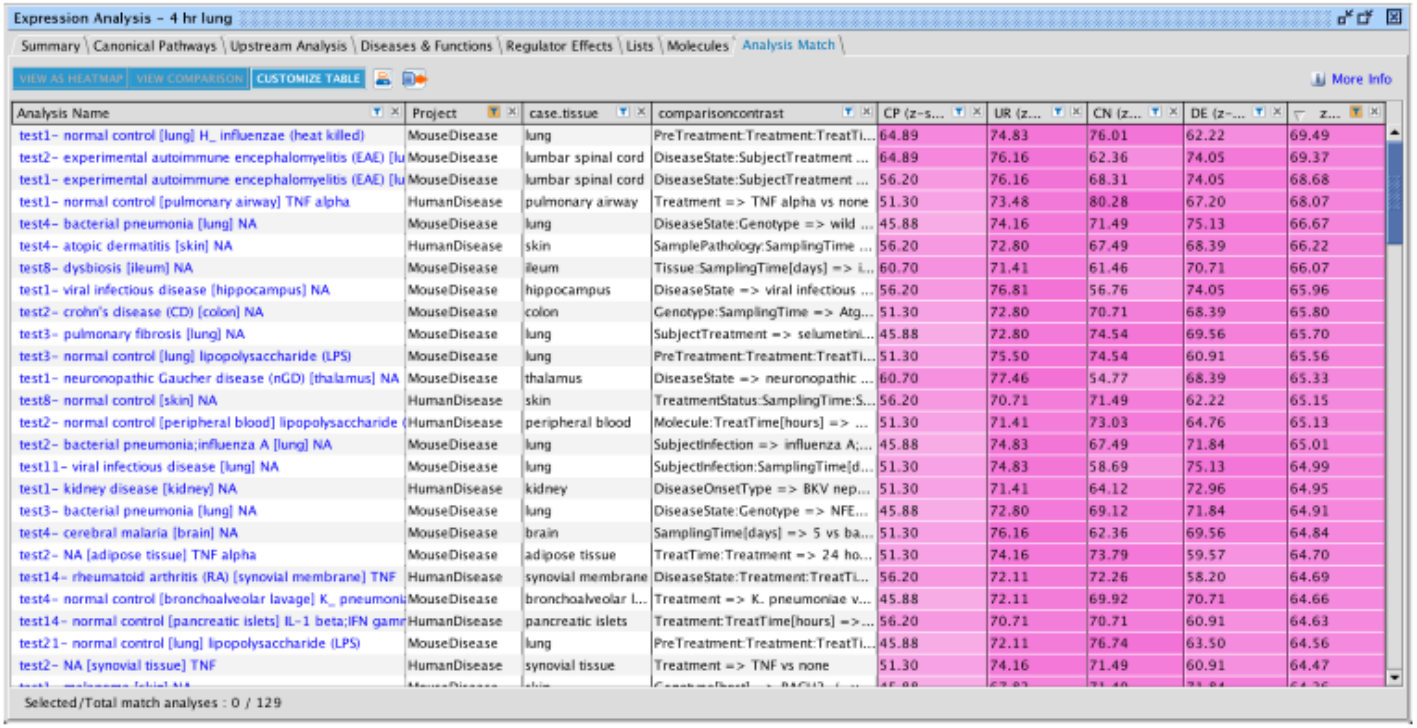
- Four new Canonical Pathways
  - GP6 Signaling Pathway
  - IL-7 Signaling Pathway
  - Sirtuin Signaling Pathway
  - Neuroinflammation Signaling Pathway



Copyright©2017 GGA Corp. All rights reserved.

Content Updates

- Analysis Match
  - Analysis Match automatically discovers other IPA Core Analyses with similar (or opposite) biological results as compared to yours, to help confirm your interpretation of the results or to provide unexpected insights into underlying shared biological mechanisms. It matches your analysis against other analyses you have created (in your Project Manager) as well as *thousands* of other human and mouse expression analyses curated from public sources.



Analysis Name	Project	case.tissue	comparisoncontrast	CP (z-s...	UR (z...	CN (z...	DE (z-...	z...
test1- normal control [lung] H_ influenzae (heat killed)	MouseDisease	lung	PreTreatment:Treatment:TreatTi...	64.89	74.83	76.01	62.22	69.49
test2- experimental autoimmune encephalomyelitis (EAE) [lu	MouseDisease	lumbar spinal cord	DiseaseState:SubjectTreatment ...	64.89	76.16	62.36	74.05	69.37
test1- experimental autoimmune encephalomyelitis (EAE) [lu	MouseDisease	lumbar spinal cord	DiseaseState:SubjectTreatment ...	56.20	76.16	68.31	74.05	68.68
test1- normal control [pulmonary airway] TNF alpha	HumanDisease	pulmonary airway	Treatment => TNF alpha vs none	51.30	73.48	80.28	67.20	68.07
test4- bacterial pneumonia [lung] NA	MouseDisease	lung	DiseaseState:Genotype => wild ...	45.88	74.16	71.49	75.13	66.67
test4- atopic dermatitis [skin] NA	HumanDisease	skin	SamplePathology:SamplingTime ...	56.20	72.80	67.49	68.39	66.22
test8- dysbiosis [ileum] NA	MouseDisease	ileum	Tissue:SamplingTime[days] => i...	60.70	71.41	61.46	70.71	66.07
test1- viral infectious disease [hippocampus] NA	MouseDisease	hippocampus	DiseaseState => viral infectious ...	56.20	76.81	56.76	74.05	65.96
test2- crohn's disease (CD) [colon] NA	MouseDisease	colon	Genotype:SamplingTime => Atg...	51.30	72.80	70.71	68.39	65.80
test3- pulmonary fibrosis [lung] NA	MouseDisease	lung	SubjectTreatment => selumetini...	45.88	72.80	74.54	69.56	65.70
test3- normal control [lung] lipopolysaccharide (LPS)	MouseDisease	lung	PreTreatment:Treatment:TreatTi...	51.30	75.50	74.54	60.91	65.56
test1- neuronopathic Gaucher disease (nGD) [thalamus] NA	MouseDisease	thalamus	DiseaseState => neuronopathic ...	60.70	77.46	54.77	68.39	65.33
test8- normal control [skin] NA	HumanDisease	skin	TreatmentStatus:SamplingTime:S...	56.20	70.71	71.49	62.22	65.15
test2- normal control [peripheral blood] lipopolysaccharide (	HumanDisease	peripheral blood	Molecule:TreatTime[hours] => ...	51.30	71.41	73.03	64.76	65.13
test2- bacterial pneumonia;influenza A [lung] NA	MouseDisease	lung	SubjectInfection => influenza A;...	45.88	74.83	67.49	71.84	65.01
test11- viral infectious disease [lung] NA	MouseDisease	lung	SubjectInfection:SamplingTime[d...	51.30	74.83	58.69	75.13	64.99
test1- kidney disease [kidney] NA	HumanDisease	kidney	DiseaseOnsetType => BKV nep...	51.30	71.41	64.12	72.96	64.95
test3- bacterial pneumonia [lung] NA	MouseDisease	lung	DiseaseState:Genotype => NFE...	45.88	72.80	69.12	71.84	64.91
test4- cerebral malaria [brain] NA	MouseDisease	brain	SamplingTime[days] => 5 vs ba...	51.30	76.16	62.36	69.56	64.84
test2- NA [adipose tissue] TNF alpha	MouseDisease	adipose tissue	TreatTime:Treatment => 24 ho...	51.30	74.16	73.79	59.57	64.70
test14- rheumatoid arthritis (RA) [synovial membrane] TNF	HumanDisease	synovial membrane	DiseaseState:Treatment:TreatTi...	56.20	72.11	72.26	58.20	64.69
test4- normal control [bronchoalveolar lavage] K_ pneumoni	MouseDisease	bronchoalveolar l...	Treatment => K. pneumoniae v...	45.88	72.11	69.92	70.71	64.66
test14- normal control [pancreatic islets] IL-1 beta;IFN gam	HumanDisease	pancreatic islets	Treatment:TreatTime[hours] =>...	56.20	70.71	70.71	60.91	64.63
test21- normal control [lung] lipopolysaccharide (LPS)	MouseDisease	lung	PreTreatment:Treatment:TreatTi...	45.88	72.11	76.74	63.50	64.56
test2- NA [synovial tissue] TNF	HumanDisease	synovial tissue	Treatment => TNF vs none	51.30	74.16	71.49	60.91	64.47

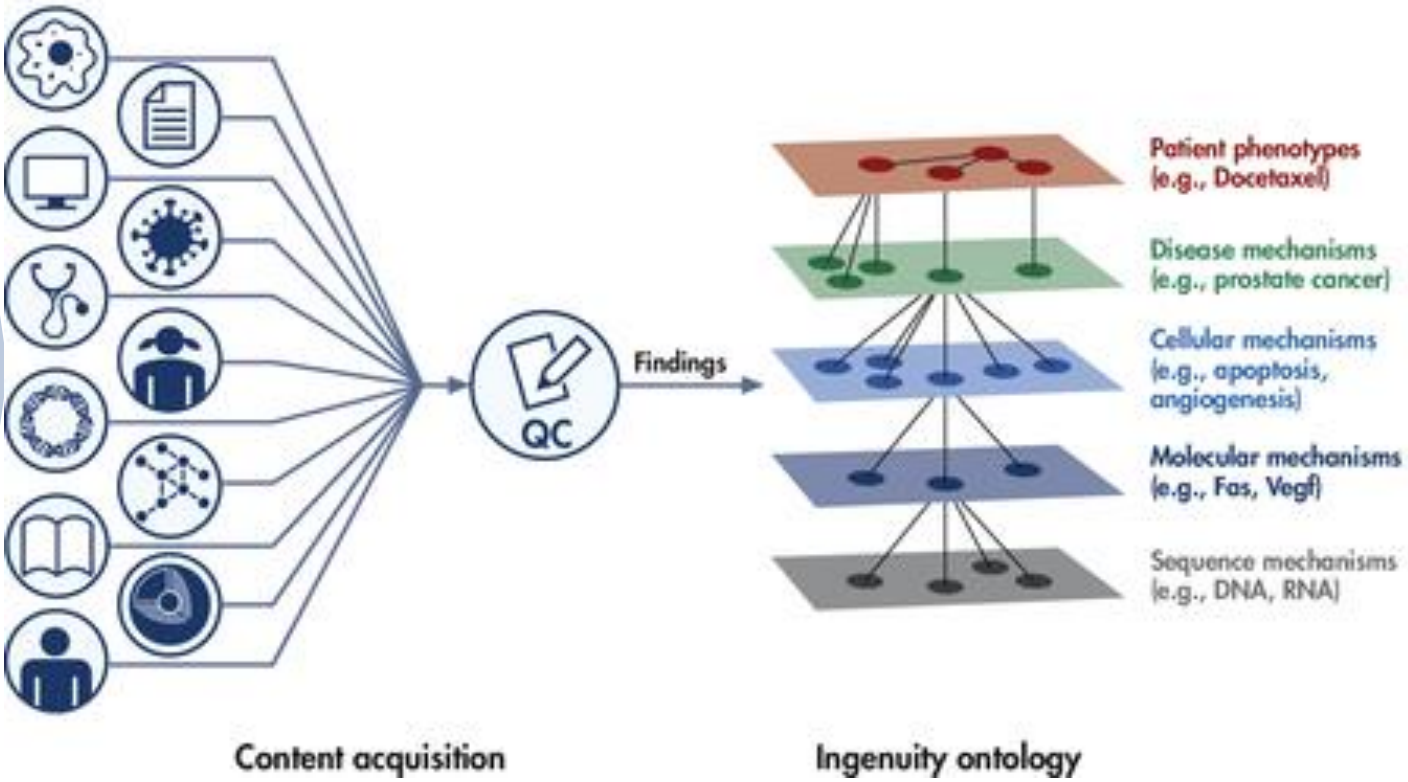
*Analysis Match requires additional licensing.

Copyright©2017 GGA Corp. All rights reserved.

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



Copyright©2017 GGA Corp. All rights reserved.

大綱

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

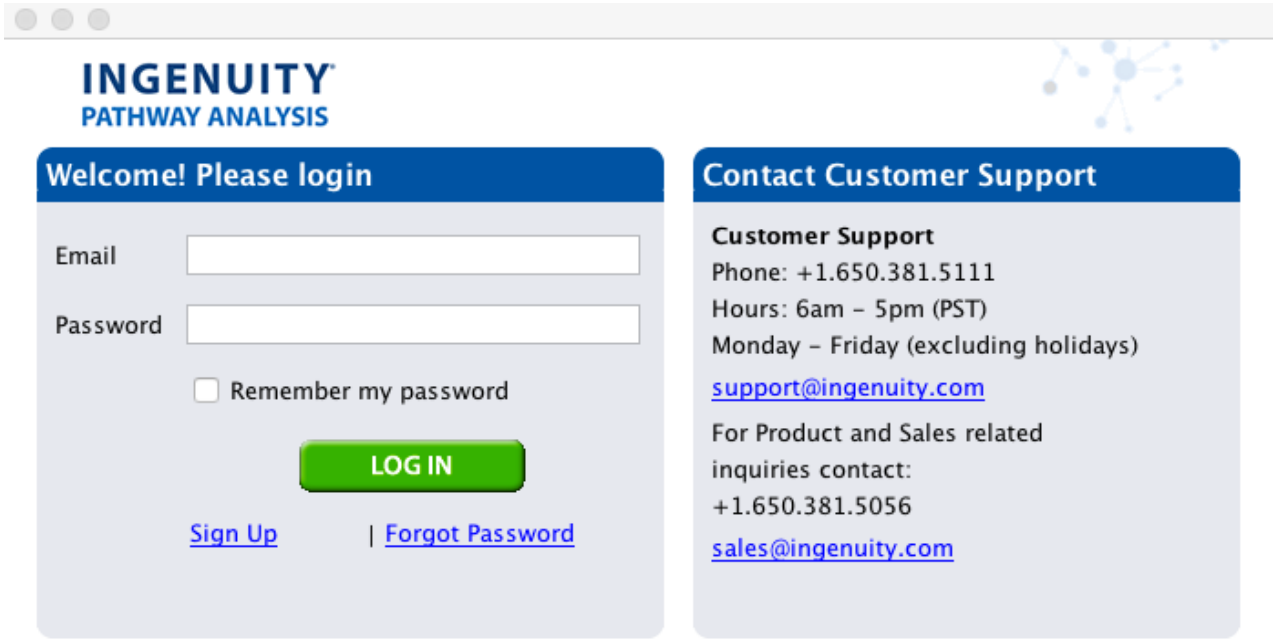
使用IPA進行分子模型建構並繪製訊息傳遞路徑

D. Q & A

Copyright©2017 GGA Corp. All rights reserved.

New IPA Client Installer

- Easier access
- Faster launch
- Can launch without a browser or Java plugin



https://www.ingenuity.com/products/login

Copyright©2017 GGA Corp. All rights reserved.

大綱

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

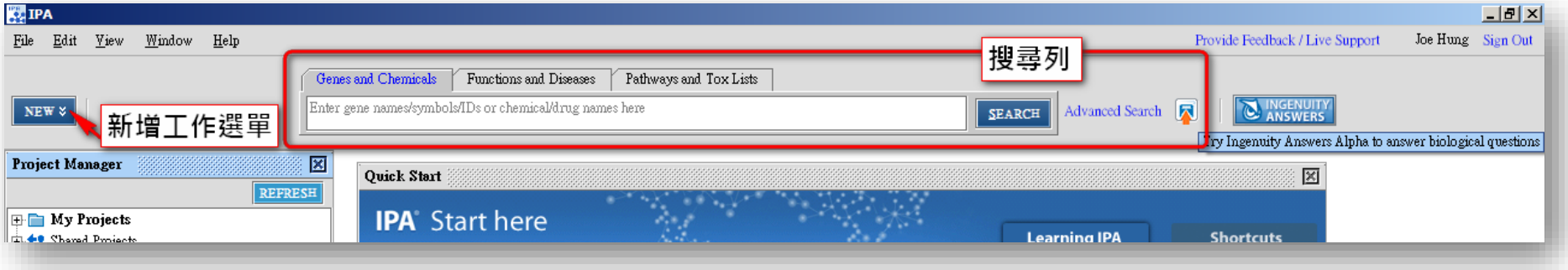
C. Building and Editing a Pathway for Publication
使用IPA進行分子模型建構並繪製訊息傳遞路徑

D. Q & A

Copyright©2017 GGA Corp. All rights reserved.

Searching

- 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



Copyright©2017 GGA Corp. All rights reserved.

Key Terminology

- **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

Copyright©2017 GGA Corp. All rights reserved.



Live Demo

Copyright©2017 GGA Corp. All rights reserved.

Hands-on Exercises I

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**?

Copyright©2017 GGA Corp. All rights reserved.

Hands-on Exercises

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

Copyright©2017 GGA Corp. All rights reserved.

大綱

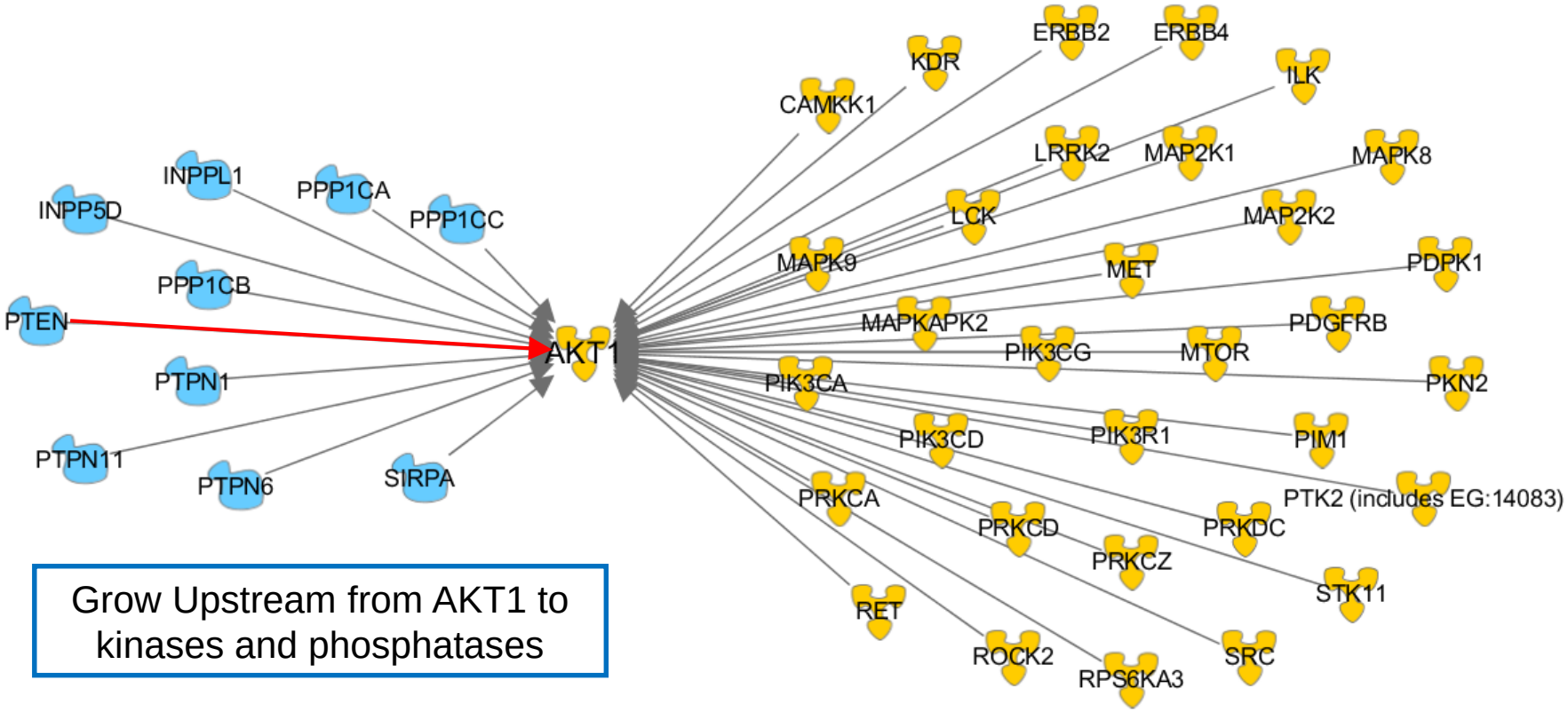
A. Introduction and Getting Started in IPA
IPA介紹與啟動IPA

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

Copyright©2017 GGA Corp. All rights reserved.

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

Copyright©2017 GGA Corp. All rights reserved.

Building Pathways

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

Copyright©2017 GGA Corp. All rights reserved.

Key Terminology

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

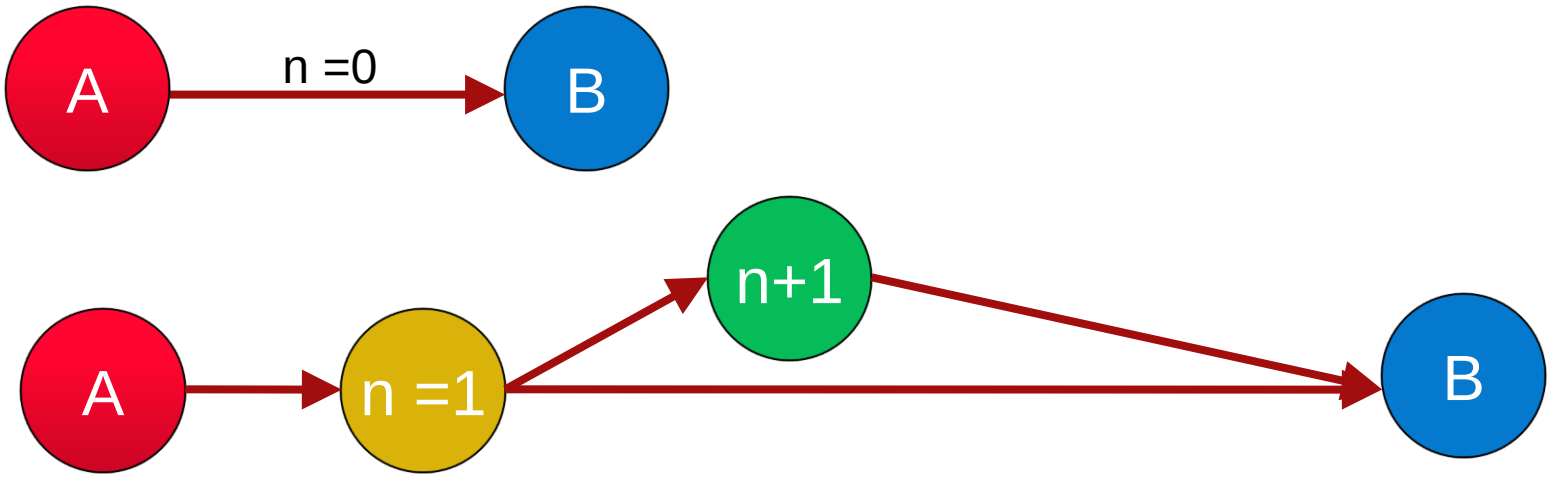
Relationship Type:

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

Copyright©2017 GGA Corp. All rights reserved.

How Path Explorer Works

- 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)



Copyright©2017 GGA Corp. All rights reserved.

Hands-on Exercises II

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?**

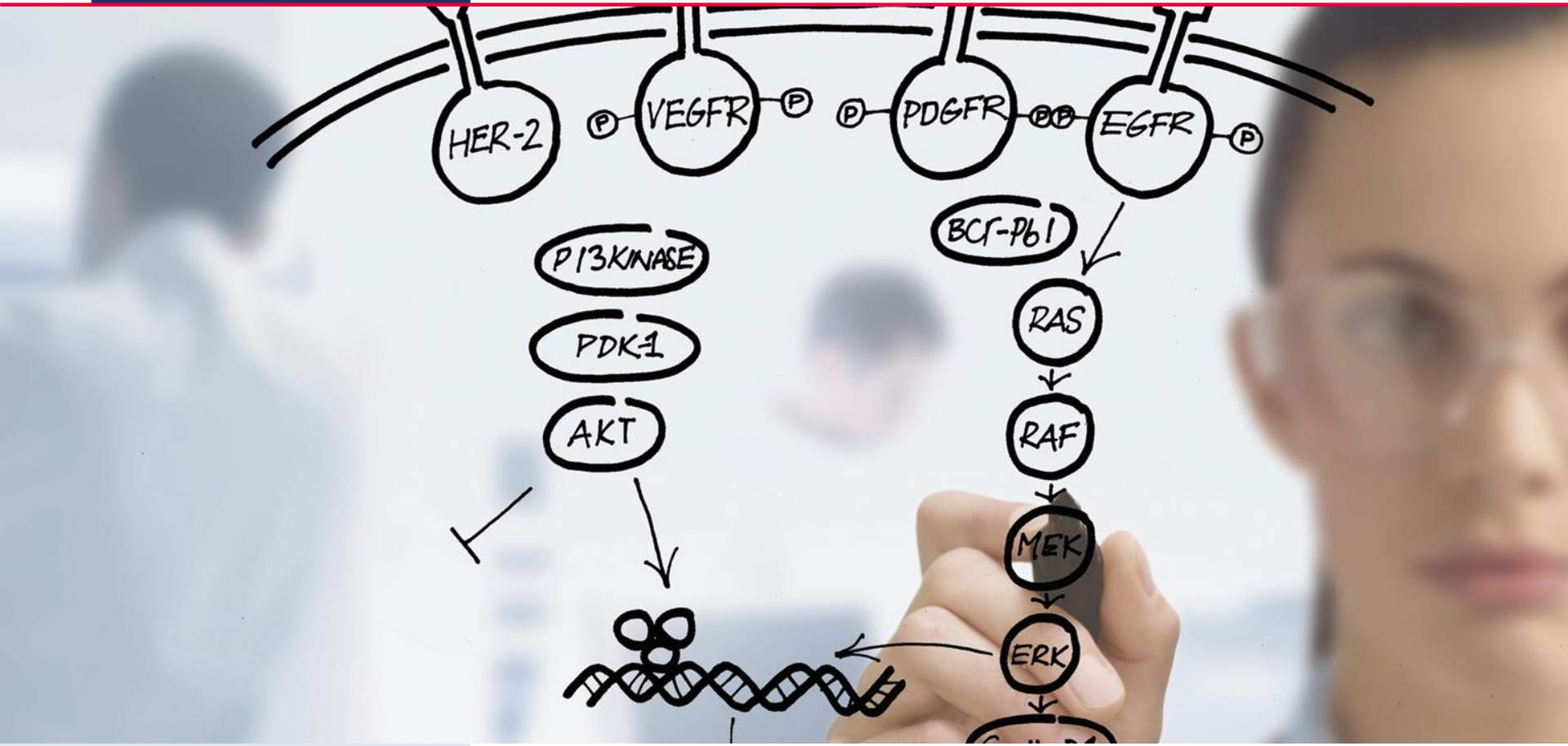
3. **Are these molecules involved in any Canonical Pathways?**

4. **Add at least one organelle or other cellular structure to your pathway and move the molecules on your pathway to the appropriate location.**

Copyright©2017 GGA Corp. All rights reserved.

Q&A

Copyright©2017 GGA Corp. All rights reserved.



歡迎與我們聯絡

創源生技
GGA

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

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

My E-mail: Genechen@gga.asia

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