

源资科技

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IPA用户培训

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2022年3月2日



源资科技

创新信息技术与整合资讯管理的知识领航者

源资信息科技（上海）有限公司成立于2008年5月，目前公司主要经营和研发生命科学与材料科学类学术专业软件、信息化管理系统和质量管理系统，同时提供从药物发现到药物开发的完整解决方案。



人数 110
30% 硕士以上学历
50% 5年以上项目经验

注册资金200万美金
ISO9001认证
高新技术企业
客户数量超过1000



公司规模

经营范围

公司资质

公司宗旨

科研计算模拟解决方案
智能信息化业务
临床电子化业务

为国内医药、化工、
材料等高科技领域客户
提供高附加价值的
优质服务

<http://www.tri-ibiotech.com/>

计算模拟类产品

源资科技

01



材料基因组计划
材料模拟
VASP计算

材料科学

04



生命科学

PK/PD
临床试验
生物信息学



量子化学
分子模拟



计算化学



02

化学信息学

波谱解析
实验信息管理
电子实验记录ELN



ACD/Labs

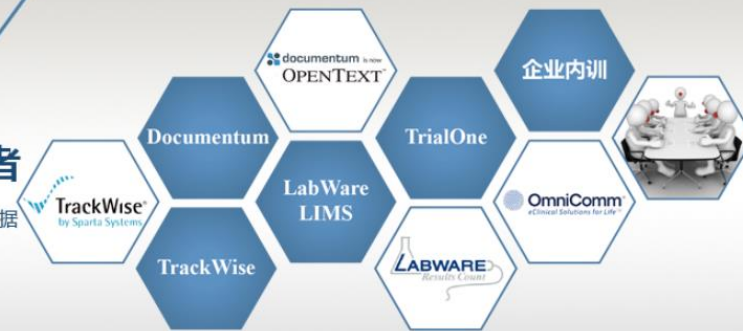


03

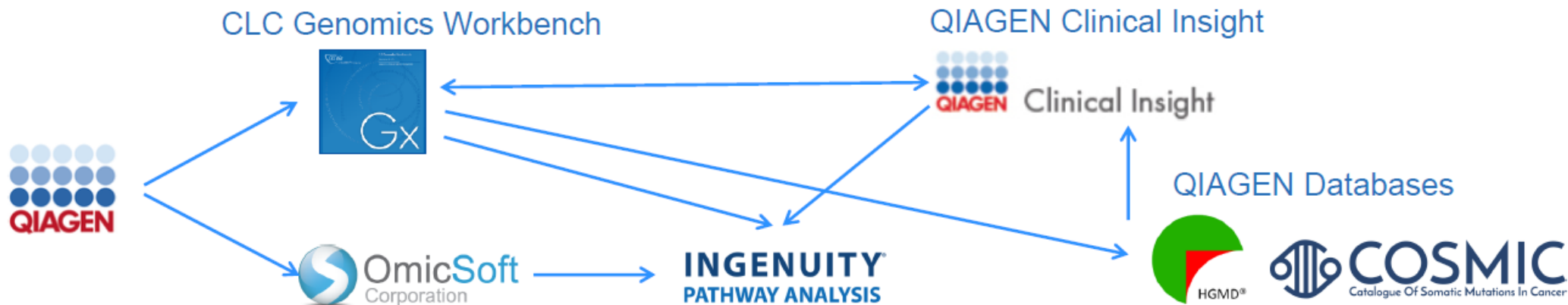
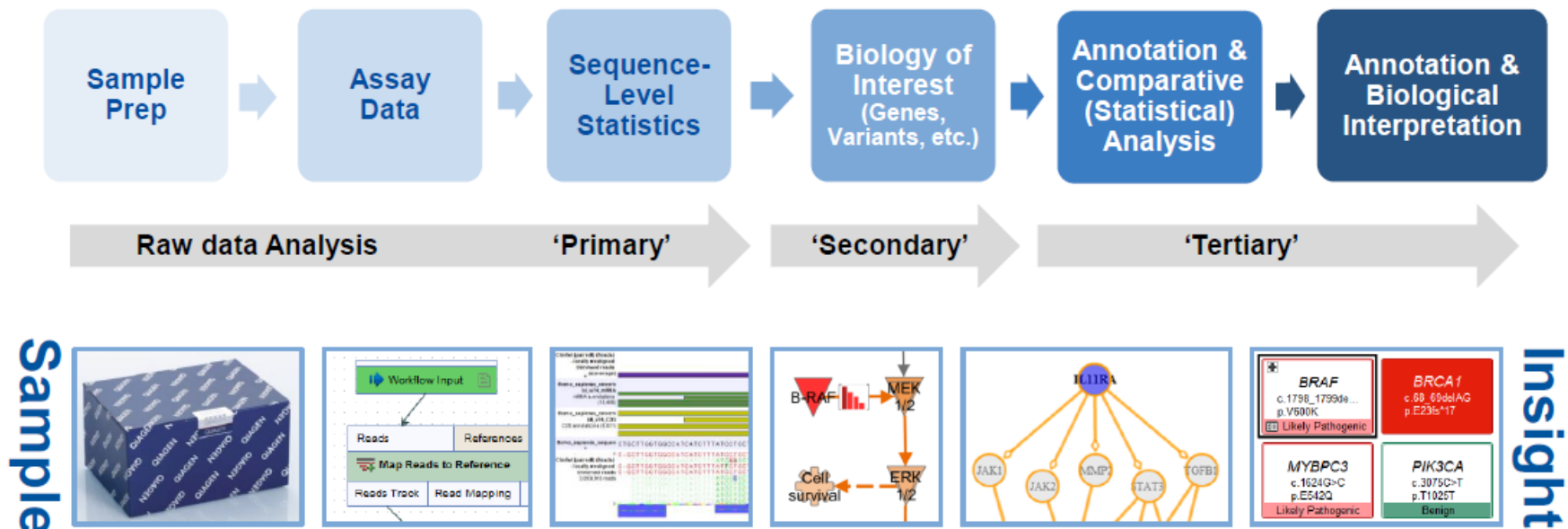


创新信息技术与整合 资讯管理的知识领航者

- 信息技术信息管理引导决策创新、大数据分析与管理模式的升级
- 专注于材料科学和生命领域



QIAGEN Digital Insight Total Solution



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Content

源资科技

1. IPA软件基本信息
2. 查询功能
3. 分子活性预测功能
4. Pathway构建
5. Causal Networks
6. MicroRNA Target Filter
7. IsoProfiler
8. IPA文献分享 (5篇)
9. IPA软件演示

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PART

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IPA软件基本信息

1

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IPA 登录



- 安装完成后，桌面会出现图标：
- 双击图标，软件进入加载界面，加载界面之后为登录界面。



Ingenuity Pathway Analysis



Welcome! Please login

Email

Password

Remember my password

LOG IN

[Find Out More](#) | [Forgot Password](#)

You are logging in from IP address 123.116.248.205

[Privacy Policy](#)

Contact QIAGEN

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Sales: +1 (650) 381-5056

Hours: 0:00 – 16:00 PST (9:00 – 0:00 CET)
Monday - Friday

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- 在登录界面中输入申请IPA账号使用的Email及密码即可进入软件

IPA with Advanced Analytics LCL

Advanced Analytics: Causal Network Analysis, BioProfiler, IsoProfiler, Relationship Export, and Phosphoproteomics Analysis

交大IPA预约: 登陆时间规定**工作日上午8点到下午5点**（寒暑假登陆时间为上午9点半到下午4点）

地点: 医学院图书馆一楼电子阅览室IPA专用电脑系统，IPA操作系统绑定在指定电脑上，使用者建议提前2到3周预约使用，每人每次使用时间不得超过4小时。

注意:

- 对于轮流申请使用的账号，请协调好不同用户登入登出的时间。自己的数据可以导出保存（.qipa文件）或删除以便下一位用户使用IPA。
- 数据上传以后超过180天，凯杰将从IPA永久删除这些老数据，注意导出保存重要数据。
- 如果要更换锁定的电脑，请联系技术支持工程师。注意不要频繁更换。

Windows Operating Systems:

- Windows 10
- Windows 8
- Windows 7
- Windows XP SP2 or later*

Windows Internet Browsers:

- Microsoft Edge 87 or later
- Firefox 5 or later
- Chrome 10 or later
- Safari 5.05 or later

Java Runtime Environment (JRE).

Not needed if using the installed version of the QIAGEN IPA client **:

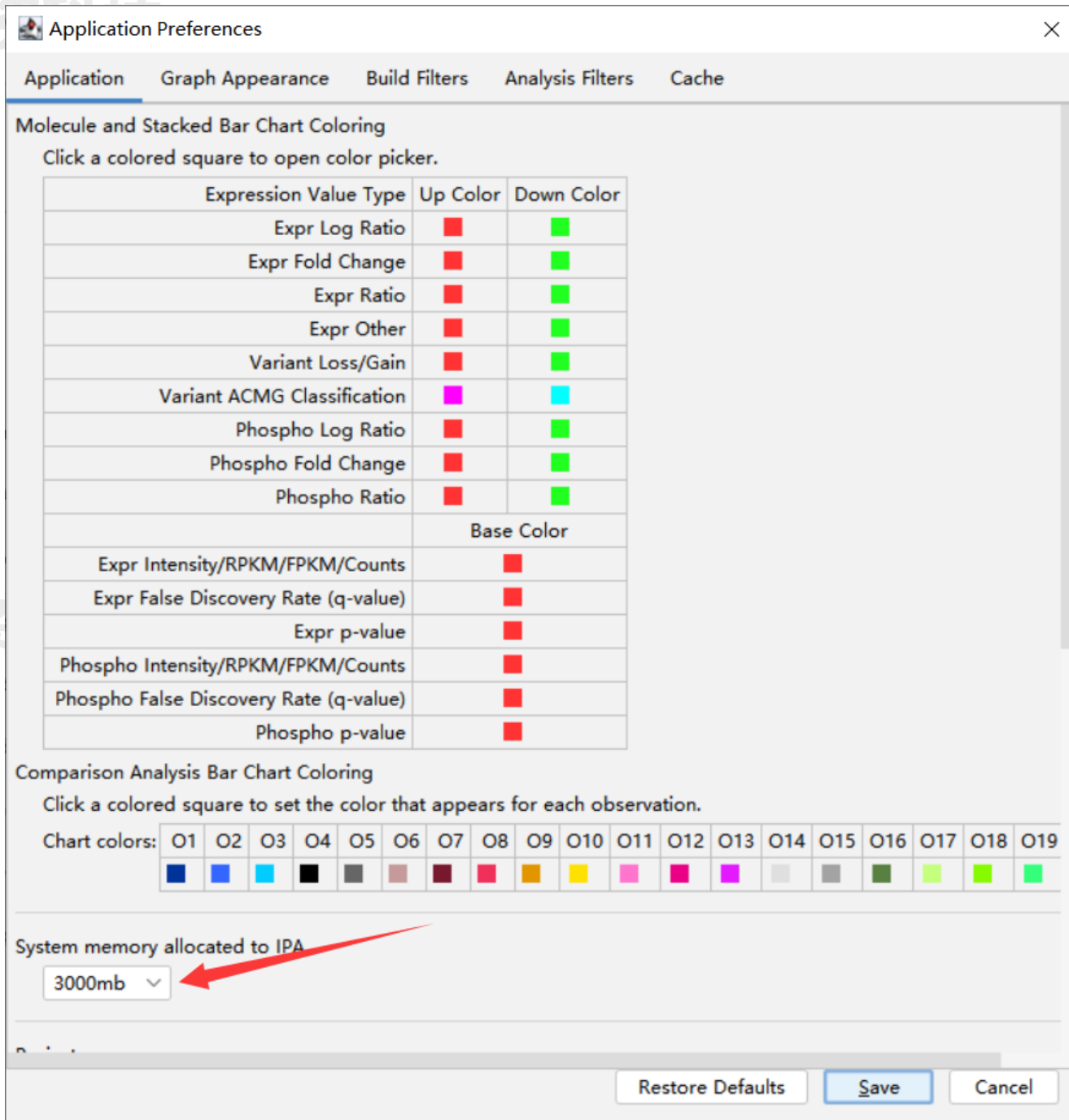
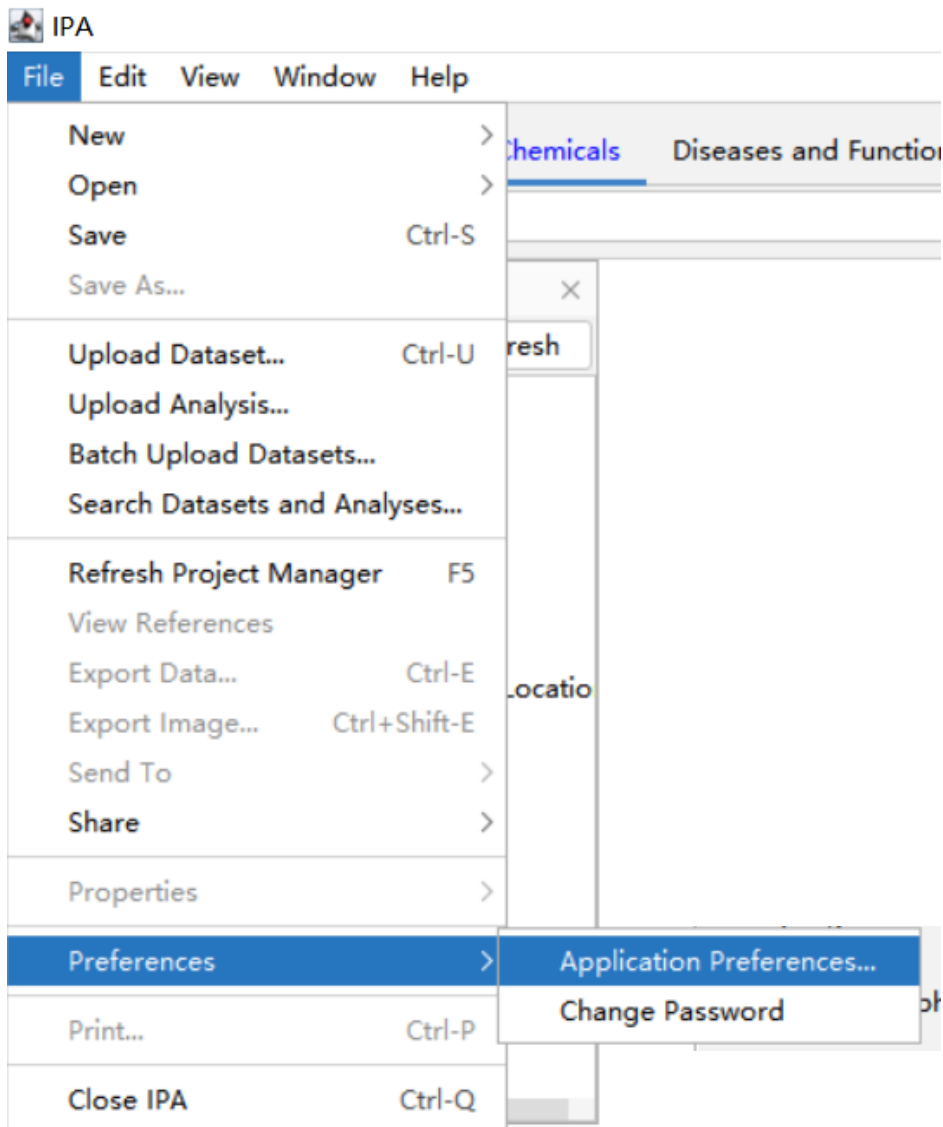
- JRE 1.8.0_xx or higher

Minimum Hardware Requirements:

- Core™ i5 processor or equivalent running at 2 GHz or higher with 64 bit OS and Java
- Minimum at least 3 GB RAM free for Java
- Minimum Screen resolution of 1280×800

Mac用户见: <https://digitalinsights.qiagen.com/products-overview/discovery-insights-portfolio/analysis-and-visualization/qiagen-ipa/>

调高IPA的系统内存



IPA指南: <https://qiagen.secure.force.com/KnowledgeBase/KnowledgeIPAPage>

视频教程、讲座等: <https://tv.qiagenbioinformatics.com/search/perform?search=ipa>



PRODUCTS AND SERVICES ▾ SOLUTIONS ▾ WEBINARS ▾ TUTORIALS ▾

All Articles **IPA** CLC Genomics Server CLC Genomics Workbench HGMD

Search

Home / Search results for *ipa*

SEARCH RESULTS FOR *IPA*



QIAGEN IPA
Systems Analysis of Cell Therapies- Demonstrating Ingenuity Pathway (IPA) on...
19 views November 30, 2021



TUTORIALS
Single-cell RNA-seq data analysis and interpretation
68 views November 12, 2021



QIAGEN IPA
QIAGEN IPA deep-dive and new features training, America - Nov 3 2021
52 views November 04, 2021

By Article Types

- Basics
- FAQs
- Knowledge
- Product Features
- System Requirements
- Tutorial & Training

IPA Legend

QIAGEN Ingenuity Pathway Analysis (IPA) | Describes the tool bar icons, colors, and more in IPA

Brief IPA help overview

QIAGEN Ingenuity Pathway Analysis (IPA) | Guide to the key help articles for QIAGEN IPA

What is IPA and how can it help your research?

QIAGEN Ingenuity Pathway Analysis (IPA) | Brief overview of QIAGEN IPA

Exploring relationships among molecules, diseases, functions, and more

Overview of the ways in which you can visually explore the curated information in IPA

Analysis Results Tutorial

Pattern Search

QIAGEN Ingenuity Pathway Analysis (IPA) | How to search the OmicSoft expression collection using a network or pathway gene pattern

Exploring large public data resources through IPA

QIAGEN Ingenuity Pathway Analysis (IPA) | A brief overview of curated 'omics data resources available in IPA

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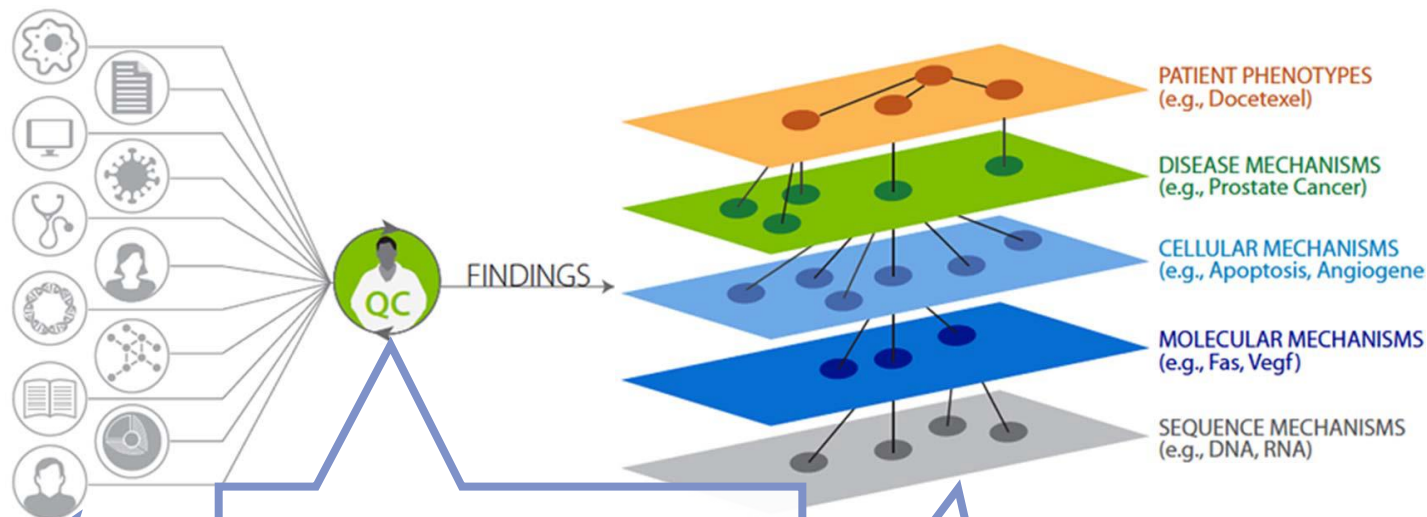
源资科技

查询功能

2

源资科技

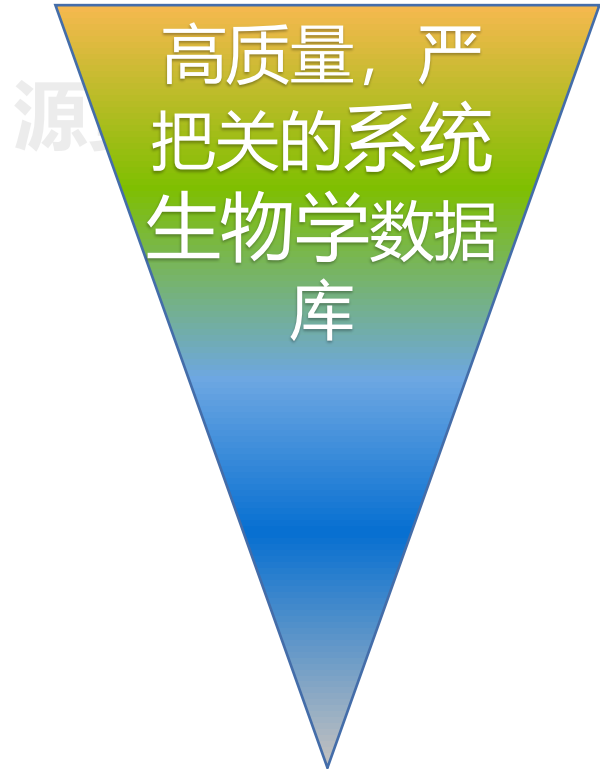
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500多名专家多轮质控

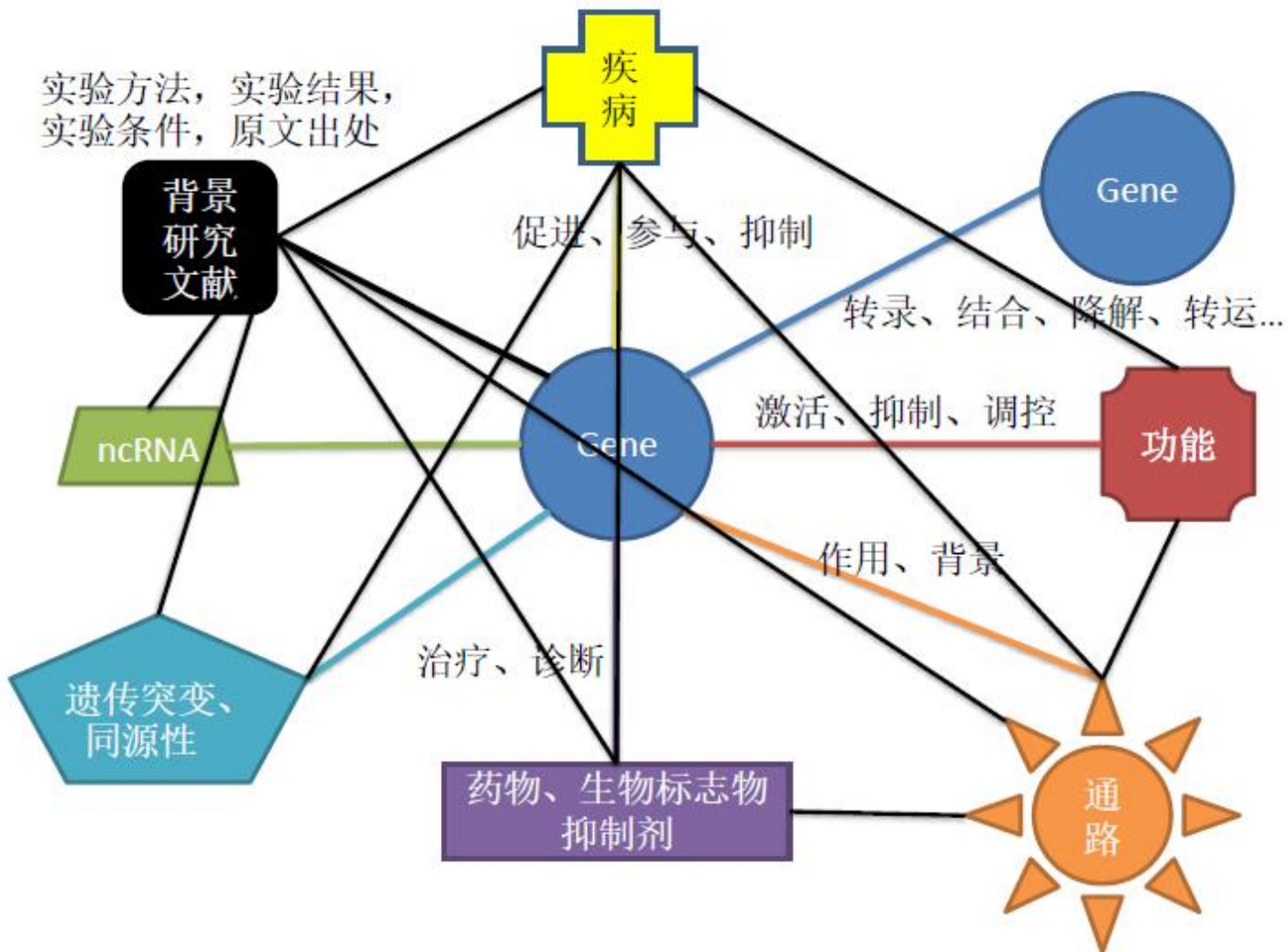
300多种顶尖杂志全文
3000多种生物学杂志摘要
30多种公共数据库
850多万条生物学知识

人、小鼠、大鼠等物种
3万多种基因、化合物
近1万种生物学功能、疾病本体论分类
超过130万种相互作用



IPA: 立体整合多组学系统的强力工具

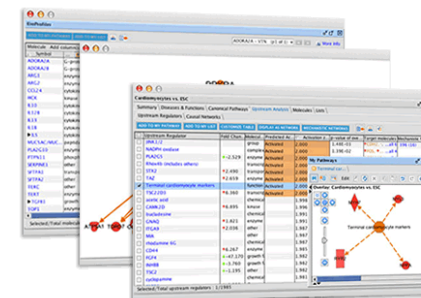
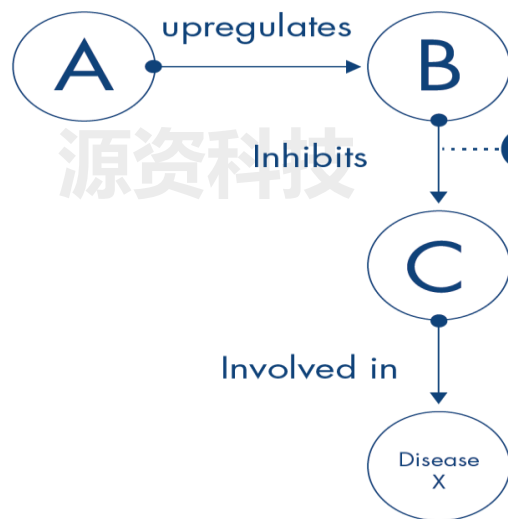
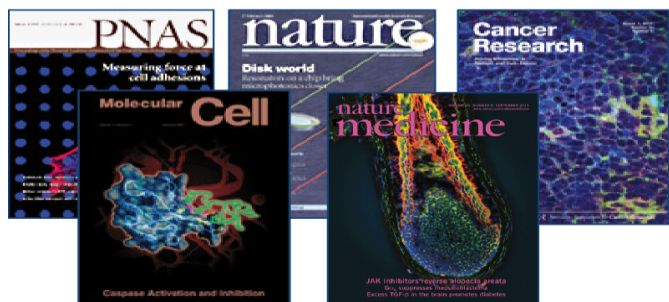
IPA 整合的第三方数据库



Entrez Gene
RefSeq
OMIM
ClinVAR
GWAS Database
Gene Ontology (GO)
Human Metabolome Database (HMDB)
GNF Tissue Expression Body Atlas
NCI-60 Cell Line Expression Atlas
HumanCyc metabolic pathway information
BIND, DIP, MINT, MIPS, BioGRID, IntAct, Cognia protein-protein interactions
Clinicaltrials.gov
Drugs@FDA
Mosby's Drug Consult
Goodman & Gilman's Pharmacological Basis of Therapeutics
DrugBank
Hazardous Substance Database (HSDB)
Chemical Carcinogenesis Research Information System Database (CCRIS)
TargetScan
miRBase
miRecords
TarBase
COSMIC
The Mouse Genome Database (MGD) from The Jackson Laboratory (JAX)

IPA: 知其然知其所以然

源资科技



- Cancer Scoring
- Hereditary Disease Scoring
- Causal Network Analysis
- Pathway Activity Analysis
- Regulator Effects

源资科技
整合

组织

分析

查看findings统计数值

IPA
File Edit View Window Help

Help and Support F1
Tutorials
Video Tutorials
Workflows >
Quick Start Ctrl-9
Legend Ctrl-Shift-I
About IPA
What's new in IPA

and Functions Pathways and Tox Lists
chemical/drug names here Search Advanced Search

What's new in IPA

- G-Protein Coupled Receptor Signaling Pathway
- Polyamine Regulation

Content updated for one pathway

- Circadian Rhythm Signaling

>325,000 new findings (bringing the total in IPA to over 8.4 million), including:

- ~143,000 Expert findings
- ~66,600 protein-protein interaction findings from BioGRID
- ~400 protein-protein findings from IntAct
- ~12,000 findings from COSMIC
- ~86,350 cancer mutation findings from ClinVar
- ~12,000 findings from the Mouse Genome Database (MGD)
- ~1,430 findings from the Online Mendelian Inheritance in Man (OMIM)
- ~1,800 Gene Ontology findings
- ~1,400 target-to-disease findings from ClinicalTrials.gov
- ~1,800 drug-to-disease findings from ClinicalTrials.gov
- ~300 newly mappable chemicals

>6,000 new datasets (for a total of >102,000) will soon be available in Analysis Match, Activity Plot, and Pattern Search

Land	Repository	Datasets Q2 2021	Datasets Q3 2021	Increase
DiseaseLand	HumanDisease	20,506	22,605	2,099
	MouseDisease	16,795	18,684	1,889
	RatDisease	7,809	7,809	
	LINCS	28,234	28,234	
	OncoGEO	9,254	10,852	1,598

IPA具有独一无二的数据库和人性化的操作界面

	公共软件	IPA
数据来源	表达谱芯片、人工上传、同源比较、自动提取文献摘要	高质量论文人工全文阅读取证 权威数据库 具备临床信息
数据组成	GO: 基因注释 KEGG: 信号通路 SRING: 相互作用 Transfac: 转录因子 mirBase: miRNA信息 Nexbio: 疾病信息	亚细胞定位, 生理过程, 分子功能 生物通路, 转录调控 药物靶标, 生物标志物 疾病表型, 遗传突变
易用性	单一的结果 无详细的参考文献信息 每种数据库都要从头学习	各类分析在同一界面完成 所有结果包含参考文献资料 界面简洁, 易学易用
准确性	数据来源、更新速度、数据提取算法均各不相同, 无法保证一致性 大多数工具不支持个性化需求 大部分数据来源于表达谱芯片, 志愿上传, 无验证结果	每周更新文献资料, 每季度更新软件分析模块 支持个性化分析需求, 构建非经典调控途径 多轮专家质控搜索结果 参考数据库、杂志、数据均为高影响力资源

Quantifiable benefits of IPA

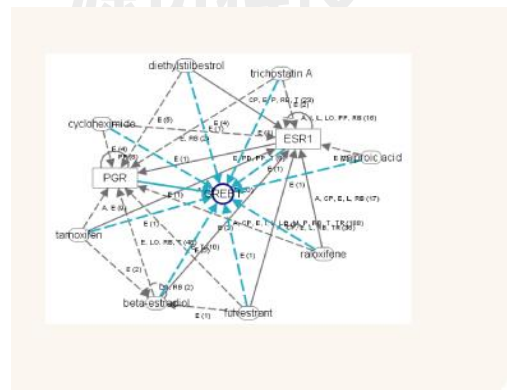
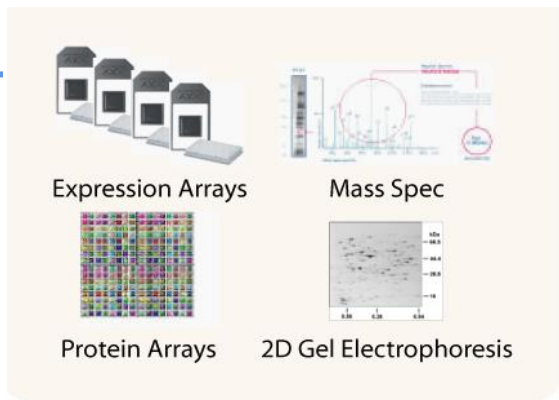
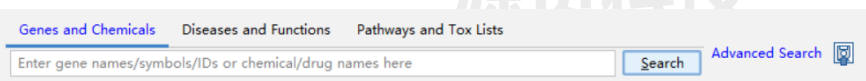
- **Quick to provide insights**
 - Upload and get analysis results in minutes. One upload, many ways to look at the data.
- **Trustworthy:** Cited frequently in publications by the top 10 academic and top 10 pharma
 - ~1400 citations in the last 5 years from institutions like Harvard, University of Cambridge, MIT, Stanford, Johns Hopkins, Pfizer, Merck, GSK, JNJ and only ~270 from MetaCore.
 - IPA cited 7x more than top competitor MetaCore since 2004.
- **Up to date:** Weekly content updates and four major software releases per year– other software is updated much less often, and some can go years without content updates.
- **Great customer support:** 1-day turnaround on customer support cases from scientists

源资科技 生物学问题

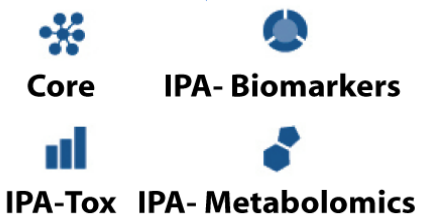
搜索

实验数据

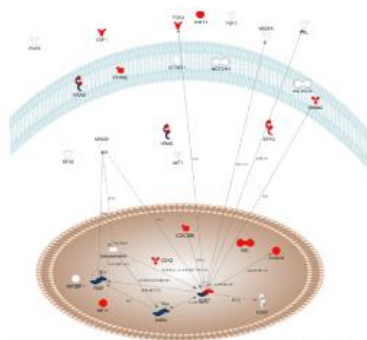
定制路径



BioProfiler



对比分析



Communicate & Collaborate

- 模拟下游效应
- 理解基因表达变化的原因
- 解释预测的调控子如何导致预测的功能效应
- 鉴定可能的新调控子网络等

软件打开界面——菜单栏

菜单栏
File可以开始所有的工作

Help帮助文件，对每一个功能和模块都有详细的解答

The screenshot shows the IPA software interface with the File menu open. The menu items are: New, Open, Save, Save As..., Upload Dataset..., Upload Analysis..., Batch Upload Datasets..., Search Datasets and Analysis..., Refresh Project Manager, View References, Export Data..., Export Image..., Send To, Share, Properties, Preferences, Print..., Close IPA. The Help menu is also open, showing: Help and Support, Tutorials, Video Tutorials, Workflows, Quick Start, Legend, About IPA, What's new in IPA, Upload Analysis..., Advanced Search, Project..., Compare, Import Pathway, Analyzing phosphoproteomics data, Analyzing genetic gain/loss data, Analyzing metabolomics data, Case studies and Support webinars, Top help articles and FAQs, Contacting Support, Shortcuts. A text box in the center of the image contains the text '菜单栏 File可以开始所有的工作' and 'Help帮助文件，对每一个功能和模块都有详细的解答'. A red box highlights the menu items.

软件打开界面——Create New 源资科技

The screenshot displays the QIAGEN IPA software interface. At the top, there are navigation tabs for 'Genes and Chemicals', 'Diseases and Functions', and 'Pathways and Tox Lists'. A search bar is located below these tabs. On the left side, a 'Create New...' menu is open, listing various analysis options such as 'Core Analysis...', 'Comparison Analysis...', 'Biomarker Filter...', 'Biomarker Comparison Analysis...', 'microRNA Target Filter...', 'BioProfiler', 'IsoProfiler', 'My Pathway', 'Path Designer', 'Filter Dataset', 'Upload Dataset...', 'Upload Analysis...', 'Advanced Search', 'Project...', 'Compare', and 'Import Pathway'. A red box highlights the 'Create New...' menu item, and a red arrow points from it to a central text box. The central text box contains the text: 'Create New: 操作的快捷键，能够开始多种操作命令和数据分析'. In the background, a 'Quick Start' dialog box is visible, featuring a large image of a cell and a virus, and a list of analysis options: 'Analyzing mRNA or proteomics data', 'Analyzing microRNA data', 'Analyzing phosphoproteomics data', 'Analyzing genetic gain/loss data', 'Analyzing metabolomics data', 'Case studies and Support webinars', 'Top help articles and FAQs', 'Contacting Support', and 'Shortcuts'. A 'News' section is also visible at the bottom right of the main interface, containing several bullet points about the IPA 2021 Winter release, trial resources, and other updates.

Create New:
操作的快捷键，能够开始多种操作命令和数据分析

软件打开界面——Project Manager

源资科技

The screenshot shows the Project Manager interface. A red callout box highlights the 'My Projects' list on the left side of the window. The list includes folders for 'Danbai', 'Shanxi', 'COVID-19', 'Cardio', 'Training Project', 'Human Genes Chromosomal Location', 'Ingenuity KEGG gene lists', 'Tissue Expression', 'Example Analyses', 'Shared Projects', and 'Libraries'. The main content area displays a search bar, a 'Quick Start' sidebar with various analysis options, and a 'News' section with a scheduled downtime announcement for the IPA 2021 Winter release.

Project Manager:
所有上传的数据、分析的结果
收集整理分子列表、通路
与其他科学家共享的结果

软件打开界面——Quick Start 源资科技

IPA

File Edit View Window Help

Genes and Chemicals Diseases and Functions Pathways and Tox Lists

Create New... Enter gene names/symbols/IDs or chemical/drug names here Search Advanced Search

Project Manager

A-Z Sort Search Refresh

My Projects

- Danbai
- Shanxi
- COVID-19
- Cardio
- Training Project
- Human Genes Chromosomes Locations
- Ingenuity KEGG gene list
- Tissue Expression
- Protein Analyses
- Projects

Quick Start

News

- Exploring large public data resources through IPA
- Exploring IPA knowledge
- Analyzing mRNA or proteomics data
- Analyzing microRNA data
- Analyzing phosphoproteomics data
- Analyzing genetic gain/loss data
- Analyzing metabolomics data
- Case studies and Support webinars
- Top help articles and FAQs
- Contacting Support
- Shortcuts

News

- The IPA downtime for the upcoming IPA 2021 Winter release has been scheduled for:
 - Pacific Standard Time: Friday, Dec 10th 5 p.m. through Sunday, Dec 12th, 12 p.m. PST (Noon)
 - Central European Time: Saturday, Dec 11th, 2 a.m. through Sunday, Dec 12th, 9 p.m.
 - Japan Standard Time: Saturday, Dec 11th, 9 a.m. through Monday, Dec 13th, 5 a.m.
 - China update set for CST (Beijing): Friday, Dec 10th, 10 p.m. through Sunday, Dec 12th, 5 p.m.
- If you are new to IPA or taking a trial please see: [IPA Trial Resources](#).
- Pave your way to greatness using advanced pathway analysis: [Learn more](#).
- Check out the QIAGEN Digital Insights [publication roundup](#).
- Visit our [blog](#) and sign up for our newsletter.
- Search Google Scholar for [publications that cite IPA](#).
- [Watch a webinar](#) about the new (and free!) [Coronavirus Network Explorer](#) web app built by the QIAGEN Digital Insights team in part using Machine Learning. The same networks are also available in IPA. Look in the lower portion of the IPA Project Manager for a folder called "QIAGEN Coronavirus Networks".
- See the latest IPA news on [LinkedIn](#) or [Twitter](#).

Don't Show at Startup

Quick Start:
IPA操作指导
新任务快捷入口

软件打开界面——搜索框

The screenshot displays the IPA software interface. At the top, there are three search tabs: "Genes and Chemicals", "Diseases and Functions", and "Pathways and Tox Lists". Below these tabs is a search input field with the placeholder text "Enter gene names/symbols/IDs or chemical/drug names here", a "Search" button, and an "Advanced Search" link. A "Project Manager" sidebar is visible on the left, showing a tree view of projects and libraries. A "Quick Start" window is open in the foreground, containing various links and information. A red box highlights the search area, and a red arrow points from the text box to the search input field.

**搜索框：
基因与化合物
疾病和功能
通路和毒理列表
三个搜索框，不能互混**

基因搜索

- EPOR是什么，其分子类型，表达位置，分子功能，参与通路等基本信息有哪些？与它相互作用的分子有哪些？上游有哪些对它进行调控的分子？在它的上游有什么可以对它进行激活的激活因子？

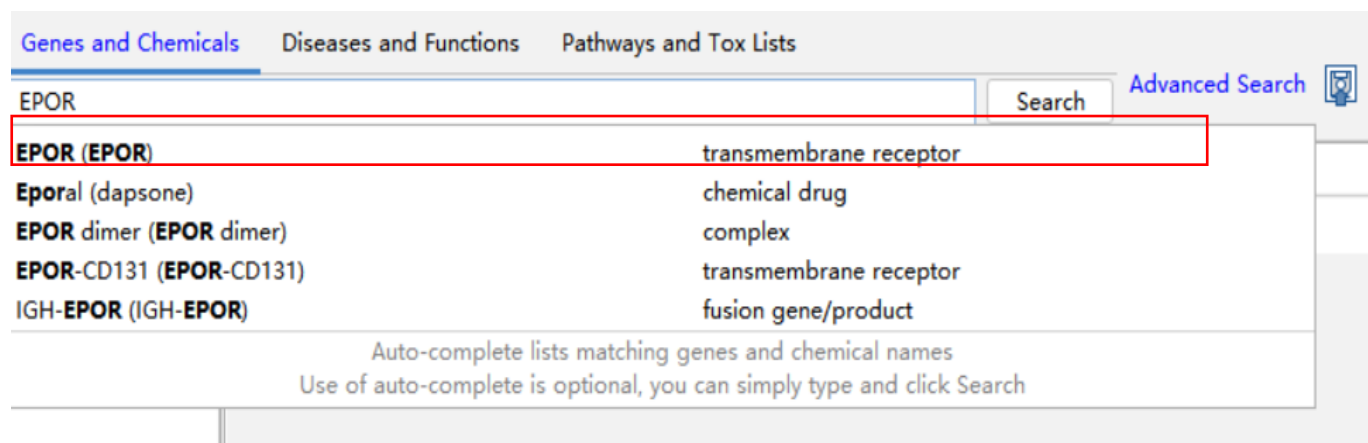
靶标基因与已知药物关系

- 靶标基因HDAC
- 药物TamiFlu作用信息
- TamiFlu与靶标基因HDAC是否有作用关系

疾病与功能基因搜索 (BioProfiler)

- 研究发现了与两千多个与肺癌相关的基因，其中哪些基因与肺癌生长和发展有关？

EPOR是什么，其分子类型，表达位置，分子功能，参与通路等基本信息有哪些？与它相互作用的分子有哪些？上游有哪些对它进行调控的分子？在它的上游有什么可以对它进行激活的激活因子？



IPA 搜索功能——举例 EPOR 基因 源资科技

Search

Add To My Pathway | Add To My List | Create Dataset | BioProfiler | Interaction Network | Activity Plot

The search for EPOR matched 5 items.

<input type="checkbox"/>	Symbol	Matched Term	Synonym(s)	Entrez Gene Name	Location	Type(s)	Biomarker Applic	Drug(s)	Target(s)	Species
<input type="checkbox"/> 1	EPOR	EPOR, Epor	EPO receptor, erythropoietin receptor	erythropoietin receptor	Plasma Mem	transmembr		EPO/filgrastim, peginesatide, EPO, epoetin beta, EPO/sargramosti darbepoetin alfa, epoetin zeta, darbepoetin alfa, continuous eryth erythropoietin/le		Human, Mouse, Rat
<input type="checkbox"/> 2	dapsone	Eporal	4-(4-aminophenyl)sulfor 4-(4-aminophenyl)sulph 4,4'-diaminodiphenyl su 4,4'-diaminodiphenyl su 4,4'-diaminophenyl sulfc 4,4'-diaminophenyl sulp 80-08-0, Aczone, aniline, 4,4'-sulfonyldi- aniline, 4,4'-sulphonyldi- Araldite Ht, Avlosulfon, Avlosulfone, Avlosulphone, benzenamine, 4,4'-sulfo		Other	chemical dr			DHPS	

IPA Gene View: EPOR (Mammalian)

[Contact Support](#) | [Help Documentation](#)

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

[Summary](#) [Human](#) [Mouse](#) [Rat](#)

Member Of: EPOR-CD131, EPOR dimer, IGH-EPOR

Entrez Gene Name: erythropoietin receptor

Synonym(s): EPO receptor, erythropoietin receptor

NCBI CDD Domains (Superfamilies / Multi-Domains): [Fibronectin type 3 domain, FN3](#)

Protein Functions / Functional Domains: Box I domain, Box II domain, cytoplasmic domain, dimerization domain, ectodomain, erythropoietin receptor, extracellular domain, identical protein binding, intracellular domain, Jak2 binding domain, negative regulatory domain, phosphotyrosine motif, PI3K binding domain, protein binding, Shp1 binding domain, Sh Ptp1 binding domain, signaling domain, Src-homology 2 binding domain, Stat5 binding domain, transmembrane/cytoplasmic domain, transmembrane domain, transmembrane receptor, tyrosine phosphorylation site, YXXP domain

Subcellular Location: cell surface, cellular membrane, Cytoplasm, dendrites, Endoplasmic Reticulum, intracellular space, membrane fraction, nuclear speckles, perikaryon, plasma, Plasma Membrane, plasma membrane extracellular face, presynaptic terminals, rod inner segments

Canonical Pathway: Erythropoietin Signaling Pathway; Role of JAK2 in Hormone-like Cytokine Signaling

Targeted By miRNA Functional Cluster: [miR-10400-3p \(and other miRNAs w/seed UGGGCUC\)](#), [miR-1179 \(miRNAs w/seed AGCAUUC\)](#), [miR-1184 \(miRNAs w/seed CUGCAGC\)](#), [miR-1188-3p \(and other miRNAs w/seed GAGGCUC\)](#), [miR-1199-5p \(and other miRNAs w/seed CUGAGCC\)](#), [miR-1200 \(miRNAs w/seed UCCUGAG\)](#), [miR-12185-3p \(and other miRNAs w/seed CAGCCAC\)](#), [miR-12192-5p \(and other miRNAs w/seed GUGGGGU\)](#), [miR-12204-5p \(and other miRNAs w/seed UGAGUCU\)](#), [miR-125b-5p \(and other miRNAs w/seed CCCUGAG\)](#), [miR-1264 \(and other miRNAs w/seed AAGUCUU\)](#), [miR-1284 \(and other miRNAs w/seed CUAUACA\)](#), [miR-1285-3p \(and other miRNAs w/seed CUGGGCA\)](#), [miR-1343-3p \(and other miRNAs w/seed UCCUGGG\)](#), [miR-1587 \(and other miRNAs w/seed UGGGCUG\)](#), [miR-17-2-3p \(and other miRNAs w/seed CUGCACU\)](#), [miR-188-5p \(and other miRNAs w/seed AUCCCUU\)](#), [miR-1896 \(and other miRNAs w/seed GGUGGGU\)](#), [miR-1909-3p \(and other miRNAs w/seed GCAGGGG\)](#), [miR-198 \(miRNAs w/seed GUCCAGA\)](#), [miR-2117 \(miRNAs w/seed GUUCUCU\)](#), [miR-2276-3p \(miRNAs w/seed CUGCAAG\)](#), [miR-2392 \(miRNAs w/seed AGGAUGG\)](#), [miR-2681-3p \(miRNAs w/seed AUCAUGG\)](#), [miR-296-3p \(miRNAs w/seed AGGGUUG\)](#), [miR-3064-5p \(and other miRNAs w/seed GGCUGUU\)](#), [miR-3065-3p \(miRNAs w/seed CAGCACC\)](#), [miR-3070-5p \(and other miRNAs w/seed GCCCCUG\)](#), [miR-3083-5p \(and other miRNAs w/seed GGCUGGG\)](#), [miR-3104-5p \(and other miRNAs w/seed AGGGGGC\)](#), [miR-3127-5p \(miRNAs w/seed UCAGGGC\)](#), [miR-3160-3p \(miRNAs w/seed GAGCUGA\)](#), [miR-3179 \(miRNAs w/seed GAAGGGG\)](#), [miR-3199 \(and other miRNAs w/seed GGGACUG\)](#), [miR-324-3p \(and other miRNAs w/seed CACUGCC\)](#), [miR-324-3p \(miRNAs w/seed CCACUGC\)](#), [miR-328-5p \(and other miRNAs w/seed GGGGGGC\)](#), [miR-342-5p \(and other miRNAs w/seed GGGGUGC\)](#), [miR-3473h-5p \(and other miRNAs w/seed AGGGGCU\)](#), [miR-3594-5p \(and other miRNAs w/seed CCAGGGC\)](#), [miR-3605-3p \(miRNAs w/seed CUCCGUG\)](#), [miR-361-3p \(miRNAs w/seed CCCCCAG\)](#), [miR-3614-3p](#)

Top findings from Ingenuity Knowledge Base (show all 3727 categorized literature findings)

regulates: JAK2, STAT3, STAT5a/b, STAT5A, EPOR, ERK1/2, PIM1, JAK1, STAT5B, STAT1, AKT1, BCL2L1, LYN, SHC1, CSN2

regulated by: EPO, KITLG, EPOR, JAK2, beta-estradiol, GATA1, ESR1, lenalidomide, CSF2, darbepoetin alfa, TFR2, Gp55, HIPK2, trans-hydroxytamoxifen, megakaryocytes

binds: EPO, JAK2, CISH, PIK3R1, PTPN6, SOCS2, STAT5A, GRB2, SOCS3, CRKL, SYK, LYN, CSF2RB, STAT5a/b, PLCG2

role in cell: proliferation, growth, differentiation, apoptosis, development, number, tyrosine phosphorylation in, phosphorylation in, mitogenesis in, survival

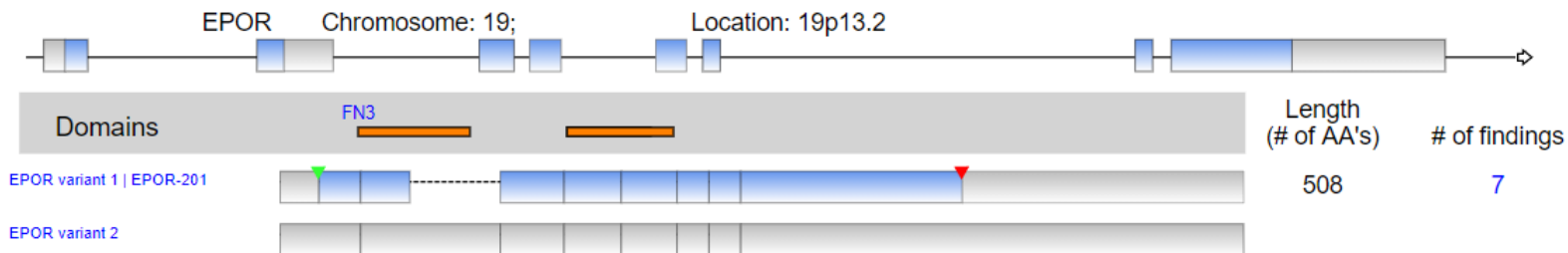
disease: erythrocytosis, anemia, chronic kidney disease, chemotherapy-induced anemia, chronic renal failure, myelodysplastic syndrome, chronic hepatitis C, polycythemia, stage V chronic kidney disease, renal failure, stage III chronic kidney disease, lymphoma, venous thrombosis, solid tumor, delayed graft function, hip fracture, hypoxic-ischemic encephalopathy, acute mountain sickness, fatigue, optic neuritis, end stage renal disease, thoracic aortic dissection, lower-risk myelodysplastic syndrome, cancer anemia, zidovudine induced anemia, hemolytic uremic syndrome, stage IV chronic kidney disease, traumatic brain injury, plasma cell myeloma, out of hospital cardiac arrest, myelodysplastic syndrome with ring sideroblasts, preterm birth, refractory anemia, non-myeloid cancer, congestive heart failure, neonatal anemia, chronic renal impairment, cognitive impairment, chronic myelomonocytic leukemia, refractory anemia with excess blasts, renal anemia, short-term memory impairment, acute myocardial infarction, osteoarthritis, HIV infection, left ventricular hypertrophy, diabetic nephropathy, heart failure, kidney disease, renal impairment, secondary hyperparathyroidism, diabetes mellitus, acute kidney injury, unclassifiable myelodysplastic syndrome, myelodysplastic syndrome with multilineage dysplasia, hypoplasia, leukemia, ventricular dysfunction, hypoplastic anemia, chronic obstructive pulmonary disease, cardiovascular disorder, acute renal failure, contrast induced nephropathy, familial erythrocytosis, cerebral malaria, edema, neoplasia, mature T-cell neoplasia, peripheral T-cell lymphoma, endometriosis, infection, Philadelphia-like B-lymphoblastic leukemia/lymphoma, global developmental delay, neoplastic cell transformation, Philadelphia-like acute lymphoblastic leukemia, benign erythrocytosis, neurodegeneration, natural killer cell neoplasia, T-cell non-Hodgkin disease, natural killer/T-cell lymphoma, primary familial congenital polycythemia, Philadelphia-like B-cell acute lymphoblastic leukemia, familial polycythemia

EPOR 其他信息

Human **Isoforms From** RefSeq

View GTEx human tissue expression (Land Explorer)

More Info



Descriptions from External Databases

Entrez Gene Summary: This gene encodes the erythropoietin receptor which is a member of the cytokine receptor family. Upon erythropoietin binding, this receptor activates Jak2 tyrosine kinase which activates different intracellular pathways including: Ras/MAP kinase, phosphatidylinositol 3-kinase and STAT transcription factors. The stimulated erythropoietin receptor appears to have a role in erythroid cell survival. Defects in the erythropoietin receptor may produce erythroleukemia and familial erythrocytosis. Dysregulation of this gene may affect the growth of certain tumors. Alternate splicing results in multiple transcript variants.[provided by RefSeq, May 2010]

GO Annotations

- Molecular Function:** cytokine receptor activity; erythropoietin receptor activity; identical protein binding; protein binding; transmembrane signaling receptor activity
- Biological Process:** aging; brain development; cardiac muscle tissue morphogenesis; decidualization; elevation of cytosolic calcium ion concentration; embryo development; erythropoietin-mediated signaling pathway; heart development; heart morphogenesis; negative regulation of neuron apoptotic process; negative regulation of nitric oxide biosynthetic process; positive regulation of cell proliferation; positive regulation of ERK1 and ERK2 cascade; positive regulation of neuron projection development; positive regulation of phosphatidylinositol 3-kinase cascade; positive regulation of Ras protein signal transduction; response to hypoxia; signal transduction; vasculogenesis involved in coronary vascular morphogenesis; ventricular cardiac muscle tissue morphogenesis; viral reproduction; visceral serous pericardium development
- Cellular Component:** cytoplasm; external side of plasma membrane; extracellular region; integral to membrane; integral to plasma membrane; membrane; nuclear speck; plasma membrane

Drug Information

Targeting Drug	Drug Brand Name(s)	Action
darbepoetin alfa/filgrastim		agonist, stimulator
EPO/filgrastim		stimulator, agonist
EPO/sargramostim		agonist, stimulator
erythropoietin/lenalidomide		binder, agonist
EPO	Abseamed; Binocrit; E.P.O.; Epogen; Epogen/Procrit; Eprex; Erythropoietin; Procrit; Retacrit	binder, stimulator, agonist
darbepoetin alfa	Aranesp; Aranest; Nesp	agonist, stimulator
continuous erythropoietin receptor activator	Mircera	activator
epoetin beta	NeoRecormon; Recormon	binder
peginesatide	Omontys; Omontys Preservative Free	stimulator
epoetin zeta	Silapo	binder

与EPOR相关的信息总结 (Findings)

3727 Categorized Literature Findings (show details)

3727 Categorized Literature Findings (hide details)

Functional Roles | Mutant Information | Modifications and Regulation | Disease | Expression and Localization | Physical Interactions | Toxicology | Additional Findings | Isoform Specific Findings

Functional Roles

Molecular Processes

activation of (100) A2M, AKT, TYK2

expression of (55) BCL2L1, C, STAT5a/b,

tyrosine phosphorylation of (44) EES, INPP

NIH National Library of Medicine
National Center for Biotechnology Information

Log in

STAT1, STAT2, STAT3, STAT5A, STAT5B, STAT5a/b,

TYC, OAS2, PIM1, SIGLEC1, SLC40A1, SOCS1, SOCS3,

PubMed.gov

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Findings: Functional Roles

Review the information that supports the gene-to-f

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<< Previous 20 | Next 20 >> Show Findings 1 - 20

Findings 1 - 20 of 100

In Cho cells, mutant **EPOR protein** (deletion 469-475) d

Experiment Type: immunoblot

12538595

Guillard C, Chré
Chem. 2003 Ma

Source: Ingenuity Expert Findings

PRL protein in cell culture **causes little or no change i**
protein fragment (substitution Y401F;Y429F;Y431F;Y4

Experiment Type: anti-phosphores

16407271

Um M, Lodish H
Jan 4.

Source: Ingenuity Expert Findings

In Cho cells, mutant **EPOR protein** (deletion 469-475) d

Experiment Type: immunoblot

12538595

Guillard C, Chré
Chem. 2003 Ma

Source: Ingenuity Expert Findings

5.157 点这里更新 > J Biol Chem. 2006 Mar 3;281(9):5648-56. doi: 10.1074/jbc.M510943200.
Epub 2006 Jan 4.

Antiapoptotic effects of erythropoietin in differentiated neuroblastoma SH-SY5Y cells require activation of both the STAT5 and AKT signaling pathways

Moonkyoung Um¹, Harvey F Lodish

Affiliations + expand

PMID: 16407271 DOI: 10.1074/jbc.M510943200

Free article

Abstract

The hematopoietic cytokine erythropoietin (Epo) prevents neuronal death during ischemic events in

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ceptor via a G(i) protein beta gamma-subunit-initiated pathway. J Biol

ient containing a **extracellular domain** from **PRLR protein** and of a mutant
SY5Y cells.

naling pathways. J Biol Chem. 2006 Mar 03;281(9):5648-56. Epub 2006

ceptor via a G(i) protein beta gamma-subunit-initiated pathway. J Biol

IPA Gen
Review t
Summary
NCE
Pr
T

Ingenuity Pathway Analysis

Report Date: 2021-10-20
Report Version:
Content Version: 68752261 (Release Date: 2021-09-06)

Canonical Pathway: **Erythropoietin Signaling Pathway**

Description: Erythropoietin (Epo) elicits cell-specific responses upon interacting with its receptor EpOR. Activation of EpOR by Epo results in receptor homodimerization, which induces a cascade of signaling events. Epo is a major activator of the Ras/MAPK pathway. This activation is achieved via signaling through GRB2, SHC, GAB2 and the PTB domain containing proteins. GRB2 constitutively associates with SOS and binds to EpOR either via an interaction with GAB2 or by binding to EpOR-associated tyrosine-phosphorylated SHC. SHC recruits the GRB2-SOS complex to the plasma membrane, thereby promoting Ras activation. PKC, a potent activator of Ras and c-Raf, plays an important role in the Epo-induced activation of MAPK. Raf1 inhibits the activity of VDAC and functions as an important Anti-apoptotic factor. Activated c-Raf phosphorylates the dual functional protein kinases MEKs, which then phosphorylate and activate ERK/MAPKs. Activated ERKs in turn enhance transcriptional activity of Elk1 and CREB, which regulate the early gene expression in erythroid cells.

Epo activates MAPK through a novel pathway dependent on Gi association to EpOR. Following Epo stimulation, Gi is released from the receptor, resulting in subsequent activation of MAPKs. The tyrosine kinase JAK2 contributes to this pathway by acting downstream of GNB-y and upstream of Ras and PI3K. Epo signaling also activates the Ras/MAPK/ERK pathway by the use of a third group of interacting partners other than the SHC/GRB2/SOS complex or the Gi proteins. The adaptor protein CrkL, interacts with and recruits C3G to the activated EpOR. C3G independently initiates Epo-mediated MAPK signaling via the activation of Ras. Activated Ras then stimulates the Raf/MEK/ERK signaling cascade leading to the activation of Elk1, which enhances transcriptional activity of immediate early factors c-Fos and c-Jun through the serum response element. CrkL and C3G are also implicated in c-Raf activation via a Ras/PI3K-dependent mechanism involving the activation of Rac.

The transcriptional activation and stability of c-Jun is accomplished by JNK1, CKII and PPTase, whereas in case of c-Fos, ERK phosphorylates c-Fos, resulting in its increased transcriptional activity. PIN1 regulates AP-1-mediated transcription. As a consequence, the mitogenic action of Epo is directly linked to transcriptional regulatory events utilizing Ras as a molecular switch relaying upstream tyrosine kinase signals to a serine/threonine kinase cascade. Active ERKs also activate Cyclin D1, the critical regulator of the cell-cycle clock apparatus directing the G1-S phase progression during the cell cycle.

Activated EpOR ensures its control over this trail via Src tyrosine kinase. JAK2-activated FAK1 activates PI3K in a Syk-dependent manner. Activated PI3K phosphorylates membrane-bound PIP2 to generate PIP3, and PTEN acts as a negative regulator of this phosphorylation event. As a result, PI3K triggers the phosphorylation of Akt via PDK-1. Akt phosphorylates various signaling molecules such as GSK3, BAD and FKHR to promote cell survival. Akt prevents the nuclear translocation of FoxO3a, which inhibits apoptosis. BAD phosphorylation also stimulates certain anti-apoptotic signals that facilitate inhibition of Cytochrome C release and inactivation of caspase 1, 3, 8, and 9. Optimal function of GATA1 is essential for the biological function of Epo, and GATA1 plays a role at a number of steps of the erythroid differentiation program. (Upgraded 07/2020)

Signaling Pathway Categories: Cellular Growth, Proliferation and Development; Growth Factor Signaling

Top Functions & Diseases: Cell Death and Survival; Cell Cycle; Cellular Function and Maintenance

Molecules: 1-phosphatidyl-D-myo-inositol 4,5-bisphosphate, Akt, Angiogenesis, Ap1, APAF1, Apoptosis, BAD, BCL2L1, BIRC2, BIRC3, Ca2+, CDND1, CDND2, Cell cycle progression, Cellular infiltration by granulocytes, CSF2RB, CTNNB1, diacylglycerol, Differentiation of erythroid precursor cells, ELK1, EPO, EPOR, EPOR dimer, EPOR-CD131, ERK1/2, FOS, FOXO3, GATA1, GRB2, Grb2-Src1-Sos, GSK3B, hemoglobin, HIF1, Hypoxia of kidney, Ikb, Ikb-NRk, Inflammation, inositol triphosphate, IRS2, ITPR, JAK2, JUN, MACROH2A2, MAP2K1/2, Maturation of erythroid cells, MDM2, MTOR, Neuroprotection, NFkB (complex), nitric oxide, NOS3

Drug Summary - Overview of drugs targeting molecules in Canonical Pathway
Showing 3 of 656 row(s) of Drug data. (Show All)

Drug Name	Targets	Actions	Brand Names	Indications/Status
1-(3-(1,4-dihydroimidazo[4,5-c]pyrazol-5-yl)-4-methylphenyl)-3-(3-(4-methyl-1H-imidazol-1-yl)-5-(trifluoromethyl)phenyl)urea	RAF1	inhibitor		
1-(5-isouquinolinesulfonyl)piperazine	Pkc(s)	inhibitor		
1-o-hexadecyl-2-o-methyl-rac-glycerol	Pkc(s)	inhibitor		

Target Information - Overview of known drug targets in Canonical Pathway
Showing 3 of 86 row(s) of Target data. (Show All)

Target (Gene Symbol)	Entrez Gene Name	Location	Type	Drug(s)	Species
Akt		Cytoplasm	group	aforesertib, Akt inhibitor XI, AT13148, ipatasertib, MSC2363318A, ONC-201, SR-13668, TAS-117, TASO612	Human, Mouse, Rat
AKT1	AKT serine/threonine kinase 1	Cytoplasm	kinase	A-443654, AKT inhibitor XIII, archexin, ARQ 751, BAY1125976, capivasertib, CCT129524, enzastaurin, GSK690693, ipatasertib, LY2780301, miransertib, MK2206, MPTOE028, perfosine, tricirbine, tricirbine phosphate, uprosertib	Human, Mouse, Rat
AKT2	AKT serine/threonine kinase 2	Cytoplasm	kinase	AKT inhibitor XIII, BAY1125976, CCT129524, enzastaurin, GSK690693, tricirbine, tricirbine phosphate	Human, Mouse, Rat

Supporting References (Show details) - References from which the Canonical Pathway was derived

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Canonical Pathways

Erythropoietin...

Build Overlay Path Designer Pattern Search View: Zoom: Export:

Canonical Pathway

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3'GGG, miR-198 (miRNAs w/seed GUCCAGA), miR-2117 (miRNAs w/seed AUCAUG), miR-296-3p (miRNAs w/seed AGGGUUG), miR-3064-5p (and other miRNAs w/seed GGCUGGG), miR-3104-5p (and other miRNAs w/seed GAAGGGG), miR-3199 (and other miRNAs w/seed GGGACUG), w/seed GGGGGGC), miR-342-5p (and other miRNAs w/seed GGGGUGC), miR-361-3p (miRNAs w/seed CUCCGUG), miR-361-3p (miRNAs w/seed CCCCCAG), miR-3614-3p (miRNAs w/seed CUGGGCU), miR-3921 (and other miRNAs w/seed UAGGGGG)...(more)

源资科技

点击欲构建网络的分子前的方框（可多选），再点击Add to my pathway按钮，在下拉菜单中点击New my pathway新建查询网络

The screenshot shows a software interface with a search bar at the top. Below it, a table lists search results for 'EPOR'. The first result is 'EPOR' with a checked checkbox. A red arrow points from the text box to this checkbox. Another red arrow points from the text box to the 'Add To My Pathway' button. Below the search results, there is a 'My Pathways' section with a toolbar containing 'Build', 'Overlay', 'Path Designer', and 'Pattern Search' buttons. A red arrow points from the text box to the 'Build' button. A large blue arrow points from the search results area towards the 'Build' button. In the bottom right, there is a diagram showing the text 'EPOR' inside a blue oval.

Symbol	Matched Term	Synonym(s)
<input checked="" type="checkbox"/> 1	EPOR	EPOR, Epor
<input type="checkbox"/> 2	dapsone	Eporal

My Pathways

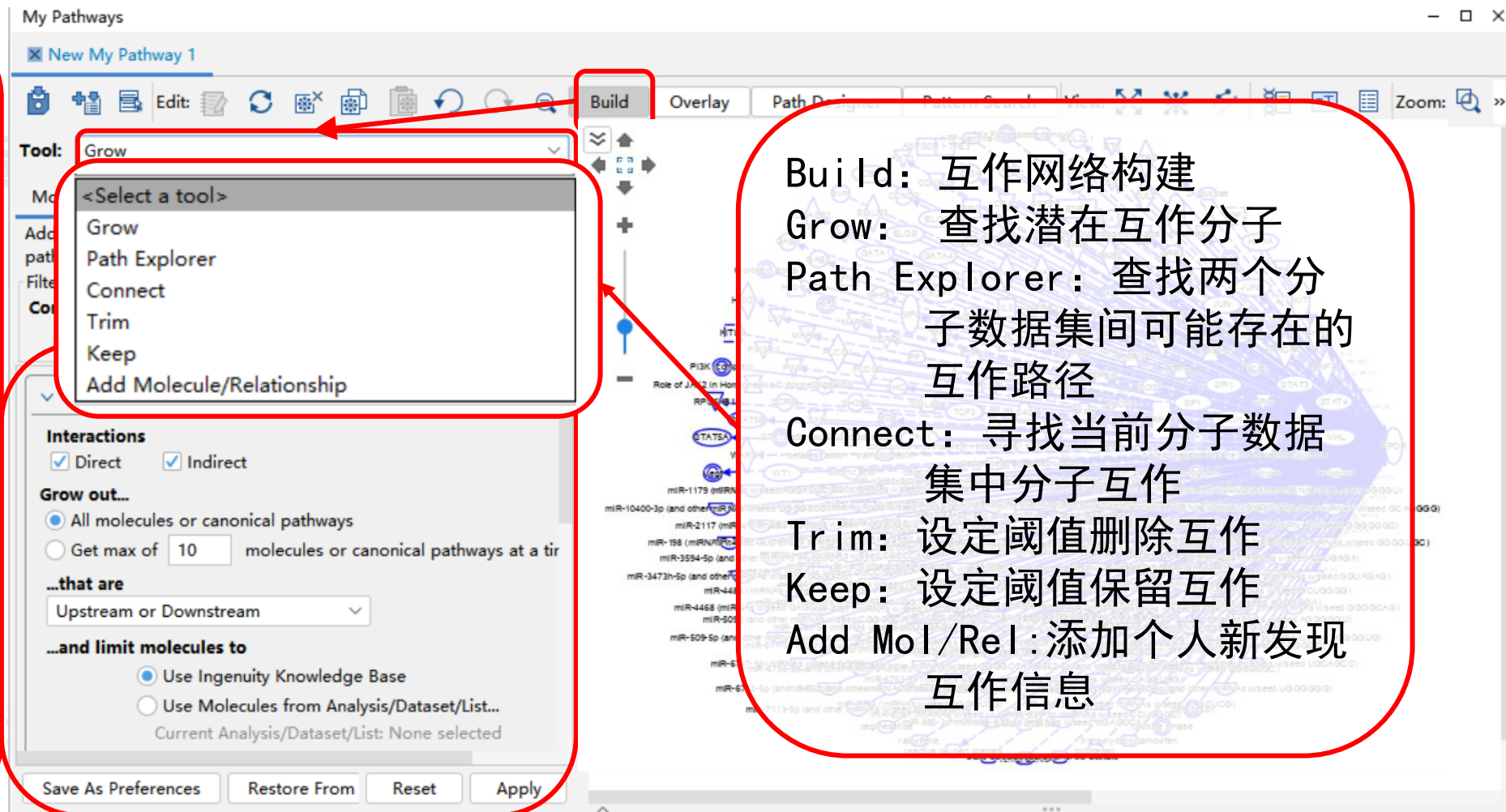
Build Overlay Path Designer Pattern Search View: [Full Screen]

EPOR

Build: 互作网络生长工具
Overlay: 功能、通路、药物等关联
Path Designer: 个性化绘图工具

通过Build构建分子互作网络：

采用Grow即可寻找与EPOR直接或间接相互作用的10个分子，也可以设定过滤参数，得到最合适的分子网络。过滤参数包括：查询数量限制；数据库；互作置信度；物种；器官组织；突变；互作类型；互作实验时限；互作分子类型等



Build: 互作网络构建
Grow: 查找潜在互作分子
Path Explorer: 查找两个分子数据集间可能存在的互作路径
Connect: 寻找当前分子数据集中分子互作
Trim: 设定阈值删除互作
Keep: 设定阈值保留互作
Add Mol/Rel: 添加个人新发现互作信息

如果双击分子与分子之间的连接线，则能看到分子间相互作用的总结，点击上方链接既可以打开IPA内部的findings

The screenshot displays the Ingenuity Pathway Analysis (IPA) software interface. At the top, a network diagram shows several nodes connected by lines. The nodes include NOSIP (continuous erythropoietin receptor activator), EPOR dimer, darbepoetin alfa, JAK, PTPRB, and SH2B2. A red box highlights a link between SH2B2 and EPOR, with an arrow pointing to a 'View relationships between: SH2B2|EPOR' button. Below this, a 'Relationship Summary' window is open, showing the text 'Click Add Relationship to create a custom relationship.' and an 'ADD RELATIONSHIP' button. A larger window titled 'IPA Relationships: SH2B2|EPOR' is open, providing detailed information about the relationship. It includes a 'PlainText' dropdown and an 'Export references' checkbox. Under the 'Ingenuity Relationships' section, two protein-protein interactions are listed:

- Binding of EPO R protein** in plasma membrane and **APS [SH2B2] protein** in cytoplasm occurs. ID: 10374881. Source: Ingenuity Expert Findings. Reference: Wakioka T, Sasaki A, Mitsui K, Yokouchi M, Inoue A, Komiya S, Yoshimura A. APS, an adaptor protein containing Pleckstrin homology (PH) and Src homology-2 (SH2) domains inhibits the JAK-STAT pathway in collaboration with c-Cbl. Leukemia. 1999 May;13(5):760-7.
- Binding of human EPOR protein** and **human SH2B2 protein** occurs. ID: 10374881. Source: BioGRID. Reference: Wakioka T, Sasaki A, Mitsui K, Yokouchi M, Inoue A, Komiya S, Yoshimura A. APS, an adaptor protein containing Pleckstrin homology (PH) and Src homology-2 (SH2) domains inhibits the JAK-STAT pathway in collaboration with c-Cbl. Leukemia. 1999 May;13(5):760-7.

On the right side, a 'Molecule Summary - SH2B2' window is open, showing details for SH2B2, including its name, symbol, description, synonyms (APS, SH2B adaptor protein 2, SH2B2alpha), and location (Cytoplasm). A 'CANCEL' button is visible at the bottom right of this window.

靶标基因与已知药物关系——举例HDAC基因

TamiFlu与靶标基因HDAC是否有作用关系?

The search for Hdac matches:

Symbol	Matched Term	Synonym(s)	Entrez Gene Name	Location	Type(s)	Biomarker Appli
1 Hdac	Hdac	Histone Deacetylase, Histone deacetyltransferase				



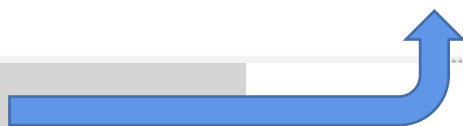
My Pathways

New My Pathway 2

Build Overlay Path Designer

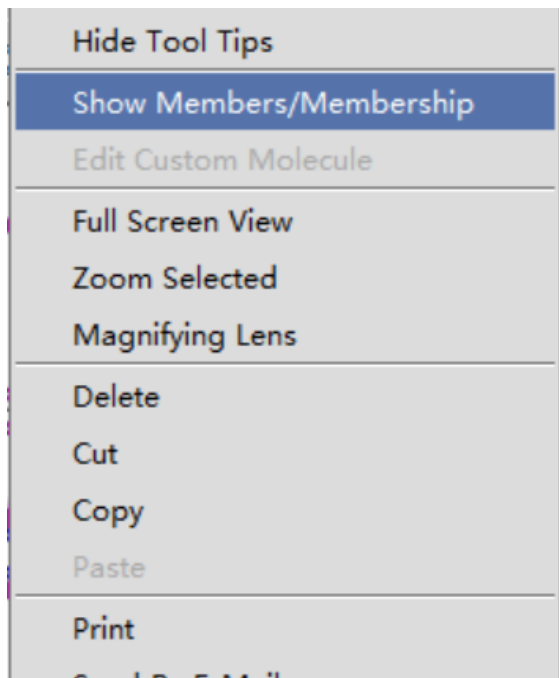
Hdac

oseltamivir



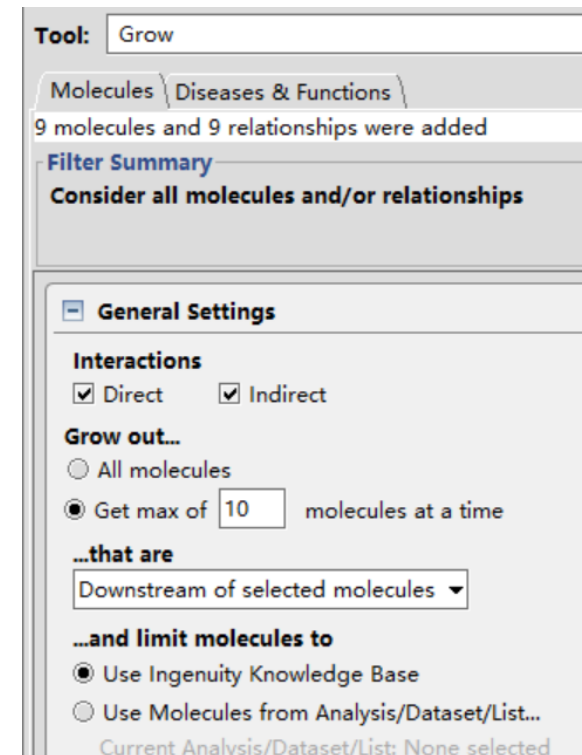
搜索HDAC与TamiFlu, 并且将他们放入同一个My Pathway中。

靶标基因HDAC与已知药物TamiFlu的关系



左键单击
oseltamivir, 选择
Build—Grow工具,
关联性选择
Downstream of
selected
molecules

右键单击HDAC, 点击Show
Members/Membership显示
所有家族分子



靶标基因HDAC与已知药物TamiFlu的关系

My Pathways

New My Pathway 4

Build Overlay Path Designer Pattern Search View: Zoom:

Tool: Path Explorer

27 shortest paths were found.

Filter Summary
Consider all molecules and/or relationships

General Settings

Interactions
 Direct Indirect

Set A
Add Remove
HDAC5
HDAC2
HDAC10

Direction: From Set A to Set B --->

Set B
Add Remove
EGFR
oseltamivir
IL1B

Use Ingenuity Knowledge Base

Save As Preferences Restore From P Reset Apply

Network diagram showing interactions between HDACs (HDAC1, HDAC2, HDAC3, HDAC5, HDAC6, HDAC10) and other molecules (EGFR, TNF, IL1B, IL1A, IL1B, IL1R1, IL1R2, IL1R3, IL1R4, IL1R5, IL1R6, IL1R7, IL1R8, IL1R9, IL1R10, IL1R11, IL1R12, IL1R13, IL1R14, IL1R15, IL1R16, IL1R17, IL1R18, IL1R19, IL1R20, IL1R21, IL1R22, IL1R23, IL1R24, IL1R25, IL1R26, IL1R27, IL1R28, IL1R29, IL1R30, IL1R31, IL1R32, IL1R33, IL1R34, IL1R35, IL1R36, IL1R37, IL1R38, IL1R39, IL1R40, IL1R41, IL1R42, IL1R43, IL1R44, IL1R45, IL1R46, IL1R47, IL1R48, IL1R49, IL1R50, IL1R51, IL1R52, IL1R53, IL1R54, IL1R55, IL1R56, IL1R57, IL1R58, IL1R59, IL1R60, IL1R61, IL1R62, IL1R63, IL1R64, IL1R65, IL1R66, IL1R67, IL1R68, IL1R69, IL1R70, IL1R71, IL1R72, IL1R73, IL1R74, IL1R75, IL1R76, IL1R77, IL1R78, IL1R79, IL1R80, IL1R81, IL1R82, IL1R83, IL1R84, IL1R85, IL1R86, IL1R87, IL1R88, IL1R89, IL1R90, IL1R91, IL1R92, IL1R93, IL1R94, IL1R95, IL1R96, IL1R97, IL1R98, IL1R99, IL1R100). The diagram shows a complex network of interactions, with HDACs at the top and other molecules at the bottom. The interactions are represented by lines of varying colors (purple, red, green, blue) and styles (solid, dashed, dotted).

Add To My Pathway Highlight View Shortest Paths (27) Paths 1 - 27

<input checked="" type="checkbox"/>	Paths	Set A Molecules	Set B Molecules
<input checked="" type="checkbox"/>	1	HDAC6	EGFR
<input checked="" type="checkbox"/>	2	HDAC3	TNF
<input checked="" type="checkbox"/>	3	HDAC4	TNF

靶标基因HDAC与已知药物TamiFlu的关系

My Pathways

× New My Pathway 4

Tool: Grow

Molecules & Canonical Pathways Diseases & Functions

Grow from selected molecules to selected diseases & functions

Indicate diseases or functions related to Any

Consider all functions

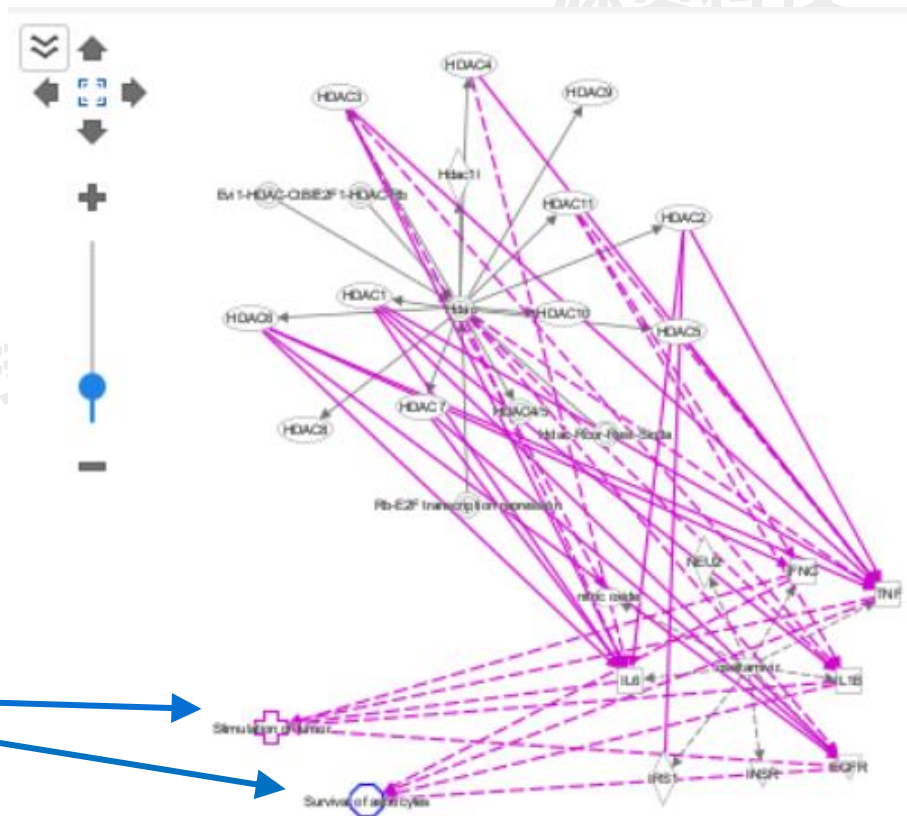
Recalculate

Diseases an...	p-value	Molecules
Synthesis of extracellu	7.60E-10	IL6, IFNG, IL1B, ...all 4
Synthesis of DNA	1.21E-09	EGFR, IFNG, IL... all 9
Synthesis of ATP	8.03E-09	INSR, IRS1, IL6, ...all 6
Swelling of joint	1.05E-08	IL6, IFNG, IL1B, ...all 4
Susceptibility to coron	1.75E-03	IRS1 ...all 1
Survival of organism	8.73E-09	EGFR, IFNG, ... all 12
Survival of astrocytes	3.97E-09	EGFR, IFNG, IL... all 4
Stimulation of tumor	5.32E-09	EGFR, IL6, IFNG, ...all 5
Stimulation of smooth	2.85E-11	IL6, IL1B, IFNG, ...all 4
Stimulation of hepator	3.02E-12	IL6, IL1B, IFNG, ...all 4
Stimulation of airway :	6.87E-10	IL1B, IFNG, TNF ...all 3
Stimulation of	4.00E-02	TNF, IL6 ...all 2

2/476

Reset Apply

全选所有需要聚类分子



靶标基因HDAC与已知药物TamiFlu的关系

My Pathways

× New My Pathway 4

Build

Overlay: MAP (Molecule Activity Predictor)

Clear

You can predict the upstream and downstream effects of activation or inhibition molecules. Begin by overlaying measurement values from a dataset or analysis, specifying activation in silico below.

Predict effect of dataset or in silico changes

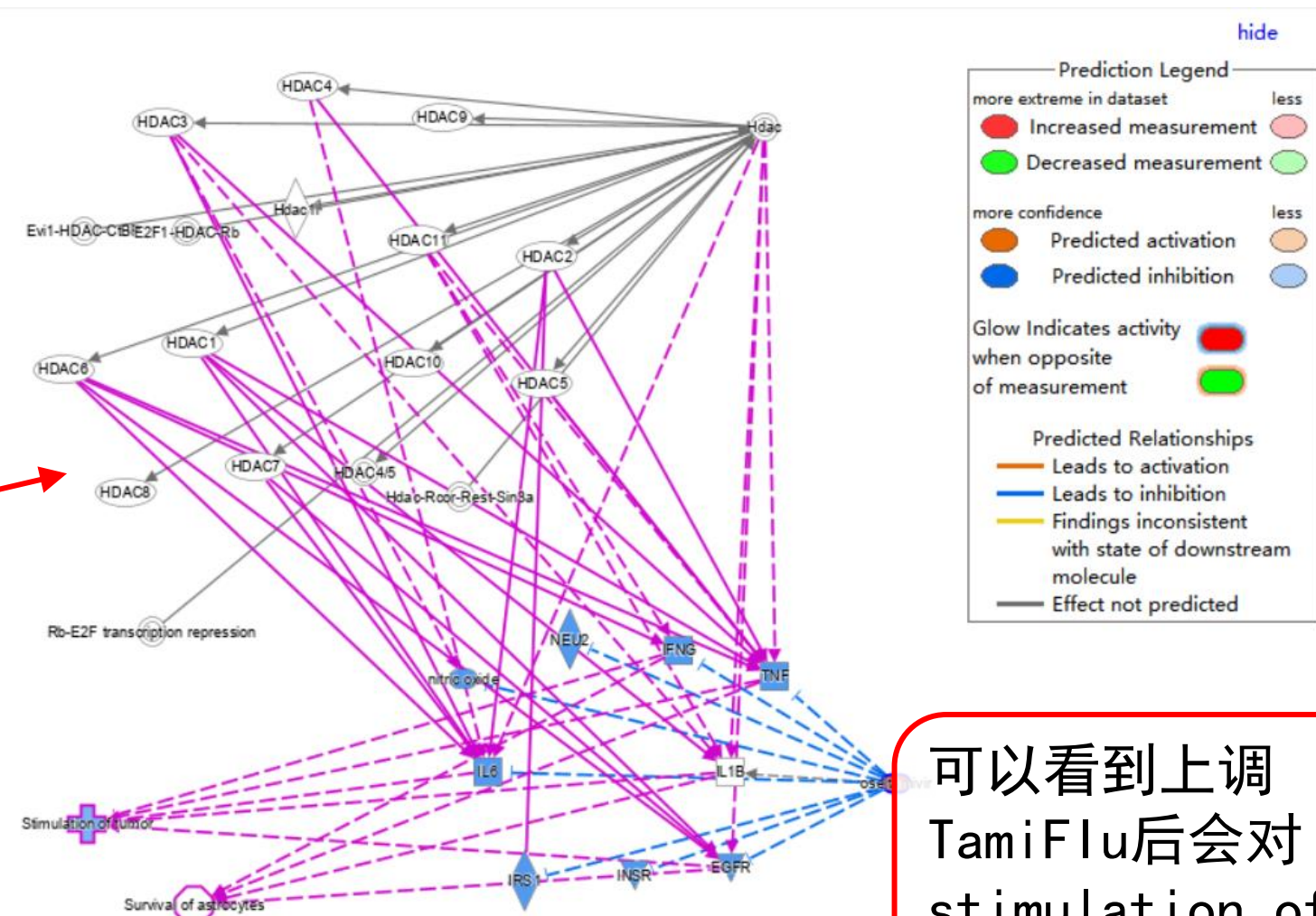
Prediction On Display prediction legend

Predict effects:
Upstream and Downstream

Activate or inhibit molecules interactively in silico
Select the value to apply and then click the molecules you wish to apply them to

Use measurement values from a Dataset or Analysis

点击预测上调或者下调的油漆图标，再点击指定为上调的节点，最后点击Start Prediction进行预测



可以看到上调TamiFlu后会对stimulation of tumor有抑制作用。

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PART

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分子活性预测功能

3

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Overlay—MAP (Molecule Activity Predictor)

The screenshot displays the MAP software interface. The top toolbar includes options like 'Build', 'Overlay', 'Path Designer', 'Pattern Search', 'View', 'Zoom', and 'Export'. The main window title is 'Overlay: Table S7 Severe and Moderate and Severe and Recovering for - 2021-09-22 05:16 下午, Expr Log Ratio'. The central area shows a complex network diagram with nodes (e.g., RPSA, RPS11, RPS2, MRPL52, NPM1, CYLD, EIF2A) and connecting edges. The left sidebar contains a 'Clear' button and a 'Predict effect of dataset or in silico changes' section with a 'Start Prediction' button and a checked 'Display prediction legend' checkbox. Below this is a 'Predict effects:' dropdown set to 'Upstream and Downstream'. At the bottom left, there are buttons for 'Activate', 'Inhibit', and 'Predict'. A red box highlights the 'Start Prediction' and 'Display prediction legend' controls. Another red box highlights the network diagram.

Predict effect of dataset or in silico changes
Start Prediction Display prediction legend

Predict effects:
Upstream and Downstream

选定某个分子，设定其为激活或者抑制状态，于此同时预测该分子上下游分子的激活或者抑制状态。

根据network中关键分子的表达变化，预测网络中其他分子的抑制或激活。

Overlay—MAP (Molecule Activity Predictor)

Canonical Pathways

Apoptosis Signaling

Build Overlay Path Designer View: Zoom: Export:

Overlay: MAP (Molecule Activity Predictor)

Clear

You can predict the upstream and downstream effects of activation or inhibition on other molecules. Begin by overlaying measurement values from a dataset or analysis, or interactively specifying activation in silico below.

Predict effect of dataset or in silico changes

Prediction On Display prediction legend

Predict effects: Upstream and Downstream

Activate or inhibit molecules interactively in silico

Select the value to apply and then click the molecules you wish to apply them to.

Use measurement values from a Dataset or Analysis

Current Analysis/Dataset/List: None selected

[Change Analysis/Dataset/List](#)

You can view the expected activation state for a canonical pathway. Toggle the expected state on and off to view the differences between it and your measurement values.

Canonical pathway activation

Color by expected activation state (press 'a' on keyboard to toggle)

Apoptosis Signaling

show legend

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Biotech

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Pathway构建

4

源资科技

源资科技

My Pathway是什么？

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源资科技

- 创建个性化通路
- 界面友好，易操作
- 功能强大，灵活
- 不受固有的经典通路限制

源资科技

源资科技

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The screenshot displays the IPA software interface. The main window shows a network diagram with nodes and edges, and a table of results. A 'Lists' dialog box is open, allowing the user to create a new list named 'test'. The dialog includes fields for 'List Name' and 'Notes', and a list of selected molecules: APCS, ARG1, C3, C1S, and CCL2. A context menu is also visible, showing options like 'Add to', 'Send to', 'Run Core Analysis', 'Run Functional Analysis', and 'Run BioProfiler'. The 'New My Pathway' option is highlighted in the 'Add to' submenu.

Lists Dialog Box:

- List Name: test
- Notes: [Empty field]
- Selected Molecules: APCS, ARG1, C3, C1S, CCL2
- Selected/Total molecules : 0/35

Context Menu:

- Add to
 - New My Pathway
 - Saved Pathway...
- Send to
- Run Core Analysis
- Run Functional Analysis
- Run BioProfiler

My Pathways

FASN Pathway

Build Overlay Path Designer Pattern Search View: Zoom: Export:

Path Designer

Path Designe...

Build Overlay View: Zoom: Export:

Molecules Relationship Line Text Cell Art Legend Background Edit Tool

Dialog 12 B I U

Overlay: <Select a tool>

<Select a tool>

Analyses, Datasets

MAP (Molecule Ac

Drug

Disease & Functio

My List

Canonical Pathway

My Pathway

Ingenuity Tox List

Biomarkers

Highlight

ENTDP5 NAGLU GNA11 CD244 ARG1 LYZ

Mup1 (includes others) Osm1 (includes others) C3

C1S CTSV ERAP1 HP LGMN

NFE2L2 NLRC5 PPARA PPARG PDCD1

Path Designer 中的多种工具，可以美化之前的通路。

哪些分子
他分子
药物相
al

Build—Grow—Molecular

My Pathways

× FASN Pathway

Build

Tool: Grow

Molecules & Canonical Pathways Diseases & Functions

Add and connect new nodes to the nodes that you select on the pathway. Click Apply to view the new network.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

Direct Indirect

Grow out...

All molecules or canonical pathways

Get max of molecules or canonical pathways at a time

...that are

Upstream or Downstream

...and limit molecules to

Use Ingenuity Knowledge Base

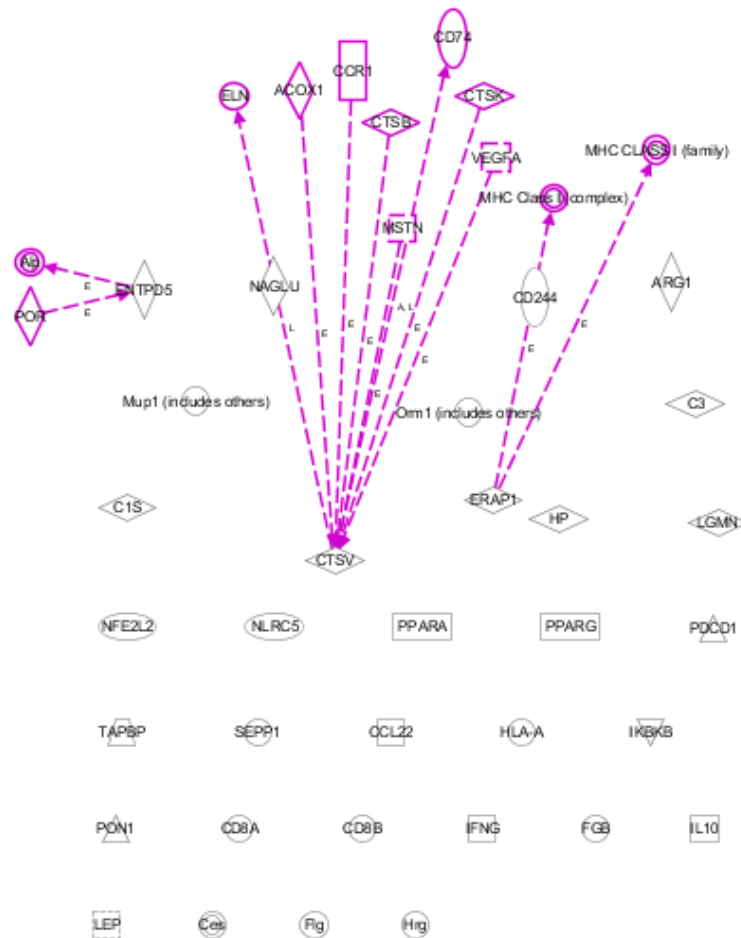
Use Molecules from Analysis/Dataset/List...

Current Analysis/Dataset/List: None selected

Change Analysis/Dataset/List

> Data Sources All

Save As Preferences Restore From Prefs Reset Apply



选择My Pathway 中一个或多个感兴趣的分子，通过Grow 工具找出与此分子相互作用的其他分子。可以设定相互作用分子数，分子来源，相互作用关系类型等参数来达到最优的结果。

Build—**Grow**—Disease & Functions

My Pathways

× FASN Pathway

Edit: [Icons] Build Overlay Path Designer Pattern Search View:

Tool: Grow

Molecules & Canonical Pathways Diseases & Functions

Grow from selected molecules to selected diseases & functions

Indicate diseases or functions related to Any of the selected molecules

Consider all functions

Recalculate

Diseases and Functi...	p-value	Molecules
Volume of prostate cancer c	2.65E-05	FASN ...all 1
Repair of pancreatic cancer	2.65E-05	FASN ...all 1
Conventional nevus	2.65E-05	FASN ...all 1
Onset of myelination of axo	5.30E-05	FASN ...all 1
Conversion of malonyl-coer	5.30E-05	FASN ...all 1
Synthesis of malonyl-coenz	1.06E-04	FASN ...all 1

Grow 中的Disease & Functions 功能可以构建所选分子与疾病间的关系。选中一个或多个分子，左侧高亮显示了该分子所参与的疾病。如果想知道选中的多个分子共同参与的疾病，可以将“Any”改成“All”。选中疾病，当点击“Apply”后，疾病就会关联到所选择的分子上。也可以通过“Filter”工具来聚焦想关注的疾病或分子。

Build—Connect

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My Pathways

FASN Pathway

Build Overlay Path Designer Pattern Search View: Zoom:

Tool: Connect

Connect selected molecules based on specified criteria. Click Apply to view new connections.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

Direct Indirect

Data Sources All

Confidence Level All

Species All

Tissues & Cell Lines All

Mutation All

Relationship Types All

Publication Date Range All

Node Types All

FASN

可以选择My Pathway 中两个或多个感兴趣的分子，通过connect工具找出这些分子间的相互关系。可以设定直接与间接作用关系，分子来源，相互作用关系类型等参数来达到最优的结果。

Build——Path Explorer

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两个/组分子间作用的最短路径。

The screenshot displays the Path Explorer software interface. The main window shows a network diagram with a central node 'Hdac' and several peripheral nodes including HDAC1, HDAC2, HDAC3, HDAC4, HDAC5, HDAC6, HDAC7, HDAC8, HDAC9, HDAC10, HDAC11, HDAC4/5, HDac-Roor-Rest-Sin3a, and Rb-E2F transcription repression. Three nodes on the left (Evi1-HDAC-CtB, E2F1-HDAC, and Rb) are highlighted with blue circles and connected to the central HDac node by blue arrows.

Below the diagram is a table titled 'Shortest Paths (11)'. The table has columns for 'Paths', 'Set A Molecules', and 'Node 1'. The first six rows are highlighted in blue.

Paths	Set A Molecules	Node 1
1	CCL22	Tnf
2	CCL22	CCR4
3	SEPP1	heparin
4	CCL22	CCL3L3
5	CCL22	TAC1
6	CCL22	Ca2+

Build——Add Molecular/Relationship

Tool: Add Molecule/Relationship

Select a molecule or relationship type then click the pathway to add it.

Molecule Types:
Select a molecule type, then click the pathway to add the molecule selected.

- ligand-dependent nuclear receptor
- mature microRNA
- microRNA
- peptidase
- phosphatase
- transcription factor
- translation factor
- transmembrane receptor
- transporter
- other

选定分子类型，在右侧空白处双击，即出现该分子图标。

如果不知道分子的类型，可以直接点other

Create/Edit Nodes

Genes & Chemicals

FASN Search

7 matches found for "FASN".

mitochondrial, 4933425A18RIK, C80494, CEM1, FASN2D, FLJ20604, KASI, KS, LOC498451, RGD1311092
Location: Cytoplasm
Family: kinase

TVB-2640 [Select]
Synonyms: 4-[1-[4-cyclobutyl-2-methyl-5-(5-methyl-1H-1,2,4-triazol-3-yl)benzoyl]piperidin-4-yl]benzotrile, 1399177-37-7, C27H29N5O, FASN inhibitor TVB-2640
Location: Other
Family: chemical drug

Node Settings

Name:

Family: chemical - protease inhibitor

Location: Other

Drug Target: Yes No

Description:
(max 4000 chars)

Save As: Custom Node

OK Cancel



双击分子图标，即可弹出分子注释对话框，搜索想要插入的分子名，找到需要的分子，点击select，分子及类型会自动编辑好。

Overlay——Analyses, Dataset & Lists

显示My Pathway中哪些分子在某个特定的network中出现，并且以不同的颜色标记这些分子表达的变化以及表达量。

Overlay: Analyses, Datasets & Lists

Clear Ignore Analysis Cutoff

Overlay datasets, analyses and lists

Index	Name (select to overlay)
	Please add a dataset, analysis or list.

▲ ▼ Add... Remove select

Matching molecules

Symbol	Display name
--------	--------------

Show node charts for multi overlay: Always For rows selected above Don't show

Graph overlay options

- 选择一组或多组观察值的分析结果。
- 在分析结果中的出现的分子会高亮显示
- 显示表达值，表达量与bar图表示。红色为上调，绿色为下调。

Overlay——Disease & Function

Overlay: Disease & Function

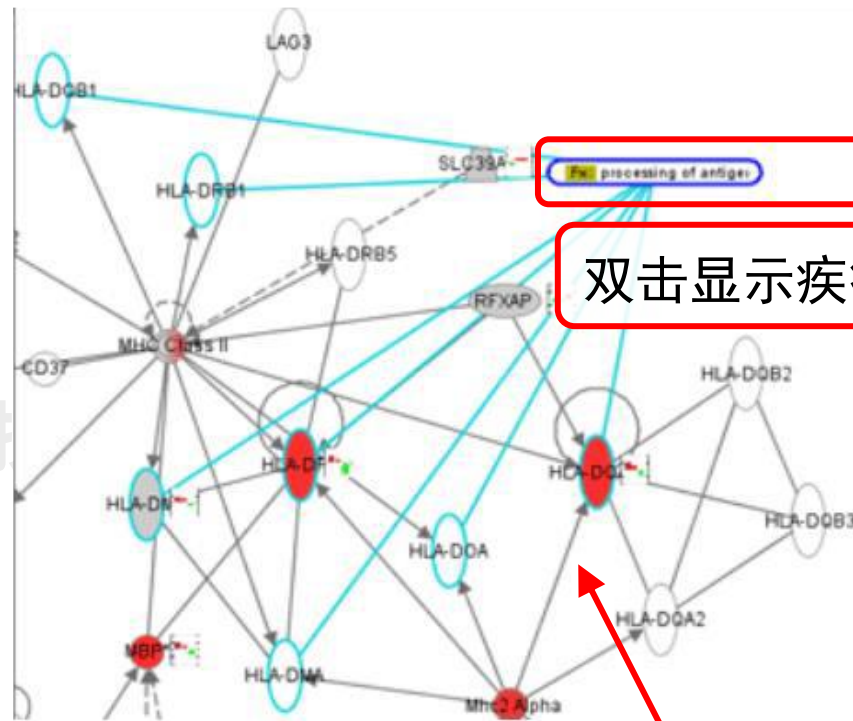
Functions Show Functions

Diseases and Functions	p-value /	# Molecules
<input type="checkbox"/> Relevant Diseases and Biological Func		22
<input type="checkbox"/> Cancer	2.32E-26 - 2...	Click to specify sort
<input checked="" type="checkbox"/> Hematological Disease	2.32E-26 - 3...	20
<input type="checkbox"/> Immunological Disease	2.32E-26 - 4...	20
<input type="checkbox"/> Organismal Injury and Abnormalitie	2.32E-26 - 6...	22
<input type="checkbox"/> Post-Translational Modification	1.37E-22 - 1...	9
<input type="checkbox"/> Cellular Development	1.11E-22 - 1...	11
<input type="checkbox"/> Connective Tissue Development	1.11E-22 - 1...	11
<input type="checkbox"/> Tissue Development	1.11E-22 - 1...	11
<input type="checkbox"/> Cell Cycle	1.11E-22 - 1...	11
<input type="checkbox"/> Cellular Assembly and Organization	2E-17 - 6.2E-9	17
<input type="checkbox"/> Cellular Function and Maintenance	2E-17 - 6.39...	20
<input type="checkbox"/> DNA Replication, Recombination, ar	2E-17 - 1.72...	17
<input type="checkbox"/> Cell Death and Survival	9.42E-16 - 1...	20
<input type="checkbox"/> Gene Expression	1.65E-15 - 6...	19
<input type="checkbox"/> Infectious Diseases	8.32E-15 - 3...	16
<input type="checkbox"/> Cellular Growth and Proliferation	6.17E-14 - 2...	19
<input type="checkbox"/> Embryonic Development	7.72E-14 - 1...	17
<input type="checkbox"/> Organismal Development	7.72E-14 - 2...	17
<input type="checkbox"/> Tissue Morphology	1.39E-13 - 2...	17
<input type="checkbox"/> Cardiovascular System Developmer	2.55E-13 - 2...	14
<input type="checkbox"/> Organ Morphology	2.55E-13 - 2...	14
<input type="checkbox"/> Organ Development	3.16E-13 - 6...	15

Looking for labels? Use [Grow to Disease & Function](#) instead

选中某个疾病过程，右侧显示网络中参与的分子。

显示网络或通路中参与的疾病。



双击作用关系，显示相关文献

Overlay——My Pathway、My list & Toxlist

Overlay: My List REFRESH

Select list labels from table to be displayed on pathway.

<input type="checkbox"/>	List Name	# Mole...	Molecule(s)
<input type="checkbox"/>	test	35	APCS, ARG1, C3, C1S*, CCL22, C...
<input type="checkbox"/>	stat	8	ARG1, C3, FGB, HP, IFNG, IL10, I...

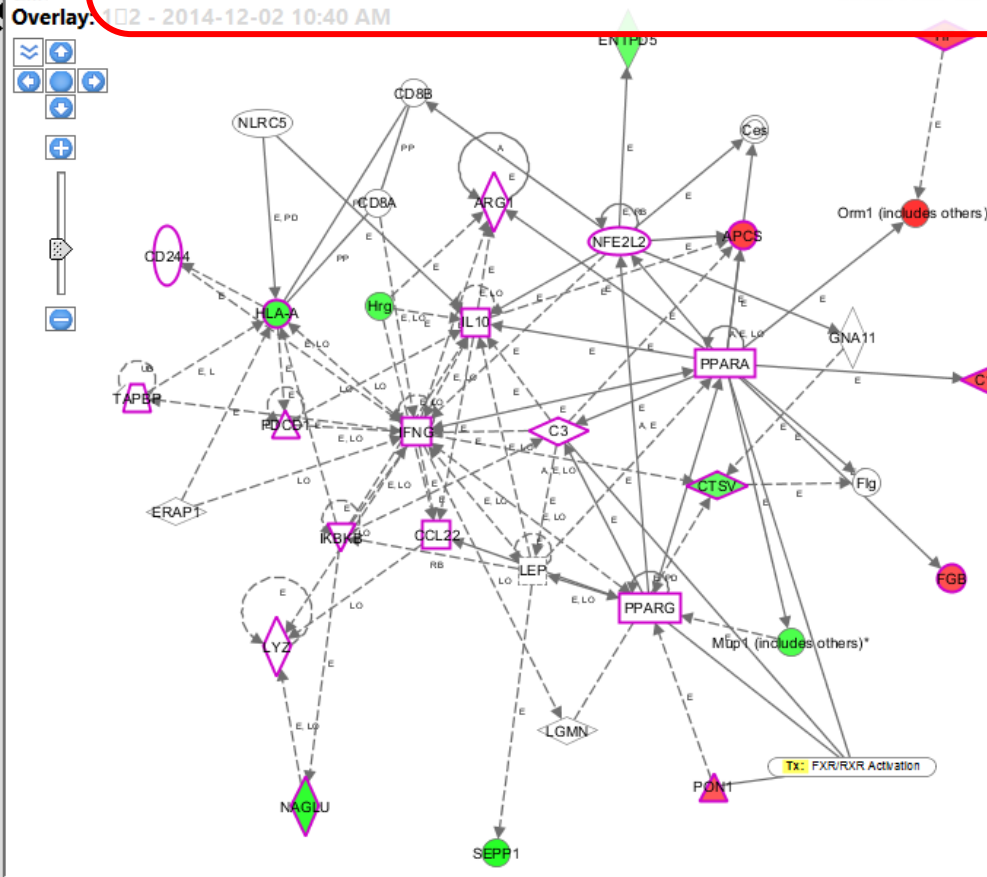
New My Overlay: Ingenuity Tox List REFRESH

Select Ingenuity Tox List labels from table to be displayed on pathway.

<input type="checkbox"/>	Ingenuity Tox Name	# Mole...	Molecule(s)
<input type="checkbox"/>	Liver Proliferation	8	C3, ENTPD5, IFNG, IKBKB, LEP,...
<input type="checkbox"/>	Liver Necrosis/Cell Death	8	C3, ENTPD5, IFNG, IKBKB, IL10...
<input type="checkbox"/>	Increases Liver Damage	5	C3, IFNG, IKBKB, PDCD1, PPARA
<input type="checkbox"/>	Positive Acute Phase Respons...	4	APCS, C3, FGB, HP
<input type="checkbox"/>	Increases Liver Hepatitis	4	IFNG, IKBKB, IL10, LEP
<input checked="" type="checkbox"/>	FXR/RXR Activation	4	C3, PON1, PPARA, PPARG
<input type="checkbox"/>	Cardiac Hypertrophy	4	GNA11, IKBKB, LEP, PPARA
<input type="checkbox"/>	Increases Renal Nephritis	3	IFNG, IL10, LEP
<input type="checkbox"/>	Cardiac Necrosis/Cell Death	3	IFNG, IKBKB, LEP
<input type="checkbox"/>	Hepatic Cholestasis	3	IFNG, IKBKB, PPARA
<input type="checkbox"/>	Mechanism of Gene Regulatio...	3	IKBKB, PPARA, PPARG
<input type="checkbox"/>	Cardiac Fibrosis	3	IFNG, PDCD1, PPARA
<input type="checkbox"/>	Increases Liver Hyperplasia/H...	3	IKBKB, LEP, PPARA
<input type="checkbox"/>	Renal Necrosis/Cell Death	3	IFNG, NFE2L2, PPARG
<input type="checkbox"/>	Hepatic Fibrosis	3	IFNG, IL10, LEP
<input type="checkbox"/>	LXR/RXR Activation	3	C3, LYZ, PON1
<input type="checkbox"/>	PPARα/RXRα Activation	3	GNA11, IKBKB, PPARA
<input type="checkbox"/>	Hepatic Stellate Cell Activation	2	IFNG, IL10
<input type="checkbox"/>	Increases Liver Steatosis	2	C3, PPARG
<input type="checkbox"/>	Oxidative Stress	2	IL10, NFE2L2
<input type="checkbox"/>	LPS/IL-1 Mediated Inhibition ...	2	Ces, PPARA
<input type="checkbox"/>	Increases Glomerular Injury	2	C3, CCL22
<input type="checkbox"/>	Xenobiotic Metabolism Signal...	2	Ces, NFE2L2
<input type="checkbox"/>	PXR/RXR Activation	2	Ces, PPARA
<input type="checkbox"/>	Persistent Renal Ischemia-Rep...	2	C3, LYZ
<input type="checkbox"/>	Increases Transmembrane Pot...	1	PPARG
<input type="checkbox"/>	Increases Cardiac Dysfunction	1	PPARA
<input type="checkbox"/>	Increases Cardiac Dilation	1	IFNG
<input type="checkbox"/>	NF-κB Signaling	1	IKBKB
<input type="checkbox"/>	NRF2-mediated Oxidative Str...	1	NFE2L2

Mode Label Interactive OFF

加入自定义通路、列表或毒性列表。确定分子之间是否有重叠，或者通路是否参与了任何分子毒理过程



Overlay——Canonical Pathways

显示My pathway中所参与的 Canonical Pathway.

Highlight: 只高亮参与某个canonical pathway 中的分子。
Label: 显示该canonical pathway 标签

OFF: 鼠标在不同canonical pathway间移动时, 右侧不显示参与的分子
On: 与OFF 功能相反。

Pathway Name	# Molecules	Molecule(s)
<input type="checkbox"/> Cardiac Hypertrophy ...	22	E2F1-HDAC-Rb, Evi1-...
<input checked="" type="checkbox"/> Coronavirus Pathoge...	21	E2F1-HDAC-Rb, Evi1-...
<input checked="" type="checkbox"/> Pancreatic Adenocar...	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Role of NFAT in Cardi...	19	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Huntington's Disease...	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Telomerase Signaling	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Molecular Mechanis...	19	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Non-Small Cell Lung ...	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Bladder Cancer Signa...	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Ovarian Cancer Signa...	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Glioma Signaling	19	E2F1-HDAC-Rb, EGF...
<input type="checkbox"/> Prostate Cancer Sign...	18	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Cell Cycle	18	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Chronic Myeloid Leu...	18	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Hereditary Breast Car...	18	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Phospholipase C Sign...	18	E2F1-HDAC-Rb, Evi1-...
<input type="checkbox"/> Small Cell Lung Canc...	18	E2F1-HDAC-Rb, Evi1-...

Overlay——Biomarker

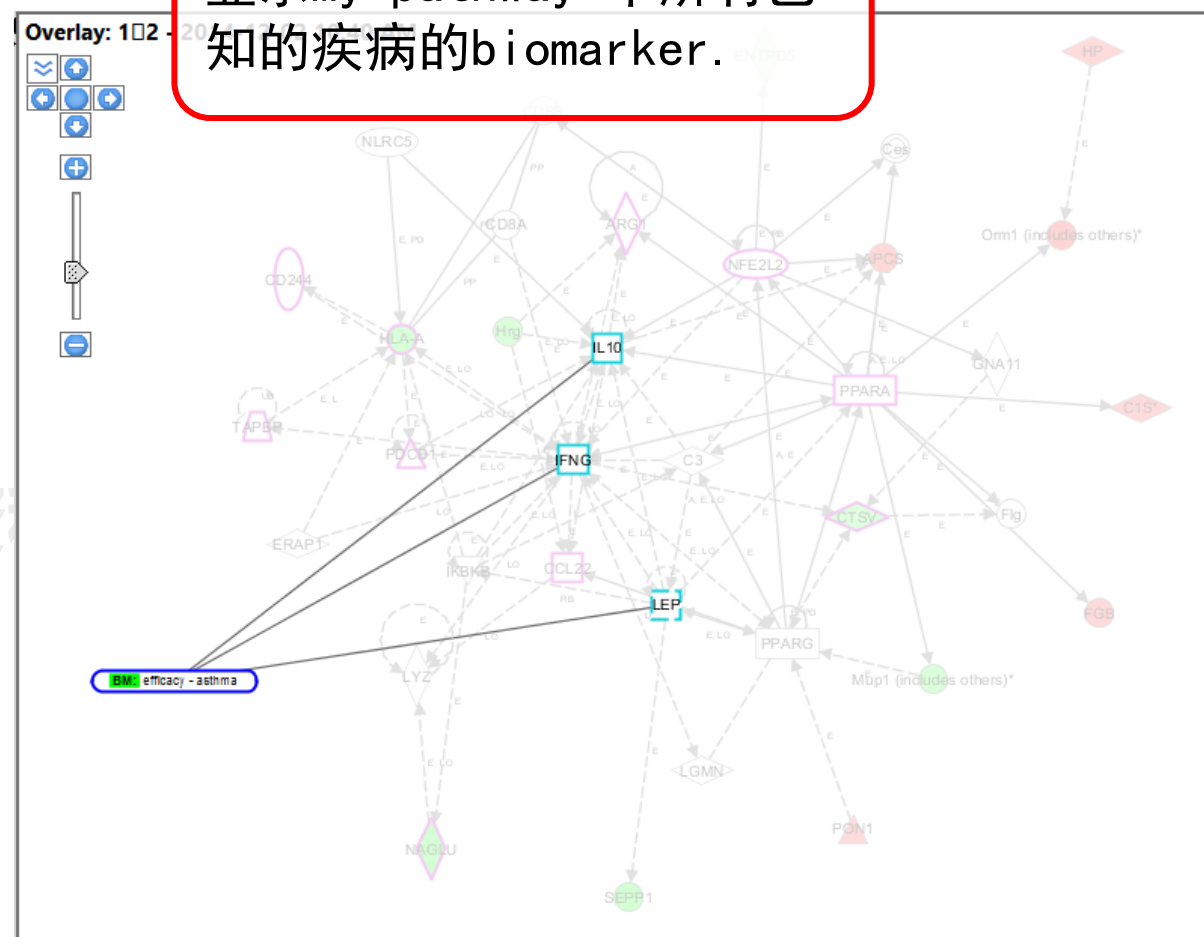
Overlay: Biomarkers

Select Biomarker labels from table to be displayed on pathway.

<input type="checkbox"/>	Application	Disease	# Molecules	Molecule(s)
<input type="checkbox"/>	efficacy	breast cancer	17	CASP3, ESR1, F...
<input type="checkbox"/>	efficacy	non-insulin-de...	17	ADIPOQ, ALB, ...
<input type="checkbox"/>	efficacy	Alzheimer's dis...	15	ALB, APOA1, A...
<input type="checkbox"/>	efficacy	atherosclerosis	14	ADIPOQ, APO...
<input type="checkbox"/>	efficacy	hypertension	13	ADIPOQ, ALB, ...
<input type="checkbox"/>	diagnosis	ovarian cancer	12	APOA1, APOE, ...
<input type="checkbox"/>	efficacy	asthma	11	CCL2, ICAM1, I...
<input type="checkbox"/>	diagnosis	breast cancer	10	APOA1, APOE, ...
<input type="checkbox"/>	unspecified ap...	Sjogren's syndr...	9	APOA1, EDN1, ...
<input type="checkbox"/>	efficacy	pancreatic can...	9	ADIPOQ, F3, F...
<input type="checkbox"/>	efficacy	cystic fibrosis	8	ALB, IL4, IL6, IL...

BM efficacy - asthma
#genes = 9
Targets: ADIPOQ,F3,FGF2,HIF1A,INS,MMP9,PTGS2,TP53,VEGFA

显示My pathway 中所有已知的疾病的biomarker.



Overlay—Drug

显示My Pathway 与FDA 批准的I, II, III期临床药物相互作用的分子

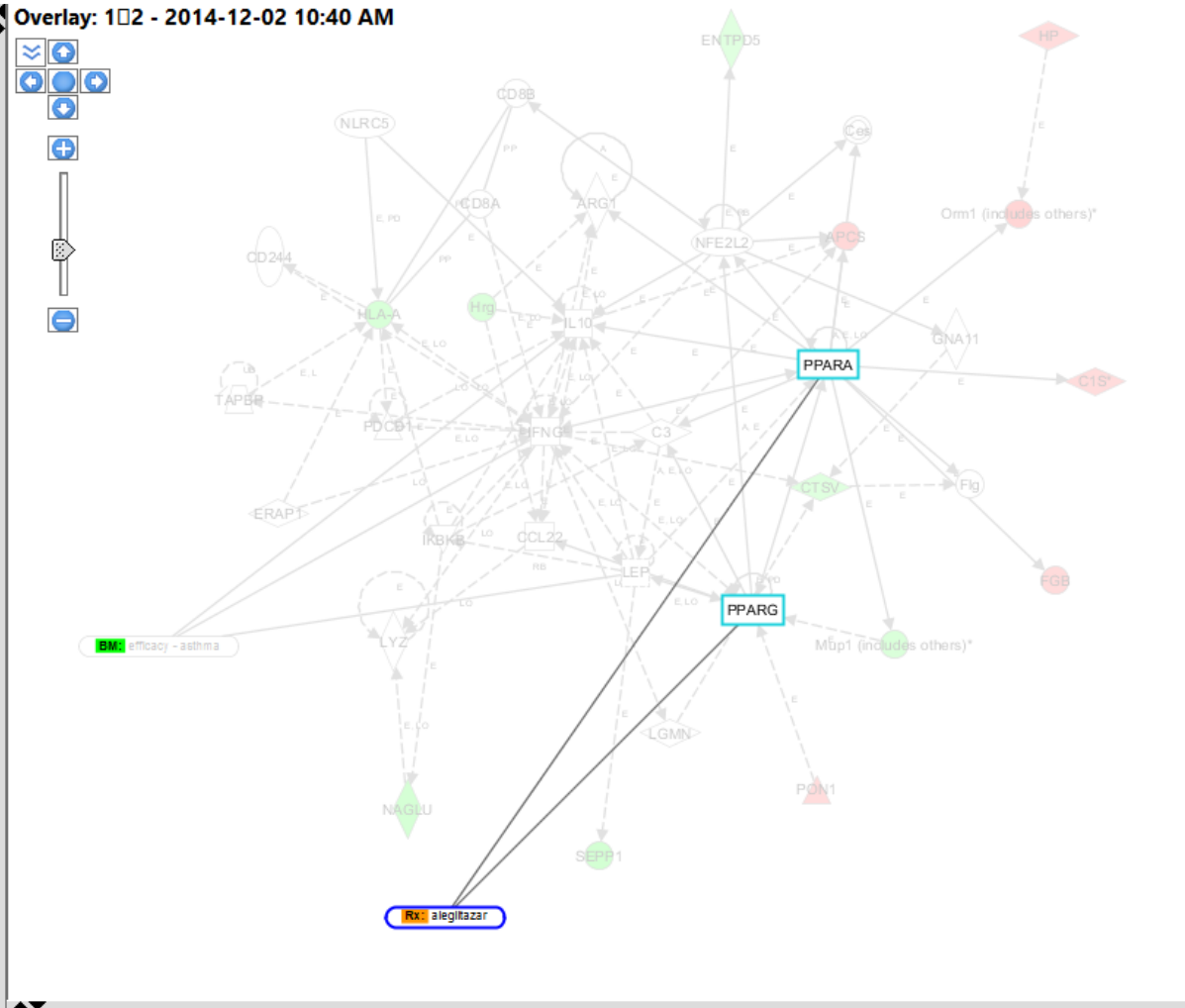
Overlay: Drug

DRUG SUMMARY

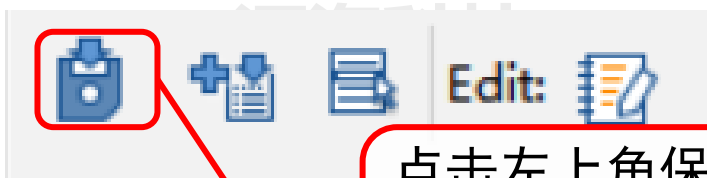
Select drug labels from table to be displayed on pathway.

<input type="checkbox"/>	Drug Name	# Mole...	Target(s)
<input checked="" type="checkbox"/>	alelitazar	2	PPARA, PPARG
<input type="checkbox"/>	bezafibrate	2	PPARA, PPARG
<input type="checkbox"/>	tesaqitazar	2	PPARA, PPARG
<input type="checkbox"/>	aspirin/dipyridamole/telmisartan	1	PPARG
<input type="checkbox"/>	nicotinic acid/pioglitazone	1	PPARG
<input type="checkbox"/>	clopidogrel/telmisartan	1	PPARG
<input type="checkbox"/>	rosiglitazone	1	PPARG
<input type="checkbox"/>	hydrochlorothiazide/telmisartan	1	PPARG
<input type="checkbox"/>	NS-220	1	PPARA
<input type="checkbox"/>	F2	1	FGB
<input type="checkbox"/>	icosapent	1	PPARG
<input type="checkbox"/>	fenofibrate	1	PPARA
<input type="checkbox"/>	nivolumab	1	PDCD1
<input type="checkbox"/>	pembrolizumab	1	PDCD1
<input type="checkbox"/>	balsalazide	1	PPARG
<input type="checkbox"/>	SERPING1	1	C1S*
<input type="checkbox"/>	dlimepiride/rosiglitazone	1	PPARG
<input type="checkbox"/>	amlodipine/telmisartan	1	PPARG
<input type="checkbox"/>	telmisartan	1	PPARG
<input type="checkbox"/>	qemfibrozil	1	PPARA
<input type="checkbox"/>	choline fenofibrate/simvastatin	1	PPARA
<input type="checkbox"/>	aloqliptin/pioglitazone	1	PPARG
<input type="checkbox"/>	clofibrate	1	PPARA
<input type="checkbox"/>	auranofin	1	IKBKB
<input type="checkbox"/>	mesalamine	1	PPARG
<input type="checkbox"/>	sulfasalazine	1	PPARG
<input type="checkbox"/>	docosahexaenoic acid	1	PPARA
<input type="checkbox"/>	ezetimibe/fenofibrate	1	PPARA
<input type="checkbox"/>	lqG	1	C3
<input type="checkbox"/>	pioglitazone	1	PPARG
<input type="checkbox"/>	troglitazone	1	PPARG
<input type="checkbox"/>	farqitazar	1	PPARG
<input type="checkbox"/>	choline fenofibrate	1	PPARA

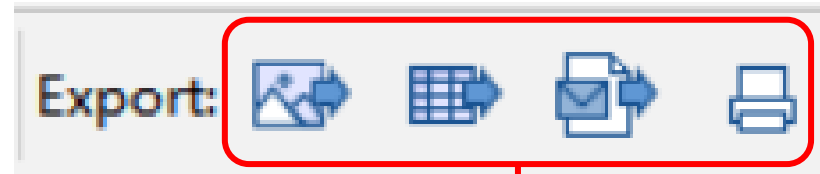
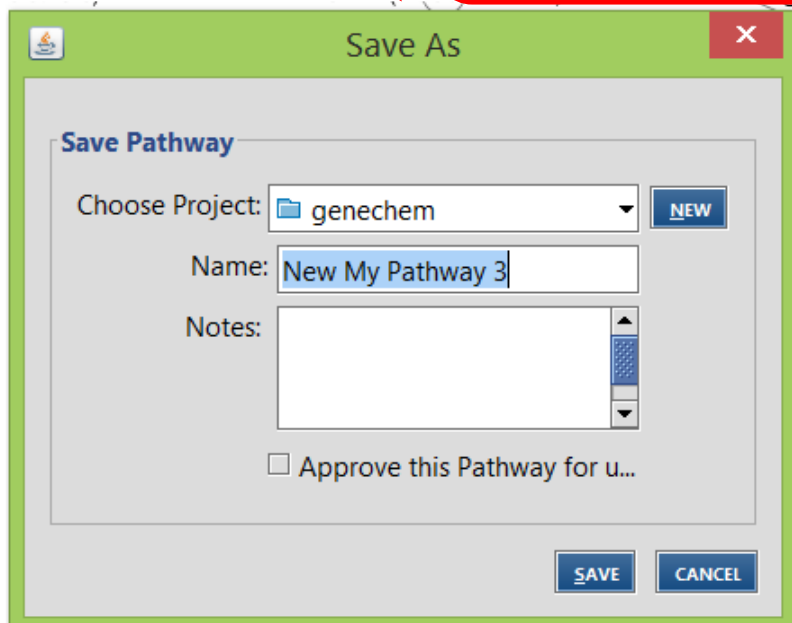
Mode Label Interactive OFF



My Pathway的保存和输出

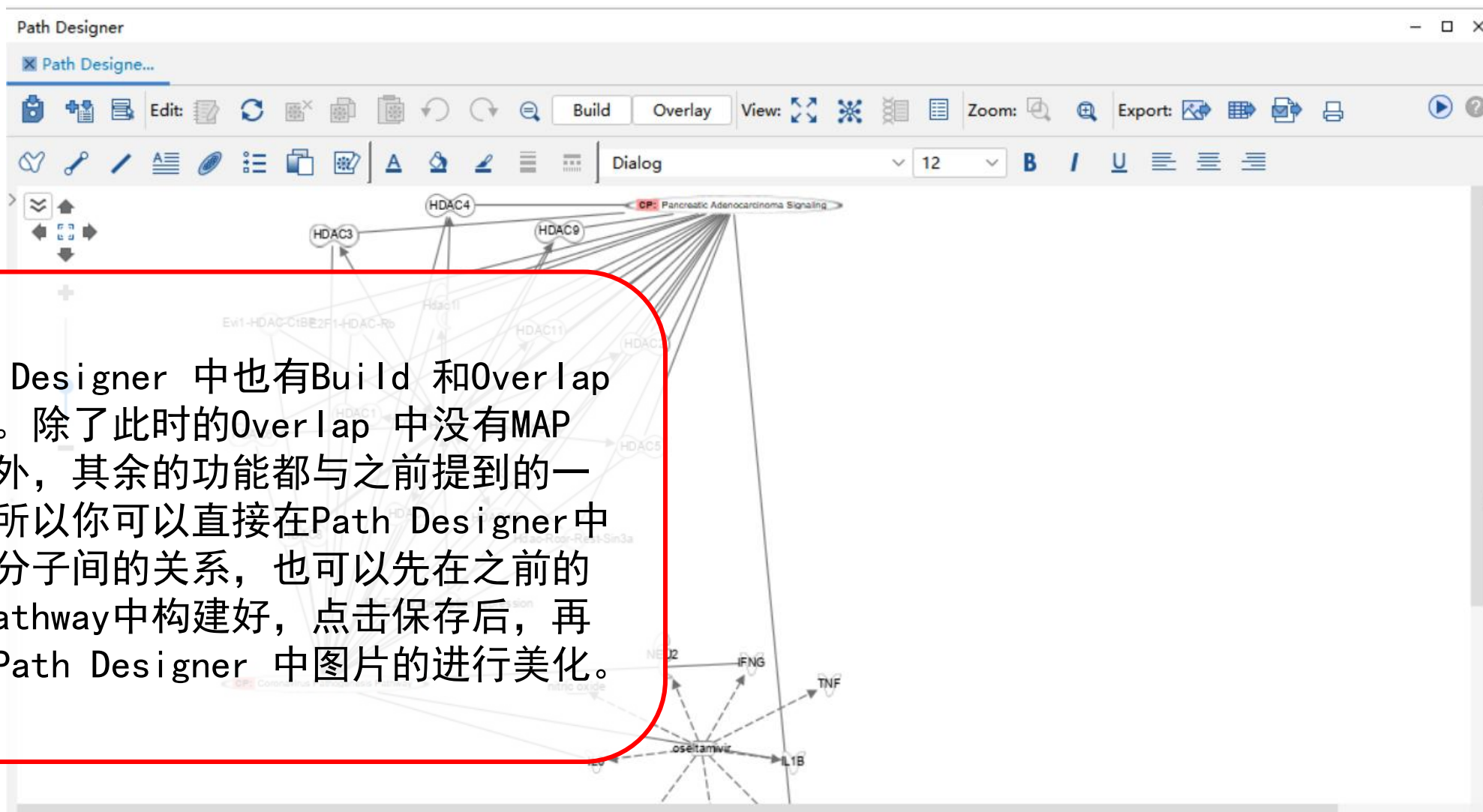


点击左上角保存按钮，选择Project folder，点击保存



My Pathway 的结果可以以图片格式，文件格式输出，也可以通过邮件发送给同事，或者打印输出。

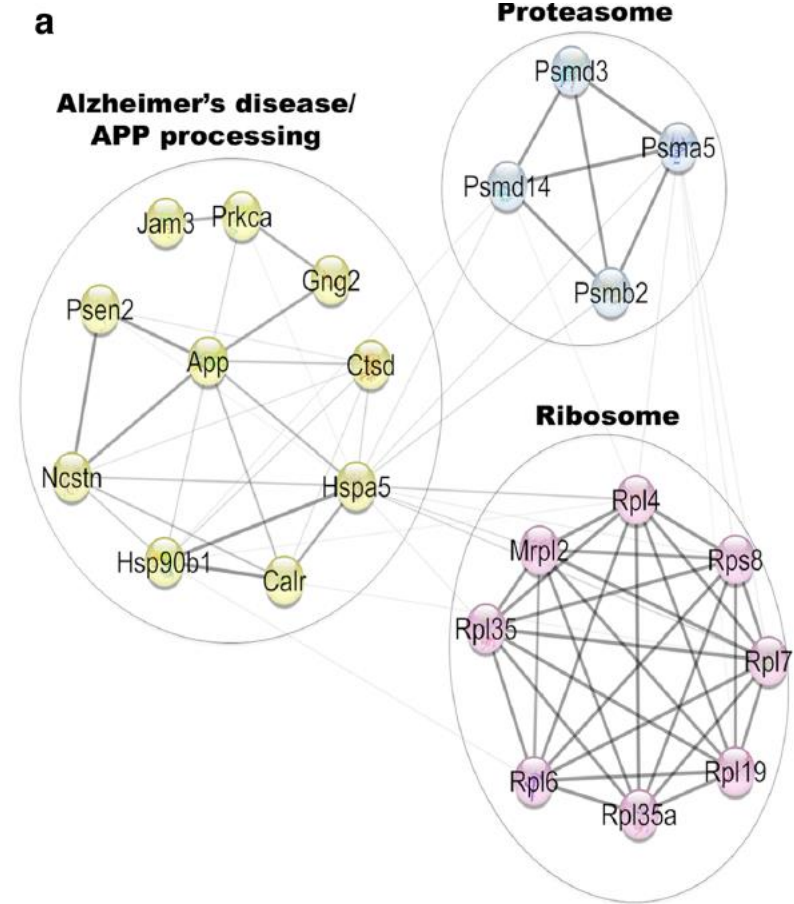
Path Designer



Path Designer 中也有Build 和Overlap 功能。除了此时的Overlap 中没有MAP 功能外，其余的功能都与之前提到的一样。所以你可以直接在Path Designer 中分析分子间的关系，也可以先在之前的My Pathway 中构建好，点击保存后，再进入Path Designer 中图片的进行美化。

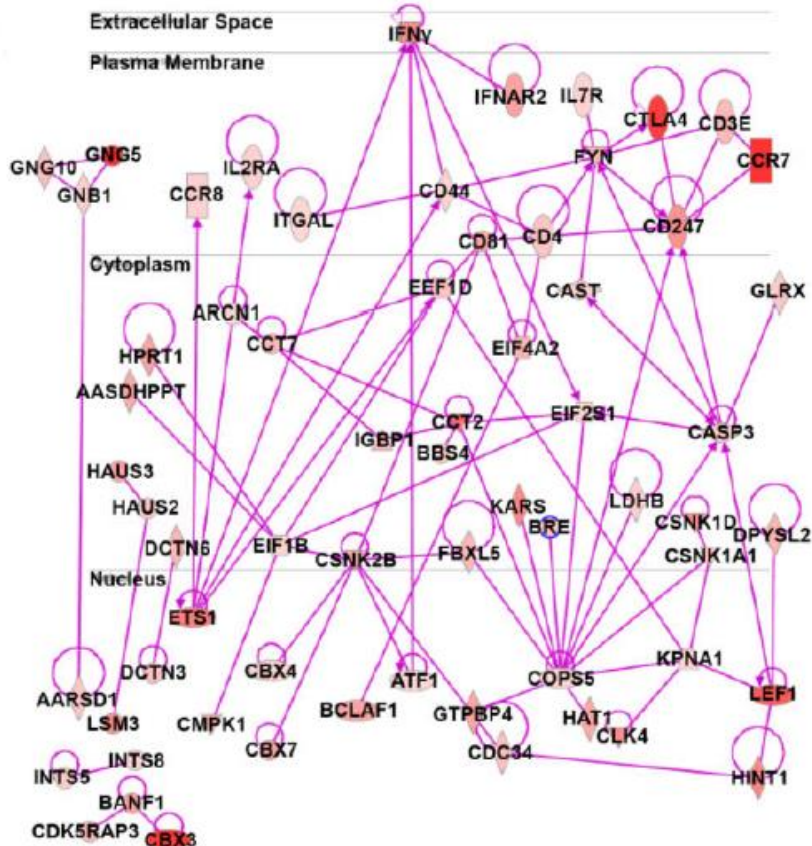
普通的分子网络图表

c	Canonical Pathway	Younger	Older	d	Diseases and Bio Function	Younger	Older
	Phagosome Maturation				Organization of cytoplasm		
	Protein Ubiquitination Pathway				Cell death		
	EIF2 Signaling				Microtubule dynamics		
	Unfolded protein response				Organization of cytoskeleton		
	Glutathione Redox Reactions II				Formation of cellular protrusions		
	Mitotic Roles of Polo-Like Kinase				Neuritogenesis		
	Endoplasmic Reticulum Stress Pathway				Movement Disorders		
	Huntington's Disease Signaling				Organismal death		
	Mitochondrial Dysfunction				Necrosis		
	Amyloid Processing				Apoptosis		
	Synaptic Long Term Depression				Reduction of hydrogen peroxide		
	RAR Activation				Development of neurons		
	ErbB4 Signaling				Anemia		
	NRF2-mediated Oxidative Stress Response				Progressive neurological disorder		
	Cleavage and Polyadenylation of Pre-mRNA				Dystrophy of apical processes		
	Mechanisms of Viral Exit from Host Cells				Quantity of neurons		
	Hypoxia Signaling in the Cardiovascular System				Myelodysplastic bone marrow neoplasm		
	Glutathione Redox Reactions I				Genitourinary tumor		
	Glucocorticoid Receptor Signaling				Cell death of tumor cell lines		
	Aldosterone Signaling in Epithelial Cells				Morphology of neurons		
	Sertoli Cell-Sertoli Cell Junction Signaling				Morphogenesis of neurons		
	RhoA Signaling				Stress response of cells		
	Axonal Guidance Signaling				Endoplasmic reticulum stress response of cells		
	L-cysteine Degradation III				Breast or ovarian cancer		
	D-myo-inositol-5-phosphate Metabolism				Malignant genitourinary solid tumor		
					Disorder of basal ganglia		

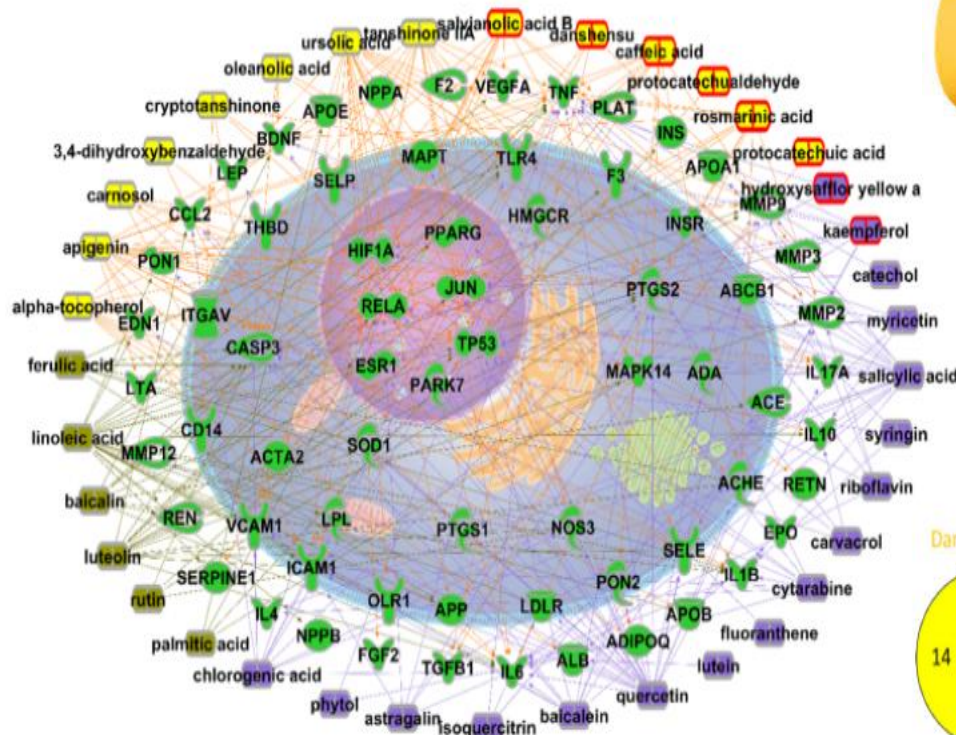


Mirzaei M , Pushpitha K , Deng L , et al. Upregulation of Proteolytic Pathways and Altered Protein Biosynthesis Underlie Retinal Pathology in a Mouse Model of Alzheimer' s Disease[J]. Molecular Neurobiology, 2019.

优秀的分子网络图



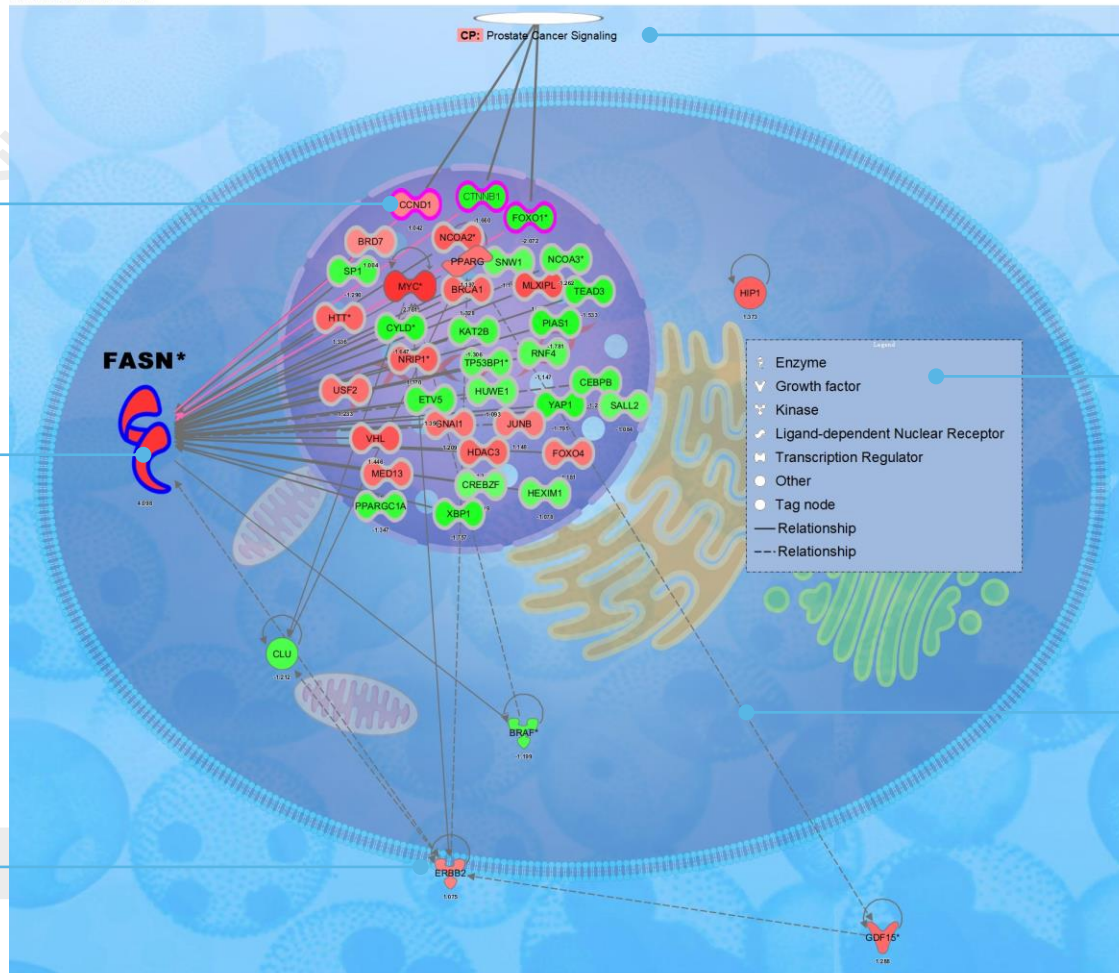
Butcher M J , Filipowicz A R , Waseem T C , et al. Atherosclerosis-Driven Treg Plasticity Results in Formation of a Dysfunctional Subset of Plastic IFN γ + Th1/Tregs[J]. Circulation Research, 2016, 119(11):CIRCRESAHA.116.309764.



Lyu, M.; Yan, C.L.; Liu, H.X.; Wang, T.Y.; Shi, X.H.; Liu, J.P.; Orgah, J.; Fan, G.W.; Han, J.H.; Wang, X.Y., et al. Network pharmacology exploration reveals endothelial inflammation as a common mechanism for stroke and coronary artery disease treatment of danhong injection. Scientific reports 2017, 7, 15427.



Path Designer New My Pathway 1



经典通路

源资科技

图例：按分子类型区分

清晰分子调控关系

源资科技

实验数据中的表达值

重点突出目标分子

精确的亚细胞定位

源资科

源资科

源资科技

源资科技

PART

源资科技

源资科技

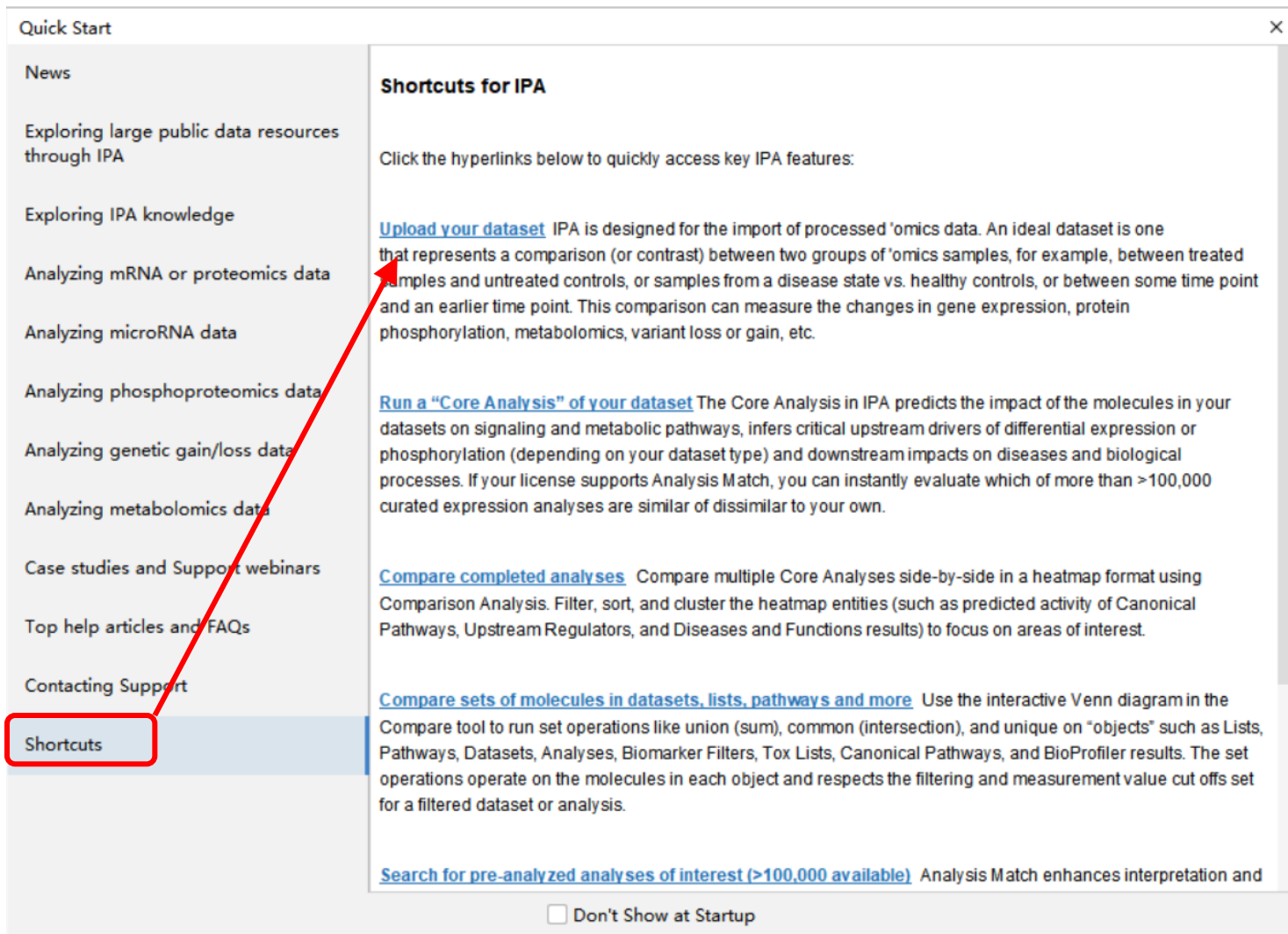
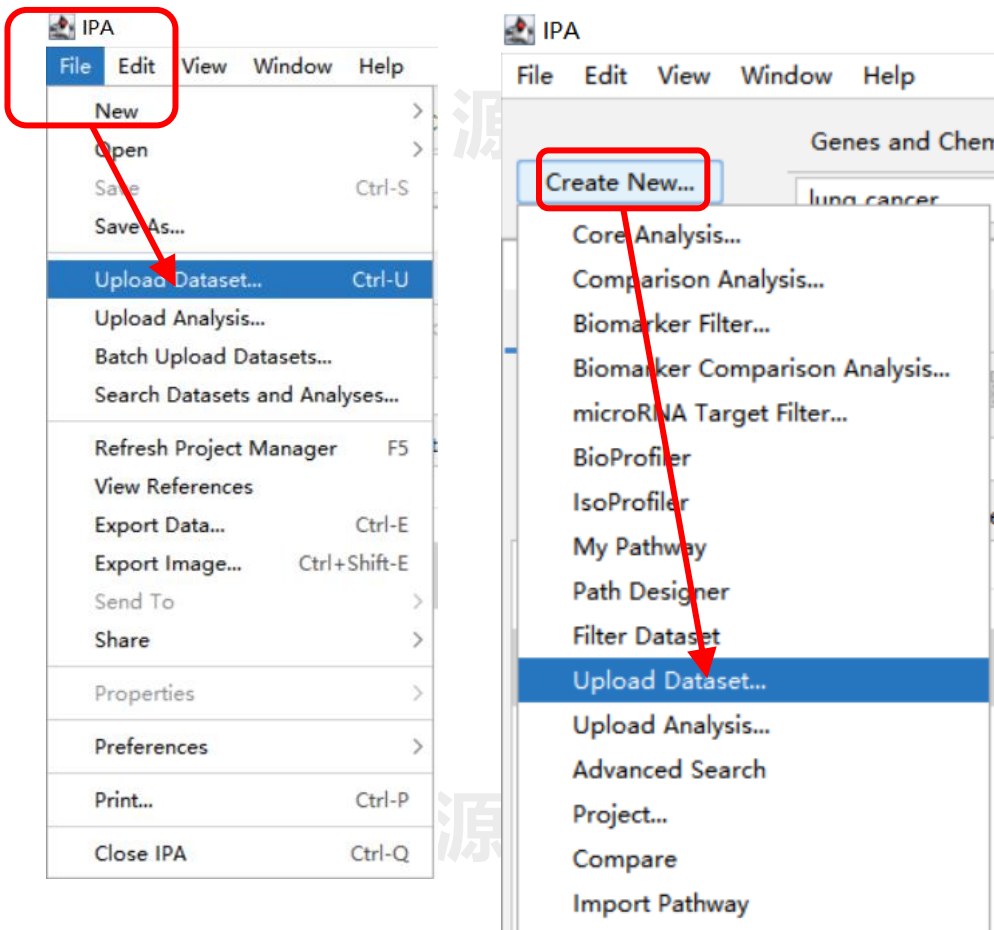
Causal Networks

5

源资科技

源资科技

将数据上传到IPA中



IPA 支持的
数据类型

Observation

- 一组分子以及它们所对应的某个实验条件下的表达量定义为一个观察组；
- 一组分子以及它们对应的不同实验条件下（比如时间系列，剂量响应实验）的表达量，构成了多个观察组；

Identifier

- 分配给某个基因，蛋白或者化学物的特定的注释。IPA会从数据文件中的 Identifier column 一栏找到每个identifier,然后将其匹配到Ingenuity Knowledge Base中具体的分子信息

Expression Value

- 代表某个分子活性程度或者重要性程度的数字。IPA 可以识别不同类型的表达量
- 选择的表达量要符合IPA数据值范围

Affymetrix®
Affymetrix SNP ID
Agilent®
CAS Registry Number
CodeLink
dbSNP
Ensembl
Entrez Gene
GenBank
Gene Symbol – mouse (Entrez Gene)
Gene Symbol – rat (Entrez Gene)
Gene Symbol – human (Hugo/HGNC)
GenPept
GI Number
Human Metabolome Database (HMDB)
Illumina
Ingenuity
International Protein Index
KEGG
Life Technologies (Applied Biosystems®)
miRBase (mature)
miRBase (stemloop)
PubChem CID
Refseq
UCSC (hg18)
UCSC (hg19)
Unigene
Uniprot/Swiss-Prot Accession
Species-specific Identifiers supported in IPA
Human
Mouse
Rat
Additional species via ortholog mapping

Observation 1

Observation 2

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
Accession ID	Gene Symbol	NAME	BPH-205	BPH-202	BPH-203	BPH-201	BPH-204	BPH Ave	PCA-402	PCA-403	PCA-404	PCA-410	PCA-408	PCA-401	PCA-409	PCA-405	PCA-406	PCA-405	PCA Ave
2	Hs.159533	MST1	0.958	1.361	2.088		1.986	1.469	0.573	0.702	1.773	0.801	0.599	0.532	0.916	0.984	1.128	1.575	-1.0435
3	9375	TM9SF2	1.218	1.146	1.103		0.846	1.15567	0.896	1.412	1.45	1.439	1.45	0.801	1.272	1.041	0.65	1.114	1.1525
4	5093	PCBP1	1.125	1.338	1.609	1.445	1.427	1.37925	1.217	1.09	1.46	1.4	1.022	0.83	1.194	1.043	0.643	0.927	1.0826
5	10057	ABCC5	1.015	1.331	1.116		0.94	1.154	0.951	0.952	1.242	1.171	1.184	1.477	1.348	0.904		0.993	1.13578
6	Hs.255431	ESTs	0.671	1.663	1.511	1.292	1.688	1.28425	0.957	1.034	1.049	0.52	0.778		0.731	0.504	0.476	0.379	-1.4001
7	Hs.100554	ESTs	0.807	1.047	1.186	1.007	1.381	1.01175	0.754	0.759	1.097	0.455	0.564	0.399	0.656	0.589	0.7	0.573	-1.5277
8	AA406027	Human mRNA for lymphoc	0.805	0.91	0.746	0.981	0.821	-1.1621		0.834	1.082	0.891	1.093		0.967	1.011	1.321	0.669	-1.0168
9	Hs.144630	NR2F1	0.889	1.705	2.243	1.359	1.353	1.549	1.228	0.711	0.998	0.867	0.691	0.811	0.839	0.927	0.658	1.173	-1.1232
10	AA425947	RIG	0.852	1.535	2.326	1.797	1.502	1.6275		1.183	0.915	0.656	0.635	0.774	0.656	0.544	0.925	0.784	-1.2726

均为Identifier，在上传到IPA中时，仅选择一列即可。

均为观察值的实验重复，需求出重复值的平均值，将平均值上传到IPA。

在IPA中选择时，仅选择平均值这一列

Dataset Upload - STAD_pembrolizumab.xlsx

- Select File Format: Flexible Format
- Contains Column Header: Yes No
- 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.
- Array platform used for experiments: Not specified/applicable. Select relevant array platform as a reference set for data analysis.
- Use the dropdown menus to specify the column names that contain identifiers and observations. For observations, select the appropriate measurement value type.

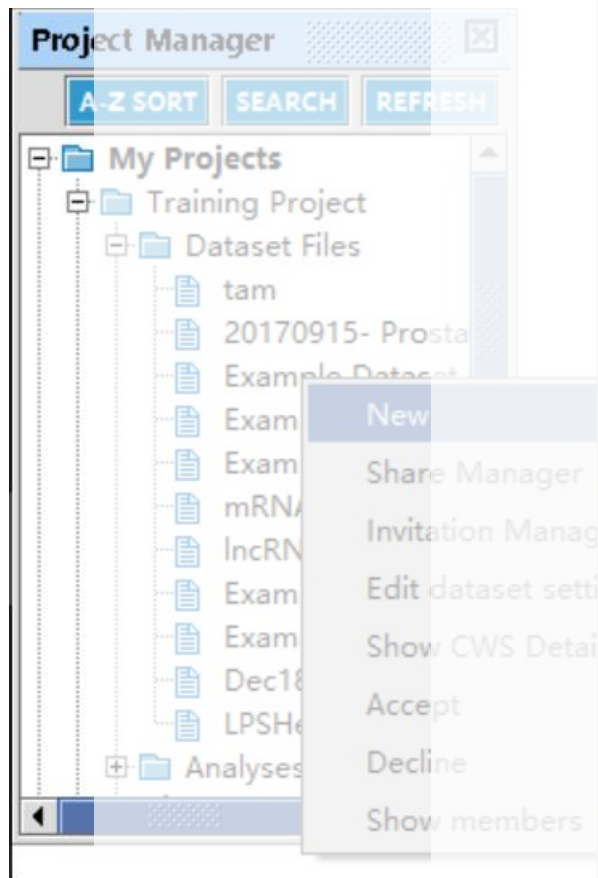
Raw Data (18705) Dataset Summary (18443) Metadata Mapped (18443) Unmapped (261)

Edit Observation Names Infer Observations

ID/Observation Name	ID	Observation 1	Observation 1	Observation 2	Observation 2
Measurement/Annotation	2 types selec...	Phospho Lo...	Expr p-value	Expr Log Ratio	Expr p-value
1	geneid	STAD vs Normal Lo...	STAD vs Normal Ra...	Pembrolizumab res...	Pembrolizumab res...
2	MARCH1	3.28999999999999...	0.9119000000000004	-8.45000000000000...	0.8191000000000005
3	MARCH1	-0.69430000000000...	0.1086	0.8869000000000002	0.1408000000000001
4	MARCH2	-0.51280000000000...	0.2457	-0.69479999999999...	0.3034999999999996
5	MARCH2	-8.77E-2	0.6823000000000002	0.3597000000000002	0.1965000000000001
6	MARCH3	0.1968	0.5383	-0.2016	0.6680000000000004
7	MARCH4	-1.0064	0.1003	1.9093	1.49E-2
8	MARCH5	-3.13000000000000...	0.8608000000000001	0.1337000000000001	0.5276999999999995
9	MARCH6	-0.2833	0.1718000000000001	1.59000000000000...	0.9543000000000004
10	MARCH7	-0.125	0.4040000000000003	0.4596000000000001	4.950000000000002..
11	MARCH8	-0.14019999999999...	0.6844000000000001	0.5526999999999997	0.2978000000000001
12	MARCH9	-0.2495	0.3795	0.2091000000000001	0.5662000000000004
13	MARCH10	0.6705999999999997	0.7317000000000002	3.6932	3.2099999999999997..
14	SEPT1	-0.30199999999999...	0.5746999999999995	-0.69869999999999...	0.3448
15	SEPT2	0.1385000000000001	0.2984	-0.1052	0.5491000000000003

Observation 1 Observation 2

开始Core analysis



File Edit View Window Help

New Core Analysis... Ctrl-N

Quick Start

News

Exploring large public data resources through IPA

Exploring IPA knowledge

Analyzing mRNA or proteomics data

Analyzing microRNA data

Analyzing phosphoproteomics data

Analyzing genetic gain/loss data

Analyzing metabolomics data

Case studies and Support webinars

Top help articles and FAQs

Contacting Support

Shortcuts

Shortcuts for IPA

Click the hyperlinks below to quickly access key IPA features:

[Upload your dataset](#) IPA is designed for the import of processed 'omics data. An ideal dataset is one that represents a comparison (or contrast) between two groups of 'omics samples, for example, between treated samples and untreated controls, or samples from a disease state vs. healthy controls, or between some time point and an earlier time point. This comparison can measure the changes in gene expression, protein phosphorylation, metabolomics, variant loss or gain, etc.

[Run a "Core Analysis" of your dataset](#) The Core Analysis in IPA predicts the impact of the molecules in your datasets on signaling and metabolic pathways, infers critical upstream drivers of differential expression or phosphorylation (depending on your dataset type) and downstream impacts on diseases and biological processes. If your license supports Analysis Match, you can instantly evaluate which of more than >100,000 curated expression analyses are similar or dissimilar to your own.

[Compare completed analyses](#) Compare multiple Core Analyses side-by-side in a heatmap format using Comparison Analysis. Filter, sort, and cluster the heatmap entities (such as predicted activity of Canonical Pathways, Upstream Regulators, and Diseases and Functions results) to focus on areas of interest.

[Compare sets of molecules in datasets, lists, pathways and more](#) Use the interactive Venn diagram in the Compare tool to run set operations like union (sum), common (intersection), and unique on "objects" such as Lists, Pathways, Datasets, Analyses, Biomarker Filters, Tox Lists, Canonical Pathways, and BioProfiler results. The set operations operate on the molecules in each object and respects the filtering and measurement value cut offs set for a filtered dataset or analysis.

[Search for pre-analyzed analyses of interest \(>100,000 available\)](#) Analysis Match enhances interpretation and

Don't Show at Startup

Ctrl+Shift-C
Ctrl+Shift-B
analysis... Ctrl+Shift-K
Ctrl+Shift-I
Ctrl+Shift-N
Ctrl+Shift-D
Ctrl+Shift-S
Ctrl+Shift-P
Ctrl-R

设置Core Analysis参数

确认参考数据和分析的分子背景一致

Population of genes to consider for p-value calculations:
Reference Set: Ingenuity Knowledge Base (Genes Only)

Relationships to consider:
 Direct and Indirect Relationships
 Direct Relationships

设置构建互作网络或上游调控因子是否考虑间接作用。互作网络寻找的最为相关的，或有分子结合作用相关的关系。

点击按钮应用过滤阈值，并查看用于分析的分子数量

设置数据过滤阈值

Set Cutoffs
Down: [] Up: []

Recalculate 681 analysis-ready molecules across observations (251 Down and 430 Up)

数据量在100-2000之间为佳，范围外的数据也能进行分析



设置Core Analysis参数

是否进行互作网络分析

是否将内源化合物加入互作网络分析中

设置互作网络的规模和结果的数量

是否进行Causal Network分析 (AA模块)

The screenshot shows the 'Create Expression Analysis' configuration window. The 'General Settings' sidebar on the left includes sections for Networks, Node Types, Data Sources, Confidence, Species, and Tissues & Cell Lines. The main configuration area is titled 'Generate the following Networks (increases analysis time)'. It features three checked checkboxes: 'Interaction networks', 'Include endogenous chemicals', and 'Causal networks'. Below these, there are two dropdown menus: 'Molecules per network' (set to 35) and 'Networks per analysis' (set to 25). A text box for 'Score master regulators...' is also present. At the bottom, a 'Preview Dataset' section shows a table of analysis-ready molecules.

Expr Fold Change	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
-1.075	Hs.9953		A1CF	APOBEC1 complementation fac...	Nucleus	other	
-1.128	AA054358		ABCA4	ATP binding cassette subfamily ...	Plasma Membrane	transporter	
-1.010	AA134400		ABCB10	ATP binding cassette subfamily ...	Cytoplasm	transporter	

设置Core Analysis参数

多种过滤条件，包括物种，节点类型等，更改过滤参数可以选择研究相关的背景数据库

将个人建立的My Pathways和My List的内容也一同纳入分析中

Analysis Filter Summary
Consider only relationships where confidence = Experimentally Observed

Dataset Column	Measurement Value Type	Range	Cutoff
BPH Ave F.C.	Expr Fold Change	-1.5314 to 3.9795	Down Up

Expr Fold Change	ID	Flags	Symbol	Entrez Gene Name	Location	Type(s)	Drug(s)
-1.075	Hs.9953		A1CF	APOBEC1 complementation fac...	Nucleus	other	
-1.128	AA054358		ABCA4	ATP binding cassette subfamily ...	Plasma Membrane	transporter	
-1.010	AA434400		ABCF10	ATP binding cassette subfamily ...	Cytoplasm	transporter	

获得 Core Analysis 分析结果

源资科技

Expression Analysis - MET

Summary Graphical Summary Canonical Pathways Upstream Analysis Diseases & Functions Regulator Effects Networks Lists My Pathways Molecules ... > ▾

Export :

- > Experiment Metadata
- > Analysis Settings
- > Top Canonical Pathways
- > Top Upstream Regulators
- > Top Diseases and Bio Functions
- > Top Tox Functions
- > Top Regulator Effect Networks
- > Top Networks
- > Top Tox Lists
- Top My Lists *(no data)*
- Top My Pathways *(no data)*
- > Top Analysis-Ready Molecules

Canonical Pathway

IPA的Canonical Pathways 是由科学家们人工摘取并构建的代谢和细胞信号通路数据库。Canonical Pathways中的信息来自于特定的杂志文章、综述、教科书和一些其它权威数据库。

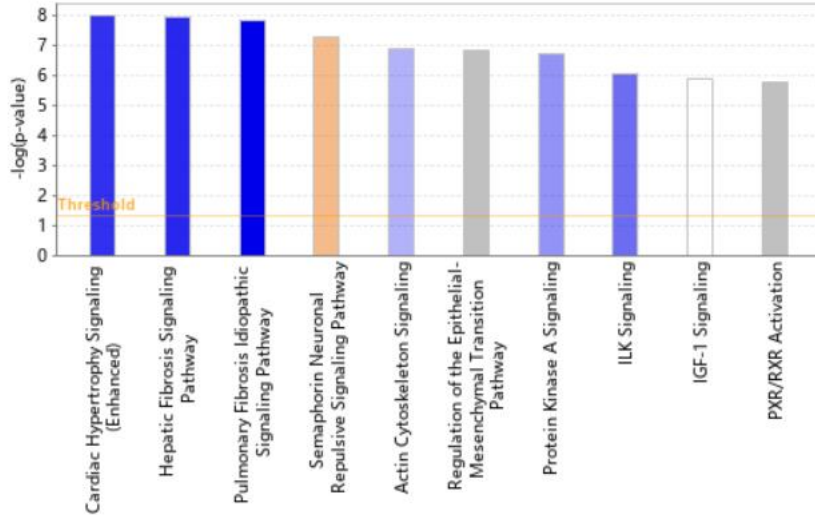
Expression Analysis - MET

Summary Graphical Summary **Canonical Pathways** Upstream Analysis Diseases & Functions Regulator Effects Networks Lists My Pathways Molecules Analysis I

Chart Overlapping

Customize Chart Horizontal Vertical Overlay: Stacked Bar Chart

positive z-score z-score = 0 negative z-score no activity pattern available

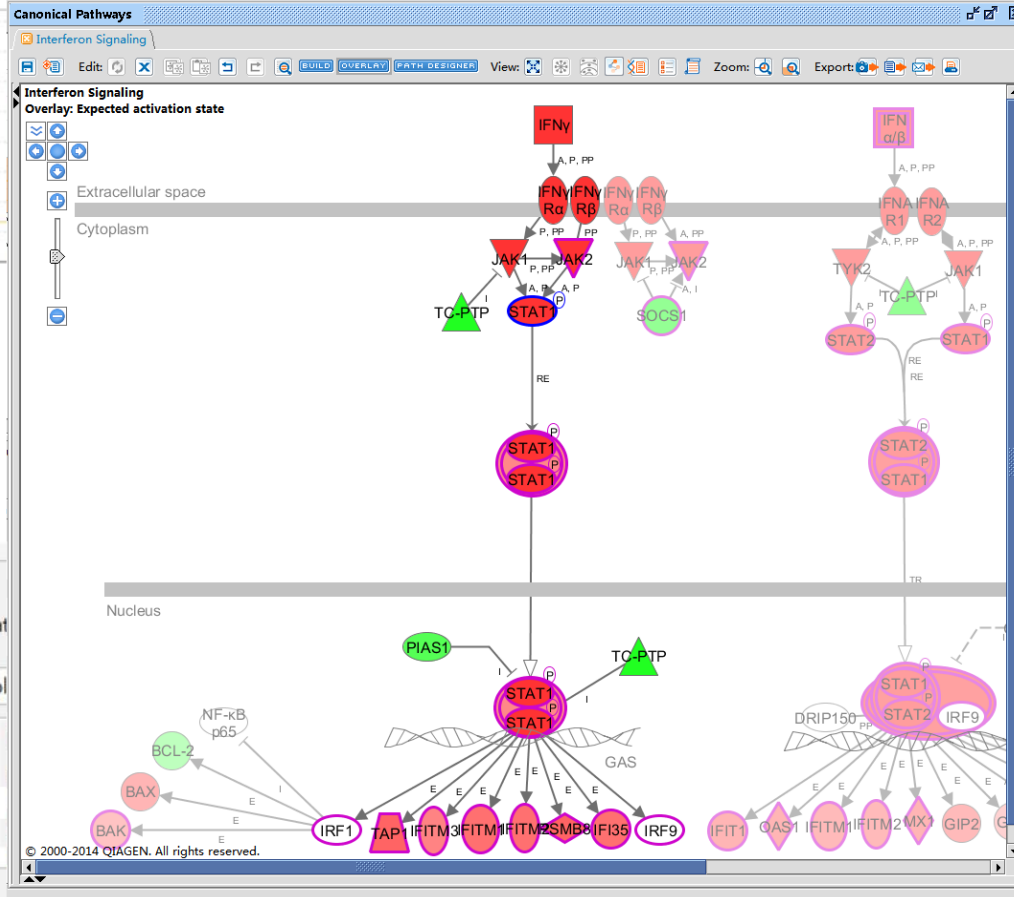


19 molecule(s) associated with **Semaphorin Neuronal Repulsive Signaling Pathway** at

Add To My Pathway Add To My List Create Dataset Customize Table

Symbol	Entrez Gene Name	Identifier
AKT3	AKT serine/threonine kinase 3	AA161465
CSPG5	chondroitin sulfate proteoglycan 5	10675
ITGA11	integrin subunit alpha 11	36721

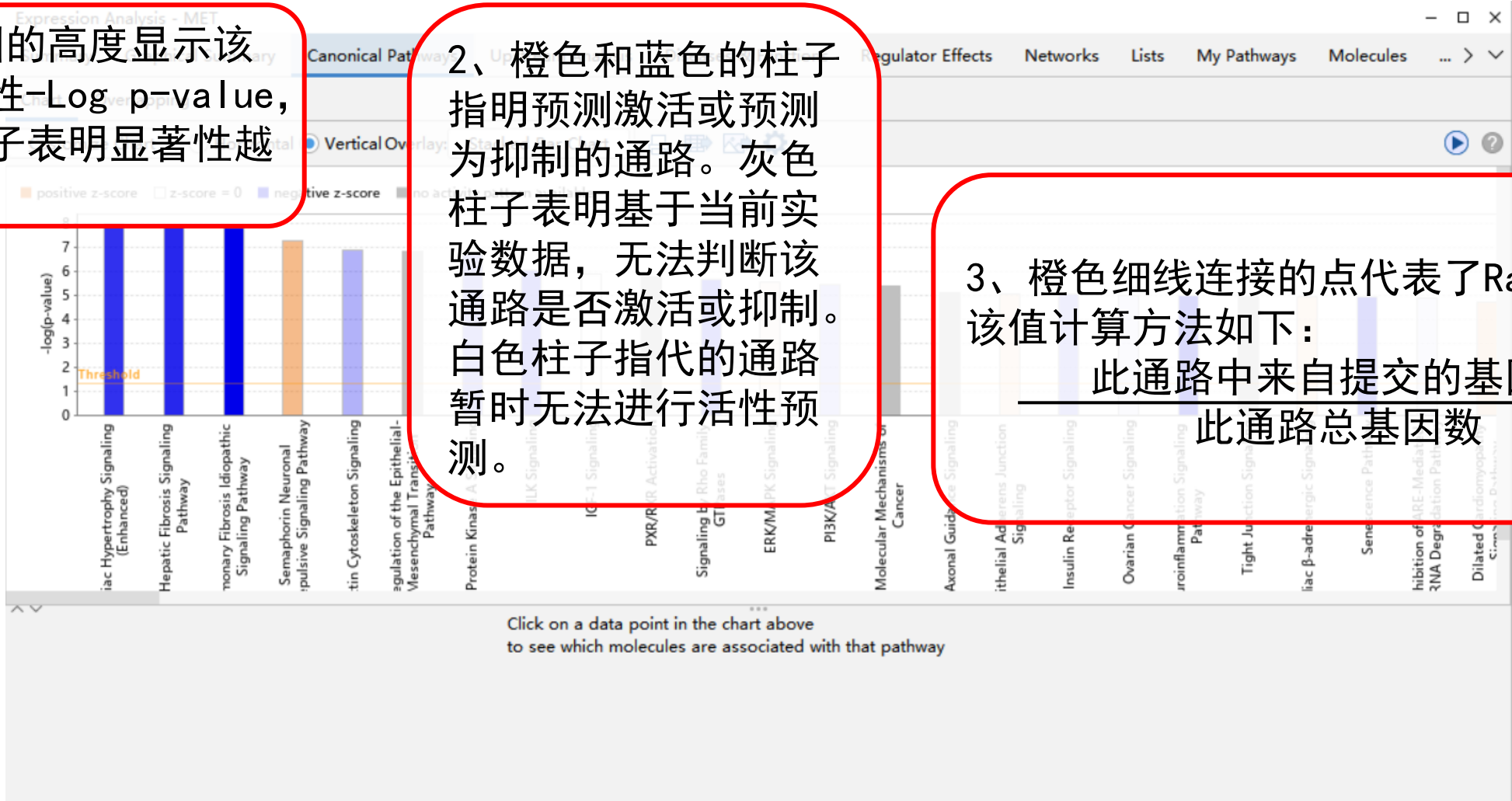
Selected/Total molecules: 0 / 19



1、柱状图的高度显示该通路显著性-Log p-value, 越高的柱子表明显著性越高。

2、橙色和蓝色的柱子指明预测激活或预测为抑制的通路。灰色柱子表明基于当前实验数据, 无法判断该通路是否激活或抑制。白色柱子指代的通路暂时无法进行活性预测。

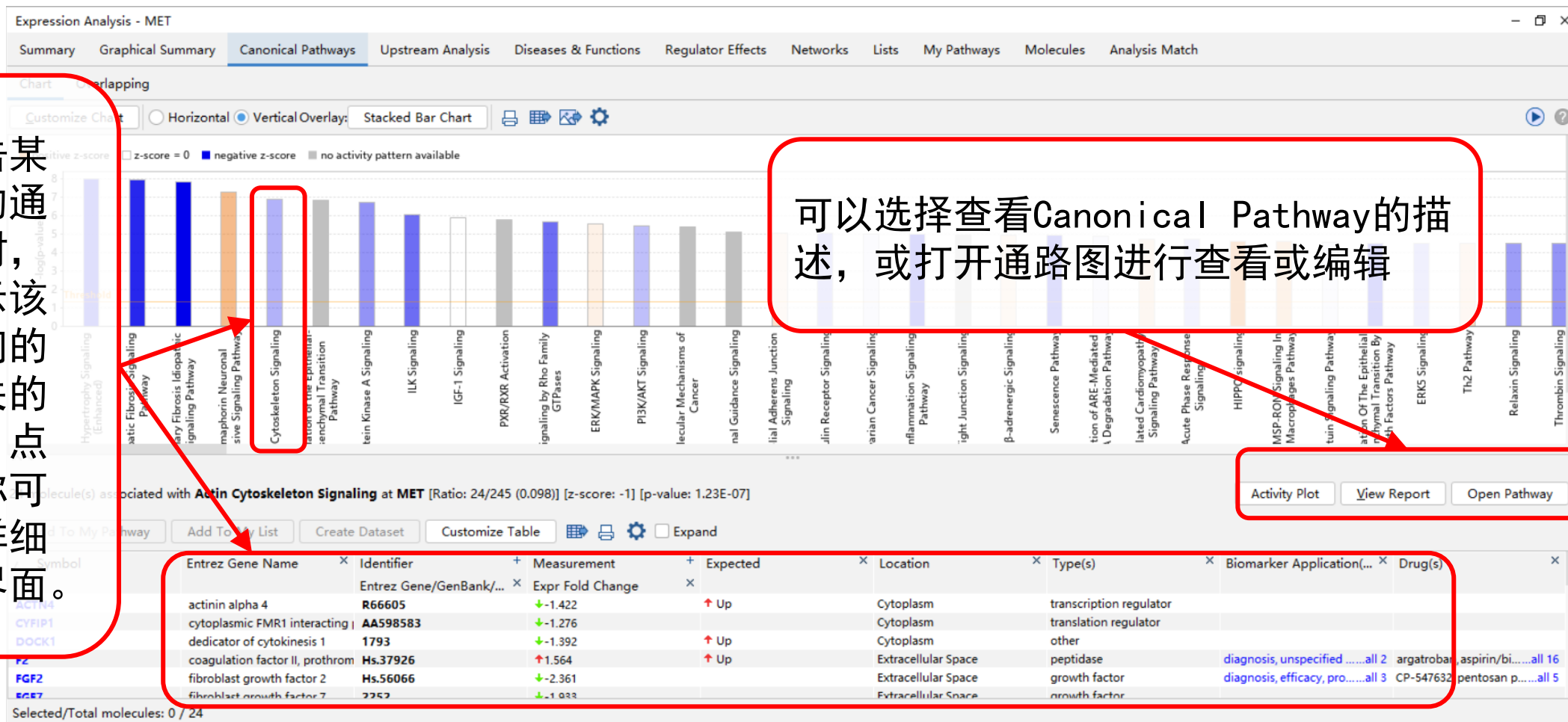
3、橙色细线连接的点代表了Ratio值, 该值计算方法如下:
$$\frac{\text{此通路中来自提交的基因数}}{\text{此通路总基因数}}$$

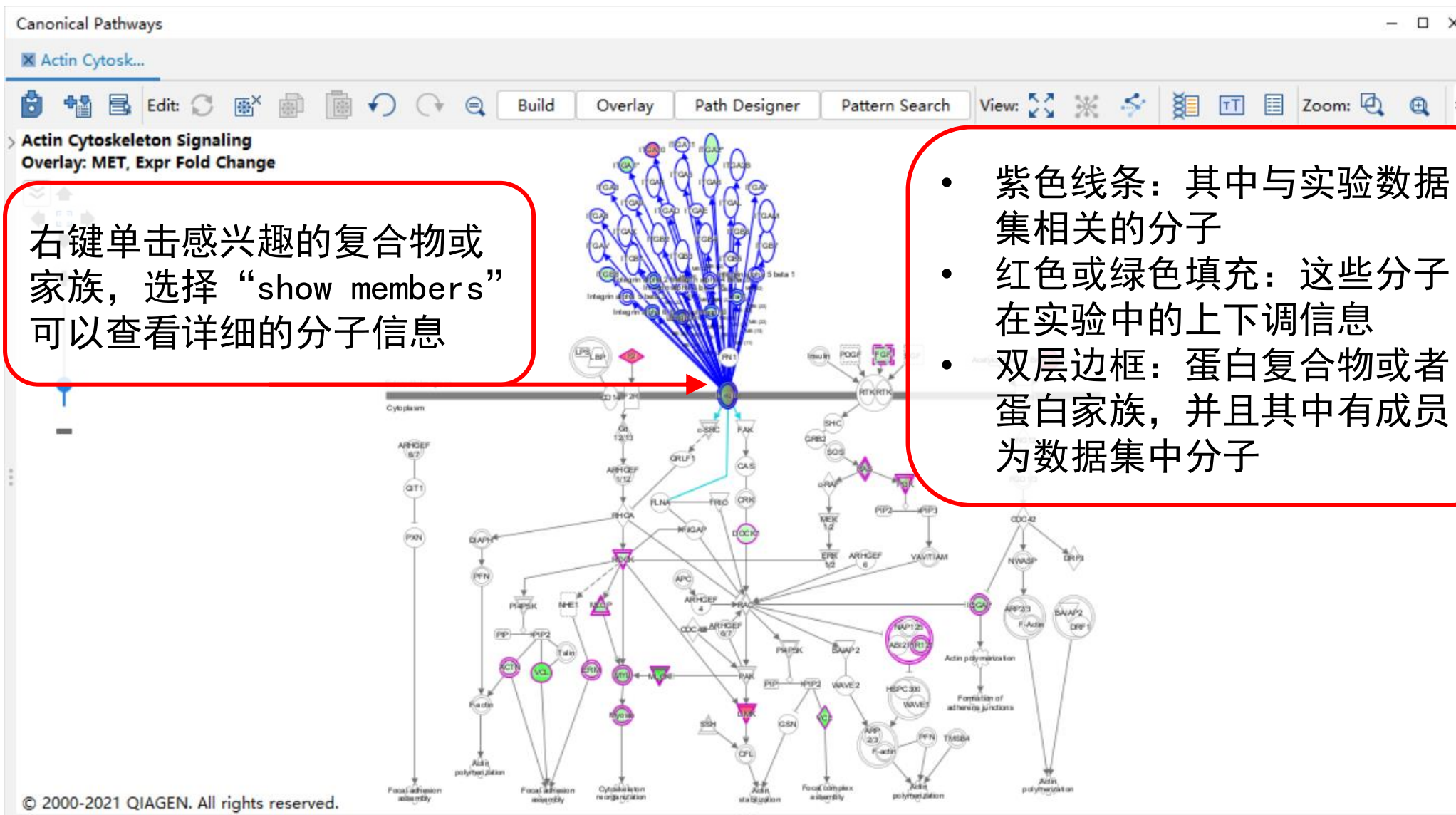


查看感兴趣的Canonical Pathway

当我们单击某个感兴趣的通路的柱子时，下方会显示该通路与我们的数据集相关的分子信息。点击基因名称可以打开其详细注释网页界面。

可以选择查看Canonical Pathway的描述，或打开通路图进行查看或编辑







Downstream Effects Analysis Evidence for Effects

Ovarian tumor (z-score 0.594). Overlap p-value **6.83E-09**

Add To My Pathway Add To My List Create Dataset Customize Table

Expr... 2.496 - 1.268 (1/3)

ID	Genes in dataset	Prediction (based on me...)	Expr Fold Change	Findings
2146	EZH2	Increased	↑2.496	Increases, (1)
AA430504	UBE2C	Affected	↑2.284	Affects, (3)
Hs.24297	MEN1	Decreased	↑1.868	Decreases, (4)
W25590	CPSF1	Affected	↑1.744	Affects, (2)
AA455102	HSPA2	Affected	↑1.721	Affects, (1)
3273	HRG	Affected	↑1.699	Affects, (1)
Hs.89887	TBXA2R	Affected	↑1.667	Affects, (1)
AA479623	MAST1	Affected	↑1.618	Affects, (2)
2305	FOXM1	Affected	↑1.614	Affects, (1)
T82022	CEP65	Affected	↑1.597	Affects, (1)
R91503	ABCC2	Affected	↑1.596	Affects, (1)
3984	IL16	Affected	↑1.564	Affects, (1)
3603	FZ	Affected	↑1.564	Affects, (1)
Hs.37926	PCLAF	Affected	↑1.563	Affects, (1)
9768	MVB12A	Affected	↑1.545	Affects, (1)
Hs.106597	NPC1L1	Affected	↑1.535	Affects, (1)
N73115	ADORA1	Affected		
H21045				

Selected 0 / 131

HRG: Literature indicates this gene is involved in Ovarian tumor but does not indicate whether it increases or decreases it.

功能分组及统计结果

关系预测依据

查看相关文献

这列为上传数据中的基因表达值

获得感兴趣的功能列表

源资科

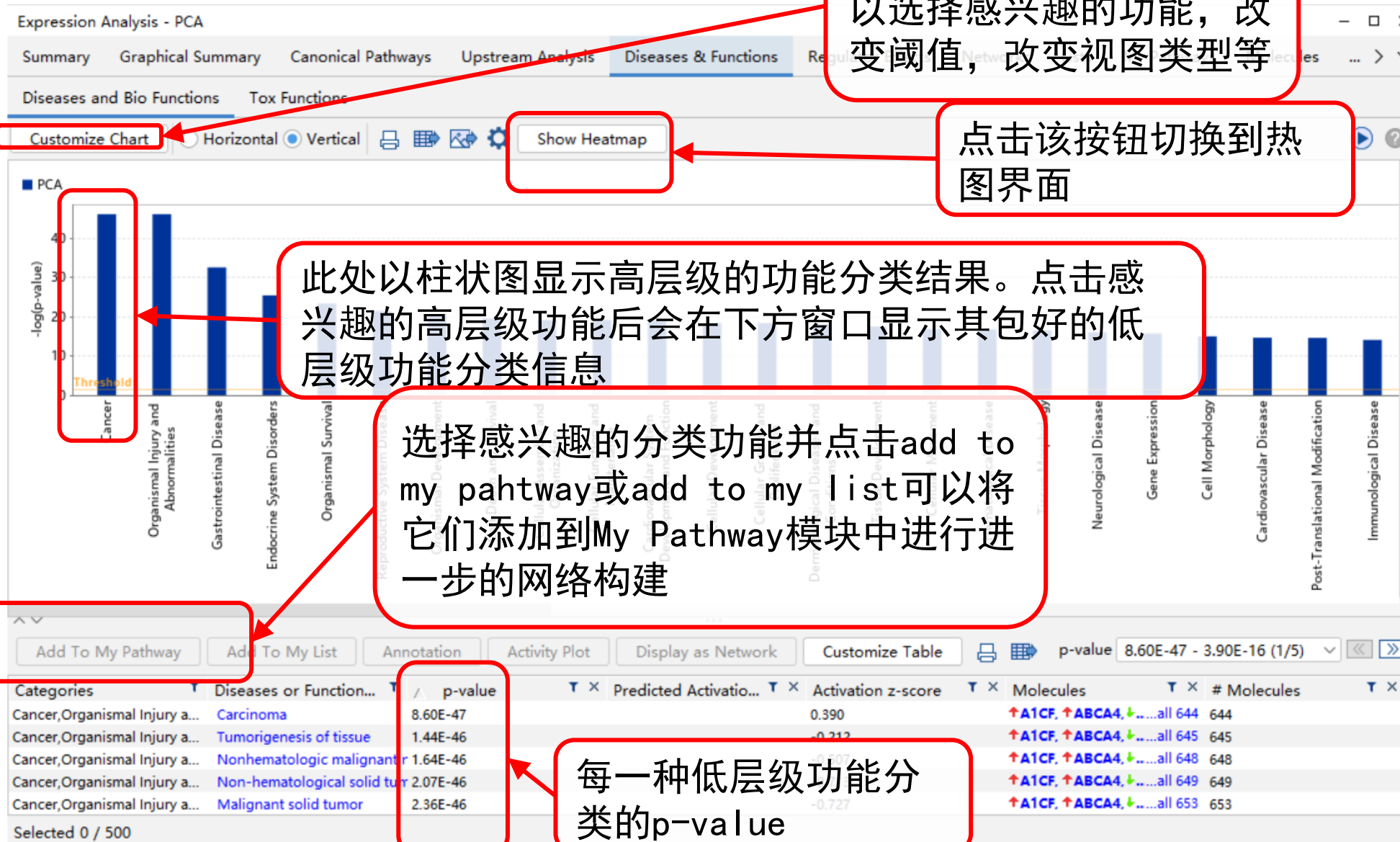
点击Customize Chart可以选择感兴趣的功能，改变阈值，改变视图类型等

点击该按钮切换到热图界面

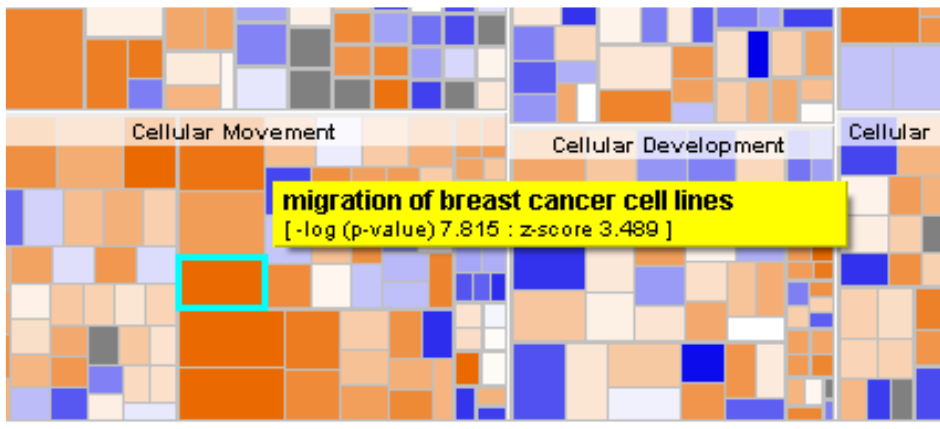
此处以柱状图显示高层级的功能分类结果。点击感兴趣的高层级功能后会在下方窗口显示其包好的低层级功能分类信息

选择感兴趣的分类功能并点击add to my pathway或add to my list可以将它们添加到My Pathway模块中进行进一步的网络构建

每一种低层级功能分类的p-value



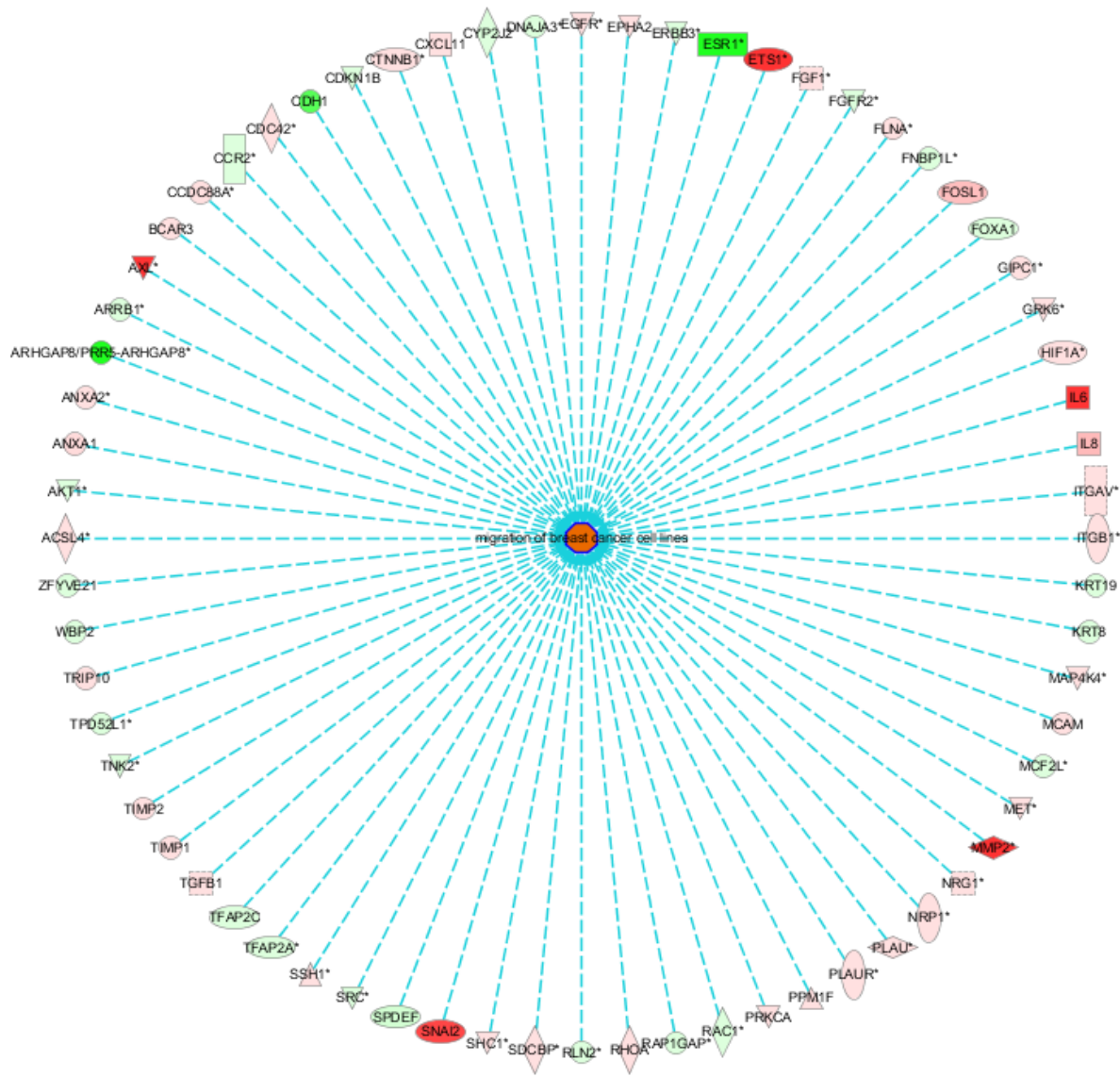
将疾病和功能以通路图显示



There are 649 unique molecules selected

Categories	Diseases or Function...	p-value
Cancer, Organismal Injury a...	Carcinoma	8.60E-47
Cancer, Organismal Injury a...	Tumorigenesis of tissue	1.44E-46
Cancer, Organismal Injury a...	Nonhematologic malignant r	1.64E-46
Cancer, Organismal Injury a...	Non-hematological solid tum	2.07E-46
Cancer, Organismal Injury a...	Malignant solid tumor	2.36E-46
Cancer, Organismal Injury a...	Extracranial solid tumor	3.84E-46

Selected 1 / 500



- Upstream regulator analysis 是基于Ingenuity® Knowledge Base中记录的 transcriptional regulators (TR)及其target genes间先验的互作关系进行分析的工具。
- 该分析工具告知在您的数据集中有多少已知的靶基因及其转录调控子，并通过和文献比对转录调控子及其靶基因可能的作用关系来预测本实验中它们的作用方向（如实验样本相对于对照组的表达量变化
- IPA对转录调控子的定义非常宽泛–任何能够影响其他分子表达量变化的均可成为转录调控子，如转录因子、microRNA、激酶、化合物或药物等。

Upstream Regulators 结果查看

源资科技

选择特定的转录因子及其靶

点击以筛选
分子类型

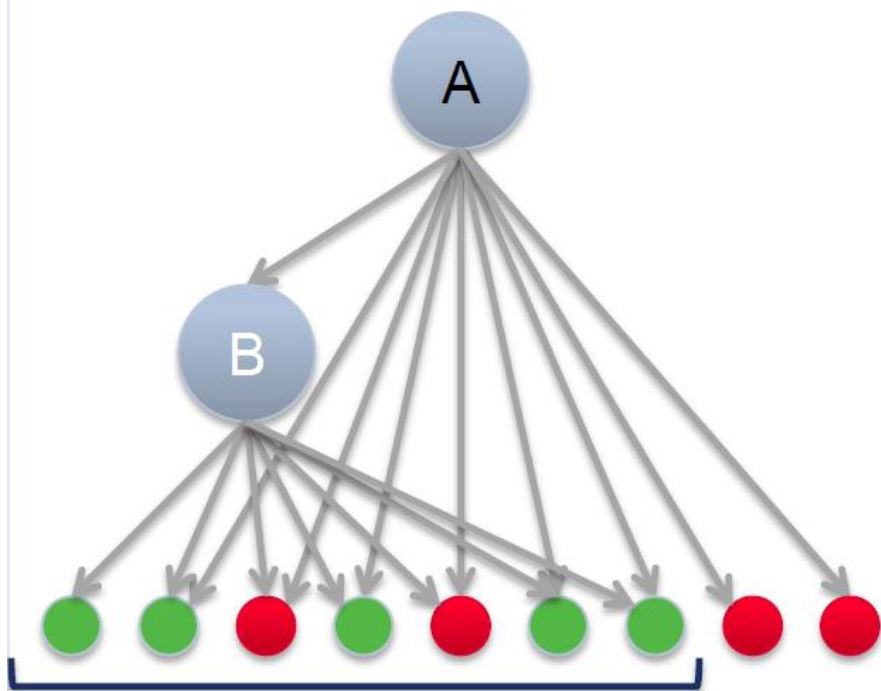
转录调节因子参考文献

点击基因名称
可以查看该转
子的所有文献
信息

鼠标置于Prediction 列上
方可以查看预测该TR会激活
或抑制对应基因判断依据

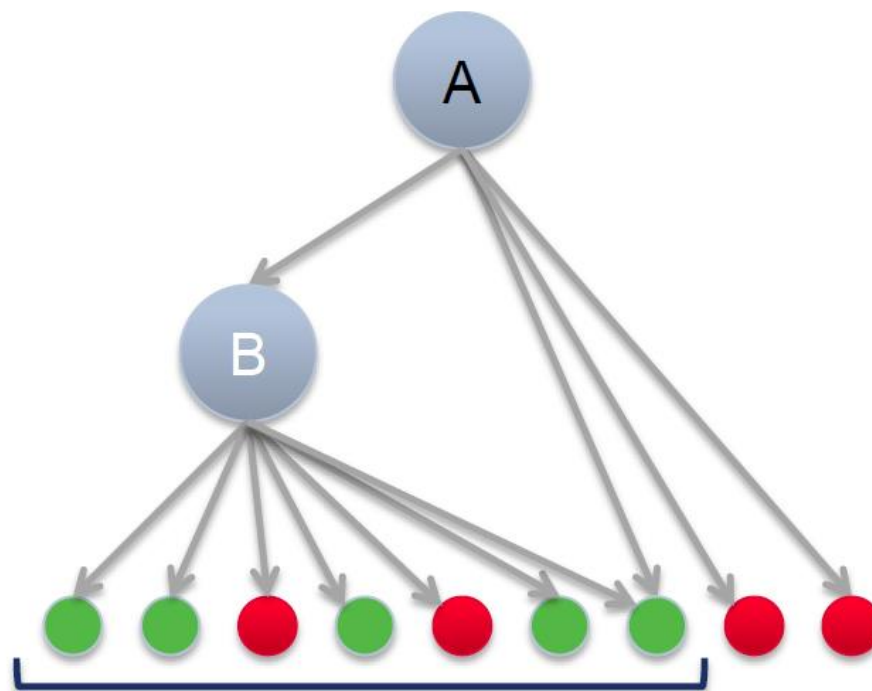
ID	Genes in dataset	Prediction (based on meas...	Expr. Fold Change	Findings
2146	EZH2	Affected	↑1.230	Regulates, (2)
2305	FOXM1	Affected	↑1.216	Regulates, (1)
TP53	Hs.19383	Affected	↑1.200	Regulates, (2)
trastuzumab	Hs.151363	Affected	↑1.188	Regulates, (1)
8-bromo		Activated	↑1.183	Upregulates, (3)
FGF2		Inhibited	↑1.136	Downregulates, (1)
FOS		Activated	↑1.133	Upregulates, (1)
KRAS		Inhibited	↑1.104	Downregulates, (1)
		Affected	↑1.097	Regulates, (2)
		Affected	↑1.084	Regulates, (2)
		Affected		Regulates, (1)
		Activated		Upregulates, (1)
6901	TAZ	Affected		Regulates, (2)
4790	NFKB1	Affected	↑1.018	Regulates, (1)
7277	TUBA4A	Affected	↓-1.001	Regulates, (2)
EGF	N77512	Affected	↓-1.016	Regulates, (2)
AGT	4613	Activated	↓-1.034	Downregulates, (2)
NSUN6	3434	Activated	↓-1.054	Downregulates, (2)
forskolin	6310	Affected	↓-1.071	Regulates, (2)

上游分子**可能**会通过其下游的调控子进行调控



共享 7个更下游靶基因中的6个

上游分子**不太可能**会通过其下游的调控子进行调控



共享 7个更下游靶基因中的1个

源资科技

源资科技

- Causal Network Analysis (因果网络分析) 可识别控制您数据集中基因表达的上游分子, 可视化您正在评估的疾病和功能, 了解主调节因子对该疾病或功能的影响, 并深入了解支持这些关系的证据。此外, 还可以通过干预分子或功能, 将假设与评估的标准联系起来, 提高预测能力。

源资科技

源资科技

源资科技

建立一个Causal Network Analysis (即Core Analysis中)

Create Expression Analysis - [analysis : xample Dataset - Prostate]

General Settings ?

Networks Interaction & Ca... ?

Node Types All ?

Data Sources All ?

Confidence Experimentally... ?

Species All ?

Tissues & Cell Lines All ?

Mutation All ?

Advanced **Save As Default**

Generate the following Networks (increases analysis time)

- Interaction networks**
- Include endogenous chemicals Molecules per network: 35 Networks per analysis: 25
- Genes are always included*
- Causal networks**
- Score master regulators for relationships to diseases, functions, genes, or chemicals (max 50)
- Score using causal paths only

Add functions and genes/chemicals [X]



Genes & Chemicals Diseases & Functions

differentiation Search

- Matching Diseases & Functions
 - Cellular Development
 - development
 - Development of cells [terminal differentiation]
 - differentiation
 - Differentiation
 - Differentiation of cells [cell differentiation,regulation of cell differentiation,...]
 - Differentiation of connective tissue [connective tissue differentiation,conjunctive
 - Differentiation of lymphatic system cells [lymphatic system cell differentiation]
 - Differentiation of mononuclear leukocytes [mononuclear phagocyte differentiat
 - Differentiation of connective tissue cells [connective tissue cell differentiation]
 - Differentiation of lymphoid cells [lymphoid cell differentiation,differentiation of
 - Differentiation of nervous system [neurological system differentiation differentiat

OK Cancel

源资科技

Add To My Pathway Add To My List Activity Plot **Customize Table**  

Master ...	Expr...	Mol...	Part...	Depth	Pre...	Note	Net...	Target...	Causal network	Targ...	Incr...	Dec...
PTPRM		phosphatase	Akt,all 43	3	Inhibited		1.00E-04	↑AB... ..all 159	159 (43)	42	HNF1B...all 3	topo... ..all 1
SPN		transmemb...	↓AGT ...all 57	3	Activated		1.00E-04	↑AB... ..all 205	205 (57)	55	beta-... ..all 1	HNR... ..all 3
FCN-159		chemical dr...	AMPK...all 43	3			1.00E-04	↑AD... ..all 159	159 (43)			
TSC22D1		transcriptio...	AKT1, ...all 50	3			6.24E-23	↑AB... ..all 191	191 (50)			
trichosanthin		chemical dr...	AKT1, ...all 55	3			1.86E-22	↑AB... ..all 187	187 (55)			
miR-96-5p (ar		mature micr...	Akt,all 25	3			3.03E-22	↑AB... ..all 153	153 (25)			
SMARCA4		transcriptio...	AR, B... ..all 8	2			4.11E-22	↑AB... ..all 153	153 (8)	8		FN1,all 5
KRAS		enzyme	Akt,all 24	2			6.07E-22	↑AB... ..all 152	152 (24)	24	5-fl... ..all 21	DGCR8...all 7
SVIL		other	APEX1...all 47	3			1.30E-21	↑AB... ..all 195	195 (47)	46	ERG ...all 1	doxo... ..all 1
PFDNS		transcriptio...	Ap1, ...all 27	3			1.91E-21	↑AB... ..all 166	166 (27)	26		
Arf		group	AKT1, ...all 50	3			2.98E-21	↑AB... ..all 182	182 (50)	45		
XRCC6	↑1.273	enzyme	AHR,all 59	3			3.97E-21	↑AB... ..all 198	198 (59)	54	CD40... ..all 3	5-aza... ..all 3
Jmy-p300		complex	AKT1, ...all 44	3			4.55E-21	↑AB... ..all 182	182 (44)	43		
Scf		complex	AR,all 49	3			4.97E-21	↑AD... ..all 152	152 (49)	42		
TMF1		transcriptio...	AKT1, ...all 43	3			5.03E-21	↑AB... ..all 160	160 (43)	42	beta-... ..all 2	ESR1 ...all 1
cobalt		chemical to...	APEX1...all 45	3			6.33E-21	↑AB... ..all 186	186 (45)	43		
TRIM29		transcriptio...	AKT1, ...all 49	3			7.59E-21	↑AB... ..all 185	185 (49)	48	TP63 ...all 1	miR-... ..all 1
bendamustin		chemical dr...	AKT1, ...all 49	3			7.97E-21	↑AB... ..all 182	182 (49)	46		
SAFB		other	Ap1,all 20	3			1.70E-20	↑AB... ..all 153	153 (20)	20		MMP3 ...all 1
SAFB2		other	Ap1,all 20	3			3.23E-20	↑AB... ..all 152	152 (20)	20	MAPK1...all 2	
tucatinib		chemical dr...	Akt,all 44	3			3.36E-20	↑AB... ..all 170	170 (44)	43		
LAMTOR5		other	AKT1, ...all 65	3			4.00E-20	↑AB... ..all 215	215 (65)	62	HOT... ..all 1	miR-... ..all 1
harmine		chemical - e...	2-a... ..all 58	3			4.15E-20	↑AB... ..all 194	194 (58)	56		
AG 1433		chemical - k...	AGall 49	3			4.85E-20	↑AB... ..all 181	181 (49)	47		
USP36		peptidase	Akt,all 43	3			6.78E-20	↑AB... ..all 164	164 (43)	42	PRKCD ...all 2	
RCHY1		enzyme	APEX1...all 44	3			7.05E-20	↑AB... ..all 186	186 (44)	43	Breas... ..all 1	decit... ..all 3
SYVN1		transporter	26sall 52	3		0.509	7.80E-20	↑AB... ..all 189	189 (52)	52	XBP1 ...all 1	
HEXIM1		transcriptio...	AJU... ..all 55	3	Inhibited	-2.392	8.12E-20	↑AB... ..all 202	202 (55)	54	5-aza... ..all 1	
OXR1		kinase	APEX1...all 42	3		1.313	8.43E-20	↑AB... ..all 188	188 (42)	40	Breas... ..all 4	

Customize Table

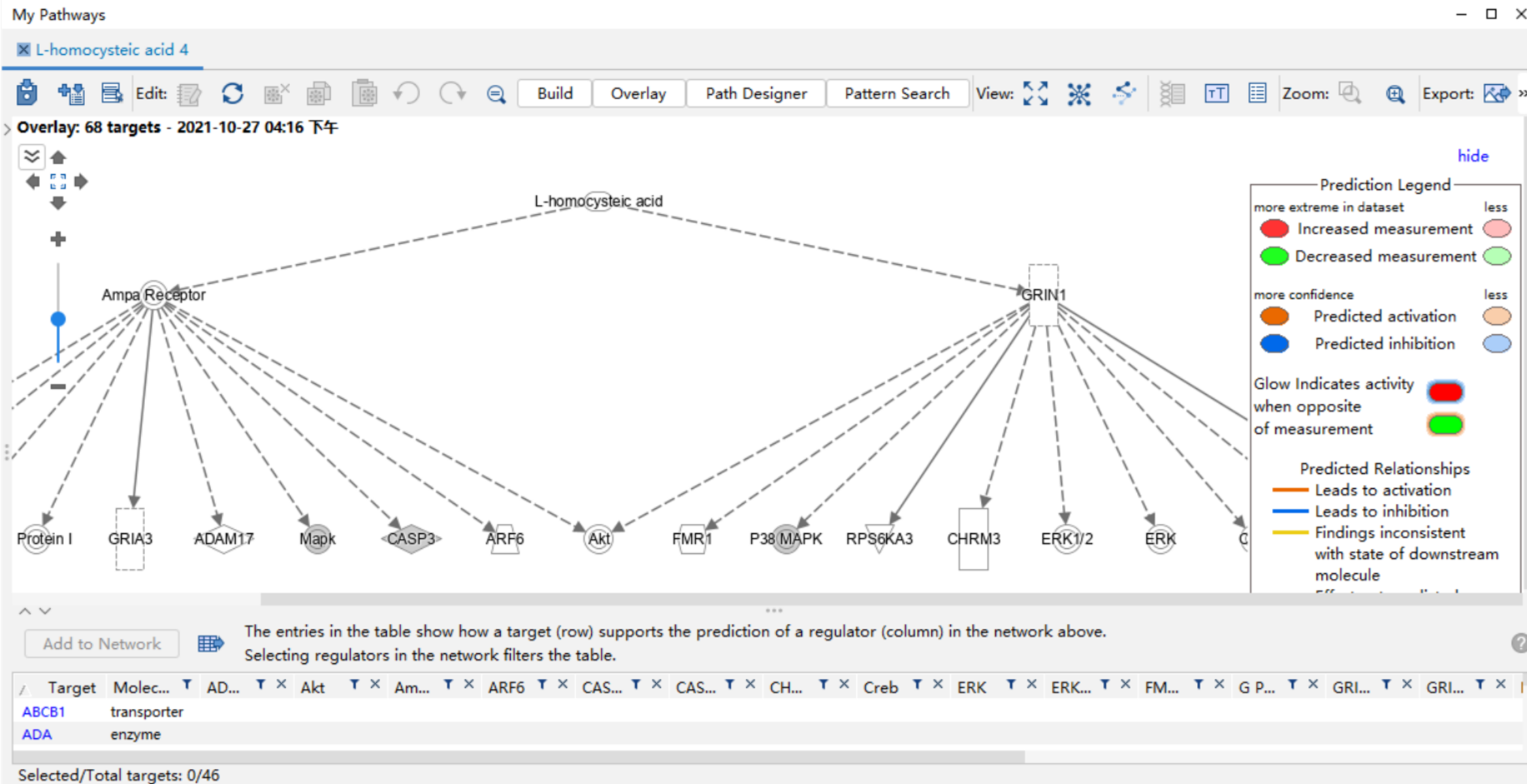
Select column(s) to be displayed in table.

- Select/Deselect all
- Master Regulator
- Expr Fold Change
- Molecule Type
- Participating regulators
- Depth
- Predicted Activation
- Notes
- Activation z-score
- p-value of overlap
- B-H corrected p-value
- Network bias-corrected p-value
- Target Molecules in Dataset
- Causal network
- Target-connected regulators
- Increases/Downstream

OK Cancel

Customize columns displayed in the table

Click on the link to access the Causal Network diagram



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PART

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源资科技

MicroRNA Target Filter

6

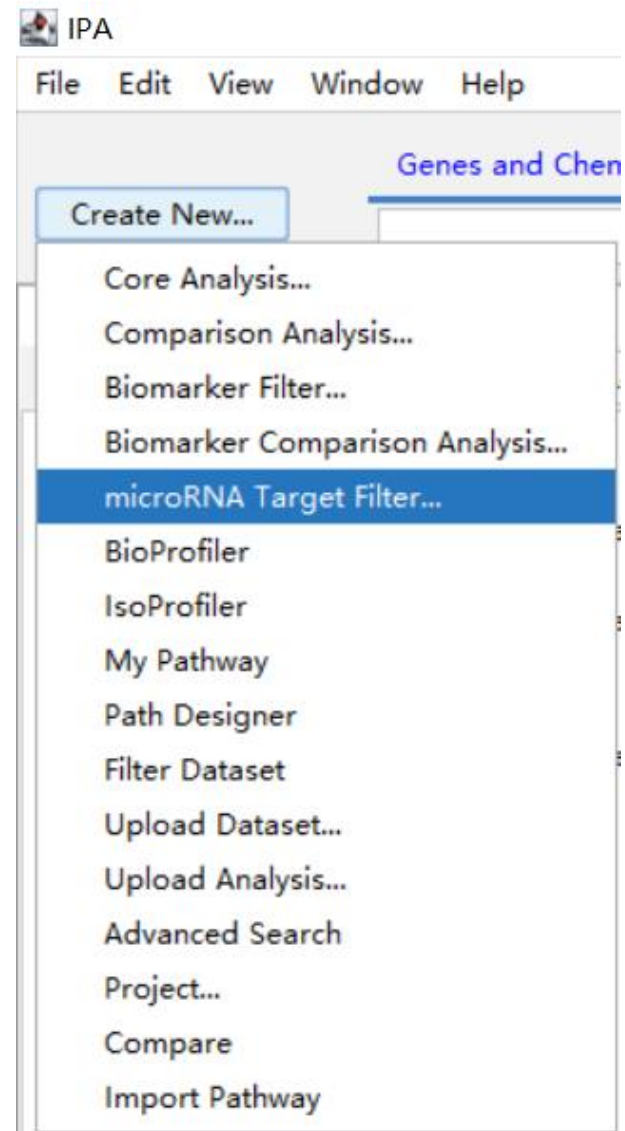
源资科技

源资科技

IPA 中的 microRNA Target Filter 通过 target 的一组 mRNAs 来探索数据集中 microRNA 的生物学特性。

使用该功能需要构建一个表格，该表格将数据集中的 microRNA 与实验观察和预测的 mRNA target 相关联，且用户可使用实验结果和 Ingenuity 知识库提供的信息对 target 进行优先排序。

注意：MicroRNA Target Filter 的数据集必须至少包含一个 microRNA。



microRNA dataset: TWEAK_microRNA_data			Relationship		mRNA	
ID	Symbol	Expr. Fold Change	Source	Confidence	Symbol	Pathway
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	AADACL3	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	AADACL4	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ABCB7	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TarBase	Experimental	ABHD11	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	High (predicted)	ABHD2	Triacylglycerol metabolism
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ABHD3	Anticardiolipin metabolism
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	AC1127152	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ACAP2	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ACBD7	
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ACER2	Ceramide Degradation, ...all 3
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ACOT4	Acyl-CoA Hydrolysis, ...all 2
<input type="checkbox"/>	hsa-miR-1	miR-1-3p (and other miRNA: ↓-3.200)	TargetScan Human	Moderate (predicted)	ACOT7	Acyl-CoA Hydrolysis, ...all 2

寻找潜在的生物学效应、导出筛选结果并保存过滤内容

Add to my pathway → 用做图Build和overlay绘制个性化的通路图

Create Data → 保存搜索结果后进行core analysis

Add to my List → 保存为列表，也可以进行core analysis

源资科技

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PART

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IsoProfiler

7

源资科技

源资科技

IsoProfiler可对RNA-seq数据集中的转录本和异构体进行筛选，找到关键异构体。

IsoProfiler主要有以下三方面用途：

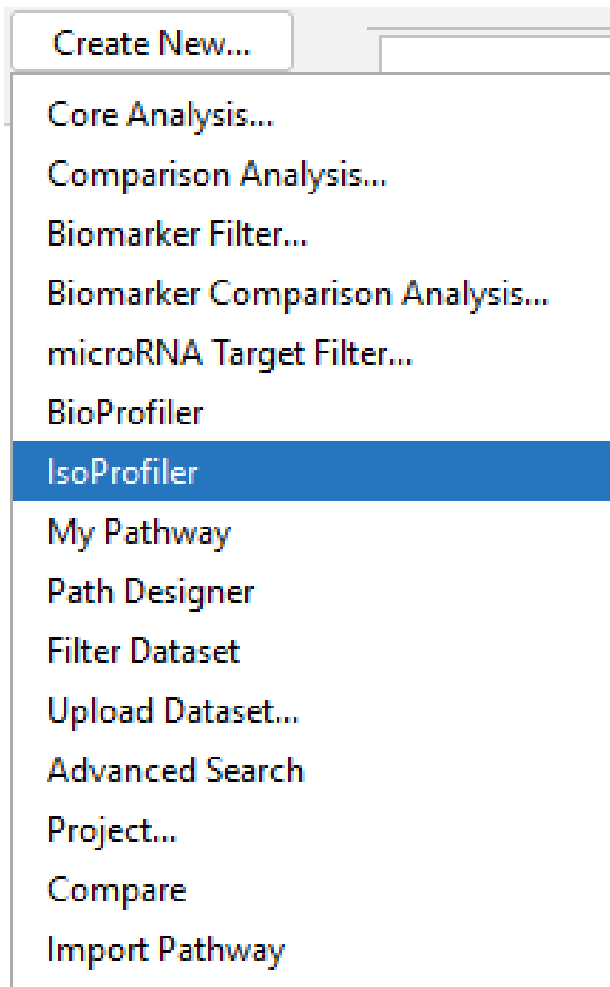
1. 从人类或小鼠数据集中发现具有特殊表达模式的异构体基因：

- 同时具有上调和下调亚型的基因
- 异构体转换——当一个基因最高丰度（例如，最高FPKM或RPKM）的异构体在数据集的实验组和对照组之间不同时
- 转录本仅在某些组织中表达的人类基因（基于人类GTEx数据）

2. 关注数据集中异构体的重要属性，例如：

- Fold change、p值和丰度（强度）截止值（cutoff）
- 与已知疾病或功能相关的亚型
- 蛋白质编码亚型
- APPRIS注释的主要亚型

3. 在一个（或多个）数据集中可视化异构体级别的表达



1. 上传异构体（即转录或剪接变体）RNA-seq数据集。
2. 数据**必须来自人类或小鼠**，并使用RefSeq、Ensembl或UCSC进行比对。不能使用基因名称或基因级ID来比对，必须使用转录本ID。例如，对于人类CDC16基因，比对的转录本ID包括NM_001078645（RefSeq）、ENST0000360383（Ensembl）或uc001vuk（UCSC）。
3. 数据集必须只有一个来源，即只有Ensembl或只有RefSeq，不能混用。因为每个来源可能对每个基因的转录本有不同的“模型”，因此不能混用。
4. **不建议使用UCSC ID**，因为蛋白质编码过滤器不适用于UCSD ID。
5. 可以直接上传CuffDiff Isoform .diff数据文件（以及随附的跟踪文件）。

IsoProfiler; Universe = Human isoforms from RefSeq with Expr Log Ratio and Expr Intensity/RPKM/FPKM/Counts

Symbol ADAM12 - CXCL12 (p1 of 5)

Symbol	Molecule T...	Gene-level Disease or Function	Expression Patterns	Isoform-specific Disease or Function
ADAM12	peptidase	Abnormal morphology of aortic valve, Abnormal morphology of... all 98	164 GTEx - 4 1 - - - - 1	Adhesion of fibroblast cell lines, Adhesion of hepatic... all 35 55
ADAM15	peptidase	Abnormal morphology of aortic valve, Abnormal morphology of... all 78	96 GTEx 4 3 - 4 - - - - -	Adhesion of breast cancer cell lines, Adhesion of mel... all 12 7
ALOX15B	enzyme	Accumulation of lipid, Adhesion of breast cancer cell lines, Adhe... all 44	84 GTEx 8 6 -	Growth of tumor, Hyperplasia of prostate gland, Oxyge... all 6 5
APP	other	Abnormal emotional behavior, Abnormal initiation of locomoti... all 972	4750 GTEx - 6 - - - 7 13 - 11 17 -	Acute myocardial infarction, Amyloidosis of vasculature... all 13 16
ATP2A3	transporter	Activation of caspase, Activation of embryonic cell lines, Activati... all 33	73 GTEx - - 2 - - - 5 - - 1 - - 3 5 -	Activation of embryonic cell lines, Activation of epitheli... all 6 9
ATP2B3	transporter	Aldosterone producing adrenocortical adenoma, Brain astrocyt... all 25	60 GTEx 7 2 2 4 10 - - 13 - - 5	Homeostasis of Ca ²⁺ , Quantity of Ca ²⁺ ... all 2 7
BCCIP	other	Amplification of centrosome, Anchoring of microtubules, Bladde... all 23	24 GTEx - - -	Homologous recombination repair of DNA double str... all 2 2
BC12L11	other	Abnormal function of B lymphocytes, Abnormal morphology of... all 321	758 more 22 y-4.943	Alzheimer disease, Annikis of fibroblast cell lines, Anno... all 19 38

Selected rows 1 / 101

Order	Transcript T...	Isoform Tracks	Protein	Schematic	Amino Aci...	APPRIS	Isoform-specific ...	GTEx	Charts	Claudin vs Luminal new	ID	Ex...	Exp...	Ex
7	protein-coding	APP695	APP695		695	ALTERNATIVE:1	Accumulation of ... all 126	3.439	13 tissues	NM_201414	↑1.134	7.42E-01	25	
3	protein-coding	APP751	APP751		751	ALTERNATIVE:1	Accumulation of a... all 58	39.447		NM_201413	↓-1.150	6.76E-01	25	
1	protein-coding	APP770	APP770		770	PRINCIPAL:4	Acute myocardial i... all 13	46.904		NM_000484	↑2.034	1.41E-01	13	
2	protein-coding	L-APP752	L-APP752		752	ALTERNATIVE:1		1.349	6 tissues		-			
4	protein-coding	APP variant 4	APP isoform d		746			0.000			-			
5	protein-coding	L-APP733	L-APP733		733	ALTERNATIVE:1		1.386			-			
6	protein-coding	APP714	APP isoform f ...		714			2.926	7 tissues	NM_001136130	↓-4.963	4.05E-01	11	
8	protein-coding	APP variant 10	L-APP677		677			0.098			-			
9	protein-coding	APP variant 7	APP isoform g		660			0.000	11 tissues		-			
10	protein-codina	APP variant 5	APP isoform e ...		639			0.202	17 tissues	NM_001136129	↓-6.897	3.48E-01	91	

IsoProfiler界面

源咨科技

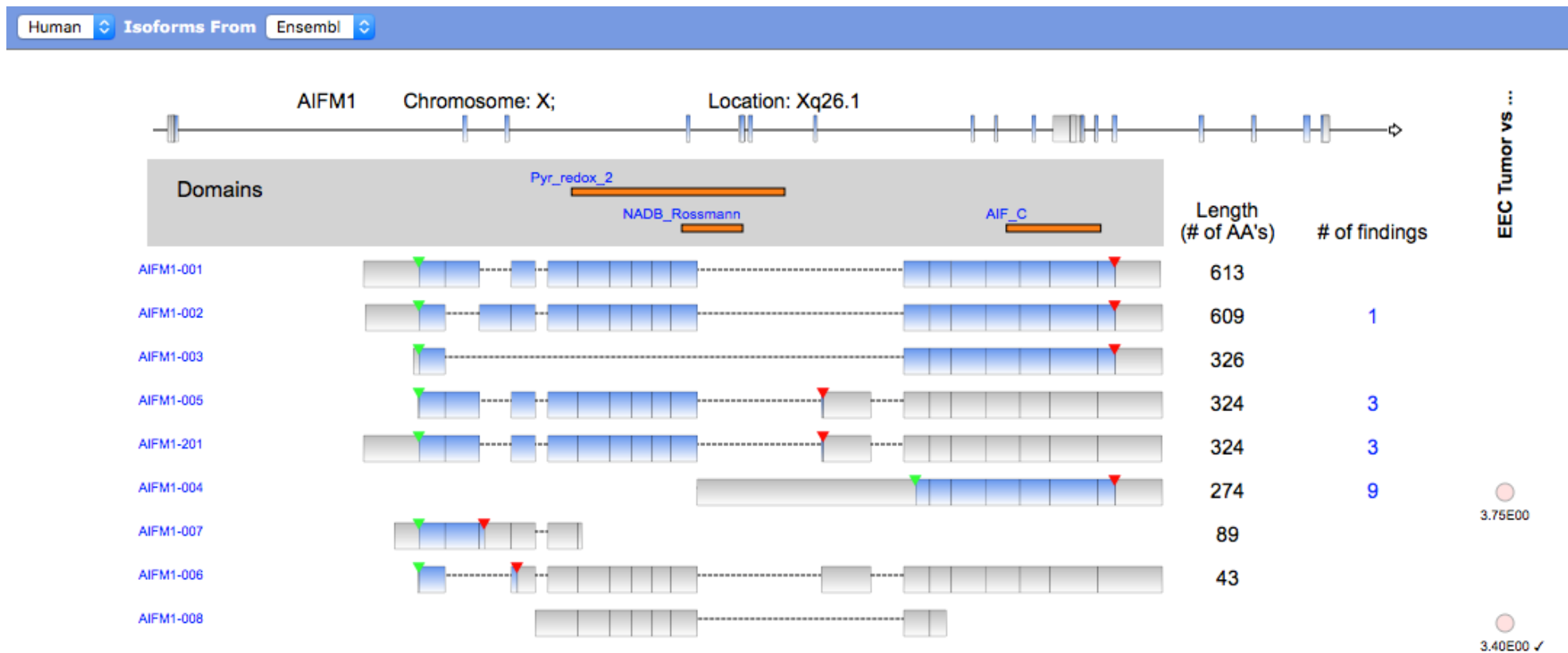
Expression Patterns (表达模式) 列中的虚线表示数据集中不存在基因的已知转录本。

Symbol	Isoform-specific Disease or Function	Expression Patterns	Max Expression Change	Transcript count	Range	Isoform-specific Findings
AGAP2	enzy... Apoptosis, Apoptosis of cancer cells, Apoptosis of tumor cel... all 11	- x - - GTEx 14 - 10 15 8	↓ -4.366	1		10
AHI1	other Chronic phase chronic myeloid leukemia ...all 1	x x x - - - - - - - - GTEx 4 - - 2 - - - 1 - 1 - - 1 - 3 - 1 2	↑ 2.163	1		5
AIFM1	enzy... Production of reactive oxygen species ...all 1	x x x - - GTEx - 8 - - -	↑ 6.640	1		1
ALOX15B	enzy... Growth of tumor, Hyperplasia of prostate gland, Oxygenatio... all 6	● ● ● GTEx 8 6 -	↓ -5490.053	3	5416.212	6
AMOT	other Enlargement of endosomal compartment ...all 1	x - - ● - - GTEx 1 - - 7 - -	↓ -4.191	1		1
AMPH	other Replication of Semliki Forest virus, Replication of Sindbis virus ...all 2	- - - - - x ● - GTEx 2 1 - - - 12 1 -	↑ 22.959	1		2

Selected rows 1 / 498

Order	Transcript Type	Isoform Tracks	Transcript	Protein	Schematic	Amino Aci...	APPRIS	Isoform-specific Disease or Funct...	GTEx	Charts	Claudin vs Luminal new	ID	Expr...	Expr ...	Exp...	Expr ...
1	protein-coding	AIFM1 variant 1	AIFM1 isoform AIF precu...	AIFM1 isoform AIF precu...		613	PRINCIPAL:4		9.072	All tissue media...	NM_004208	x	↓ -1.018	9.71E-01	23548.855	
4	protein-coding	PDCD8-short	PDCD8-short	PDCD8-short		274		Cell death of cervical cancer cell... all 3	0.464		NM_001130846	x	↓ -1.093	8.54E-01	2227.456	
2	protein-coding	AIFM1 variant 2	AIFM1 isoform AIF-exB p...	AIFM1 isoform AIF-exB p...		609	ALTERNATIV...		0.136		NM_145812	x	↑ 1.988	4.40E-01	315.051	
3	protein-coding	AIFSH2	AIFSH2	AIFSH2		324		Production of reactive oxygen s... all 1	0.000		NM_001130847	○	↑ 6.640	1.38E-01	529.458	
5	non protein-coding	AIFM1 variant 6							0.000				-			

- 点击蓝色超链接AIFM1基因，即可显示Isoform视图中有重叠的数据集。
- IsoProfiler中的转录本顺序与Isoform视图中的顺序相同。如果亚型为非蛋白质编码，则排序顺序为从最长到最短的蛋白质编码区，然后是从最长到最短的核苷酸长度。



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IPA文献

8

源资科技

源资科技

期刊: Cell

影响因子: 41.58

关键词: metastasis tumor, microenvironment, pre-metastatic niche, cancer immunology, immune suppression, stem cell niche, immunotherapy...

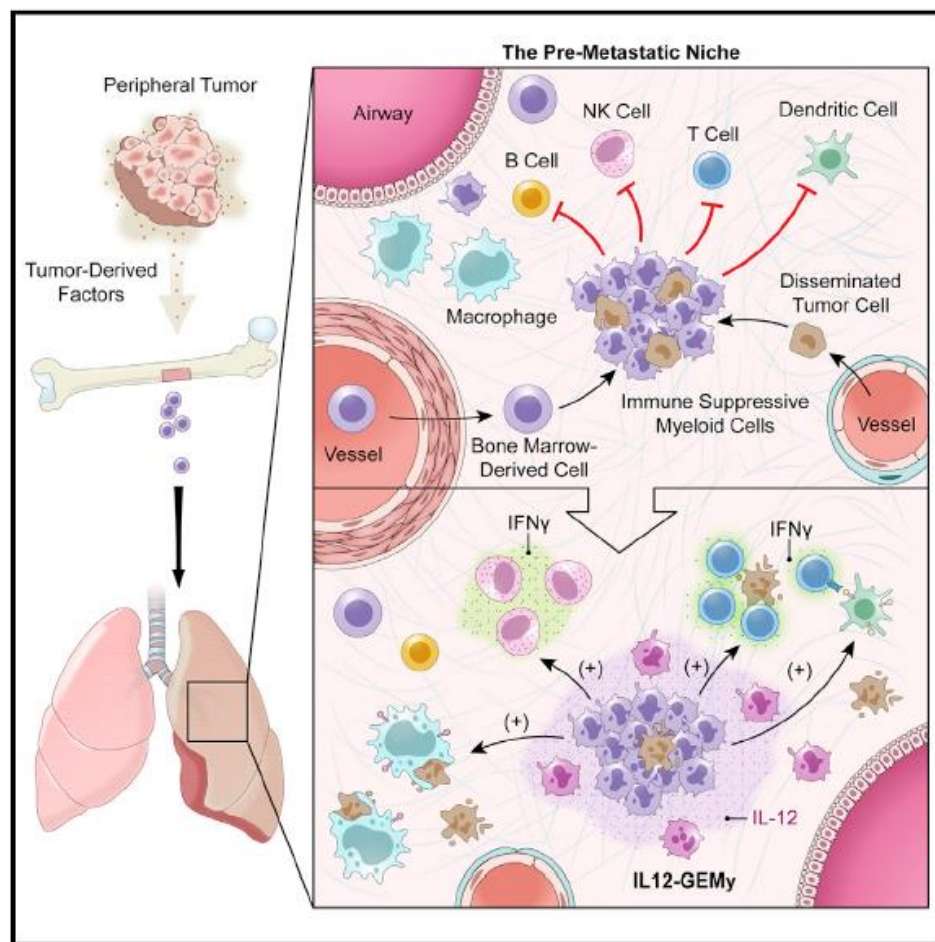
目的: 探索癌症转移过程中的关键生态位调节信号特征

实验对象: 基因工程髓样细胞 (GEMys)

IPA分析: Ingenuity pathway analysis (IPA) indicated a significant enrichment in multiple **pathways** of myeloid cell-mediated immune suppression

Genetically engineered myeloid cells rebalance the core immune suppression program in metastasis

Graphical abstract



Authors

Sabina Kaczanowska, Daniel W. Beury, Vishaka Gopalan, ..., Sridhar Hannenhalli, Michael C. Kelly, Rosandra N. Kaplan

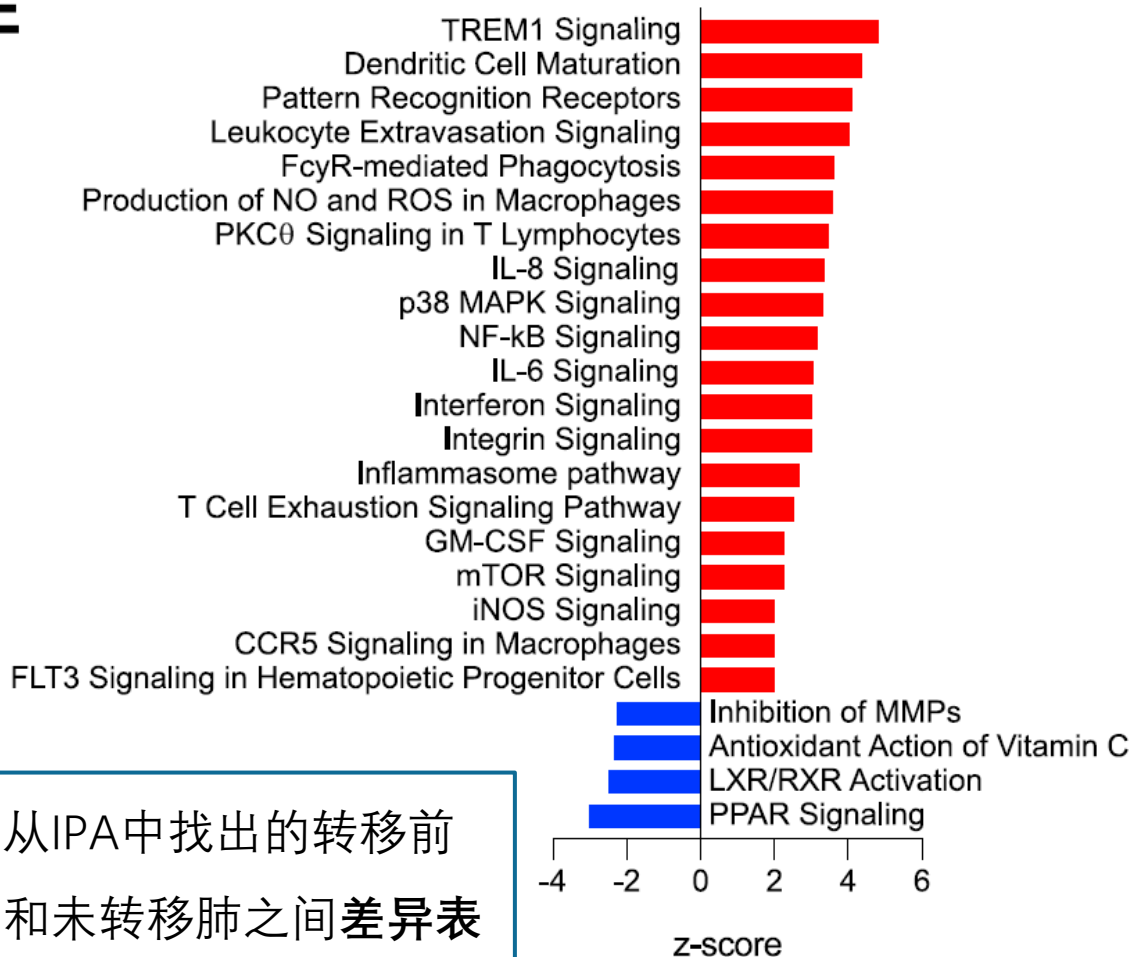
Correspondence

rosie.kaplan@nih.gov

In brief

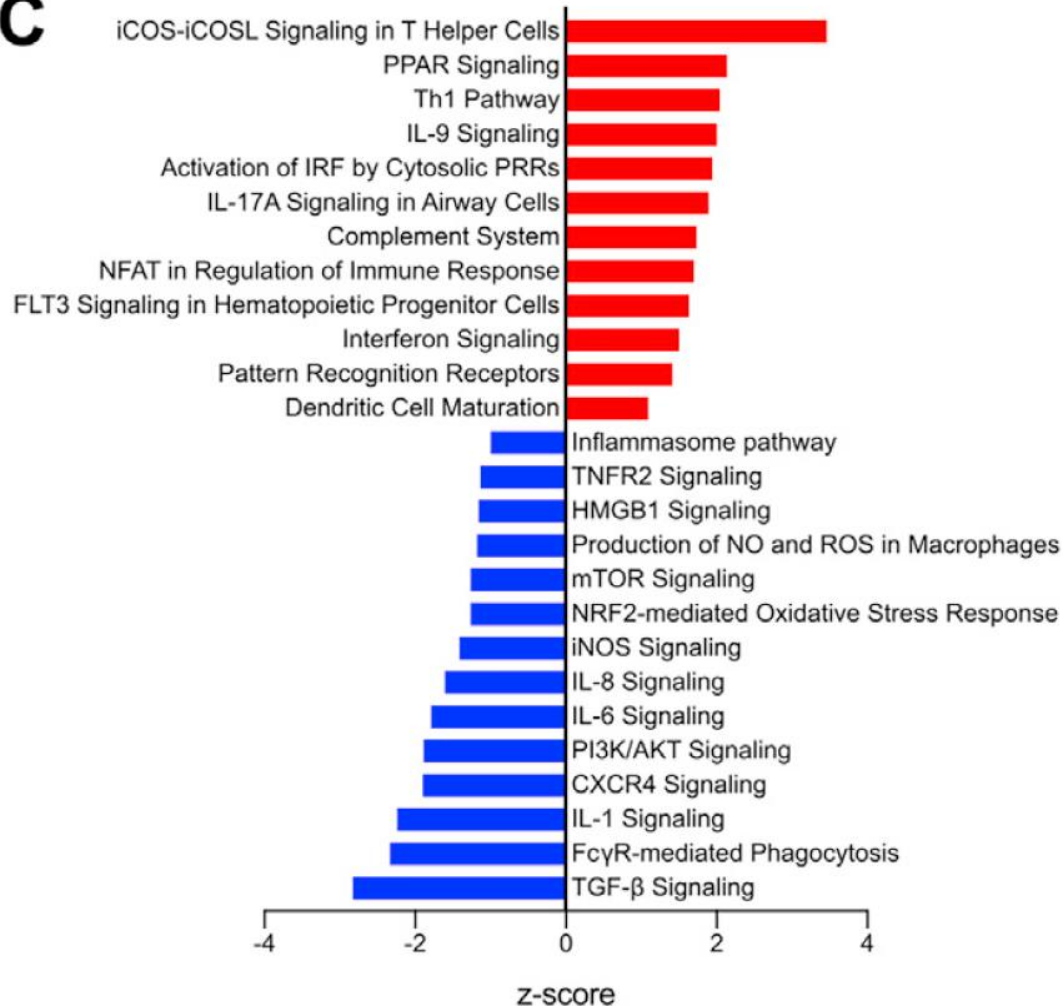
Genetically engineered myeloid cells expressing IL-12 can reverse the immunosuppressive environment developed during metastatic progression by augmenting T cell responses and reducing metastatic burden in preclinical models.

E



从IPA中找出的转移前和未转移肺之间差异表达基因的通路。

C



通过IPA找出的IL12-GEMy治疗小鼠中显著上调和下调的通路。

期刊: Cell

影响因子: 41.58

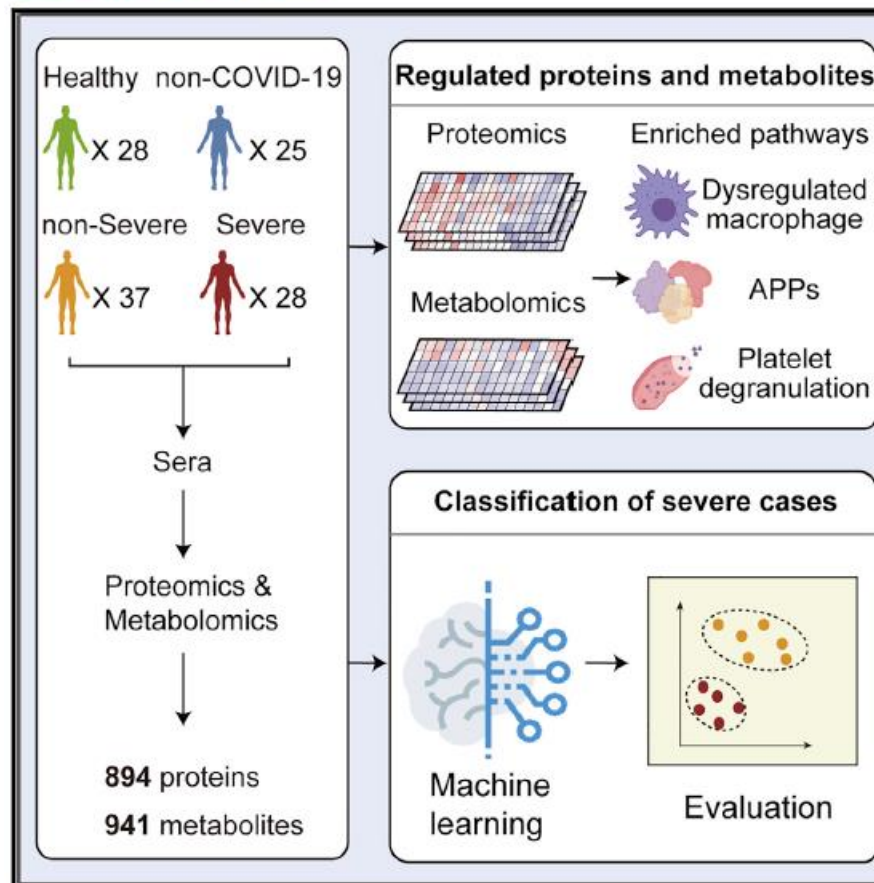
关键词: proteomics,
metabolomics, COVID-19,
serum, severity

研究对象: COVID-19患者血清46份, 正常对照53份

IPA分析: Ingenuity pathway analysis (Kramer et al., 2014) of the regulated proteins identifies most **significantly relevant pathways** with p value of determined based on right-tailed Fisher's Exact Test with the overall activation or inhibition states of enriched pathways were predicted by z-score.

Proteomic and Metabolomic Characterization of COVID-19 Patient Sera

Graphical Abstract



Authors

Bo Shen, Xiao Yi, Yaoting Sun, ...,
Huafen Liu, Haixiao Chen, Tiannan Guo

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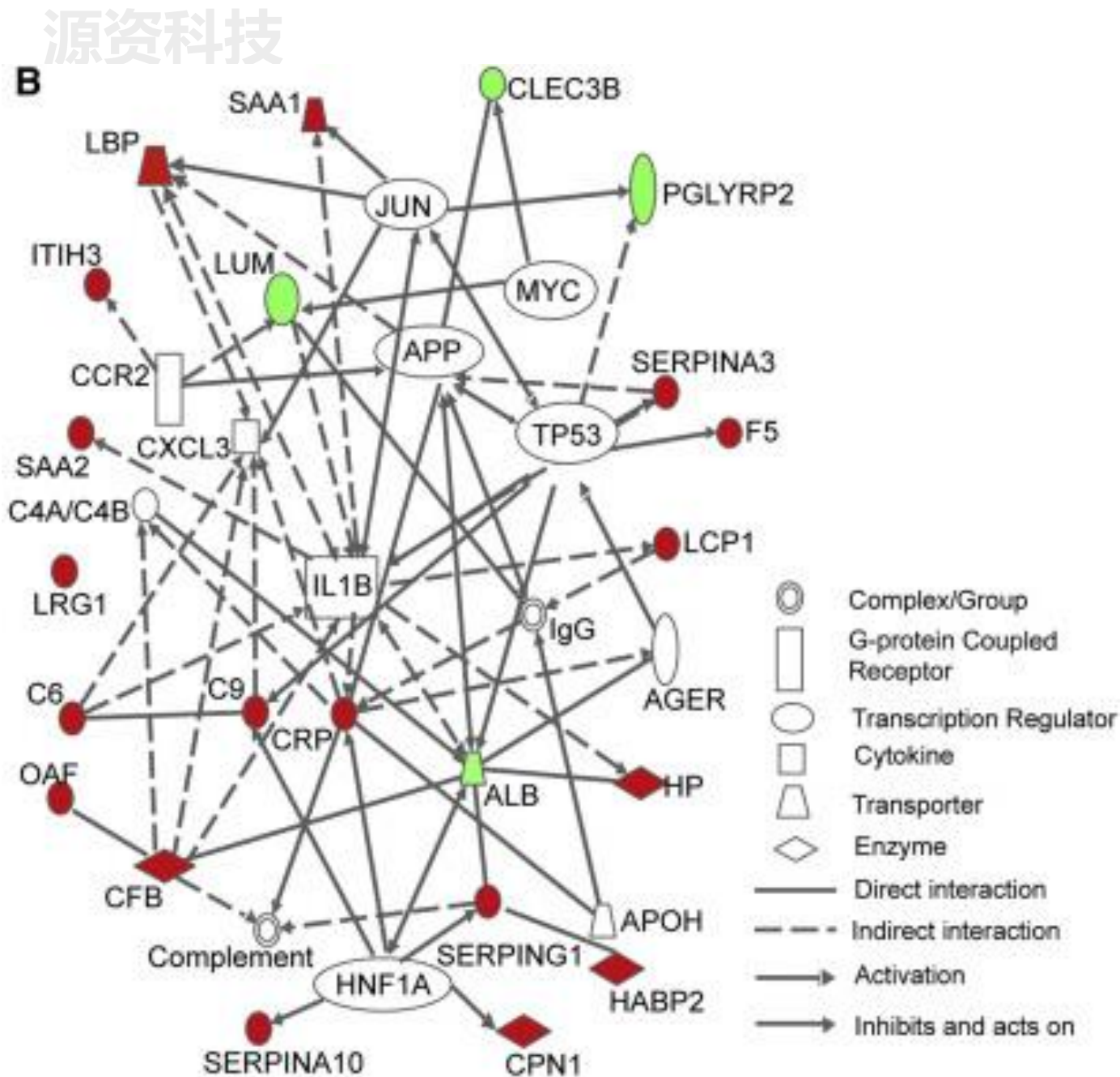
In Brief

Proteomic and metabolomic analysis of COVID-19 sera identifies differentially expressed factors that correlate with disease severity and highlights dysregulation of multiple immune and metabolic components in clinically severe patients.

文献二

研究者基于18名非重症患者和13名重症患者的蛋白质组学和代谢组学数据建立了一个随机森林机器学习模型，从而对29个重要变量进行了排序，包括22个蛋白质和7个代谢物。

如图为优先的**蛋白质网络**。红色和绿色节点分别表示上调和下调的分子。白色节点表示数据集中未检测到的分子。

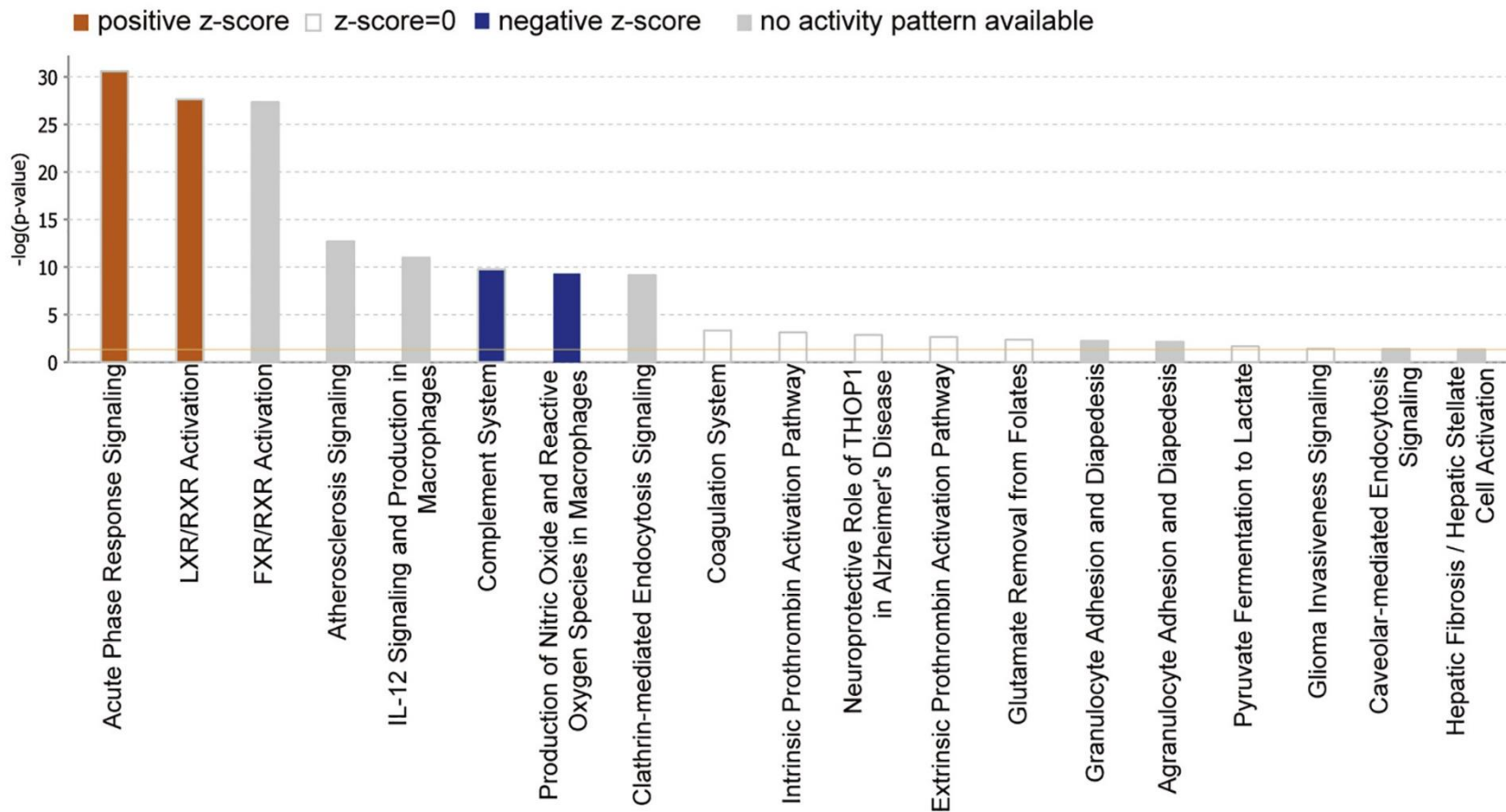


COVID-2019 93种差异表达蛋白的通路分析

IPA预测的最显著相关通路的激活或抑制状态。

源资科技

源资科技



源资科技

期刊: Cancer Cell

影响因子: 31.74

关键词: tumor microenvironment, cancer-associated fibroblast lineages, pancreatic cancer, CyTOF, tumor-restrictive fibroblast...

目的: 完善成纤维细胞异种细胞关系的功能注释和表征

研究对象: 18个小鼠组织和5个自发性肿瘤模型

IPA分析: Ingenuity Pathway Analysis (IPA)

highlighted several differentially engaged

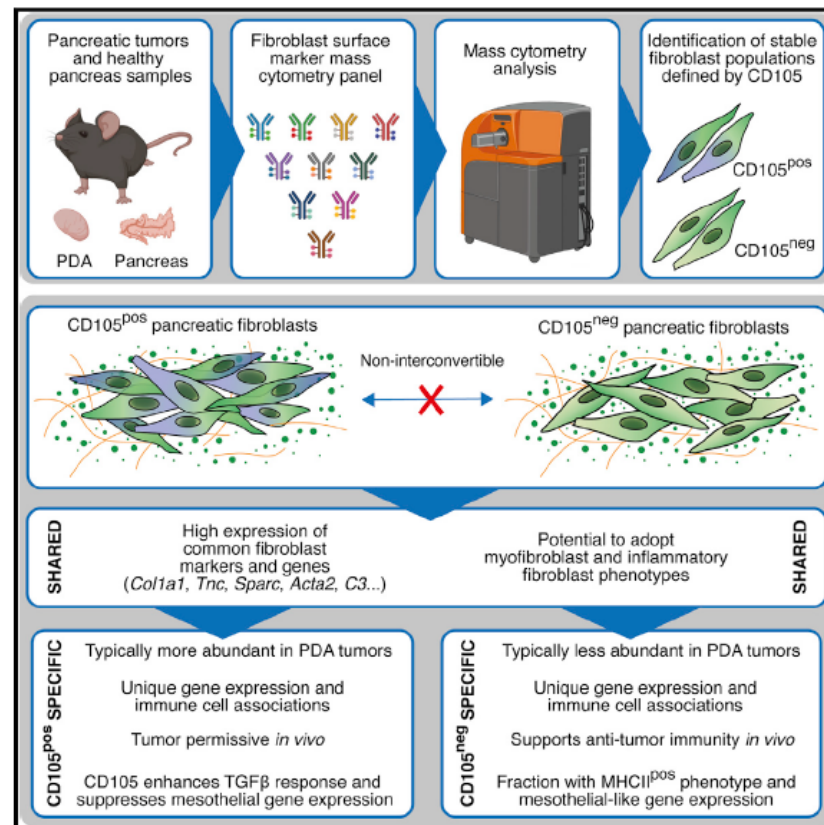
upstream regulators and pathways. IPA

revealed engagement of pathways and upstream regulators with established roles in productive anti-tumor immune responses.

Cancer Cell

Single-cell analysis defines a pancreatic fibroblast lineage that supports anti-tumor immunity

Graphical abstract



Authors

Colin Hutton, Felix Heider, Adrian Blanco-Gomez, ..., Santiago Zelenay, Jennifer P. Morton, Claus Jørgensen

Correspondence

claus.jorgensen@cruk.manchester.ac.uk

In brief

Hutton et al. use mass cytometry to chart stromal cells and describe mesenchymal states and lineages in pancreatic ductal adenocarcinoma. CD105 (*Eng*) expression distinguishes two pancreatic fibroblast lineages with distinct functions. CD105^{pos} fibroblasts are tumor permissive, whereas CD105^{neg} fibroblasts suppress tumor growth in a manner dependent on adaptive immunity.

源资科技

对分离的PDA（胰腺导管腺癌）CAF基因表达进行IPA分析，得到**通路激活评分**。如图为正富集（CD105pos中的富集，黄色）和负富集（CD105neg中的富集，紫色）的图。

源资科技

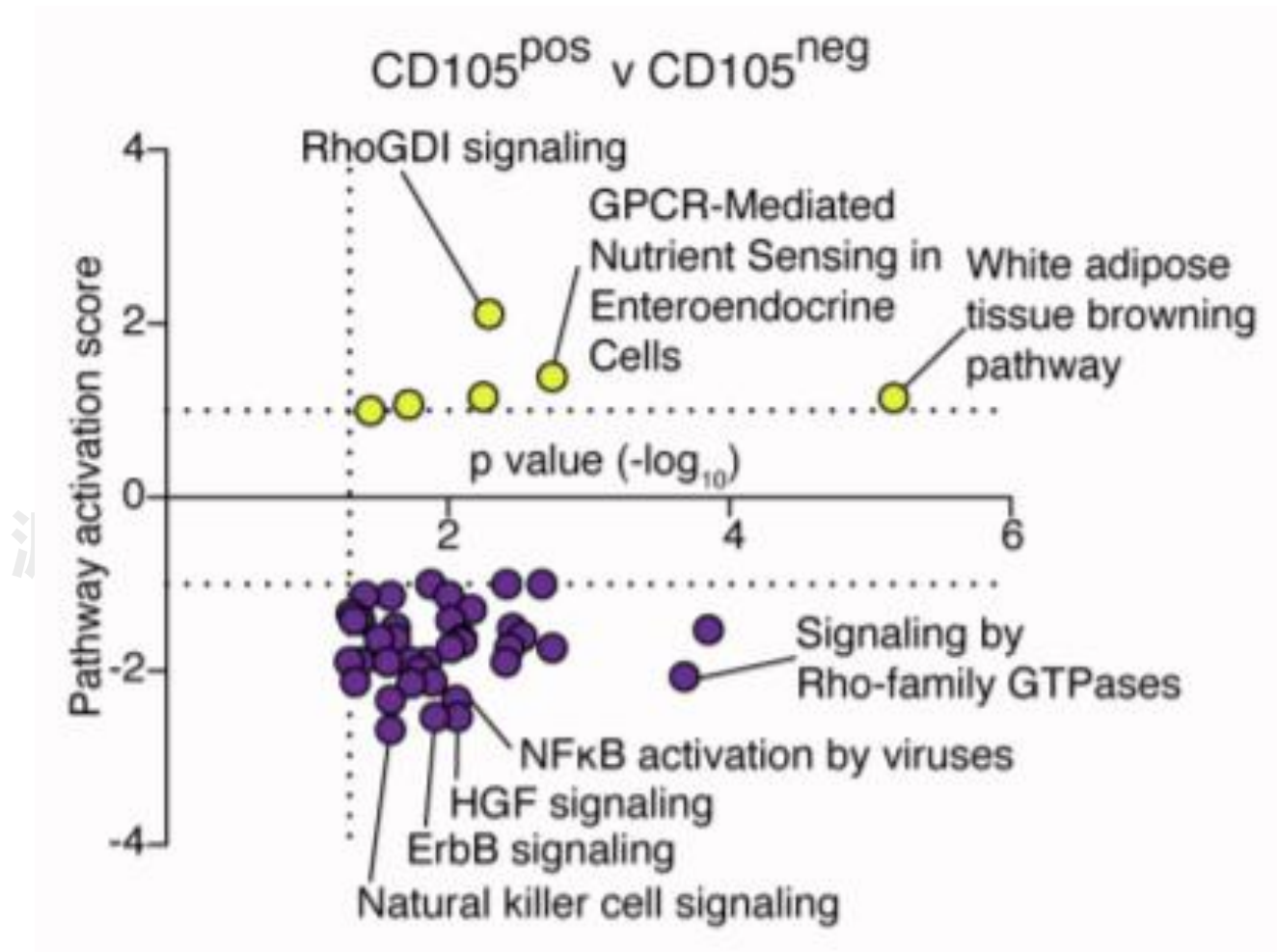


Table S3. Isolation and analysis of CD105pos and CD105neg CAFs, related to Figure 3

IPA Pathway analysis of RNAseq of KPC CD105pos (n=6) and CD105neg CAFs

Ingenuity Canonical Pathways	-log(p-value)	z-score	Molecules
Rho GDI Signaling	2'29	2'111	ARHGAP4, ARHGDIB, ARHGEF15, ARHGEF6, CDH2, CDH23, EZR, GNA14, GNG1
GPCR-Mediated Nutrient	2'74	1'387	ADCY2, ADCY7, CACNA1D, CACNA1H, CACNB2, CACNG7, CACNG8, GNA14, GNG1
P2Y Purigenic Receptor	2'25	1'155	ADCY2, ADCY7, CREB3L3, GNG11, ITGA2B, P2RY1, P2RY6, PIK3CB, PIK3R3, PIK3R5
White Adipose Tissue Br	5'17	1'147	ADCY2, ADCY7, ADRB3, ANGPT2, BMP7, CACNA1D, CACNA1H, CACNB2, CACNG7
Adrenomedullin signaling	1'72	1'069	ADCY2, ADCY7, CALCRL, CTH, GNA14, GUCY1A2, GUCY1B1, IL18, KCNH2, KCNQ1
Role of p14/p19ARF in T	1'45	1	CDKN2A, PIK3CB, PIK3R3, PIK3R5
Osteoarthritis Pathway	2'67	-1	ALPL, ANKH, BMP2, CASQ1, COL10A1, CREB3L3, GREM1, IL18RAP, IL1RAPL1, IL1R1

Table S3. Isolation and analysis of CD105pos and CD105neg CAFs, related to Figure 3

IPA upstream regulator analysis of RNAseq of KPC CD105pos (n=6) and CD105neg CAFs

Upstream Regulator	Expr Log Ratio	Molecule Type	Activation z-score	p-value of overlap	-log10pvalue	Target Molecules in Dataset	Mechanistic Network
Bvht		other	2'496	0'000043	4'366531544	ALDH1A3, ALX4, CYGB, EBF1, FOXP1	
Tgf beta		group	2'449	0'002	2'698970004	CCL11, CSF3, CXCL3, IL10, IL16, M64 (5)	
C3AR1		G-protein coupled receptor	2'385	0'00538	2'269217724	C5, CD40, CD80, CSF3, IL10, LTBF	
TP53		transcription regulator	2'308	0'0168	1'774690718	Abcb1b, ABCB4, ACE, ADRB3, AH1	
EBF2	1'834	transcription regulator	2'236	0'00308	2'511449283	DIO2, ENTPD2, MEOX1, QPRT, RIN1	
DMD	1'114	other	2'176	0'00128	2'89279003	CASQ1, Cmah, COL23A1, DMD, G	

Table S6. In vivo analysis, related to Figure 6

IPA canonical pathway analysis of bulk RNAseq of co-transplantd tumours

Ingenuity Canonical Pathways	-log(p-value)	Ratio	z-score	Molecules
PD-1, PD-L1 cancer immunotherapy pathway	4'69	0'0645	2'449	HLA-DMA, HLA-DMB, HLA-DQB1, IL2RB, LCK, ZAP70
Fcy Receptor-mediated Phagocytosis in Macrophage	2'64	0'0435	-2	FCGR3A/FCGR3B, FYB1, PLD4, RAC2
IL-15 Production	2'29	0'0348	-2	CSF1R, LCK, MERTK, ZAP70
Th1 Pathway	3'31	0'0463	-2'236	CD3D, HLA-DMA, HLA-DMB, HLA-DQB1, TBX21
Dendritic Cell Maturation	2'55	0'0312	-2'236	FCGR3A/FCGR3B, HLA-DMA, HLA-DMB, HLA-DQB1, TREM2
Natural Killer Cell Signaling	2'46	0'0298	-2'236	FCGR3A/FCGR3B, IL2RB, LCK, RAC2, ZAP70

IPA upstream regulators analysis of bulk RNAseq of co-transplantd tumours

Upstream Regulator	Molecule Type	Activation z-score	p-value of overlap	-log10p-value	Target Molecules in Dataset
IL10RA	transmembrane rece	2'891	0'0000404	4'393618635	CALHM6, CLEC12A, CYFIP2, CYP2S1, ECM1, ERO1A, GHR, HGFA, Ly6a (includes others), Serpin
PIK3CG	kinase	2'449	0'000228	3'642065153	AIF1, CTSW, FCGR3A/FCGR3B, IL2RB, LCK, SOX9
RHO	G-protein coupled re	2'236	0'000231	3'63638802	C1QA, CD74, CSF1R, NCAM1, NT5E
NCSTN	peptidase	2'219	0'0000173	4'761953897	CSF1R, CSF2RB, GRN, Ly6a (includes others), SPI1
ATF4	transcription regulatc	2'2	0'00111	2'954677021	ERO1A, NDRG1, NUPR1, PRRX2, TNFRSF12A, VEGFA

期刊: Cancer Cell

影响因子: 31.74

关键词: rectal cancer, neoadjuvant therapy, cancer-associated fibroblasts, IL-1 signalling, senescence, IL1RN SNP

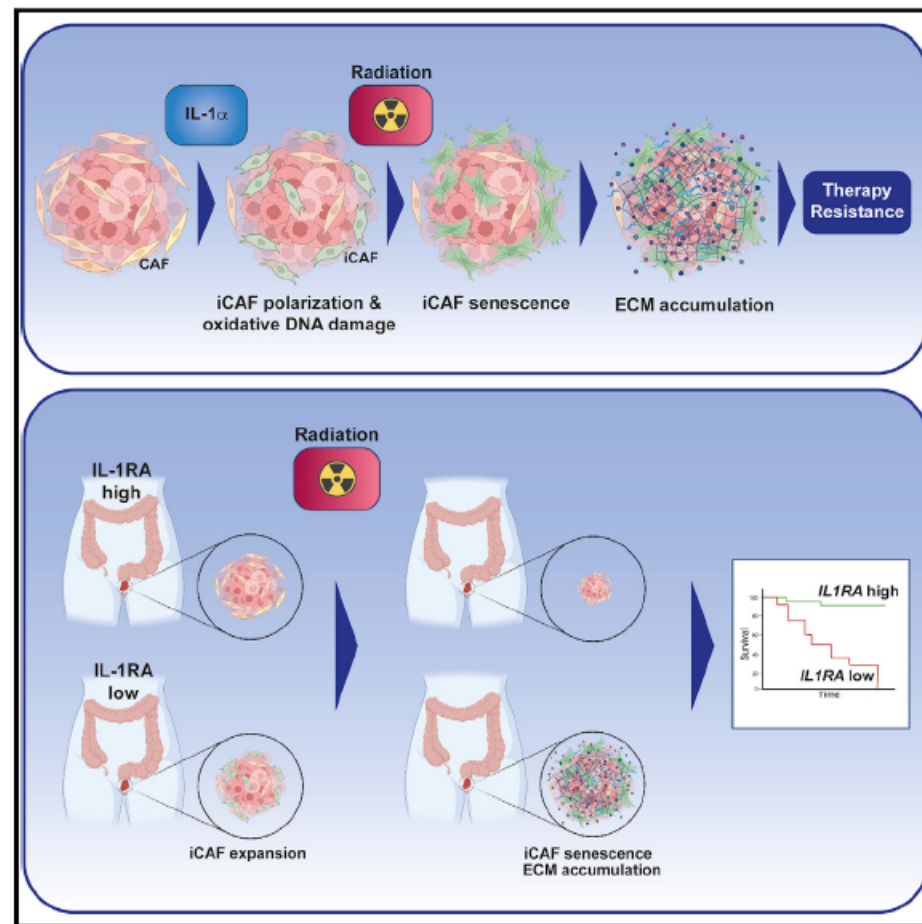
目的: 探索炎症成纤维细胞介导直肠癌对新辅助治疗的耐药性

IPA分析: Analyses of each cluster signature upstream regulators and generation of mechanistic network maps were performed using ingenuity pathway analysis software

Cancer Cell

Inflammatory fibroblasts mediate resistance to neoadjuvant therapy in rectal cancer

Graphical abstract



Authors

Adele M. Nicolas, Marina Pesic, Esther Engel, ..., Claus Rödel, Emmanouil Fokas, Florian R. Greten

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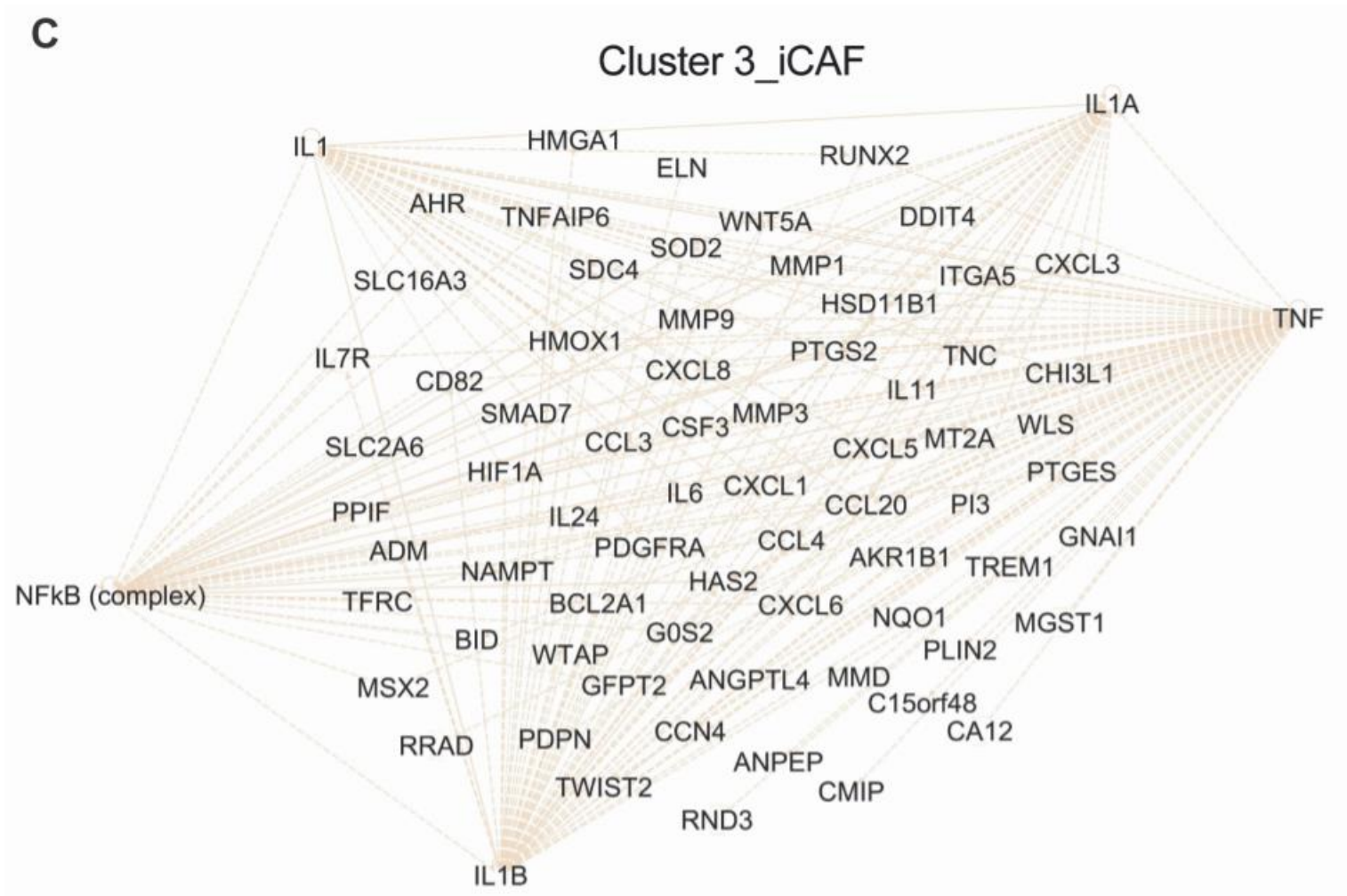
In brief

Nicolas et al. highlight the important role of inflammatory cancer-associated fibroblasts (iCAFs) for therapy response of rectal cancer patients. They demonstrate that IL-1-dependent signaling elevates oxidative DNA damage in iCAFs, which upon irradiation undergo senescence. This causes tissue remodeling and therapy resistance that can be overcome by inhibiting IL-1.

源资科技

炎症性CAF Cluster C3的**机制网络图**，预测上游调节因子及其差异表达基因的变化 (Log2FoldChange ≥ 1 , adjusted p-value threshold为0.05)。TNF、IL-1 β 、IL-1 α 、IL-1和NF κ B激活z-score分别为：6.178、6.047、4.617、4.575和4.506。p-value <0.0001。

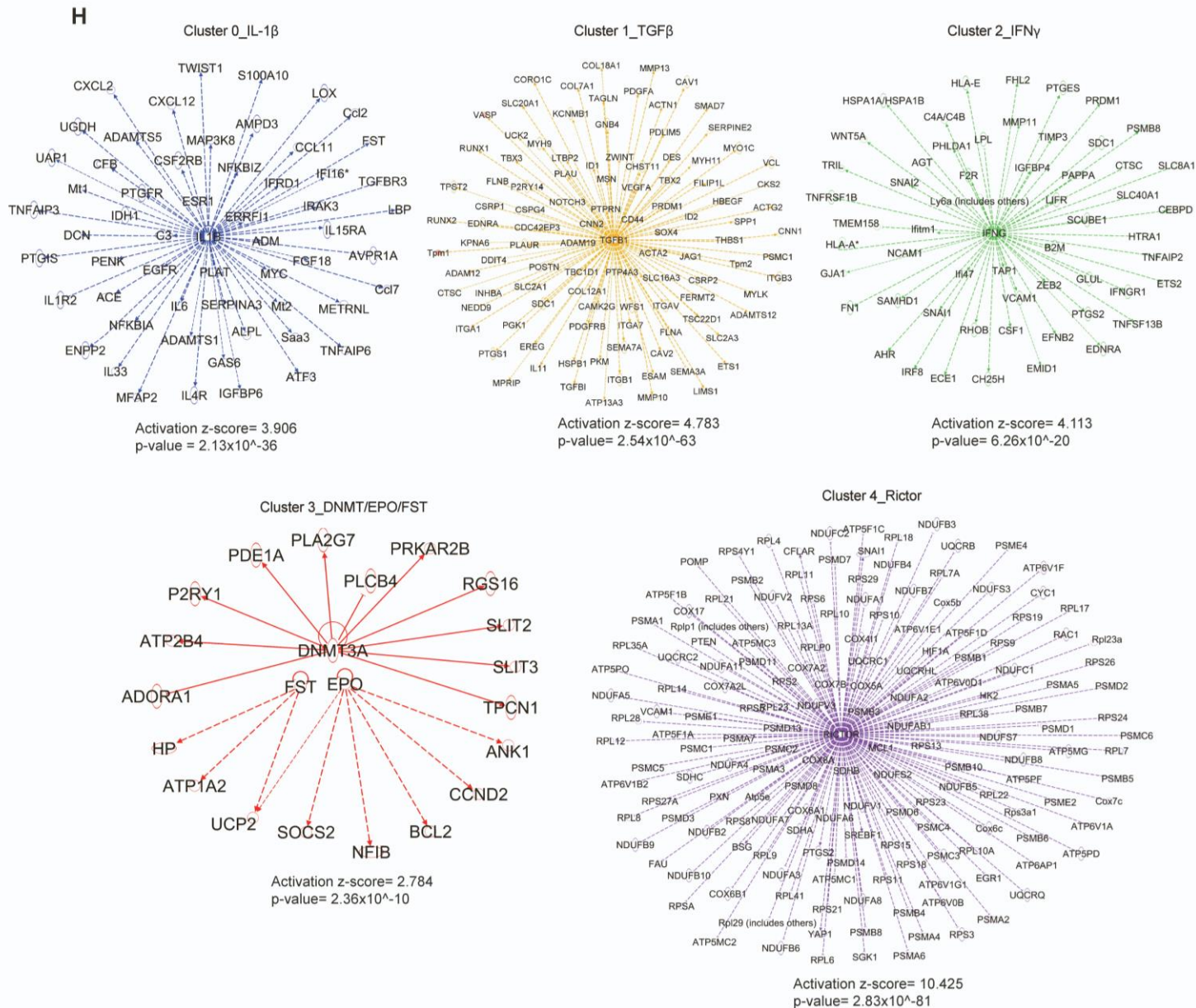
源资科技



直肠癌原位肿瘤类器官小鼠模型中的CAF分子异质性

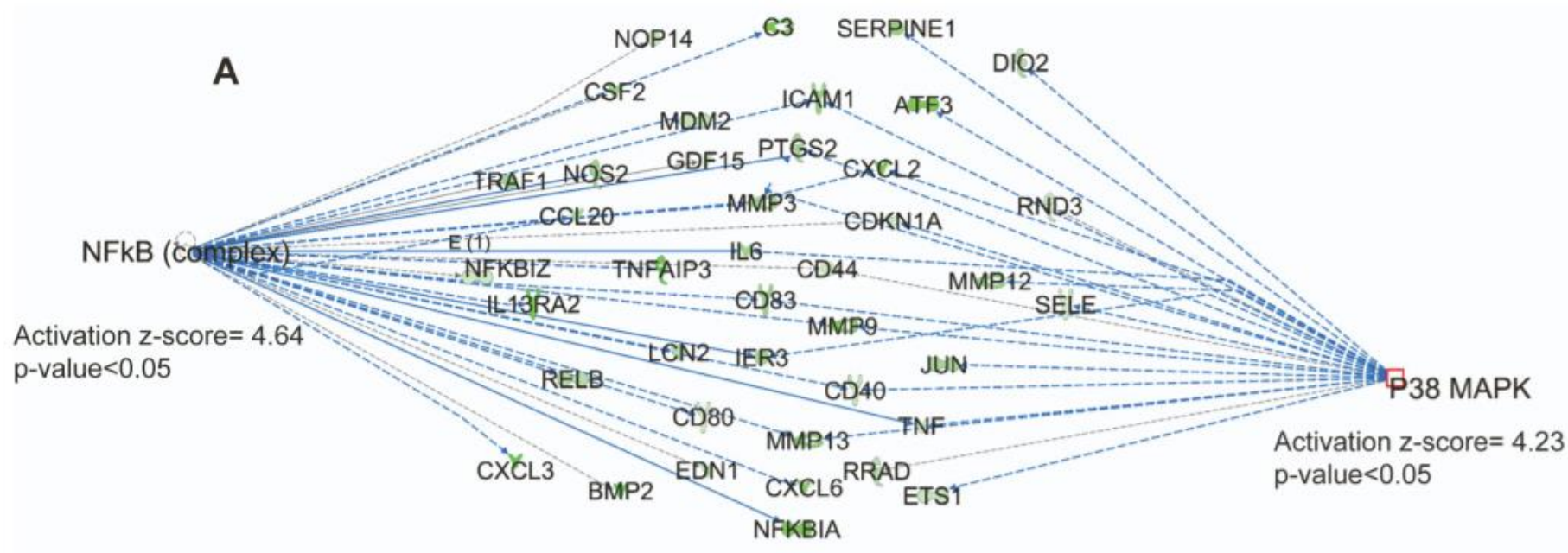
源资科技

Cluster 0_IL-1 β 、Cluster 1_TGF β 、Cluster 2_IFN γ 和Cluster 3_DNMT/EPO/FST中CAF上游调节因子及其相关差异上调基因的机制网络图，以及Cluster 4_Rictor CAF上游调节因子及其相关的显著下调基因。单细胞测序数据代表了从APTKA原位肿瘤 (n=4只小鼠) 中分离的624个CAF，通过IPA软件进行分析。激活z-score>2, p-value of overlap<0.0001。



IPA表明NF- κ B和p38激活是负责炎症基因表达谱的主要信号通路

如图为APTKA条件培养基处理的成纤维细胞上游调节因子及其差异表达基因的**机制网络图** (Log2FoldChange ≥ 1 , adjusted p-value threshold为0.05)。NF- κ B和p38激活z-score分别为4.64和4.23。p-value of overlap<0.05。

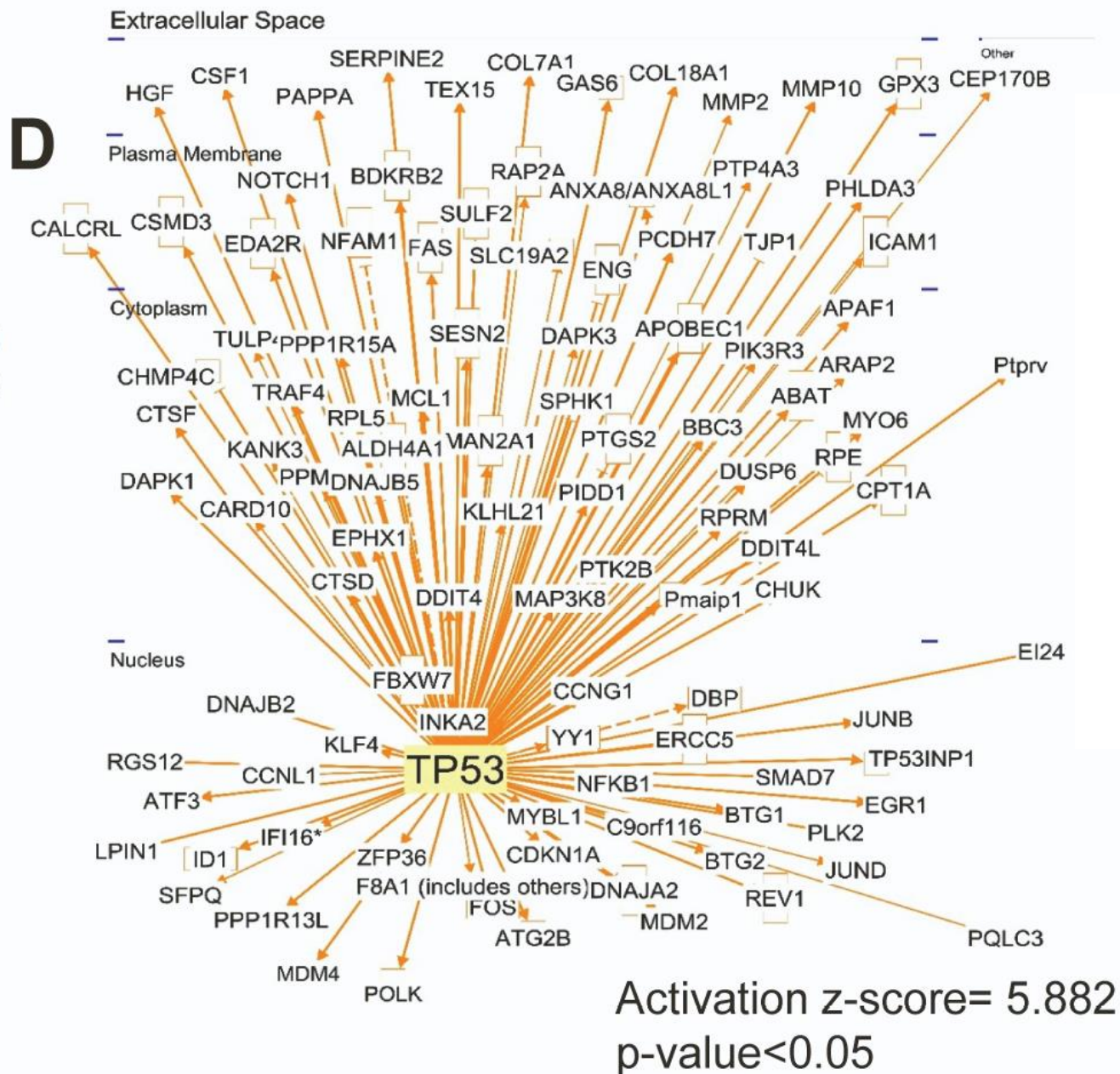


文献四

p53信号网络图

辐照后APTKA成纤维细胞及其差异表达基因的上游调节因子（adjusted p-value threshold为0.05）。

IPA表明，我们在matrisome分析中发现的许多诱导基因，包括编码各种分泌因子（细胞外蛋白：胶原蛋白、蛋白多糖、生长因子、ECM调节因子、ECM相关蛋白）的基因，以及细胞周期抑制剂Cdkn1a，均以p53依赖的方式调节。



Inherent hepatocytic heterogeneity determines expression and retention of edited *F9* alleles post-AAV/CRISPR infusion

Qiang Wang^{a,1}, Lin Zhang^{a,1}, Guo-Wei Zhang^{a,2}, Jian-Hua Mao^a, Xiao-Dong Xi^a, Lu Jiang^a, Gang Lv^a, Jing Lu^a, Yan Shen^b, Zhu Chen^{a,3}, Jiang Zhu^{a,3}, and Sai-Juan Chen^{a,3}

^aShanghai Institute of Hematology, State Key Laboratory of Medical Genomics, National Research Center for Translational Medicine, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China; and ^bResearch Center for Experimental Medicine, Ruijin Hospital, Shanghai Jiao-Tong University School of Medicine, Shanghai 200025, China

Contributed by Zhu Chen, September 2, 2021 (sent for review June 13, 2021; reviewed by Marina Cavazzana and Qingyu Wu)

期刊: PNAS

影响因子: 11

关键词: gene therapy,
hemophilia B, AAV/CRISPR,
liver immunity

源咨科技

目的: 探索AAV/CRISPR介导肝脏基因编辑的应用范围、潜在机制和潜在局限性

研究对象: C57BL/6背景的HB小鼠 (因子IX启动子和外显子1至3敲除[F9-KO])

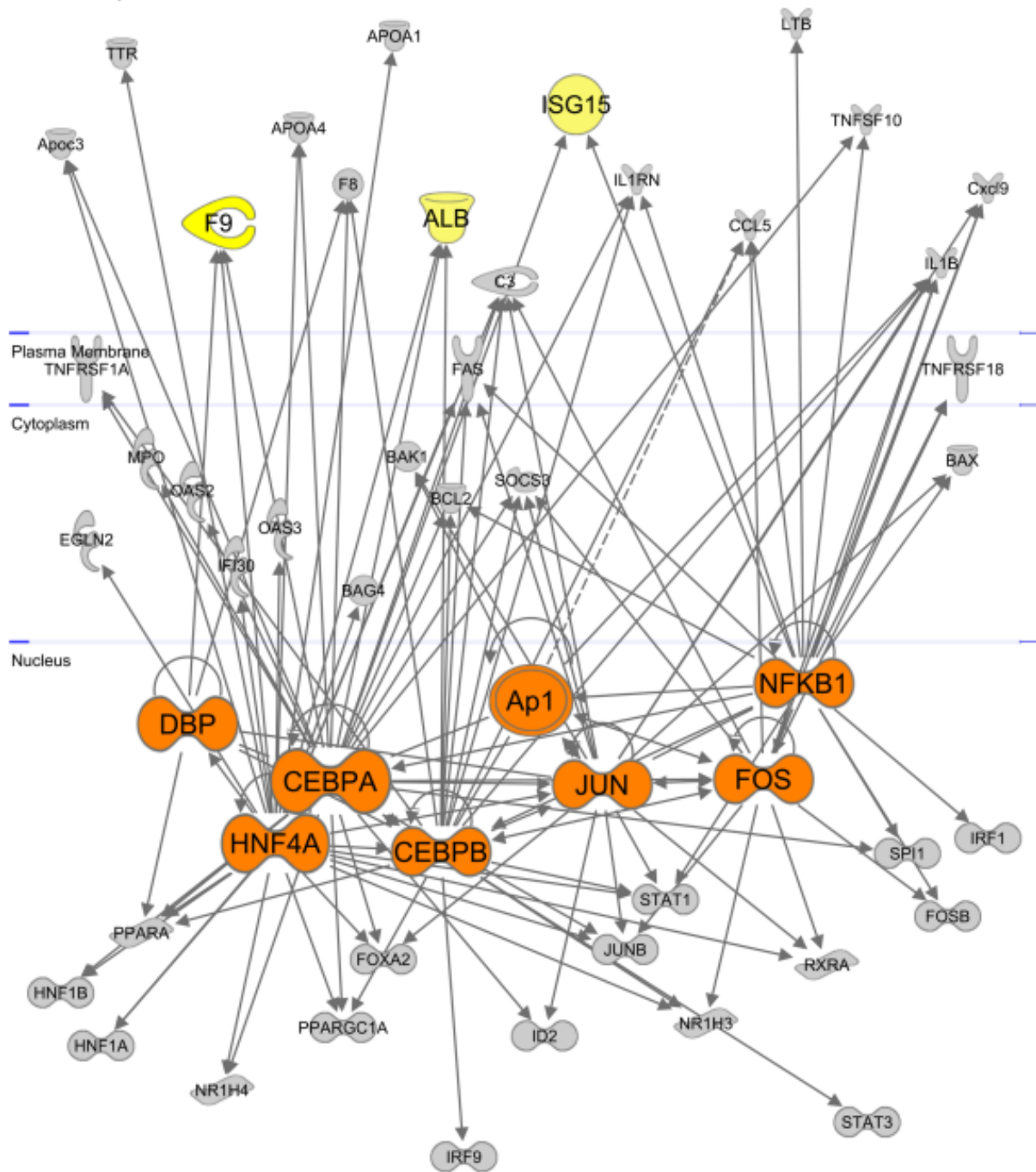
IPA分析: IPA analysis was used to **determine pathways** or **gene networks** that may be altered across clusters based on scRNA-seq results. Via Qiagen Digital Insights (<https://www.qiagenbioinformatics.com>), we uploaded each cluster marker gene to IPA, and used the “**core analysis**” function to analyze **upstream transcriptional regulators and gene networks**.

文献五



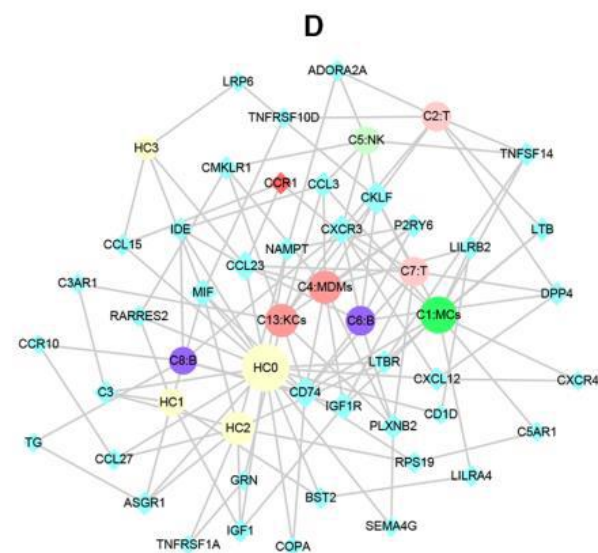
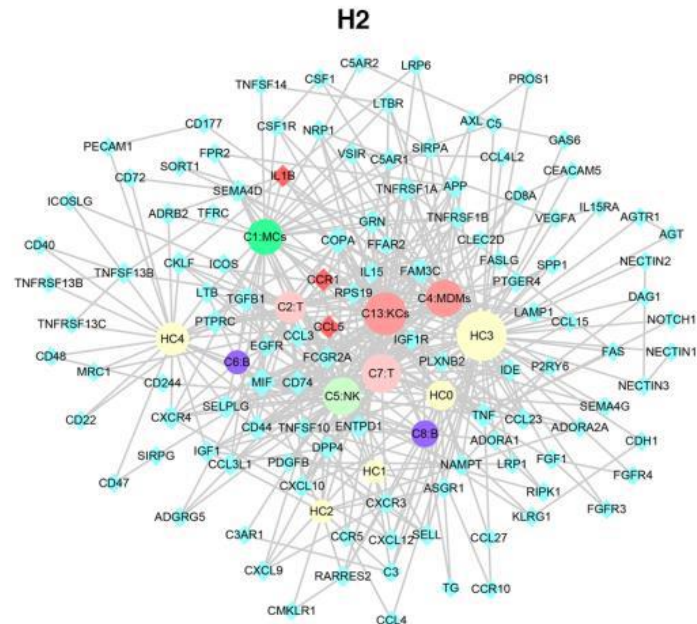
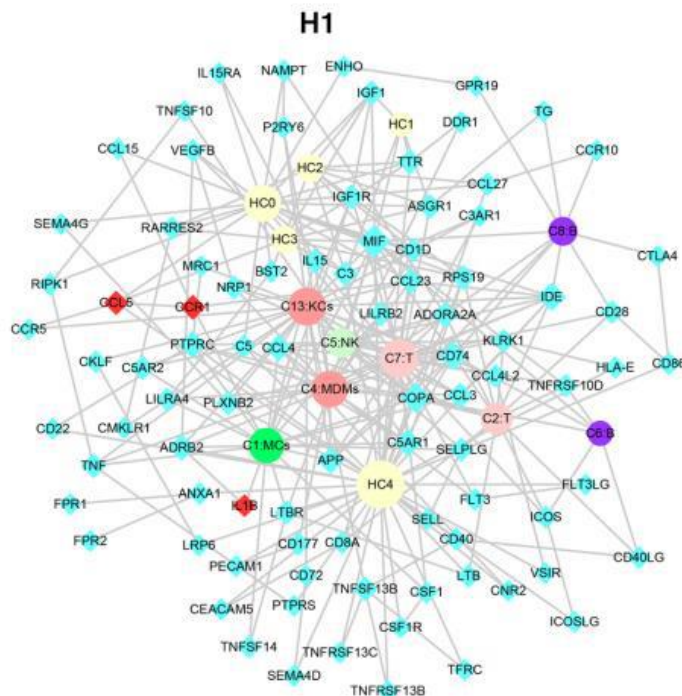
发现：炎症信号通过调节离散的
LETF（肝脏富集转录因子），以肝
细胞亚群依赖的方式，调节P2驱动
的F9表达

IPA图中显示了Alb派生的P2序列中
专门针对I类LEFT和II类LEFT的大量响
应元素的分布。



各种类型的免疫细胞和炎症因子之间相互作用的特征

IPA图中显示了在H1 (injected with PBS)、H2 (dual AAVs without DXM treatment) 和D (dual AAVs treated with DXM) 条件下，主要免疫细胞和肝细胞亚群之间的细胞因子通讯网络所构成的肝脏炎症簇。



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