# Ingenuity Pathway Analysis(IPA)



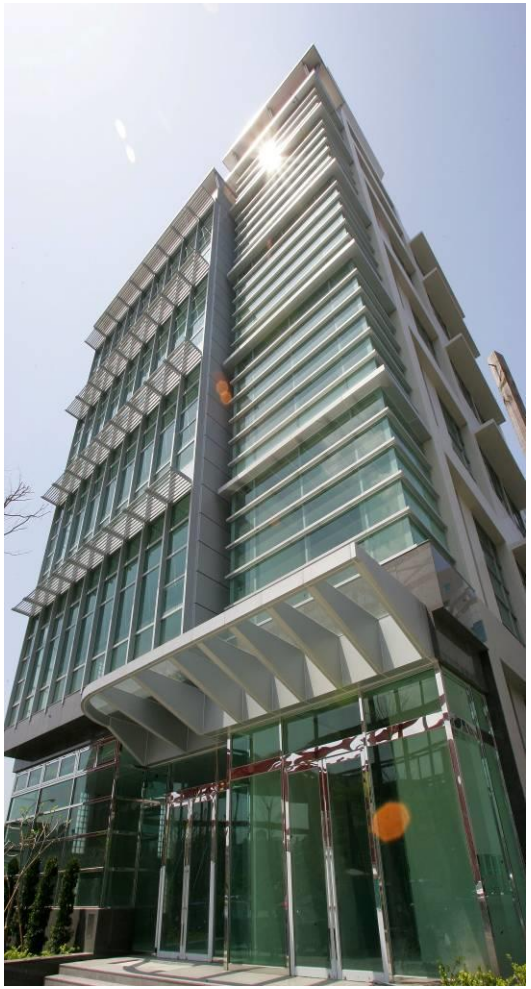

## Basic Training Course

IPA資料庫使用介紹：如何查找資訊、繪製路徑及上傳dataset

**Clair Tsai　蔡宜庭**

**創源生技 業務主任**

# About GGA



## GGA is part of the BIONET Group (訊聯生物科技)

CEO: Christopher Tsai, Ph.D. 蔡政憲 博士

Established: Nov. 2008

Main Product & Service Areas:

- Genetic Testing & Molecular Diagnosis
- **Scientific Informatics & Bio IT**

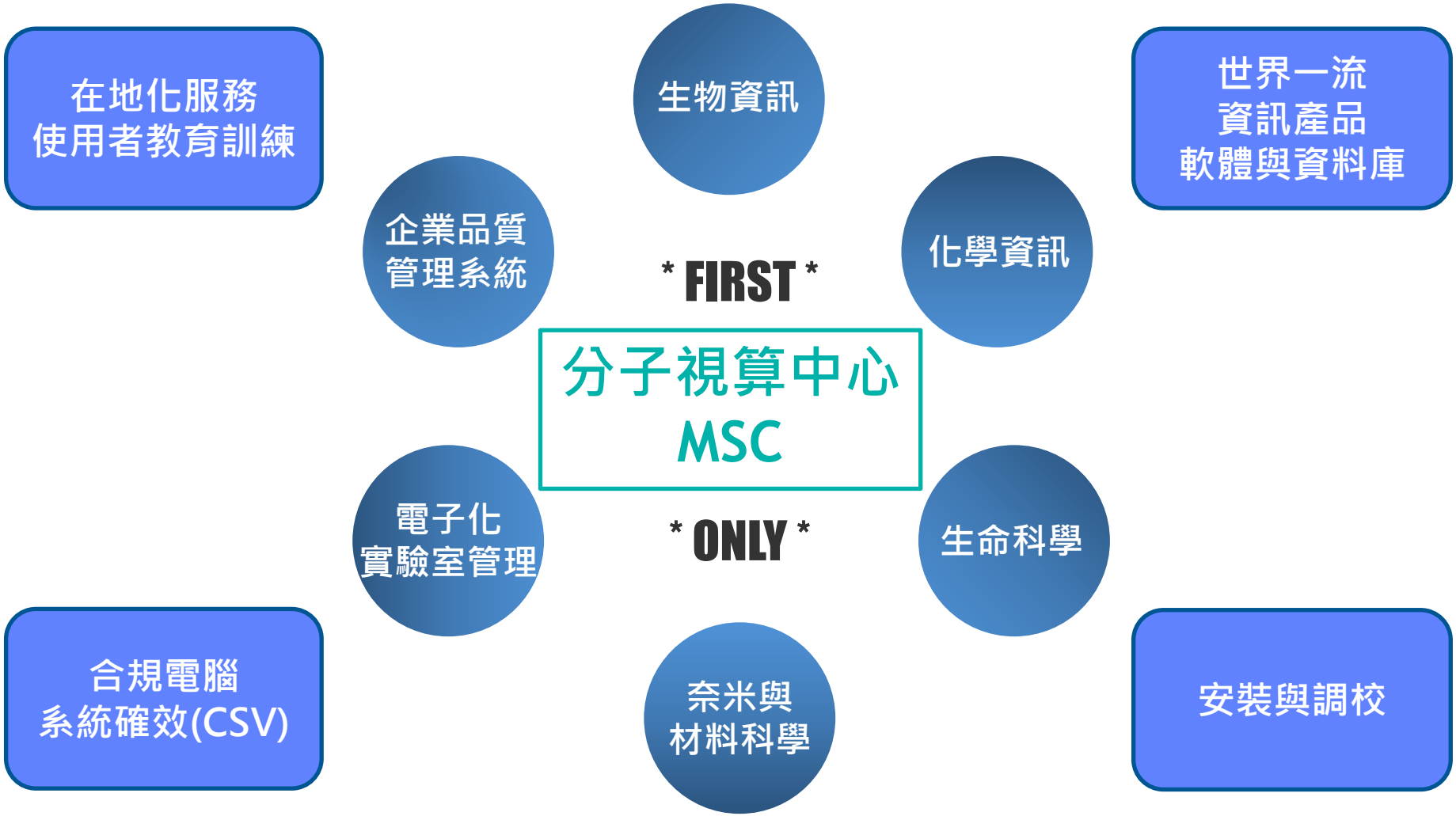
IPO Date: September 17, 2012

Stock Ticker: 4160 (Taiwan OTC)



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# Molecular Science Center in GGA




02-2795-1777#3012



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# IPA功能及操作介紹

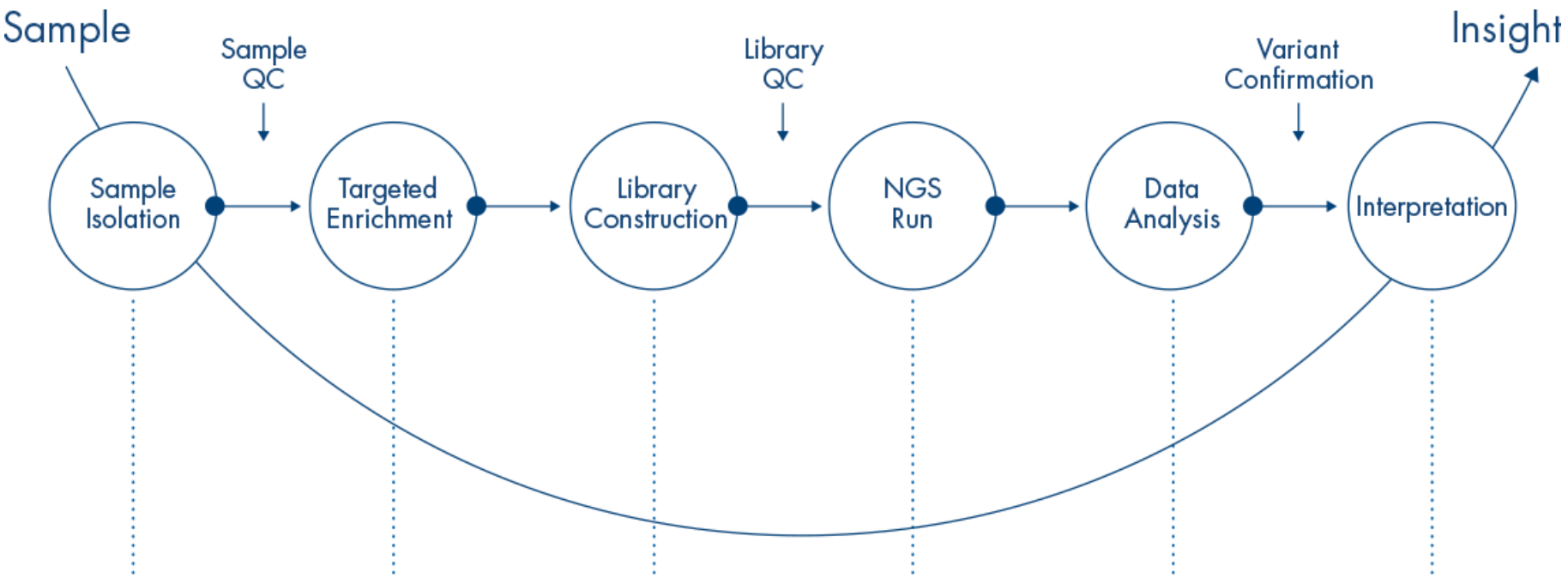
1. IPA功能介紹
2. 使用IPA進行分子模型建構並繪製訊息傳遞路徑
3. 實驗資料上傳與條件設定





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# QIAGEN Bioinformatics Solution




QIAamp DNA kits

PAXgene RNA/DNA kits

GeneRead DNA FFPE Kit

QIAamp Circulating NA Kit

exoRNeasy Kits

RNeasy Kits

QIAseqTargeted RNA Panels

QIAseq DNAseq Panels v3

QIAseq FX Library Kits

QIAseq 1-step Amplicon KIt

QIAseq Ultralow Input Kit

REPLI-g® Single Cell Kits

**Biomedical Genomics Workbench & Biomedical Genomics Server Solution**

**QIAGEN® Clinical Insight Analyze (QCI-A)**

**Ingenuity Variant Analysis**

**QIAGEN® Clinical Insight Interpret (QCI-I)**

**Ingenuity Pathway Analysis**

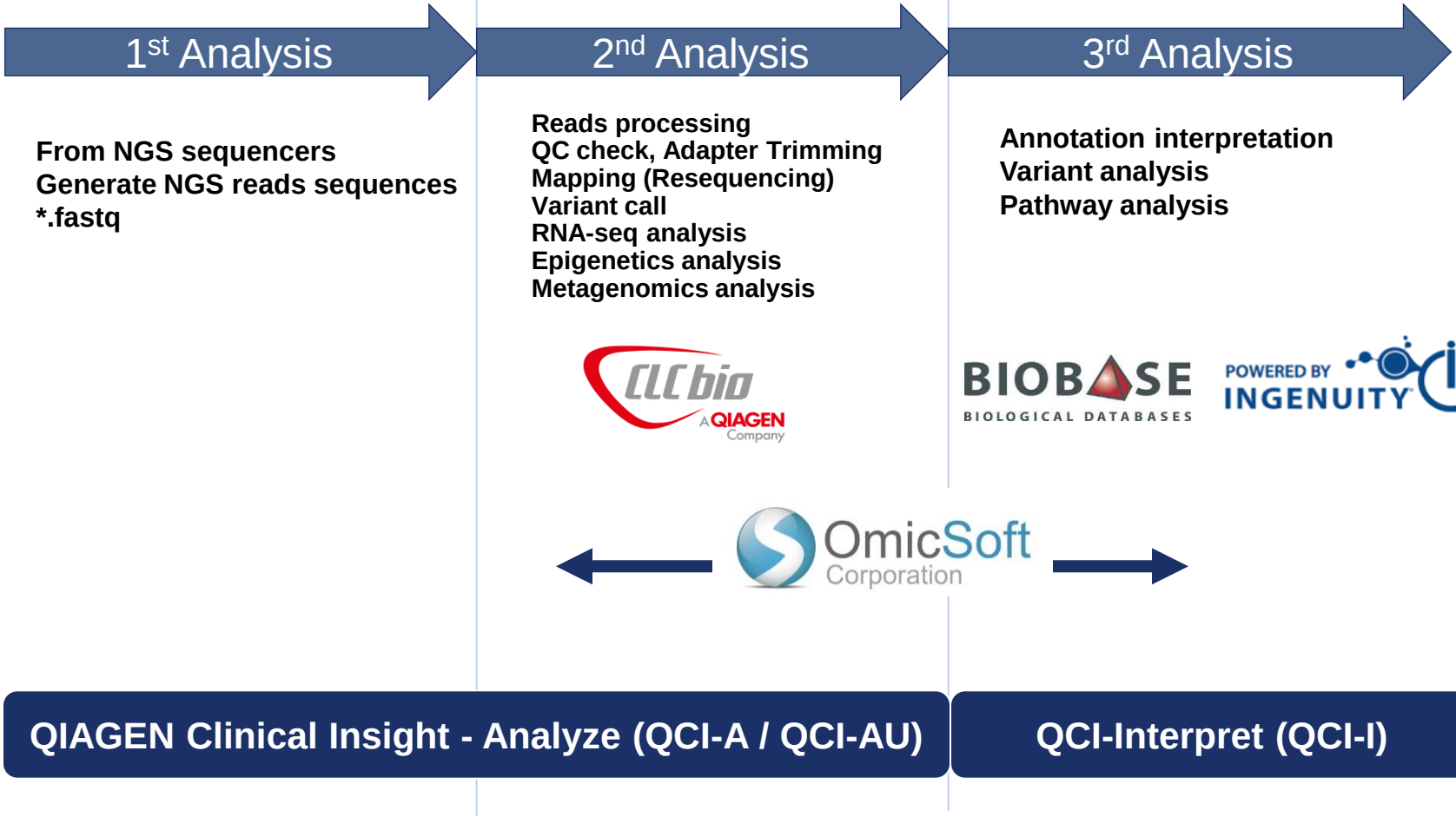
**HGMD®**



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# QIAGEN BioX Product Portfolio

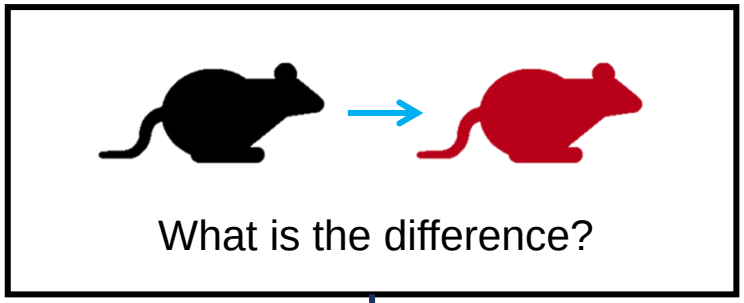
## By NGS Data analysis workflow






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# Why are we using IPA?



What is the difference?

Your dataset

pathway

Relationship With other Observation

Disease

function

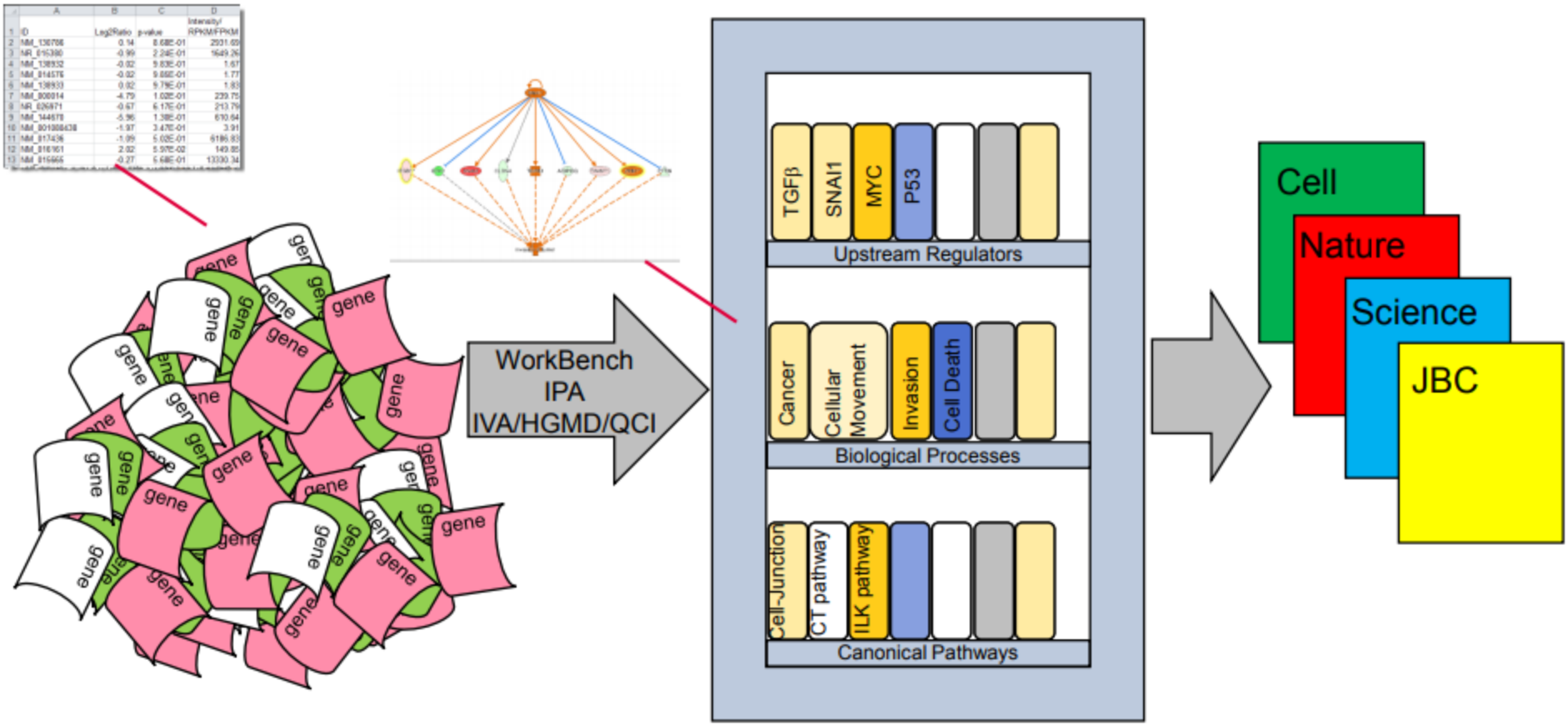
What are the relationship between each molecules?

What do they relate to each other?



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# What can Qiagen bioinformatics products do for you?

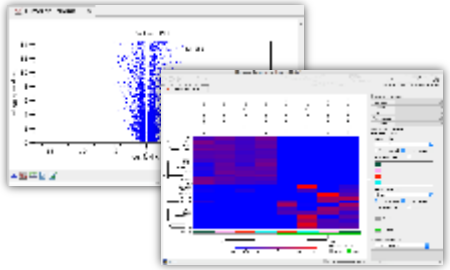


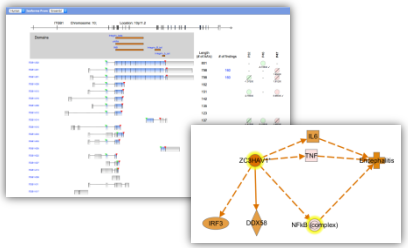



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# QIAGEN solution: NGS 數據串接分析處理

CLC製圖：
多功能分析
2D 階層式分群
PCA與火山圖
文氏圖





IPA：分辨轉錄異構物與生物意義

資料與描述型資料匯入 (CLC)

定序資料之序列比對

定量並找出顯著表現的基因

標準化&統計分析

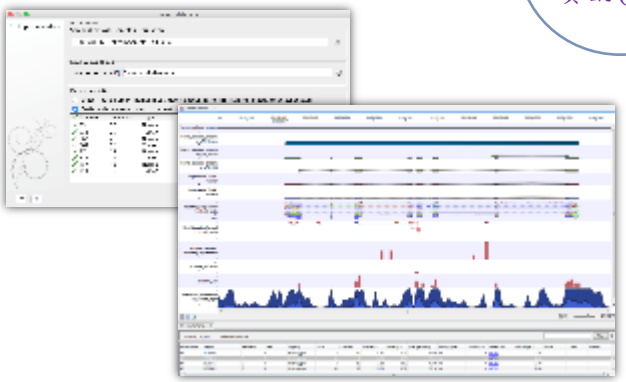
辨識定序資料內之變異資訊 (IVA)

變異位點註解以及找出潛在性生物意義變異點

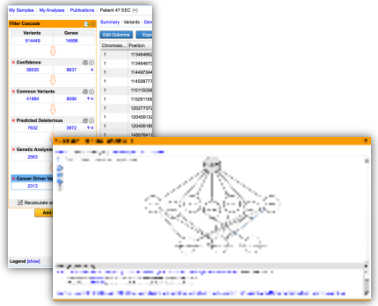
生物路徑分析 (IPA)

找尋上游調控因子

產生可能因子假說



CLC序列分析頁面：
視覺化基因表現圖譜與變異圖譜，
並能整合在同一個瀏覽頁面內



IVA變異位點分析：
區分變異點以及其生物、路徑至表型關係



IPA：
了解上下游基因表現對生物途徑的影響



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# IPA

## IPA orthologous :

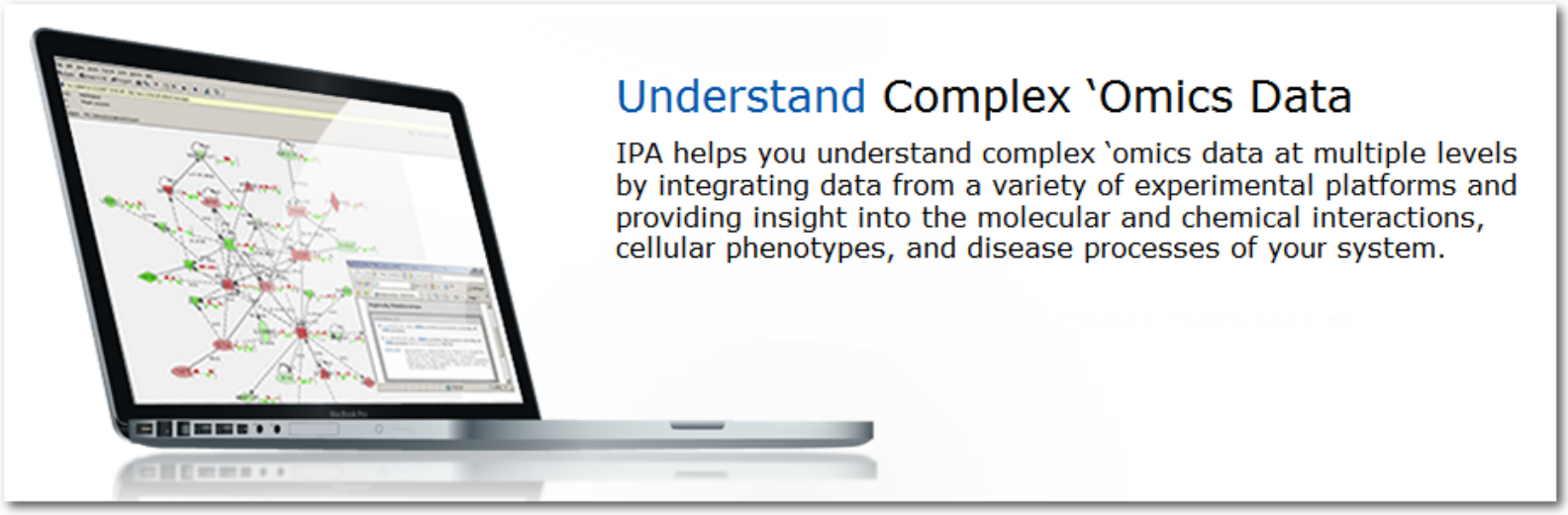
Arabidopsis thaliana
Bos taurus (bovine)
Caenorhabditis elegans
Gallus gallus (chicken)
Pan troglodytes (chimpanzee)
Danio rerio (zebrafish)
Canis lupus familiaris (canine)
Drosophila melanogaster
Macaca mulatta (Rhesus Monkey)
Saccharomyces cerevisiae
Schizosaccharomyces pombe

## IPA supported platform :

- **Gene expression:**
  - qPCR analysis
  - Microarray
  - RNA-Seq (NGS)
  - microRNA
  - mRNA
- **Proteomics**
  - PhosphoProteomics[New]
- metabolomics

## IPA application:

- Biomarker finding
- Toxicity Functions
- Diseases regulation





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# Supported Identifiers for Data Upload

Get more complete mapping during dataset 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 | | | | | |



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# Peer-reviewed publications citing Ingenuity apps

>17,000 publications that used IPA -- and growing!

**Best matches for ingenuity pathway analysis:**

Causal **analysis** approaches in **Ingenuity Pathway Analysis**.
Krämer A et al. Bioinformatics. (2014)

Gene set enrichment **analysis** and **ingenuity pathway analysis** of metastatic clear cell renal cell carcinoma cell line.
Khan MI et al. Am J Physiol Renal Physiol. (2016)

**Ingenuity Pathway Analysis** of Gene Expression Profiles in Distal Nerve Stump following Nerve Injury: Insights into Wallerian Degeneration.
Yu J et al. Front Cell Neurosci. (2016)

Switch to our new best match sort order

**Sort by:**

Best match | Most recent

**Results by year**

Downlo

**Search results**

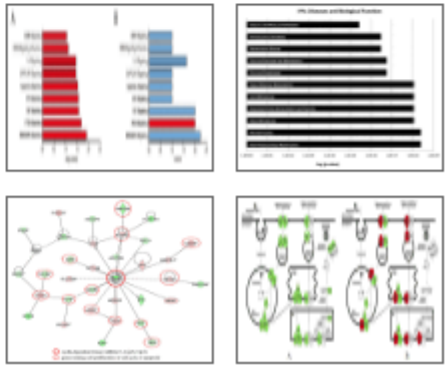
**Items: 1 to 20 of 2318**

<< First < Prev Page 1 of 116 Next > Last >>

1. 17beta-hydroxysteroid dehydrogenase type 5 is negatively correlated to apoptosis inhibitor GRP78 and tumor-secreted protein PGK1, and modulates breast cancer cell viability and proliferation.
Xu D, Aka JA, Wang R, Lin SX.
J Steroid Biochem Mol Biol. 2017 Jul;171:270-280. doi: 10.1016/j.jsbmb.2017.04.009. Epub 2017 Apr 27.
PMID: 28457968
Similar articles

2. 2D-gel based proteomics unravels neurogenesis and energetic metabolism dysfunction of the olfactory bulb in CUMS rat model.

**PMC Images search for** *ingenuity pathway analysis*





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# Multi-Omics Analysis using IPA

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

RESEARCH ARTICLE

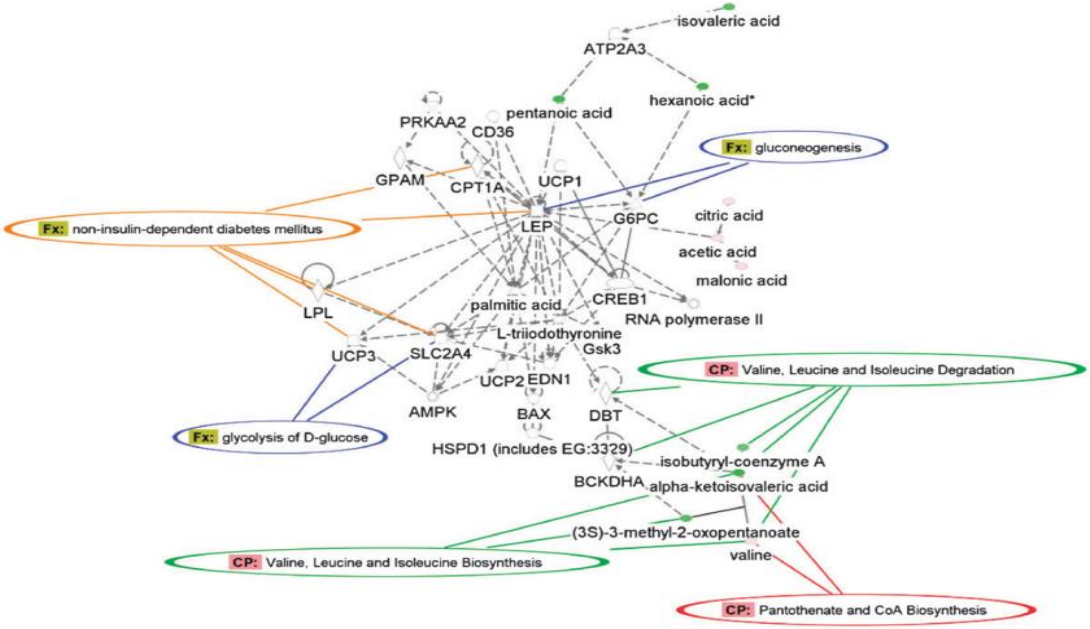
## A Multi-Omics Approach Identifies Key Hubs Associated with Cell Type-Specific Responses of Airway Epithelial Cells to Staphylococcal Alpha-Toxin

Erik Ric … ukoti[3], …
Jan-Pe…

**Integ… … id bi…**
**disco…**

Susan …
Terence…

*Received …*
*First pub…*
DOI: 10…




Multi Experiment

↓

Phosphorylation

+

Protein Expression

+

mRNA Expression

+

miRNA Expression

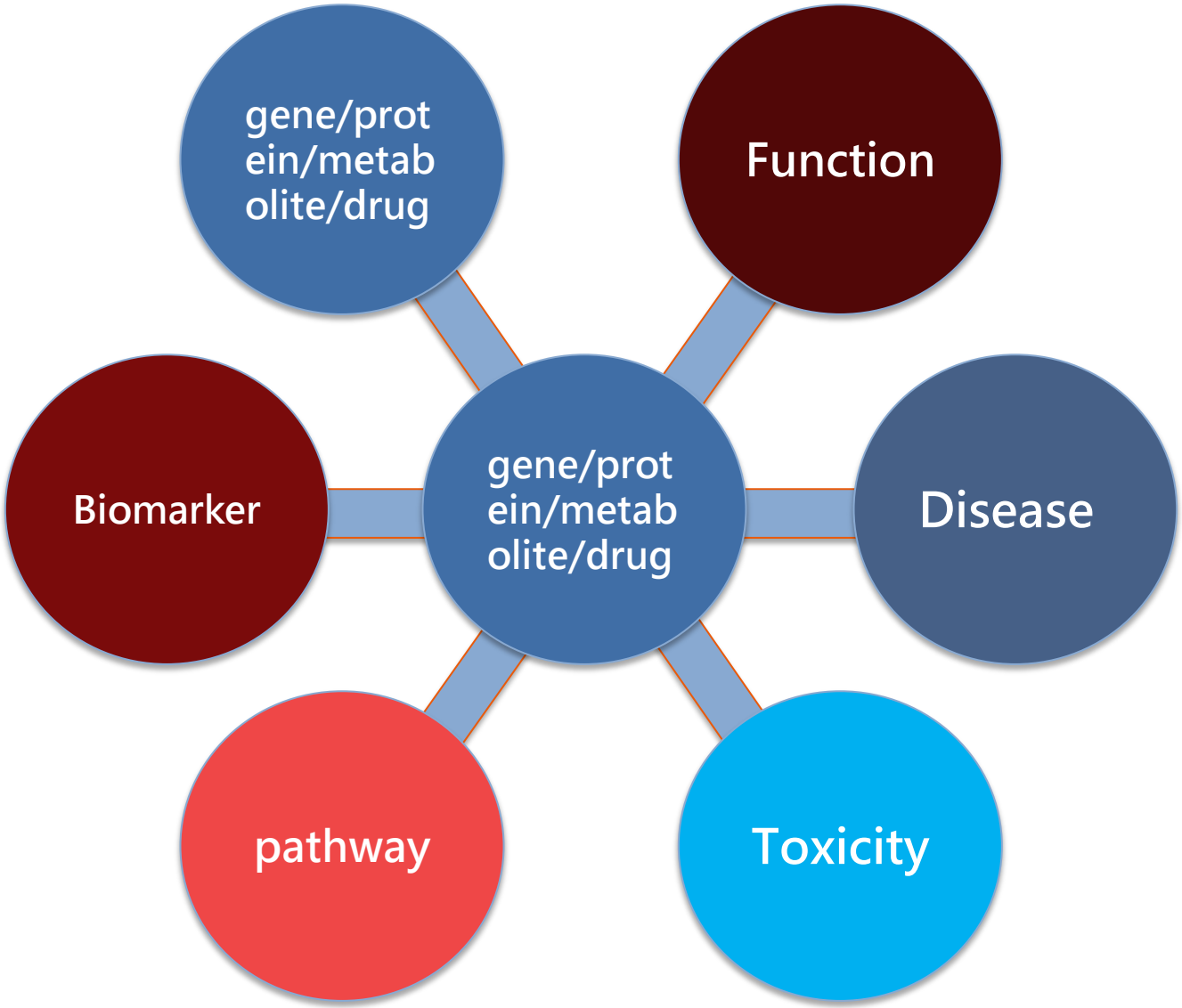
↓

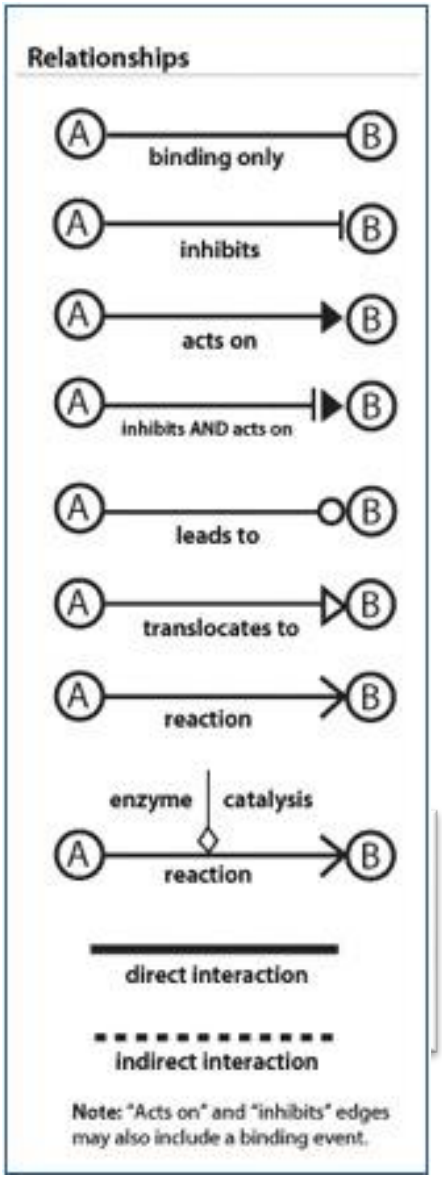
IPA analysis

Sample t…

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# 用IPA來發掘實驗資料中各類型關係

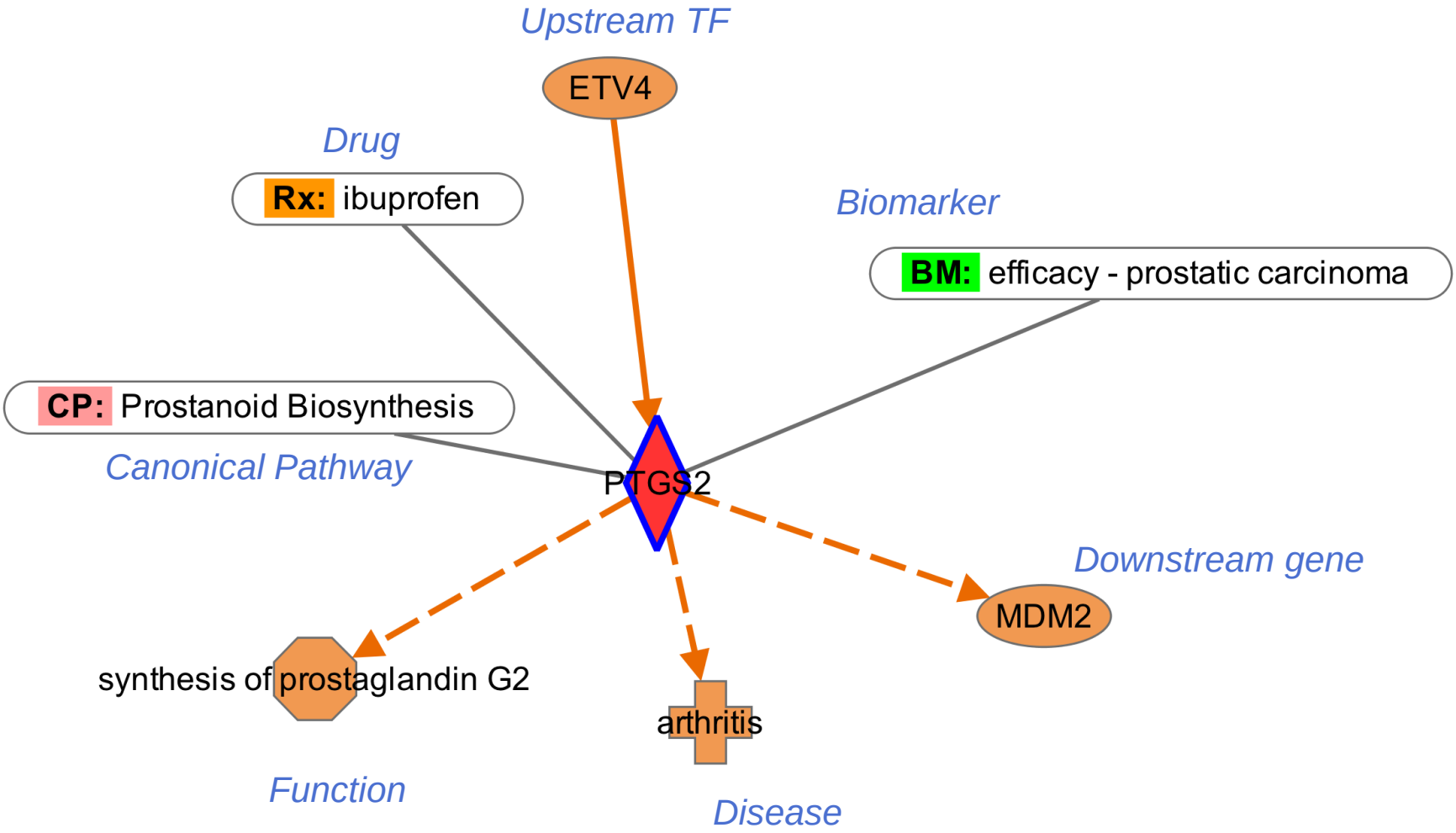





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# Capturing molecular information from the literature

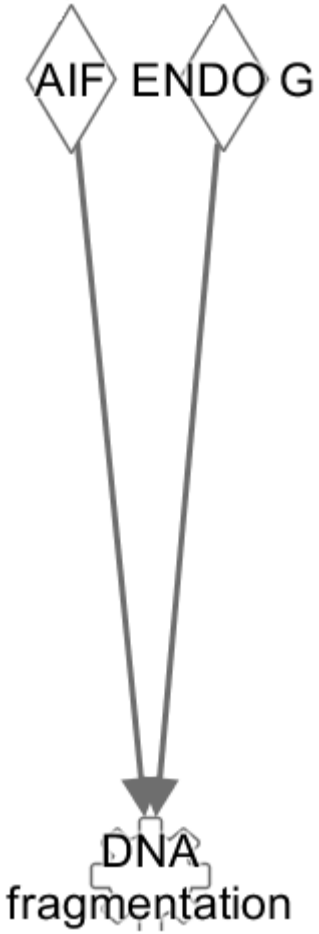



Gather this type of information for nearly every gene. Inferences can be made from the resulting networks.



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




## IPA Relationships: ENDO G|DNA fragmentation

Review the information that supports the gene-to-function relationship. Click the plus icon to view the reference infor

EndNote ▼ EXPORT REFERENCES

### Ingenuity Relationships

causation [16]

**Translocation of ENDONUCLEASE G [ENDOG] protein to** nuclei from mammal cultured hepatocytes **increases**

18691057 Gómez-Lechón MJ, O'Connor JE, Lahoz A, Castell JV, Donato MT. Identification of apo 2008;15(20):2071-85.

Source: Ingenuity Expert Findings

**Rat Endog protein** in a cell free system **increases fragmentation of** nucleosomal **Deoxyribonucleic Acid** in nuc

Experiment Type: agarose gel electrophoresis

16407272 Ishihara Y, Shimamoto N. Involvement of endonuclease G in nucleosomal DNA fragm 10;281(10):6726-33. Epub 2006 Jan 4.

Source: Ingenuity Expert Findings

In cytoplasm, **Endo G protein increases fragmentation of DNA.**

15182854 Lemarié A, Lagadic-Gossmann D, Morzadec C, Allain N, Fardel O, Vernhet L. Cadmiur oxidative stress-related impairment of mitochondria and relocation of endonuclease

Source: Ingenuity Expert Findings

**ENDOG protein** in a cell-free system **increases fragmentation of DNA** in nuclei.

15077142 Cregan SP, Dawson VL, Slack RS. Role of AIF in caspase-dependent and caspase-ind

Source: Ingenuity Expert Findings

**zVAD causes little or no change in fragmentation of DNA** that is mediated by **ENDOG protein.**

15077142 Cregan SP, Dawson VL, Slack RS. Role of AIF in caspase-dependent and caspase-ind

Source: Ingenuity Expert Findings



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# 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[New], MINT, Cognia, etc.
- **miRNA/mRNA target databases**
  - TarBase, TargetScan, miRecords
- **Gene to Disease Associations**
  - OMIM, GWAS databases
- **Metabolomics**
  - HumanCyc[New]
- **Clinical Trial information**
  - ClinicalTrials.gov

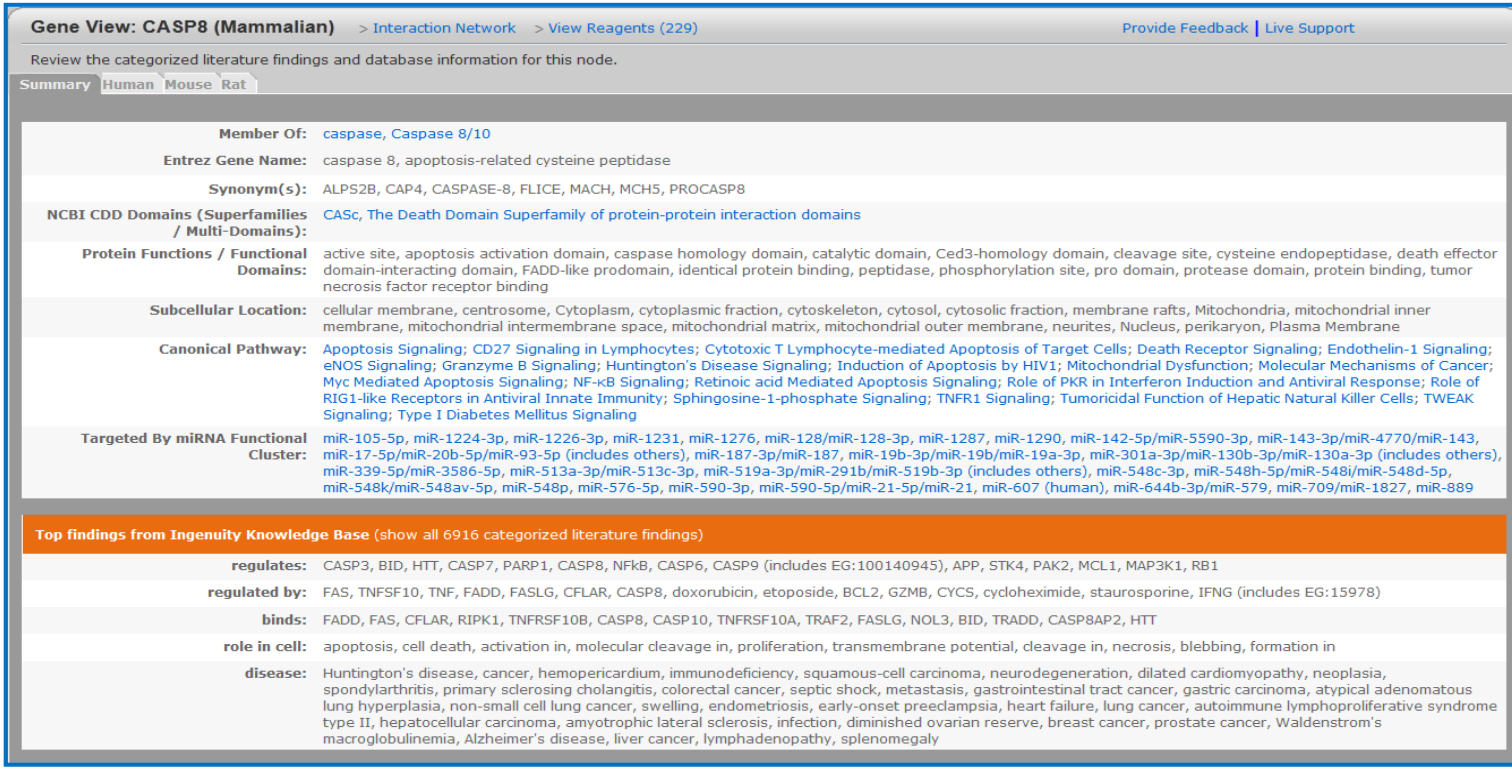




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# Unique Tools for Biological Analysis and Interpretation

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- Human & Mouse Isoform Views
- BioProfiler
- Diseases & Bio Functions
- Canonical Pathways
- Upstream Regulator Analysis
- Build & Overlay and Interactions



**Gene View: CASP8 (Mammalian)** > Interaction Network > View Reagents (229) Provide Feedback | Live Support

Review the categorized literature findings and database information for this node.

Summary | Human | Mouse | Rat

| | |
|---|---|
| **Member Of:** | caspase, Caspase 8/10 |
| **Entrez Gene Name:** | caspase 8, apoptosis-related cysteine peptidase |
| **Synonym(s):** | ALPS2B, CAP4, CASPASE-8, FLICE, MACH, MCH5, PROCASP8 |
| **NCBI CDD Domains (Superfamilies / Multi-Domains):** | CASc, The Death Domain Superfamily of protein-protein interaction domains |
| **Protein Functions / Functional Domains:** | active site, apoptosis activation domain, caspase homology domain, catalytic domain, Ced3-homology domain, cleavage site, cysteine endopeptidase, death effector domain-interacting domain, FADD-like prodomain, identical protein binding, peptidase, phosphorylation site, pro domain, protease domain, protein binding, tumor necrosis factor receptor binding |
| **Subcellular Location:** | cellular membrane, centrosome, Cytoplasm, cytoplasmic fraction, cytoskeleton, cytosol, cytosolic fraction, membrane rafts, Mitochondria, mitochondrial inner membrane, mitochondrial intermembrane space, mitochondrial matrix, mitochondrial outer membrane, neurites, Nucleus, perikaryon, Plasma Membrane |
| **Canonical Pathway:** | Apoptosis Signaling; CD27 Signaling in Lymphocytes; Cytotoxic T Lymphocyte-mediated Apoptosis of Target Cells; Death Receptor Signaling; Endothelin-1 Signaling; eNOS Signaling; Granzyme B Signaling; Huntington's Disease Signaling; Induction of Apoptosis by HIV1; Mitochondrial Dysfunction; Molecular Mechanisms of Cancer; Myc Mediated Apoptosis Signaling; NF-κB Signaling; Retinoic acid Mediated Apoptosis Signaling; Role of PKR in Interferon Induction and Antiviral Response; Role of RIG1-like Receptors in Antiviral Innate Immunity; Sphingosine-1-phosphate Signaling; TNFR1 Signaling; Tumoricidal Function of Hepatic Natural Killer Cells; TWEAK Signaling; Type I Diabetes Mellitus Signaling |
| **Targeted By miRNA Functional Cluster:** | miR-105-5p, miR-1224-3p, miR-1226-3p, miR-1231, miR-1276, miR-128/miR-128-3p, miR-1287, miR-1290, miR-142-5p/miR-5590-3p, miR-143-3p/miR-4770/miR-143, miR-17-5p/miR-20b-5p/miR-93-5p (includes others), miR-187-3p/miR-187, miR-19b-3p/miR-19b/miR-19a-3p, miR-301a-3p/miR-130b-3p/miR-130a-3p (includes others), miR-339-5p/miR-3586-5p, miR-513a-3p/miR-513c-3p, miR-519a-3p/miR-291b/miR-519b-3p (includes others), miR-548c-3p, miR-548h-5p/miR-548i/miR-548d-5p, miR-548k/miR-548av-5p, miR-548p, miR-576-5p, miR-590-3p, miR-590-5p/miR-21-5p/miR-21, miR-607 (human), miR-644b-3p/miR-579, miR-709/miR-1827, miR-889 |

**Top findings from Ingenuity Knowledge Base** (show all 6916 categorized literature findings)

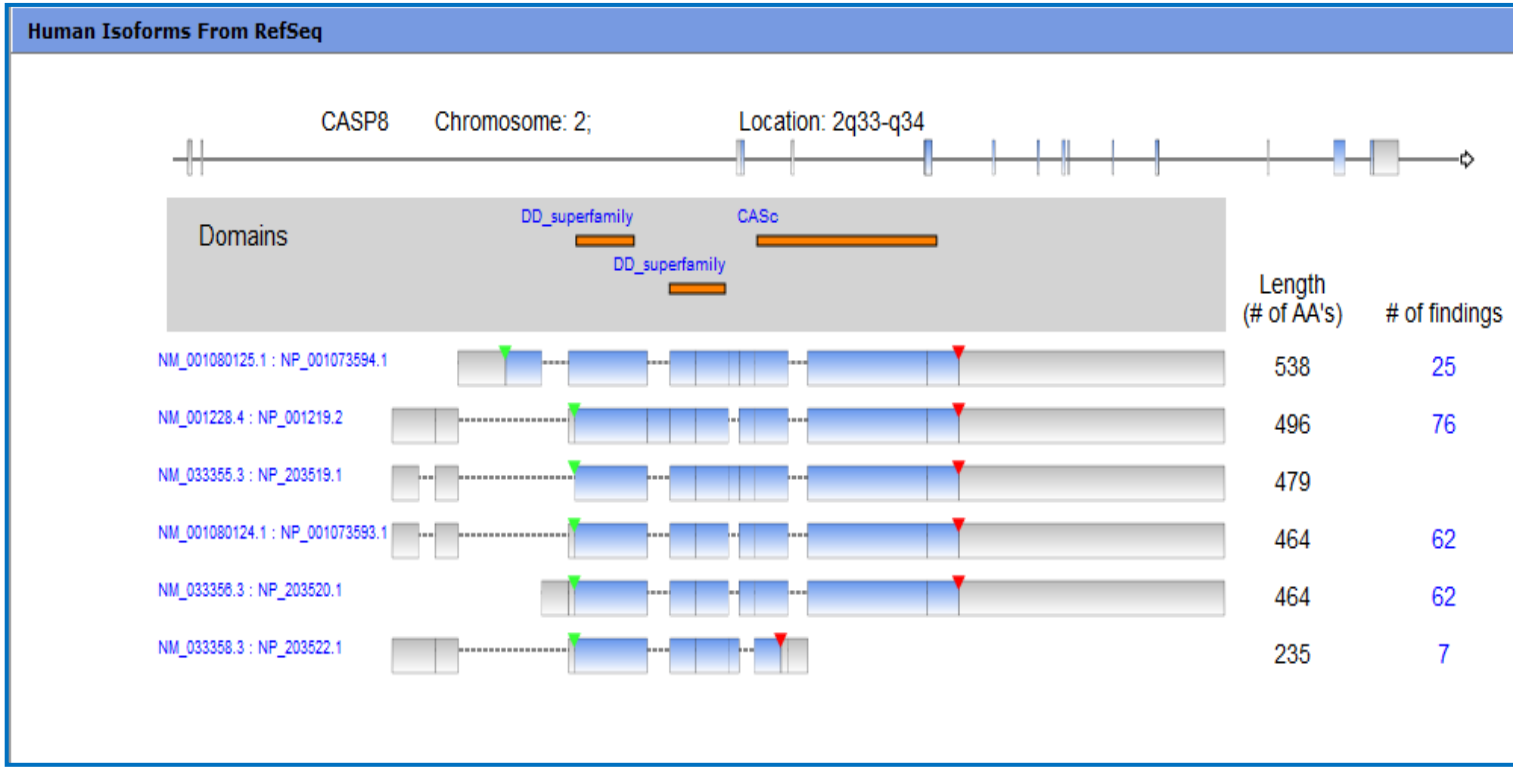
| | |
|---|---|
| **regulates:** | CASP3, BID, HTT, CASP7, PARP1, CASP8, NFkB, CASP6, CASP9 (includes EG:100140945), APP, STK4, PAK2, MCL1, MAP3K1, RB1 |
| **regulated by:** | FAS, TNFSF10, TNF, FADD, FASLG, CFLAR, CASP8, doxorubicin, etoposide, BCL2, GZMB, CYCS, cycloheximide, staurosporine, IFNG (includes EG:15978) |
| **binds:** | FADD, FAS, CFLAR, RIPK1, TNFRSF10B, CASP8, CASP10, TNFRSF10A, TRAF2, FASLG, NOL3, BID, TRADD, CASP8AP2, HTT |
| **role in cell:** | apoptosis, cell death, activation in, molecular cleavage in, proliferation, transmembrane potential, cleavage in, necrosis, blebbing, formation in |
| **disease:** | Huntington's disease, cancer, hemopericardium, immunodeficiency, squamous-cell carcinoma, neurodegeneration, dilated cardiomyopathy, neoplasia, spondylarthritis, primary sclerosing cholangitis, colorectal cancer, septic shock, metastasis, gastrointestinal tract cancer, gastric carcinoma, atypical adenomatous lung hyperplasia, non-small cell lung cancer, swelling, endometriosis, early-onset preeclampsia, heart failure, lung cancer, autoimmune lymphoproliferative syndrome type II, hepatocellular carcinoma, amyotrophic lateral sclerosis, infection, diminished ovarian reserve, breast cancer, prostate cancer, Waldenstrom's macroglobulinemia, Alzheimer's disease, liver cancer, lymphadenopathy, splenomegaly |



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- Upstream Regulator Analysis
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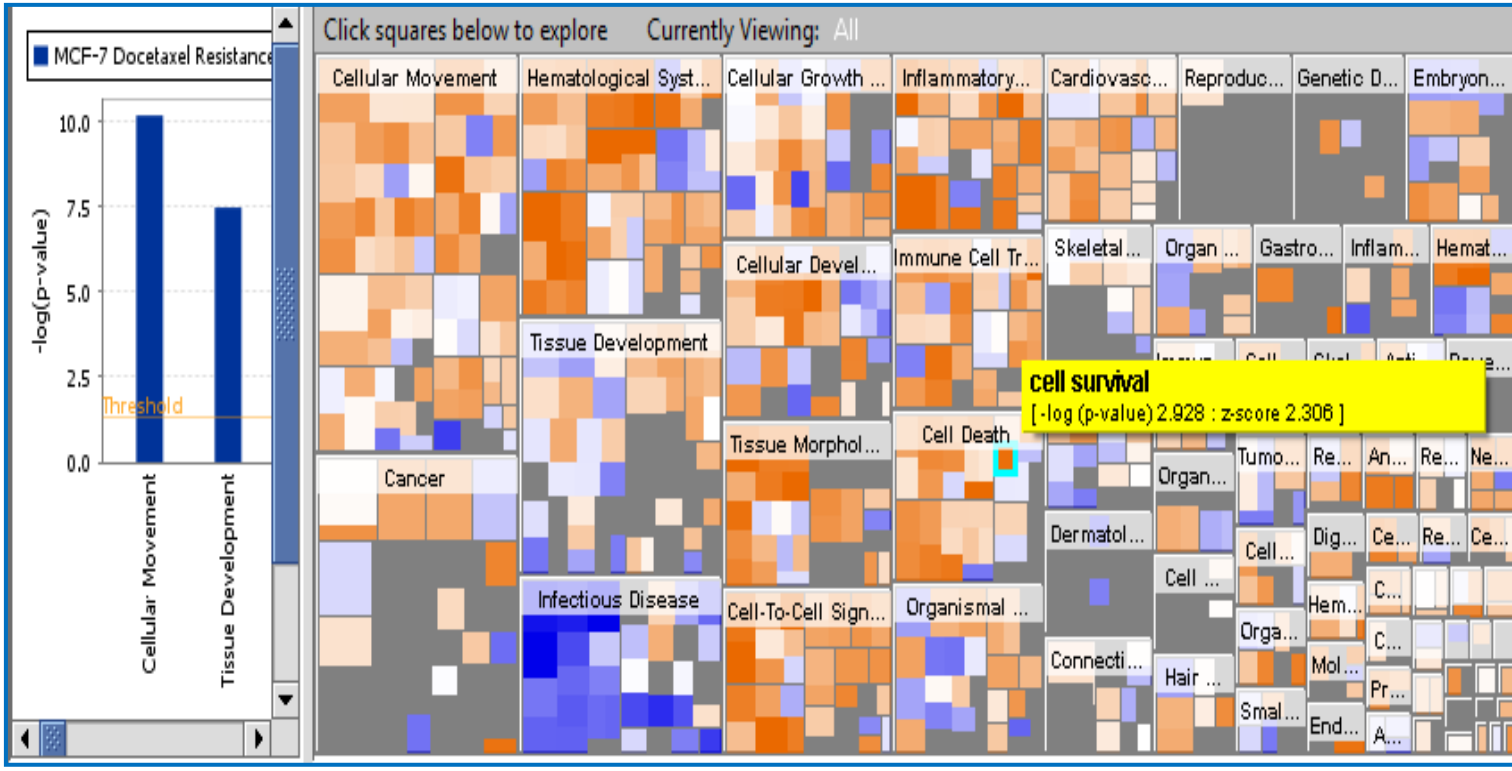
Add column(s) | Diseases & Functions Evidence

| Symbol | Molecule ... | Effect on ... | Disease | Mutation ... | Biomarke... | Species E... | Drug targ... | Expressio... |
|---|---|---|---|---|---|---|---|---|
| 2,3,4,7,8-pentachlo... | increased activity | increases | hepatic steatosis | wild type | not applicable | Rat | not applicable | not applicable |
| 3,4,5,3',4'-pentachl... | increased activity | increases | hepatic steatosis | wild type | not applicable | Rat | not applicable | not applicable |
| ABCA1 | decreased activity | increases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| ABCB11 | increased activity | decreases | hepatic steatosis | wild type | not applicable | Mouse | not applicable | not applicable |
| ABCG1 | decreased activity | decreases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| ABHD5 | decreased activity | increases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| ACACA | increased activity | affects | hepatic steatosis, ... | wild type | not applicable | Human | not applicable | upregulation |
| acadesine | increased activity | decreases | hepatic steatosis | wild type | not applicable | Rat | not applicable | not applicable |
| ▼ACADL | decreased activity,i... | affects,increases | hepatic steatosis, ... | homozygous,knock... | not applicable | Mouse,Human | not applicable | not applicable,upre... |
| | decreased activity | increases | hepatic steatosis | [homozygous, knoc... | not applicable | Mouse | not applicable | not applicable |
| | decreased activity | increases | hepatic steatosis | wild type | not applicable | Human | not applicable | not applicable |
| | increased activity | affects | hepatic steatosis, ... | wild type | not applicable | Human | not applicable | upregulation |
| ACADM | decreased activity | increases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| ACADVL | decreased activity | increases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| acetaminophen | increased activity | increases | hepatic steatosis | wild type | not applicable | Mouse | not applicable | not applicable |
| ACOT11 | decreased activity | decreases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| ACOT13 | decreased activity | decreases | hepatic steatosis | homozygous,knock... | not applicable | Mouse | not applicable | not applicable |
| ▶ACOX1 | decreased activity,i... | affects,increases | hepatic steatosis, ... | heterozygous,homo... | not applicable | Mouse,Human | not applicable | not applicable,upre... |
| ACOX2 | increased activity | affects | hepatic steatosis, ... | wild type | not applicable | Human | not applicable | upregulation |


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- Upstream Regulator Analysis
- Build & Overlay and Interactions

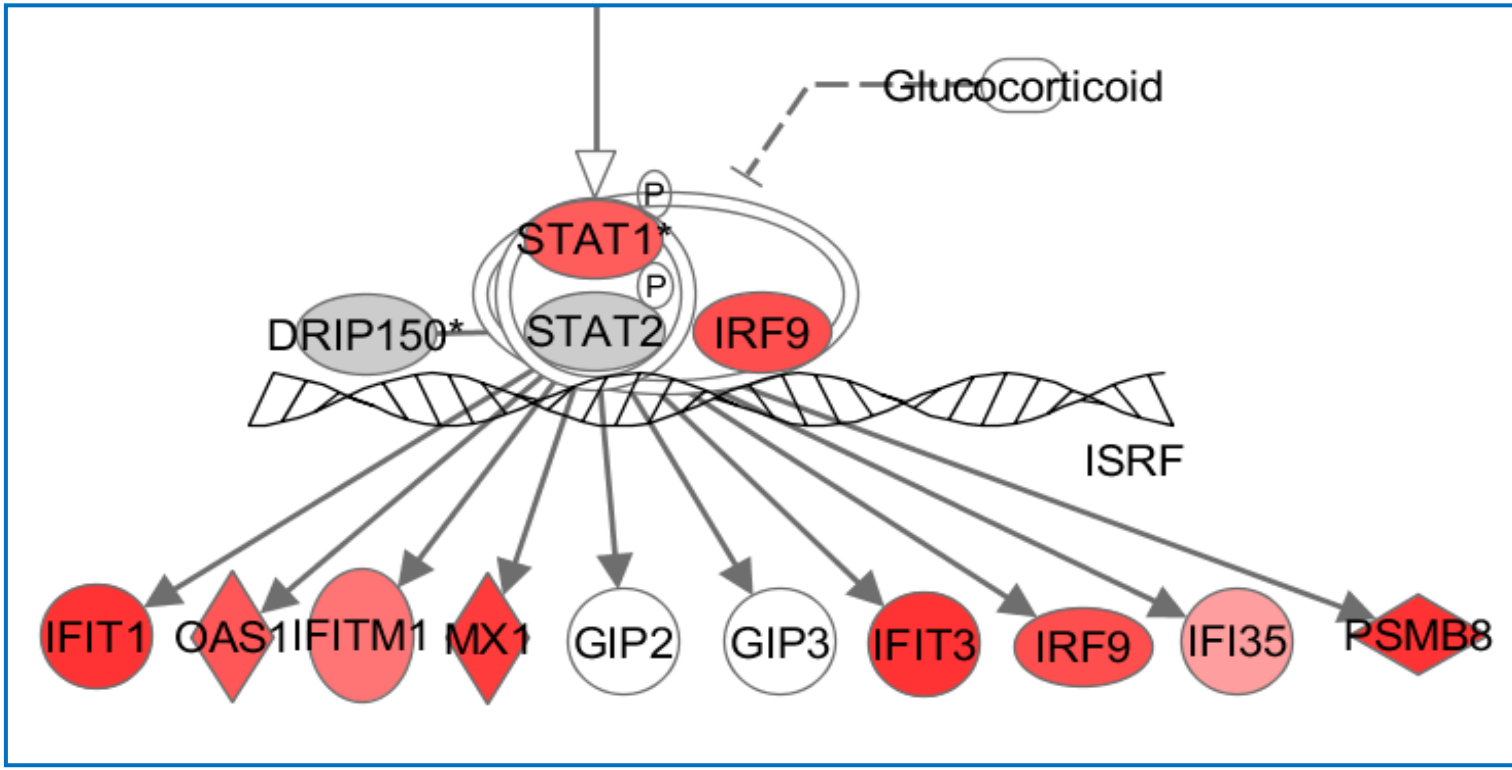





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# Unique Tools for Biological Analysis and Interpretation

- Gene View Summaries
- Human & Mouse Isoform Views
- BioProfiler
- Diseases & Bio Functions
- Canonical Pathways
- Upstream Regulator Analysis
- Build & Overlay and Interactions






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# Unique Tools for Biological Analysis and Interpretation

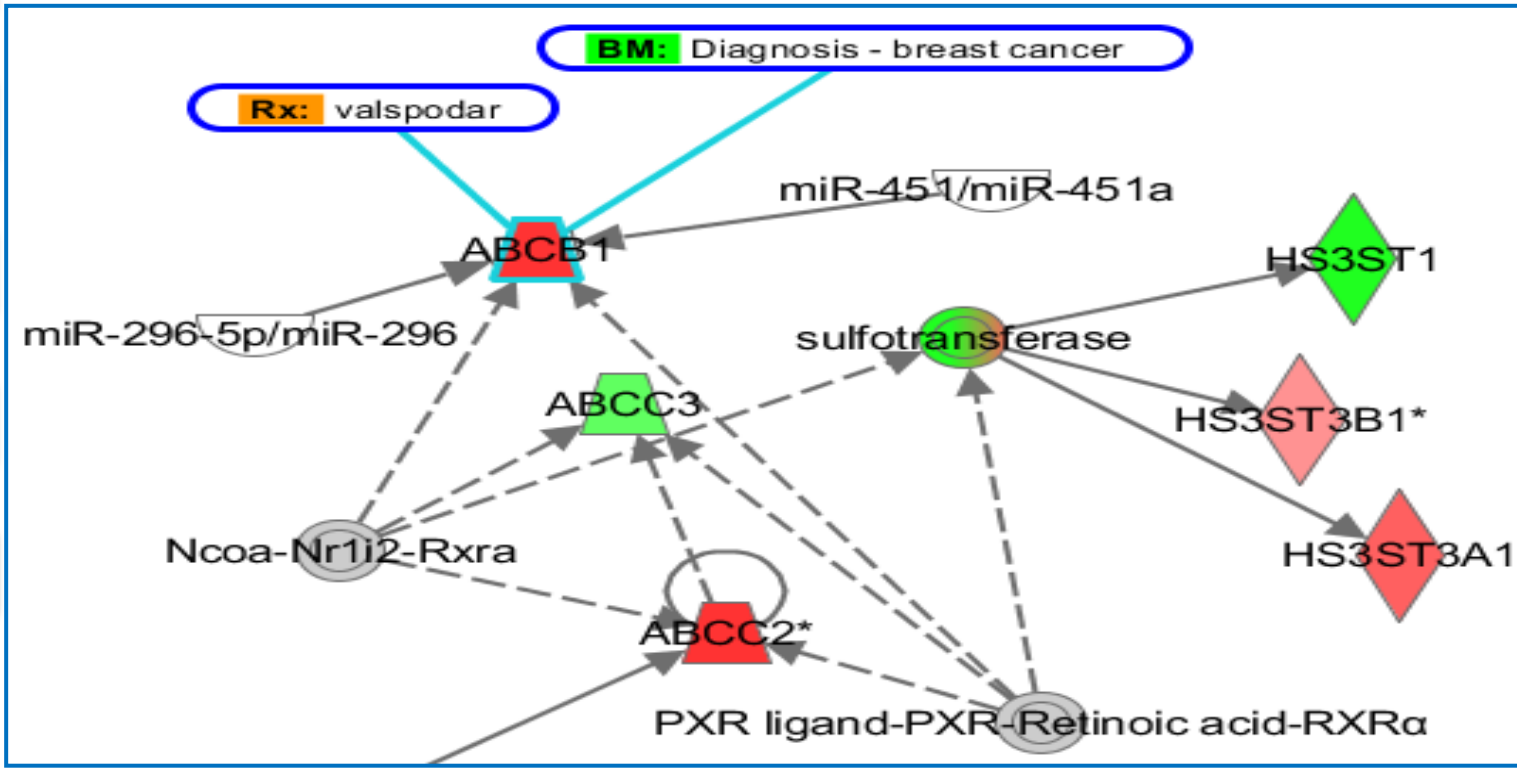
- Gene View Summaries
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- Upstream Regulator Analysis
- Build & Overlay and Interactions

| Upstream Regulator | Molecule Type | Predicted ... | Activation z... | p-value... |
|---|---|---|---|---|
| IFNA2 | cytokine | Activated | 7.729 | 3.83E-42 |
| MAPK1 | kinase | Inhibited | -6.204 | 4.47E-36 |
| IRF7 | other | Activated | 6.513 | 8.22E-34 |
| IFNG (includes EG:15 | cytokine | Activated | 8.418 | 1.96E-31 |
| IL1RN | cytokine | Inhibited | -5.911 | 2.72E-30 |
| TNF | cytokine | Activated | 5.710 | 3.09E-26 |
| Interferon alpha | group | Activated | 6.916 | 1.56E-25 |
| lipopolysaccharide | chemical drug | Activated | 6.673 | 7.17E-25 |


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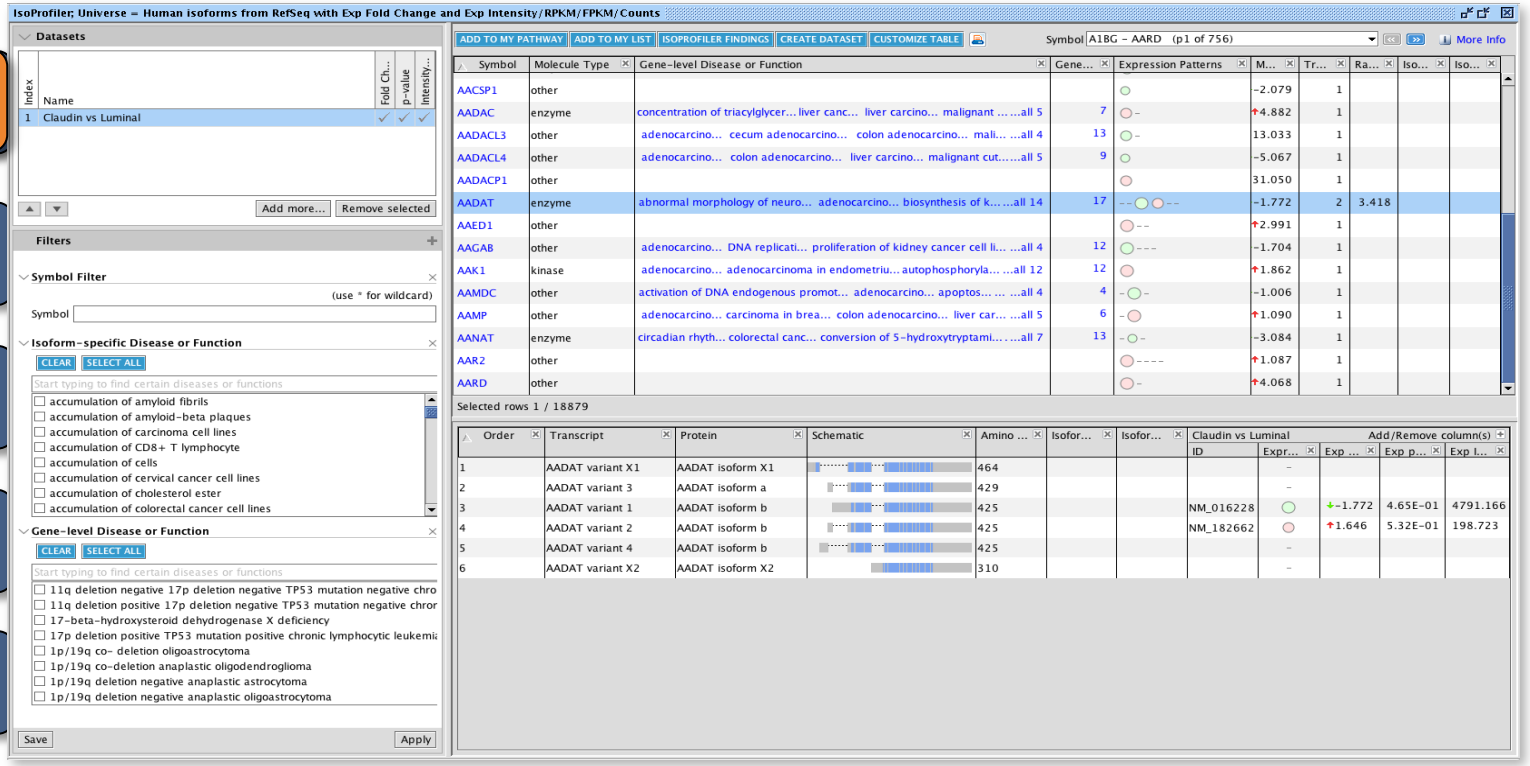





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# Unique Tools for Biological Analysis and Interpretation

- IsoProfiler
- Multi-omics Overlay
- Phosphorylation Analysis
- Comparison Analysis
- Analysis Match w/ OmicSoft Lands

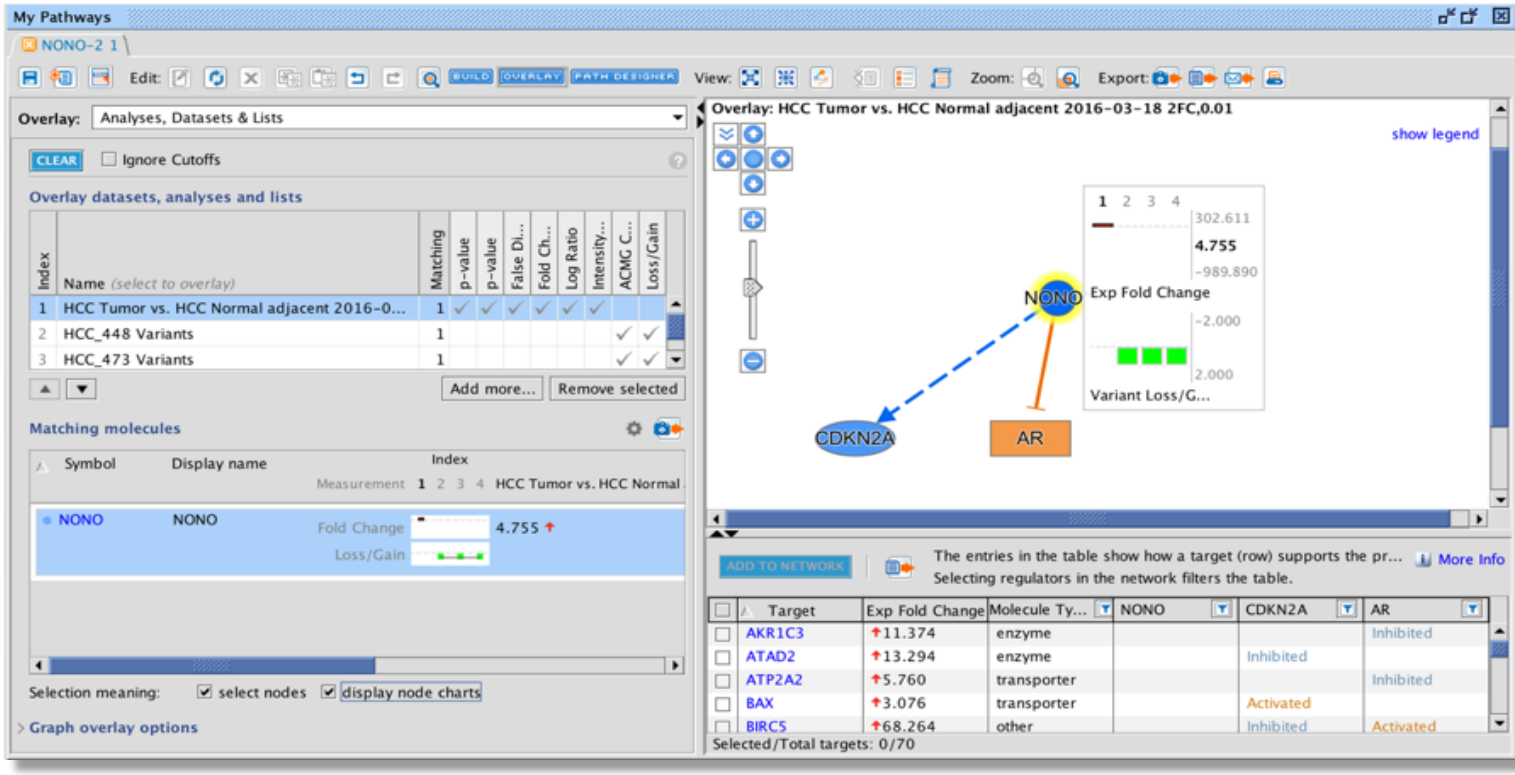





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# Unique Tools for Biological Analysis and Interpretation

- IsoProfiler
- Multi-omics Overlay
- Phosphorylation Analysis
- Comparison Analysis
- Analysis Match w/ OmicSoft Lands

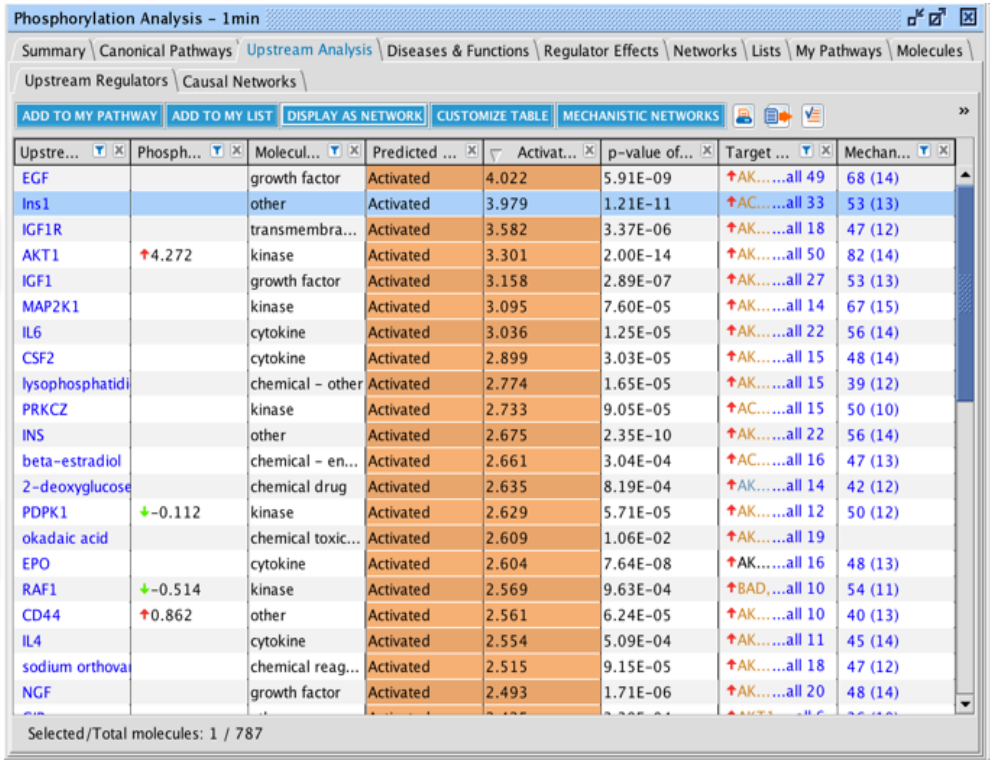





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# Unique Tools for Biological Analysis and Interpretation

- IsoProfiler
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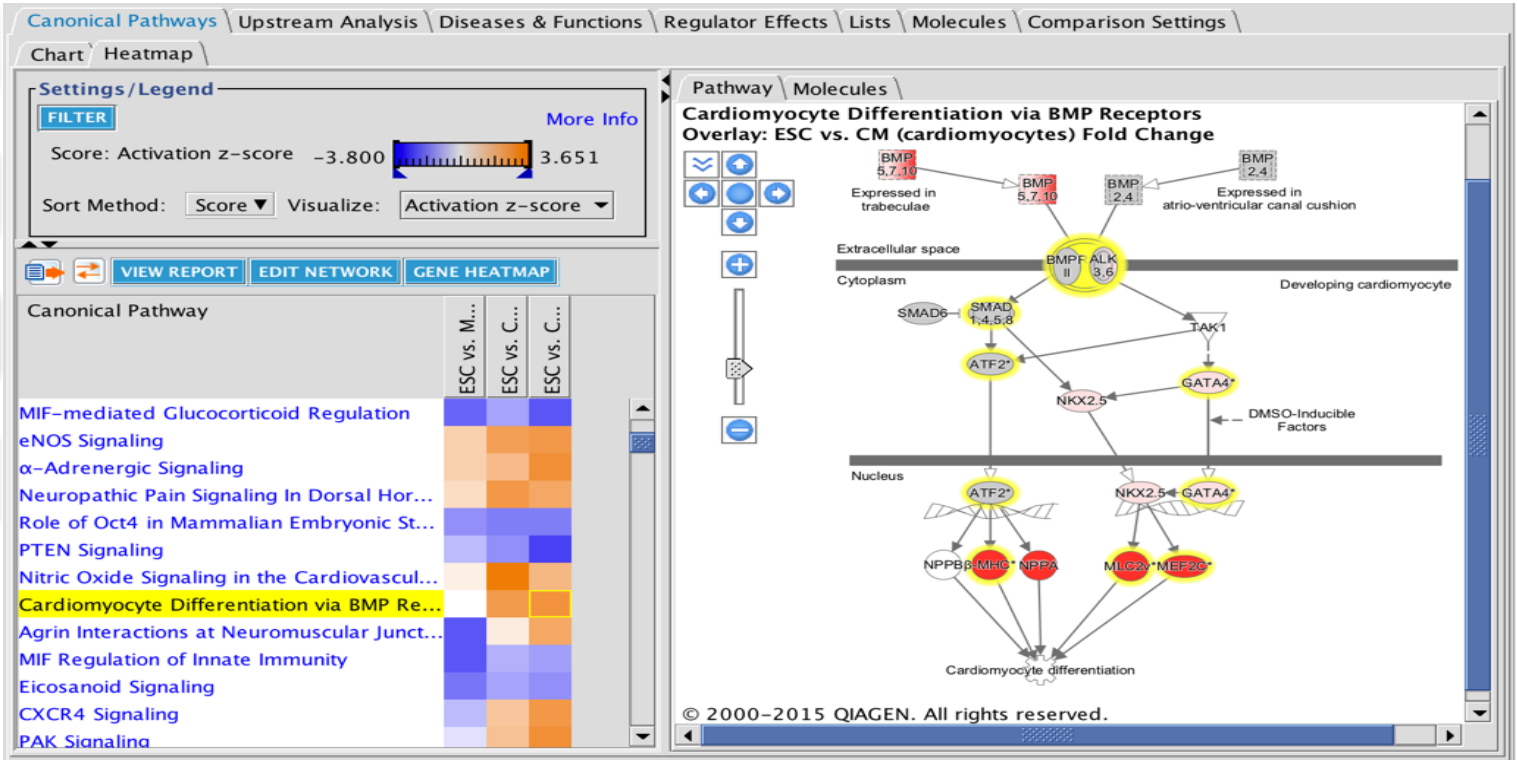





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# Unique Tools for Biological Analysis and Interpretation

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- Multi-omics Overlay
- Phosphorylation Analysis
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- Analysis Match w/ OmicSoft Lands

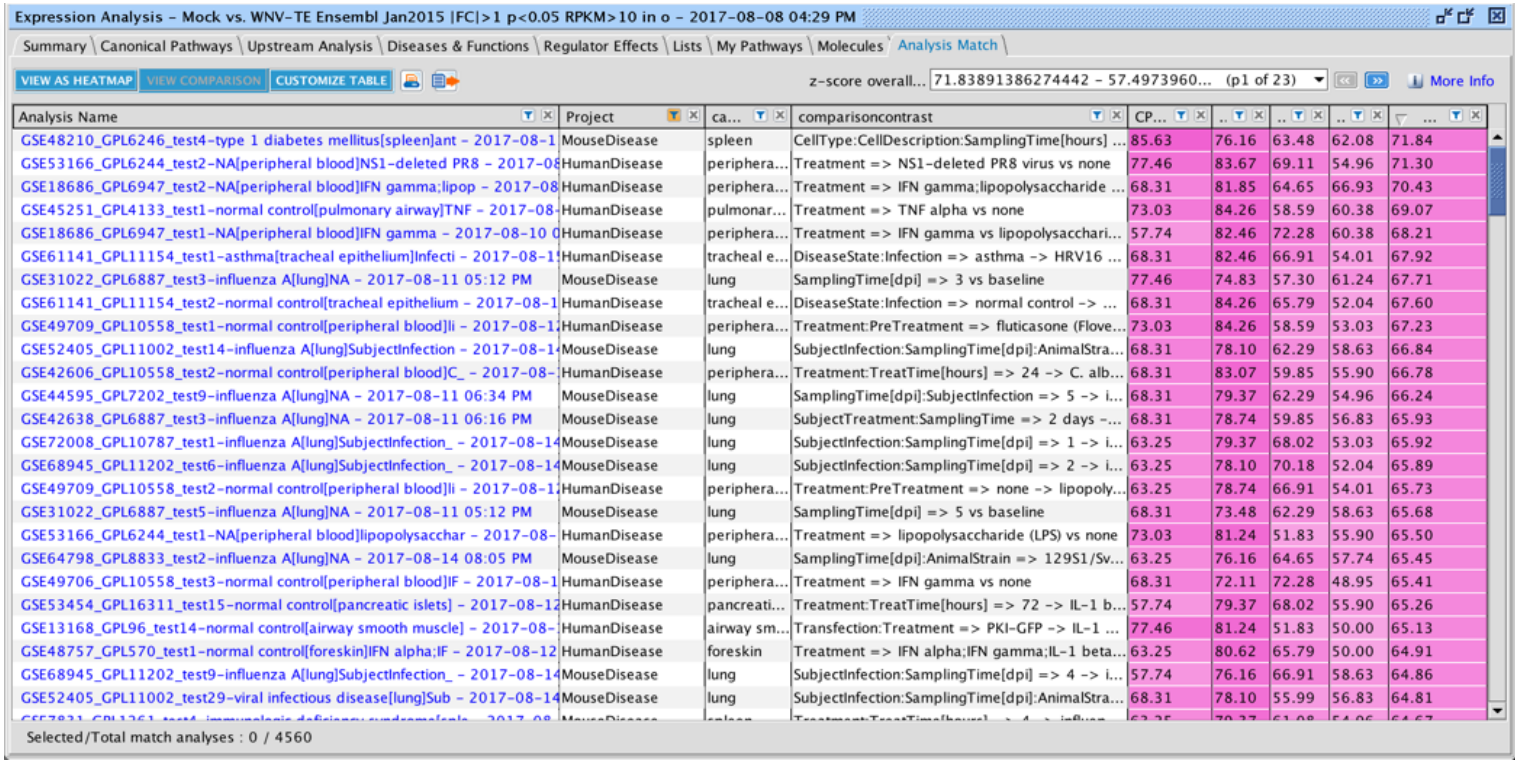





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# Unique Tools for Biological Analysis and Interpretation

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- Multi-omics Overlay
- Phosphorylation Analysis
- Comparison Analysis
- Analysis Match* w/ OmicSoft Lands



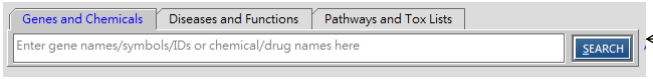



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# Entry Points in IPA

## Biological Questions

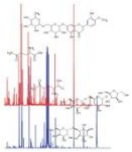
### Search




### Experiment Data



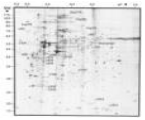
Expression arrays



Mass spec

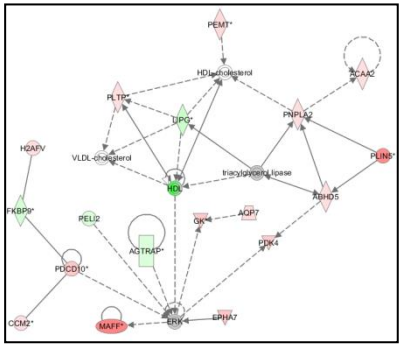


Protein arrays



2D Gel electrophoresis

### Custom Pathway



Networks



Core



IPA-Biomarker

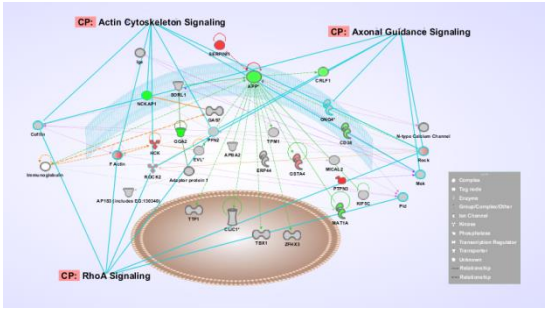


IPA-Tox



IPA-Metabolomics

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

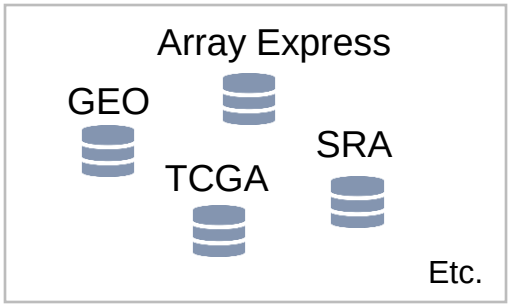


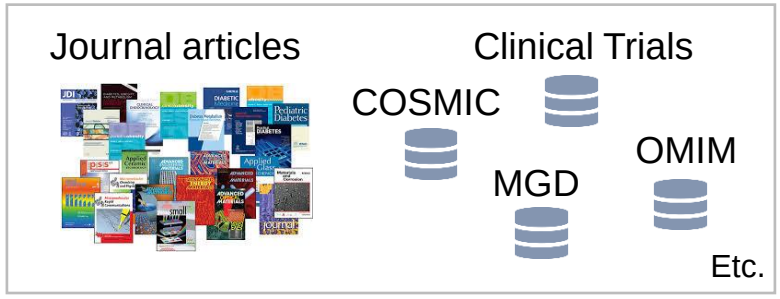

**Communicate & Collaborate**



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# Unprecedented discovery, together




Curation, Processing, & QA

Curation & QA

**Datasets integrated into OmicSoft Lands**

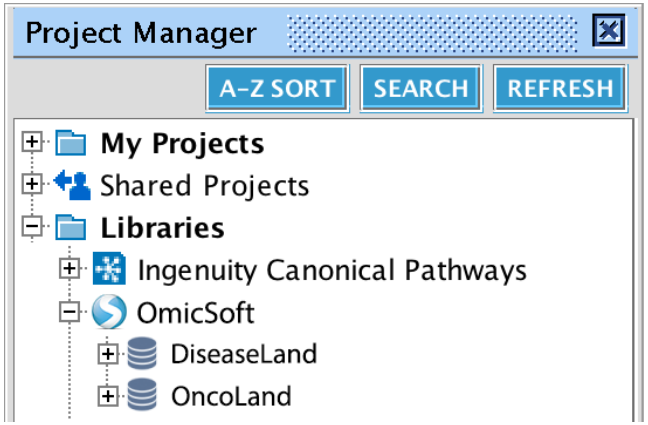
**Curated Findings**

OmicSoft Array Suite

OncoLand
DiseaseLand

49,000+ Expression comparison datasets

INGENUITY PATHWAY ANALYSIS






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

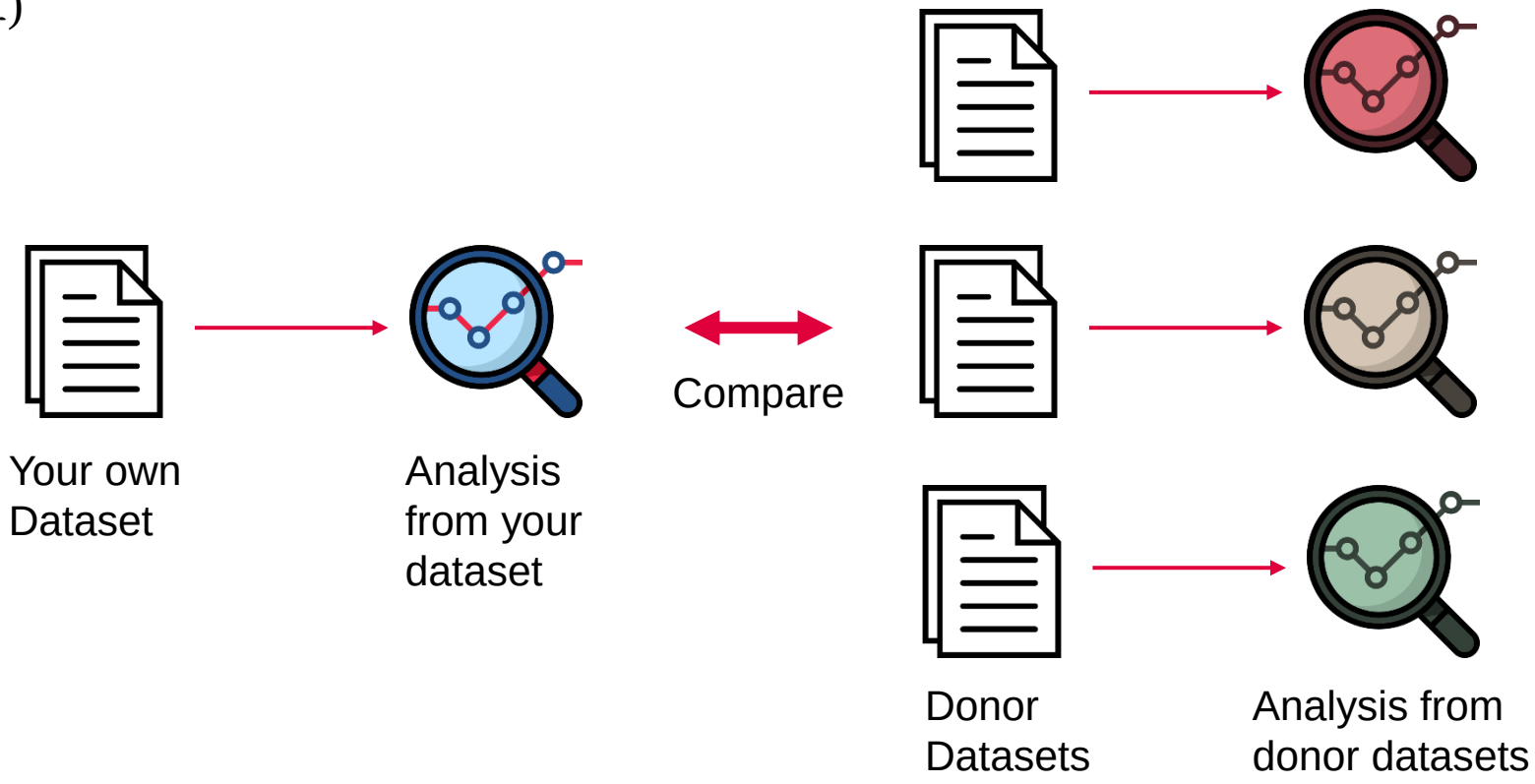


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# Analysis Match

截至今日，本次更新增加了19,000組分析完成的數據至Analysis Match分析功能中，您可以在Analysis Match分析模組當中，比較您的實驗資料與外部資料庫如TCGA、LINCS等，在不同的癌症類型，疾病類型與實驗組中分析其相似及相異關係度。

並於七月中旬，會自**LINCS（NIH Library of Integrated Network-Based Cellular Signatures）**再添加大約**28,000**個分析組，總數將超過**49,000**個(相較於上季僅有8100+個分析組)



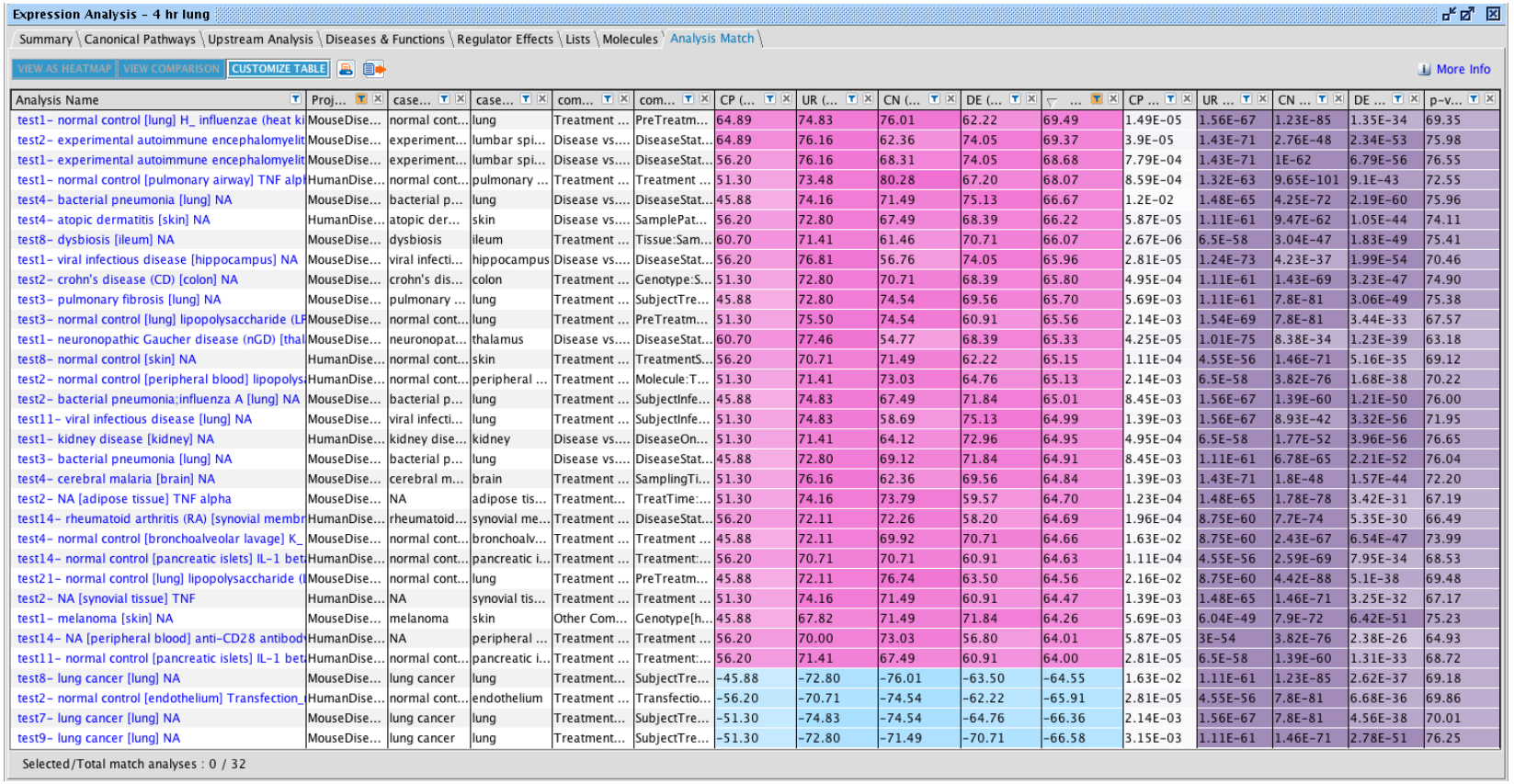


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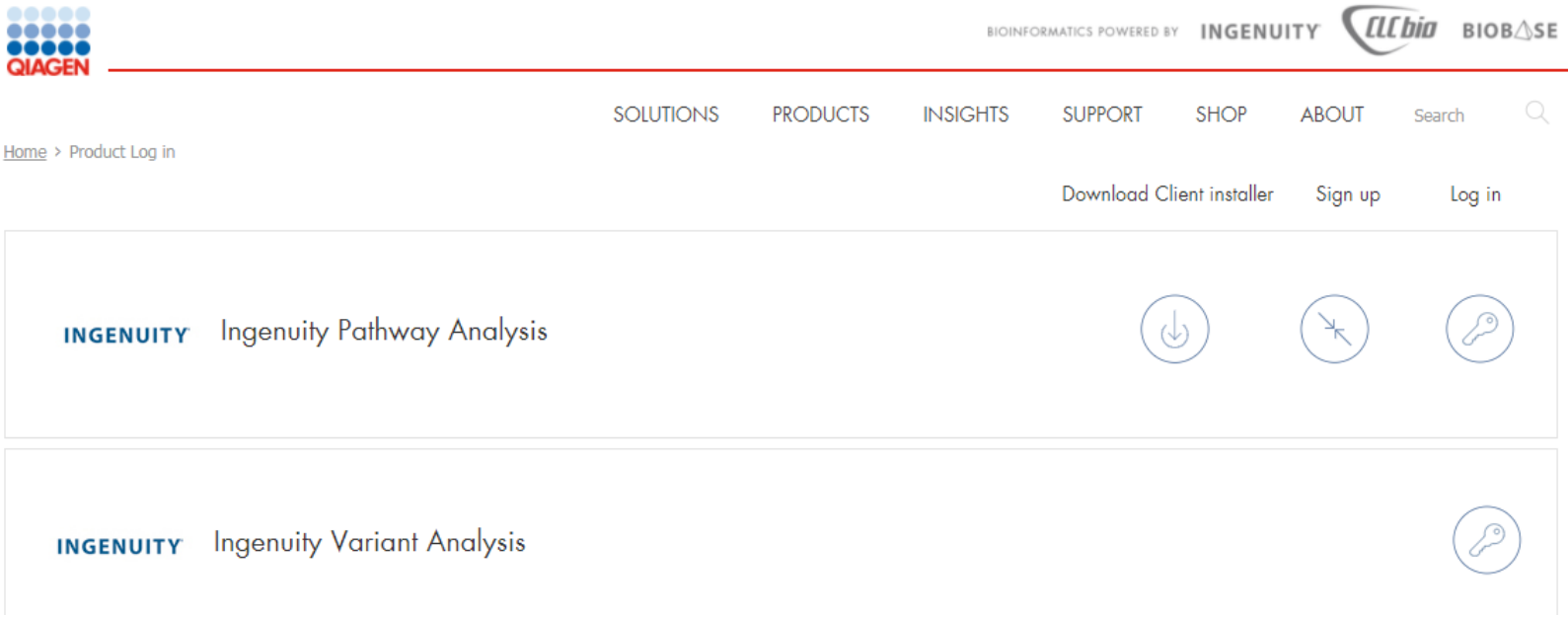
並於七月中旬，會自**LINCS（NIH Library of Integrated Network-Based Cellular Signatures）**再添加大約**28,000**個分析組，總數將超過**49,000**個(相較於上季僅有8100+個分析組)




| Analysis Name | Proj... | case... | case... | com... | com... | CP (... | UR (... | CN (... | DE (... | ... | CP ... | UR ... | CN ... | DE ... | p-v... |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| test1- normal control [lung] H_ influenzae (heat ki | MouseDise... | normal cont... | lung | Treatment ... | PreTreatm... | 64.89 | 74.83 | 76.01 | 62.22 | 69.49 | 1.49E-05 | 1.56E-67 | 1.23E-85 | 1.35E-34 | 69.35 |
| test2- experimental autoimmune encephalomyelit | MouseDise... | experiment... | lumbar spi... | Disease vs.... | DiseaseStat... | 64.89 | 76.16 | 62.36 | 74.05 | 69.37 | 3.9E-05 | 1.43E-71 | 2.76E-48 | 2.34E-53 | 75.98 |
| test1- experimental autoimmune encephalomyelit | MouseDise... | experiment... | lumbar spi... | Disease vs.... | DiseaseStat... | 56.20 | 76.16 | 68.31 | 74.05 | 68.68 | 7.79E-04 | 1.43E-71 | 1E-62 | 6.79E-56 | 76.55 |
| test1- normal control [pulmonary airway] TNF alpl | HumanDise... | normal cont... | pulmonary ... | Treatment ... | Treatment ... | 51.30 | 73.48 | 80.28 | 67.20 | 68.07 | 8.59E-04 | 1.32E-63 | 9.65E-101 | 9.1E-43 | 72.55 |
| test4- bacterial pneumonia [lung] NA | MouseDise... | bacterial p... | lung | Disease vs.... | DiseaseStat... | 45.88 | 74.16 | 71.49 | 75.13 | 66.67 | 1.2E-02 | 1.48E-65 | 4.25E-72 | 2.19E-60 | 75.96 |
| test4- atopic dermatitis [skin] NA | HumanDise... | atopic der... | skin | Disease vs.... | SamplePat... | 56.20 | 72.80 | 67.49 | 68.39 | 66.22 | 5.87E-05 | 1.11E-61 | 9.47E-62 | 1.05E-44 | 74.11 |
| test8- dysbiosis [ileum] NA | MouseDise... | dysbiosis | ileum | Treatment ... | Tissue:Sam... | 60.70 | 71.41 | 61.46 | 70.71 | 66.07 | 2.67E-06 | 6.5E-58 | 3.04E-47 | 1.83E-49 | 75.41 |
| test1- viral infectious disease [hippocampus] NA | MouseDise... | viral infecti... | hippocampus | Disease vs.... | DiseaseStat... | 56.20 | 76.81 | 56.76 | 74.05 | 65.96 | 2.81E-05 | 1.24E-73 | 4.23E-37 | 1.99E-54 | 70.46 |
| test2- crohn's disease (CD) [colon] NA | MouseDise... | crohn's dis... | colon | Treatment ... | Genotype:S... | 51.30 | 72.80 | 70.71 | 68.39 | 65.80 | 4.95E-04 | 1.11E-61 | 1.43E-69 | 3.23E-47 | 74.90 |
| test3- pulmonary fibrosis [lung] NA | MouseDise... | pulmonary ... | lung | Treatment ... | SubjectTre... | 45.88 | 72.80 | 74.54 | 69.56 | 65.70 | 5.69E-03 | 1.11E-61 | 7.8E-81 | 3.06E-49 | 75.38 |
| test3- normal control [lung] lipopolysaccharide (LF | MouseDise... | normal cont... | lung | Treatment ... | PreTreatm... | 51.30 | 75.50 | 74.54 | 60.91 | 65.56 | 2.14E-03 | 1.54E-69 | 7.8E-81 | 3.44E-33 | 67.57 |
| test1- neuronopathic Gaucher disease (nGD) [thal | MouseDise... | neuronopat... | thalamus | Disease vs.... | DiseaseStat... | 60.70 | 77.46 | 54.77 | 68.39 | 65.33 | 4.25E-05 | 1.01E-75 | 8.38E-34 | 1.23E-39 | 63.18 |
| test8- normal control [skin] NA | HumanDise... | normal cont... | skin | Treatment ... | TreatmentS... | 56.20 | 70.71 | 71.49 | 62.22 | 65.15 | 1.11E-04 | 4.55E-56 | 1.46E-71 | 5.16E-35 | 69.12 |
| test2- normal control [peripheral blood] lipopolys | HumanDise... | normal cont... | peripheral ... | Treatment ... | Molecule:T... | 51.30 | 71.41 | 73.03 | 64.76 | 65.13 | 2.14E-03 | 6.5E-58 | 3.82E-76 | 1.68E-38 | 70.22 |
| test2- bacterial pneumonia;influenza A [lung] NA | MouseDise... | bacterial p... | lung | Treatment ... | SubjectInfe... | 45.88 | 74.83 | 67.49 | 71.84 | 65.01 | 8.45E-03 | 1.56E-67 | 1.39E-60 | 1.21E-50 | 76.00 |
| test11- viral infectious disease [lung] NA | MouseDise... | viral infecti... | lung | Treatment ... | SubjectInfe... | 51.30 | 74.83 | 58.69 | 75.13 | 64.99 | 1.39E-03 | 1.56E-67 | 8.93E-42 | 3.32E-56 | 71.95 |
| test1- kidney disease [kidney] NA | HumanDise... | kidney dise... | kidney | Disease vs.... | DiseaseOn... | 51.30 | 71.41 | 64.12 | 72.96 | 64.95 | 4.95E-04 | 6.5E-58 | 1.77E-52 | 3.96E-56 | 76.65 |
| test3- bacterial pneumonia [lung] NA | MouseDise... | bacterial p... | lung | Disease vs.... | DiseaseStat... | 45.88 | 72.80 | 69.12 | 71.84 | 64.91 | 8.45E-03 | 1.11E-61 | 6.78E-65 | 2.21E-52 | 76.04 |
| test4- cerebral malaria [brain] NA | MouseDise... | cerebral m... | brain | Treatment ... | SamplingTi... | 51.30 | 76.16 | 62.36 | 69.56 | 64.84 | 1.39E-03 | 1.43E-71 | 1.8E-48 | 1.57E-44 | 72.20 |
| test2- NA [adipose tissue] TNF alpha | MouseDise... | NA | adipose tis... | Treatment... | TreatTime:... | 51.30 | 74.16 | 73.79 | 59.57 | 64.70 | 1.23E-04 | 1.48E-65 | 1.78E-78 | 3.42E-31 | 67.19 |
| test14- rheumatoid arthritis (RA) [synovial membr | HumanDise... | rheumatoid... | synovial me... | Treatment ... | DiseaseStat... | 56.20 | 72.11 | 72.26 | 58.20 | 64.69 | 1.96E-04 | 8.75E-60 | 7.7E-74 | 5.35E-30 | 66.49 |
| test4- normal control [bronchoalveolar lavage] K_ | MouseDise... | normal cont... | bronchoalv... | Treatment ... | Treatment ... | 45.88 | 72.11 | 69.92 | 70.71 | 64.66 | 1.63E-02 | 8.75E-60 | 2.43E-67 | 6.54E-47 | 73.99 |
| test14- normal control [pancreatic islets] IL-1 bet | HumanDise... | normal cont... | pancreatic i... | Treatment ... | Treatment:... | 56.20 | 70.71 | 70.71 | 60.91 | 64.63 | 1.11E-04 | 4.55E-56 | 2.59E-69 | 7.95E-34 | 68.53 |
| test21- normal control [lung] lipopolysaccharide (I | MouseDise... | normal cont... | lung | Treatment ... | PreTreatm... | 45.88 | 72.11 | 76.74 | 63.50 | 64.56 | 2.16E-02 | 8.75E-60 | 4.42E-88 | 5.1E-38 | 69.48 |
| test2- NA [synovial tissue] TNF | HumanDise... | NA | synovial tis... | Treatment ... | Treatment ... | 51.30 | 74.16 | 71.49 | 60.91 | 64.47 | 1.39E-03 | 1.48E-65 | 1.46E-71 | 3.25E-32 | 67.17 |
| test1- melanoma [skin] NA | MouseDise... | melanoma | skin | Other Com... | Genotype[h... | 45.88 | 67.82 | 71.49 | 71.84 | 64.26 | 5.69E-03 | 6.04E-49 | 7.9E-72 | 6.42E-51 | 75.23 |
| test14- NA [peripheral blood] anti-CD28 antibod | HumanDise... | NA | peripheral ... | Treatment ... | Treatment ... | 56.20 | 70.00 | 73.03 | 56.80 | 64.01 | 5.87E-05 | 3E-54 | 3.82E-76 | 2.38E-26 | 64.93 |
| test11- normal control [pancreatic islets] IL-1 bet | HumanDise... | normal cont... | pancreatic i... | Treatment ... | Treatment:... | 56.20 | 71.41 | 67.49 | 60.91 | 64.00 | 2.81E-05 | 6.5E-58 | 1.39E-60 | 1.31E-33 | 68.72 |
| test8- lung cancer [lung] NA | MouseDise... | lung cancer | lung | Treatment... | SubjectTre... | -45.88 | -72.80 | -76.01 | -63.50 | -64.55 | 1.63E-02 | 1.11E-61 | 1.23E-85 | 2.62E-37 | 69.18 |
| test2- normal control [endothelium] Transfection_ | HumanDise... | normal cont... | endothelium | Treatment ... | Transfectio... | -56.20 | -70.71 | -74.54 | -62.22 | -65.91 | 2.81E-05 | 4.55E-56 | 7.8E-81 | 6.68E-36 | 69.86 |
| test7- lung cancer [lung] NA | MouseDise... | lung cancer | lung | Treatment... | SubjectTre... | -51.30 | -74.83 | -74.54 | -64.76 | -66.36 | 2.14E-03 | 1.56E-67 | 7.8E-81 | 4.56E-38 | 70.01 |
| test9- lung cancer [lung] NA | MouseDise... | lung cancer | lung | Treatment... | SubjectTre... | -51.30 | -72.80 | -71.49 | -70.71 | -66.58 | 3.15E-03 | 1.11E-61 | 1.46E-71 | 2.78E-51 | 76.25 |


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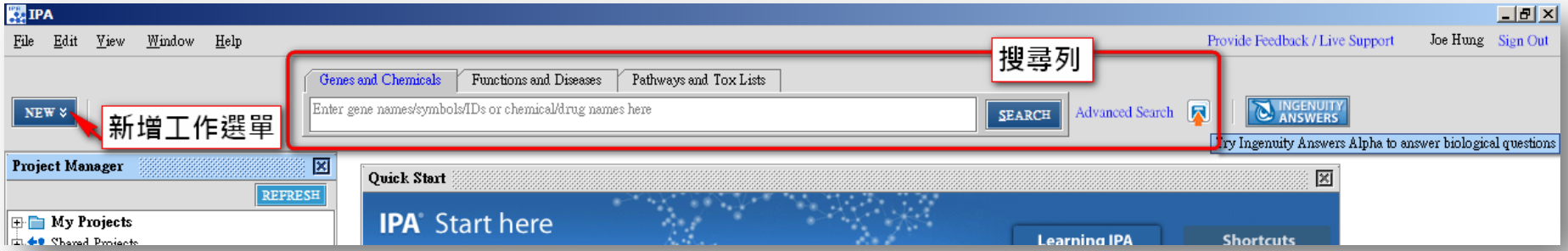
Dataset: https://goo.gl/mx2nuj






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- **Genes and chemicals**
- **Diseases and Functions**
- **Pathways and tox lists**
- Advanced search: Limiting results to a molecule type, family or subcellular location



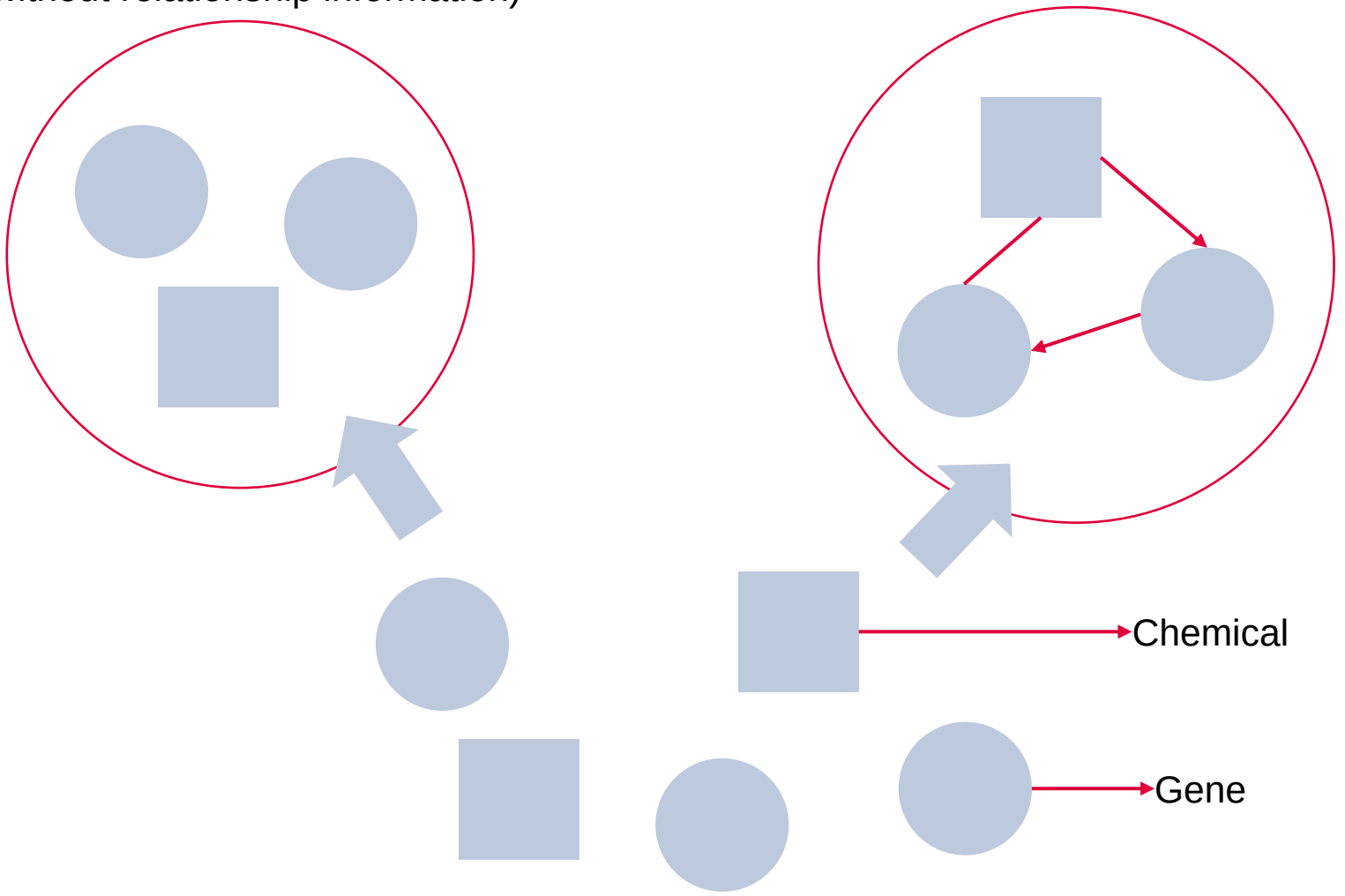


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# Scales for Gene/Chemical, Disease, Pathway

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

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

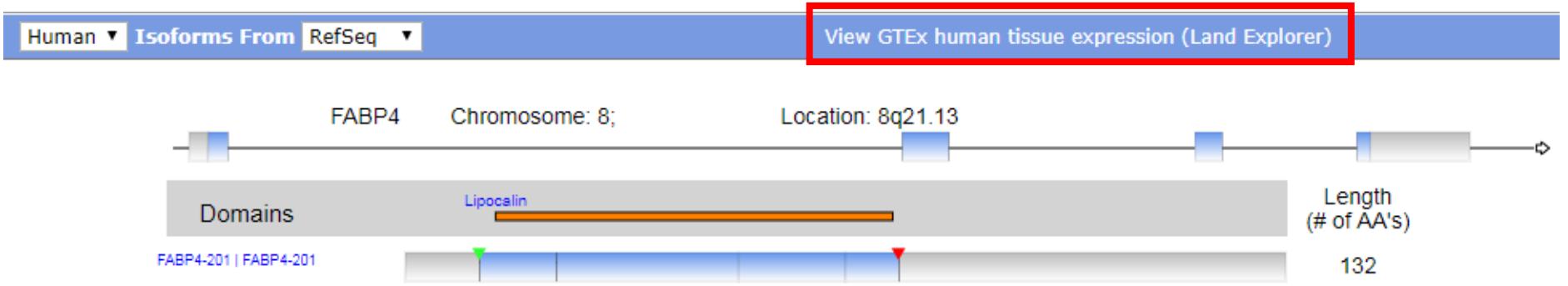





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# Gene View

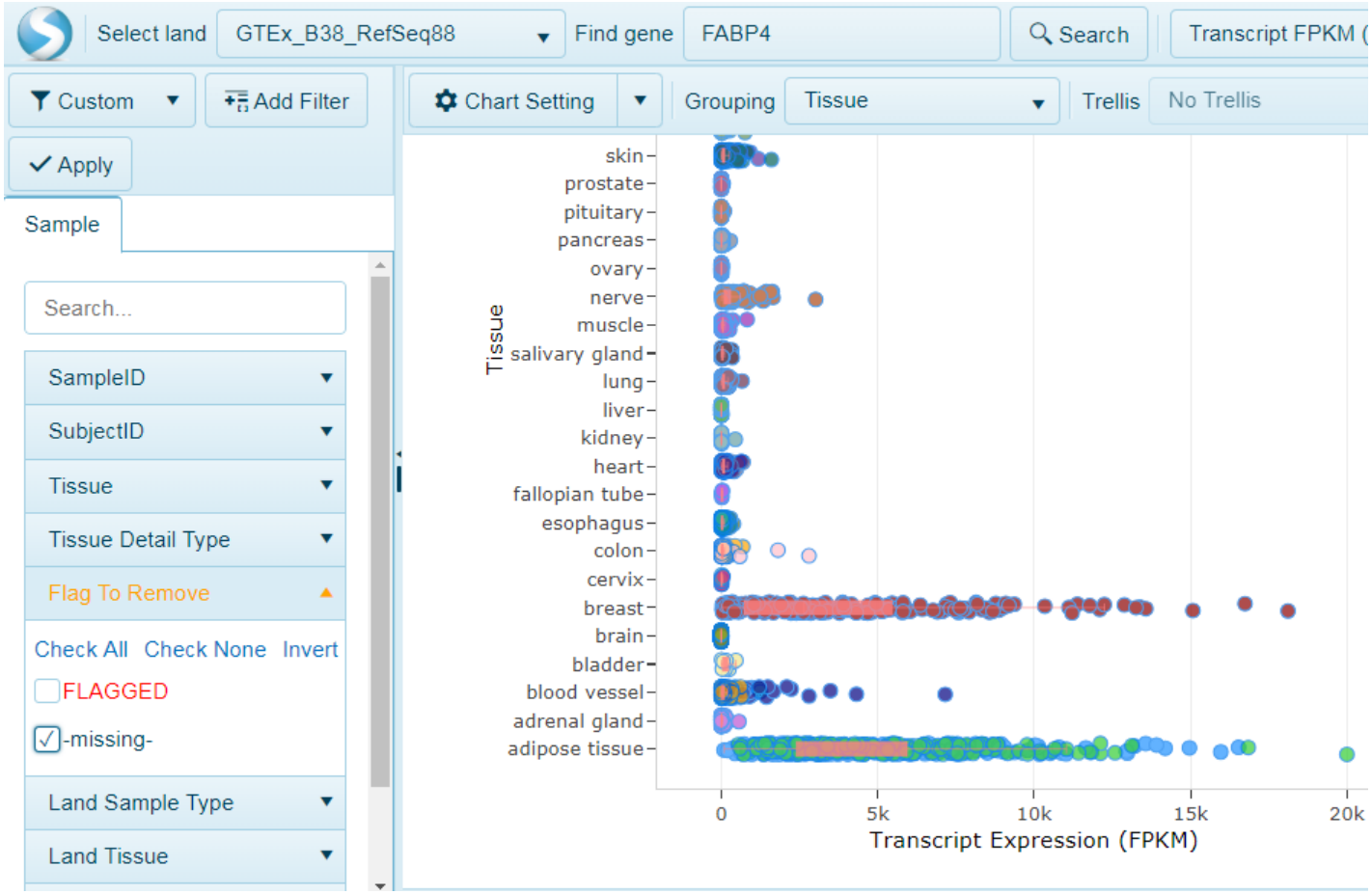
- **Explore sample-level human tissue expression through OmicSoft Land Explorer**




Now you can examine detailed expression patterns across human tissues directly from IPA's Isoform Views. IPA now offers access to a lite version of OmicSoft Land Explorer. With this new feature, you can provide interactive plots of gene expression in 51 different human tissues from the GTEx project, for both gene level and individual splice variants. You can filter the view for a particular tissue, or filter on metadata, such as tissue donor age or gender. You can also download the detailed sample-level expression data for the gene.


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- **View of human isoform-level expression in human tissue samples for FABP4**





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# Key Terminology

- **Finding:6.6 million**
  - 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


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# 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)

**Node**

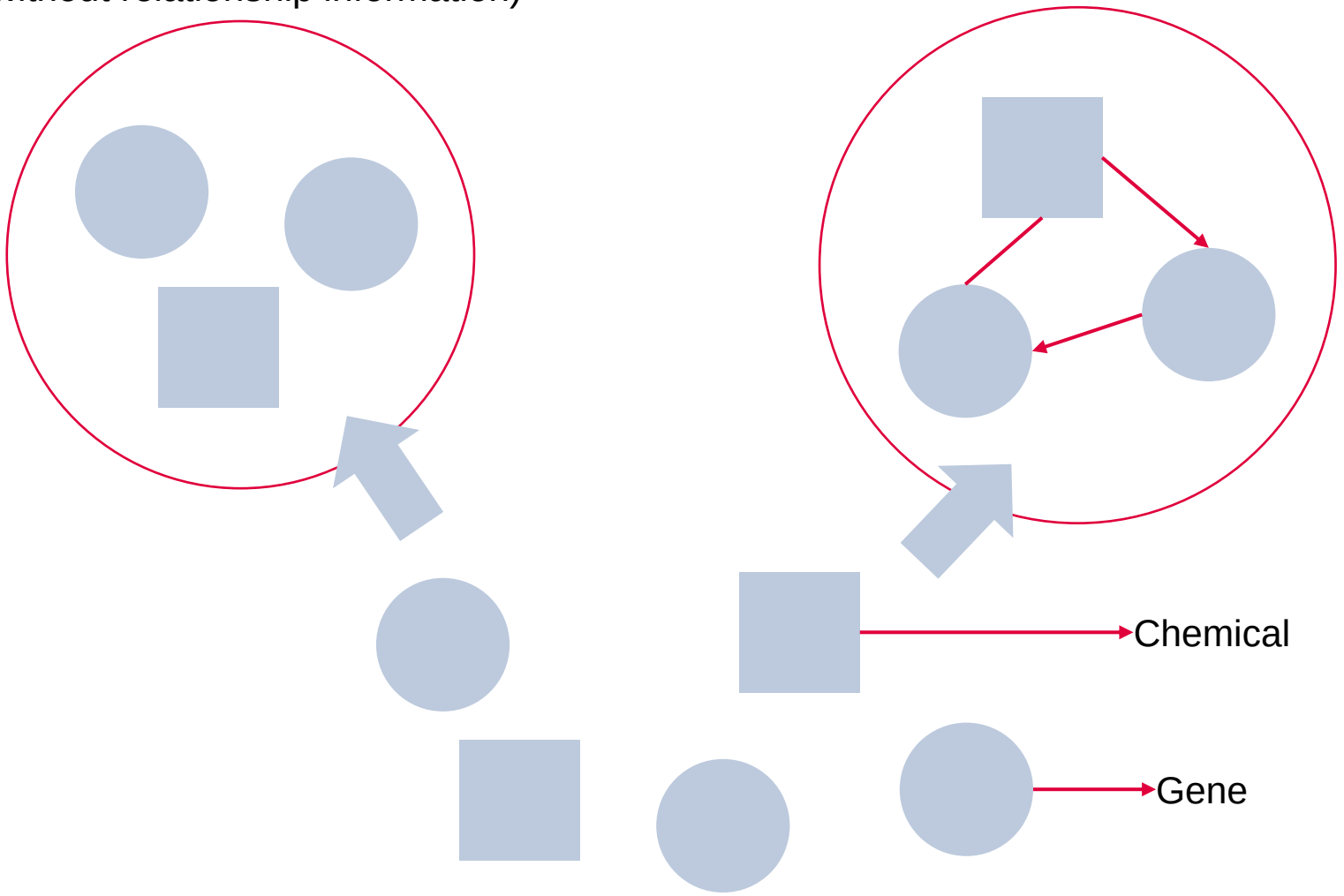
- Single molecule in Network such as Gene, Chemicals, Disease, and Pathway


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# Scales for Gene/Chemical, Disease, Pathway

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

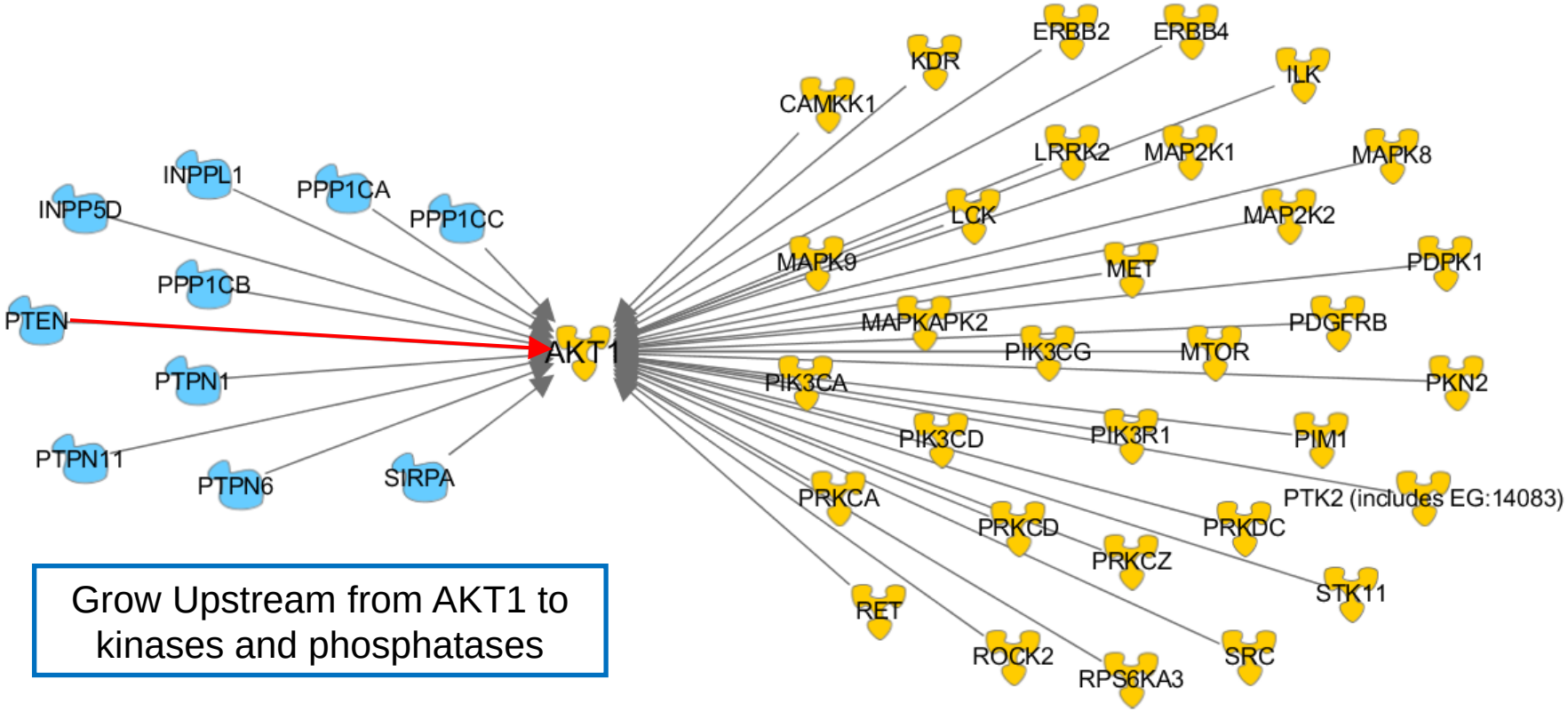
Set of Genes and Chemicals associated with Disease/Function (with relationship information)






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# 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.

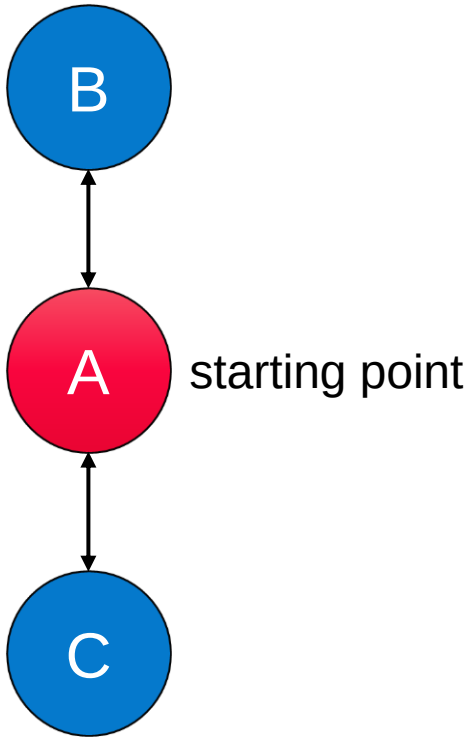
Source: Ingenuity Expert Findings



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# Grow

- 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.

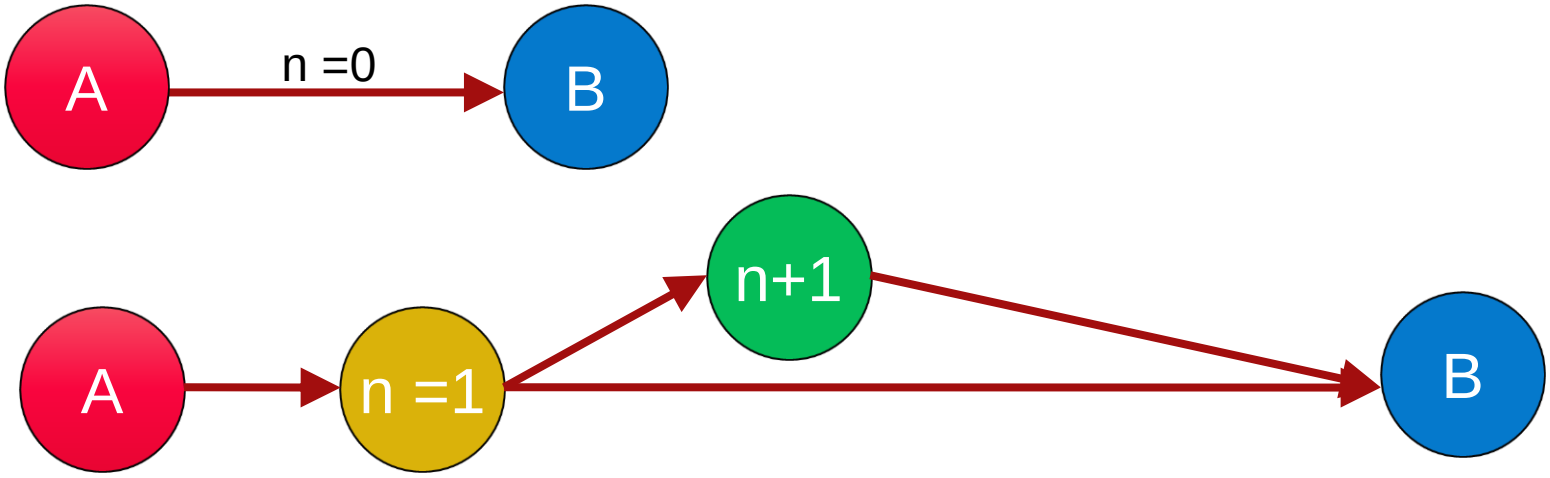




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# How Path Explorer Works

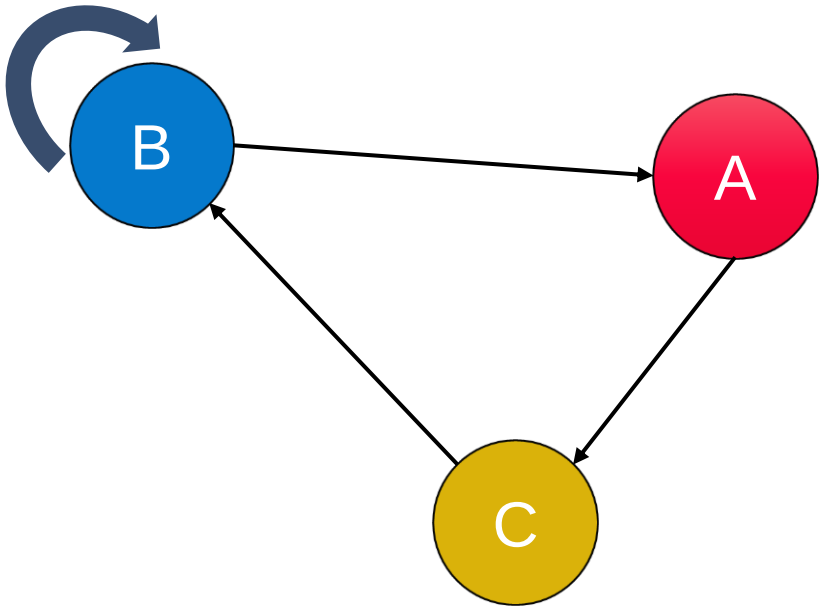
- Calculates the “Shortest Path” between 2 molecules or 2 sets of molecules
- If 2 molecules/sets don’t have specific connections in IPA, Path Explorer will find how many and which molecules can be added to this pathway to create the shortest path
  - Shortest Path (n)
  - Shortest Path + 1 (n+1)





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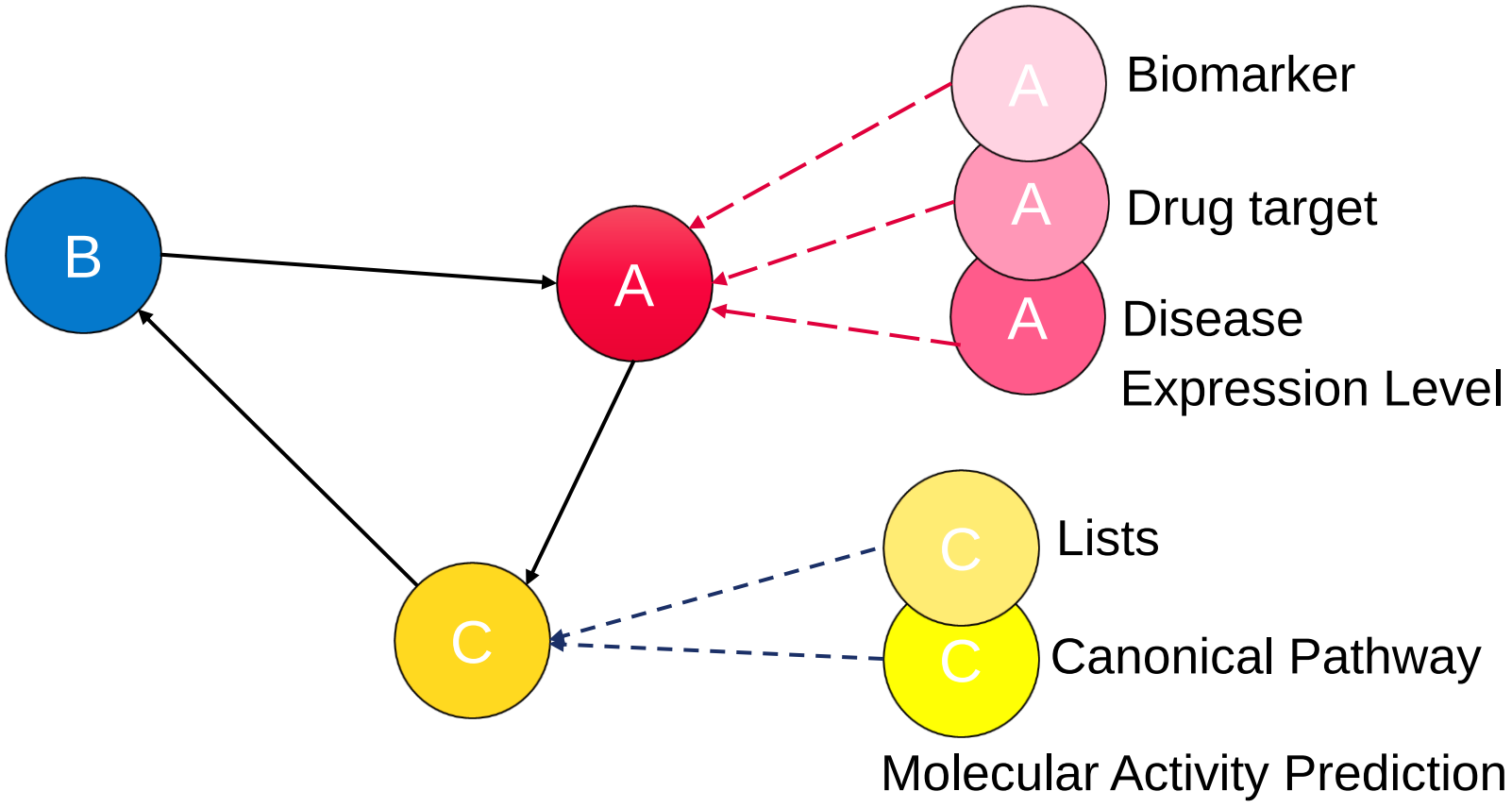
- Connect allows you to see specific molecular interactions between nodes or groups of nodes.





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

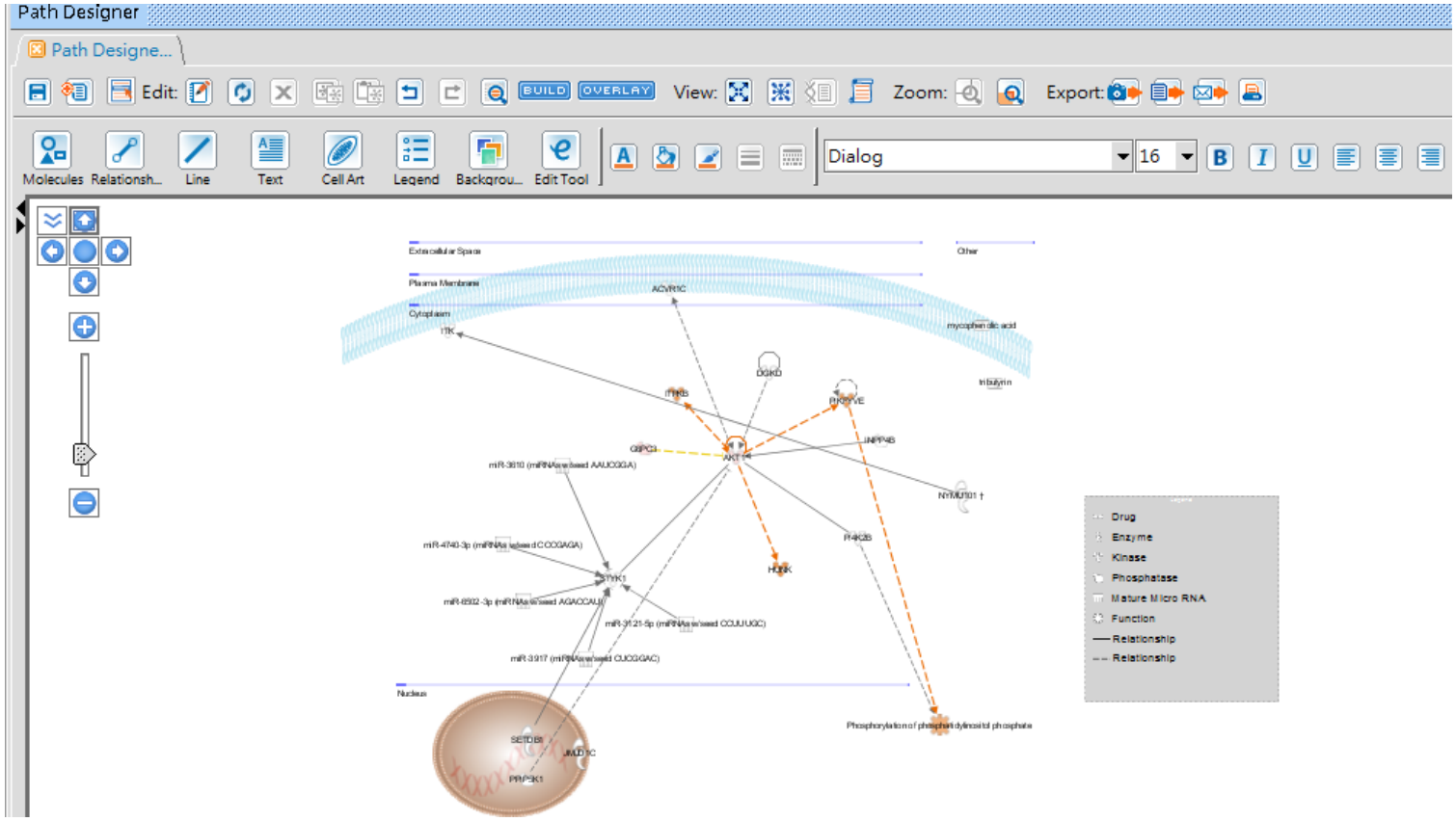




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# Path Designer

- 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.






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# Live Demo


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# 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 | 1-10-10-18 | 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 ho | 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 |



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- **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。


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# Get more complete mapping during dataset upload

IPA can now improve your success of mapping identifiers in your datasets by evaluating more than one column of gene or chemical IDs.

1. Select File Format: Flexible Format More Info
2. Contains Column Header: Yes No
3. Select Identifier Type: Please assign at least one column below as "ID", and assign the identifier type(s).
   Assign additional columns as ID to improve mapping coverage if desired.
4. Array platform used for experiments: Not specified/applicable Select relevant array platform as a reference set for data analysis.
5. Use the dropdown menus to specify the column names that contain identifiers and observations. For observations, select the appropriate measurement value type.

Raw Data (410) | Dataset Summary (379) | Metadata

EDIT OBSERVATION NAMES | INFER OBSERVATIONS | More Info

| ID/Observation Name | ID | ID | ID | ID | FoldChange | FoldChange | FoldChange |
|---|---|---|---|---|---|---|---|
| | | | | | Expr Fold C... | Expr p-value | Expr False D... |
| Measurement/Annotation | PubChem | CAS | KEGG | HMDB | | | |
| 1 | PUBCHEM | CAS | KEGG | HMDB | FoldChange | RawPValue | FDR_BH |
| 2 | 5283469 | 2277-28-3 | --- | --- | -1.153 | 0.0807 | 0.1866 |
| 3 | 643975 | 146-14-5;8436... | C00016 | HMDB0001248 | 1.2117 | 0.4047 | 0.5399 |
| 4 | 754 | 29849-82-9 | C00093 | HMDB0000126 | 1.1347 | 0.4695 | 0.607 |
| 5 | 182230 | 2490-97-3 | C02716 | HMDB0006029 | 1.2527 | 0.1435 | 0.2743 |
| 6 | 5283565 | 104404-17-3 | --- | HMDB0004950 | -1.572 | 3.27E-06 | 0.000038615 |
| 7 | 9547101 | --- | --- | --- | -1.2166 | 0.0367 | 0.102 |
| 8 | --- | 56421-10-4 | --- | HMDB0008038 | 7.8962 | 2.55E-20 | 1.12E-17 |
| 9 | 440120 | 23284-33-5 | C03793 | HMDB0001325 | 1.1721 | 0.0977 | 0.2139 |
| 10 | 92105 | 332-80-9 | C01152 | HMDB0000001 | 1.4374 | 2.03E-06 | 0.000025366 |
| 11 | 187488 | 86321-32-6 | --- | --- | 1.2989 | 0.0002 | 0.0015 |
| 12 | 673 | 1118-68-9 | C01026 | HMDB0000092 | 1.2614 | 0.0001 | 0.0009 |
| 13 | 5282807 | 7370-49-2 | C16533 | HMDB0061714 | 1.2144 | 0.1393 | 0.2729 |
| 14 | 11439 | 123-56-8 | C07273 | --- | 10.2482 | 0.2813 | 0.4438 |
| 15 | 2802421 | 3077-46-1 | --- | HMDB0061684 | 1.0268 | 0.6567 | 0.7588 |
| 16 | 92751 | 314-50-1 | --- | HMDB0000788 | 1.2056 | 0.4893 | 0.6198 |
| 17 | 6453725 | 85187-10-6;85... | C00550 | HMDB0001348 | -1.2915 | 0.0229 | 0.0673 |
| 18 | 193270 | --- | --- | --- | -1.6398 | 4.60E-06 | 0.000051519 |
| 19 | 892 | 87-89-8 | C00137 | HMDB0000211 | 1.1548 | 0.1619 | 0.3036 |
| 20 | 446640 | --- | --- | --- | 1.2473 | 0.037 | 0.1025 |
| 21 | 203 | 99-16-1 | C00499 | HMDB0001209 | 1.1974 | 0.3231 | 0.477 |

SAVE | CANCEL | HELP



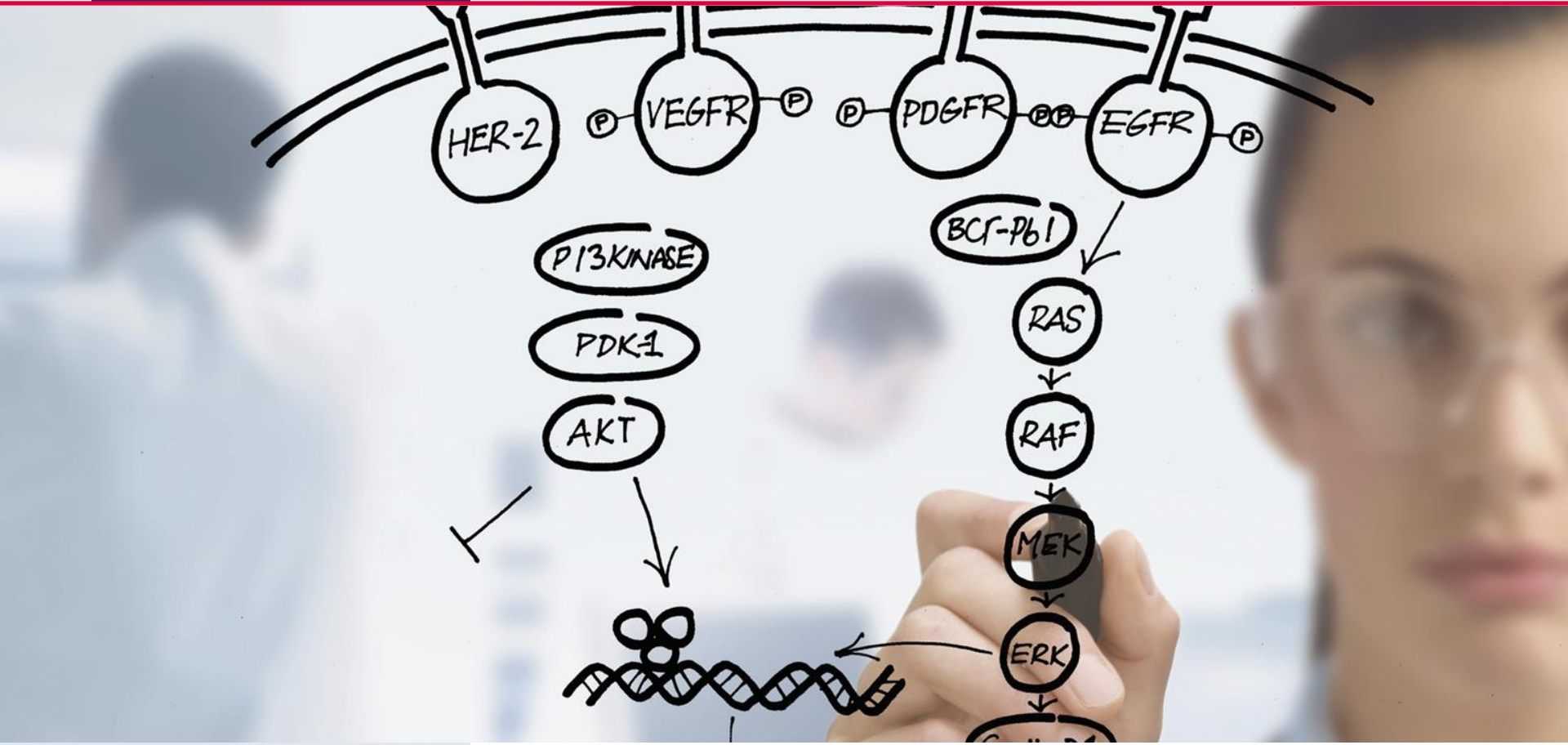
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# Live Demo


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# Q&A


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## 歡迎與我們聯絡

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