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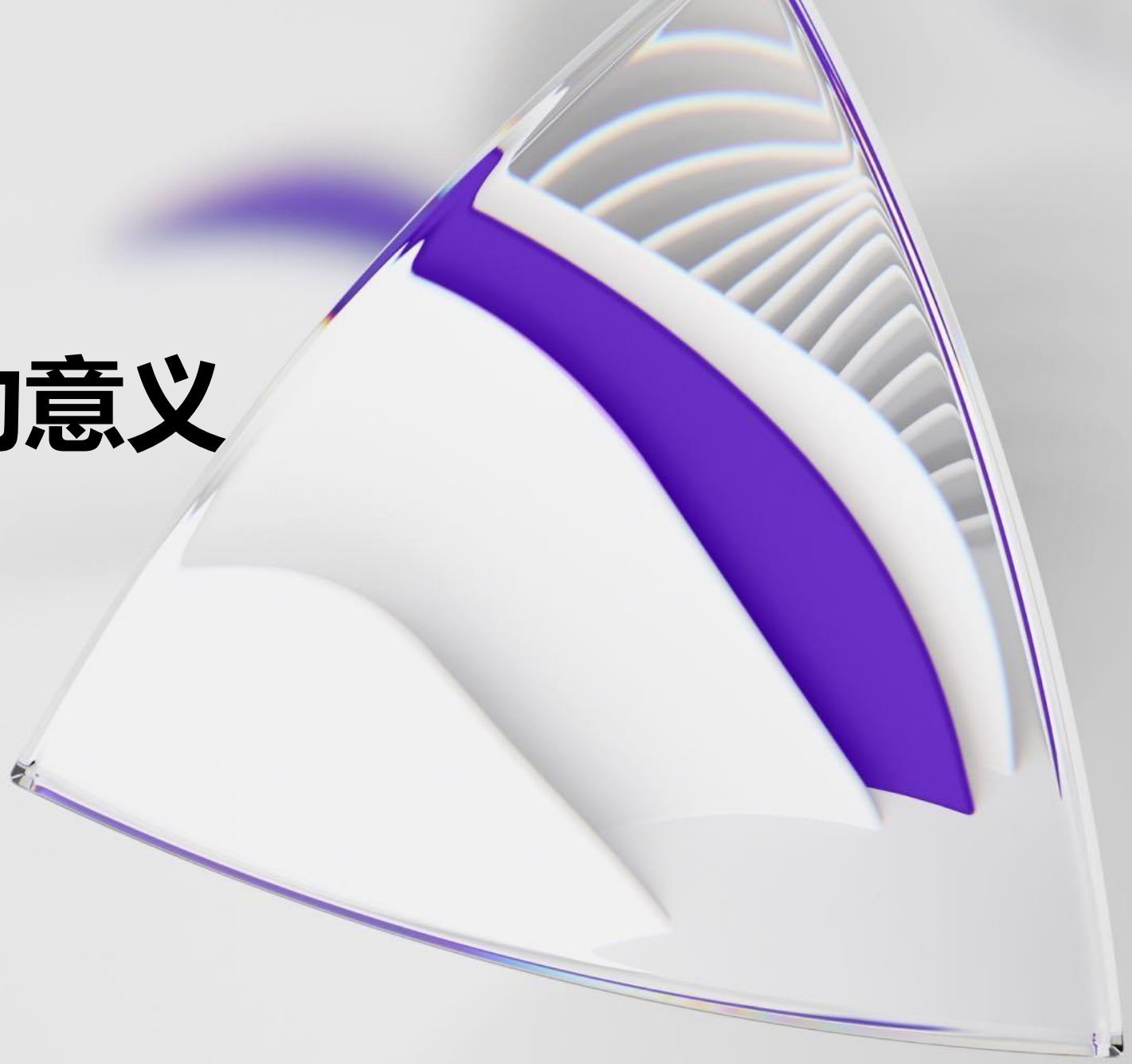
探索数据背后的意义

MetaCore助力疾病通路研究



科睿唯安：专业信息服务提供商，致力于加快创新步伐

我们与180多个国家的

18,000

多家客户合作

总部位于**英国伦敦**

纽约证券交易所上市公司，代码：**CCC**

50/TOP50

国际制药企业及生物技术公司

+600

投资公司、政府基金

17/TOP20

全球国际医疗器械企业

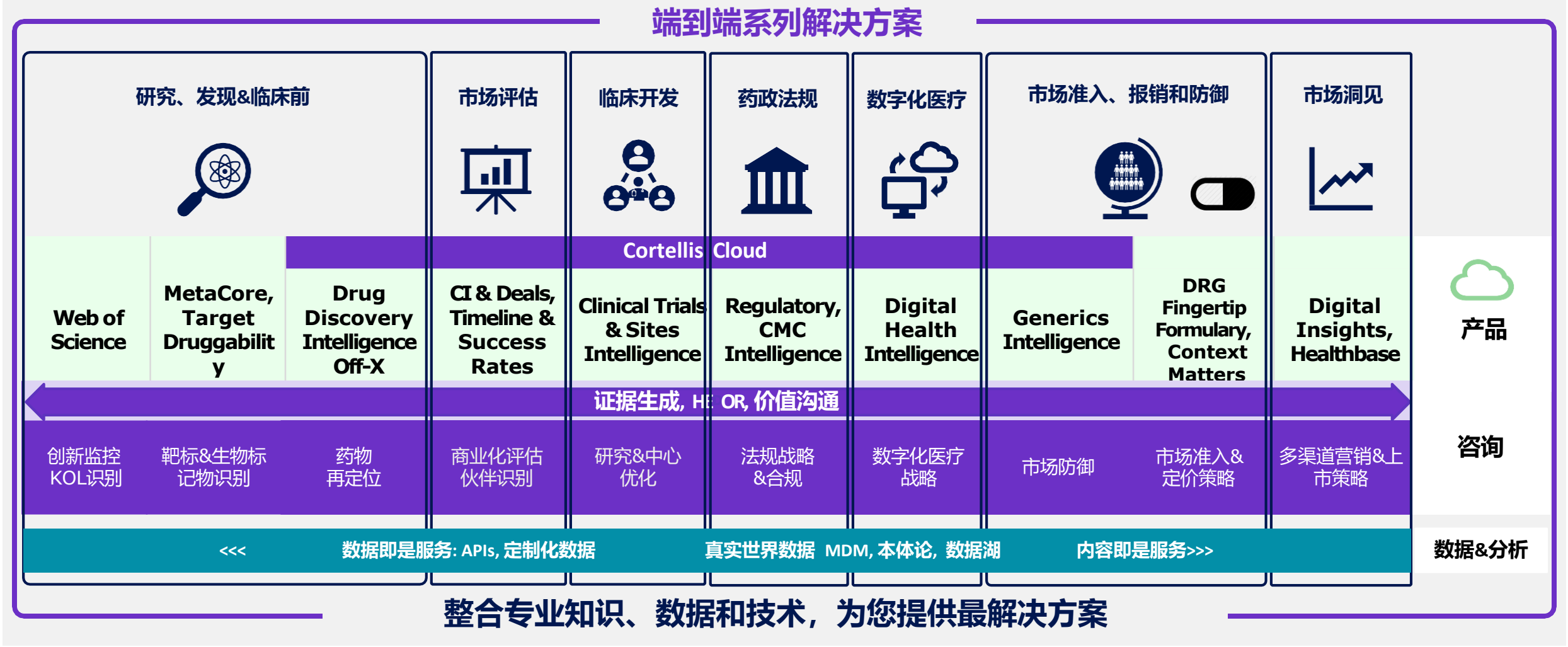
+7,000

领先的学术机构、非盈利组织及政府单位

~200

中国领先的制药企业及生物技术公司

科睿唯安生命科学与医疗健康提供药品全生命周期解决方案



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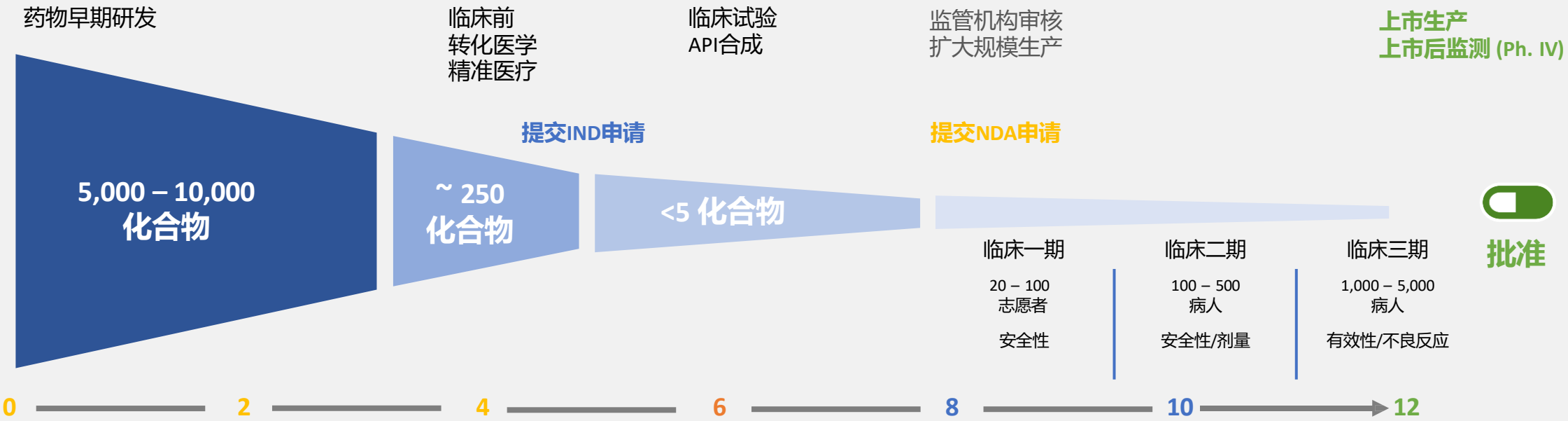
科睿唯安生命科学领域数据库：覆盖药物研发全流程



Cortellis Cloud™

METACORE + METADRUG	CDDI DRA OFF-X	竞争情报 CCI	交易情报 CDI 临床情报 CTI	药物研发时间轴和成功率预测: DTSR	CRI, CMC, PV, CIRS, CMR (年度付费报告)	DIGITAL HEALTH INTELLIGENCE	CGI	咨询服务 Data Lake API
		CORTELLIS						

Clarivate™

内容覆盖全面

内容来源

- 临床试验注册中心
- 专利
- 药理学研究
- 法规监管
- 组学
- 动物模型
- 公司官网
- 年报& 券商分析报告

简单化

综合化

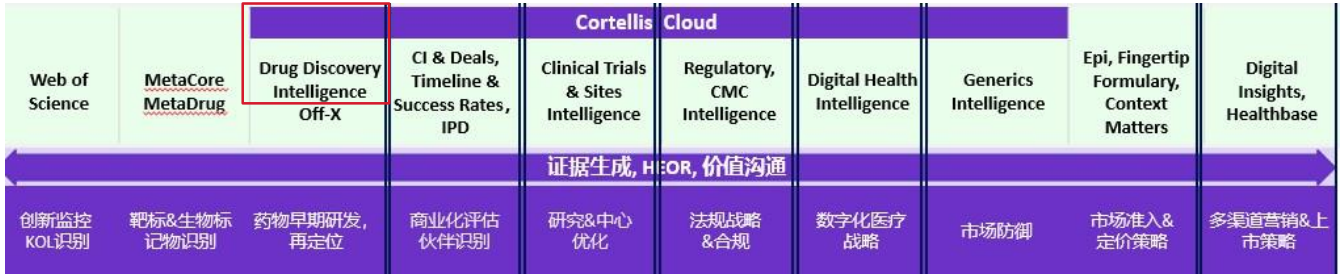
系统化

专有、全面和整合的内容

Cortellis竞争&交易情报	行业领先的产品管线数据库
Cortellis分析服务	咨询服务
Cortellis药政法规情报	最全面的药政法规内容和分析 CMC、药物警戒、信号检测、CIRS
Cortellis临床试验情报	最广泛的临床试验情报来源 时间轴与成功上市预测 CMR 组合基准测试
Cortellis数字健康情报	为法规和业务拓展战略提供额外见解
MetaCore, Cortellis解决方案	专有分析工具，用于发现生物学路径
CDDI, Cortellis解决方案	独家来源的、多方面的药物研究、临床前、转化医学和精准医疗情报
Cortellis Generic解决方案	行业领先的仿制药、专利、市场可及性和API情报解决方案

Clarivate™

Cortellis Drug Discovery Intelligence
早期研发情报数据库，含Biomarker（已订购）



Cortellis药物早期研发情报提供

For Scientists， By Scientists

700000+
药物(含大分子药物、疫苗细胞治疗、基因治疗)

47000+
靶点及基因

19w+
动物实验模型

3200000+
药理学数据

1380000+
药代动力学数据

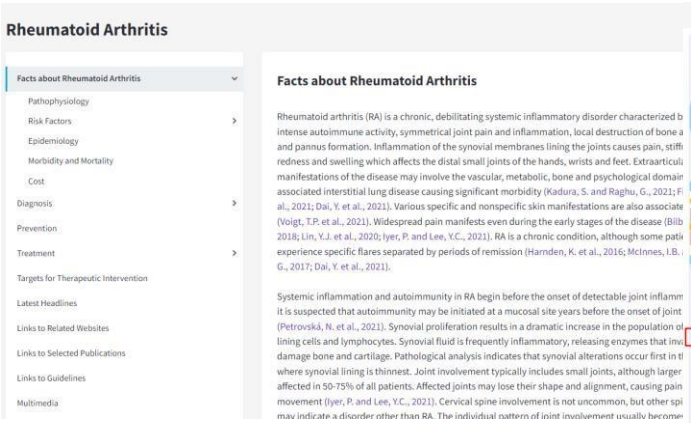
36000+
药物药物相互作用

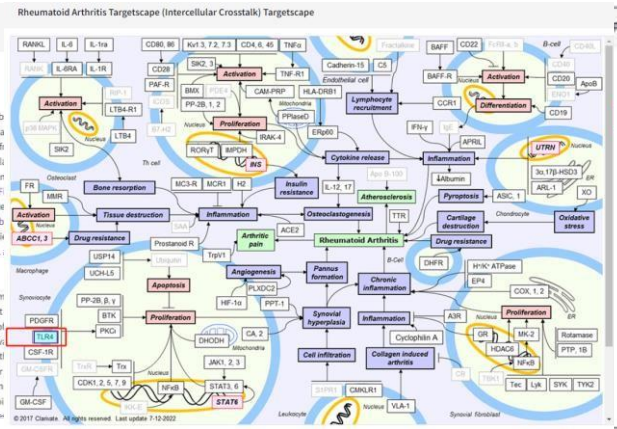
530000+
专利

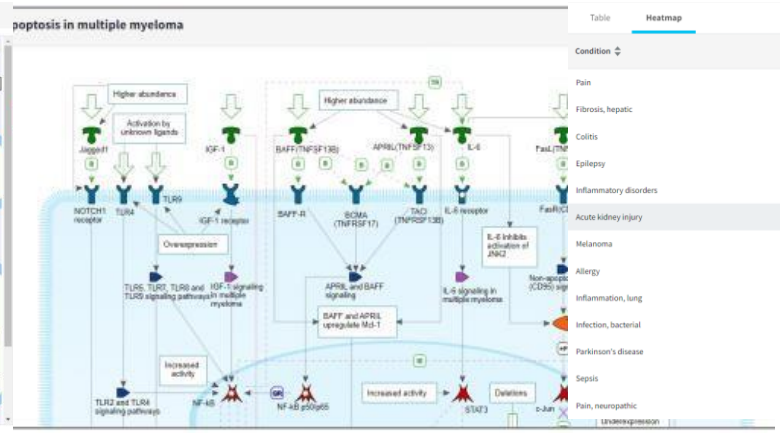
3020000+
文献

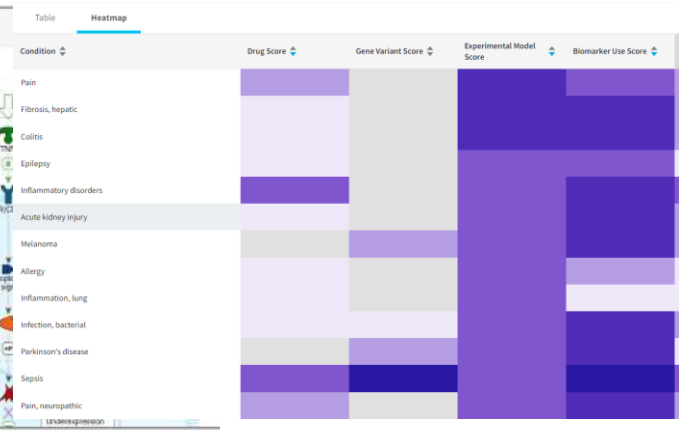
50000+
药物代谢

Administered Product	Dosage	Measured Product	Parameter	Value	Compartment	Method	Organism	Source
Sotorasib	10 mg/kg	Sotorasib	t1/2	24 min	Plasma		Dogs	Am Che Natl Me
Sotorasib	10 mg/kg	Sotorasib	Vss	700 ml/kg			Mice	Am Che Natl Me
Sotorasib	1 mg/kg	Sotorasib	t1/2	30 min	Plasma		Mice	J Med C
Sotorasib	1 mg/kg	Sotorasib	Cl	3.4 l/h/kg	Plasma		Rats	J Med C
Sotorasib	10 mg/kg	Sotorasib	Vss	2 l/kg			Rats	Am Che Natl Me
Sotorasib	1 mg/kg	Sotorasib	Vss	700 ml/kg			Mice	J Med C









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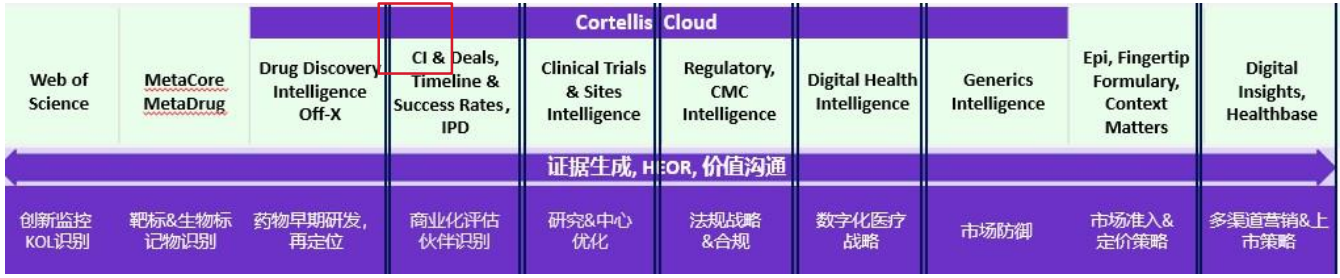
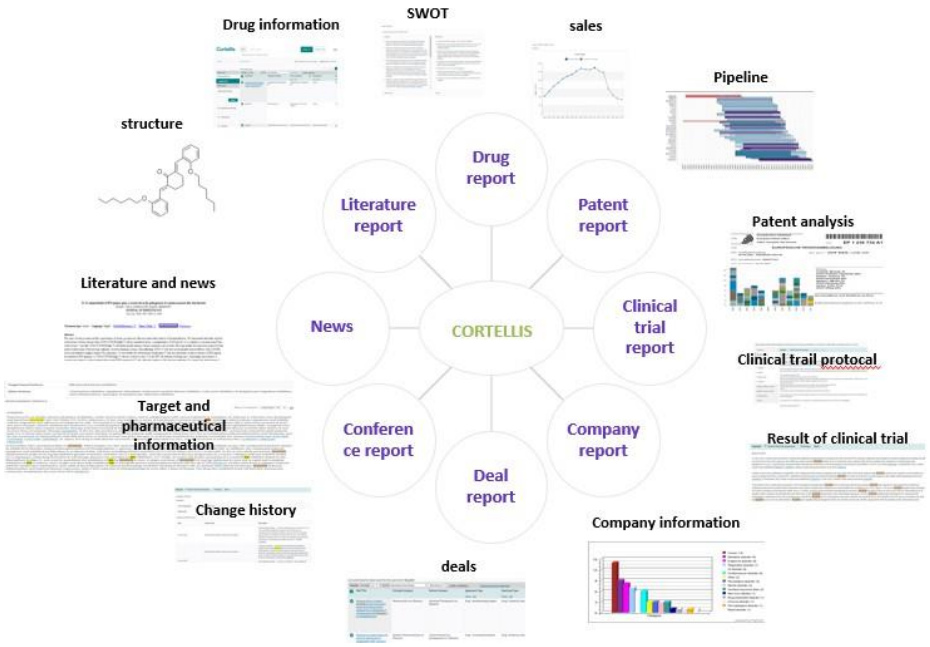
Cortellis Competitive Intelligence
竞争情报数据库

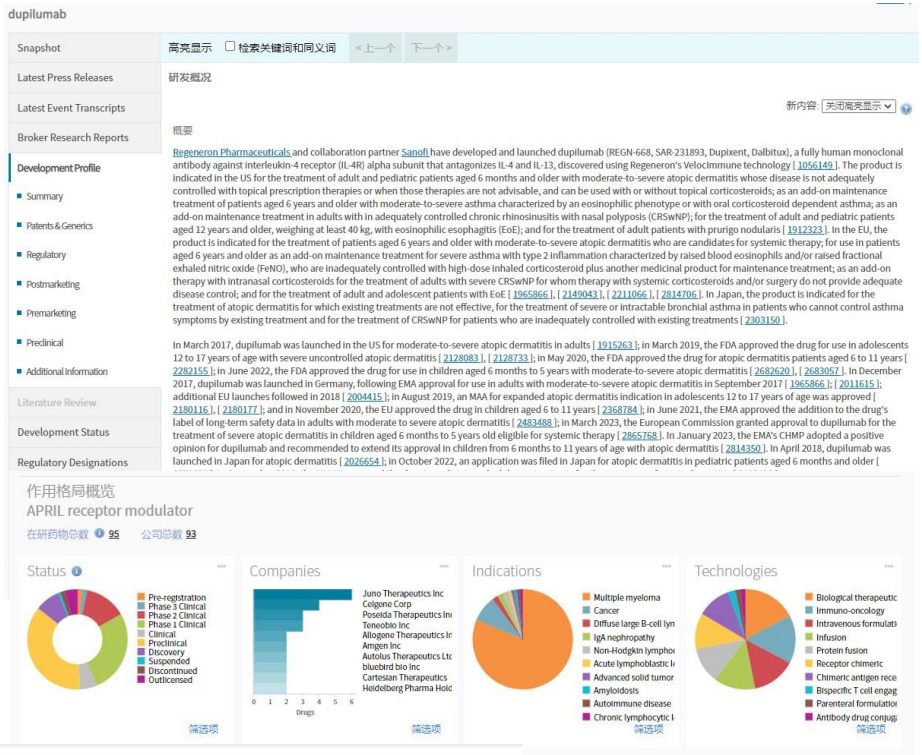


Cortellis: a comprehensive collection of innovative drugs information



Data for innovation:

- ✓Drugs: 90,000+
- ✓Clinical trials: 600,000+*
- ✓Deals: 140,000+*
- ✓Patents: 5,700,000+
- ✓Disease briefing: 169*
- ✓Regulatory: 200,000+*
- ✓Conferences: 100,000+
- ✓Companies: 260,000+
- ✓Literature: 2,700,000+
- ✓Broker research: 1,900,000+
- ✓News: 560,000+
- ✓Venture funding: 10,000+



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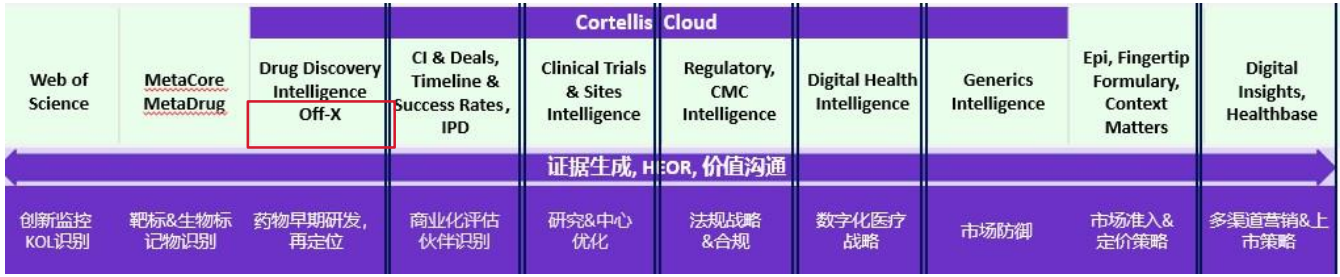
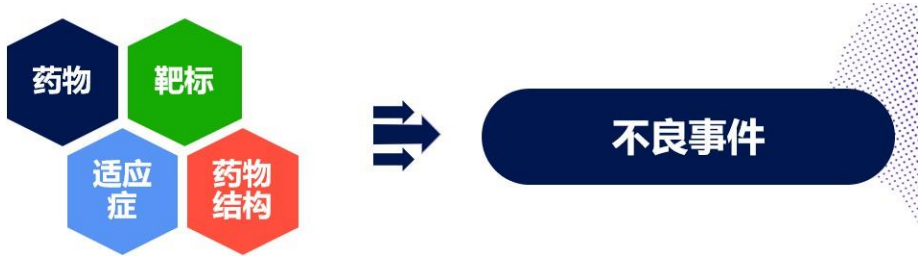
药物安全信息平台
OFF-X





美国食品和药品监督管理局将能够继续使用科睿唯安旗下药物安全信息平台 OFF-X™

近日，全球领先的专业信息服务提供商科睿唯安（纽约证券交易所股票代码：CLVT）**宣布将与美国食品和药品监督管理局签署的《材料转移协议》(MTA) 延长三年，**确保美国食品和药品监督管理局能够继续使用**科睿唯安旗下药物安全信息平台 OFF-X™**。该平台提供综合的临床前毒理、临床和上市后不良事件数据、可视化工具和分析。

临床研究的成功可能会受到意外安全问题的影响。在药物研发过程中，尽早识别潜在安全责任至关重要。通过融合临床前和临床的药物安全数据转化，可以减少患者负担并提高研发成功率。

随着双方合作关系进入第六个年头，美国食品和药品监督管理局将继续使用 OFF-X，以识别与分子靶点，新药及上市药物相关的潜在不良事件，**并为监管审查过程提供支持。**该协议通过评估加强人用药品及相关分子靶点安全性评价的方法，继续支持美国食品和药品监督管理局履行保护公众健康的使命。

> **科睿唯安合作伙伴关系副总裁 Gavin Coney 表示：**“科睿唯安利用深度数据、深厚的洞察力和专业知识，帮助生命科学合作伙伴预测并克服向患者提供创新治疗的障碍。美国食品和药品监督管理局与科睿唯安之间的这项协议将赋能研究人员和药物安全专业人员在药物研发和上市后所有阶段预测和监测潜在安全责任的准备。”

Master view

Showing **1,784 adverse events** for **25 System Organ Classes**

Filter | Columns | View: AE/SOC

Adverse event • System Organ Class	OFF-X Target/Class Score	Classifier tags	Alert type: Number of alerts	Alert type: Class alerts	Alert type: Drug alerts	Alert phase: Preclinical	
Death • General disorders and administration site conditions	Very high	On-Target, Causality, Severity	227	40	10	7	217	40	9	8
Decreased appetite • Metabolism and nutrition disorders	Very high	On-Target, Causality, Severity, Pharmacogenomics	449	66	12	9	437	66	0	0
Dermatitis acneiform • Skin and subcutaneous tissue disord…	Very high	On-Target, Causality, Severity, Pharmacogenomics	347	50	16	7	331	50	1	2
Diarrhoea • Gastrointestinal disorders	Very high	On-Target, Causality, Severity, Pharmacogenomics	1114	81	44	14	1070	81	18	8
Hypomagnesaemia • Metabolism and nutrition disorders	Very high	On-Target, Causality, Severity	138	26	10	4	128	25	1	1
Interstitial lung disease • Respiratory, thoracic and mediasti…	Very high	On-Target, Causality, Severity, Pharmacogenomics	323	28	20	8	303	28	2	2
Mucosal inflammation • General disorders and administrati…	Very high	On-Target, Causality, Severity, Pharmacogenomics	189	25	19	9	170	25	0	0

Filter | Columns | AE/SOC

Adverse event • System Organ Class	OFF-X Target/Class Score	Biological Role & Preclinical Pharmacological Evidence: Target Expression	Human Genetic variants	KO/KD Animal data	In vitro Data / Patient samples	Preclinical	Clinical Pharmacological Evidence: Phase I	Phase II	Phase III	Clinical Regulatory	Postmarketing	Phase not specified
Weight decreased • Investigations	Medium					30 17 Species 4	25 22	54 23	24 11	28 14	9 6	9 4
Mutagenic effect • Congenital, familial and genetic disorders	Not associated				7 6 Species 3	26 10 Species 3					1 1	
Diarrhoea • Gastrointestinal disorders	Very high	DM	1		1 2 Species 1	16 8 Species 3	202 74	312 47	137 23	66 15	258 21	199 28
Infertility male • Reproductive system and breast disorders	Very low	DM				12 7 Species 3				1 1	1 1	
Foetal disorder • Pregnancy, puerperium and perinatal cond…	Medium					10 8 Species 2	1 1		1 1	12 10		

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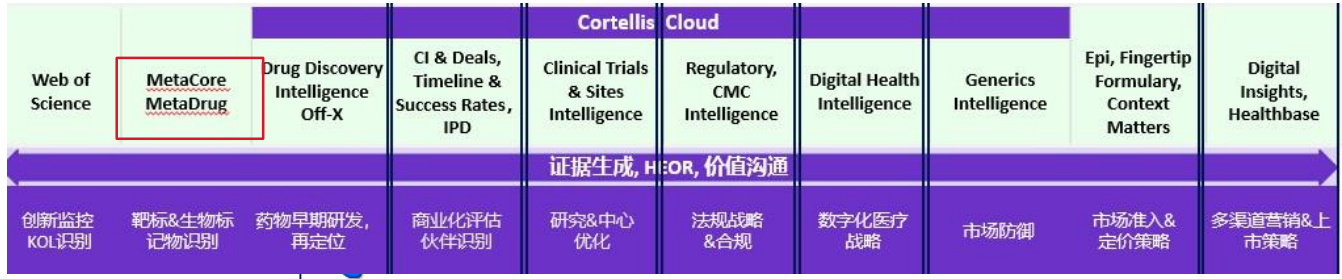
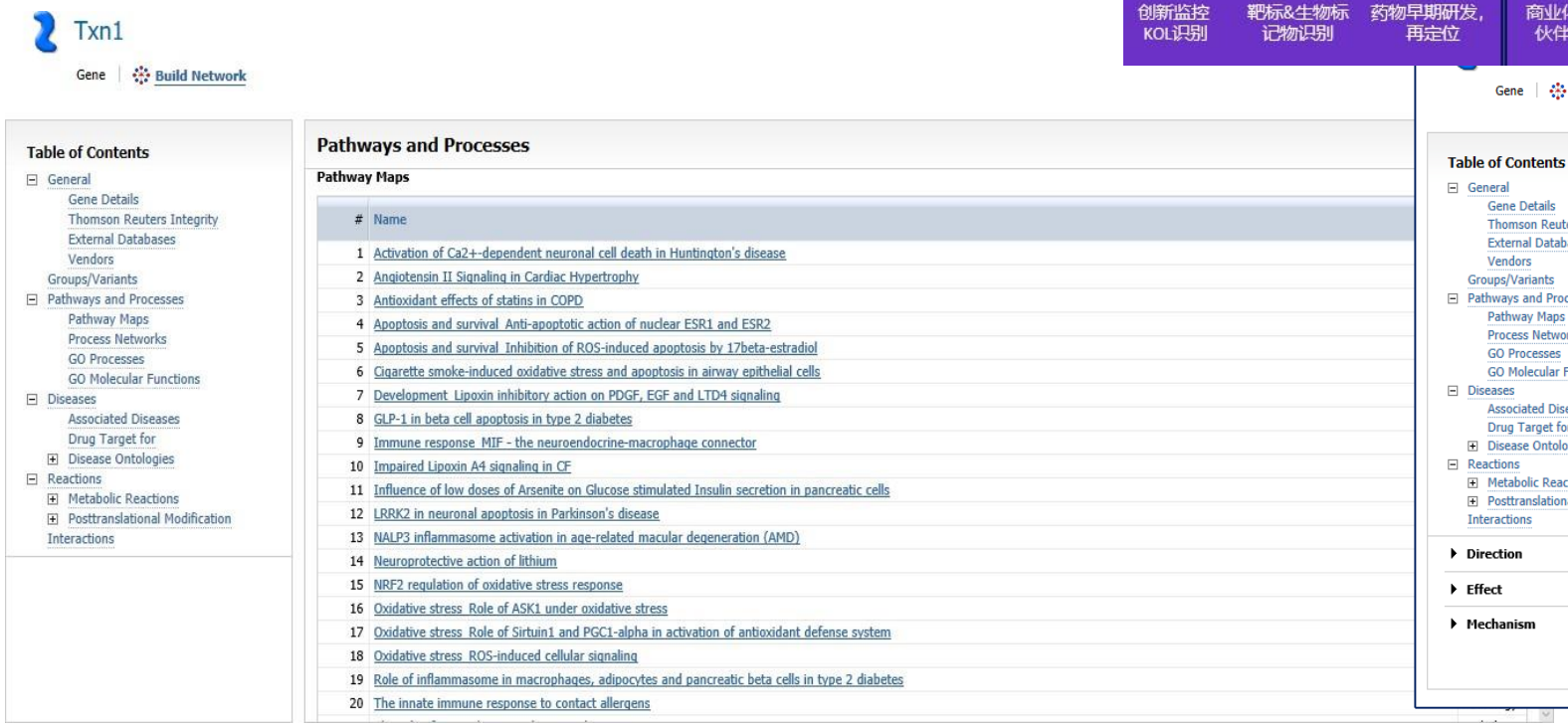
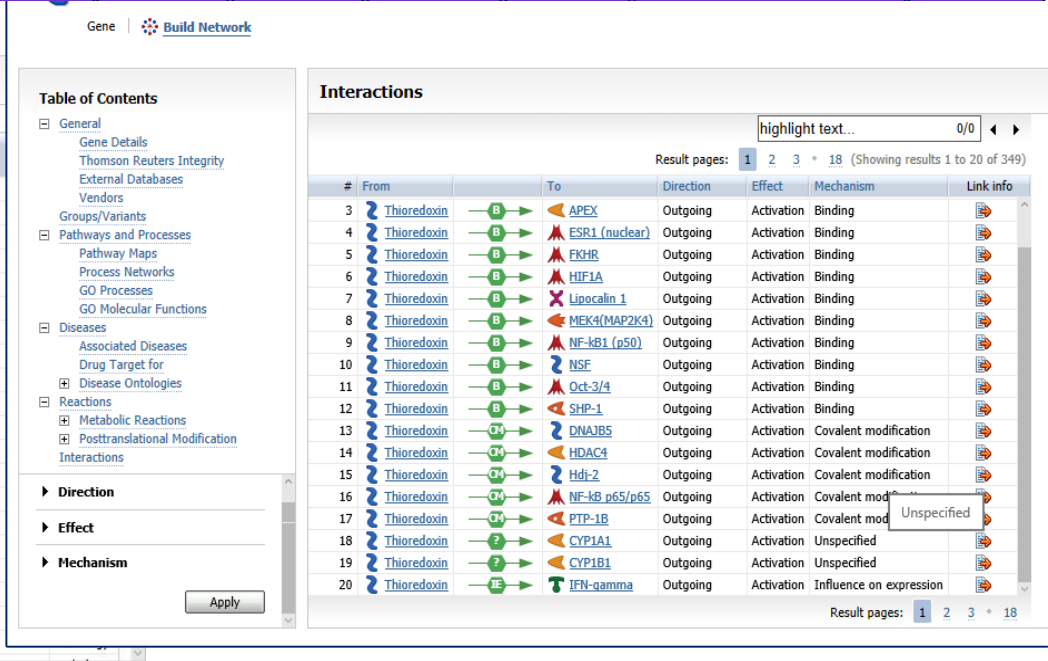
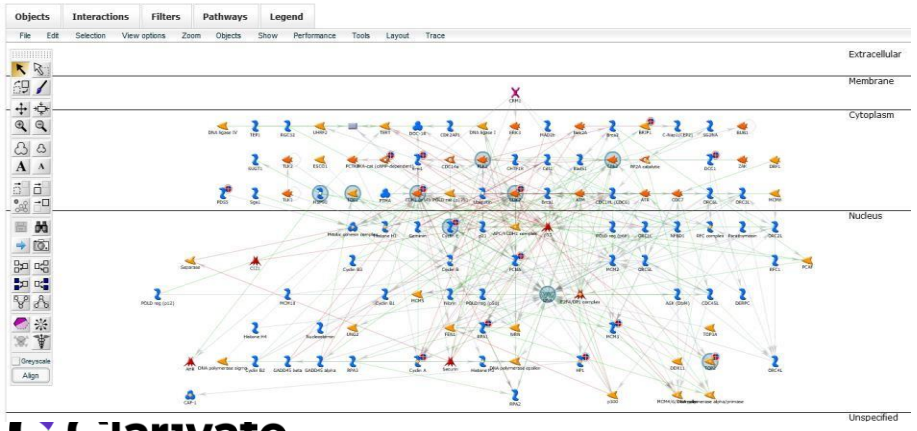
Metacore, Metadrug









- Accelerate disease research, biomarker, and drug target identification
  加快疾病研究、生物标志物和药物靶标鉴定进程
- MetaCore has prepared the code and algorithms, and the data can be uploaded for omics data analysis
  MetaCore已做好代码和算法，上传数据即可进行组学数据分析
- Build the signaling network you want
  构建您想要的信号传导网络

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日程

第一部分：MetaCore数据平台简介

第二部分：MetaCore重点功能介绍

第三部分：系统生物学案例分享

第四部分：内容回顾与总结

Clarivate™

MetaCore （原GeneGo产品）概览

加快疾病研究、生物标志物和药物靶标鉴定进程

METACORE 可用于：

- 药物发现（drug discovery）中组学（OMICS）数据的通路分析
- 在数据库中进行知识挖掘，产生假设
- 靶标和生物标记物的评估与验证
- 全面疾病通路的建立和发病机制的研究
- 病患分层、综合性比对和功能性指纹图谱

适合以下专业人员：

- 生物学研究人员
- 发现生物学家
- 生物信息学家
- 生物标记小组和临床前研究人员
- 治疗领域方向高层人员
- 首席调研员（临床医生等 PI）
- 转化医学研究人员

- **数据精准：**完全通过人工阅读全文文献和实验数据后进行整合的高准确率 的数据库，包含分子互作作用，通路，基因与疾病关联，化学代谢物与毒理信息。
- **功能强大：**涵盖药物研究各个方面 ，包括药物靶标的发现及验证；药物代谢的通路分析及药物作用靶标及活性和毒性的预测；药物临床实验数据的功能分析等。
- **使用方便：**从实验数据的上传、统 计分析一直到靶标的验证、新的靶标的选择和生物标记物的发现都可以实时显示，图形界面和可视化工具非常友好。

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近年来利用MetaCore发表的高影响力文章部分列表

1. *(2023) Subcellular location defines GPCR signal transduction. Science Advances IF=13.6*
2. *(2023) Exploring the possible mechanism(s) underlying the nephroprotective effect of Zhenwu Decoction in diabetic kidney disease: An integrated analysis. PHYTOMEDICINE IF=7.9*
3. *(2022) A lymphocyte–microglia–astrocyte axis in chronic active multiple sclerosis. Nature, IF=64.2*
4. *(2021) Deletion of Abi3 gene locus exacerbates neuropathological features of Alzheimer's disease in a mouse model of Aβ amyloidosis. Science Advances IF=13.6*
5. *(2021) Differences in transcriptome response to air pollution exposure between adult residents with and without chronic obstructive pulmonary disease in Beijing: A panel study. JOURNAL OF HAZARDOUS MATERIALS IF=13.6*
6. *（2019）Metastatic-niche labelling reveals parenchymal cells with stem features. Nature, IF=64.2*
7. *（2016）Dual Targeting of P53 and C-Myc Selectively Eliminates Leukaemic Stem Cells. Nature IF= 64.2*
8. *（2016）A Core Viral Protein Binds Host Nucleosomes to Sequester Immune Danger Signals。 Nature IF= 64.2*
9. *(2013) Molecular Profiling of Human Mammary Gland Links Breast Cancer Risk to a p27(+) Cell Population with Progenitor Characteristics. Cell Stem Cell. IF=23.9*
10. *(2011)The JAK2/STAT3 signaling pathway is required for growth of $CD44^{+}CD24^{-}$ stem cell-like breast cancer cells in human tumors. J Clin Invest.; IF=12.812*
11. *(2008). Core signaling pathways in human pancreatic cancers revealed by global genomic analyses. Science.IF=56.9*
12. *(2008). An integrated genomic analysis of human glioblastoma multiforme. Science . IF=56.9*
13. *(2008). Regulation of in situ to invasive breast carcinoma transition. Cancer Cell. IF=50.3*
14. *(2007). The genomic landscapes of human breast and colorectal cancers. Science IF=56.9*

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Metacore是组学分析的有效分析工具

Article | Published: 08 September 2021

A lymphocyte–microglia–astrocyte axis in chronic active multiple sclerosis

Martina Absinta, Dragan Maric, Marjan Gharagozloo, Thomas Garton, Matthew D. Smith, Jing Jin, Kathryn C. Fitzgerald, Anya Song, Poching Liu, Jing-Ping Lin, Tianxia Wu, Kory R. Johnson, Dorian B. McGavern, Dorothy P. Schafer, Peter A. Calabresi & Daniel S. Reich

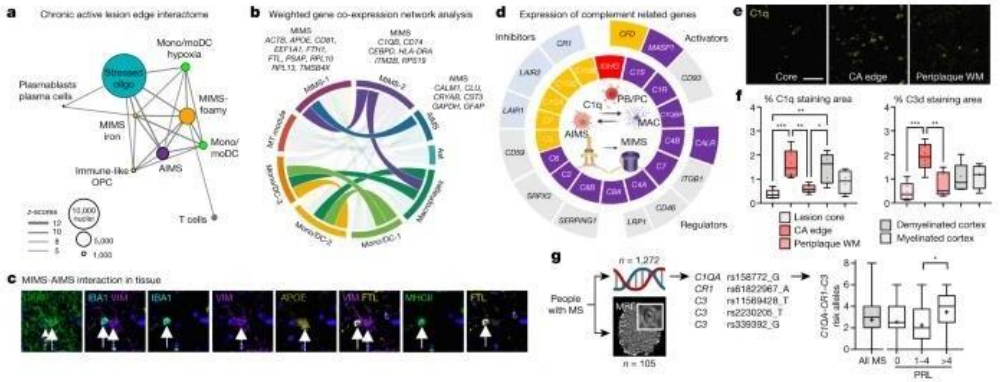
Nature **597**, 709–714 (2021) | Cite this article

42k Accesses | **270** Citations | **213** Altmetric | Metrics

Abstract

Multiple sclerosis (MS) lesions that do not resolve in the months after they form harbour ongoing demyelination and axon degeneration, and are identifiable in vivo by their paramagnetic rims on MRI scans[1,2,3]. Here, to define mechanisms underlying this disabling, progressive neurodegenerative state[4,5,6] and foster development of new therapeutic agents, we used MRI-informed single-nucleus RNA sequencing to profile the edge of demyelinated white matter lesions at various stages of inflammation. We uncovered notable glial and immune cell diversity, especially at the chronically inflamed lesion edge. We define 'microglia inflamed in MS' (MIMS) and 'astrocytes inflamed in MS', glial phenotypes that demonstrate

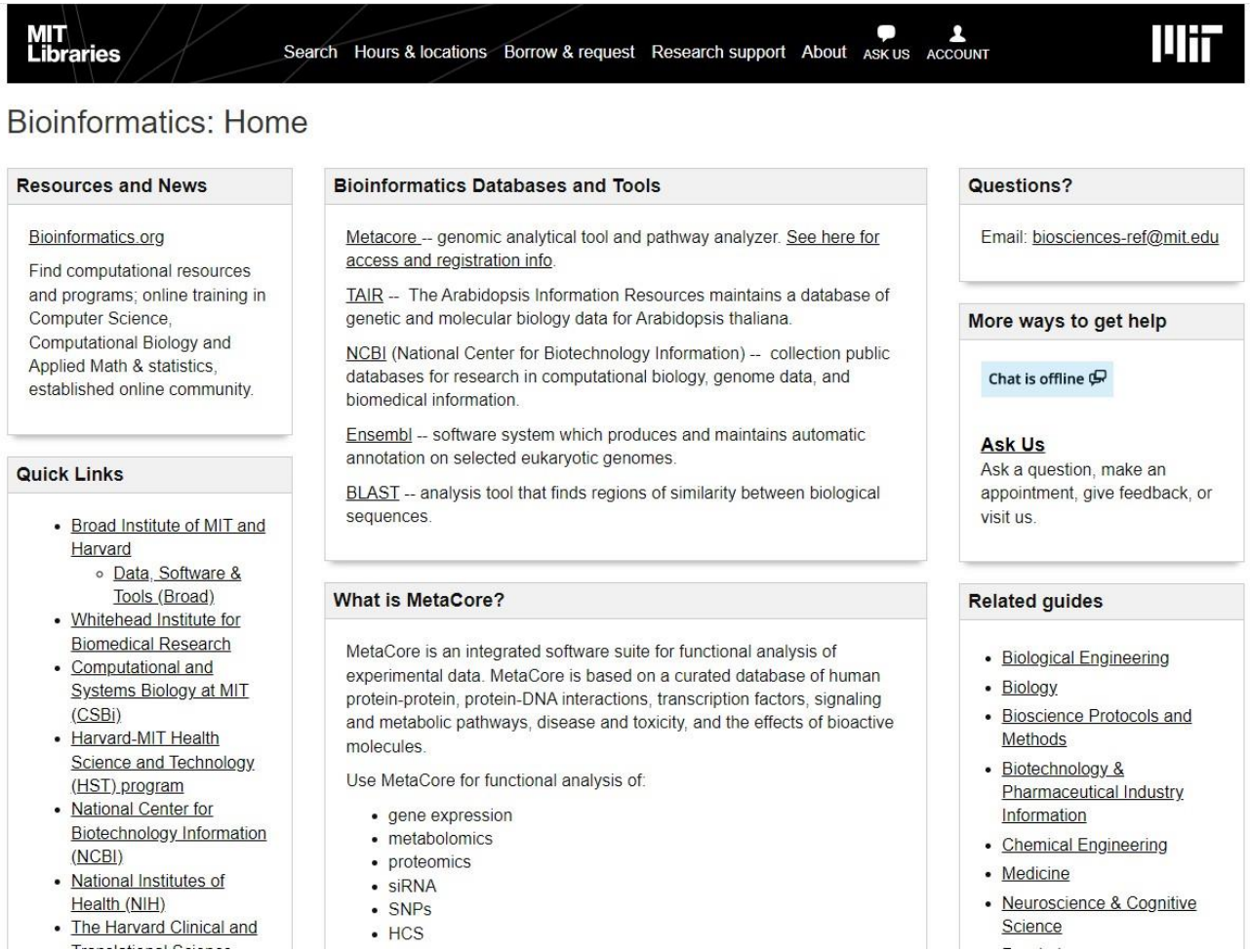
Fig. 3: MIMS–AIMS interactions anchor the glial interactome, and C1q and C3 activity is increased in chronic active white matter lesions.



a, Glial interactome map of the chronic active lesion edge (first 20 significant connections, $P < 0.05$). Each node indicates a cell-type cluster; node size is proportional to number of nuclei and connector thickness is proportional to *z*-scores of the MetaCore interactome output. **b**, Correlations among gene modules in immune and astrocyte clusters using WGCNA, retaining only genes that are differentially expressed in chronic active edge versus control white matter; module size < 50 genes. Ribbon colour scale: eigengene adjacency matrix values (highest quartile, dark colour; corresponding heat map and scale bar are shown in Extended Data Fig. 8c). MIMS and AIMS gene modules are highly correlated. DC, dendritic cells. MT, mitochondria. **c**, Spatial interaction between MIMS (dashed white arrow) and AIMS (white arrow) in tissue at the chronic active edge. **d**, *z*-scores (>1.5 relative to all

https://www.nature.com/articles/s41586-021-03892-7

众多知名院校在使用metacore



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- Broad Institute of MIT and Harvard
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- Whitehead Institute for Biomedical Research
- Computational and Systems Biology at MIT (CSBi)
- Harvard-MIT Health Science and Technology (HST) program
- National Center for Biotechnology Information (NCBI)
- National Institutes of Health (NIH)
- The Harvard Clinical and

Bioinformatics Databases and Tools

Metacore -- genomic analytical tool and pathway analyzer. See here for access and registration info.

TAIR -- The Arabidopsis Information Resources maintains a database of genetic and molecular biology data for Arabidopsis thaliana.

NCBI (National Center for Biotechnology Information) -- collection public databases for research in computational biology, genome data, and biomedical information.

Ensembl -- software system which produces and maintains automatic annotation on selected eukaryotic genomes.

BLAST -- analysis tool that finds regions of similarity between biological sequences.

What is MetaCore?

MetaCore is an integrated software suite for functional analysis of experimental data. MetaCore is based on a curated database of human protein-protein, protein-DNA interactions, transcription factors, signaling and metabolic pathways, disease and toxicity, and the effects of bioactive molecules.

Use MetaCore for functional analysis of:

- gene expression
- metabolomics
- proteomics
- siRNA
- SNPs
- HCS

Questions?

Email: biosciences-ref@mit.edu

More ways to get help

Chat is offline

Ask Us

Ask a question, make an appointment, give feedback, or visit us.

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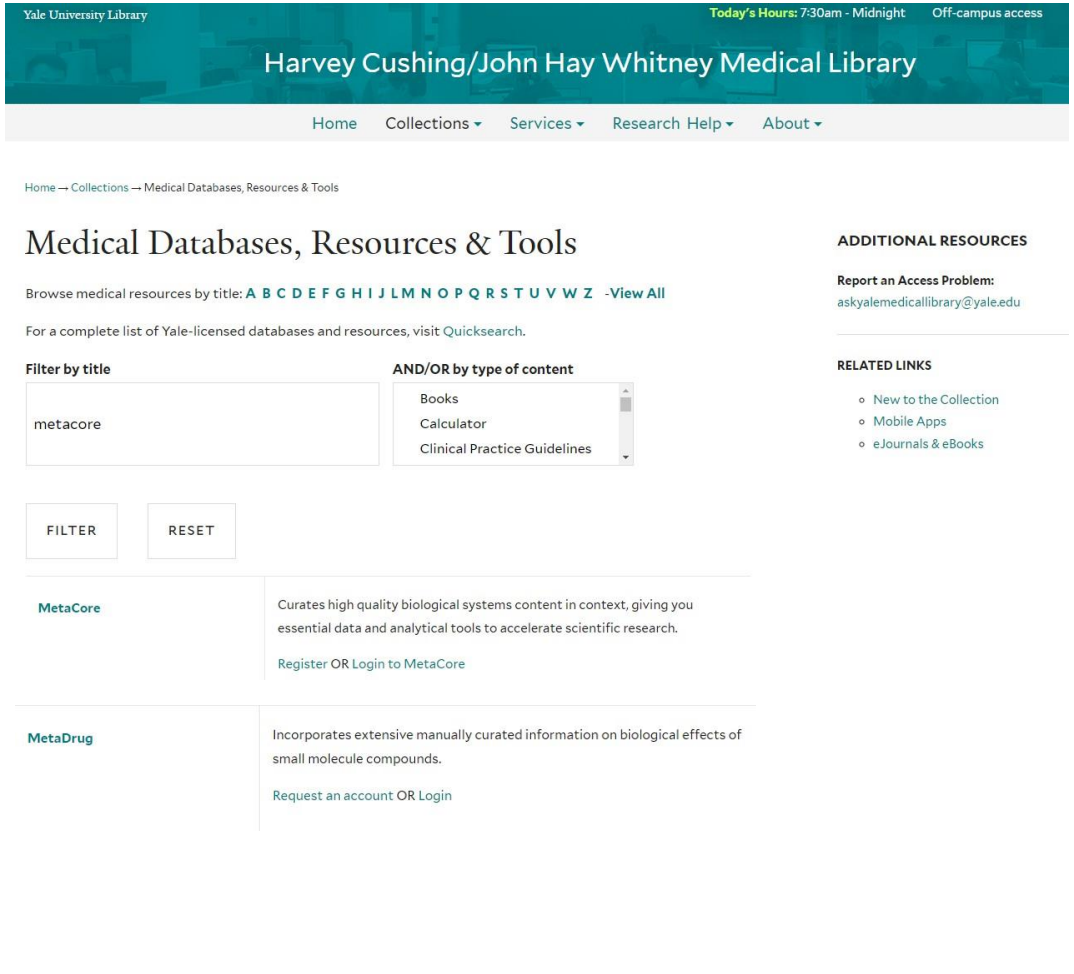
- Medicine
- Neuroscience & Cognitive Science



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Home → Collections → Medical Databases, Resources & Tools

Medical Databases, Resources & Tools

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Filter by title

metacore

AND/OR by type of content

Books
Calculator
Clinical Practice Guidelines

FILTER RESET

MetaCore

Curates high quality biological systems content in context, giving you essential data and analytical tools to accelerate scientific research.

Register OR Login to MetaCore

MetaDrug

Incorporates extensive manually curated information on biological effects of small molecule compounds.

Request an account OR Login

ADDITIONAL RESOURCES

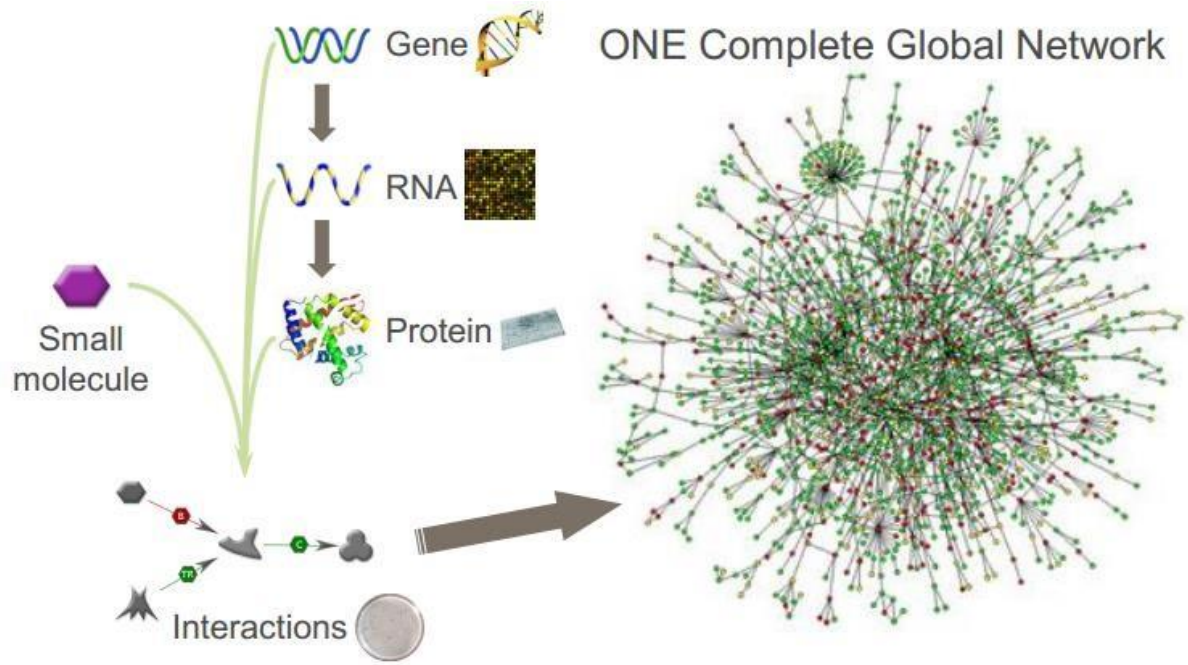
Report an Access Problem:
askyalemedicallibrary@yale.edu

RELATED LINKS

- New to the Collection
- Mobile Apps
- eJournals & eBooks

什么是MetaCore?

系统生物学简化复杂系统

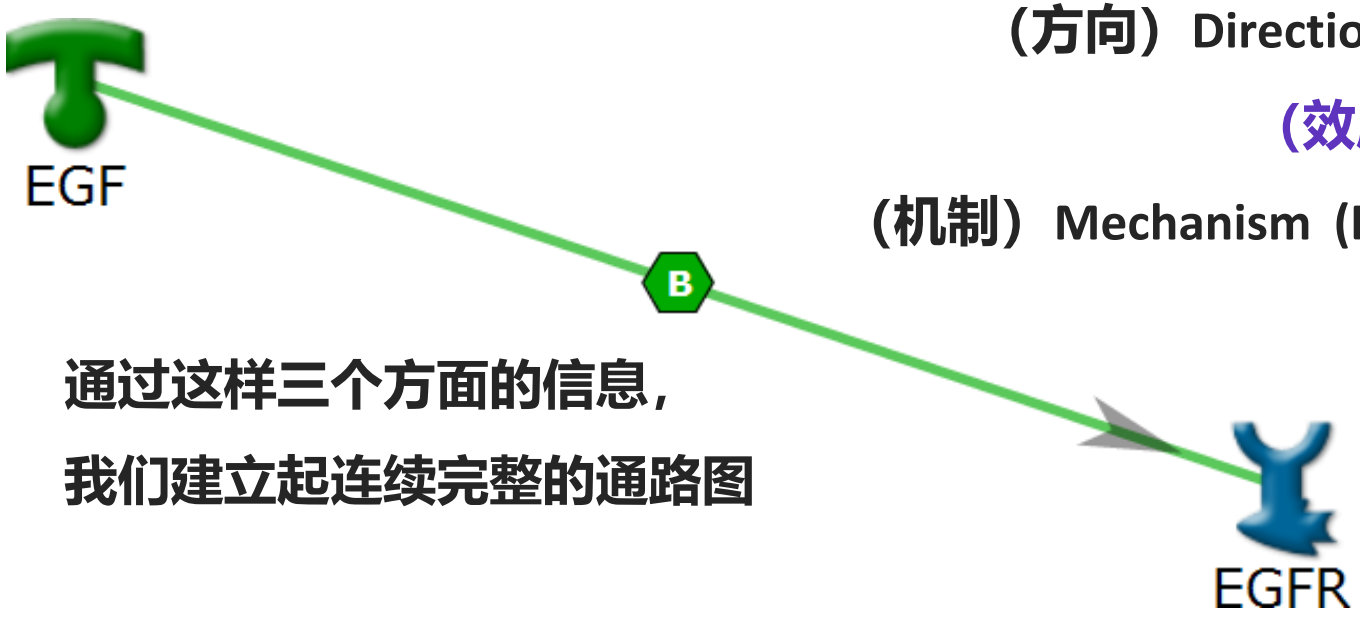


Cortellis Cloud™ （科睿唯安数据库）

MetaCore

Enrichment Analysis	Build Network	Interactome Analysis	Data mining
基因可以通过富集分析映射到已知的pathway/network上，并支持多组高通量数据分析	可根据实验数据或网络节点构建网络	分析互作关系，寻找重要的靶点/基因	通过快速检索或高级检索快速找到疾病/基因/蛋白等文献数据。

MetaCore 中的分子相互作用数据——包含：方向，效应，机制



（方向）Directionality (→)

（效应）Effect

（机制）Mechanism（B=Binding)

通过这样三个方面的信息，

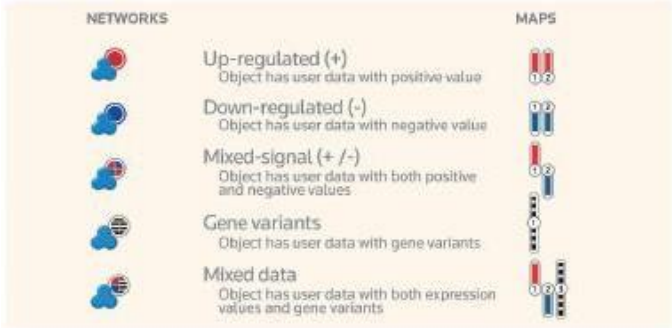
我们建立起连续完整的通路图

Clarivate™

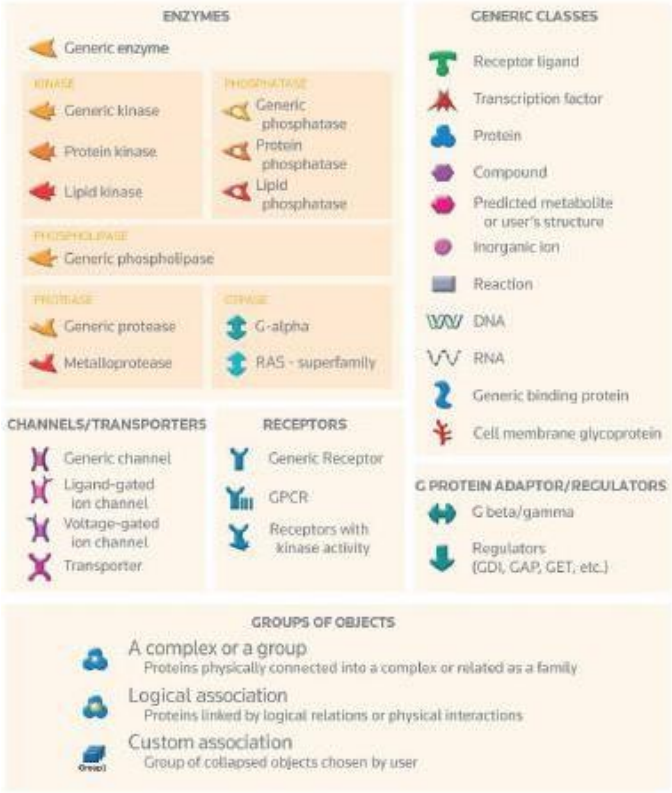
MetaCore

Quick reference guide

User Data

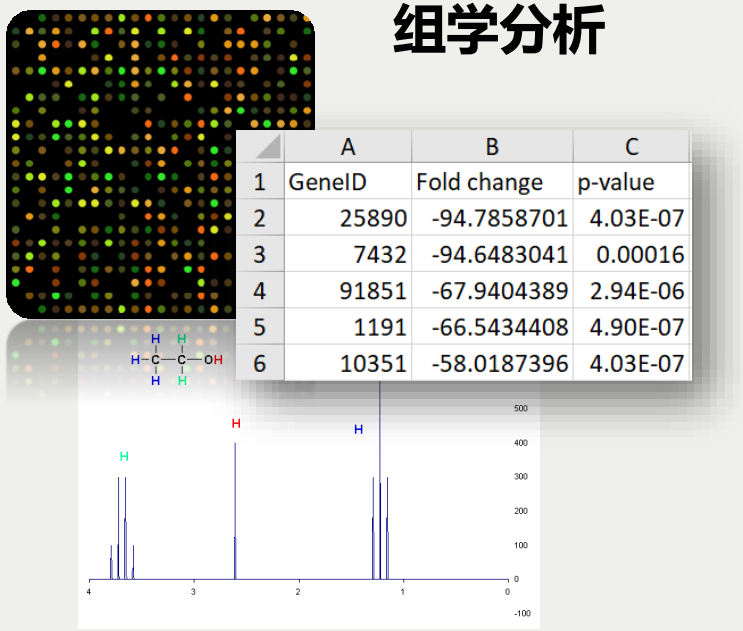


Network Objects



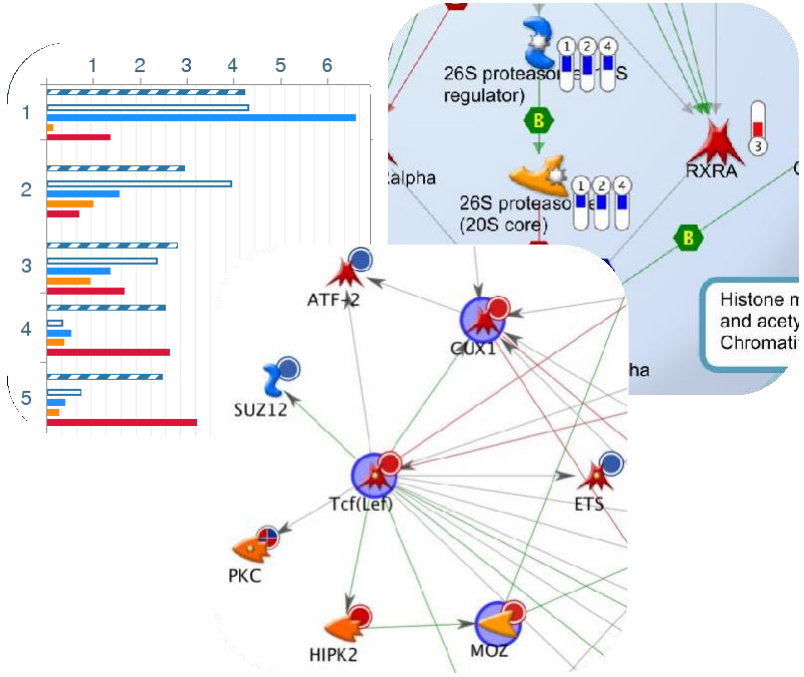
搜索/浏览

组学分析



	A	B	C
1	GeneID	Fold change	p-value
2	25890	-94.7858701	4.03E-07
3	7432	-94.6483041	0.00016
4	91851	-67.9404389	2.94E-06
5	1191	-66.5434408	4.90E-07
6	10351	-58.0187396	4.03E-07

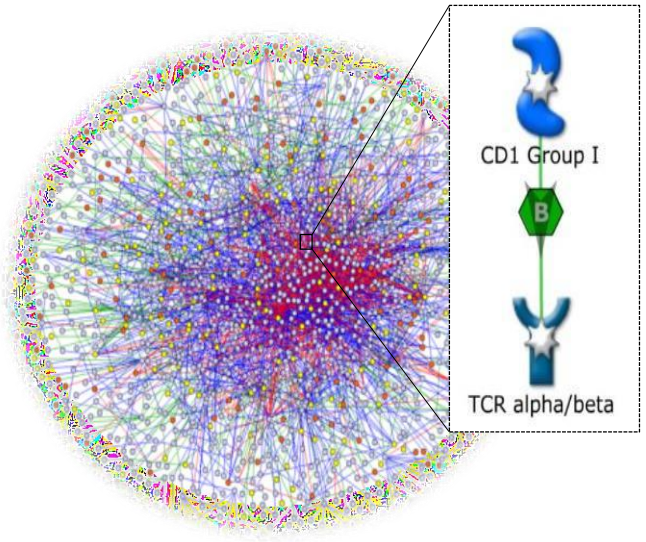
MetaCore



- 在经过验证的生物途径的背景下了解实验数据
- 生成并确认新靶标和生物标志物的假设

MetaBase

3700 种期刊，由科学家手动策划



Clarivate™

MetaCore / MetaBase的数据载量

Content Overview

- 每季度更新
- 科学家手动上传

MetaBase	number
Human Genes	63885
Human SwissProt proteins	20385
Mouse genes	73080
Mouse SwissProt proteins	17082
Rat genes	43048
Rat SwissProt proteins	8135
Compounds	983111
Compounds with structure	966368
Endogenous compounds	5464
Nutritional compounds	127
Metabolites of xenobiotic	40335
Drugs	9117
- Biologics	1360
- Small Molecules	7757
- Approved drugs	2290
- Withdrawn drugs	261
- Clinical trial drugs	4993
- Discontinued drugs	1187
- Preclinical drugs	250
- Unknown	136
- Drug combination regimens	8445

MetaCore	number
Human genes in network	29503
Mouse genes in network	28505
Rat genes in network	18685
Chemical compounds	528016
Drugs	4944
Endogenous compounds	3602
Metabolic reactions	50304
Transport reactions	4591
Processing Reactions	4459
Pubmed journals	3765
Pubmed records	3584562
Pubmed articles (unique)	319065
Total amount of interactions	3181746
- Protein – Protein	1398912
- Compound – Protein	990222
- Compound – Compound	12180
- Metabolic enzyme -Reaction	61429
- Transporter – Reaction	5217
- Substrate, Product – Reaction	134335
- RNA – Protein	579451
Pathway maps	1590
- Human genes in maps	8132
- Mouse genes in maps	7409
- Rat genes in maps	7213
- Interactions in maps	35698

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Meta Core 支持的浏览器

考虑到如果使用不支持的浏览器，会遇到的问题，特此建议使用metacore推荐的以下四种。

Latest Chrome version

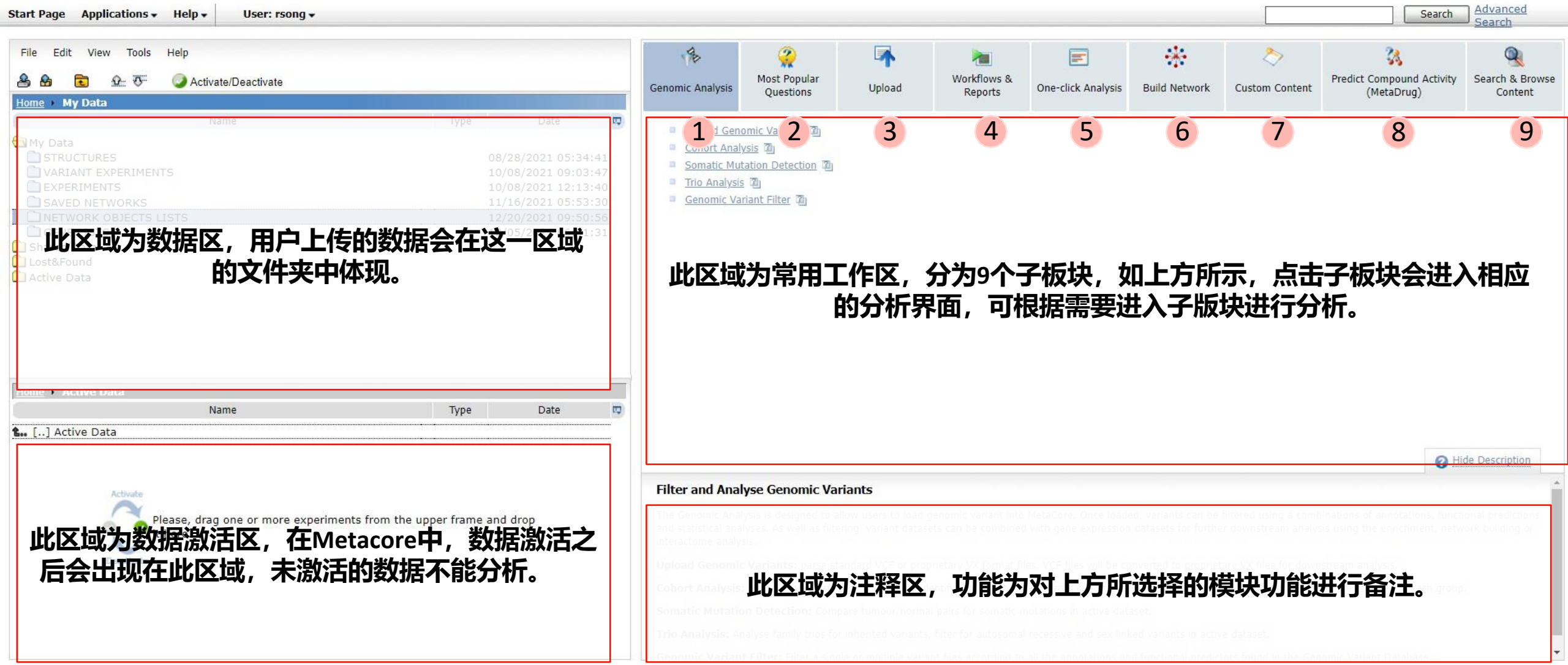
Latest FireFox version

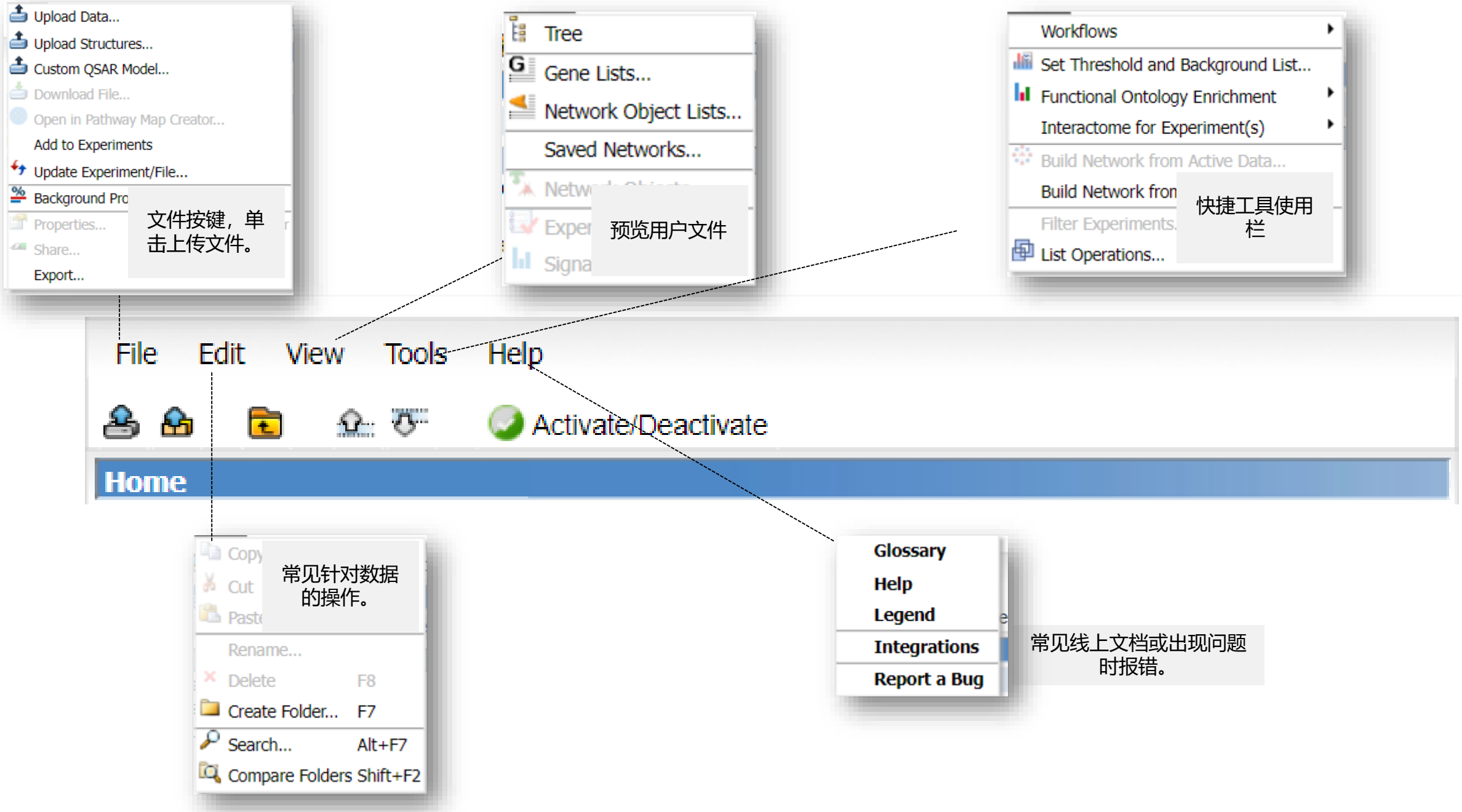
Latest MS Edge version

Safari version 12.0.3 and higher

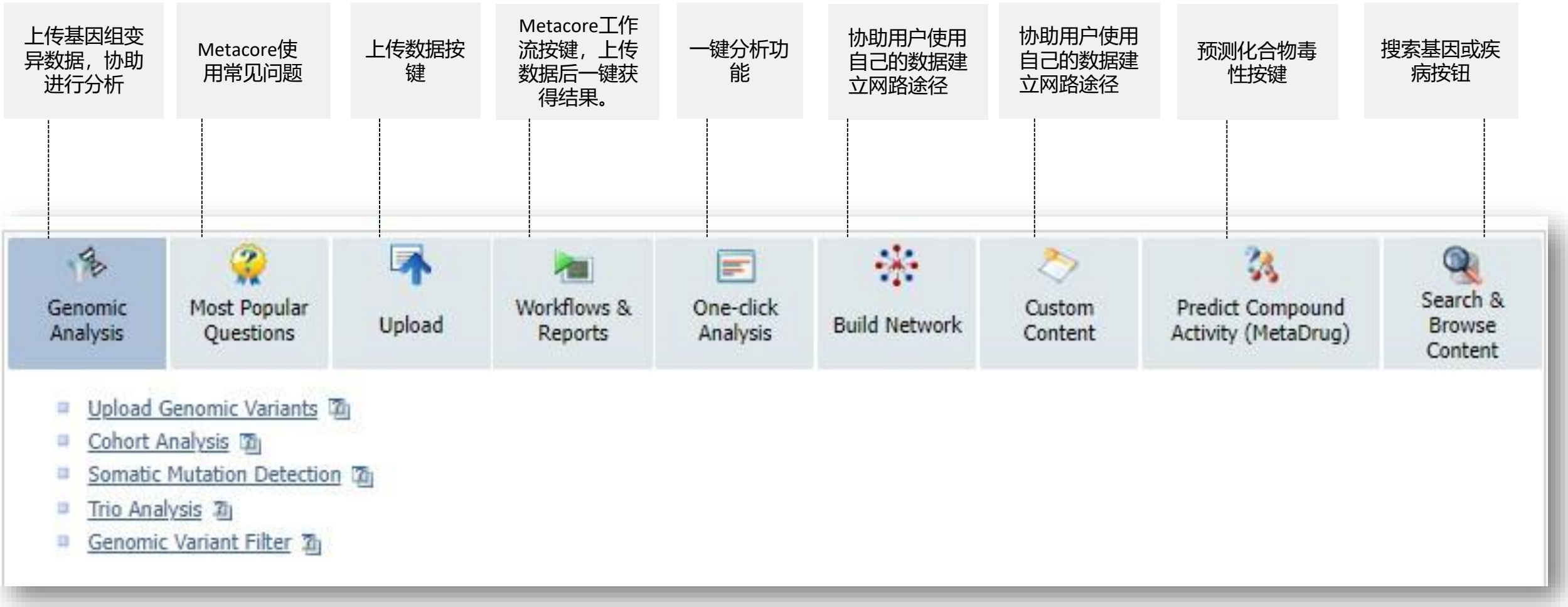
TIP： Microsoft are withdrawing support for the Internet Explorer from August 17, 2021 and therefore, from October 1, **2021 Clarivate will no longer support IE**. You may continue to use IE for MetaCore, but over time you may encounter issues that our support team will not be able to help with. To ensure you continue to have the best experience with MetaCore we encourage you to upgrade to MS Edge or other supported browsers.

Meta Core 界面概览




Upload Data...
Upload Structures...
Custom QSAR Model...
Download File...
Open in Pathway Map Creator...
Add to Experiments
Update Experiment/File...
Background Pro
Properties...
Share...
Export...
文件按键，单击上传文件。
Tree
Gene Lists...
Network Object Lists...
Saved Networks...
预览用户文件
Workflows
Set Threshold and Background List...
Functional Ontology Enrichment
Interactome for Experiment(s)
Build Network from Active Data...
Build Network fron
Filter Experiments...
List Operations...
快捷工具使用栏
File
Edit
View
Tools
Help
Activate/Deactivate
Home
Copy
Cut
Paste
Rename...
Delete F8
Create Folder... F7
Search... Alt+F7
Compare Folders Shift+F2
常见针对数据的操作。
Glossary
Help
Legend
Integrations
Report a Bug
常见线上文档或出现问题时报错。

Meta Core 界面功能介绍



日程

第一部分：MetaCore数据平台简介

第二部分：MetaCore重点功能介绍

第三部分：系统生物学案例分享

第四部分：内容回顾与总结

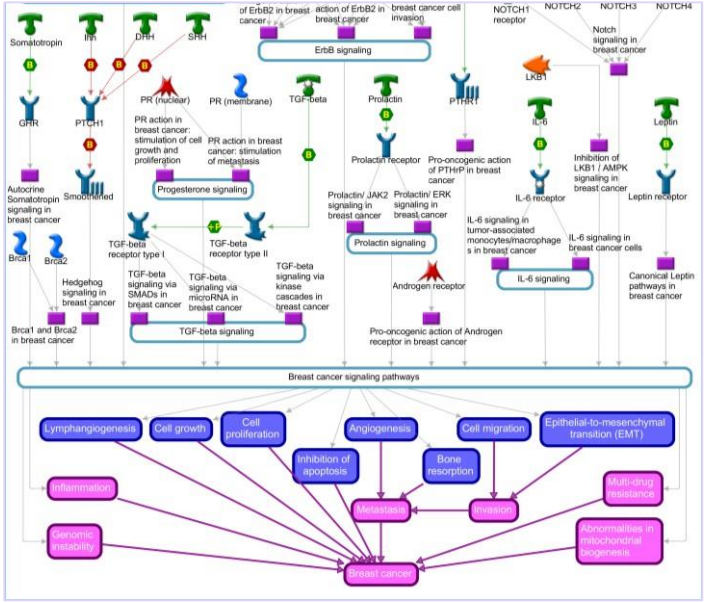
Clarivate™

MetaCore, a Cortellis Solution

- **关键问题**
- 我的组学数据在健康和患病分子途径的背景下意味着什么?
- 在我的疾病领域已经做了什么研究，可以帮助我开发新的假设?
- 在我感兴趣的途径或网络中，每种分子相互作用的机制，方向性和作用是什么?
- **功能和数据源**
- 一键式分析和节省时间的工作流程，如富集分析、实验比较、生物标志物评估等
- 来自同行评审文献的 1，500 多种**手动策划的途径**
- 3 M+分子相互作用的机制、方向性和效果

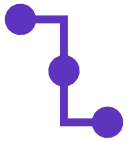
关键解决方案

- 模拟疾病途径并研究因果机制
- 发现药物靶点和生物标志物
- 可视化生物关系



MetaCore 基础功能与应用价值-概述

EZ Search



Build Network

Enrichment Analysis

功能

- 检索某对象的基因/突变/蛋白/药物/疾病等基本信息；
- 查看某对象参与的重要疾病过程及信号通路；
- 查看与该对象有直接相互作用关系的其他对象；
- 多种算法构建单个/多个对象的相互作用关系网络；
- 多组学数据同时分析，富集相关性最高的通路；

价值

- 帮助科研人员快速、全面、准确了解某个新的领域，提供项目/课题所需的基本资料，提高科研效率；
- 通过构建相互作用网络，发现潜在的分子间相互作用关系，为项目/课题顺利进行提供可能的方向；
- 通过上传数据富集分析，挖掘实验数据中隐藏的逻辑关系，帮助科研人员研究疾病机制、药物靶标、发现生物标记物及药物研发等；

查资料

指方向

定逻辑

日程

第一部分：MetaCore数据平台简介

第二部分：MetaCore重点功能介绍

第三部分：系统生物学案例分享

第四部分：内容回顾与总结

Clarivate™

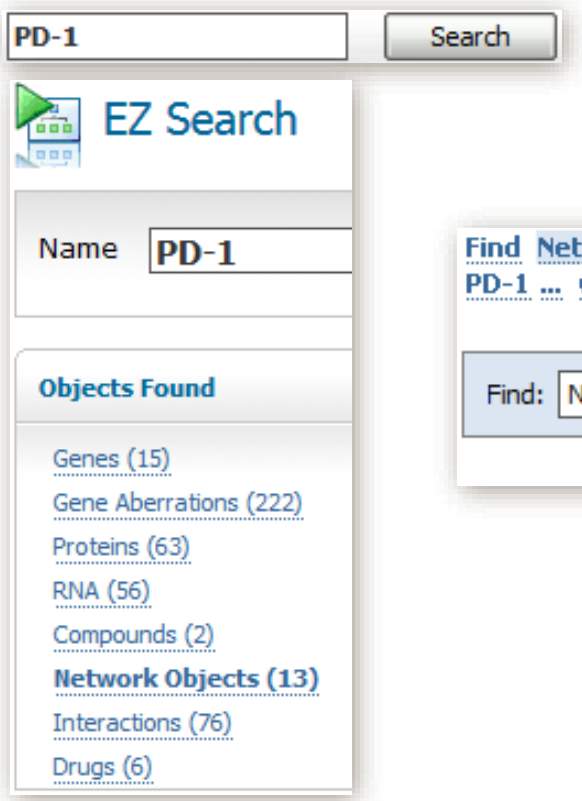
1-检索和靶点机制相关药物

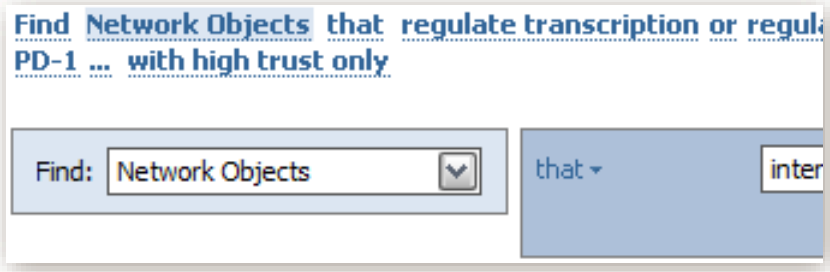
- MetaCore具有丰富的检索功能，协助高效检索。

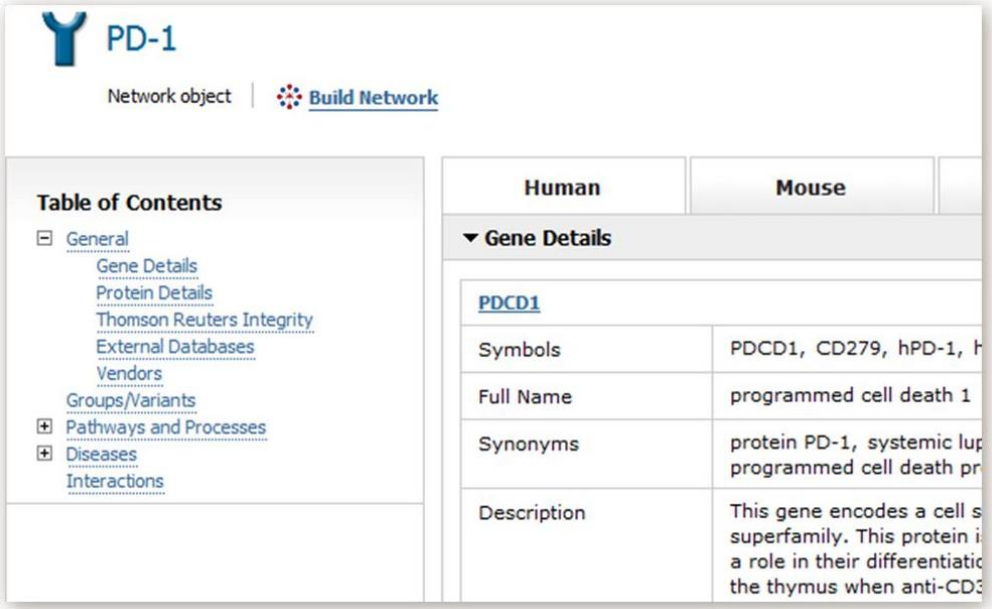
CASE-通过知识挖掘了解肿瘤免疫靶点PD-1

EZ search

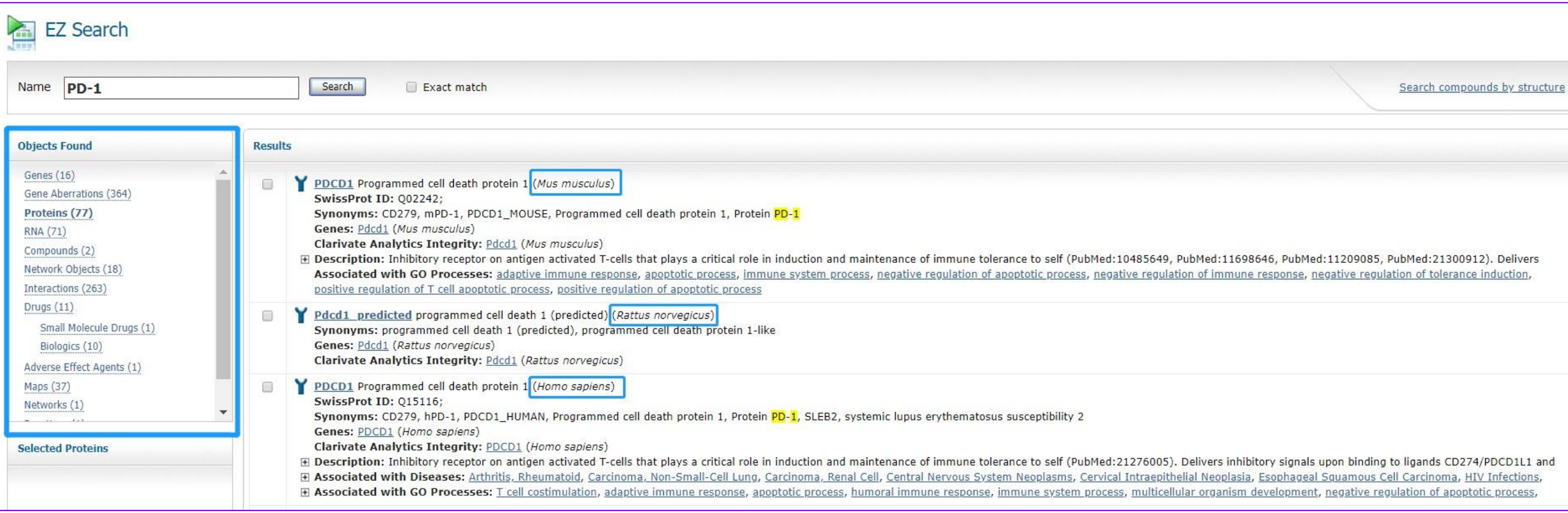
EZ search → Advanced Search → Export to MetaCore







通过知识挖掘了解肿瘤免疫靶点PD-1



通过知识挖掘了解肿瘤免疫靶点PD-1

PDCD1_HUMAN

Protein | Build Network

Table of Contents

- General
  - Protein Details
  - Clarivate Analytics Integrity
  - External Databases
  - Vendors
- Groups/Variants
- Pathways and Processes
  - Pathway Maps
  - Process Networks
  - GO Processes
  - GO Molecular Functions
- Diseases
  - Associated Diseases
  - Drug Target for
- Interactions

General

Protein Details

PDCD1_HUMAN	
Name	PDCD1_HUMAN / Programmed cell death protein 1
Synonyms	CD279, hPD-1, PDCD1_HUMAN, Programmed cell death protein 1, Protein PD-1, SLEB2, systemic lupus erythematosus susceptibility 2
Description	Inhibitory receptor on antigen activated T-cells that plays a critical role in induction and maintenance of immune tolerance to self (PubMed:21276005). Delivers inhibitory signals upon binding to ligands CD274/PDCD1L1 and CD273/PDCD1LG2 (PubMed:21276005). Following T-cell receptor (TCR) engagement, PDCD1 associates with CD3-TCR in the immunological synapse and directly inhibits T-cell activation (By similarity). Suppresses T-cell activation through the recruitment of PTPN11/SHP-2: following ligand-binding, PDCD1 is phosphorylated within the ITSM motif, leading to the recruitment of the protein tyrosine phosphatase PTPN11/SHP-2 that mediates dephosphorylation of key TCR proximal signaling molecules, such as ZAP70, PRKCQ/PKCtheta and CD247/CD3zeta (By similarity). The PDCD1-mediated inhibitory pathway is exploited by tumors to attenuate anti-tumor immunity and escape destruction by the immune system, thereby facilitating tumor survival (PubMed:28951311). The interaction with CD274/PDCD1L1 inhibits cytotoxic T lymphocytes (CTLs) effector function (PubMed:28951311). The blockage of the PDCD1-mediated pathway results in the reversal of the exhausted T-cell phenotype and the normalization of the anti-tumor response, providing a rationale for cancer immunotherapy (PubMed:22658127, PubMed:25034862, PubMed:25399552).
Molecular Weight	31647
Genes	PDCD1
Network objects	PD-1
Precursor	PDCD1 (HUMAN) transcript
Localization	external side of plasma membrane, integral component of membrane, plasma membrane
Organ/Tissue/Fluid Expression (RNA)	Adrenal Cortex; Adrenal Glands; Amniotic Fluid; Amygdala; Appendix; Atrioventricular Node; Blood; Bone Marrow; Brain; Caudate Nucleus; Cerebellum; Cerebral Cortex; Ciliary ganglion; Conjunctiva; Corpus Uterus; Fetal Brain; Fetal Liver; Fetal Lung; Fetal Thyroid; Frontal Lobe; Ganglia, Spinal; Globus Pallidus; Gyrus Cinguli; Heart; Hippocampus; Hypothalamus; Kidney; Lacrimal Apparatus; Lens, Crystalline; Leydig Cells; Liver; Lung; Lymph Nodes; Medulla Oblongata; Muscle, Skeletal; Muscle, Smooth; Myometrium; Occipital Lobe; Olfactory Bulb; Ovary; Palatine Tonsil; Pancreas; Parietal Lobe; Pituitary Gland; Placenta; Plasma; Pons; Prefrontal Cortex; Prostate; Respiratory Mucosa; Salivary Glands; Seminiferous Tubules; Spinal Cord; Superior Cervical Ganglion; Temporal Lobe; Testis; Thalamus; Thymus Gland; Thyroid Gland; Tongue; Trachea; Trigeminal Ganglion; Urinary Bladder; Urothelium; Uterus

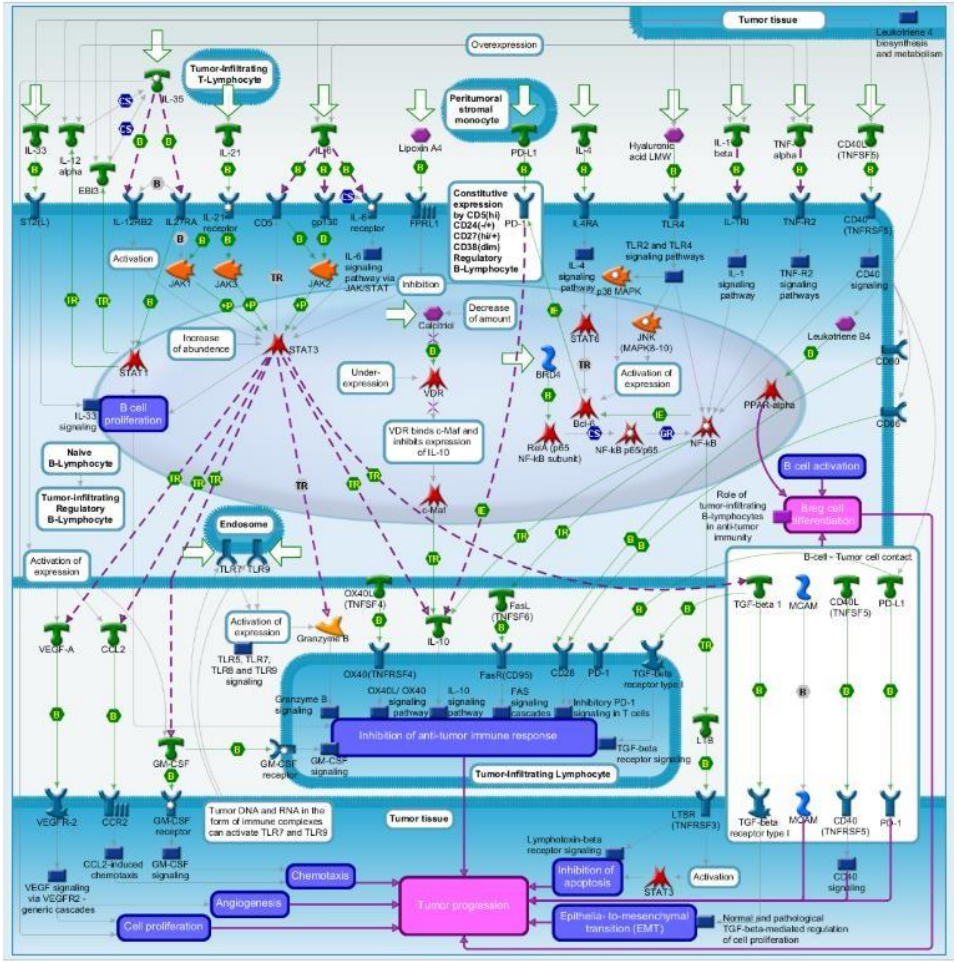
Clarivate Analytics Integrity

External Databases

Vendors

通过知识挖掘了解肿瘤免疫靶点PD-1

调节性B细胞与肿瘤细胞的相互作用



B-regulatory cells and tumor cells intercellular interaction

Abstract:

In neoplastic disorders, B-regulatory cells (Bregs) are generated in response to signals from the tumor microenvironment and in turn promote tumor growth through expression of number of mediators that can act directly and indirectly on the diversity of leukocyte subsets infiltrating developing tumors and evolving neoplastic cells. Bregs express a variety of cytokines and other immunosuppressive molecules including IL-10, IL-35, TGF-beta 1, PD-L1, PD-1, FasL(TNFSF6), CD40L(TNFSF5), CD40(TNFRSF5) and OX40L(TNFSF4). This cell subset may also express proteases, such as Granzyme B, that directly impair T cell function.

Details:

In neoplastic disorders, B-regulatory cells (Bregs) are generated in response to signals from the tumor microenvironment and in turn promote tumor growth through expression of number of mediators that can act directly and indirectly on the diversity of leukocyte subsets infiltrating developing tumors and evolving neoplastic cells [1], [2], [3], [4], [5]. In addition to secreting mediators, tumor cells can promote Breg cells generation via direct cell-to-cell contact [6], [7], [8].

Bregs infiltration has been identified in a many malignancies including ovarian, gastric, non-small cell lung cancer, pancreatic, esophageal, head and neck, tongue squamous cell carcinoma and hepatocellular carcinomas [5], [9], [10], [11], [12], [13], [14], [15], [16], [17].

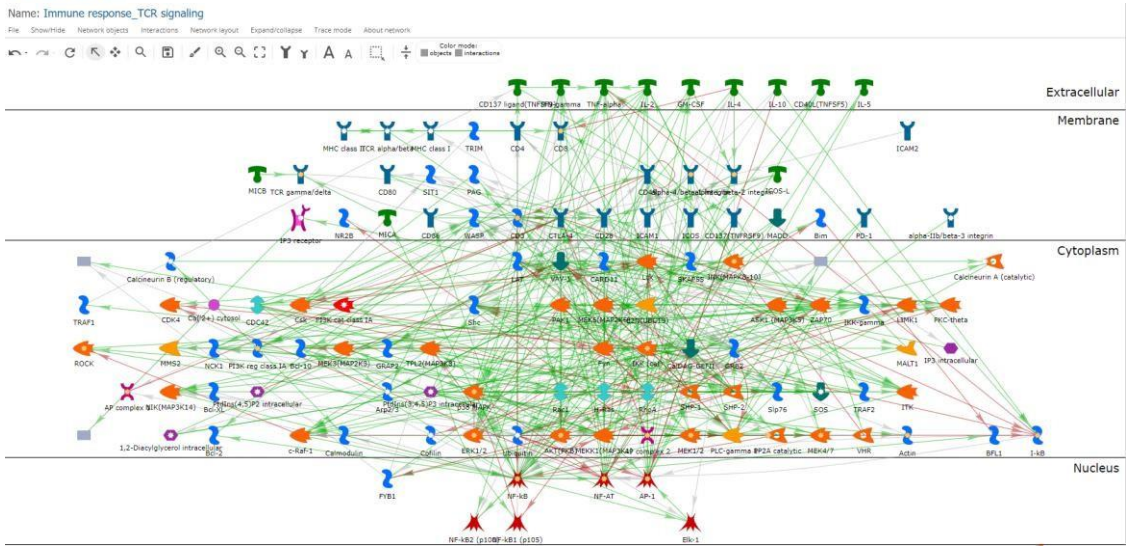
Bregs express a variety of suppressive cytokines and ligands which are implicated in the suppression of anti-tumor immunity including IL-10, IL-35, TGF-beta 1, PD-L1, PD-1, FasL(TNFSF6), CD40L(TNFSF5), CD40(TNFRSF5) and OX40L(TNFSF4). This cell subset may also express proteases, such as Granzyme B, which directly impair T cell function [3], [4], [5], [18], [19], [20].

Capability of tumor-infiltrating B cells to differentiate into Bregs subset is regulated by B cell antigen receptor (BCR), IL-35, IL-21, IL-6, PD-L1, IL-4, TLR4, IL-1 beta, TNF-alpha, CD40L(TNFSF5) and Calcitriol signaling pathways [15], [21], [22], [23], [24], [25].

IL-35, via IL-12RB2 and IL27RA, activates STAT1 and STAT3, thereby inducing Breg subset, and promotes the expression of IL-35 subunits IL-12 alpha and EBI3, and IL-10 expression [26], [27]. Bregs-mediated production of IL-35 can lead to tumor cell proliferation [19], [20]. Overexpression of IL-12 alpha and EBI3 in tumor tissue can result in higher induction of Bregs subset, elevated production of IL-35 and IL-10, which in turn promote tumor progression [28], [29], [30], [31], [32].

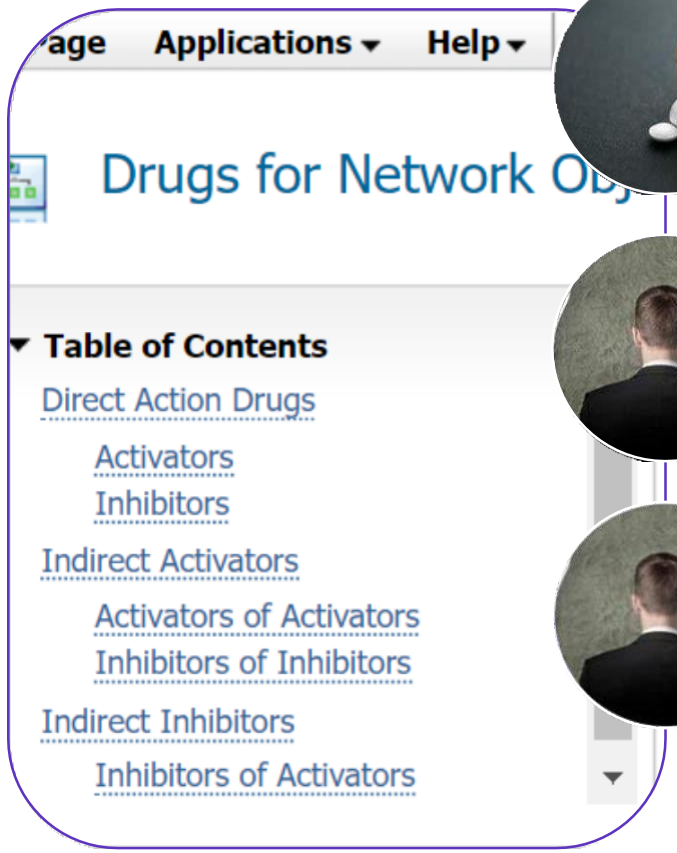
B cells stimulated with IL-21 also respond with the development of a population of B cells expressing IL-10. IL-21 via IL-21 receptor induces JAK1 and JAK3-dependent STAT3 pathway. Activated STAT3 promotes the expression of suppressors of anti-tumor immune response IL-10 and Granzyme B [5], [22], [33]. Moreover, tumor DNA and RNA in the form of immune complexes can activate TLR7 and TLR9 that elevate the expression levels of Granzyme B [22], [34], [35], [36].

IL-6 can induce the expression of IL-10 via CD5 and IL-6 receptor-dependent activation of STAT3. IL-6 directly binds to CD5 and gp130 that leads to activation of JAK2 and its downstream transcription factor STAT3. STAT3 upregulates CD5 expression, thereby forming a feed-forward loop in the B cells. In addition, IL-6, possibly via STAT3 activation, promotes the expression of VEGF-A, CCL2 and GM-CSF, by B cells, which leads to tumor cell population proliferation, angiogenesis and chemotaxis [23], [37], [38], [39], [40], [41], [42], [43], [44]. Overexpression of IL-6 in tumor can lead to increased production of IL-10 by Bregs [45], [46], [47].



查找网络对象的药物-Drugs for Network Object

MetaCore提供直接或间接地激活或抑制所选对象的药物。这些药物被安排在三个主要组别，每个组别有两个分组，说明如下：



Direct action drugs

- Activators：**直接激活**原始网络对象的药物。
- Inhibitors：**直接抑制**原始网络对象的药物。

Indirect activators

- Activators of activators：激活原始网络对象的药物。
- Inhibitors of inhibitors：抑制原始网络对象的药物

Indirect inhibitors

- Inhibitors of activators：抑制网络对象的药物，能激活原有的网络对象。
- Activators of inhibitors：激活网络对象的药物，抑制了原有的网络对象。

CASE： PD-1 网络对象的药物-Drugs for Network Object

▼ Indirect Activators

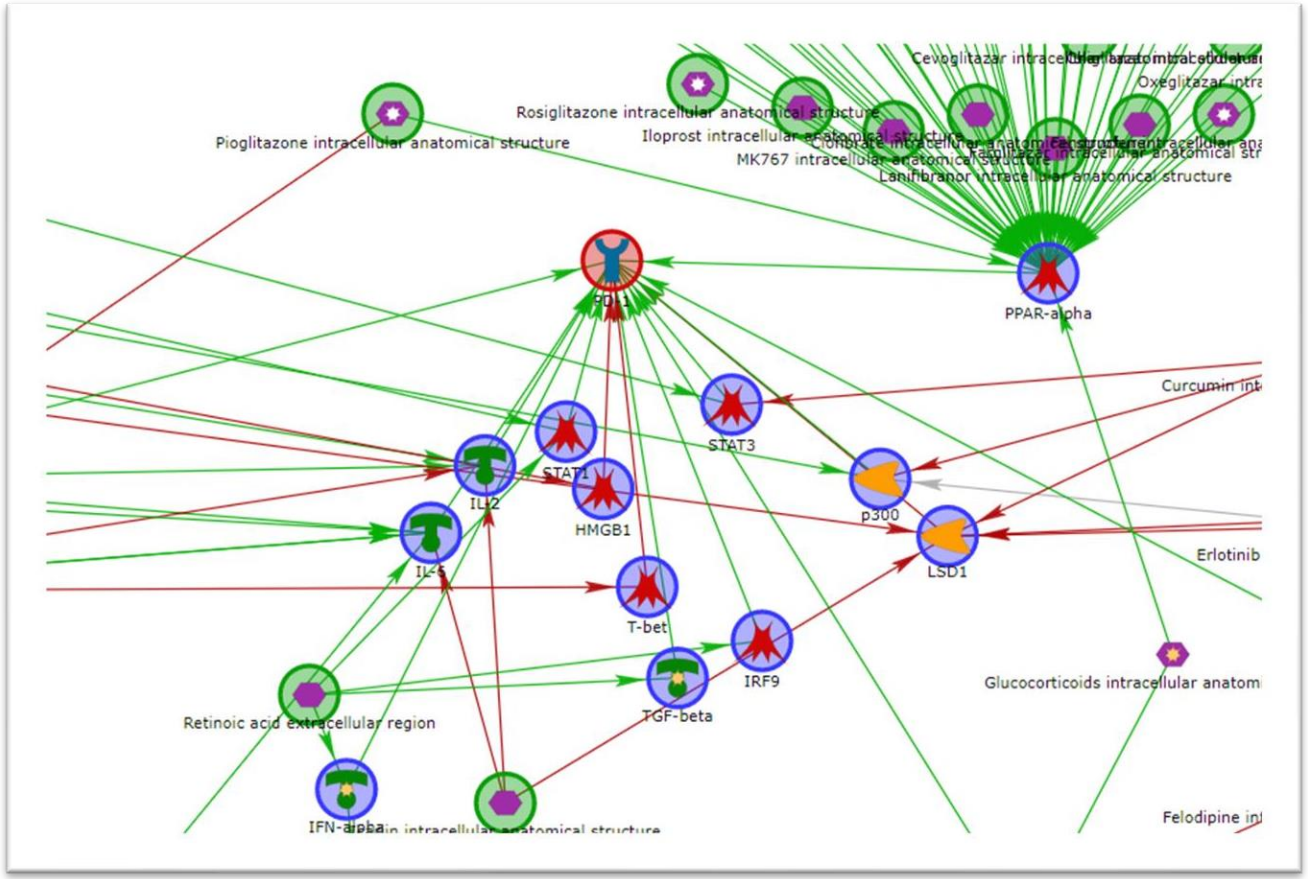
Indirect Activators

▼ Activators of Activators

NW Object	#	NW Object 2	Reference (NW Obj-NW Obj2)	Drug	Mechanism	Reference (NW Obj2-Drug)
PD-1	1.	PPAR-alpha		Imiglitazar intracellular anatomical structure	Binding	15219816
				Oleic acid intracellular anatomical structure	Binding	10198642,10529898,10691680,16731579,16731579,8611035,16731579
				Eicosapentaenoic acid intracellular anatomical structure	Binding	9113986,10198642,10529898
				Linolenic acid intracellular anatomical structure	Binding	16731579,10198642,16731579,9113986,16731579
				GW501516 intracellular anatomical structure	Binding	12699745,16797985,17512197,12699745
				Chiglitazar intracellular anatomical structure	Unspecified	
				Flufenamic acid intracellular anatomical structure	Unspecified	9013583
				Muraglitazar intracellular anatomical structure	Binding	15771468

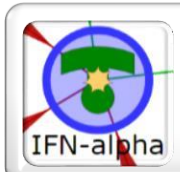
CASE： PD-1 网络对象的药物-Drugs for Network Object

Indirect Activators



原始对象，红色圈。

药物，绿色圈。



中间物体，蓝色圈。

2-按细胞类型/组织或细胞定位确定基因的优先级

- 从筛选中了解候选基因列表，更有效地识别和优先处理有前途的靶标。

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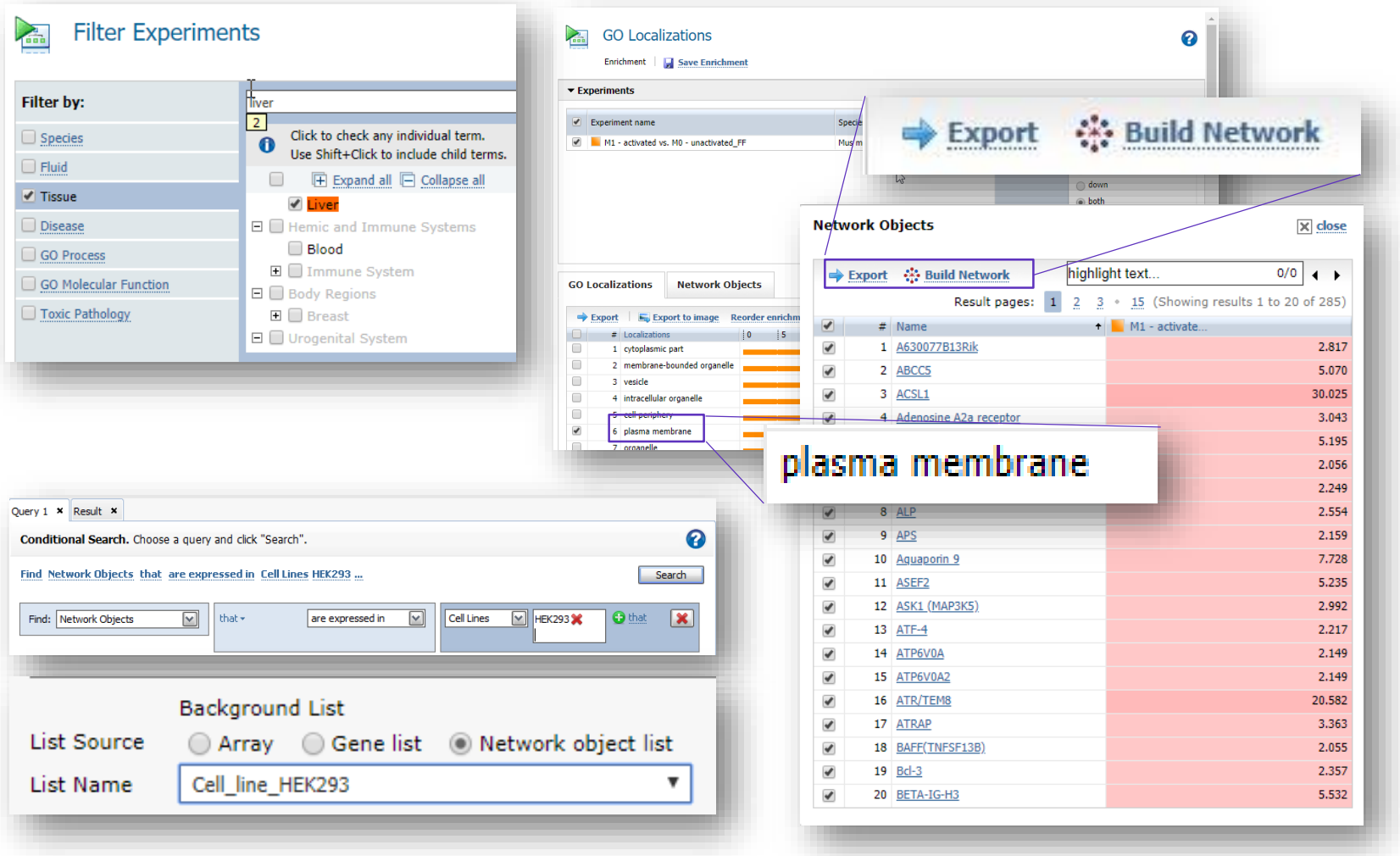
2.按细胞类型/组织或细胞定位确定基因的优先级



- 从候选基因列表中识别潜在靶标
-
- 优先考虑位于plasma membrane-细胞膜中的候选物或已知在特定细胞系或组织中表达的候选物，以专注于那些成功可能性较大的候选物。

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3-了解靶点和疾病之间的关联

- 加速并简化查找文献证据,高效确定候选目标的过程。

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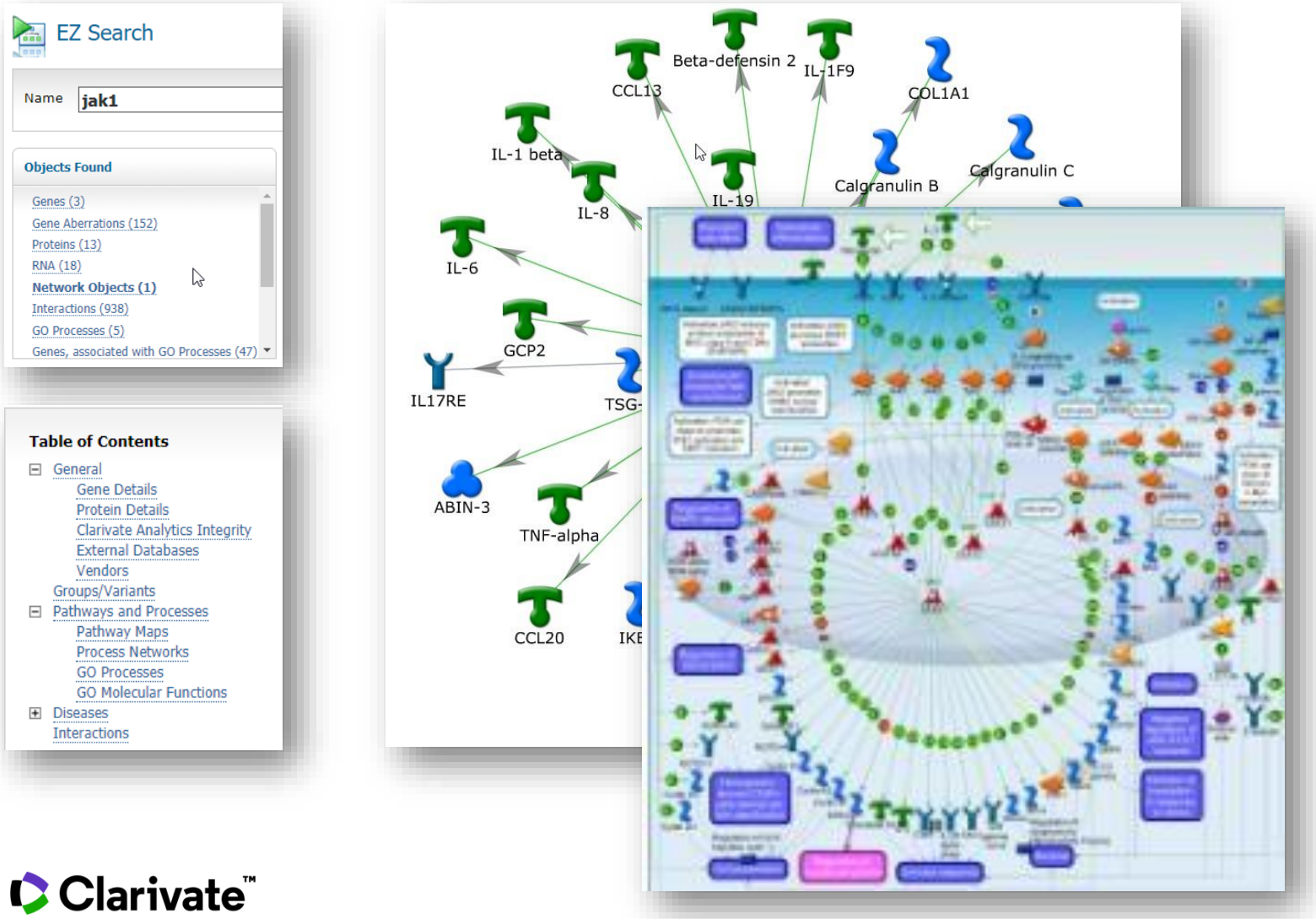
3.靶点– 疾病关联



- 加速并简化查找文献证据以确定候选目标的过程
- 建立基因- 疾病背后的生物学原理关联，以便更支持做出选择决策。

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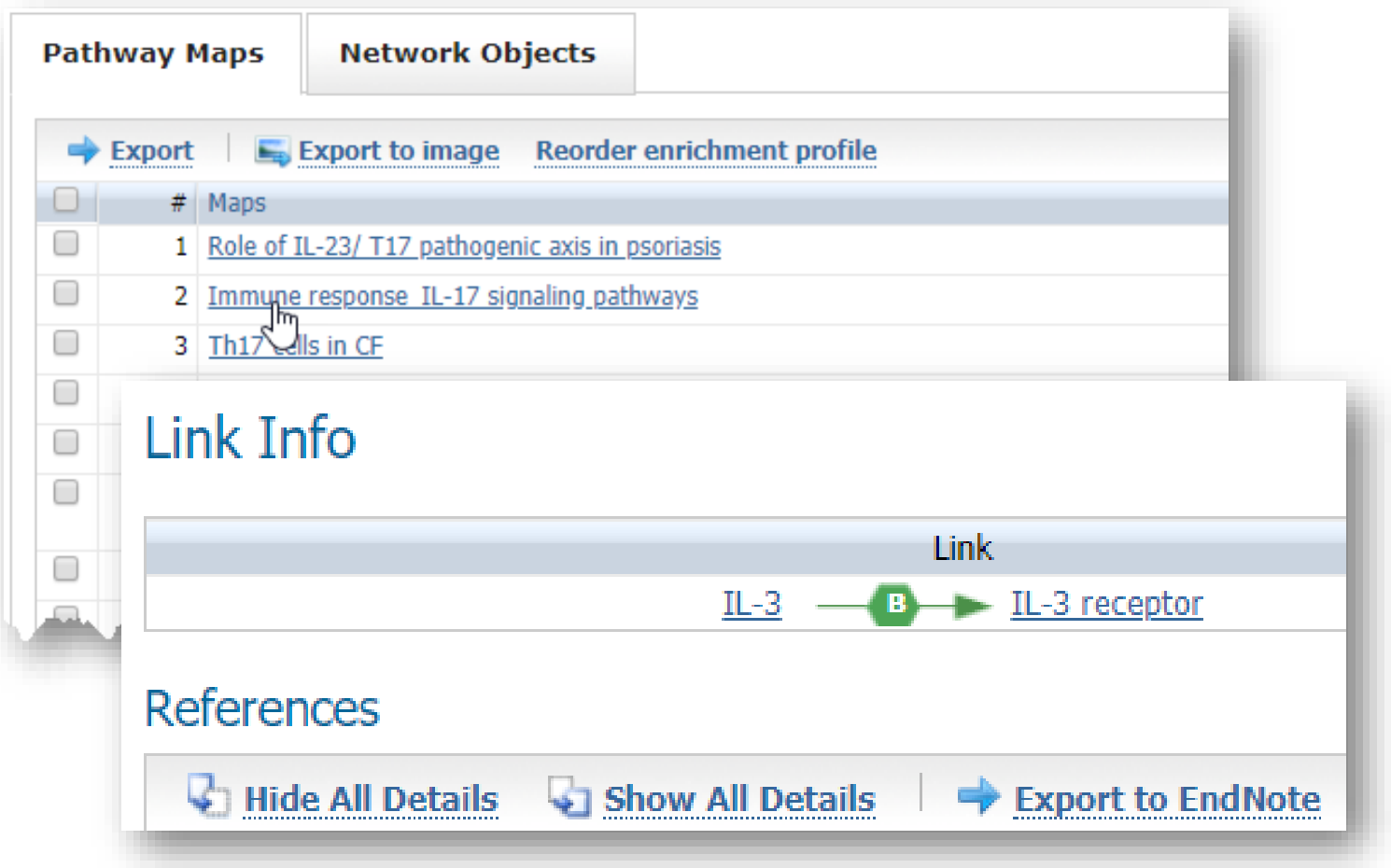
3.靶点– 疾病关联



- 加速并简化查找文献证据以确定候选目标的过程
- 每一条疾病通路都有专业编辑进行注释。

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4-定义特殊的疾病机制

- 加速并简化查找文献证据以确定候选目标的过程。
- 通过建立自己的路径并使用metacore专有知识进行注释，以确保研究相关人员之间拥有之间清晰一致的沟通。

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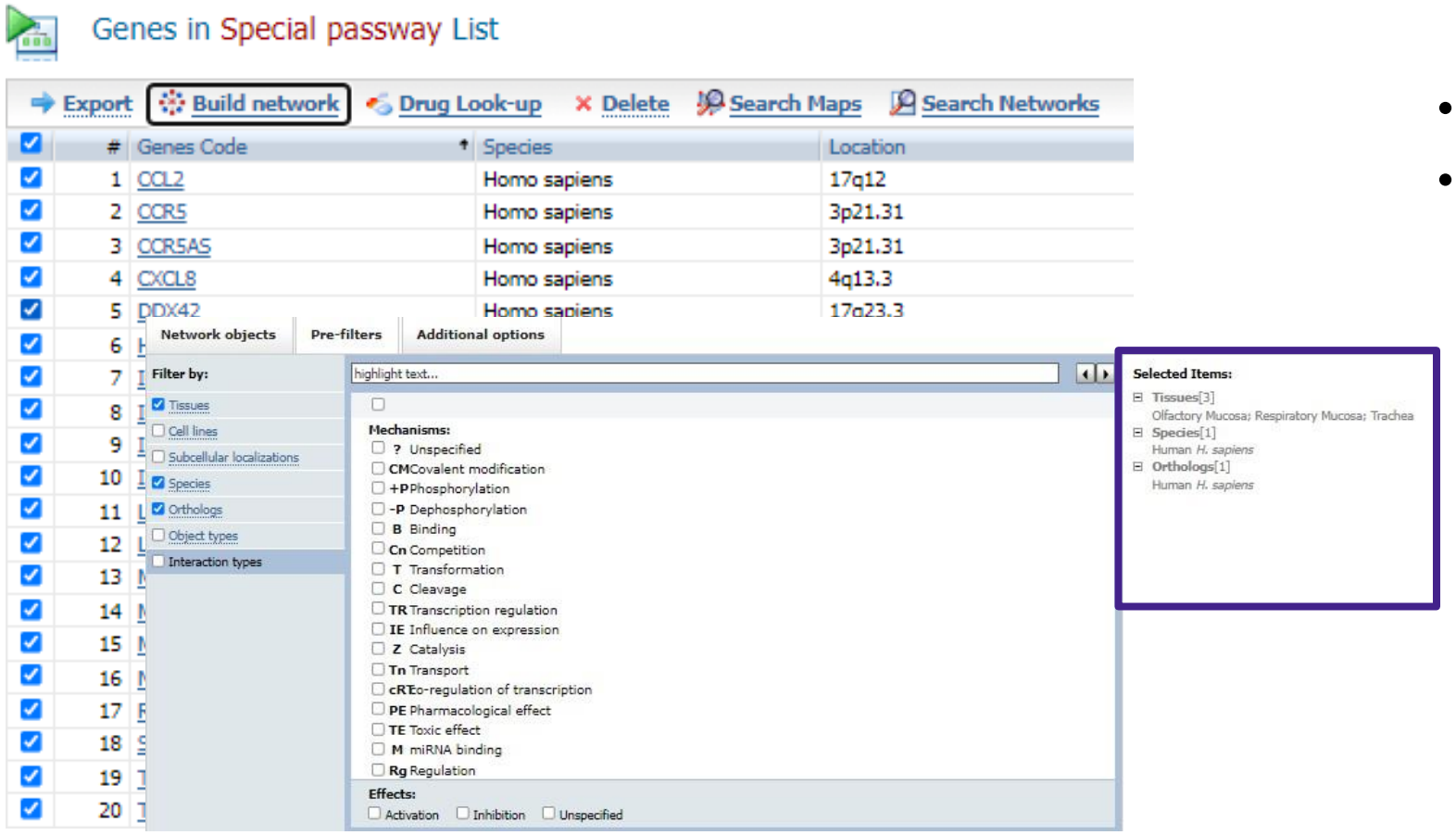
4.建立研究特殊路径



- 分析特殊的基因列表。
- 过滤特殊研究偏好：组织（呼吸道黏膜，气管位置，）物种过滤等。

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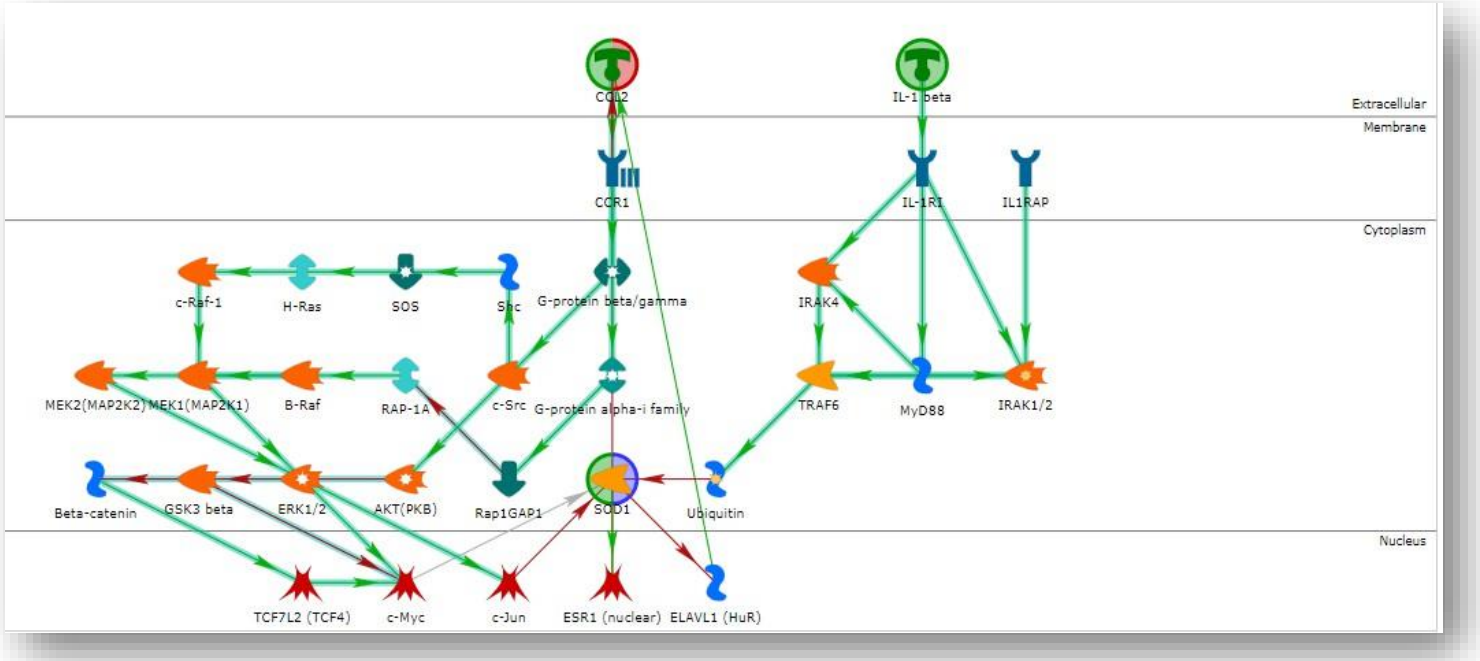
4.建立研究特殊路径



- 可调节通路图
- 提供多种数据进行筛选。
- 建立研究路径，用metacore专有知识进行注释，确保研究相关人员之间拥有之间清晰一致的沟通。

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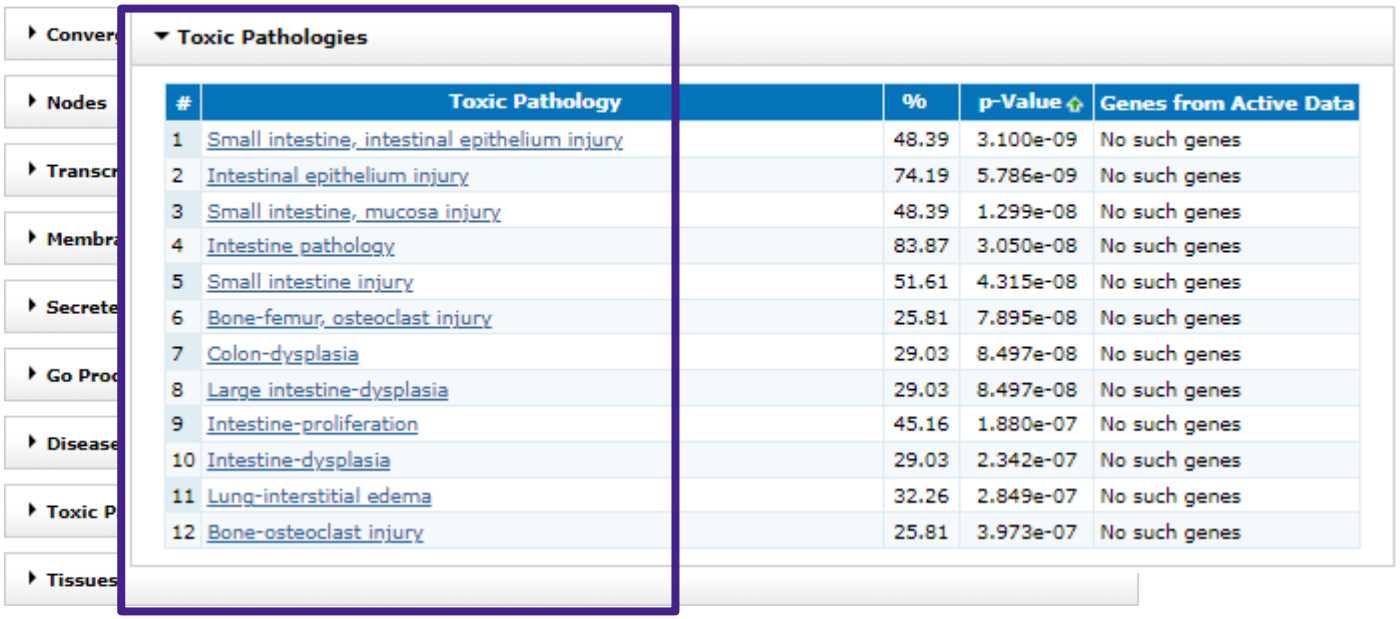
4.通路图分析



#	Toxic Pathology	%	p-Value	Genes from Active Data
1	Small intestine, intestinal epithelium injury	48.39	3.100e-09	No such genes
2	Intestinal epithelium injury	74.19	5.786e-09	No such genes
3	Small intestine, mucosa injury	48.39	1.299e-08	No such genes
4	Intestine pathology	83.87	3.050e-08	No such genes
5	Small intestine injury	51.61	4.315e-08	No such genes
6	Bone-femur, osteoclast injury	25.81	7.895e-08	No such genes
7	Colon-dysplasia	29.03	8.497e-08	No such genes
8	Large intestine-dysplasia	29.03	8.497e-08	No such genes
9	Intestine-proliferation	45.16	1.880e-07	No such genes
10	Intestine-dysplasia	29.03	2.342e-07	No such genes
11	Lung-interstitial edema	32.26	2.849e-07	No such genes
12	Bone-osteoclast injury	25.81	3.973e-07	No such genes

- 一键获得关于通路图注解以及相关疾病网络。
- 快速进一步挖掘相关疾病机制。

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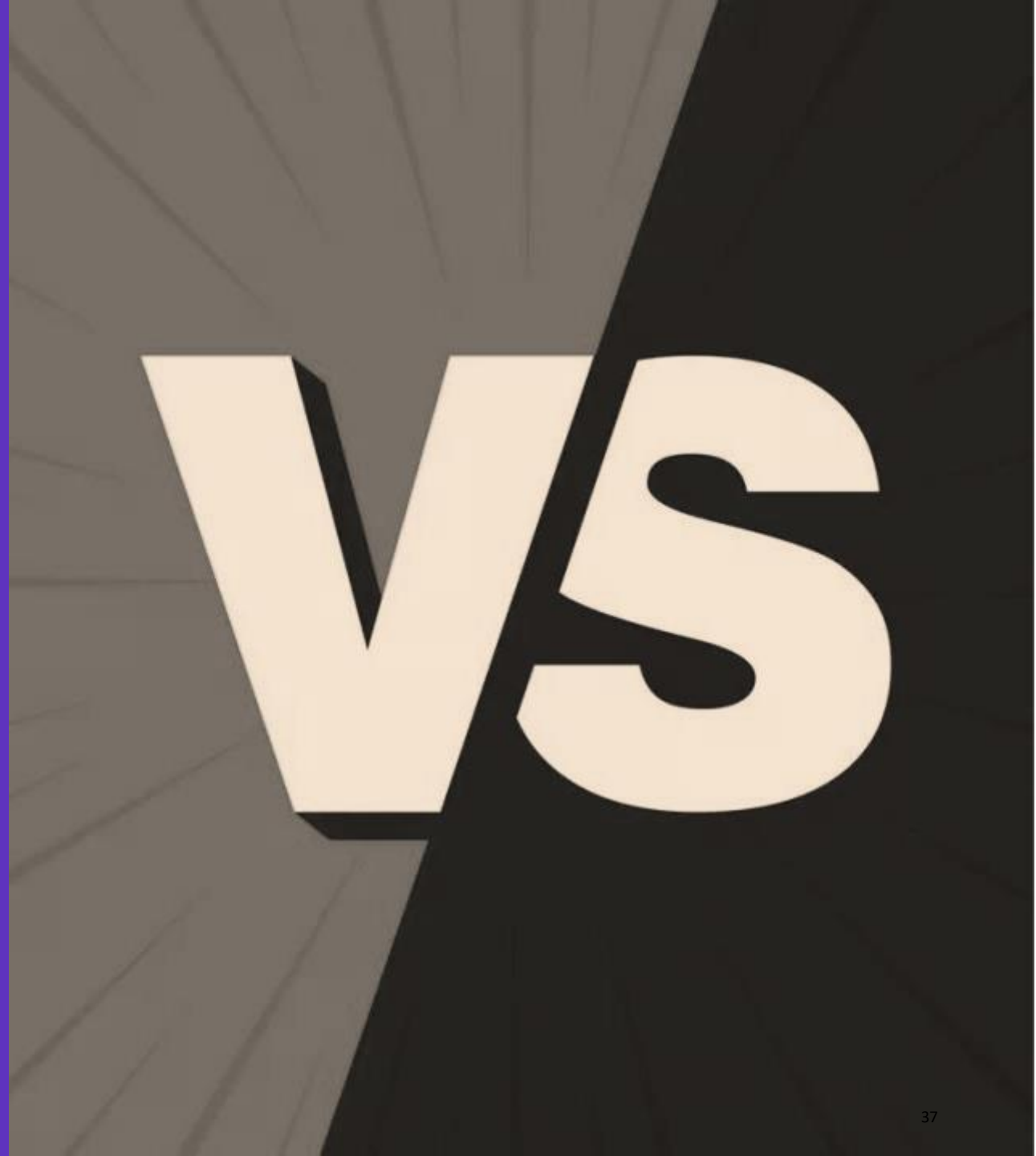
5-对比研究工作流
Compare Experiments Workflow

实用场景

- 多个数据集情况。
- 希望了解哪些过程（通路、网络、基因本体、疾病等）是独特的，哪些是数据集共有的。

- 例：已在组学数据中识别出两个患者亚组，并希望了解每个亚组独有的生物学过程



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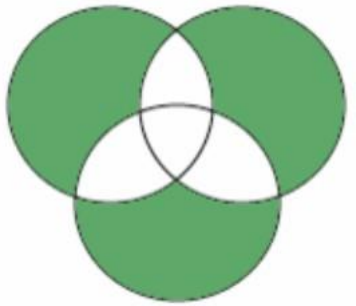
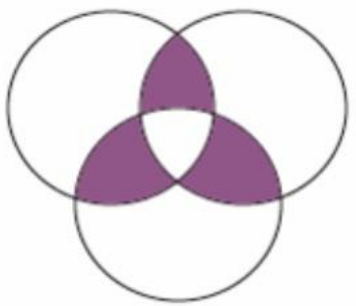
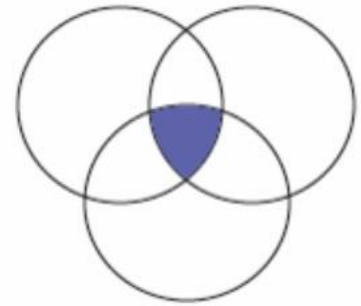
5.数据集意义

Figure 2. Datasets

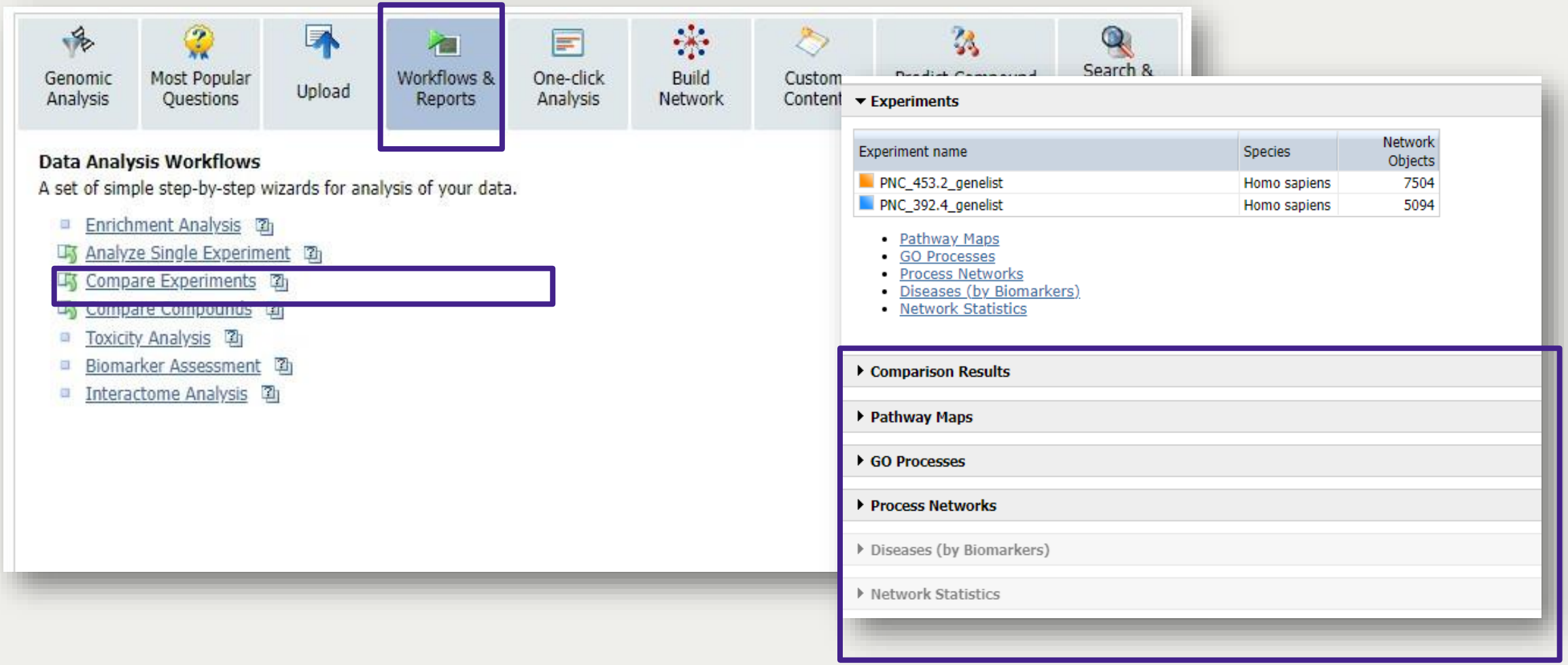
Unique (one separate set for each experiment)	Similar (the set comprising all partial intersections of experiments)	Common (the set which is the common part of all experiments)
		

- “Unique”set:每个单独的实验（由该实验特有的对象组成）。
- “Similar”set： 由所有既不唯一，也不常见的对象组成)。
- ”Common“set:（由每个实验中发现的所有网络对象组成）。

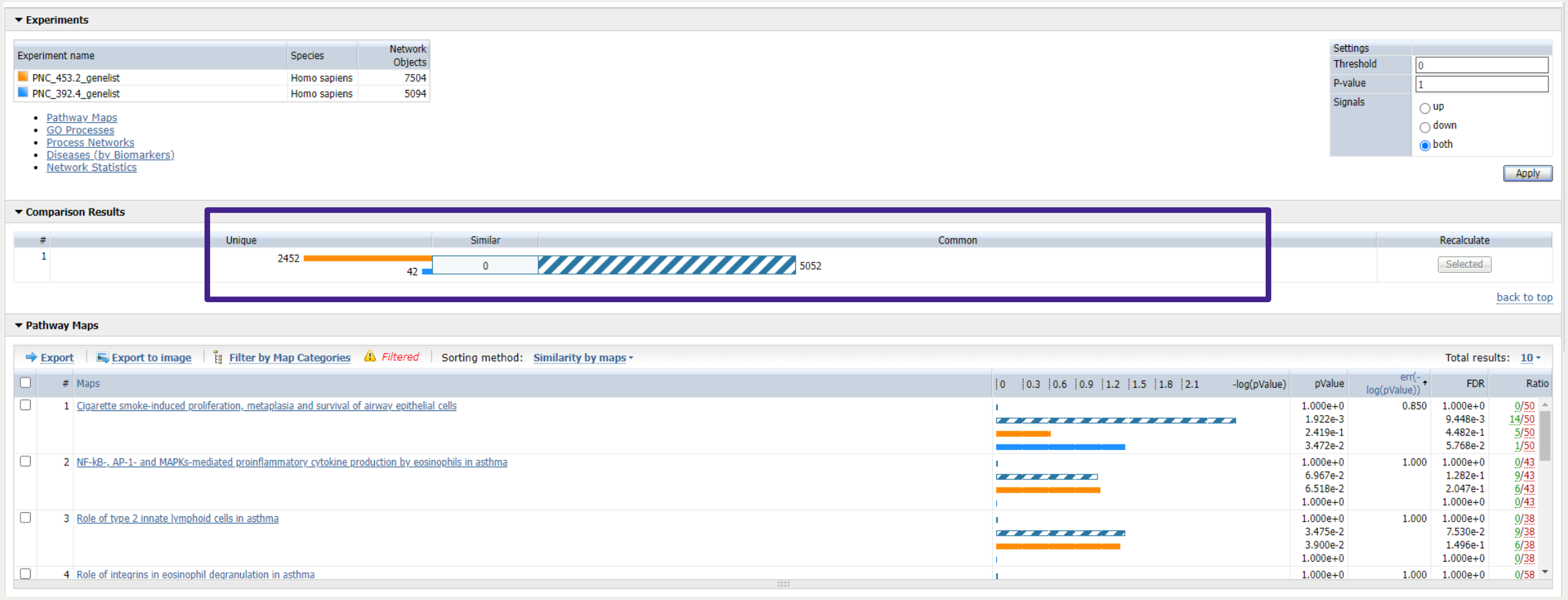
分析后数据颜色

- Unique”set 着彩色
- “similar” set 不着色
- “common” set：斑马纹

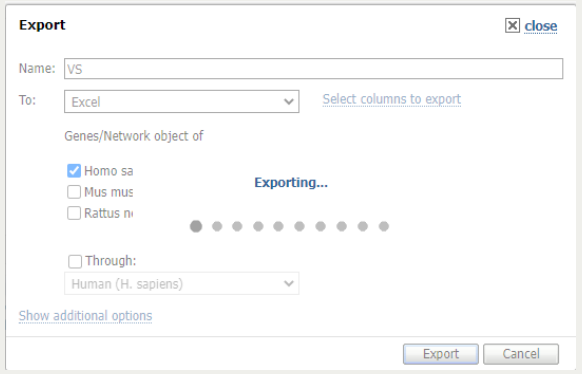
5.Compare Experiments Workflow-操作步驟



5.Compare Experiments Workflow



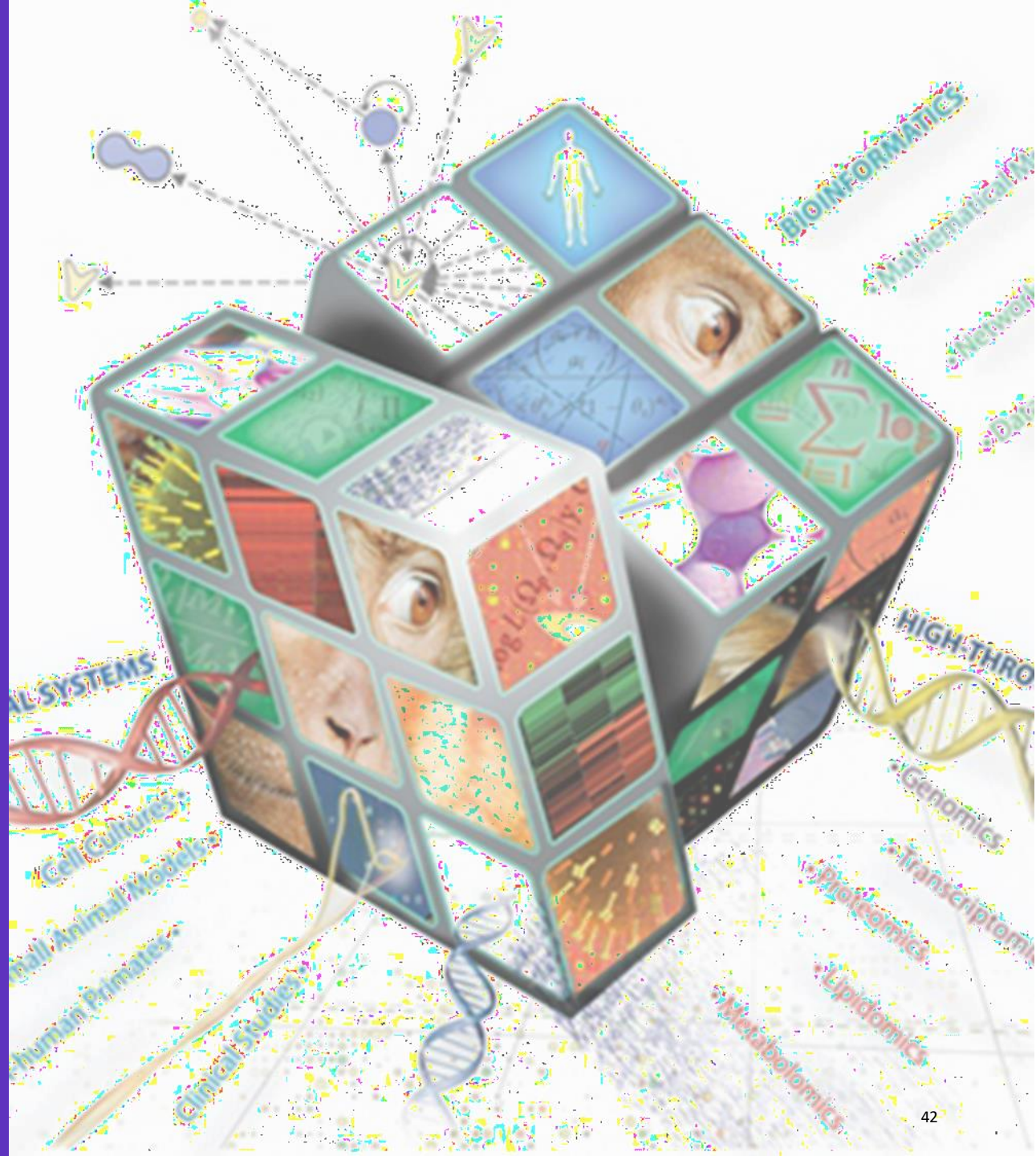
Compare Experiments Workflow-结果



MetaCore Data								CDDI Data				PNC_392.4_genelist		PNC_453.2_genelist	
#	Input IDs	Network Object Na	Gene Symbol	Unit (protein or chem	Object Type	Description	Therapeutic Drugs	CDDI Biomarke	CDDI Biomarker Role	CDDI Biomarker Type	CDDI Genes & Targets	Signal	p-value	Signal	p-value
4	ENSG00000175793	0	0	0	Generic binding protein			0	Diagnosis; Predicting Drug Resistance; Predicting Treatment Efficacy	Genomic	C-X-C motif chemokine ligand 5; ENAH actin regulator; Kruppel like factor 5; MIB E3 ubiquitin protein ligase 1; S100 calcium binding	1	0	1	0
5	ENSG00000175793	0	0	0	Generic binding protein			0	Predicting Treatment Efficacy	Genomic	G protein subunit gamma 7; H2B clustered histone 8; H2B clustered histone 7; ISG15 ubiquitin like modifier; RecQ like helicase; SEL1L	1	0	1	0
6	ENSG00000175793	0	0	0	Generic binding protein			0	Predicting Treatment Efficacy	Genomic	0	1	0	1	0
7	ENSG00000175793	0	0	0	Generic binding protein			0	Diagnosis	Genomic	0	1	0	1	0
8	ENSG00000175793	0	0	0	Generic binding protein			0	Diagnosis	Genomic; Proteomic	0	1	0	1	0
9	ENSG00000175793	0	0	0	Generic binding protein			0	Prognosis	Genomic	2'-5'-oligoadenylate synthetase 3; 2'-5'-oligoadenylate synthetase like; 3-hydroxy-3-methylglutaryl-CoA synthase 1; 5'-nucleotidase,	1	0	1	0
10	ENSG00000175793	0	0	0	Generic binding protein			0	Differential Diagnosis	Genomic	0	1	0	1	0
11	ENSG00000175793	0	0	0	Generic binding protein			0	Diagnosis	Proteomic	0	1	0	1	0
12	ENSG00000175793	0	0	0	Generic binding protein			0	Prognosis - Risk Stratification	Genomic	Aly/REF export factor; H2A.J histone; H2A.Z variant histone 1; NADH:ubiquinone oxidoreductase subunit B10; eukaryotic translation	1	0	1	0
13	ENSG00000175793	0	0	0	Generic binding protein	0		0	Diagnosis; Differential Diagnosis; Disease Profiling; Monitoring Treatment Efficacy;	Genomic; Proteomic	0	1	0	1	0

6. 多基因列表或多组学数据通路分析

- 全面了解生物学背景，以帮助推动研究计划的下一步。
- 最大限度地提高生成多类型数据的投资回报。



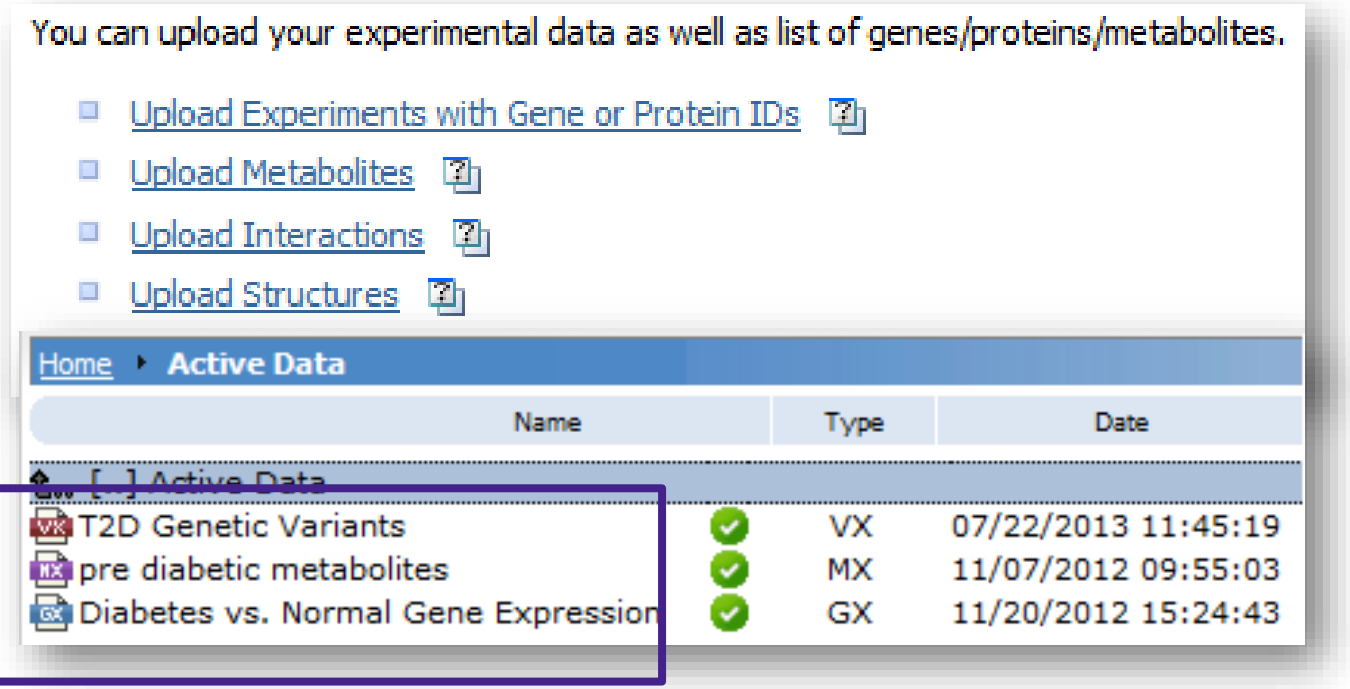
多组学数据分析的小技巧

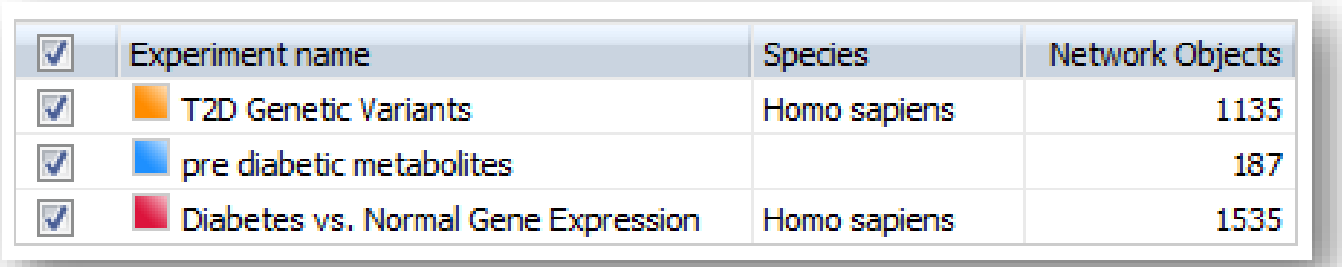
- 代谢物变化和转录变化可以帮助我们找到引起代谢变化的通道和酶
- **蛋白组和转录组学的分析**可以有助于找到与翻译水平相关的表达
- 代谢组和蛋白组学的分析可以有助于找到生物标志物.

TIPS：

比较不同的组学数据时，我们需要想一想他们是怎样相互关联的?

多组学方法已被证明是发现样本量有限的疾病表型的强大工具





方法：过滤结直肠癌（CRC）.vcf文件，使用优先变体运行通路图富集以及整合来自MetaCore微阵列存储库的CRC转录组学数据。

案例说明：围绕CRC的机制提出了多个假设，使用MetaCore中可用的知识和数据驱动方法的组合。

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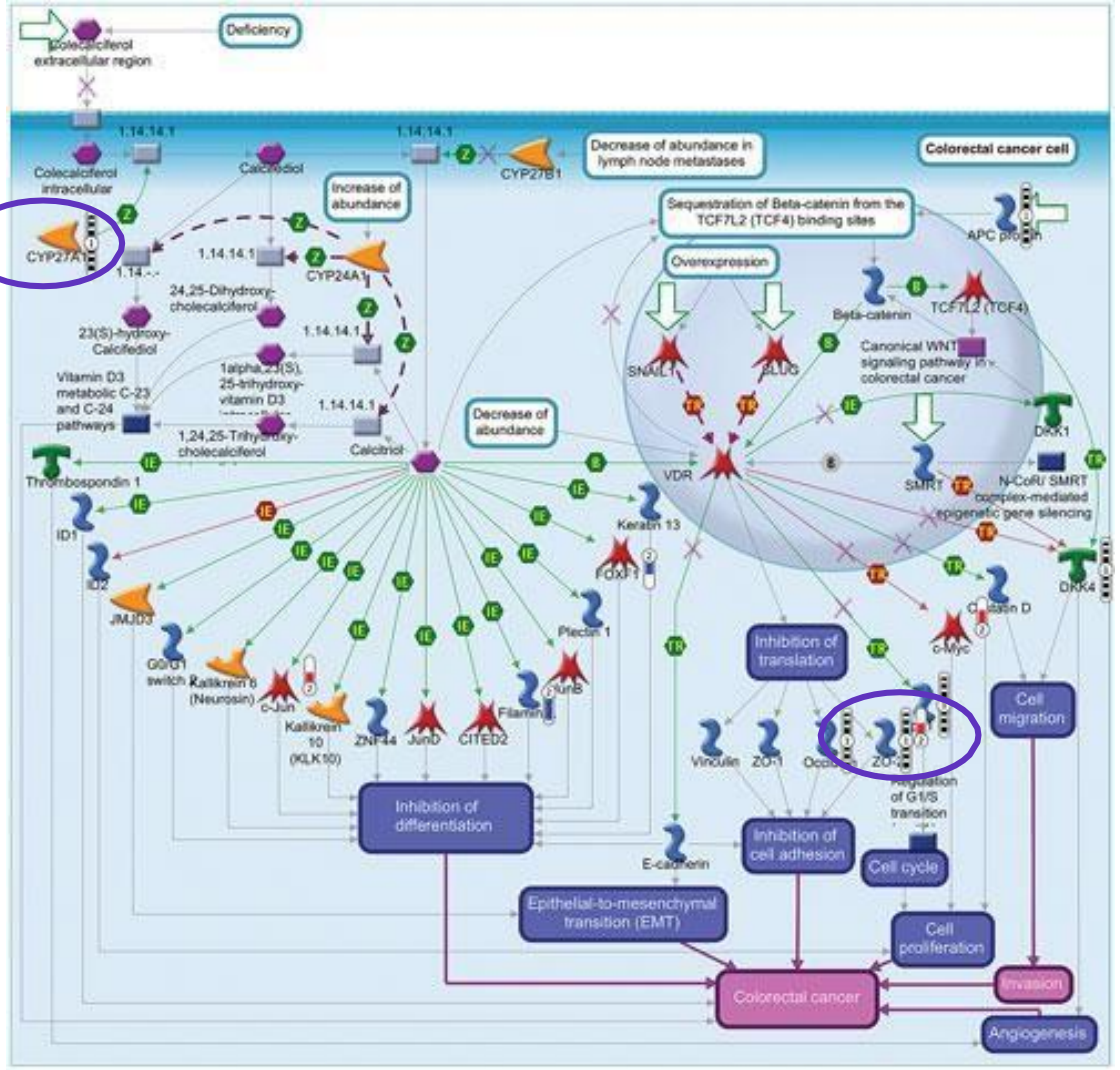
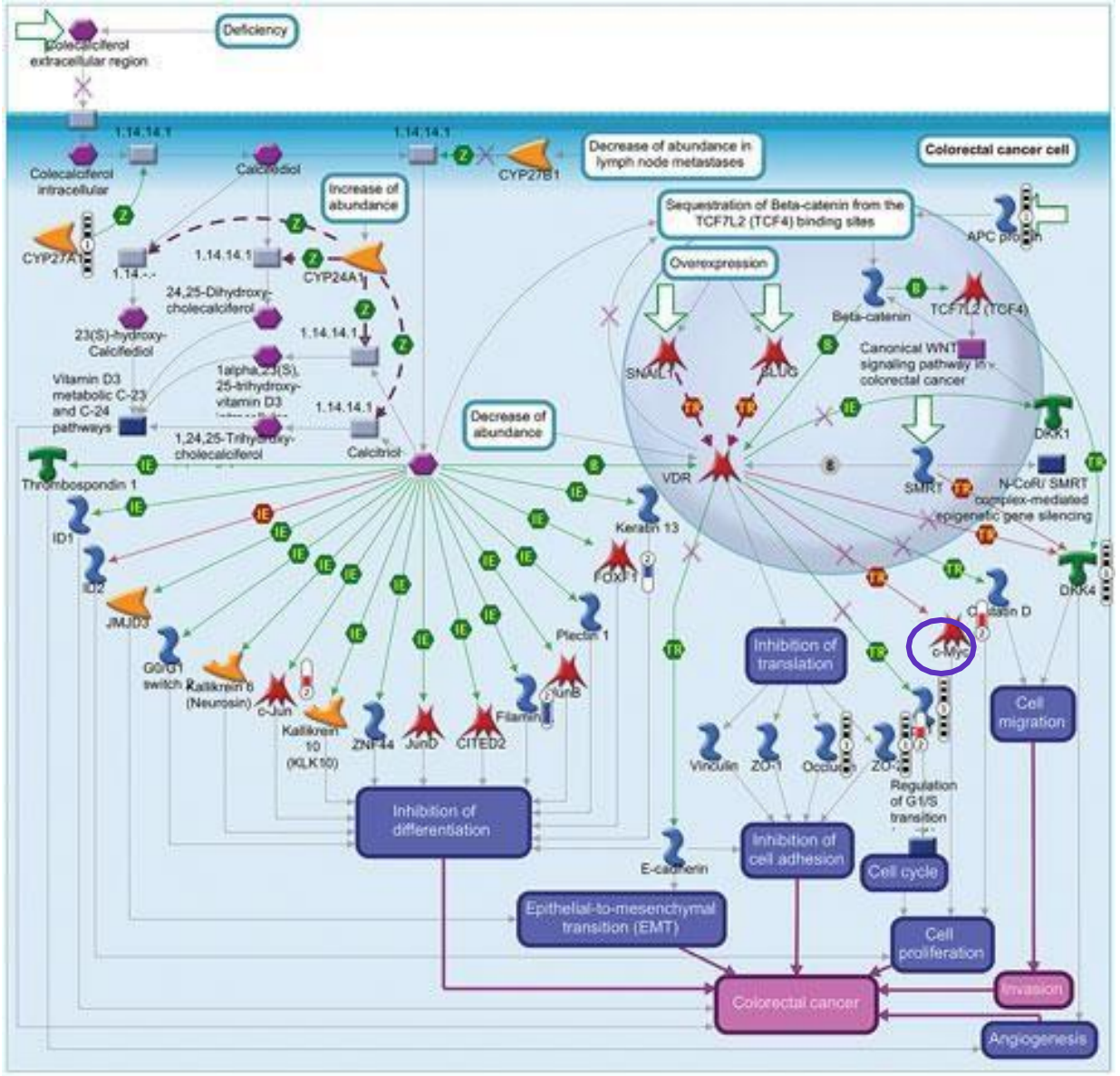


结果解读

1. CYP27A1（过滤后的三个变体）催化胆钙化醇（colecalciferol）转化为骨化二醇（calcifediol），后者通过另一种酶转化为骨化三醇。 CRC 中骨化三醇信号下调; 因此，这些 CYP27A1 突变可能代表功能缺失突变，这些突变降低了胆钙化醇的催化作用和整体降低的 VDR 信号传导。
2. CRC基因组数据显示ZO2（TJP2基因）在C>T SNP 71865988位置的变异，转录组学数据显示 TJP2基因上调1.8倍（p值= .021）。**可以假设这种变异导致TJP2的产生增加，并改变生物过程，例如通过细胞粘附机制的CRC进展。**



结果解读

3. 这张图描述了细胞周期中的细胞增殖,对CRC表型有影响。数据显示细胞周期蛋白依赖性激酶抑制剂1A或p21中的两种变体（位置36651971 C>A和36652122 C>G），它们可能参与细胞周期的失调，导致细胞增殖的变化。

该图还显示了c-Myc在mRNA水平上的上调（折叠变化= +2.3和p值= .0009），这也可能有助于增加细胞增殖。因此，可以**假设基因组和转录组学变化的这种组合通过失调的细胞增殖来驱动CRC。**.

日程

第一部分：MetaCore数据平台简介

第二部分：MetaCore重点功能介绍

第三部分：系统生物学案例分享

第四部分：内容回顾与总结

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Meta Core 功能总结

MetaCore™是所有产品的Back Bone。它包含许多功能和工具，主要八项功能及作用如下所示：

Data Manager：

- 安全的个人数据存储平台。可存储实验,基因列表,进程列表和其他数据集;协作工作。

comparison tool

- 对比实验中的不同数据

Enrichment Analysis tool ：

- 允许在多种ontologies 和 GO ontologies选择进行数据的富集分析。

Network Building engine：

- **数十种独家算法。**（专门为转录因子和受体分析而设计的算法。）允许根据所上传的数据自定义网络。

Interactome 工具：

- 显示网络对象与从的实验数据中获取/推断的对象之间的交互的统计数据。

向导及工作流程工具：

- 帮助运行连续的任务.
- 仅需数次点击便可获得说明性的报告。

搜索工具：

- 支持围绕整个MetaCore™数据库查找基因、网络中的对象、疾病、路径等。

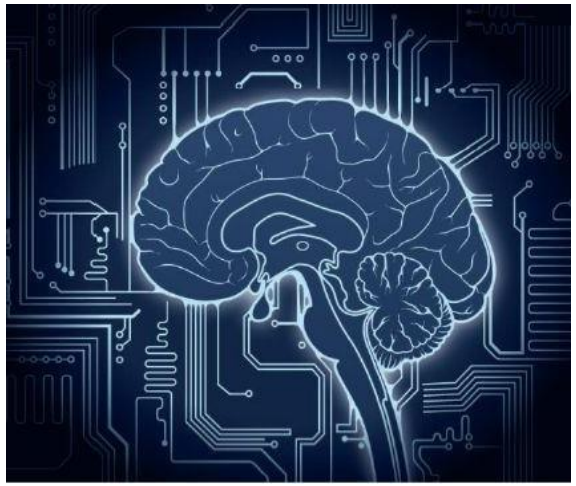
数据过滤工具：

- 灵活方便（对于VCF文件等）

数据库特点总结：

数据挖掘

协助挖掘感兴趣的基因和靶点之间关系



智能分析

多种算法，支持一键分析

无需编写代码

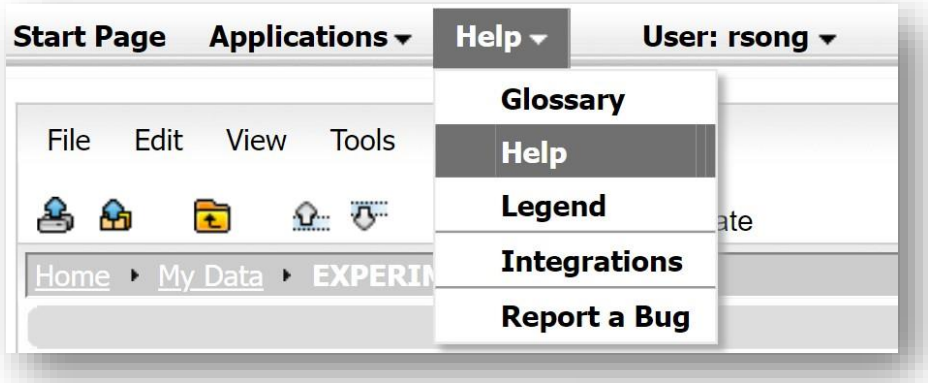
操作简便

团队新成员上手方便，点击即可分析。

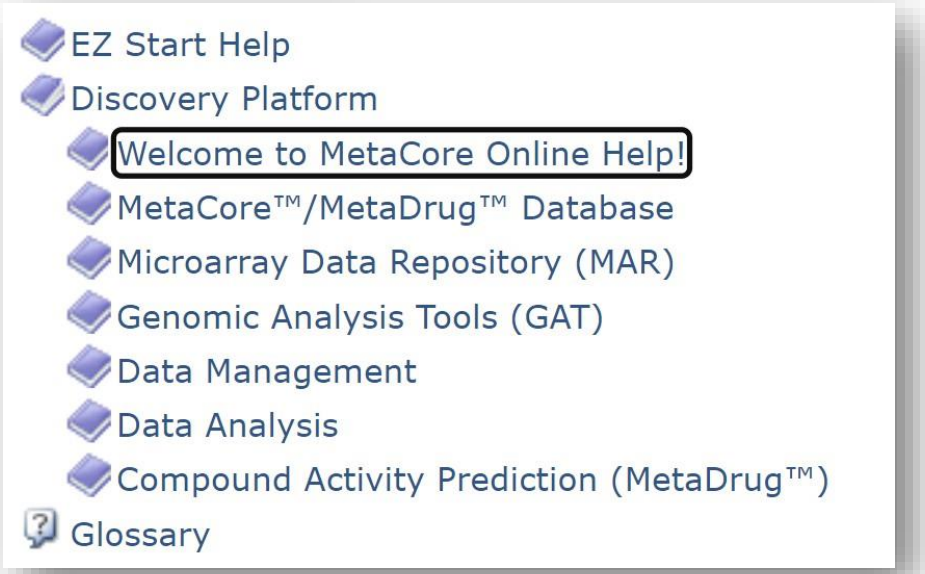
详实的线上帮助文档

关于数据库使用操作以及多种功能介绍。

系统生物学领域知识体系概况。



支持关键词检索查询
线下操作详细介绍
帮助文档互联



售后服务支持

- 数据库培训：为订购客户提供免费培训交流活动；
- 在线培训：组织俱乐活动，定期在线解答大家的疑问，提供最新的检索技巧，分享检索经验；
- 技术支持：我们会为我们的客户提供400电话和Email咨询服务，保证您们在工作时间内有任何疑问都可以通过我们人工服务获得解答；TS技术支持团队：400 8424 896 ； ts.support.china@Clarivate.com
- 行业资讯：可访问科睿唯安在线学院或者官方微信：

  http://clarivate.com.cn/e-Clarivate/