MetaCore+MetaDrug 教育訓練

法德利科技
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Instructor

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- 國立台灣大學 理科博士
- **經歷**

農委會科技計畫

陽明大學微生物與免疫學 計畫研究

台灣大學生命科學院 動物實驗 講師

法德利科技股份有限公司　　產品管理部

(負責產品 : Clarivate Cortellis MetaDrug+MetaCore, Cortellis CDDI, BIOVIA Pipeline Pilot)

- **專長**

生理學、內分泌學、分子內分泌、生物資訊

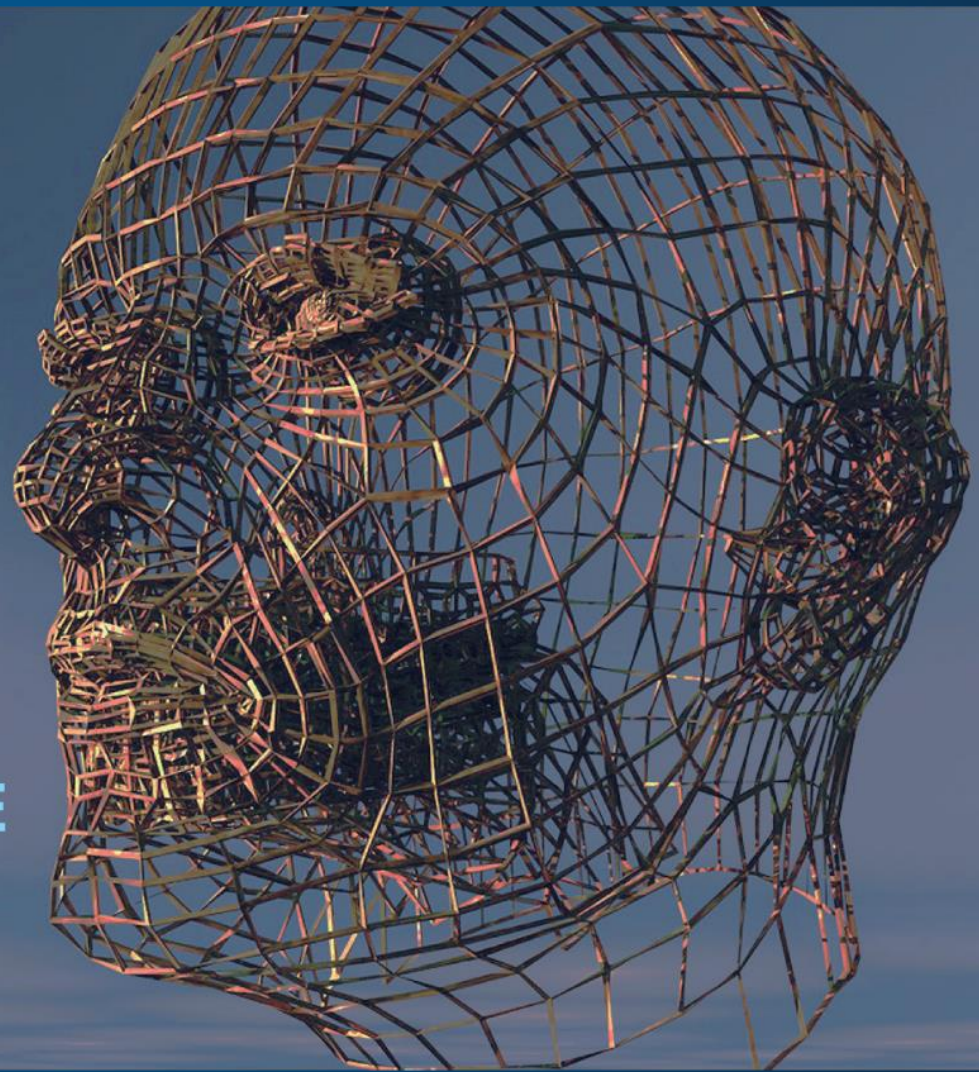
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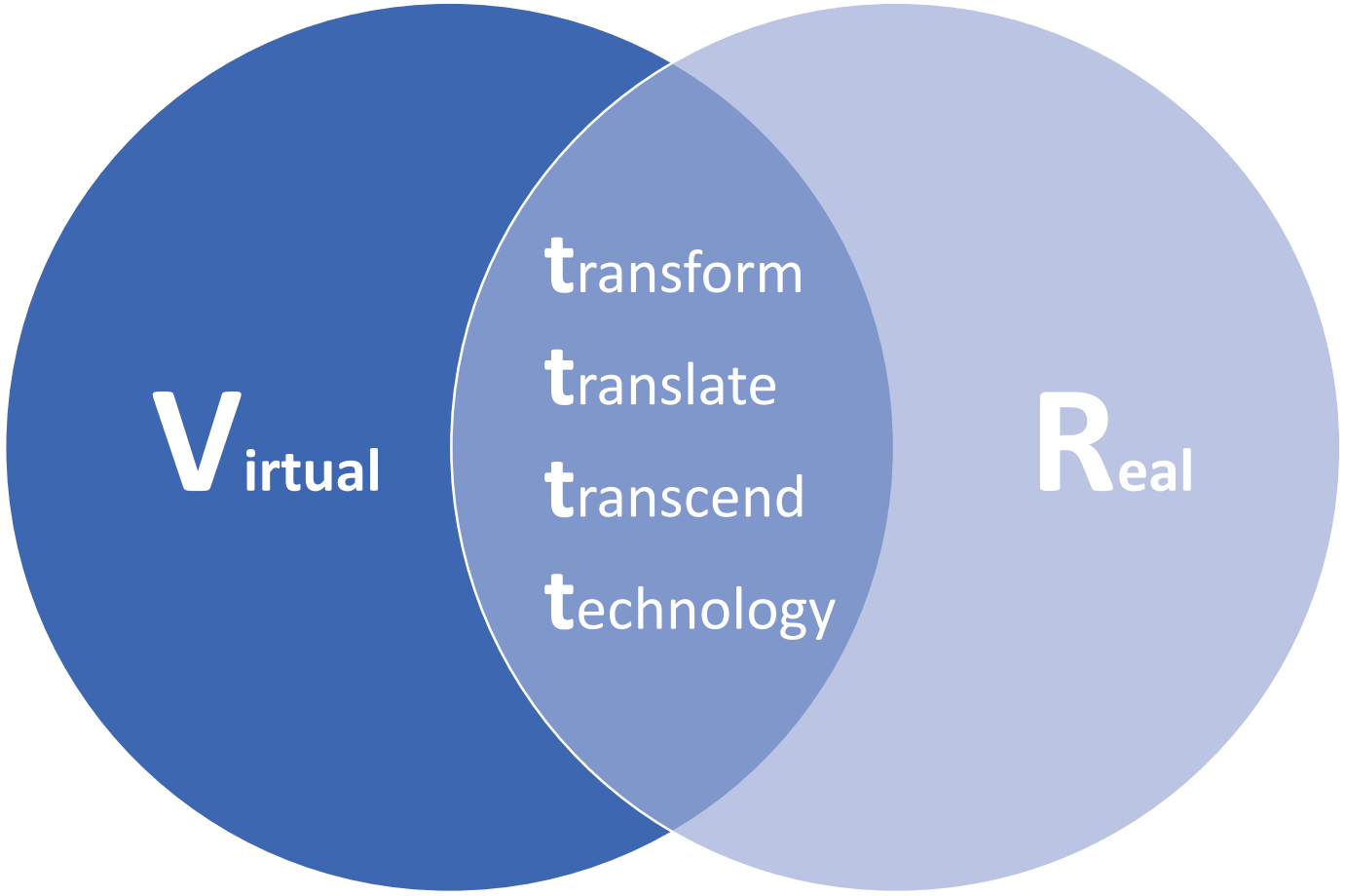
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Harnessing the Power of
Virtual Technology to
transform the
Real World!

SIMULATION - INNOVATION - QUALITY - COMPLIANCE - INTELLIGENCE



What VtR means

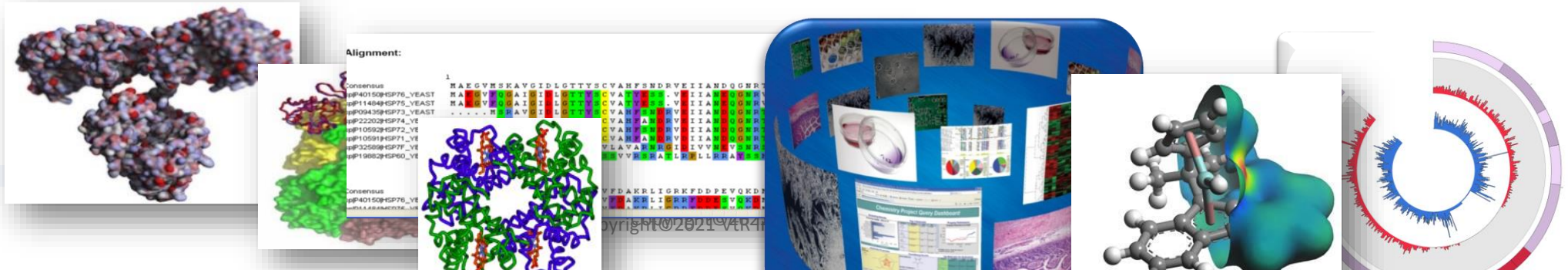


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法德利科技 科學資訊事業

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- 法德利科技是提供完整**高端科學資訊服務**的在地團隊。
- 法德利服務以科技產業為主，包含生技藥業、醫療服務業、電子半導體產業、能源石化業等，提供從R、D、Q、到M (**研究、發展、品質、製造**)一貫之資訊解決方案。
- 法德利的產品及服務項目涵括**生物資訊**、**化學資訊**、**生命科學**、**奈米與材料科學**、**電子化臨床與實驗室管理**、**製程監控分析**、及**企業品質管理系統**等。
- 法德利除提供先進之軟體及資料庫外，更包含安裝調校、合規**電腦系統確效**(CSV)、委託研究、系統客製開發、使用者教育訓練等服務，客戶遍及產、官、學、研各界。



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產業資訊與合規之完整解決方案

符合法規之電子系統確效與整合實驗研究成果之資訊解決方案



實驗室合規管理系統
電腦系統確效服務
系統整合維護與硬體資源提供



合規的文檔及品質管理與臨床資訊解決方案



企業品質及文檔管理系統
電腦系統確效服務
電子送件提交系統
系統整合維護

Unified Solutions



製程、化學品配方之研發解決方案

生命與材料科研軟體及資料庫
委託研究
實驗室合規管理系統
系統整合維護與硬體資源提供

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法德利 資訊產品



效率與合規

- 工作流程設計、第三方工具整合、客製化功能開發 (Dassault Systèmes 3DEXPERIENCE, BIOVIA Foundation, Pipeline Pilot)
- 合規、品質、與文檔管理系統：含文件、教育訓練、偏差、矯正預防、變更管制等管理 (Sparta Systems TrackWise; QUMAS EDMS & EQMS; Navitas pharmaREADY)
- 合規電子文件提交系統 (EXTEDO eCTDmanager)
- 實驗室資訊管理系統：含庫存、樣品規格、儀器調校、安定性測試、環境監控等管理 (BIOVIA Inventory, Samples, EM, CISPro, Instrument, Task Plan)
- 電子實驗記錄簿 (BIOVIA ELN)
- 實驗執行系統 (BIOVIA Compose & Capture)
- 發展與製造資料之分析研判 (BIOVIA Discoverant; Tableau BI)

創新與研發

- 化合物合成設計 (BIOVIA MS)
- 材料設計與模擬 (BIOVIA MS)
- 小分子與大分子新藥開發設計 (BIOVIA DS)
- 代謝、活性、與毒性分析 (BIOVIA DS)
- 生命科學建模與模擬 (BIOVIA DS)
- 高速高通量藥物篩選 (BIOVIA DS)
- 生物序列資料分析 (BIOVIA PP; MacVector)
- 動態3D人體數位心臟模型 (Dassault Systèmes Living Heart Project)
- 生物實體與化學物質註冊系統 (BIOVIA Registration)

資料與知識

- 基因體學、蛋白質體學、及系統生物學 (BIOVIA DS & PP; Cortellis MetaCore/MetaDrug)
- 化學物質分析與管理系統 (BIOVIA Insight, CISPro)
- 藥品安全警戒與監控 (EXTEDO SafetyEasy PV; Navitas safetyREADY)
- 化合物資料庫 (BIOVIA ACD, SCD)
- 臨床試驗設計及結果預測、分析、與管理 (Medidata)
- 最新產業全方位數據及情報收集、整理、分析、報告 (Clarivate WebOfScience, Cortellis, Derwent, Medtech 360)
- 精準醫療與臨床醫學資料倉儲、人工智慧、與大數據應用 (Dassault Systèmes 3DEXPERIENCE, BIOVIA PP; Wiley Current Protocol; Tableau)

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Outline

- Introduction
- What is MetaCore?
  - ◆ 介面介紹
  - I. 知識挖掘
  - ● Exercise I
  - II. 建構網絡及分子路徑圖
  - ● Exercise II
  - III. 體學數據上傳及分析
  - ● Case study
- What is MetaDrug?
  - IV. 化合物活性預測
  - ● 針對靶點的藥物活性預測
  - ● Metadrug預測工具
- Summary

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科睿唯安是專業研發及市場情報的提供者，專業傳承超過150年

1864
Zoological Society of London 及 British Museum 建立 Zoological Records動物生物學資料庫

1926
Society of Bacteriologists 及 Botanical Society 建立BIOSIS 生物學資料庫

1955
Eugene Garfield 博士發明引文索引



1957
成立 Institute for Scientific Information (ISI)公司

1963
專利家族之父 Monty Hyams 開始製作發行Derwent 專利摘要



1986
湯森公司收購商標檢索公司 Thomson & Thomson 及 COMPUMARK

1997
推出 Web of Science

2003
湯森公司收購 Techstreet

2011
推出 Cortellis

2012
湯森路透收購 MarkMonitor

2016
智權與科學事業部自湯森路透獨立，成立科睿唯安 (Clarivate Analytics)

Clarivate Analytics

2017
收購 Publons

2018
收購 Kopernio

Kopernio

2018
收購 TrademarkVision

TrademarkVision

2019
與Churchill 公司合併，科睿唯安 (Clarivate) 正式在紐約證交所上市

2019
收購 SequenceBase

SequenceBase

2020

darts-ip
Part of Clarivate

London, UK, Philadelphia, US, & Brussels, Belgium, December 2, 2019— Clarivate Analytics plc (NYSE:CCC;CCC.WS), a global leader in providing trusted insights and analytics to accelerate the pace of innovation, today announced it has acquired Darts-ip, a leading provider of case law data and analytics for intellectual property (IP) professionals. Recently awarded best legal tech company by Trends Legal Awards in Belgium, Darts-ip's case law data and supporting analytics solutions will be offered alongside Clarivate's trusted patent, trademark and domain data and solutions, across Derwent™, CompuMark™ and MarkMonitor™, to help companies make smarter, faster decisions.

2020

DRG
Part of Clarivate

London, UK, & Philadelphia, US, March 2, 2020– Clarivate Analytics plc (NYSE:CCC; CCC.WS) ("Clarivate"), a global leader in providing trusted insights and analytics to accelerate the pace of innovation, today announced it has completed its acquisition of Decision Resources Group ("DRG"). Previously, Clarivate announced on January 17, 2020 its intent to acquire DRG from Piramal Enterprises Limited ("PEL", NSE: PEL, BSE: 500302), part of global business conglomerate Piramal Group.

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科睿唯安和您一起走在加速創新到市場實踐的進展

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科學研究及發現 → 研發及上市申請 → 上市監控及優化


學術機構


生技公司


醫療器材


政府監管


法規政策


醫療支付

從專業觀點出發引領生命科學產業

Institute for Scientific Information

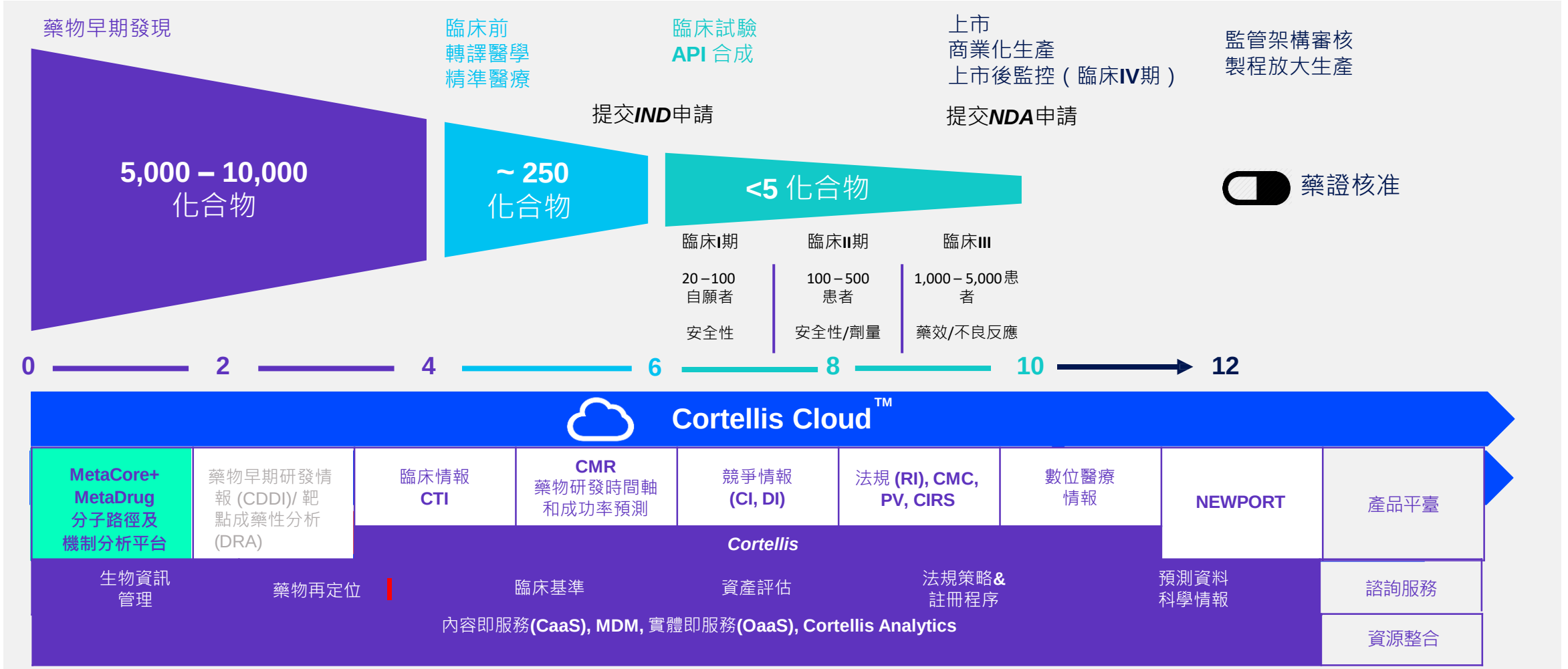
The Centre for Medicines Research

The Centre for Innovation in Regulatory Science

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科睿唯安產品全線支撐整個藥品開發生命週期

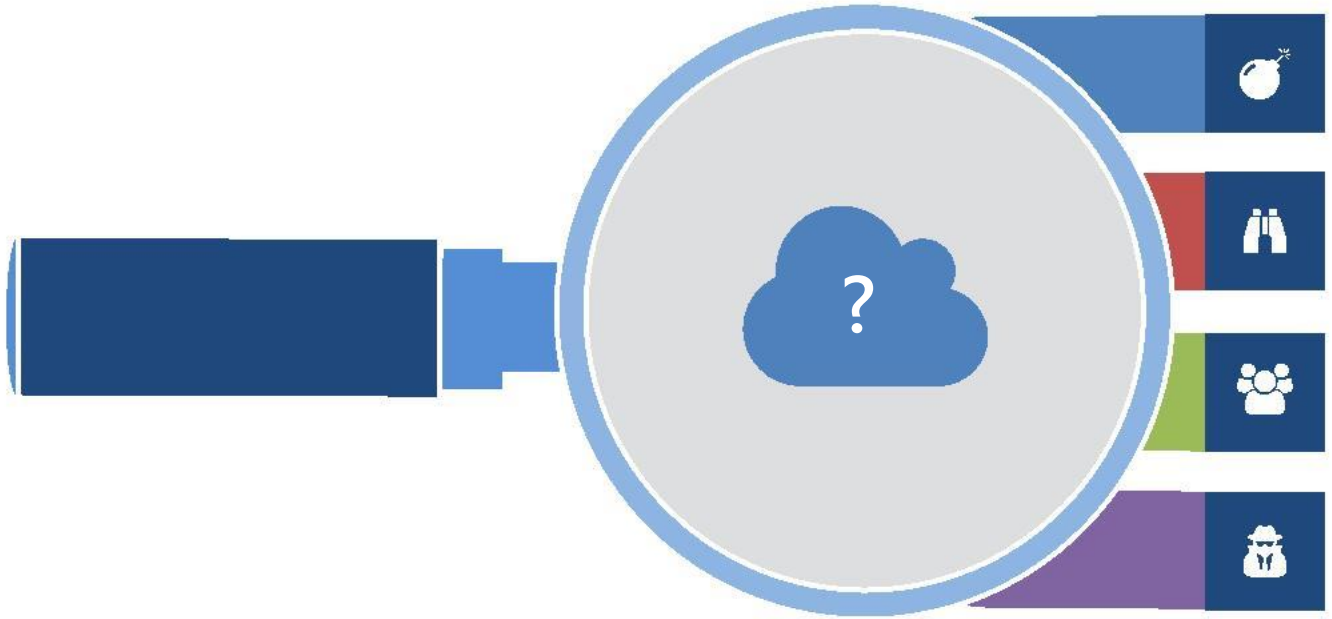


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What is MetaCore?

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藥物早期開發分子路徑分析的重要性



瞭解疾病的發病機制（通過知識挖掘和多體學資料的分析）

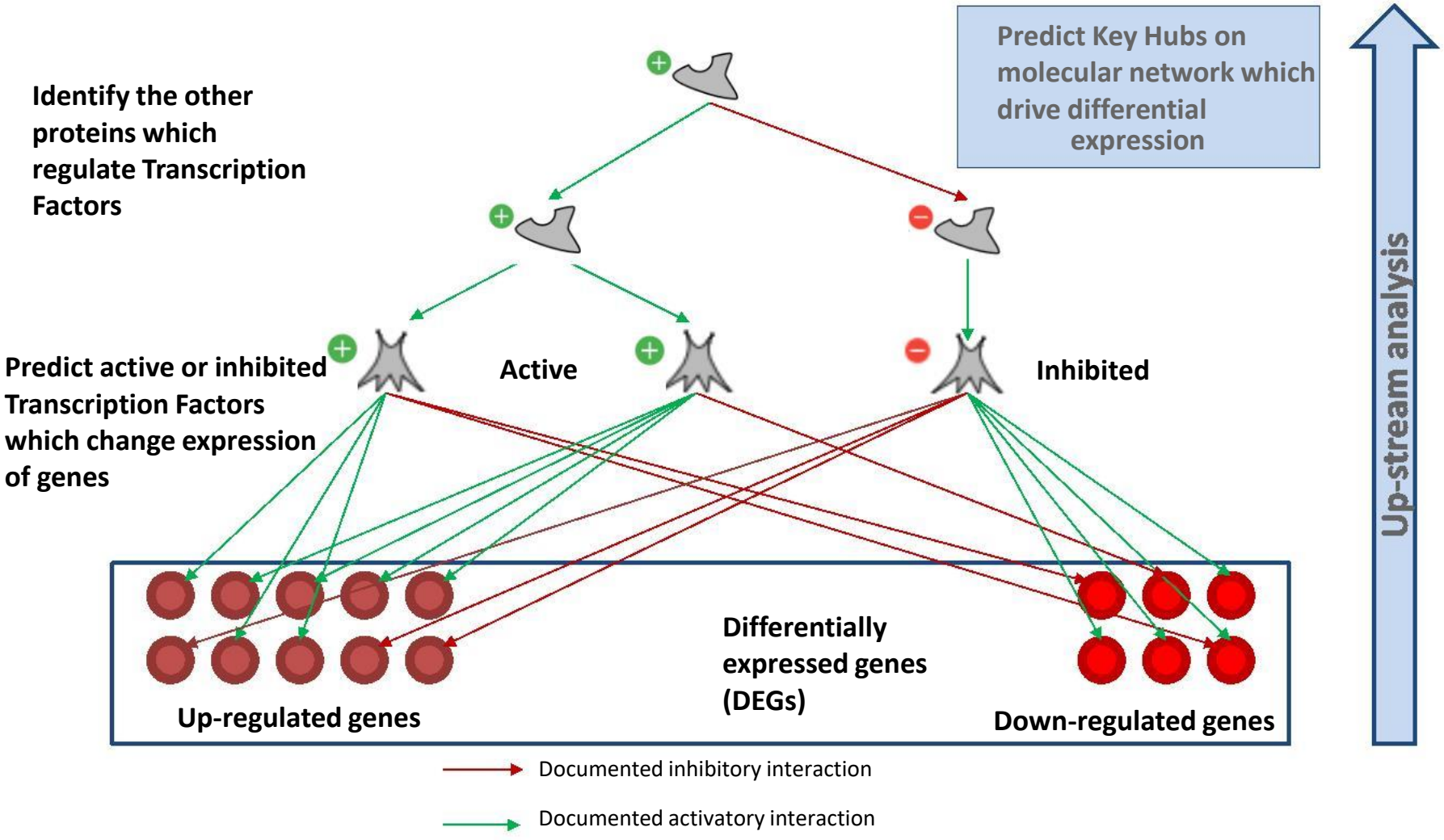
在您感興趣的治療領域裡發現潛力的藥物靶點

發現藥物的作用機制並預測它的毒性

確定生物標記，可以說明您加速臨床前，轉化醫學及臨床研究進展

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Powerful analytics – causal reasoning



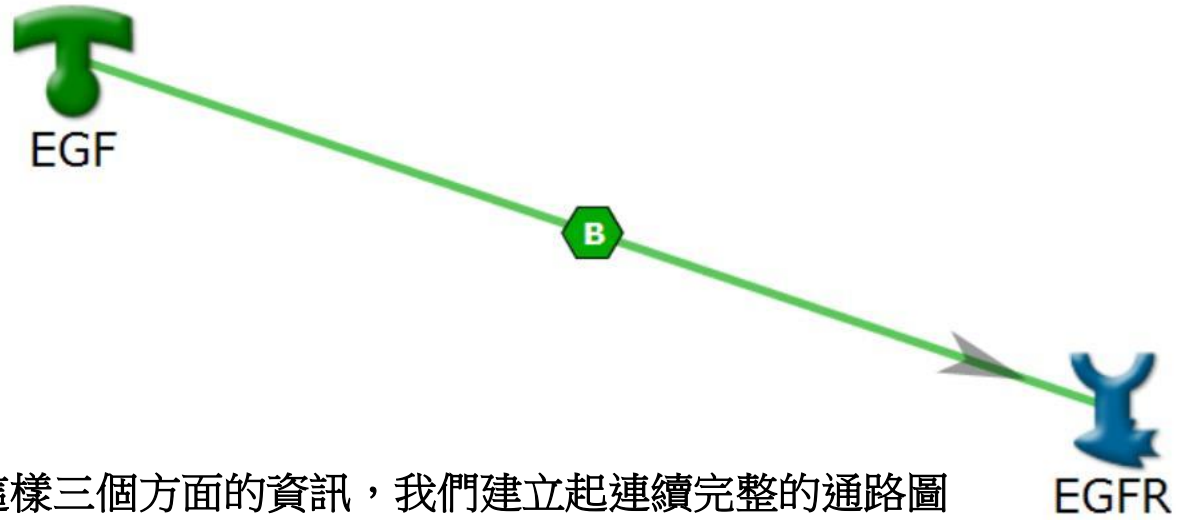
1. Chindelevitch L, Ziemek D, Enayetallah A, Randhawa R, Sidders B, et al. (2012) Causal reasoning on biological networks: interpreting transcriptional changes. Bioinformatics 28: 1114-1121.
2. Pollard J Jr, Butte AJ, Hoberman S, Joshi M, Levy J, Pappo J. (2005) A computational model to define the molecular causes of type 2 diabetes mellitus. Diabetes Technol Ther. 2005 Apr;7(2):323-36.

MetaCore 中的分子相互作用資料——包含：方向，效應，機制

（方向）Directionality

（效應）Effect

（機制）Mechanism (B=Binding)



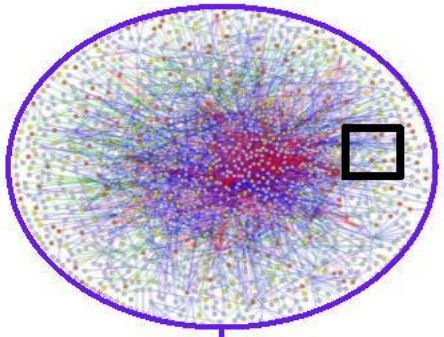
通過這樣三個方面的資訊，我們建立起連續完整的通路圖

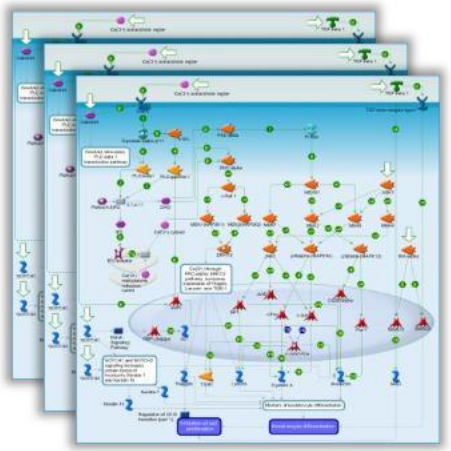
Metacore 全、準、新——高品質的底層內容和演算法

全面、準確、詳細的分子生物學資料加速疾病研究和藥物靶點的發現









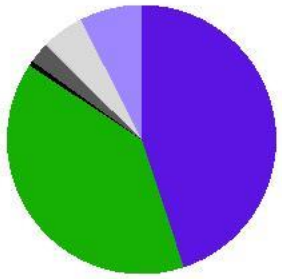
Publications

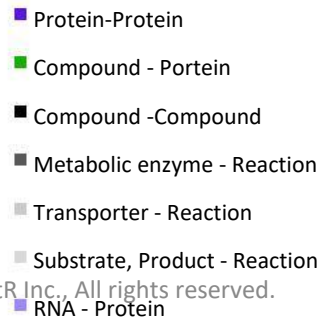
Manual annotation from publications

- Team of PhDs, MDs
- More than 10 years

Molecular Interaction

2 million interactions





Global Network

Pathway maps

1600+ canonical and disease signaling pathways

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介面介紹

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登入首頁

MetaCore
A Cortellis solution

Clarivate Analytics

Home Support Training About Us



*"Something that I do with **MetaCore** in one afternoon now, would have taken a week before."*

Dr. Charles Lecellier
Principal Investigator
IGMM

Your GPS in Pathway Analysis

Whether you want to reduce the risk in your OMICs analysis, realize the potential of your biomarkers, or establish a target's mechanism of action, Clarivate has the right solution for you.

MetaCore

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

MetaMiner Partnerships

A series of industry-academy partnerships on systems biology of common human diseases and stem cells, led by Clarivate.

MetaDrug

A leading systems pharmacology solution that incorporates extensive manually curated information on biological effects of small molecule compounds.

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Password

Remember me

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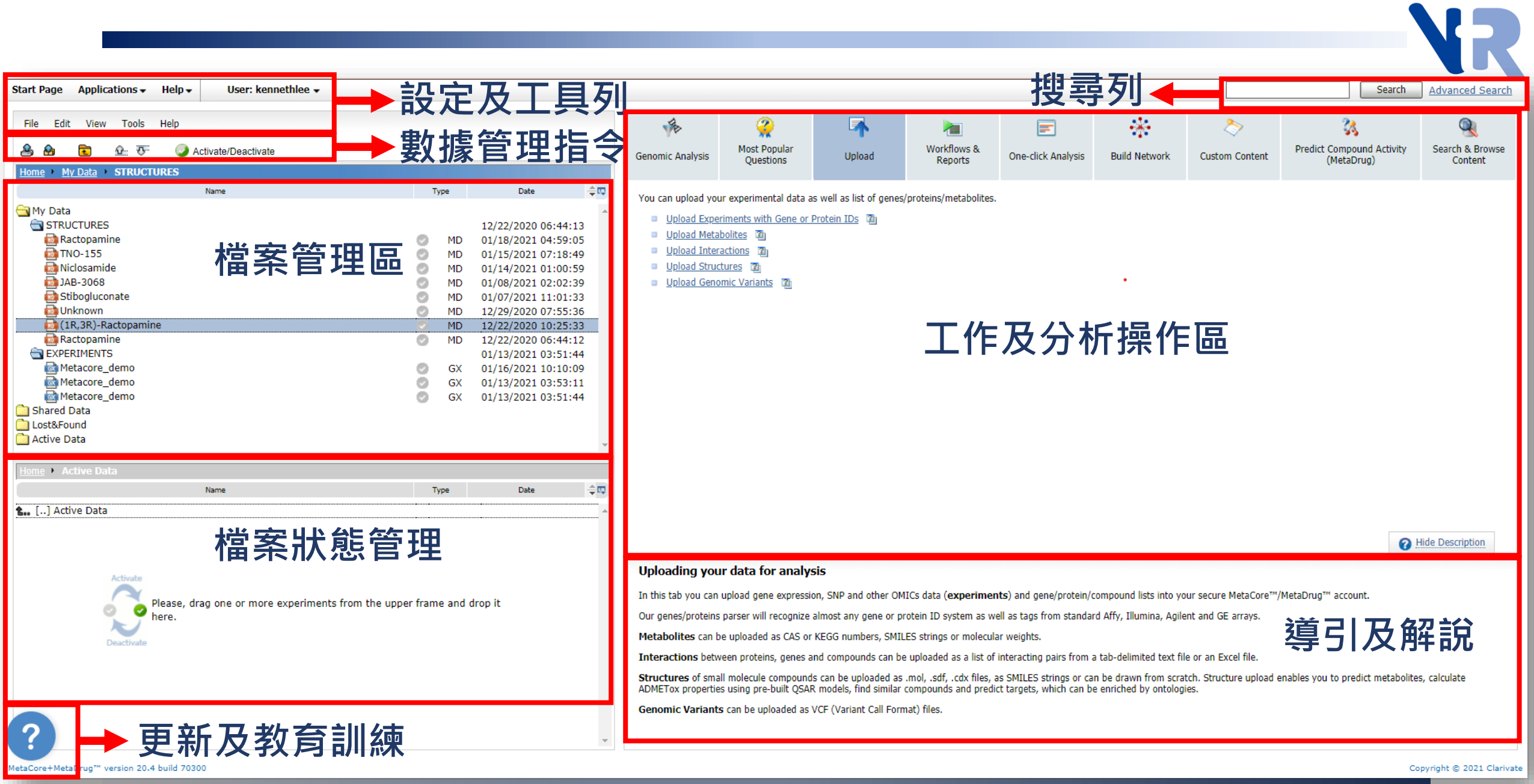
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使用者帳號

密碼

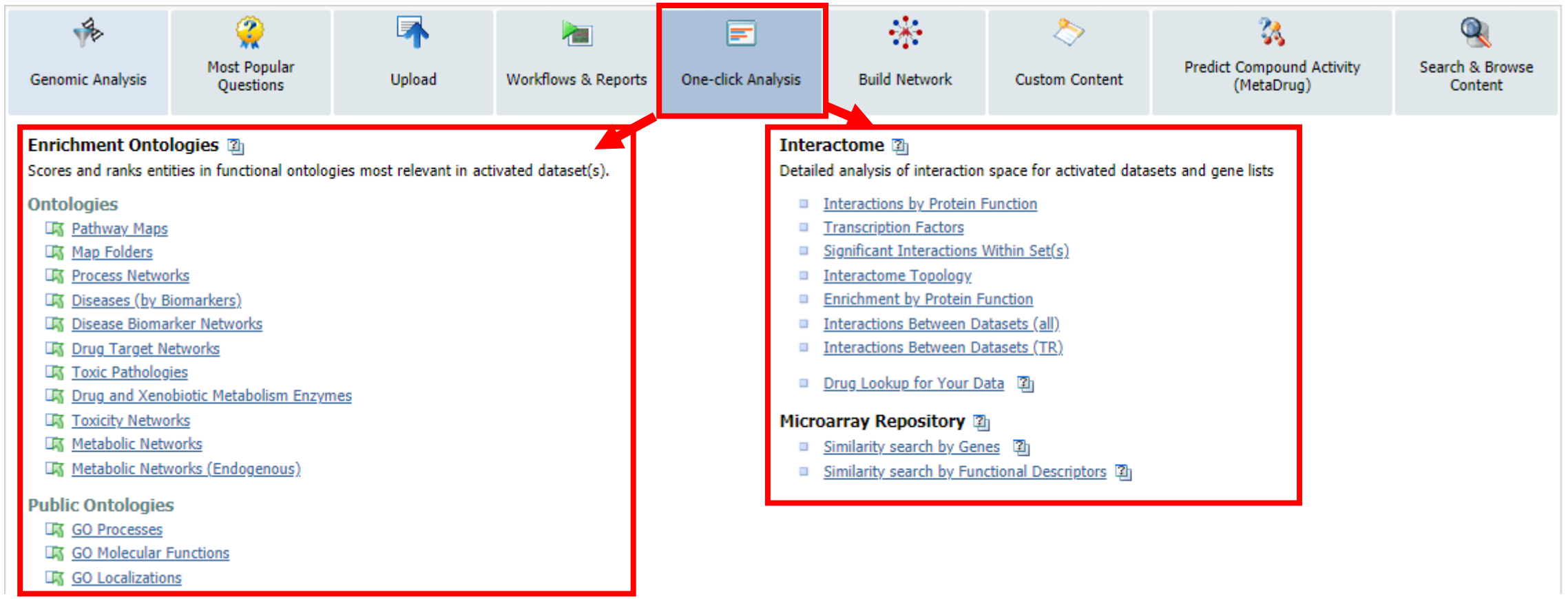
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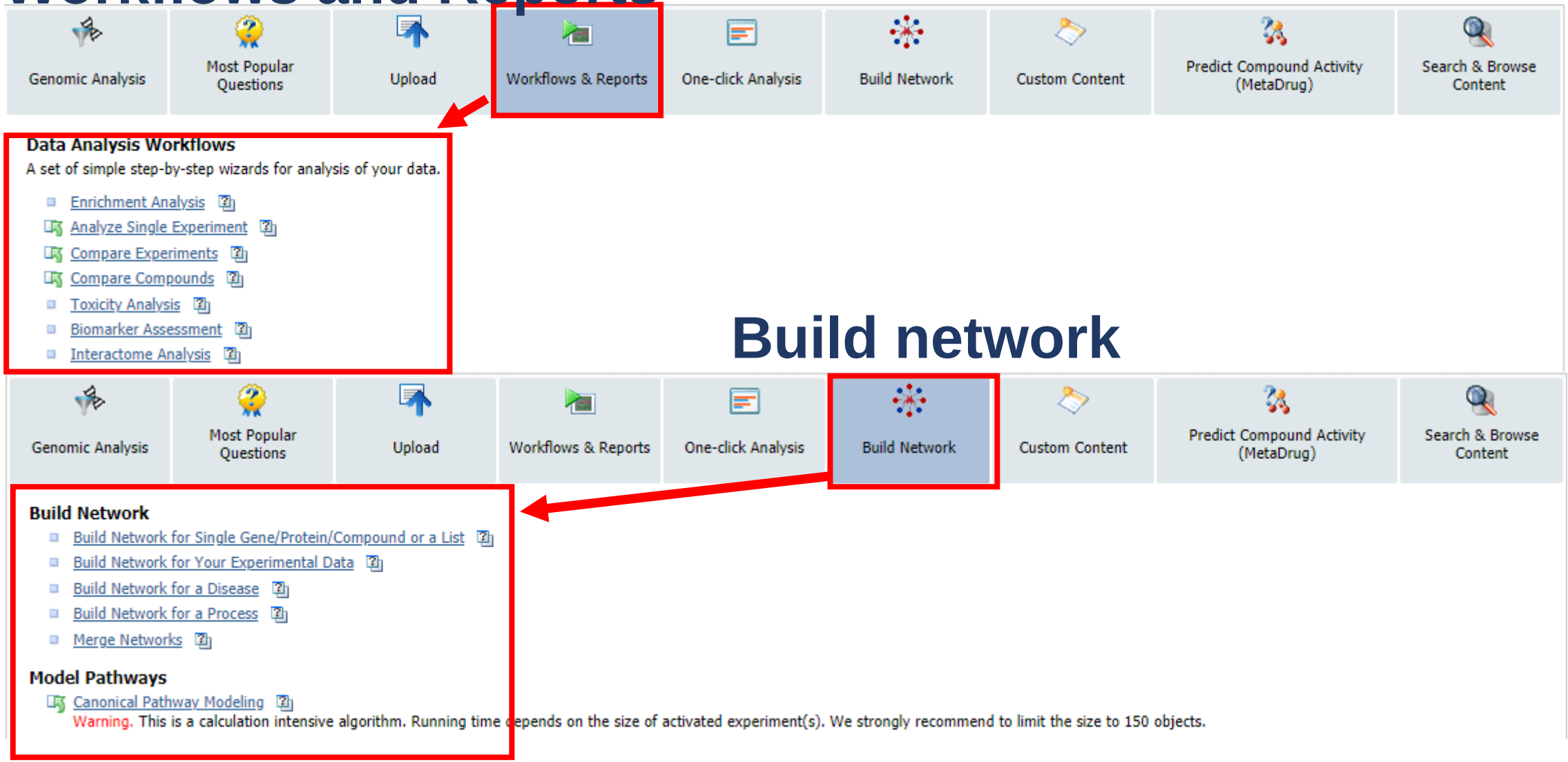
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One-click analysis

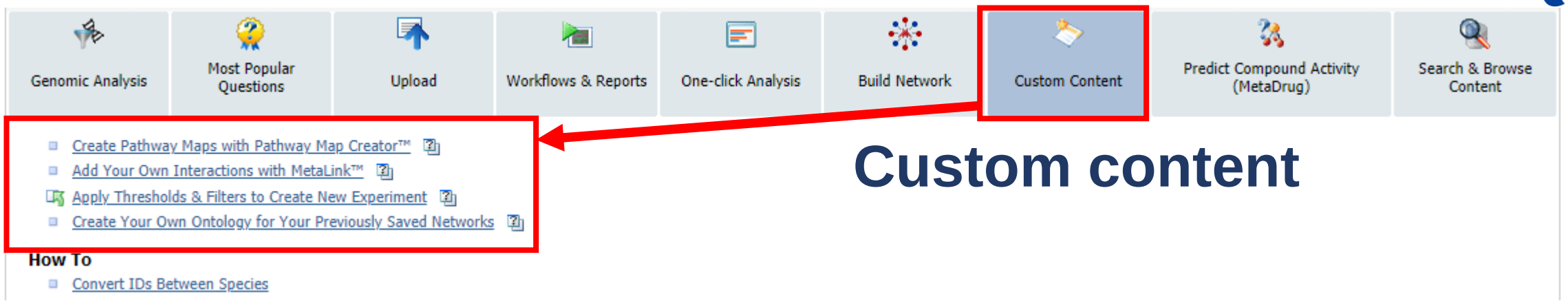


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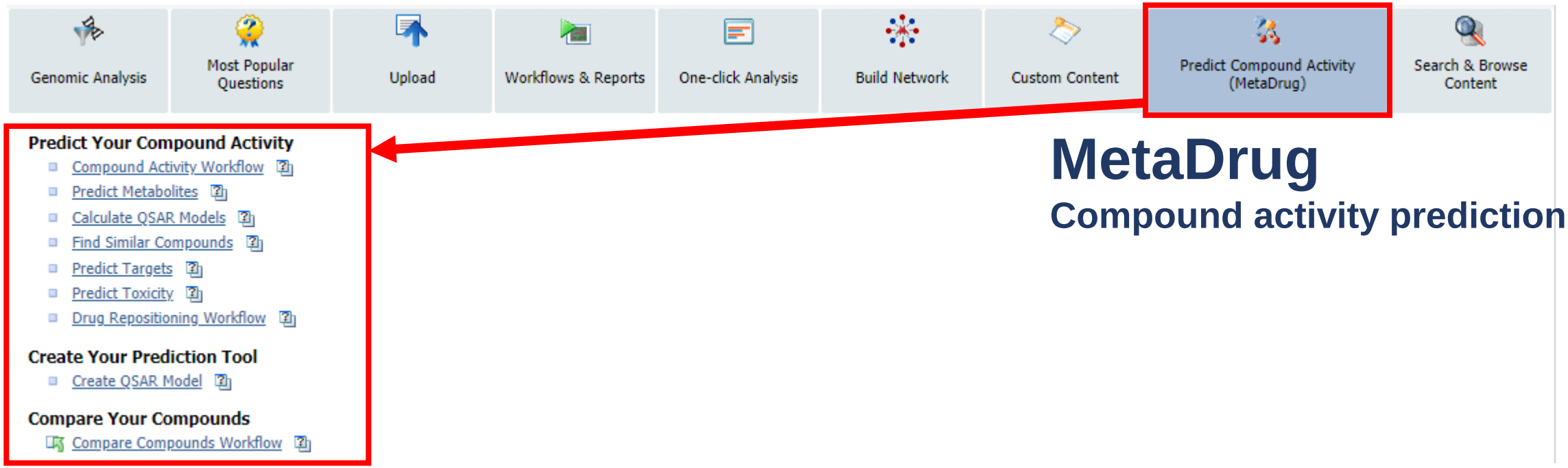
Workflows and Reports



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Custom content

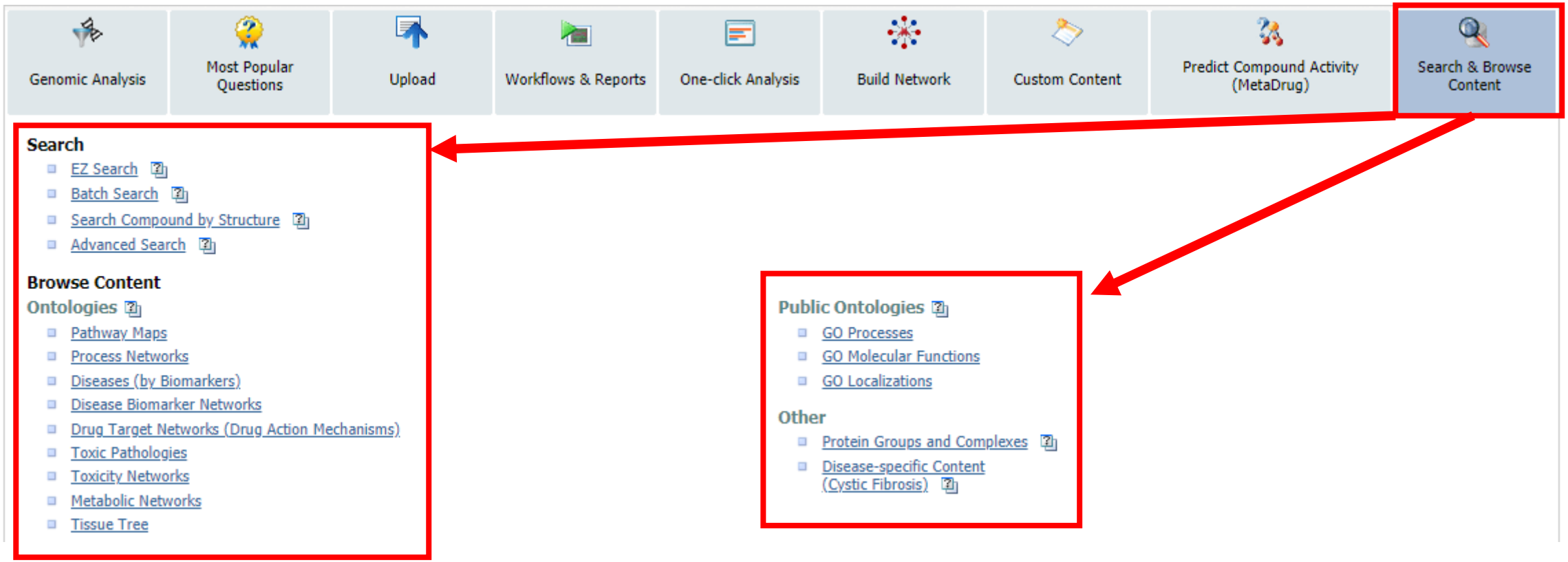


MetaDrug

Compound activity prediction

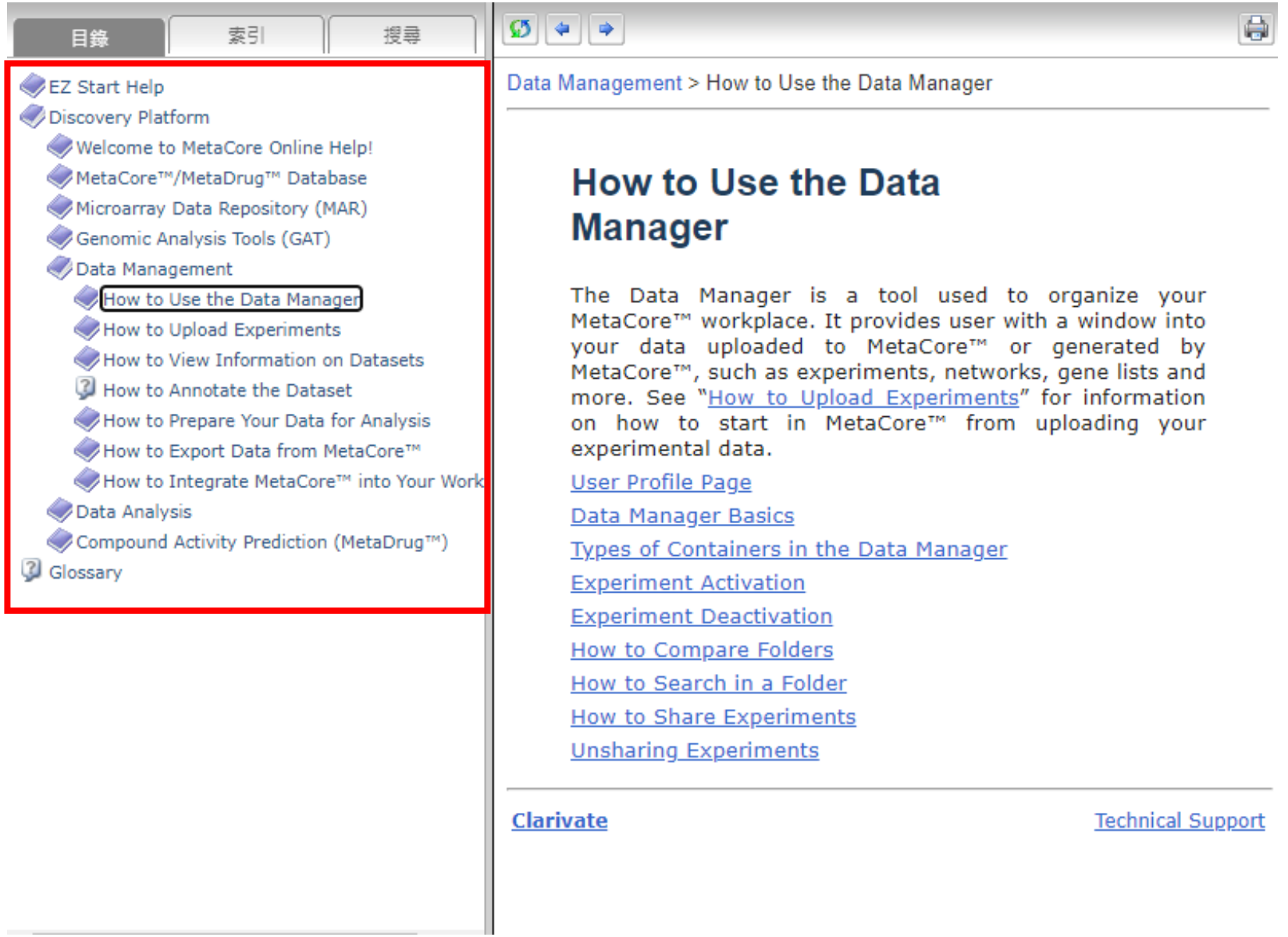
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Searching and Browsing



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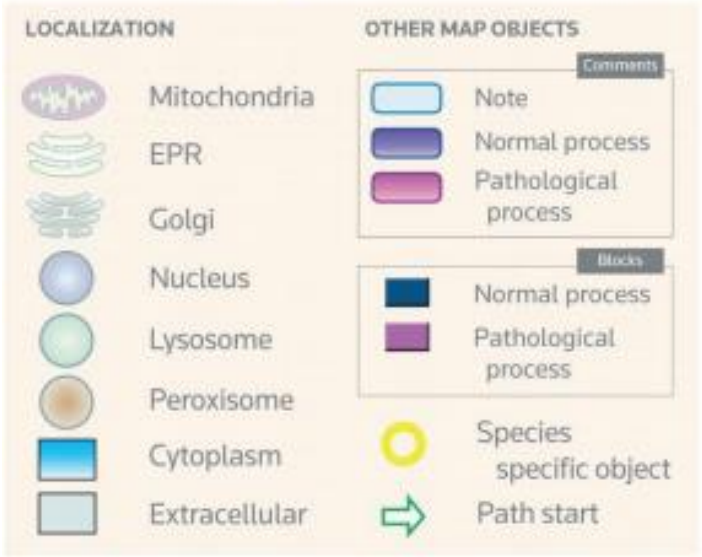
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圖示及註解

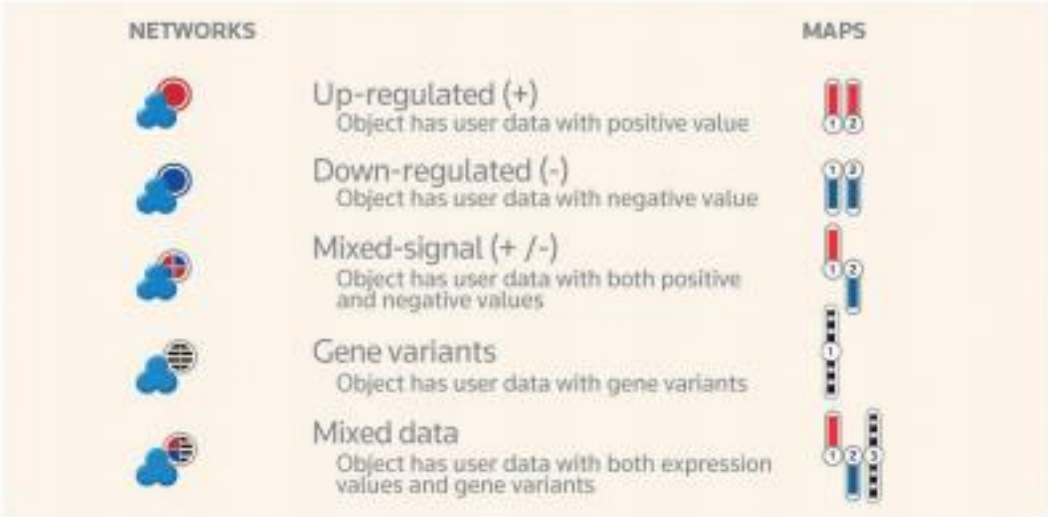
Objects on maps



Network Objects

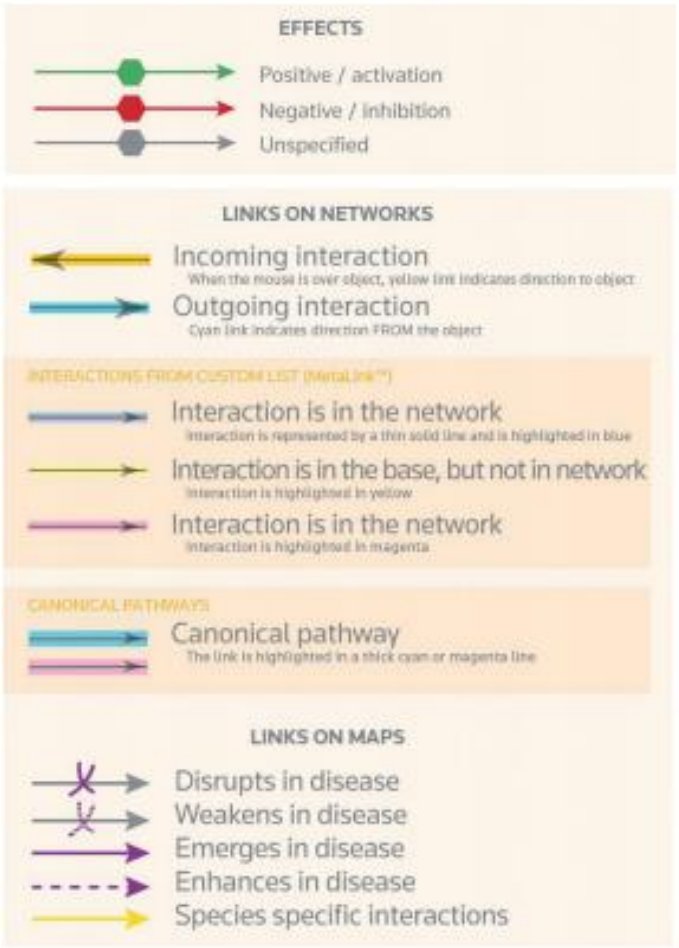


User Data



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Interactions between objects







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Live demo

MetaCore + MetaDrug 介面介紹

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I. 知識挖掘

- Understanding immuno-oncology targets through knowledge mining: a PD-1 use case

- 通過知識挖掘瞭解腫瘤免疫標的：以PD-1為例

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Questions:

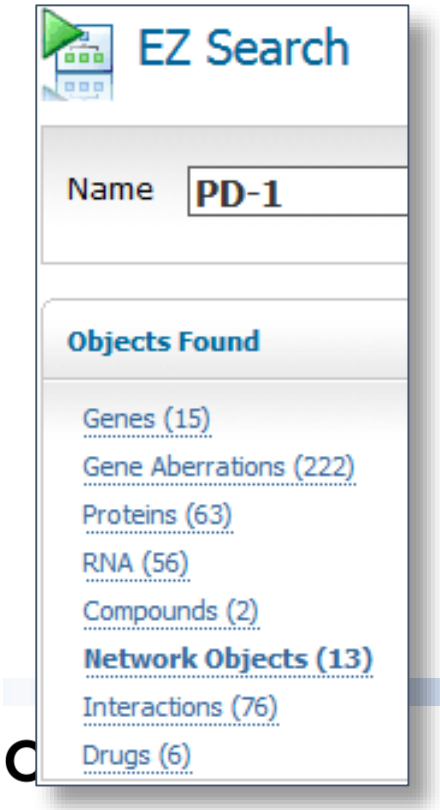
- 我們能檢索到PD-1的哪些資訊？
- 哪些蛋白質可以調節PD-1的表現？
- 哪些訊息傳導路徑可以調節PD-1的表現？
- 哪些訊息傳導路徑可能成為患者分級的良好生物標記以及潛在的治療標的？

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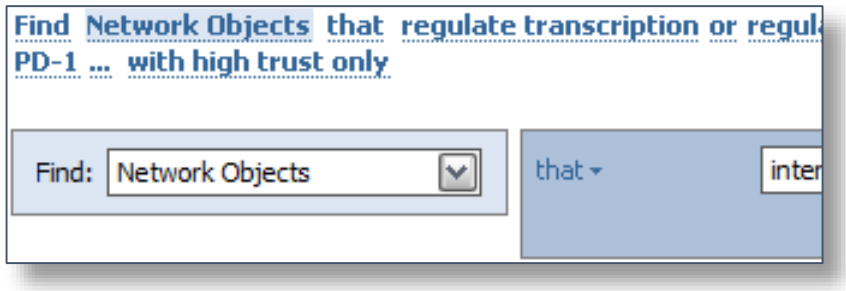
以PD-1進行檢索，並匯出相關資訊

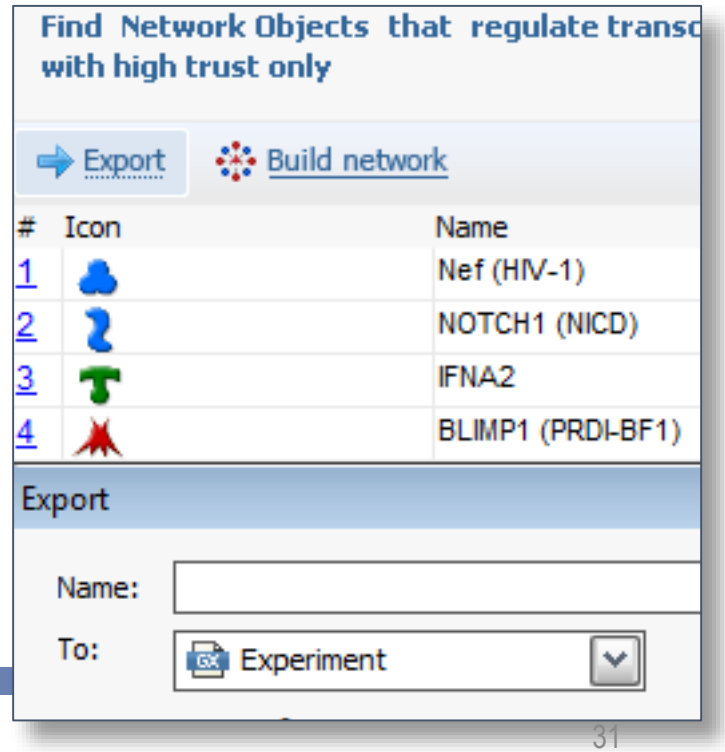
EZ Search → **Advanced Search** → **Export to MetaCore**





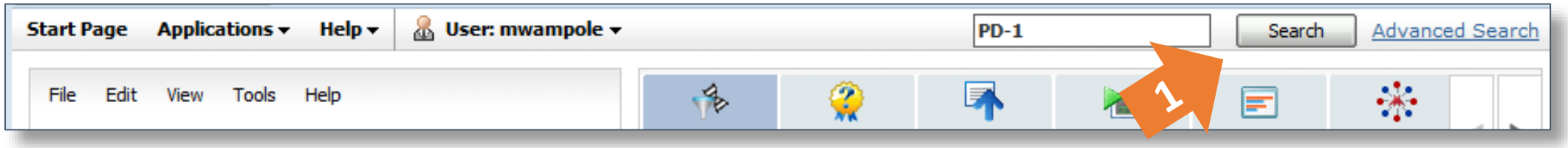
- Questions:
  - 我們能檢索到關於PD-1的哪些資訊
  - 哪些蛋白可以調節和影響PD-1的表現？

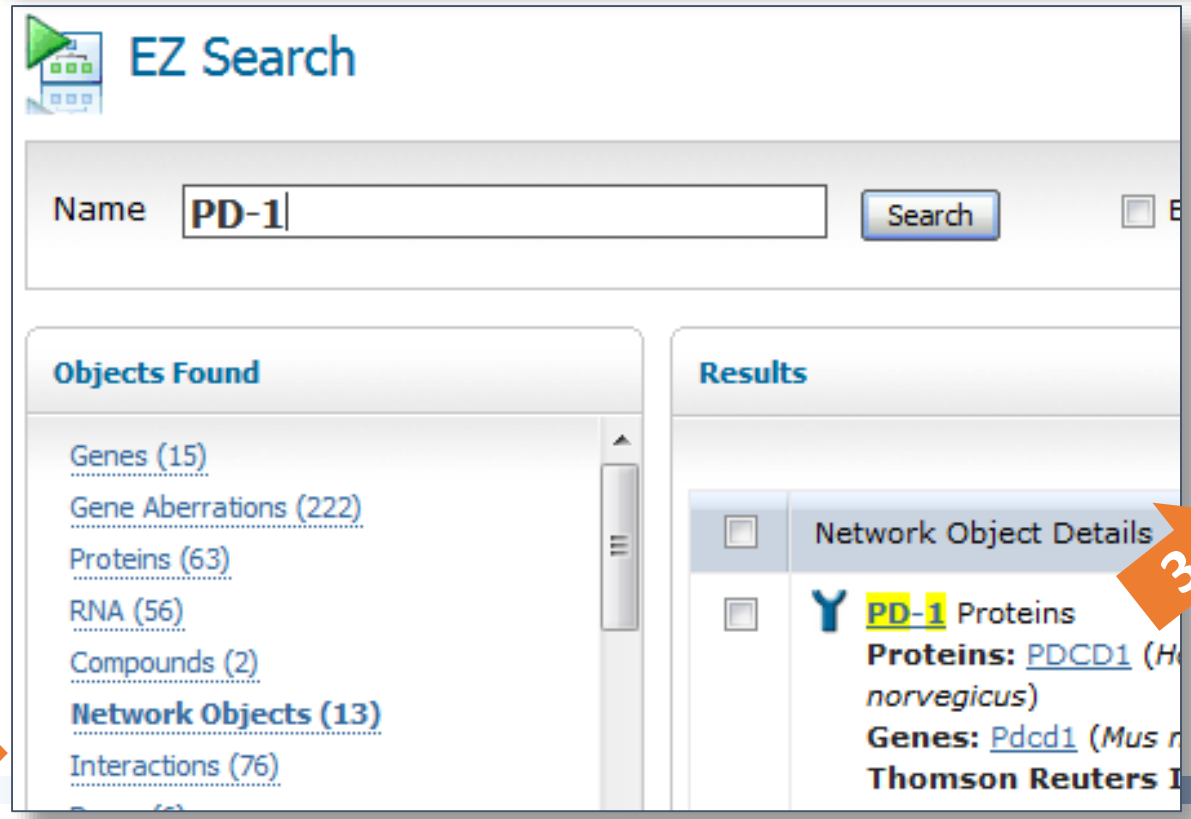


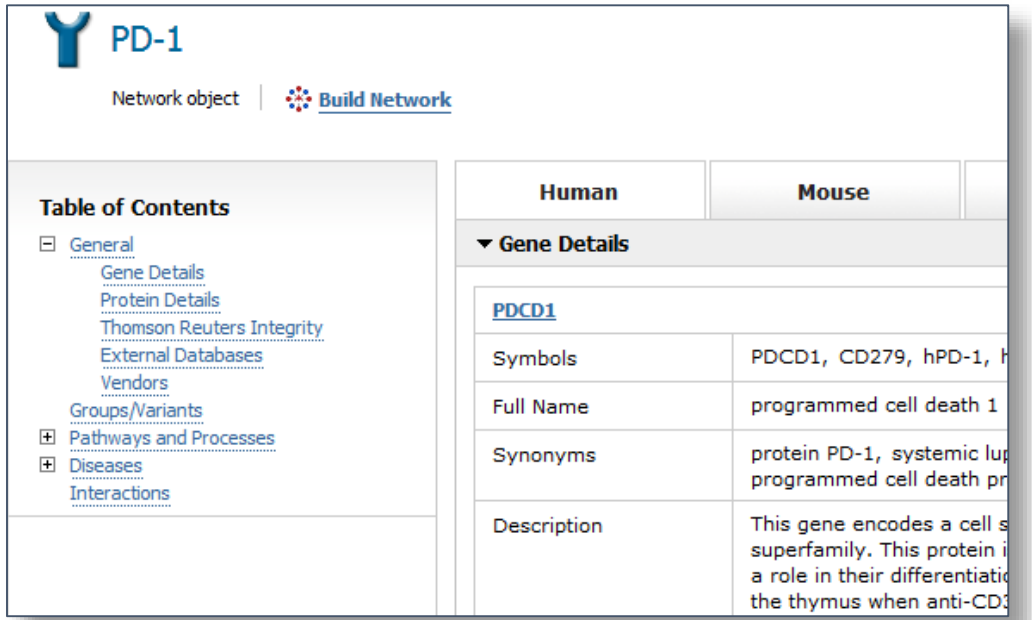


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以簡單檢索找到PD-1的相關資訊

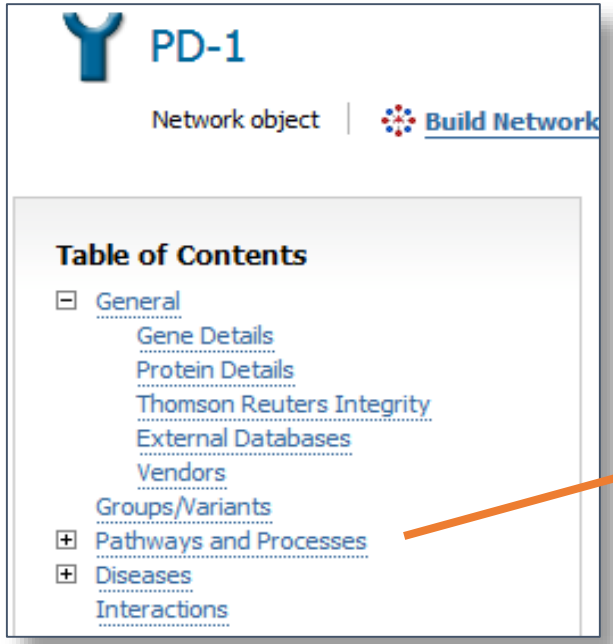




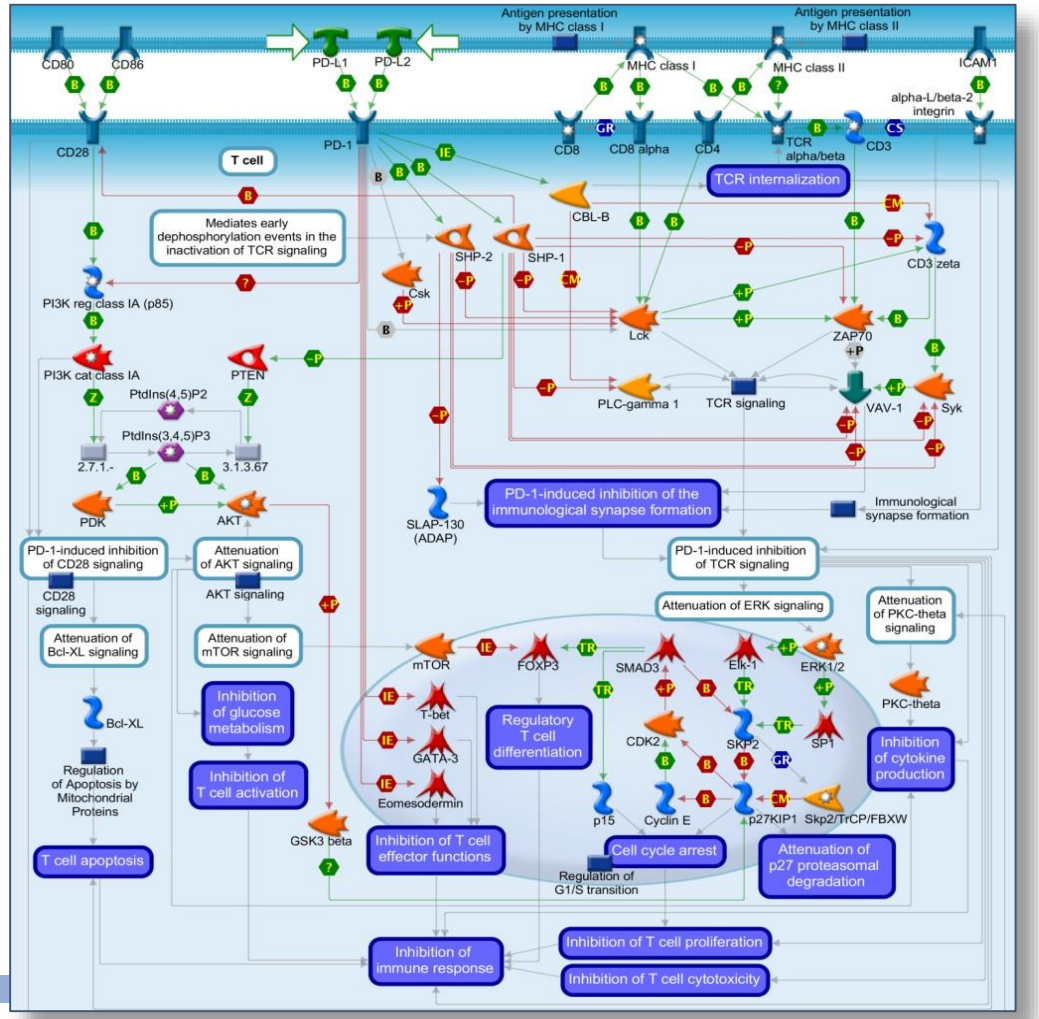


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我們能檢索到PD-1的哪些資訊?

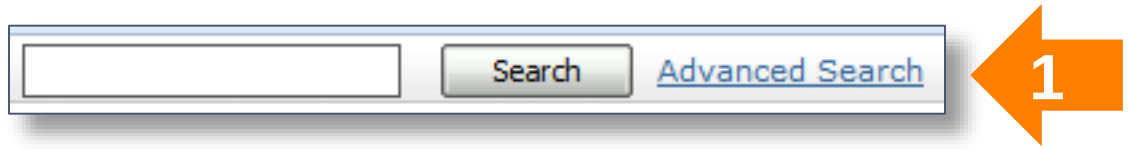


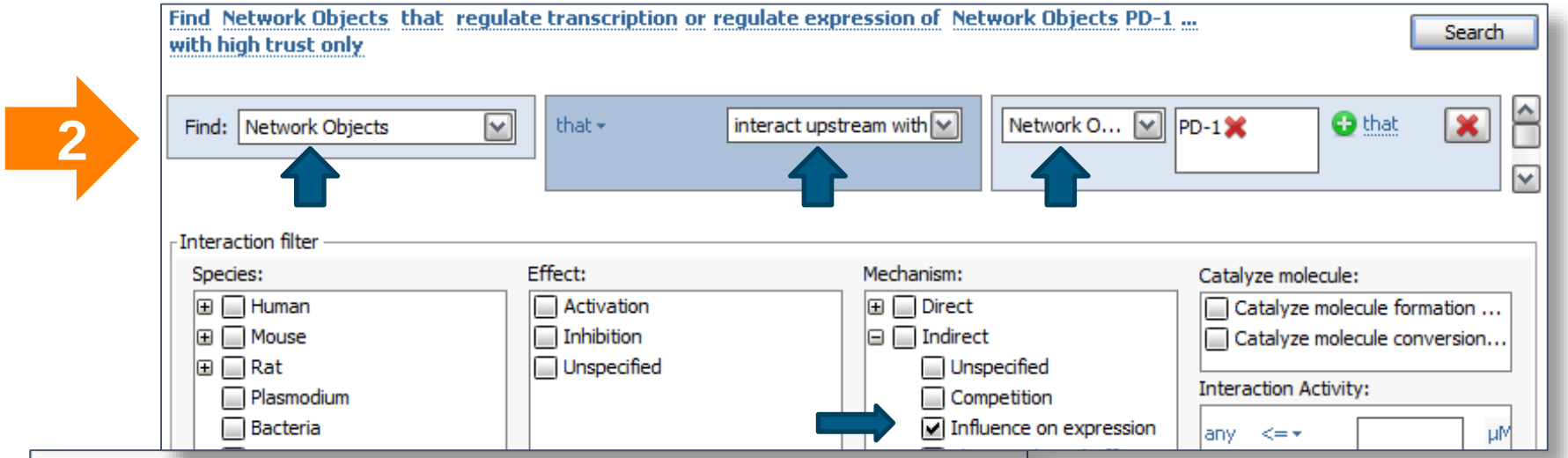
#	From		To	Direction	Effect	Mechanism	Link info
1	CTCF	TR	PD-1	Incoming	Activation	Transcription regulation	
2	FKHR	TR	PD-1	Incoming	Activation	Transcription regulation	
3	IRF9	TR	PD-1	Incoming	Activation	Transcription regulation	
4	NF-AT2(NFATC1)	TR	PD-1	Incoming	Activation	Transcription regulation	
5	RBP-J kappa (CBF1)	TR	PD-1	Incoming	Activation	Transcription regulation	

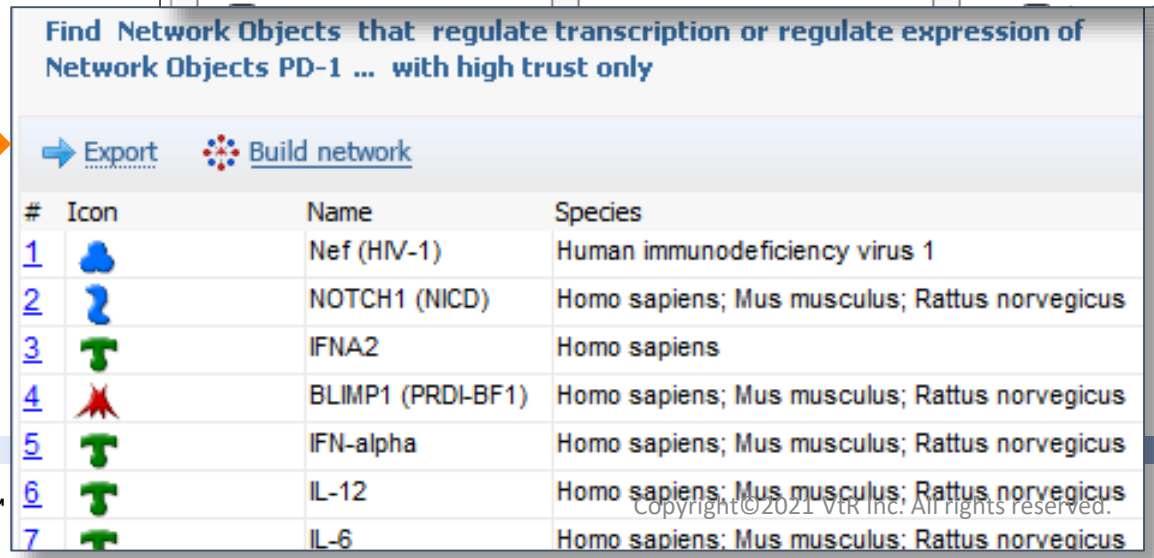


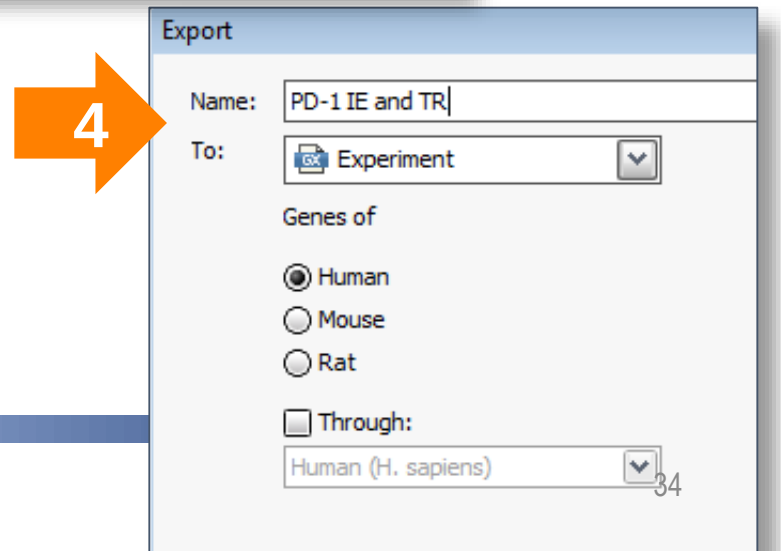
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進階檢索



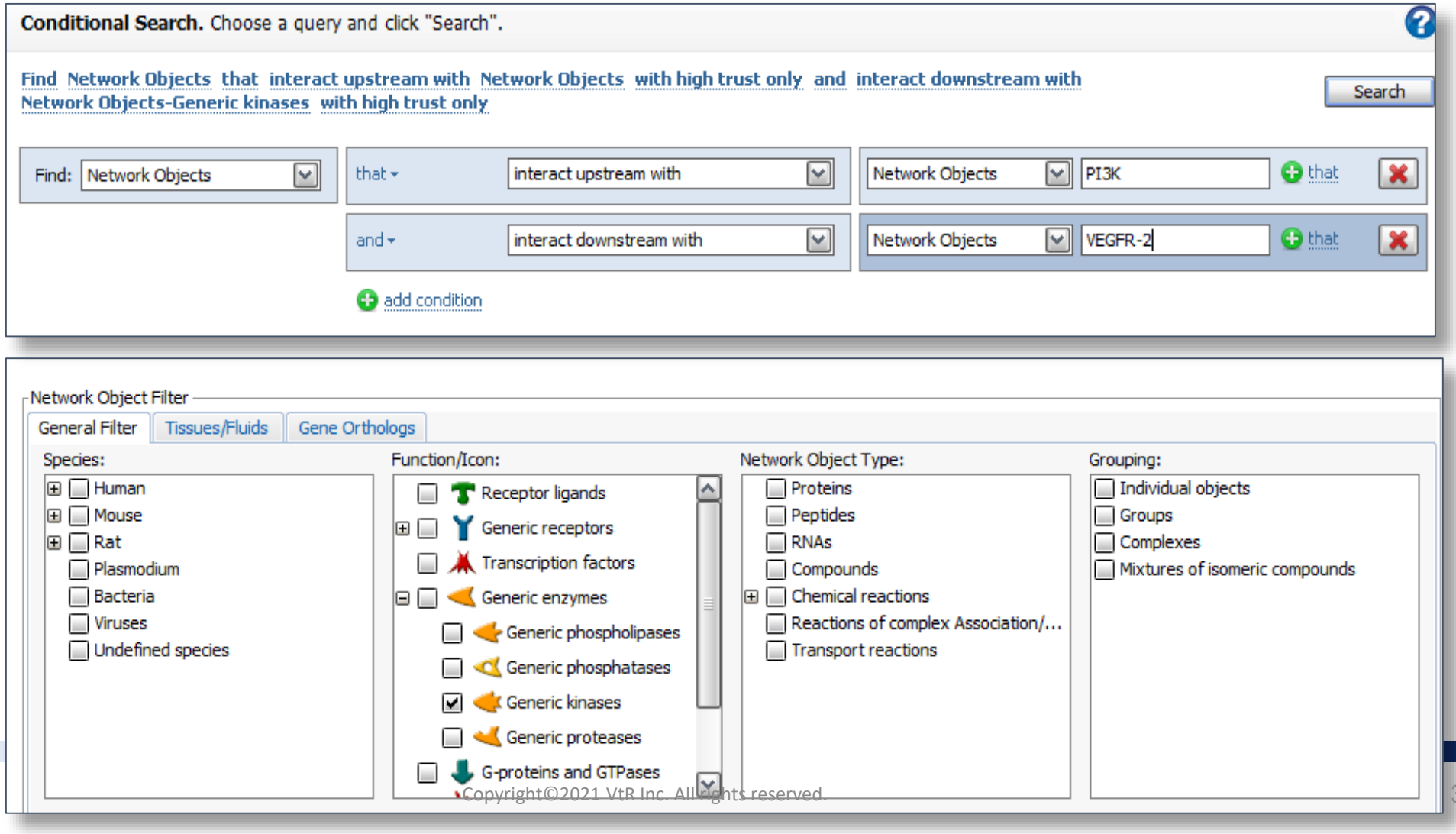






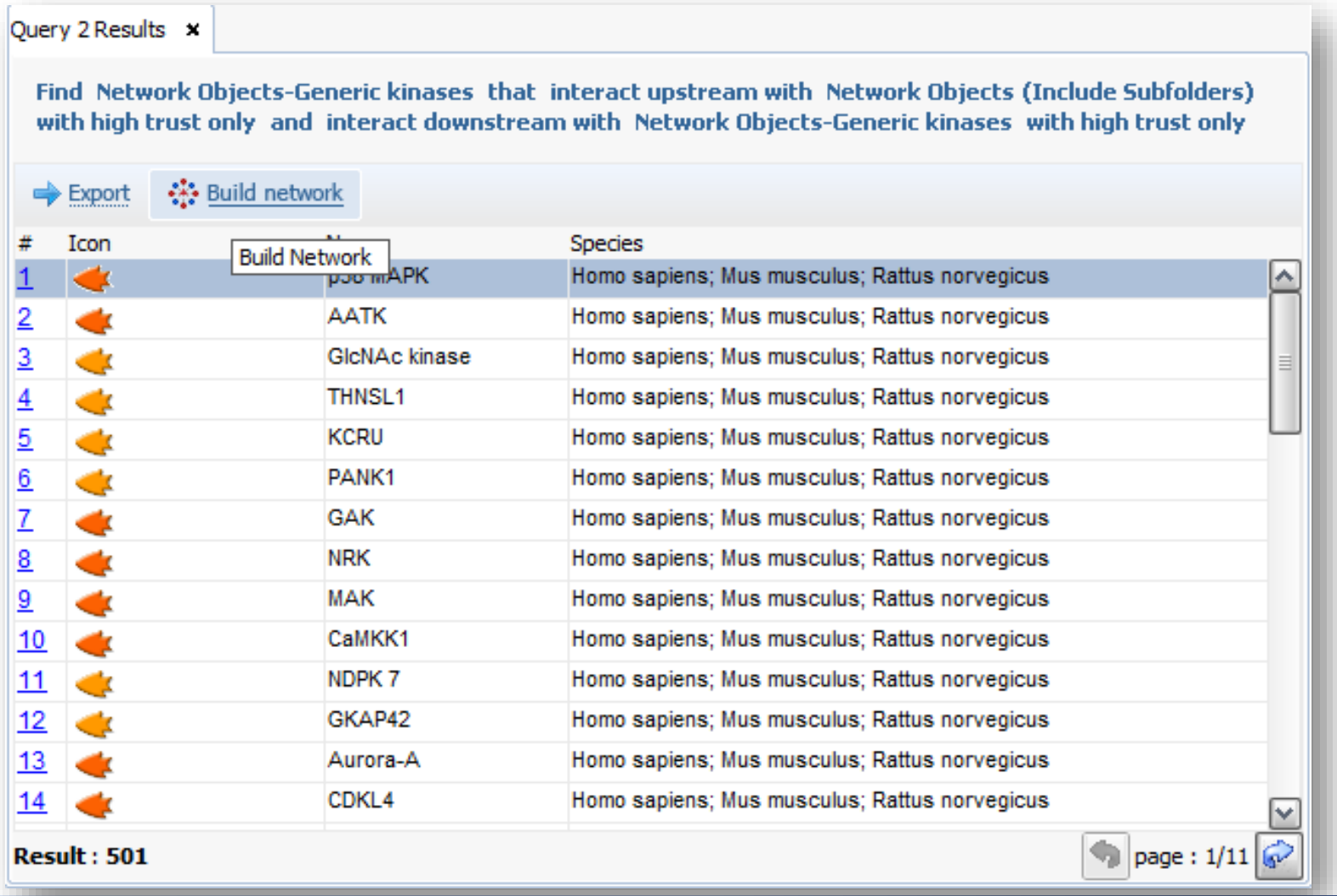
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舉例: VEGFR-2 的下游與PI3K的上游，相互(共同)作用的激酶 (Kinases) 都有哪些？



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VEGFR-2 下游與PI3K上游具作用的 Kinases



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Live demo

資料查詢與檢索

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Exercise I

資料查詢與檢索

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實作練習

以EZ search 進行關鍵字搜尋

- 基因、蛋白質
- 適應症、疾病
- 藥物標的、化合物
- Pathway maps

選擇想進一步了解的分子

以 Advanced search 搜尋分子間相互作用的機制

- 藥物標的
- 分子路徑
- 機制
- 作用物件
- 聚焦搜尋

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時事題: 查詢 “Ractopamine”

EZ Search

Name ractopamine Search Exact match

Objects Found

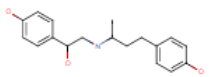
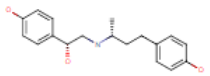
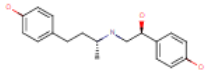
- Compounds (10)
- **Network Objects (10)**
- Interactions (14)
- Drugs (1)
  - Small Molecule Drugs (1)
- Reactions (9)
- Articles (3)

Selected Network Objects

Results

Network Object Details
Ractopamine extracellular region Compound group **Compound Group:** Ractopamine
Ractopamine 10-glucuronide intracellular Compound **Compounds:** Ractopamine 10-glucuronide
(1S,3R)-Ractopamine intracellular Compound **Compounds:** (1S,3R)-Ractopamine
(1R,3R)-Ractopamine intracellular Compound **Compounds:** (1R,3R)-Ractopamine
(1R,3R)-Ractopamine C10-glucuronide intracellular Compound **Compounds:** (1R,3R)-Ractopamine C10-glucuronide
(1S,3R)-Ractopamine C10'-sulfate intracellular Compound **Compounds:** (1S,3R)-Ractopamine C10'-sulfate
(1S,3R)-Ractopamine C10-glucuronide intracellular Compound **Compounds:** (1S,3R)-Ractopamine C10-glucuronide
(1R,3R)-Ractopamine C10'-sulfate intracellular Compound **Compounds:** (1R,3R)-Ractopamine C10'-sulfate
(1R,3R)-Ractopamine C10-glucuronide C10'-sulfate intracellular Compound **Compounds:** (1R,3R)-Ractopamine C10-glucuronide C10'-sulfate
(1S,3R)-Ractopamine C10-glucuronide C10'-sulfate intracellular Compound **Compounds:** (1S,3R)-Ractopamine C10-glucuronide C10'-sulfate

Results

Compound Details
Ractopamine 
(1R,3R)-Ractopamine 
(1S,3R)-Ractopamine 

Results

Interaction Details
Ractopamine extracellular region —B→ DNA **Effect:** Unspecified **Mechanism:** Binding **Species:** Homo sapiens, Mus musculus, Rattus norvegicus **Description:** Ractopamine binds to DNA.
Ractopamine extracellular region —?→ TAR1 **Effect:** Activation **Mechanism:** Unspecified **Species:** Homo sapiens, Mus musculus, Rattus norvegicus **Description:** Ractopamine activates TAR1.
Ractopamine extracellular region —B→ Beta-2 adrenergic receptor **Effect:** Activation **Mechanism:** Binding **Species:** Homo sapiens, Mus musculus, Rattus norvegicus **Description:** Ractopamine is potent agonist of Beta-2 adrenergic receptor
Ractopamine extracellular region —B→ Beta-1 adrenergic receptor **Effect:** Unspecified **Mechanism:** Binding **Species:** Homo sapiens, Mus musculus, Rattus norvegicus **Description:** Ractopamine shows potent binding to Beta-1 adrenergic receptor
Ractopamine extracellular region —B→ Beta-3 adrenergic receptor **Effect:** Unspecified **Mechanism:** Binding **Species:** Homo sapiens, Mus musculus, Rattus norvegicus **Description:** Ractopamine shows weak binding to Beta-3 adrenergic receptor

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時事題: 查詢 “COVID-19”與挖掘資訊

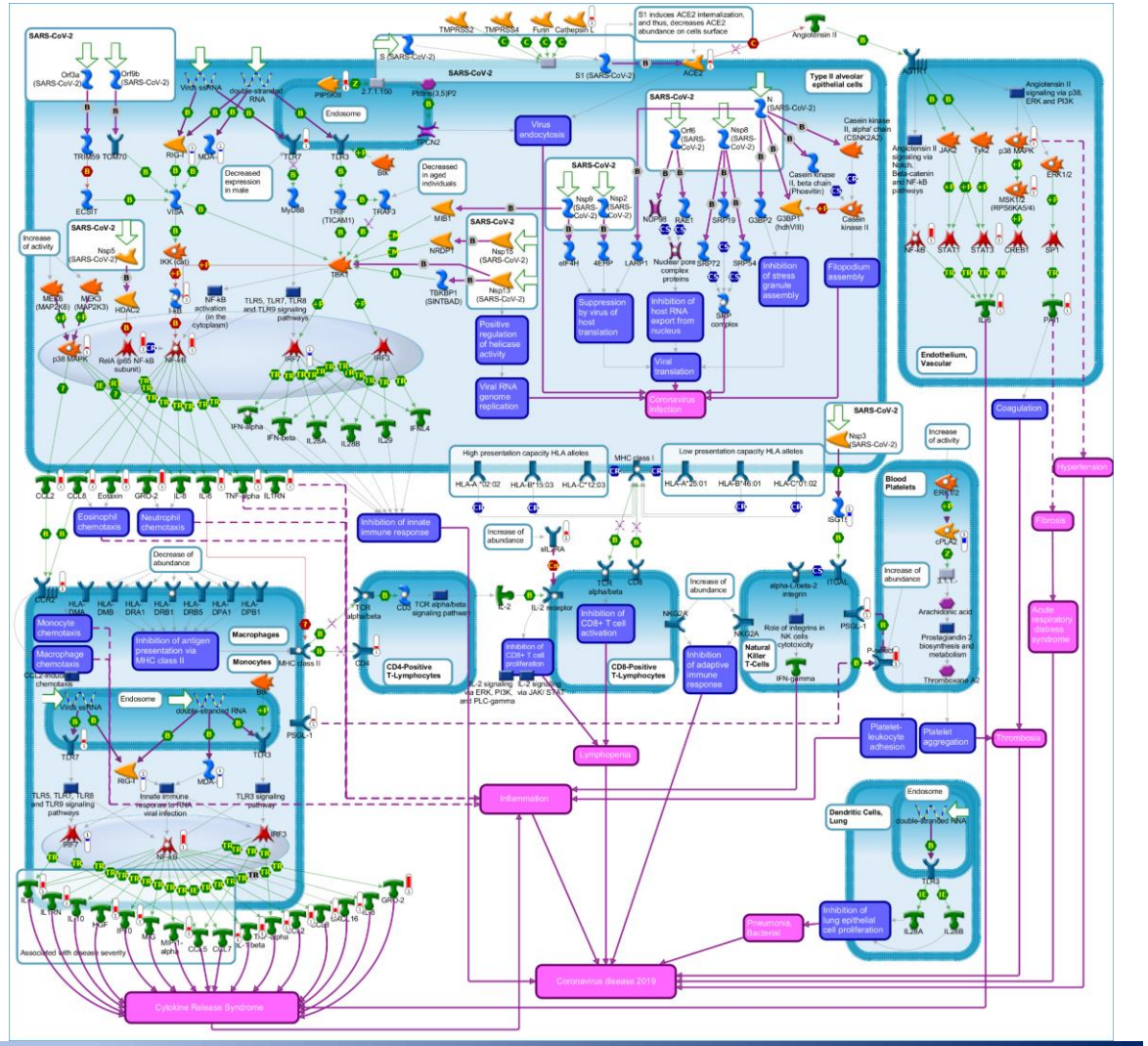
Coronavirus disease 2019

EZ Search

Name: covid-19

Results

	Potential Disease Biomarker Details
☐	CKB creatine kinase B (*Homo sapiens*)
	Potential Disease Biomarkers for: Alzheimer Diseas
☐	TNNI3 troponin I3, cardiac type (*Homo sapiens*)
	Potential Disease Biomarkers for: Acute Coronary S
☐	ALB albumin (*Homo sapiens*)
	Potential Disease Biomarkers for: Acute Coronary S
☐	HBB hemoglobin subunit beta (*Homo sapiens*)
	Potential Disease Biomarkers for: Alzheimer Diseas
☐	GPT glutamic--pyruvic transaminase (*Homo sapiens*)
	Potential Disease Biomarkers for: Alstrom Syndrom
☐	IL6 interleukin 6 (*Homo sapiens*)
	Potential Disease Biomarkers for: Abortion, Habitua
☐	HBA1 hemoglobin subunit alpha 1 (*Homo sapiens*)
	Potential Disease Biomarkers for: Alzheimer Diseas
☐	IL2RA interleukin 2 receptor subunit alpha (*Homo sapi*
	Potential Disease Biomarkers for: Acquired Immunc
☐	NPPB natriuretic peptide B (*Homo sapiens*)
	Potential Disease Biomarkers for: Acromegaly, Acut
☐	TNF tumor necrosis factor (*Homo sapiens*)
	Potential Disease Biomarkers for: Abortion, Habitua
☐	IL1B interleukin 1 beta (*Homo sapiens*)
	Potential Disease Biomarkers for: Abortion, Habitua
☐	CKM creatine kinase, M-type (*Homo sapiens*)
	Potential Disease Biomarkers for: Alzheimer Diseas



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II. 建構網絡及分子路徑圖

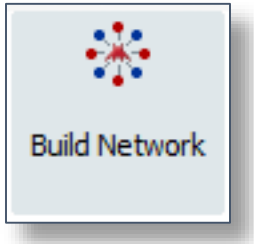
- 在這些蛋白中，哪些訊息路徑可以調節PD-1的表現?
- 哪些訊息路徑可能成為患者分級的良好生物標記以及潛在的治療標的?

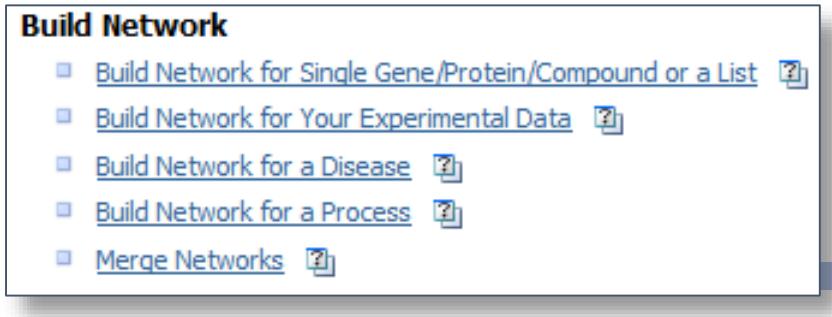
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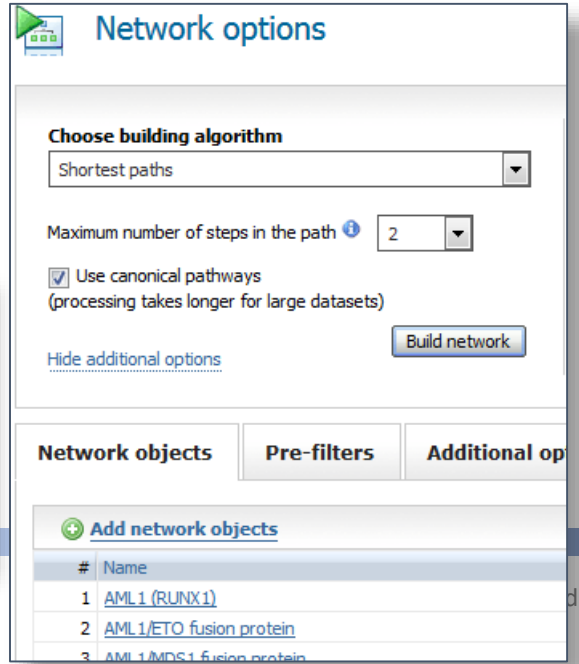
建立一個網路來推測哪些路徑可以影響PD-1的表現

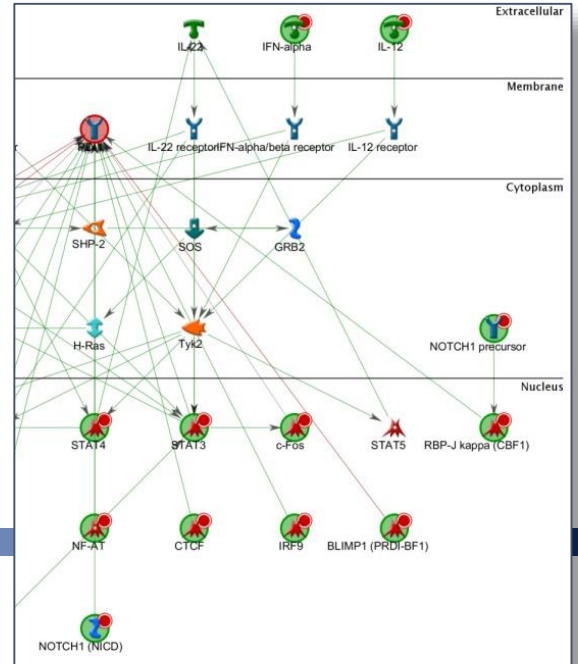
- Questions:
  - 在這些蛋白中，哪些訊息路徑可以調節PD-1的表現?
  - 哪些訊息路徑可能成為患者分級的良好生物標記以及潛在的治療標的?

Build network from experiment → **Set network building options** → **Arrange Layout**

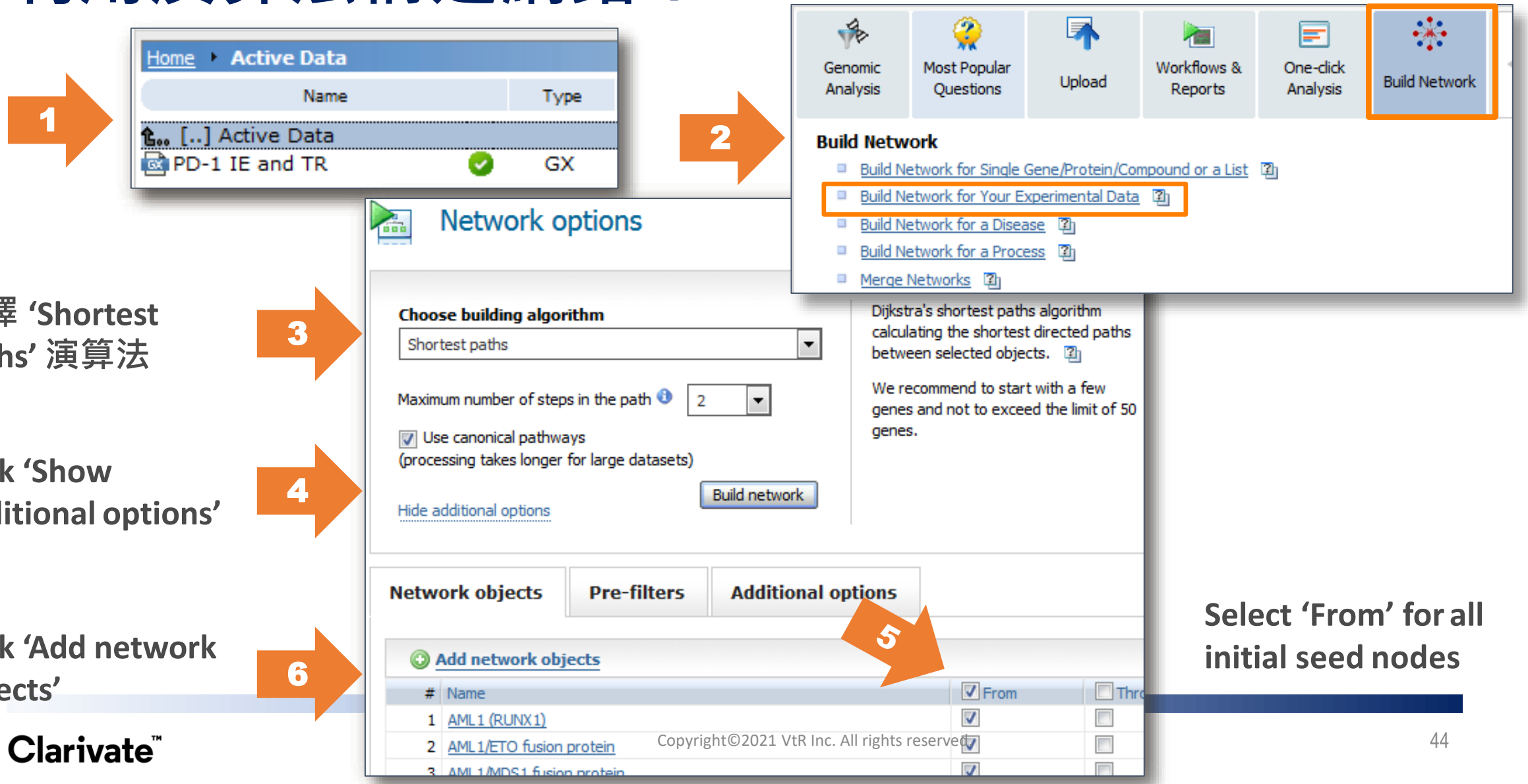








利用演算法構建網路 1

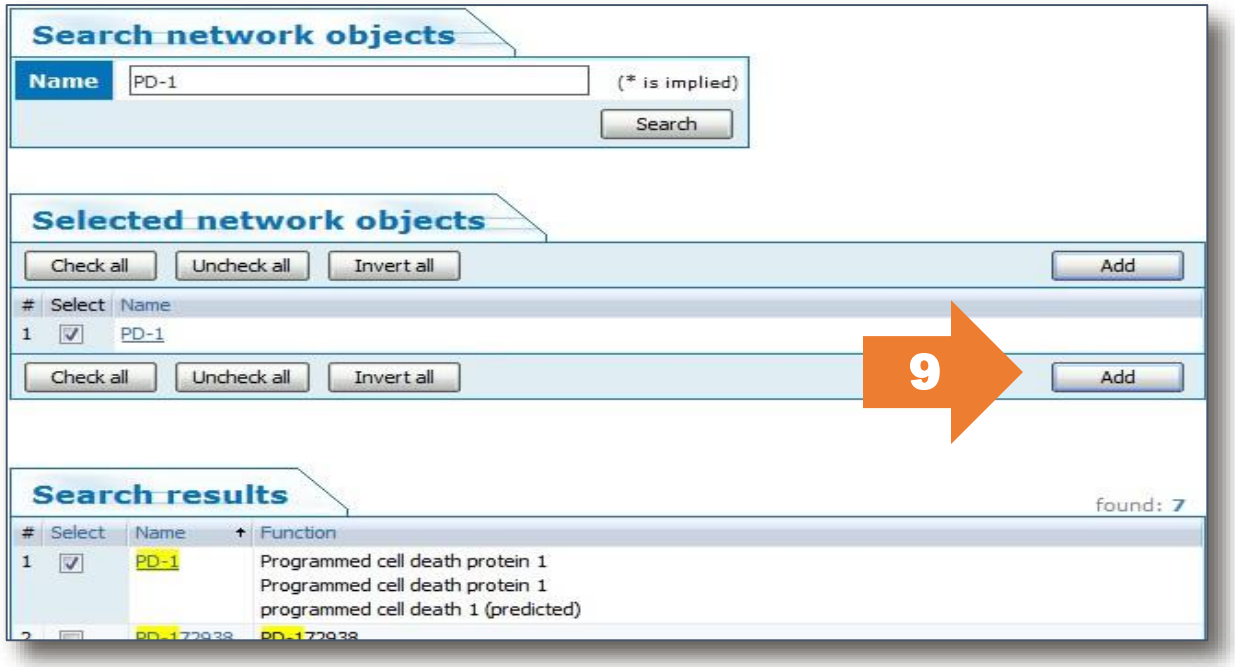


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利用演算法構建網路 2

Type PD-1 into search

7



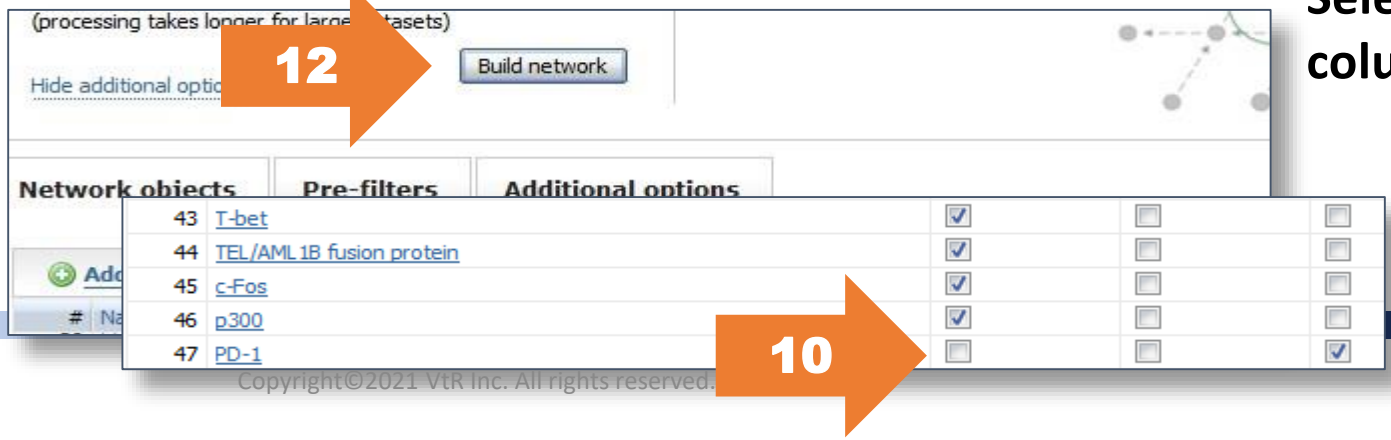
9

Add to seed list

Select the correct PD-1

8

12



11

Select PD-1 in 'To' column

10

Deselect PD-1 in 'From' column

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Analyze network

Generates sub-networks enriched with seed nodes (nodes from root list = activated experiments). Sub-networks are ranked by a P-value and G-Score and interpreted in terms of Gene Ontology processes.

We recommend 300-600 genes in input list for this algorithm. Analysis of larger datasets (>2,000 genes) is possible but calculation will take longer.



Show legend

Network options

Choose building algorithm

Analyze network

Number of nodes in a network 50

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

- Initial (seed) node included in network
- Other objects included in network
- Object not included in network
- Link included in network
- Link not included in network

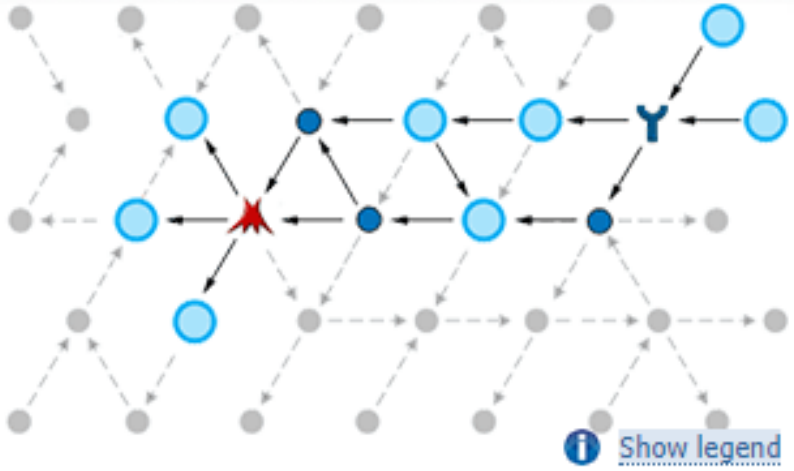
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Analyze network (TF)

For every transcription factor (TF) with direct target(s) in the root list, this algorithm generates a sub-network consisting of all shortest paths to this TF from the closest receptor with direct ligand(s) in the root list.

We recommend 300-600 genes in input list for this algorithm. Analysis of larger datasets (>2,000 genes) is possible but calculation will take longer.



Choose building algorithm

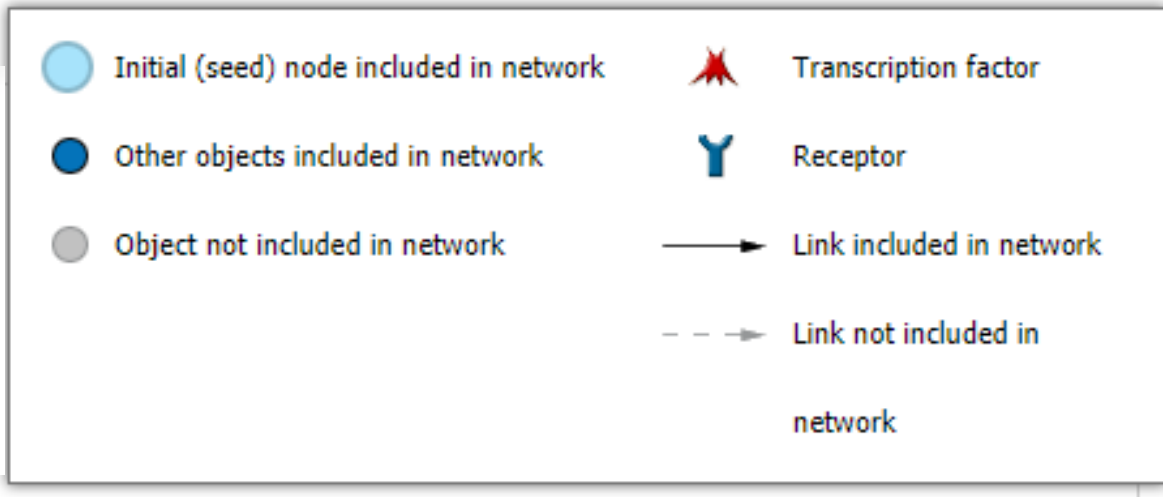
Analyze network (transcription factors)

Add ligands and TF targets

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options



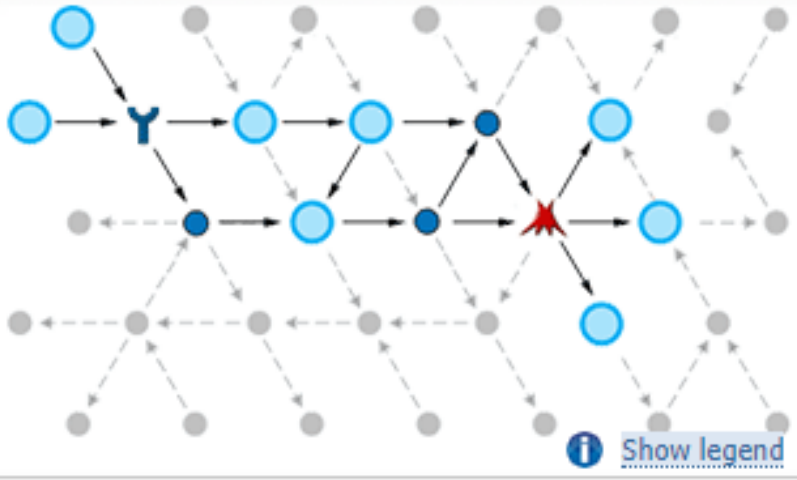
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Analyze network (Receptors)

For every receptor with direct ligand(s) in the root list, this algorithm generates a sub-network consisting of all shortest paths from that receptor to the closest TF with direct target(s) in the root list.

We recommend 300-600 genes in input list for this algorithm. Analysis of larger datasets (>2,000 genes) is possible but calculation will take longer.



Choose building algorithm

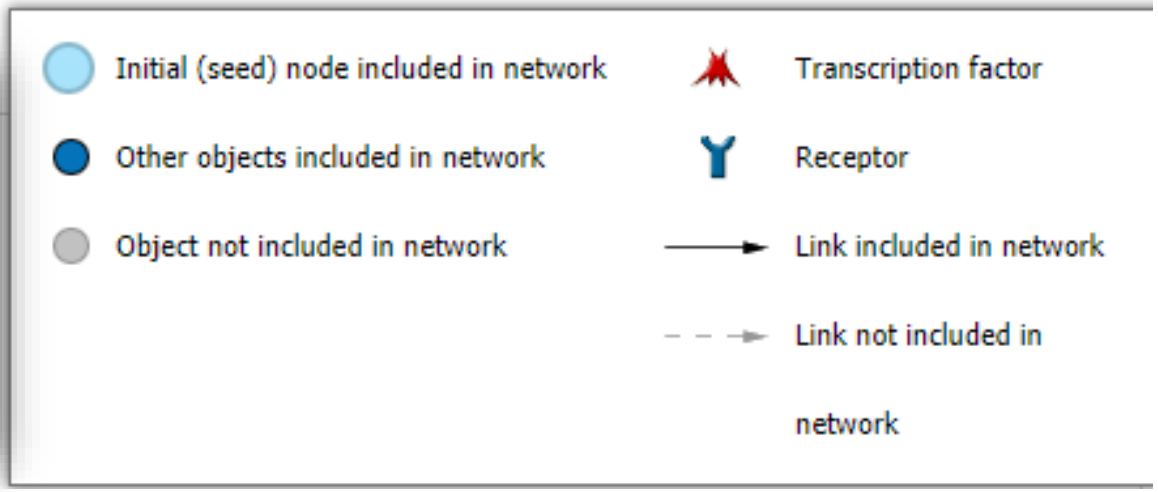
Analyze network (receptors)

Add ligands and TF targets

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

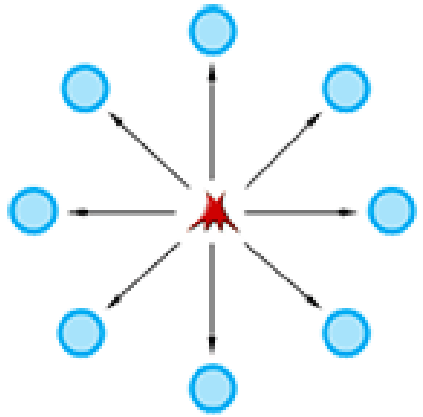


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Transcription regulation

Generates sub-networks centered on transcription factors. Sub-networks are ranked by a P-value and interpreted in terms of Gene Ontology.

We recommend 300-600 genes in input list for this algorithm. Analysis of larger datasets (>2,000 genes) is possible but calculation will take longer.



Show legend

Choose building algorithm

Transcription regulation

Number of nodes in a network 50

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

Initial (seed) node included in network

Transcription factor

Link included in network

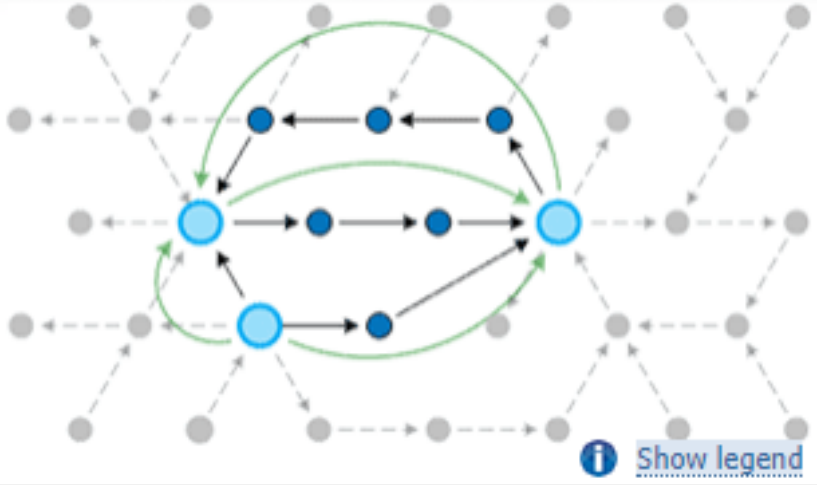
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Shortest paths

Dijkstra's shortest paths algorithm calculating the shortest directed paths between selected objects.

We recommend to start with a few genes and not to exceed the limit of 50 genes.



Choose building algorithm

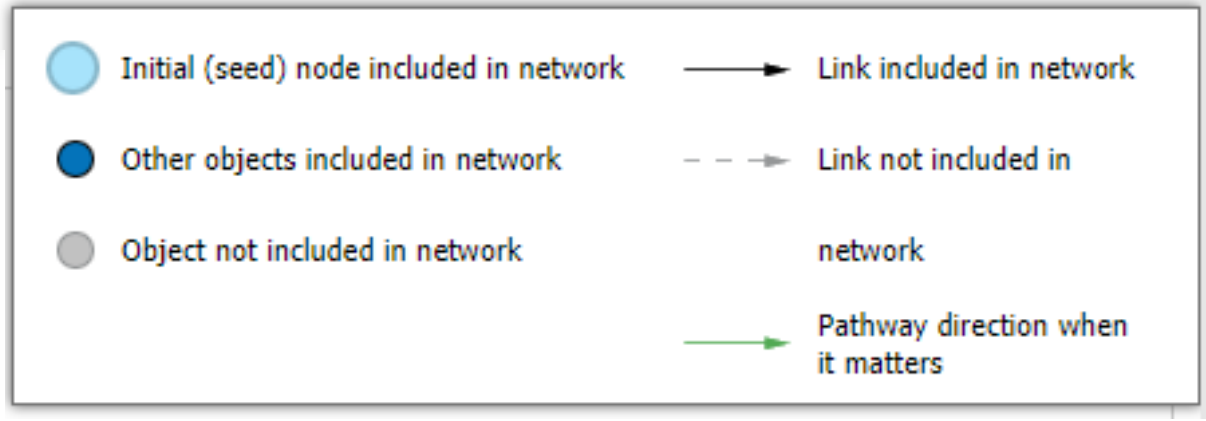
Shortest paths

Maximum number of steps in the path 2

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

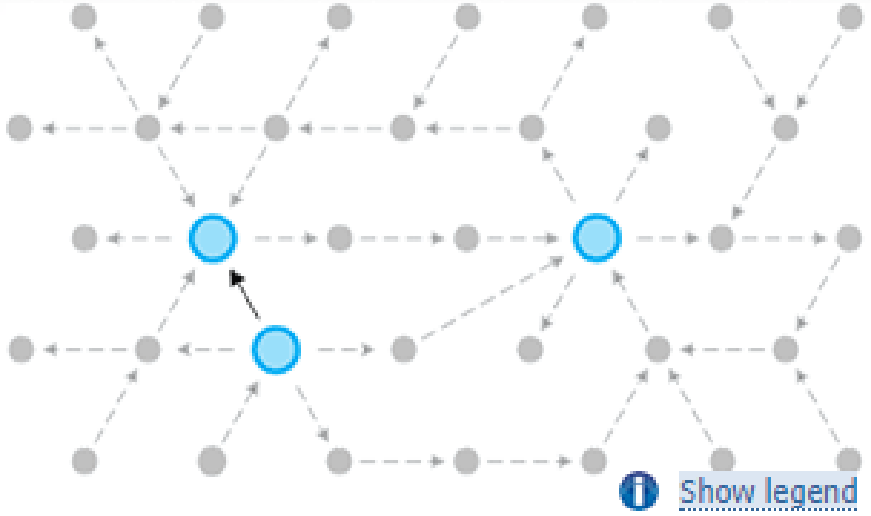


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Direct interactions

Draws direct interactions between selected objects. No additional objects are added to the network.

We recommend not to exceed the limit of 100 genes per network.



Choose building algorithm

Direct interactions

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

Initial (seed) node included in network

Object not included in network

Link included in network

Link not included in network

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Self regulation

Choose building algorithm

Self regulation

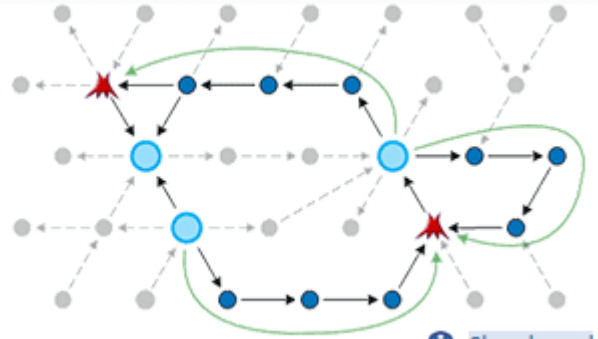
Maximum number of steps in the path 2

Use canonical pathways (processing takes longer for large datasets)

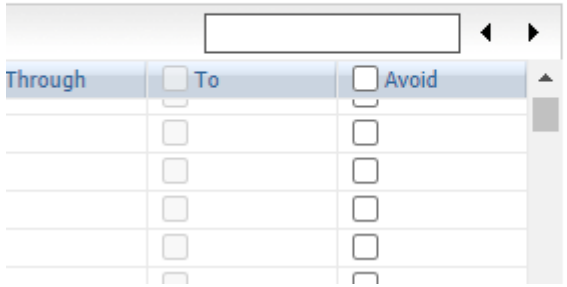
Hide additional options

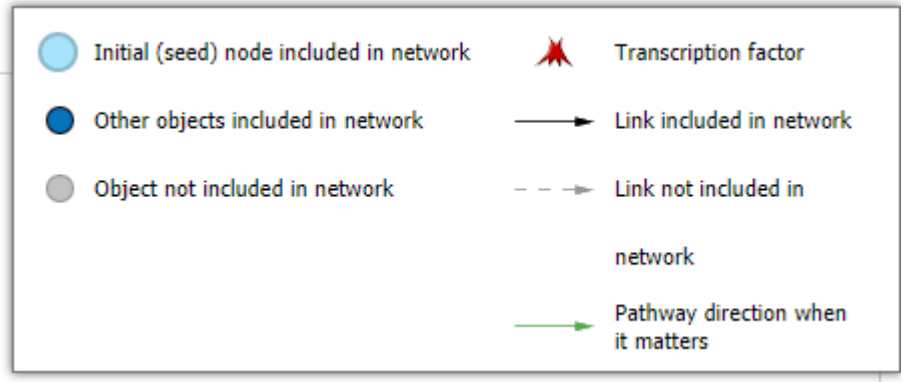
Finds the shortest directed paths containing transcription factors between the selected objects.

We recommend to start with a few genes and not to exceed the limit of 50 genes.



Show legend



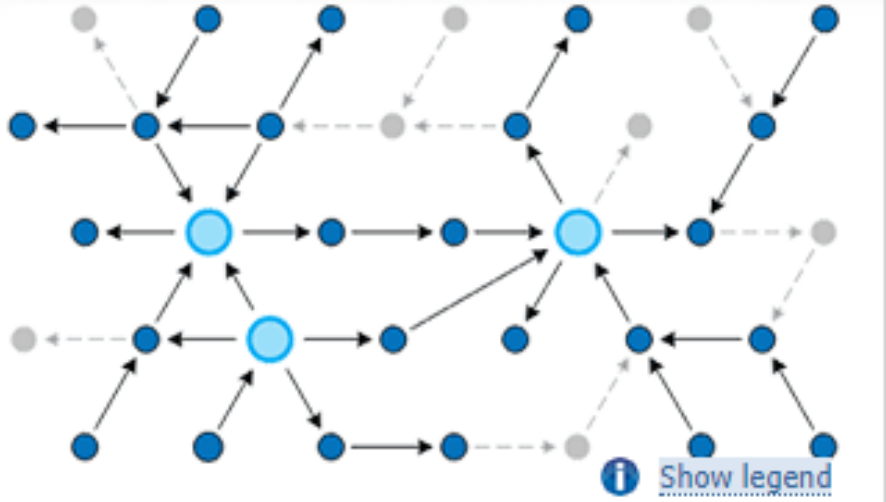


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Auto expand

Draws sub-networks around the selected objects. Expansion halts when the sub-networks intersect.

We recommend to select one to several genes (1-3) for this algorithm.



Choose building algorithm

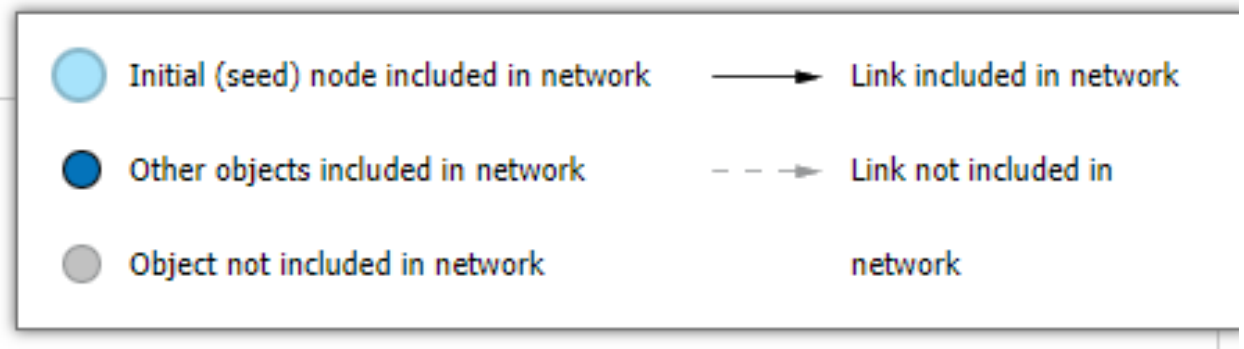
Auto expand

Number of nodes in a network 50

Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

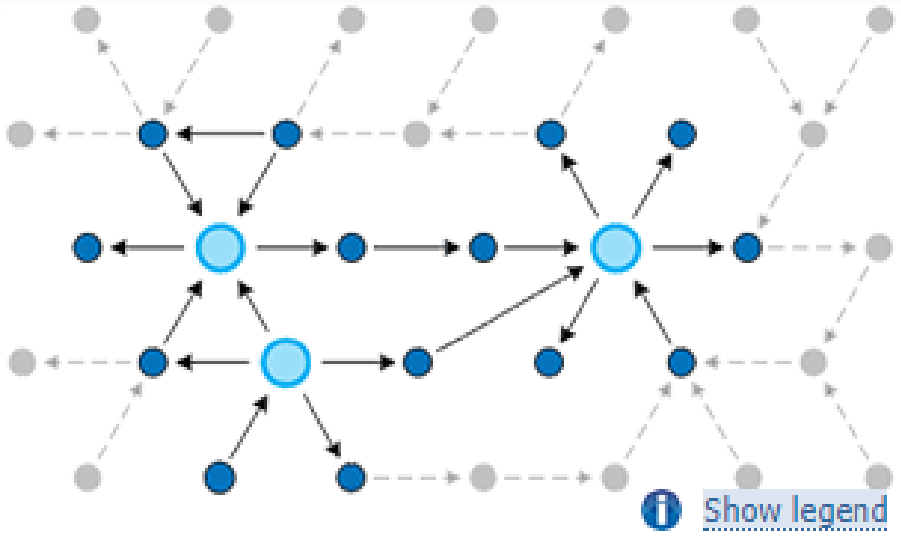


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Expand by one interaction

Draws all the one step interactions around the selected objects.

We recommend to select one to several genes (1-3) for this algorithm.



Choose building algorithm

Expand by one interaction

Directions ◯ Upstream ◯ Downstream ◉ Both

☑ Use canonical pathways (processing takes longer for large datasets)

Build network

Hide additional options

Initial (seed) node included in network

Other objects included in network

Object not included in network

Link included in network

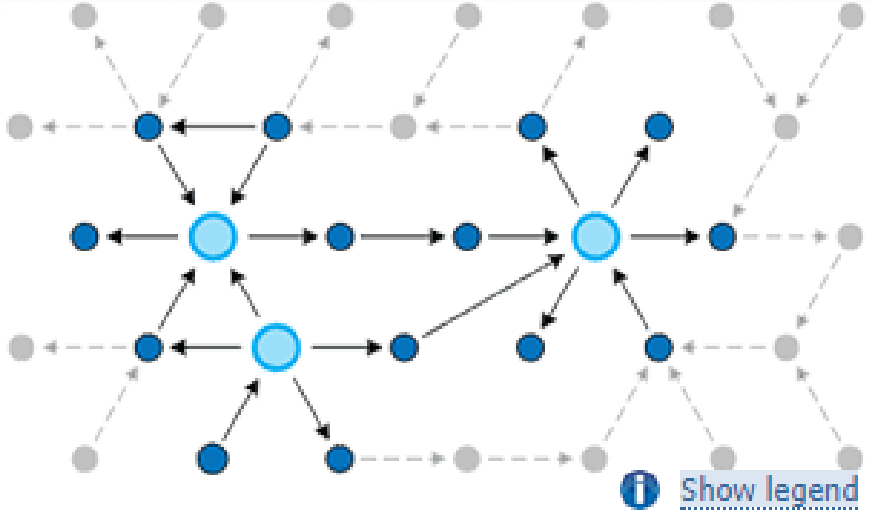
Link not included in network

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Manual expand

"Neighborhood" analysis. Expand network manually around selected objects.



Choose building algorithm

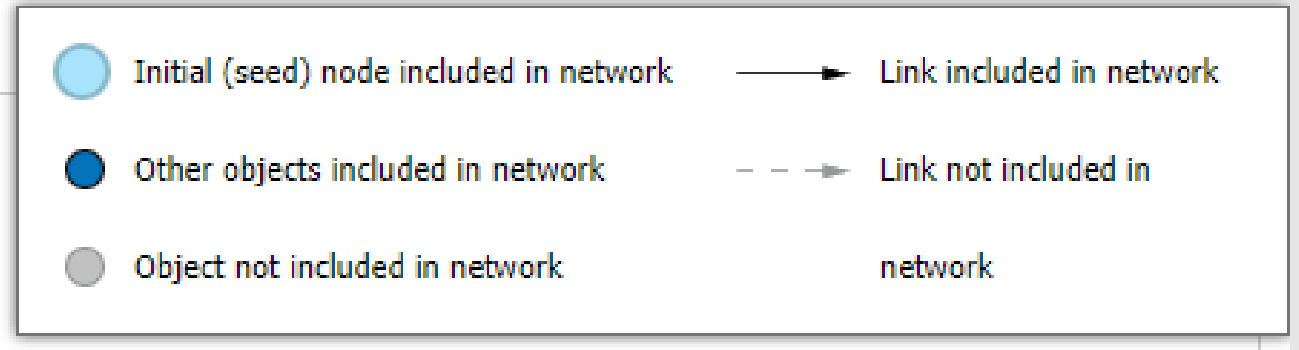
Manual expand

Maximum number of steps 2

Use canonical pathways (processing takes longer for large datasets)

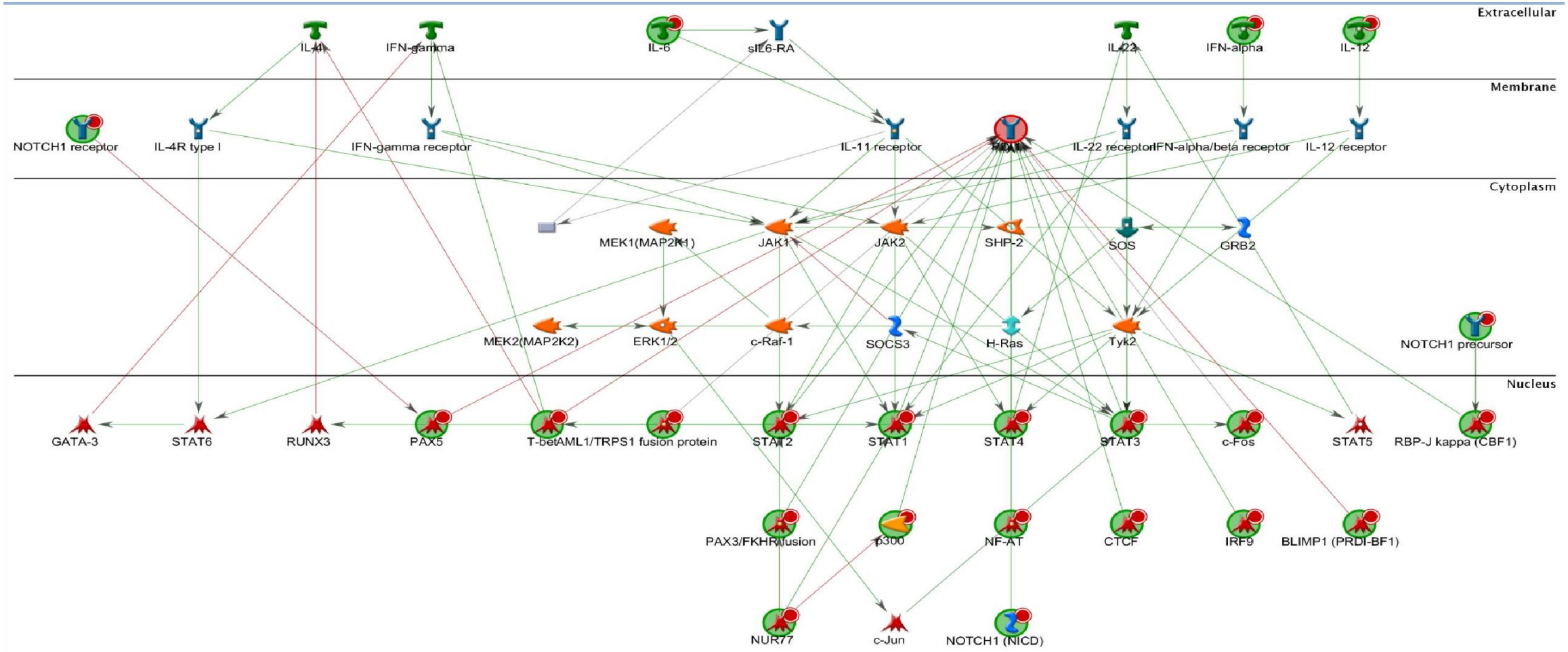
Build network

Hide additional options



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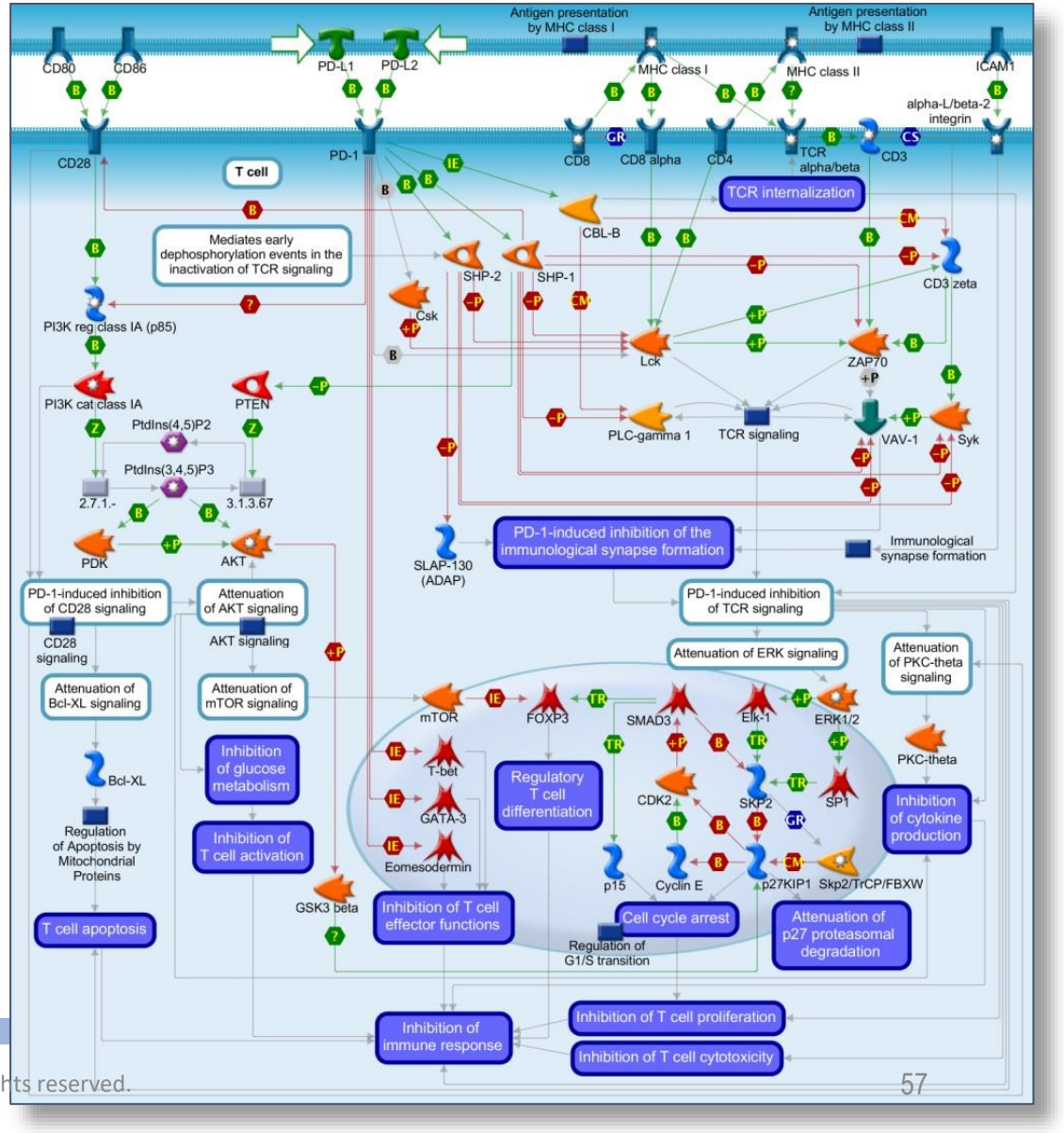
調節PD-1表現的訊息傳導路徑有哪些?



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SUMMARY

- PD-1通過與PD-L1或PD-L2結合而活化，可以抑制T細胞活化的重要訊息路徑，影響重要轉錄因子的表現。
- PD-1的表現主要集中在JAK/STAT路徑的啟動上。
- 患者分級生物標記或聯合用藥標的包括IFN- gamma、NOTCH1、STATs



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Live demo

建構網絡及分子路徑

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Exercise II

建構網絡及分子路徑

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實作練習

選擇實作 1 搜尋後感興趣的分子或物件

- 基因、蛋白質
- 藥物標的、化合物

以1-2種 model 建立分子網絡

解釋分子間相互作用的機制及可能的功能

- 藥物標的
- 分子路徑
- 機制
- 適應症、疾病

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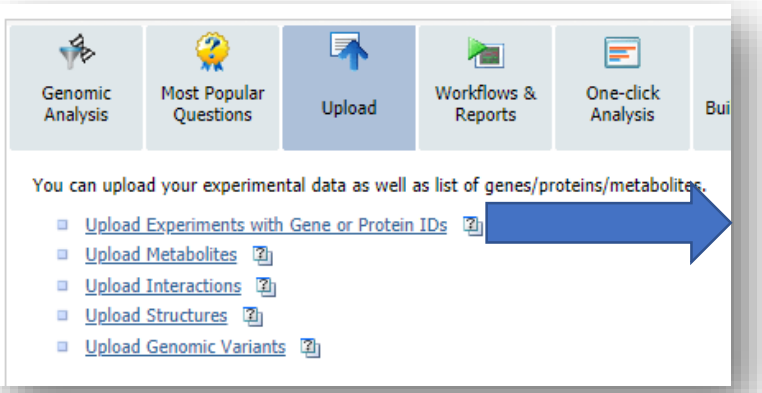
III. 體學數據上傳及分析

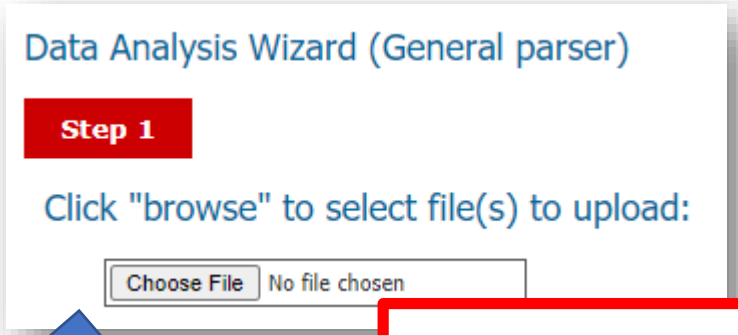
- Biomarker discovery in patients with degraded kidney function through the analysis of metabolomic, proteomic, and RNA-seq data

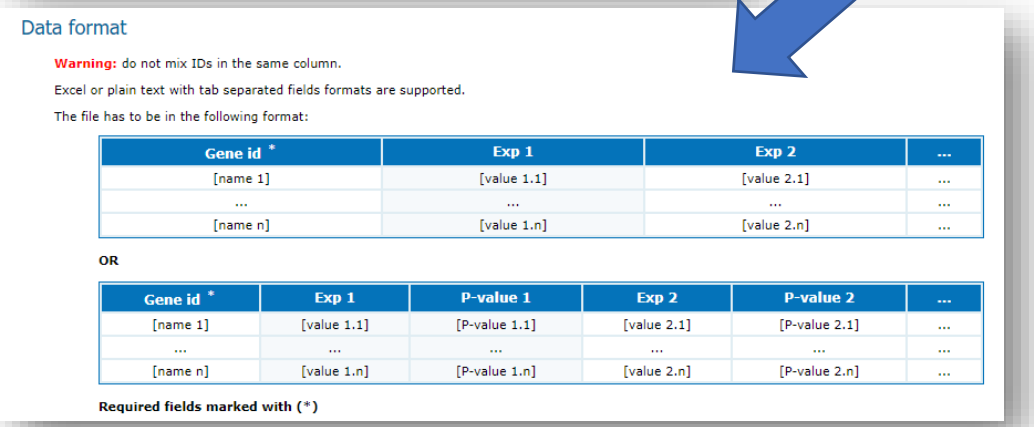
- 通過代謝體學、蛋白質體學和RNA-seq數據分析，發現腎功能退化患者的生物標記

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上傳體學數據







可上傳的數據格式

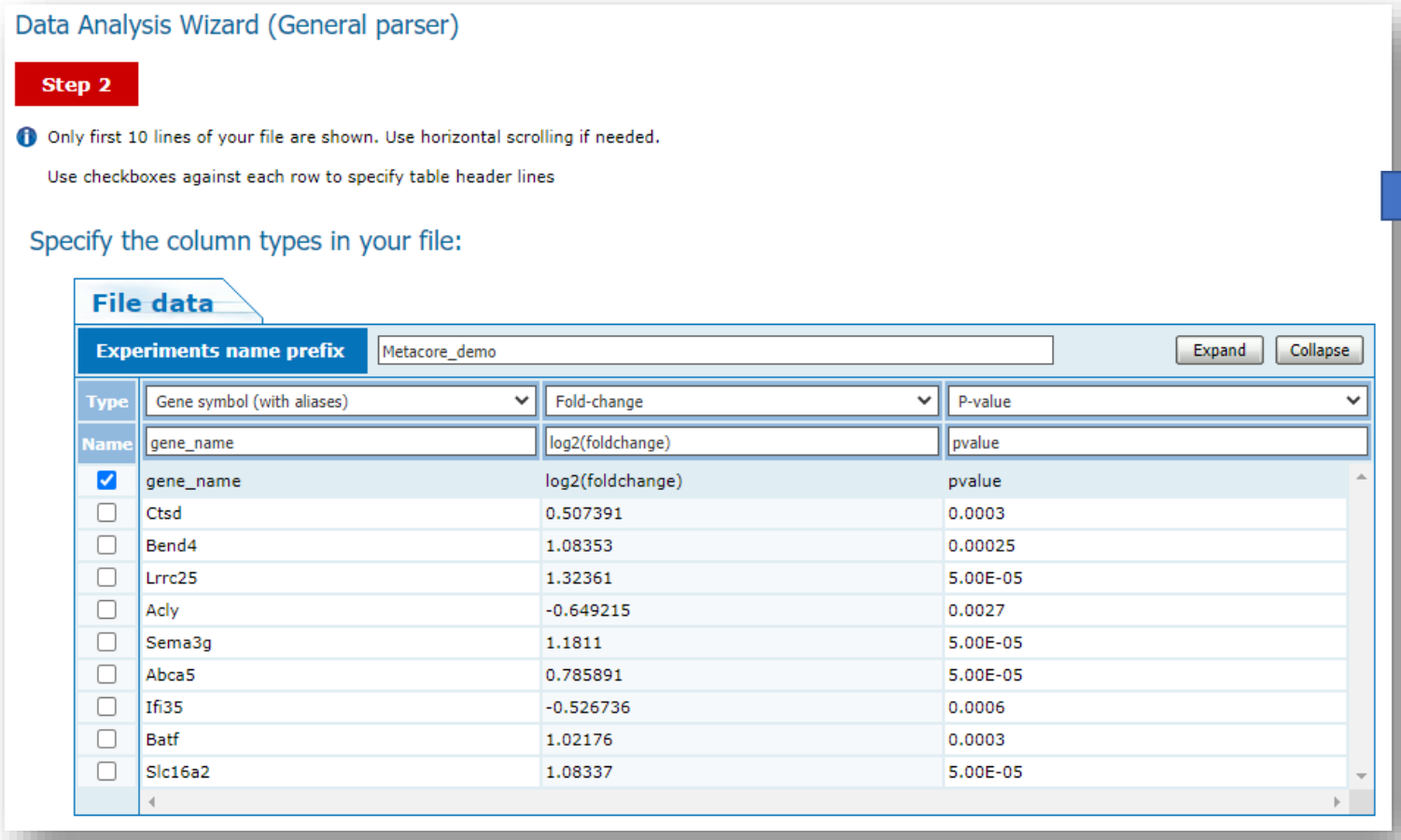
Most files are of «General» type. The following identifiers are recognized:

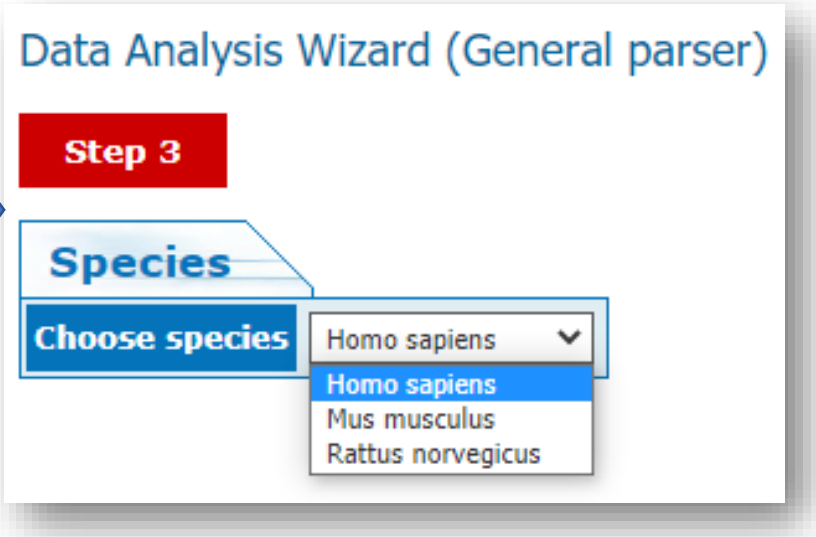
- EntrezGene (LocusLink) IDs — Mouse, Rat, Bovine, Chimpanzee, Dog, Zebra
  Baker's yeast IDs are supported as well (via orthologs)
- Gene symbol (e.g. TP53, etc.)
- Affymetrix tag ID (expression)
- Affymetrix tag ID (exon)
- Affymetrix tag IDs (SNP)
- Illumina tag IDs (expression)
- Agilent tag IDs (expression)
- Codelink tag IDs (expression)
- OMIM IDs
- RefSeq IDs
- Unigene IDs
- ENSEMBL IDs (including Sus scrofa)
- rsSNP IDs
- SwissProt IDs
- IPI IDs
- GeneBank IDs
- miRBase IDs
- Panther IDs
- MetaCore gene IDs

All entries in one column should have same type of IDs. Mixed IDs are not

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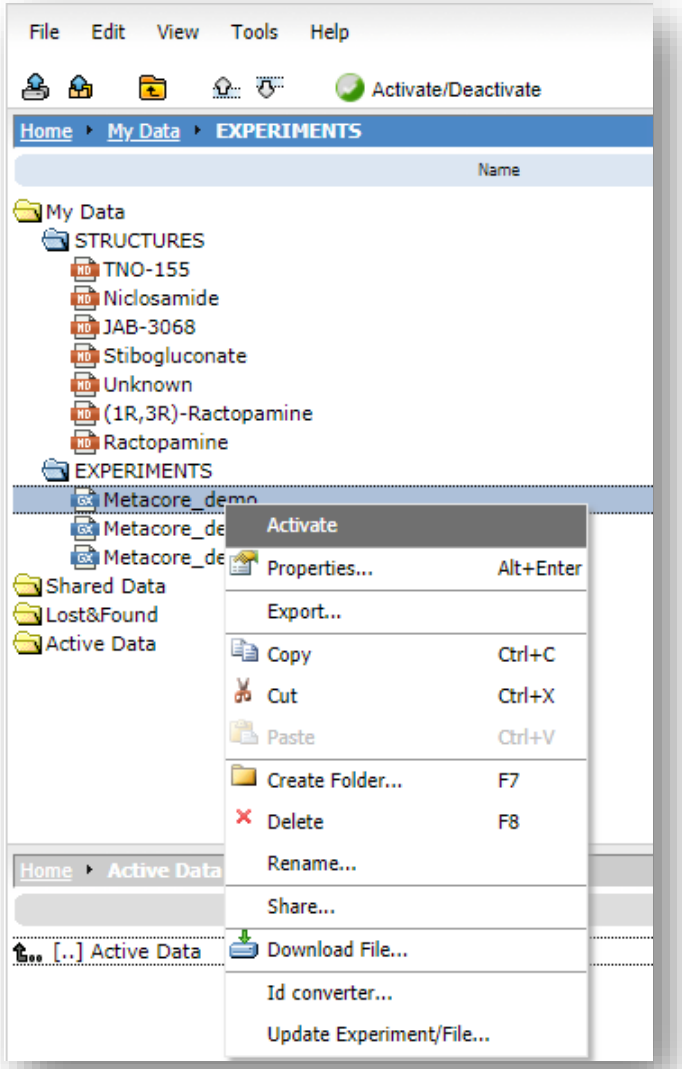
上傳體學數據的欄位對應

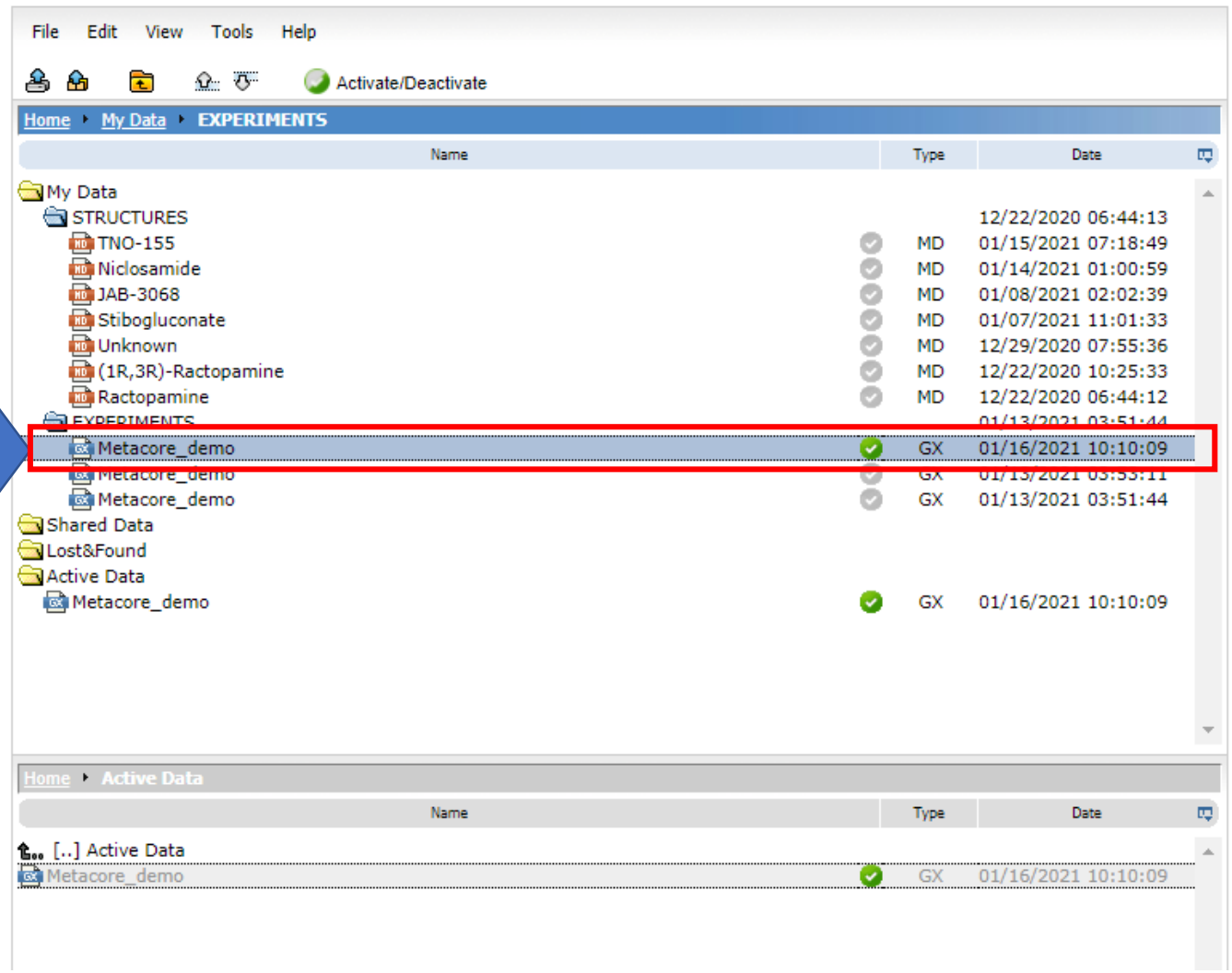




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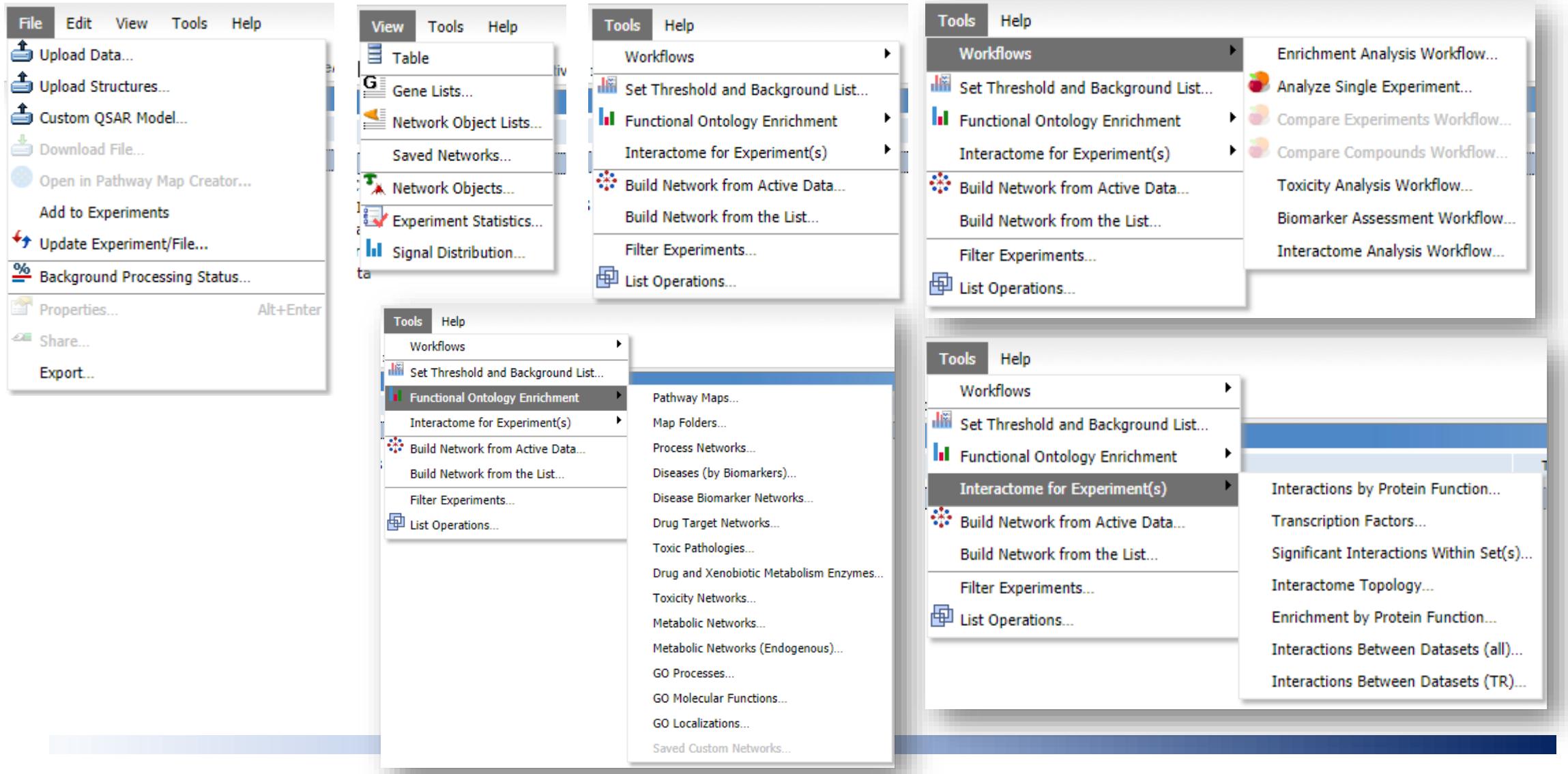
開始分析體學數據





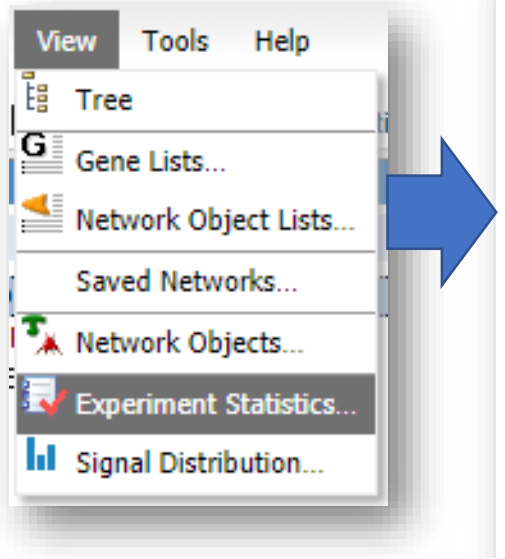
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開始分析體學數據 (可選擇的分析工具及數據呈現方式)



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透過統計分析，進入挖掘機制與網絡分析結果



Statistics

Active Experiments:

#	Experiment name	Species (Defined by genes origin)	Tag type
1.	Metacore_demo	Homo sapiens	Gene Symbol

IDs uploaded		Signal distribution
IDs on maps		
With threshold	1257	Maps
Total	1257	
IDs on networks		
With threshold	2154	Network objects
Total	2154	
IDs on diseases		
With threshold	2120	Diseases
Total	2120	
IDs on GO processes		
With threshold	2055	GO processes
Total	2055	
IDs on Process Networks		
With threshold	1059	

Pathway Maps | Network Objects

Export | Export to image | Reorder enrichment profile — Total results: 50

#	Maps	-log(pValue)	pValue	FDR	Ratio
1	Chemokines in inflammation in adipose tissue and liver in obesity, type 2 diabetes and metabolic syndrome X		1.285e-18	1.119e-15	31/48
2	Development_Regulation of epithelial-to-mesenchymal transition (EMT)		1.514e-18	1.119e-15	36/64
3	Cell adhesion_ECM remodeling		2.675e-18	1.318e-15	33/55
4	IL-1 beta- and Endothelin-1-induced fibroblast/ myofibroblast migration and extracellular matrix production in asthmatic airways		6.342e-16	2.343e-13	26/40
5	Mast cell migration in asthma		3.372e-15	8.975e-13	35/73

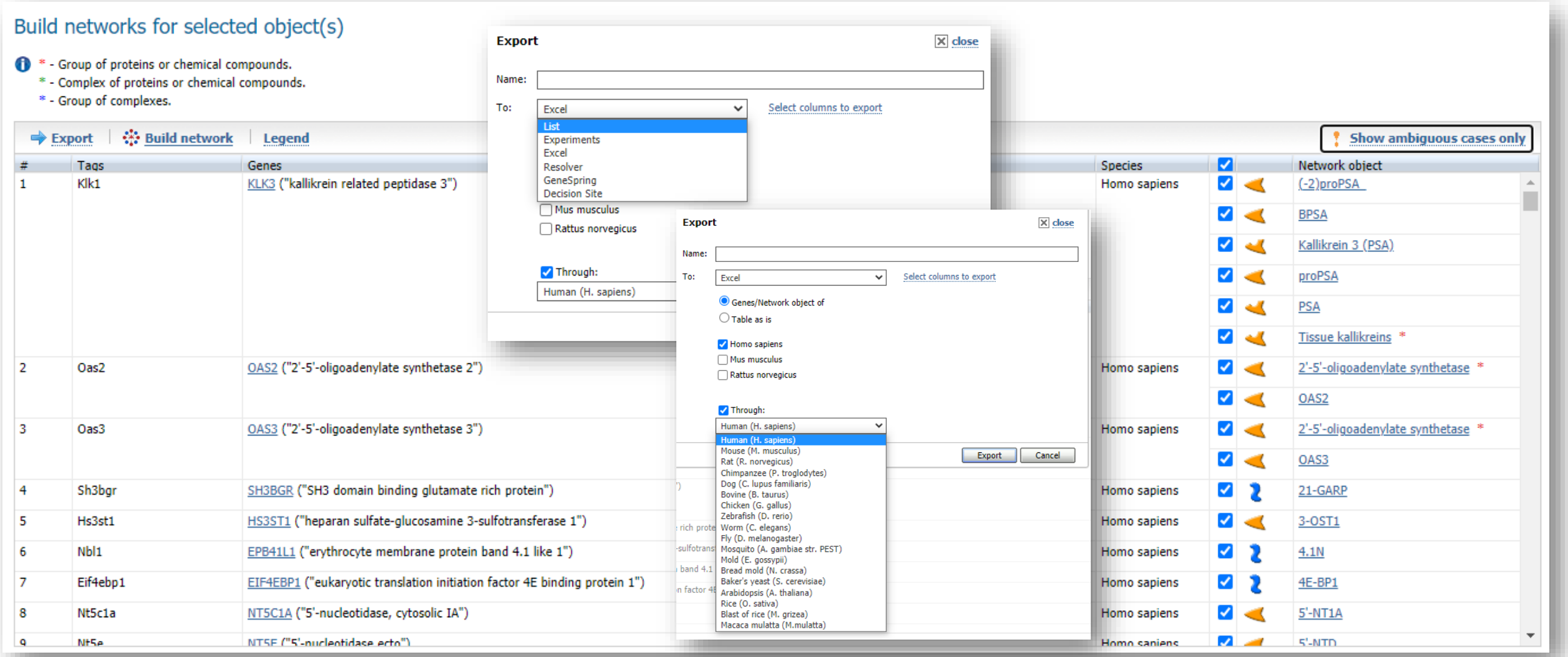
Diseases (by Biomarkers) | Network Objects

Export | Export to image | Reorder enrichment profile — Total results: 50

#	Diseases	-log(pValue)	pValue	FDR	Ratio
1	Connective Tissue Diseases		3.052e-139	9.060e-136	823/3764
2	Rheumatic Diseases		1.729e-138	2.443e-135	734/3136
3	Joint Diseases		2.469e-138	2.443e-135	746/3222
4	Arthritis		2.175e-136	1.614e-133	733/3155
5	Pathologic Processes		1.188e-135	7.054e-133	894/4349

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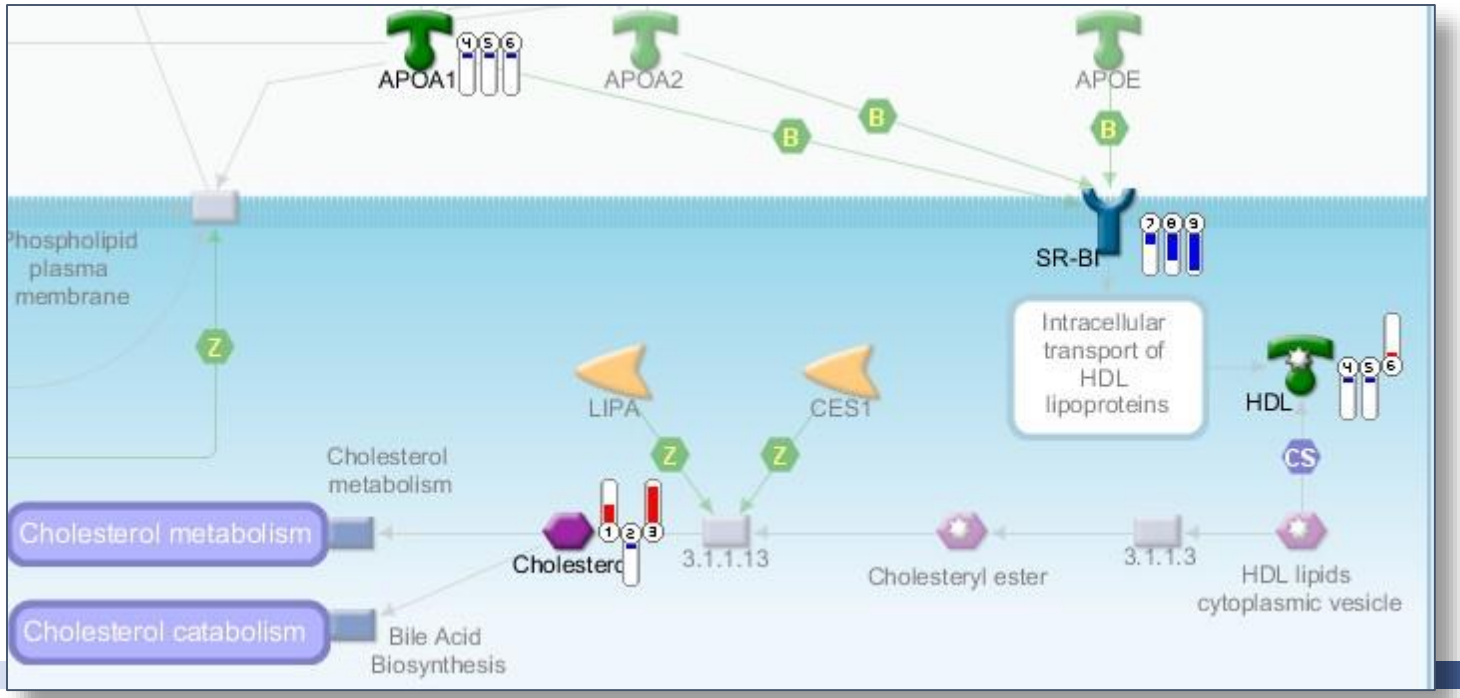
輸出網絡分析結果



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Questions:

- 我們能在代謝體學和轉錄體學資料之間找到什麼代謝關係?
- 患者血漿中哪些代謝物和蛋白質濃度的變化可以作為疾病進程的生物標記？



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多體學數據同時分析

- Combining metabolomic, transcriptomic and gene variants for side by side – omics enrichment analysis

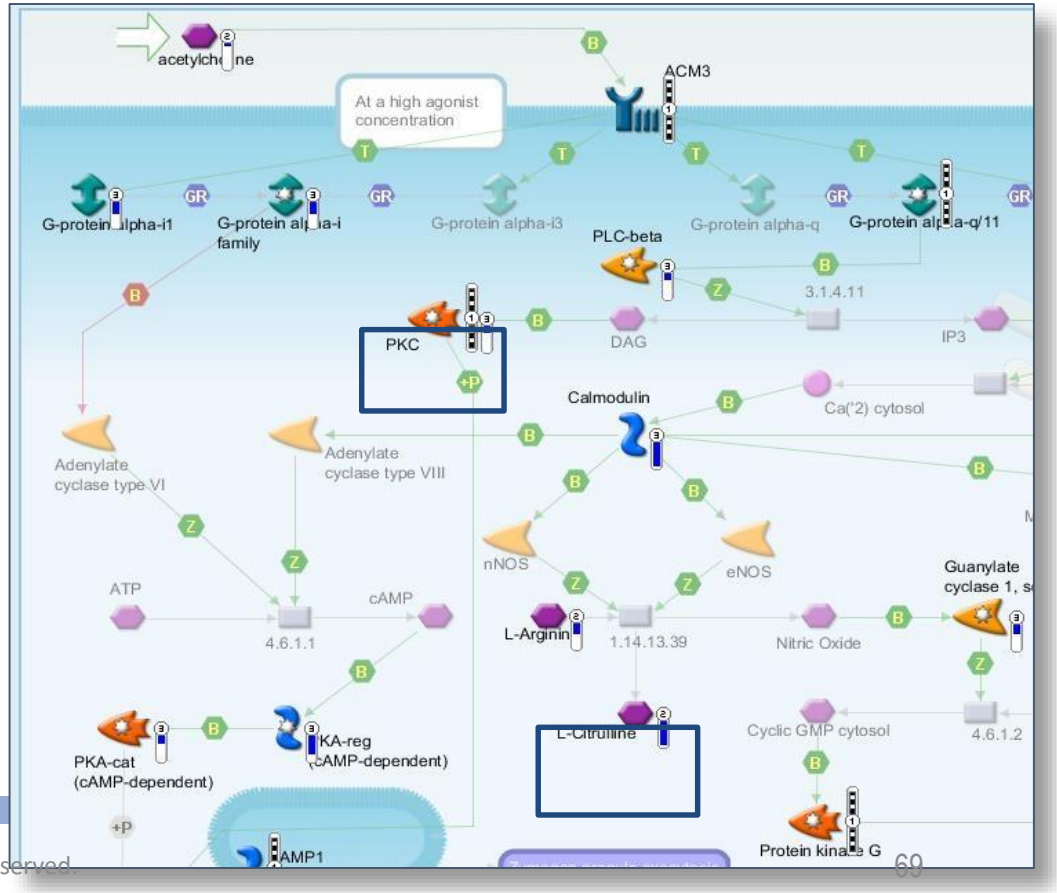
You can upload your experimental data as well as list of genes/proteins/metabolites.

- Upload Experiments with Gene or Protein IDs
- Upload Metabolites
- Upload Interactions
- Upload Structures
- Upload Gene Variants

Home ▸ **Active Data**

Name	Type	Date
[..] Active Data		
T2D Genetic Variants	VX	07/22/2013 11:45:19
pre diabetic metabolites	MX	11/07/2012 09:55:03
Diabetes vs. Normal Gene Expression	GX	11/20/2012 15:24:43

Experiment name	Species	Network Objects
T2D Genetic Variants	Homo sapiens	1135
pre diabetic metabolites		187
Diabetes vs. Normal Gene Expression	Homo sapiens	1535



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多體學數據分析的小技巧

- 在比較不同的體學數據時，我們需要想一想他們是怎樣相互關聯的？

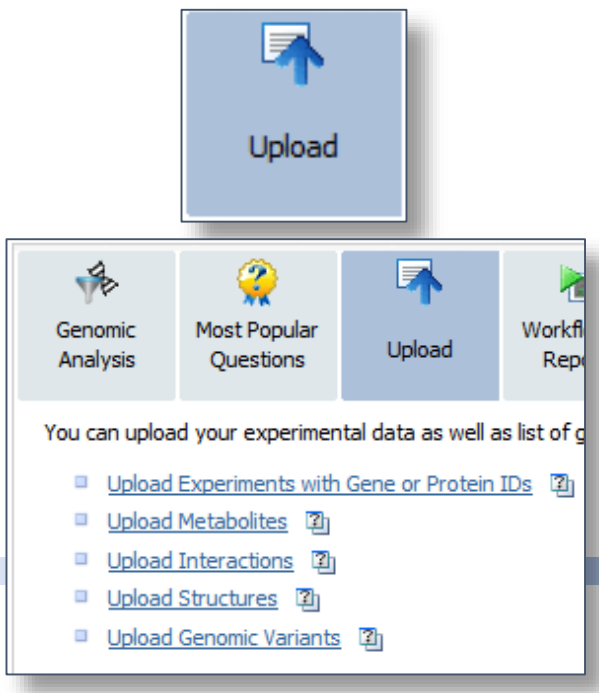
1. 代謝體學、轉錄體學的分析可以幫助我們找到引起代謝變化的路徑和酶
2. 蛋白體學、轉錄體學的分析可以有助於找到與轉譯水準相關的表現
3. 代謝體學、蛋白體學的分析可以有助於找到生物標記

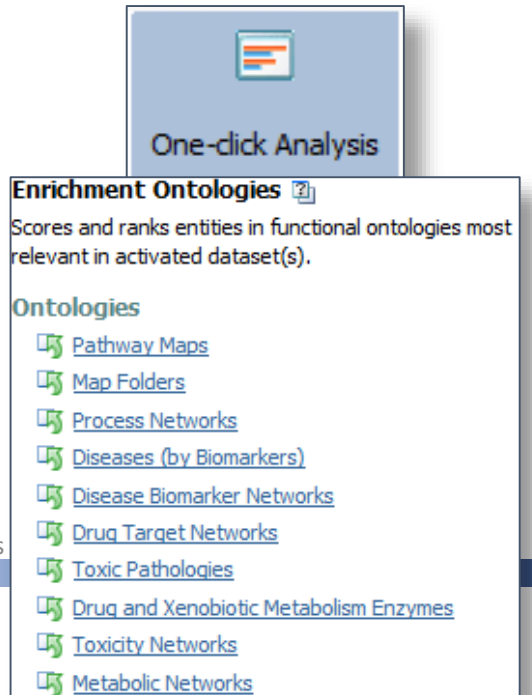
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用內源代謝網路來分析代謝體學和轉錄體學

- Question: 我們能在代謝體學和轉錄體學資料之間找到什麼代謝關係?

Upload metabolomic data → **Metabolic Networks (Endogenous) Enrichment**

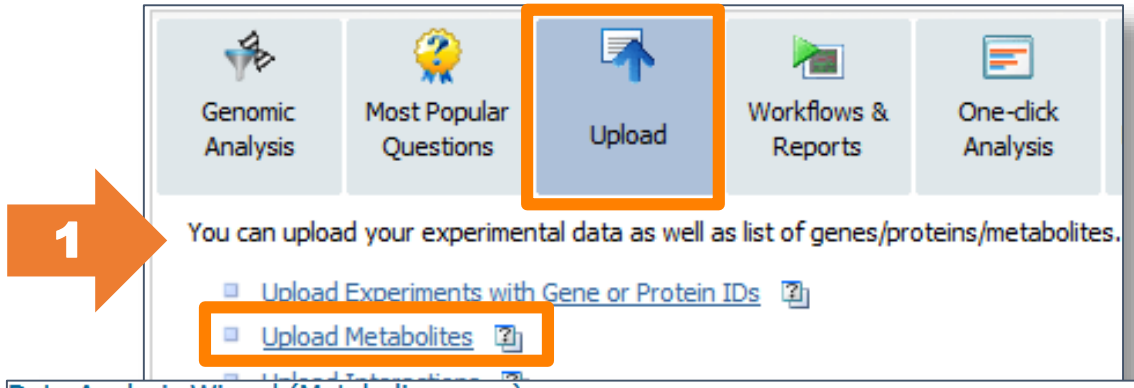


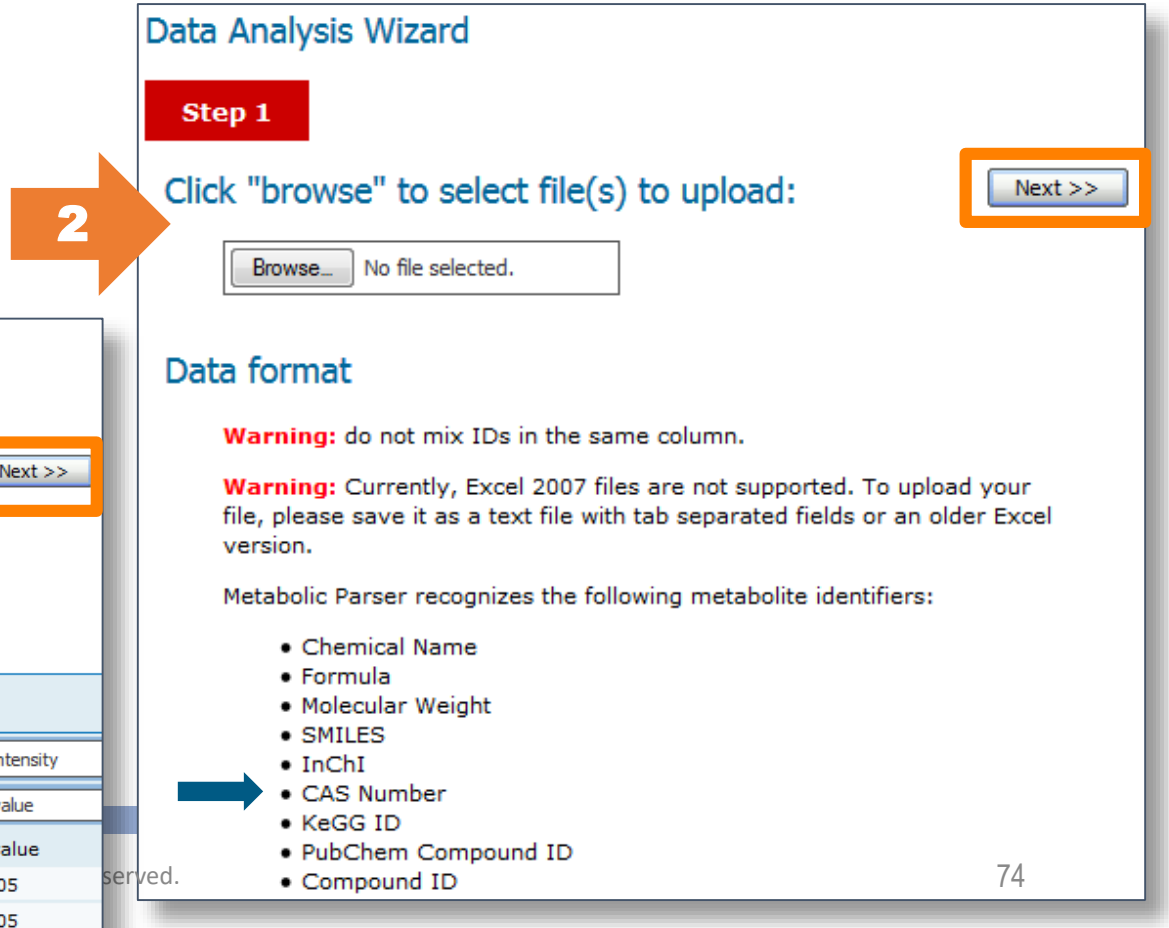


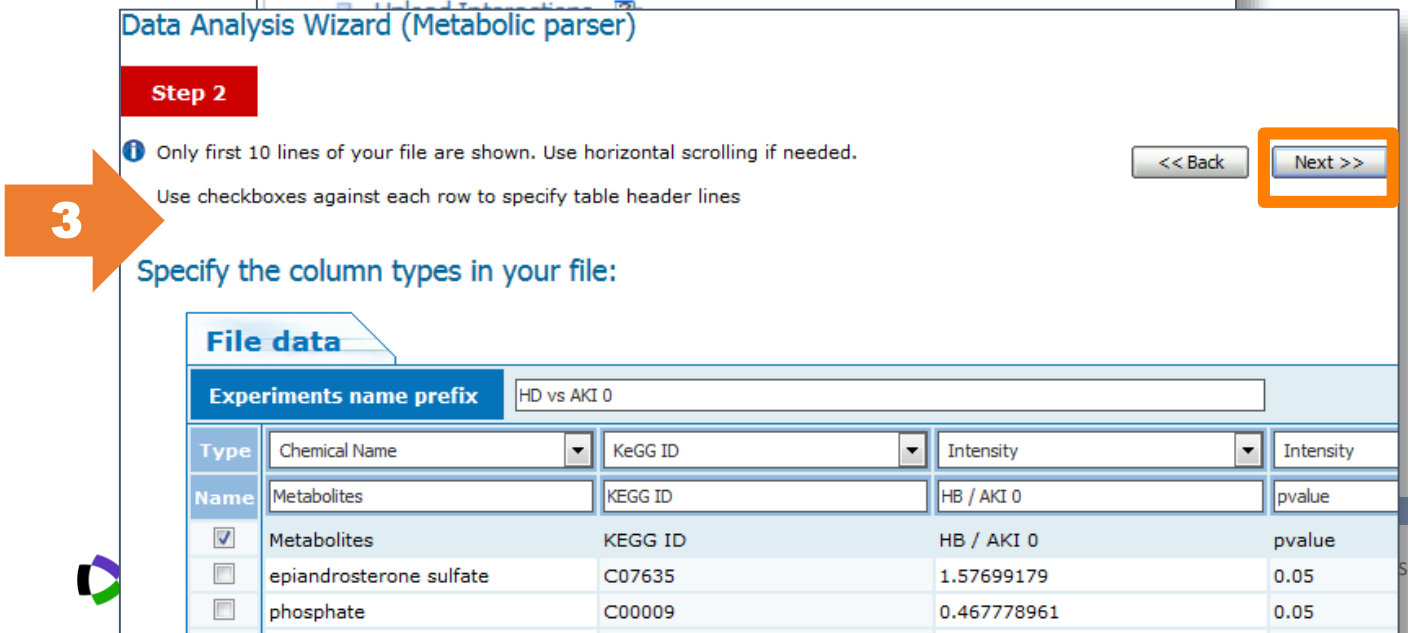
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上傳代謝體學數據到MetaCore中

- Tip: You can include multiple identifiers when uploading metabolites



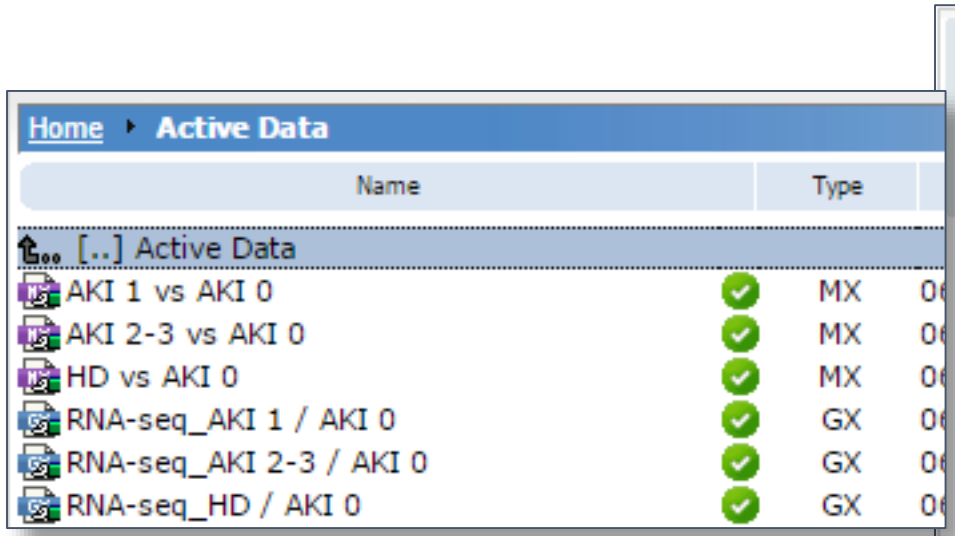


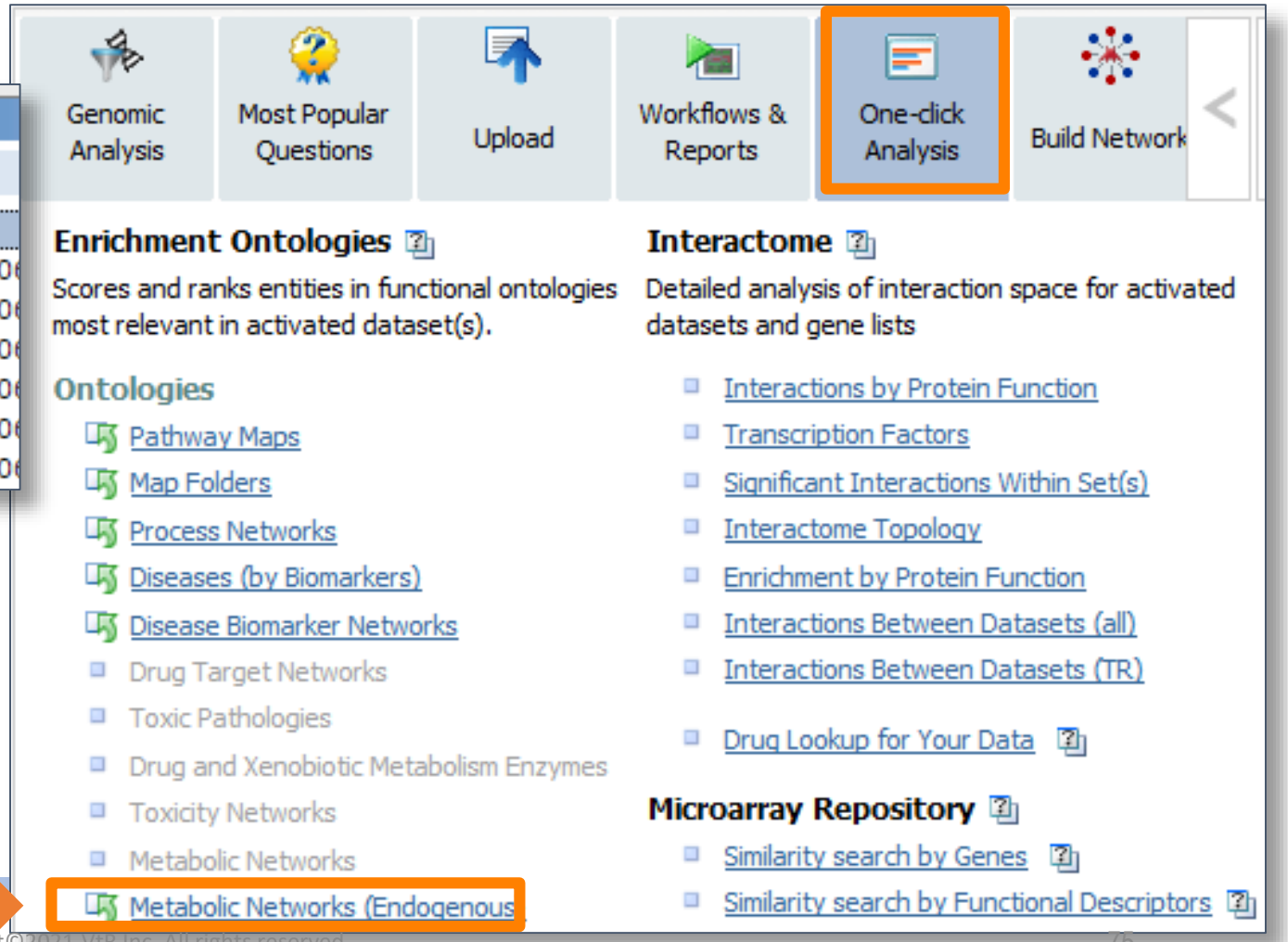


served.

透過代謝體學和基因體學的分析，我們能發現怎樣的代謝關係？

1





2

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通過代謝體學和基因體學的分析，我們能發現怎樣的代謝關係？

- Top 10 networks involved amino acid metabolism and glutamic acid processes.

Network Objects	# of Networks containing Network Object
SLC6A19	18
SLC7A9	16
L-Tryptophan intracellular	15
L-Tryptophan extracellular region	
L-Cysteine intracellular	
L-Alanine intracellular	
L-Cysteine extracellular region	
Glycogen phosphorylase	
L-Tyrosine intracellular	
SGK1	
L-Alanine extracellular region	
SHMT1	
PLC-beta	
Urea intracellular	

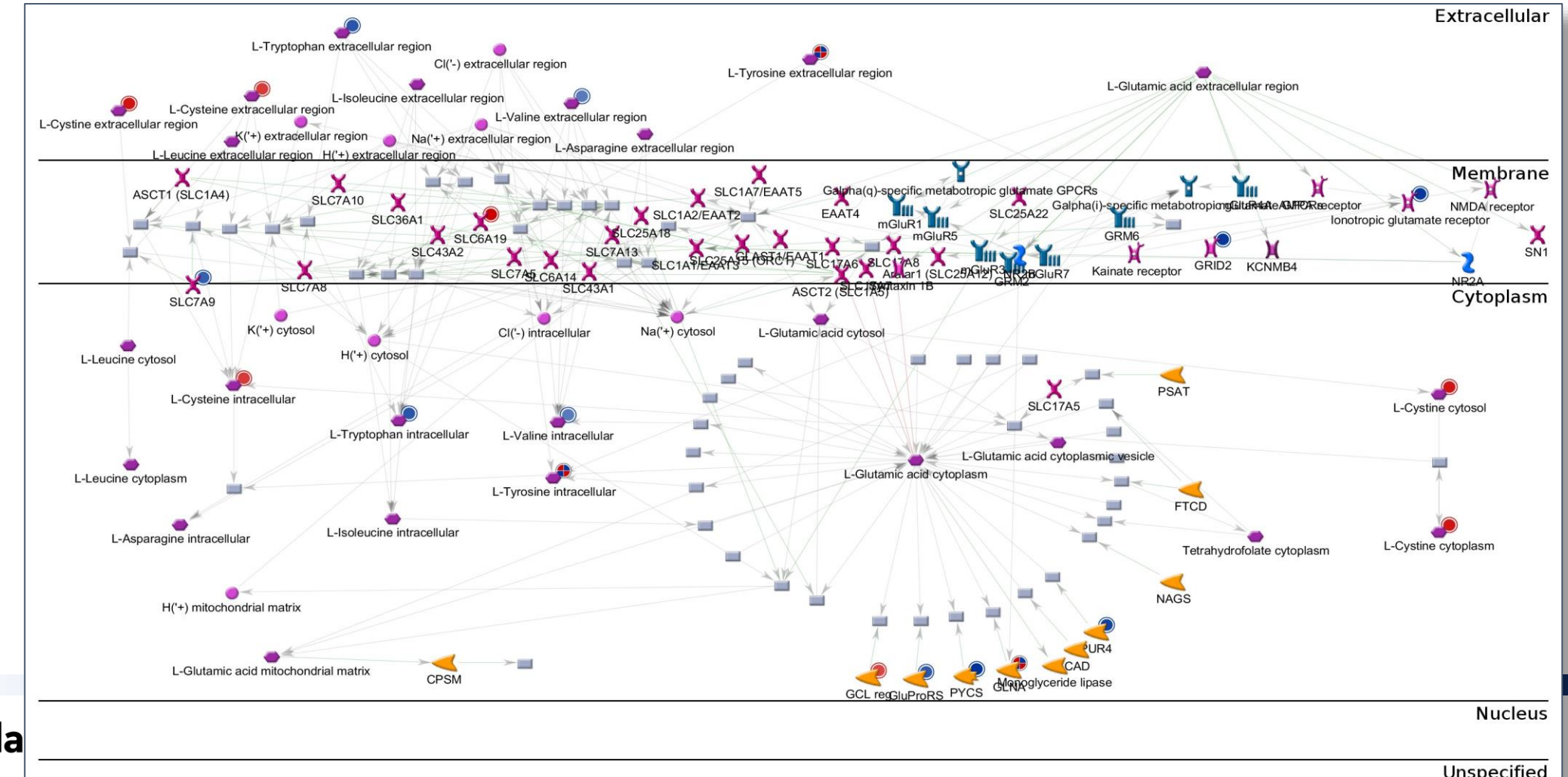
Experiment name	Species	Network Objects
AKI 1 vs AKI 0		161
AKI 2-3 vs AKI 0		161
HD vs AKI 0		161
RNA-seq_AKI 1 / AKI 0	Homo sapiens	1931

#	Networks	0 1 2 3 4 5 -log(pValue)	pValue	min(pValue)	FDR	Ratio
1	Glutamic acid pathways and transport		1.093e-7	1.093e-7	7.214e-6	11/143
			1.093e-7		7.214e-6	11/143
			1.093e-7		7.214e-6	11/143
			2.018e-1		5.823e-1	9/143
			1.981e-1		5.738e-1	9/143
			2.018e-1		5.823e-1	9/143
2	L-glutamate pathways and transport		4.290e-5	4.290e-5	1.416e-3	8/132
			4.290e-5		1.416e-3	8/132
			4.290e-5		1.416e-3	8/132
			7.643e-2		2.952e-1	10/132
			7.455e-2		3.212e-1	10/132
			7.643e-2		2.952e-1	10/132
3	Aminoacid metabolism_Ala,Ser,Cys,Met,His,Pro,G... metabolism and transport		1.204e-4	1.204e-4	1.987e-3	9/196
			1.204e-4		1.987e-3	9/196
			1.204e-4		1.987e-3	9/196
			4.007e-1		8.159e-1	10/196
			3.949e-1		8.185e-1	10/196
			4.007e-1		8.159e-1	10/196

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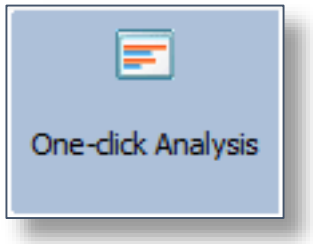
麩胺酸訊息傳導路徑是如何被影響的？SLC7A9和SLC6A19的表達變化可能影響胺基酸濃度的失調

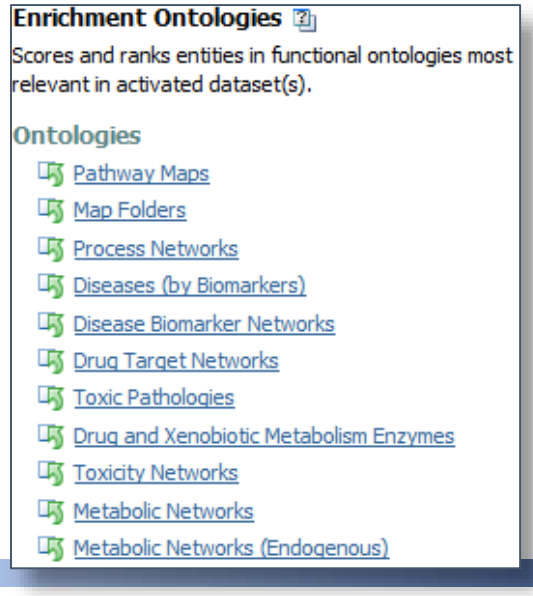


代謝體學和蛋白體學資料都涉及到的訊息傳導路徑有哪些？

- Question:
  - 患者血漿中哪些代謝物和蛋白濃度的變化可能是疾病進程的生物標記

Pathway Map Enrichment

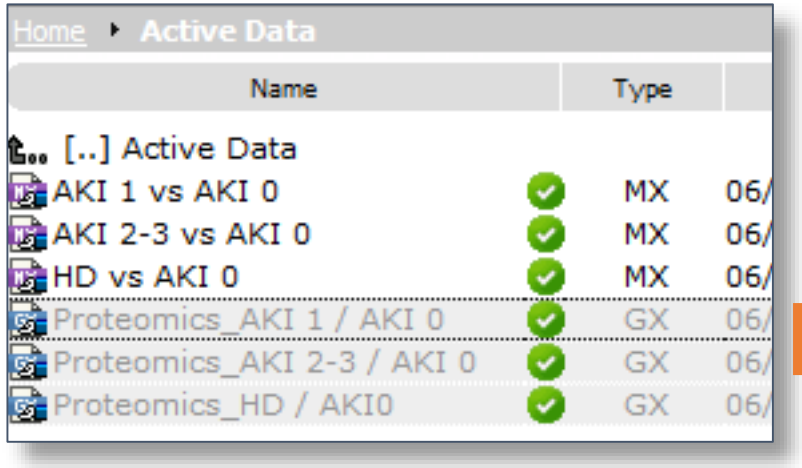




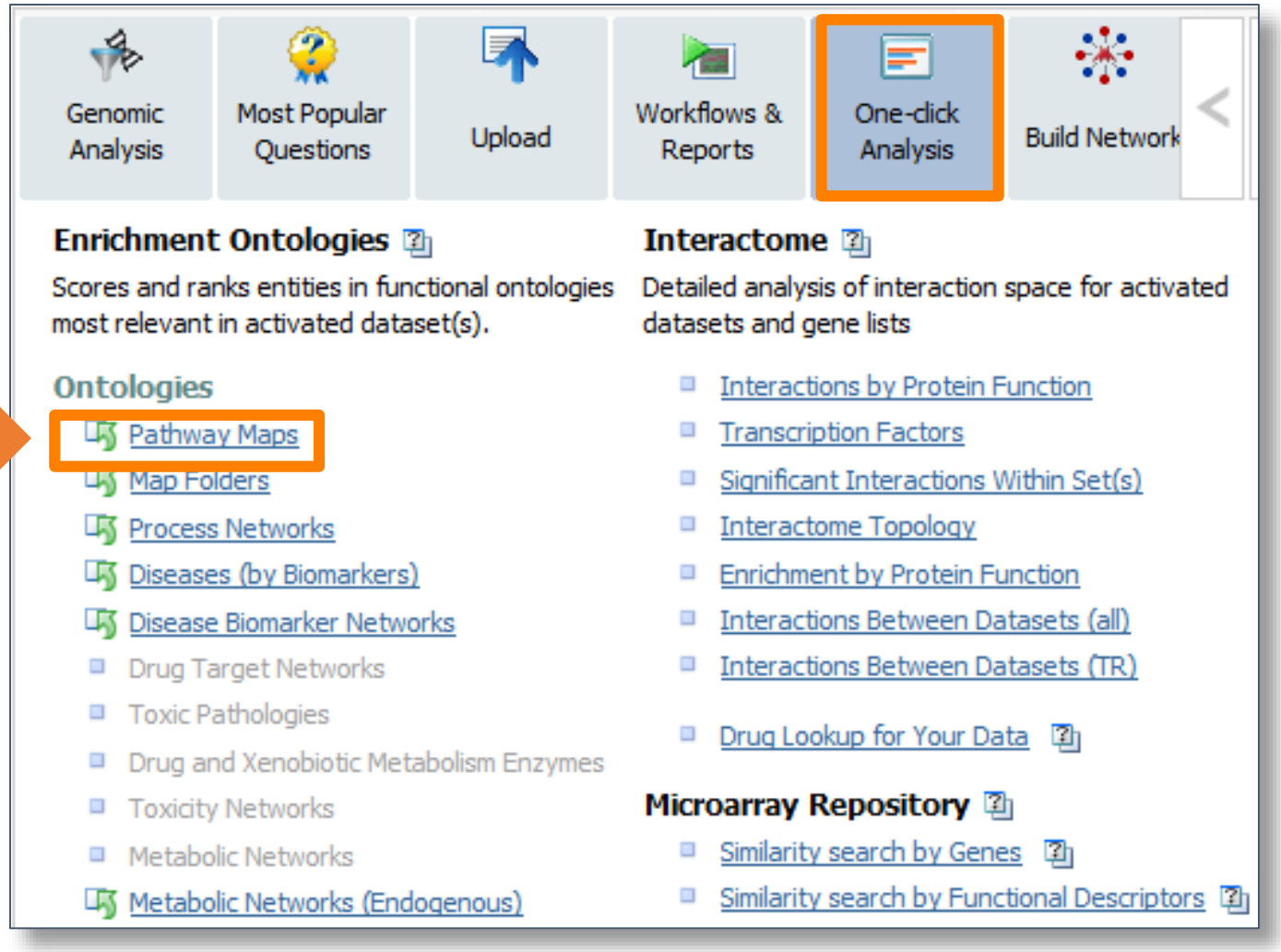
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在代謝和表現數據之間我們能找到什麼代謝關係?

1

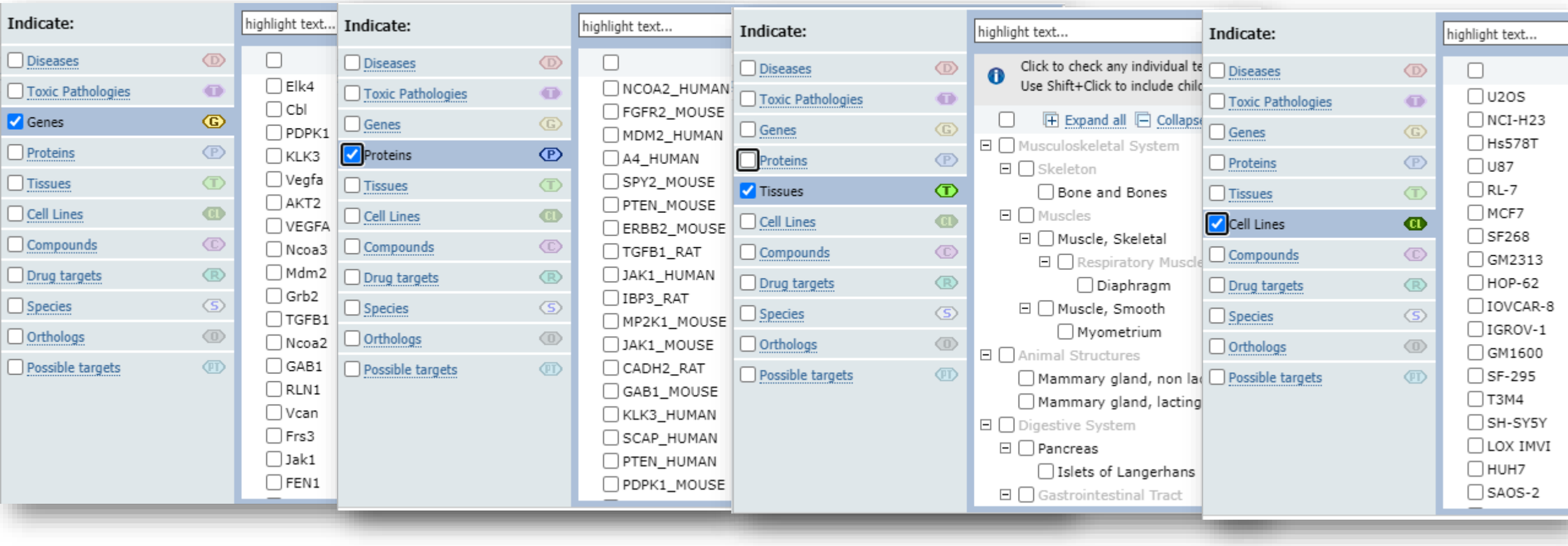


2

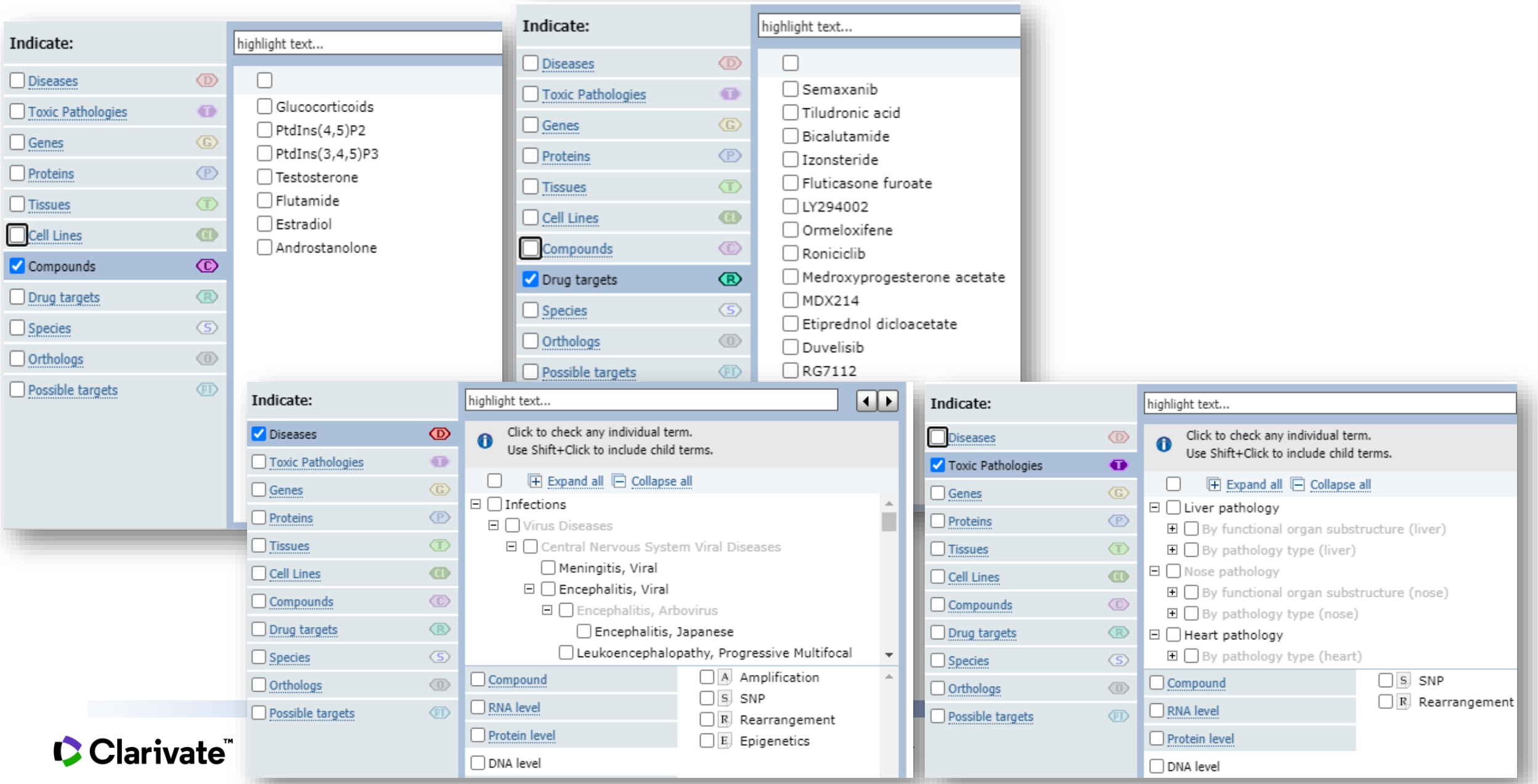


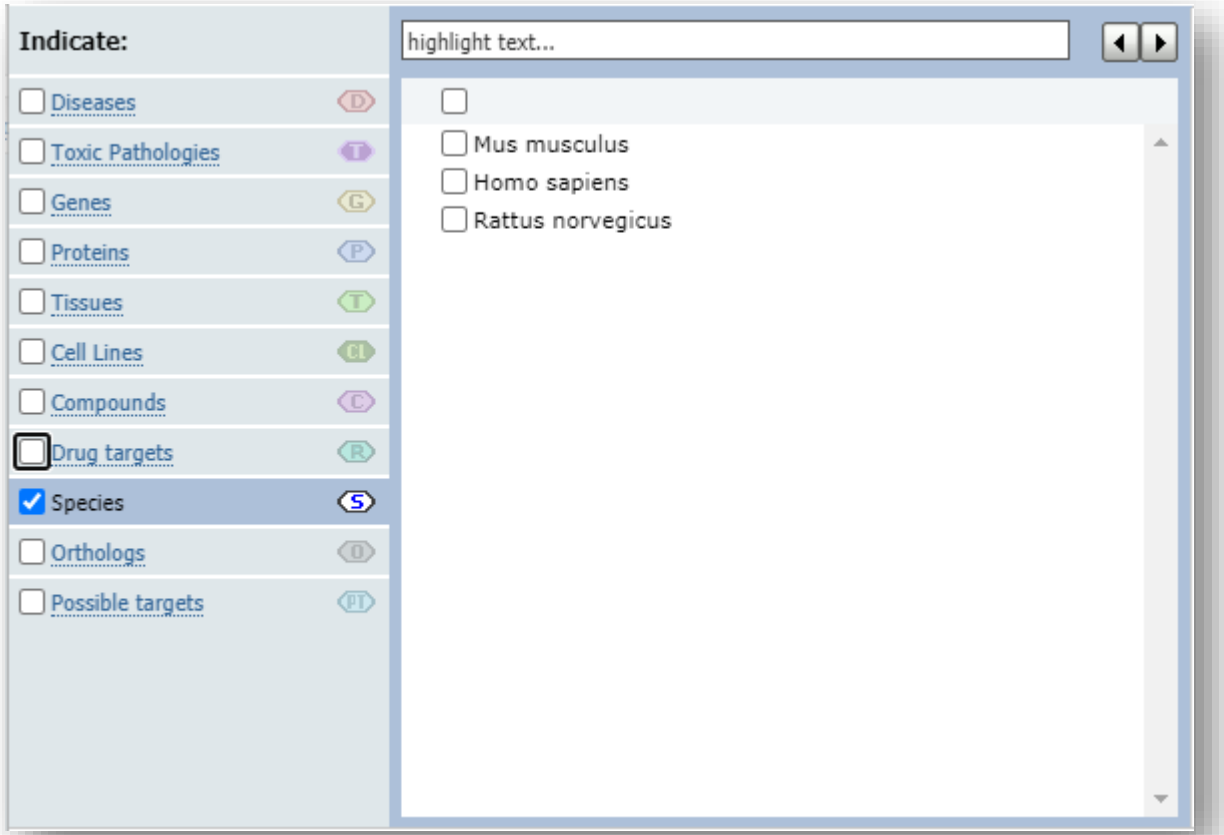
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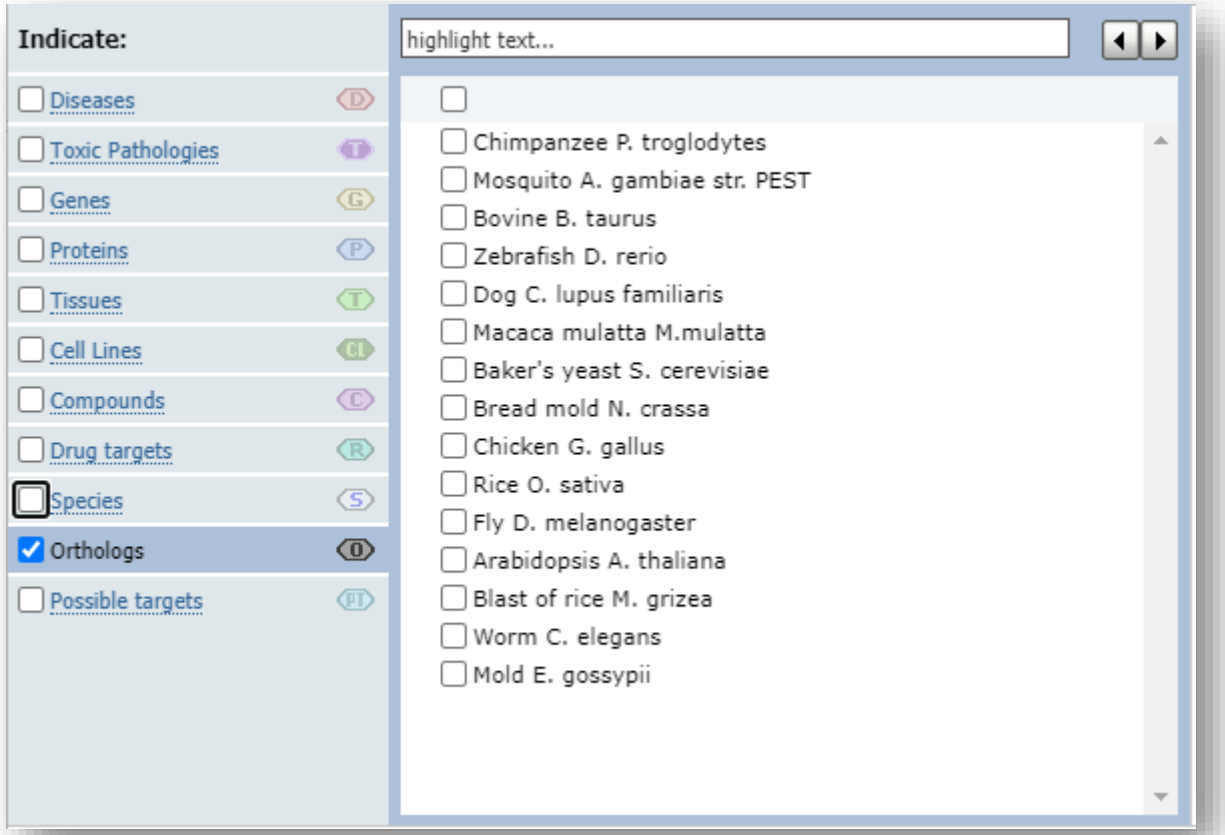
網絡建構時，可選擇想了解的資訊進行分析。



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Indicate:
highlight text...
Diseases
Toxic Pathologies
Genes
Proteins
Tissues
Cell Lines
Compounds
Drug targets
Species
Orthologs
Possible targets
Glucocorticoids
PtdIns(4,5)P2
PtdIns(3,4,5)P3
Testosterone
Flutamide
Estradiol
Androstanolone
Semaxanib
Tiludronic acid
Bicalutamide
Izonsteride
Fluticasone furoate
LY294002
Ormeloxifene
Roniciclib
Medroxyprogesterone acetate
MDX214
Etiprednol dicloacetate
Duvelisib
RG7112
Click to check any individual term.
Use Shift+Click to include child terms.
Expand all
Collapse all
Infections
Virus Diseases
Central Nervous System Viral Diseases
Meningitis, Viral
Encephalitis, Viral
Encephalitis, Arbovirus
Encephalitis, Japanese
Leukoencephalopathy, Progressive Multifocal
Compound
RNA level
Protein level
DNA level
Amplification
SNP
Rearrangement
Epigenetics
Liver pathology
By functional organ substructure (liver)
By pathology type (liver)
Nose pathology
By functional organ substructure (nose)
By pathology type (nose)
Heart pathology
By pathology type (heart)





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患者血漿中哪些代謝物和蛋白質濃度的變化可以作為生物標記?

- 膽固醇相關路徑和補體路徑都與這些體學數據變化有關。

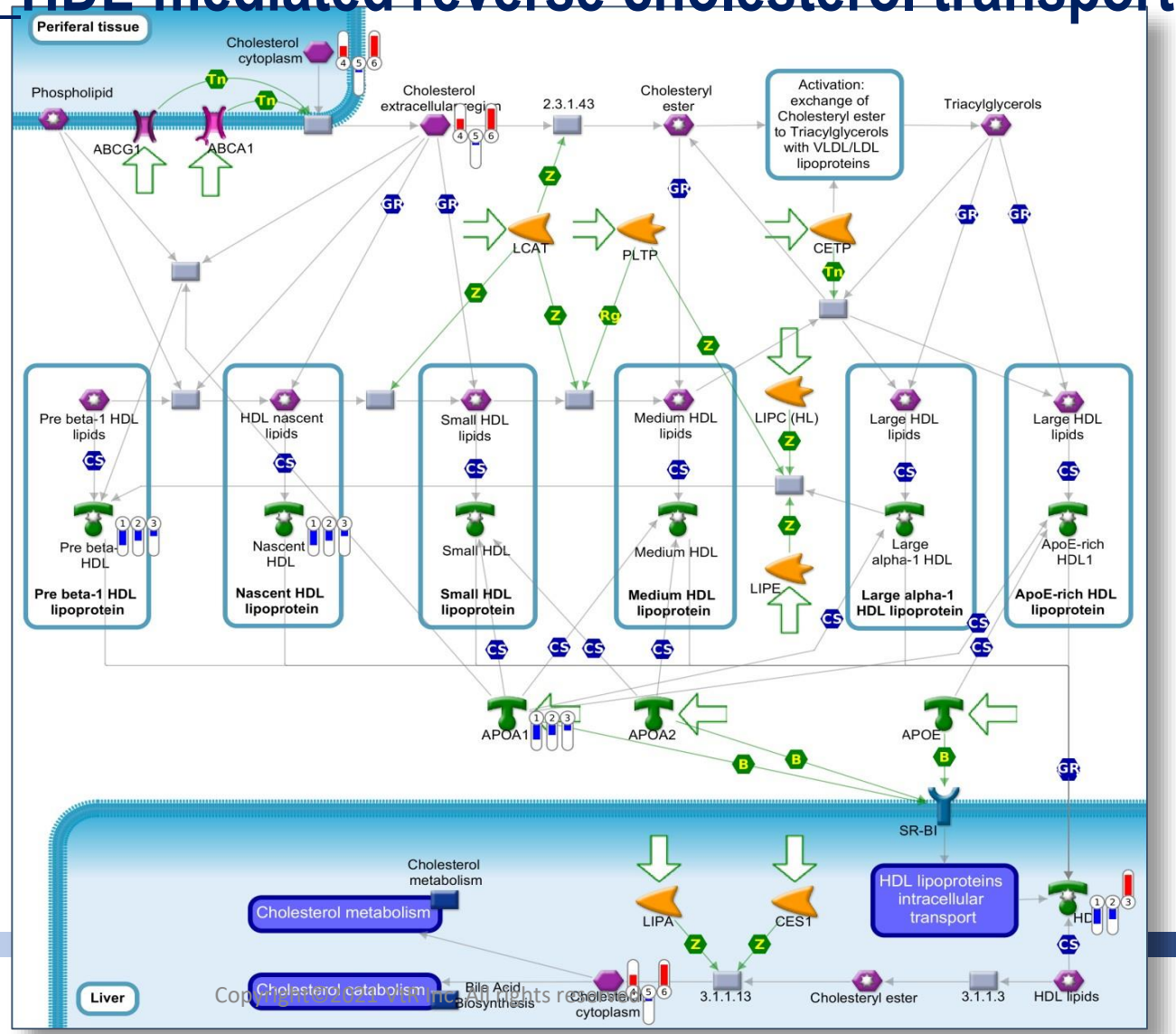
#	Maps	0 1 2 3 4 5 6 7 -log(pValue)	pValue	min(pValue)	FDR	Ratio
1	Transport_Intracellular cholesterol transport		1.279e-9	1.279e-9	5.287e-8	9/83
			1.279e-9		5.287e-8	9/83
			1.279e-9		5.287e-8	9/83
			3.962e-2		1.657e-1	2/83
			5.015e-2		1.894e-1	2/83
			5.015e-2		1.894e-1	2/83
2	Immune response_Alternative complement pathway		2.750e-1	1.514e-6	3.667e-1	1/53
			2.750e-1		3.667e-1	1/53
			2.750e-1		3.667e-1	1/53
			1.514e-6		6.966e-5	5/53
			2.947e-6		1.503e-4	5/53
			2.947e-6		1.503e-4	5/53
3	Transport_HDL-mediated reverse cholesterol transport		2.315e-3	2.163e-5	2.609e-2	3/44
			2.315e-3		2.609e-2	3/44
			2.315e-3		2.609e-2	3/44
			2.163e-5		4.975e-4	4/44
			3.656e-5		9.324e-4	4/44
			3.656e-5		9.324e-4	4/44
4	Cholesterol and Sphingolipid transport / Recycling to plasma membrane in lung (normal and CF)		3.853e-4	3.853e-4	5.308e-3	3/24
			3.853e-4		5.308e-3	3/24

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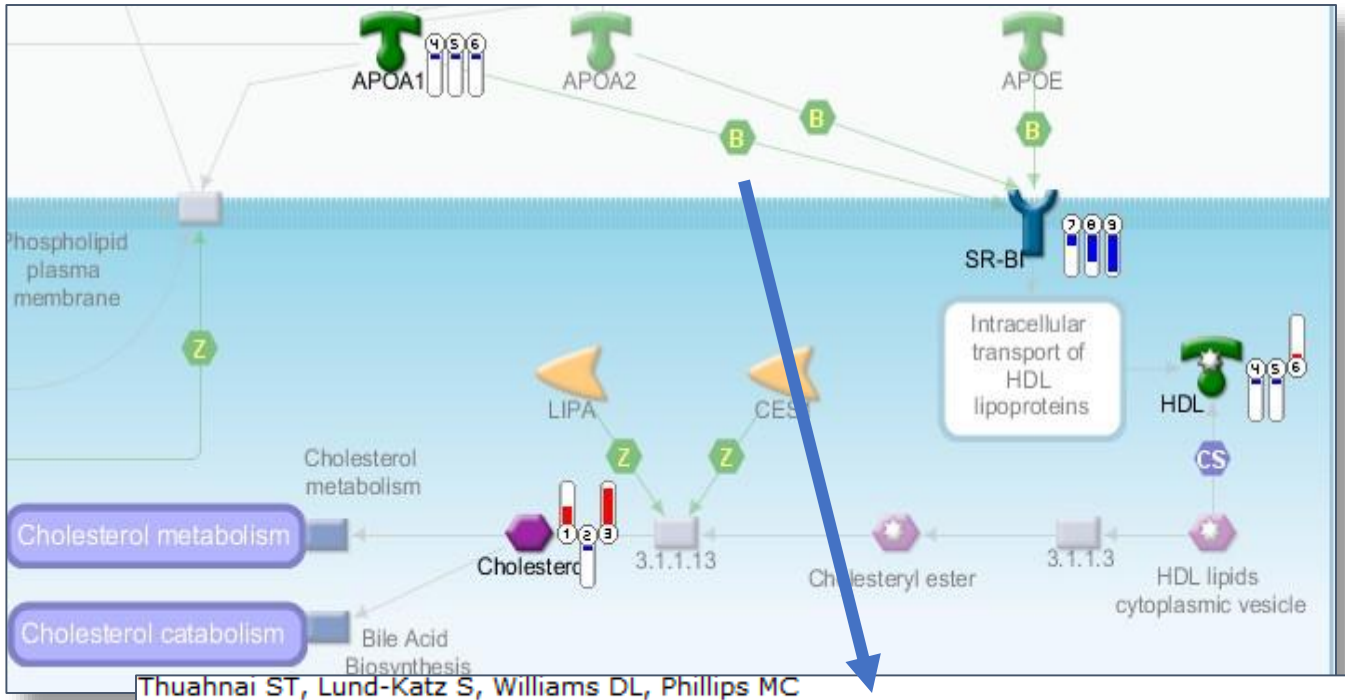
高密度脂蛋白和膽固醇與腎衰竭有關

Transport_HDL-mediated reverse cholesterol transport



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參考文獻的資訊一目了然



- SR-B1 expression appears to decrease as kidney injury worsens and could be indicative of cholesterol metabolism dysregulation.

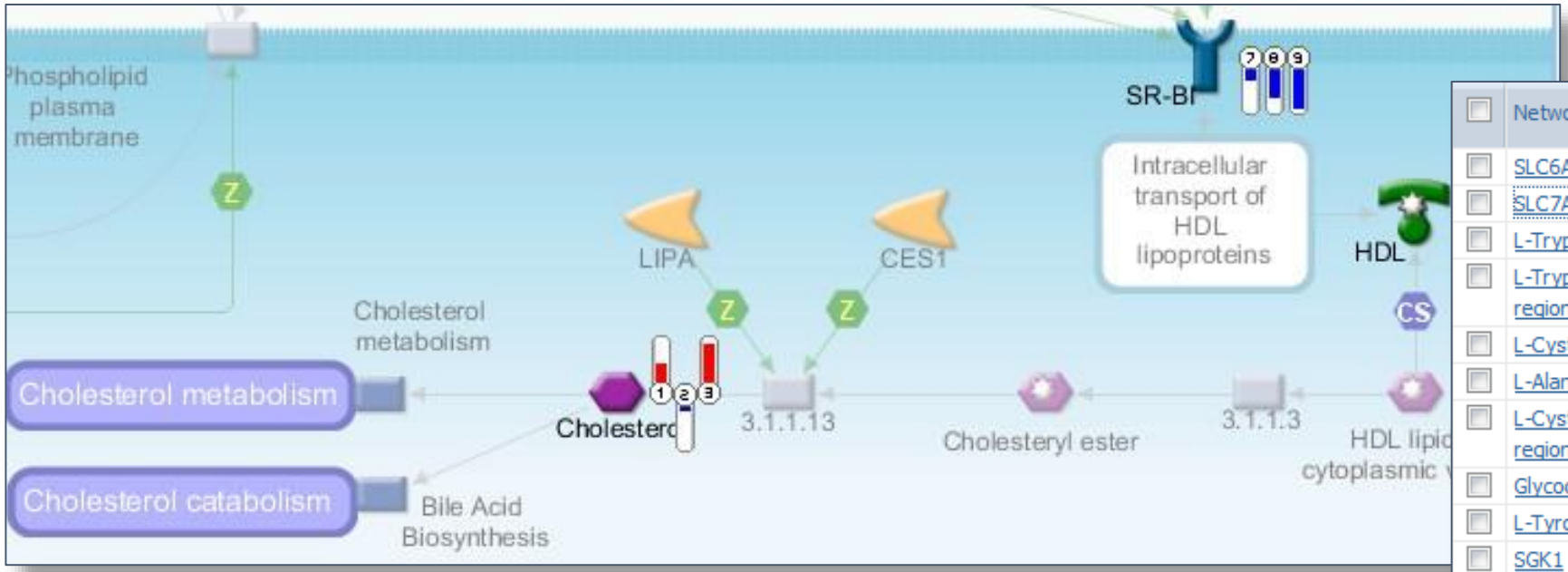
Thuahnai ST, Lund-Katz S, Williams DL, Phillips MC
Scavenger receptor class B, type I-mediated uptake of various lipids into cells. Influence of the nature of the donor particle interaction with the receptor.
The Journal of biological chemistry 2001 Nov 23;276(47):43801-8
PMID: 11564739

Experiment Details

Note	APOA1 state	Mechanism	Effect	SR-BI state	Methods	Cell line/Tissue
APOA1 increases HDL binding to SRBI and selective uptake of Cholesterol ester.	APOA1_HUMAN	Binding	Activation	SCRB1_HUMAN	3h radiolabel, 125i radiolabel, transfection, binding assay, transport activity determination	COS7

Summary

- 麩胺酸和胺基酸相關的代謝和轉運途徑包含代謝體學和RNA-seq數據
- SLC7A9和SLC6A19等路徑可能在胺基酸進出細胞的過程中發揮作用。
- 血液中APOC3和膽固醇的增加可能與肝細胞SR-B1表現的減少有關。



Network Objects	# of Networks containing Network Object
SLC6A19	18
SLC7A9	16
L-Tryptophan intracellular	15
L-Tryptophan extracellular region	14
L-Cysteine intracellular	10
L-Alanine intracellular	8
L-Cysteine extracellular region	8
Glycogen phosphorylase	8
L-Tyrosine intracellular	7
SGK1	7
L-Alanine extracellular region	7
SHMT1	7
PLC-beta	7
Urea intracellular	6

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Live demo

上傳體學數據進行分析

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由分子路徑分析找到藥物標靶，
並進一步了解相關藥物的活性預測。

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癌症轉移重要標靶 SHP2 (PTPN11) 的深度知識挖掘及檢索，及資訊收集

PTPN11

Gene | Build Network

Table of Contents

- General
  - Gene Details
  - Clarivate Integrity
  - Cortellis Drug Discovery Intelligence
  - External Databases
  - Vendors
- Groups/Variants
- Pathways and Processes
  - Pathway Maps
  - Process Networks
  - GO Processes
  - GO Molecular Functions
- Diseases
  - Associated Diseases
  - Drug Target for
  - Disease Ontologies
    - Disease Biomarker Networks

Diseases

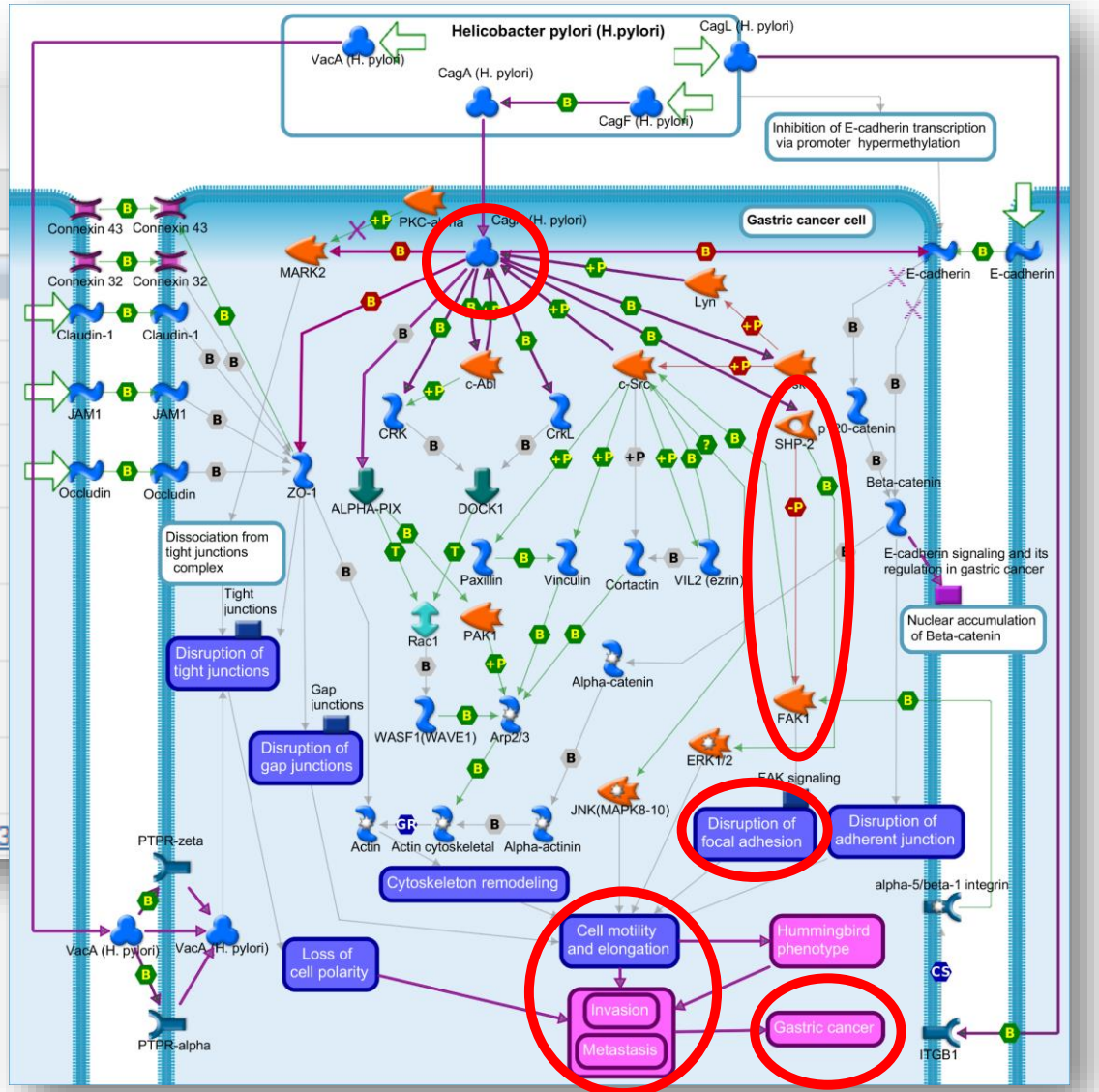
Associated Diseases

#	Name	Reference
1	Aortic Coarctation	PubMed: 15940693
2	Astrocytoma	PubMed: 28035384
3	Atrophy	PubMed: 18712962
4	Cafe-au-Lait Spots	PubMed: 12161596
5	Carcinoma, Ductal, Breast	PubMed: 18643929
6	Carcinoma, Non-Small-Cell Lung	PubMed: 20840817
7	Cardiomyopathy, Hypertrophic, Familial	PubMed: 16488201
8	Central Nervous System Neoplasms	PubMed: 28403515
9	Cervical Intraepithelial Neoplasia	PubMed: 22528229
10	Colitis, Ulcerative	PubMed: 19160029, 3

Pathways and Processes

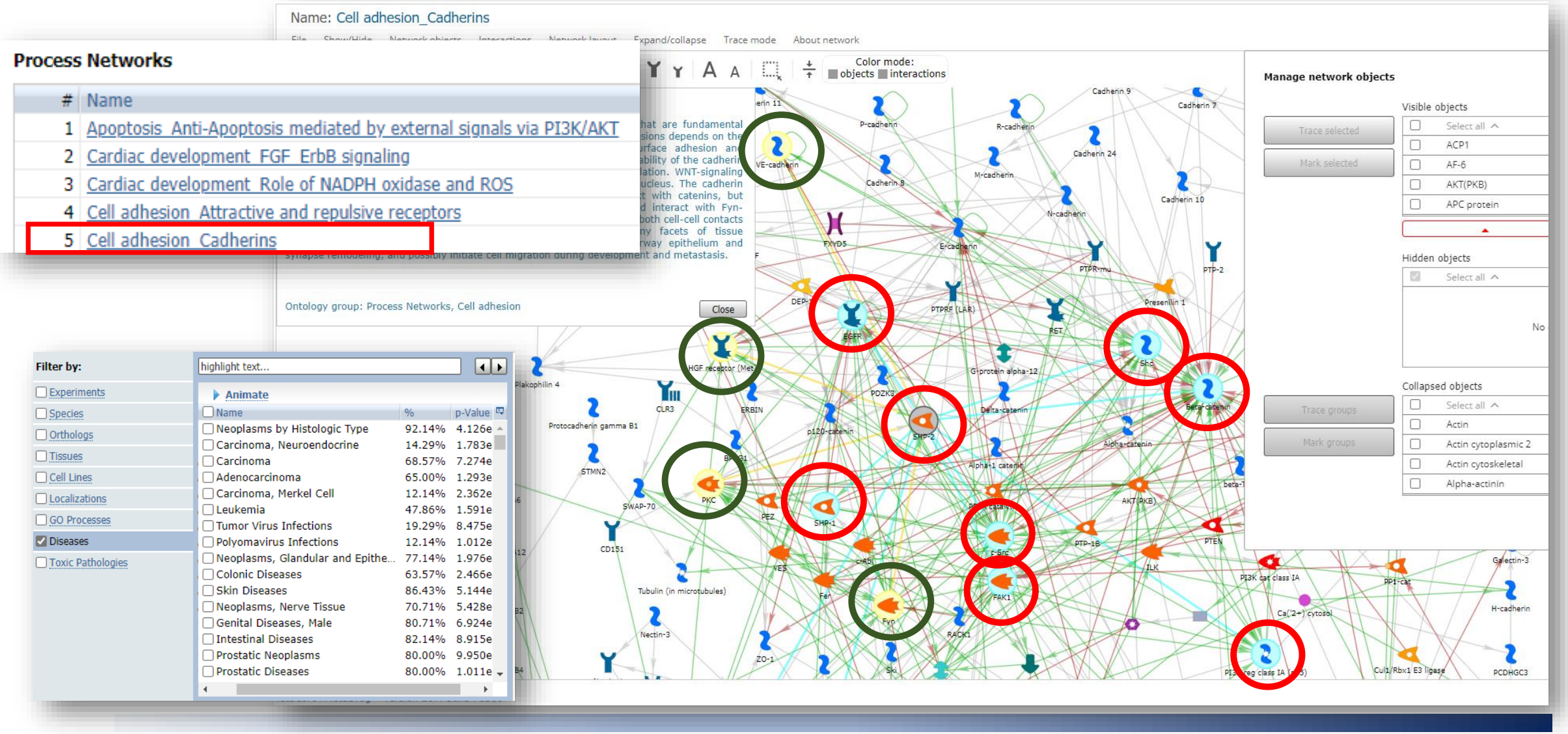
Pathway Maps

#	Name
1	Androgen receptor activation and downstream signaling in Prostate cancer
2	Canonical Leptin pathways in breast cancer
3	CHDI_Correlations from Discovery data_Causal network (positive)
4	Down-regulation of mast cell functions through ITIM-containing inhibitory receptors in asthma
5	Effect of H. pylori infection on gastric epithelial cell proliferation
6	Effect of H. pylori infection on gastric epithelial cells motility



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以 SHP2 (PTPN11) 建構靶點與生物標記的識別與驗證

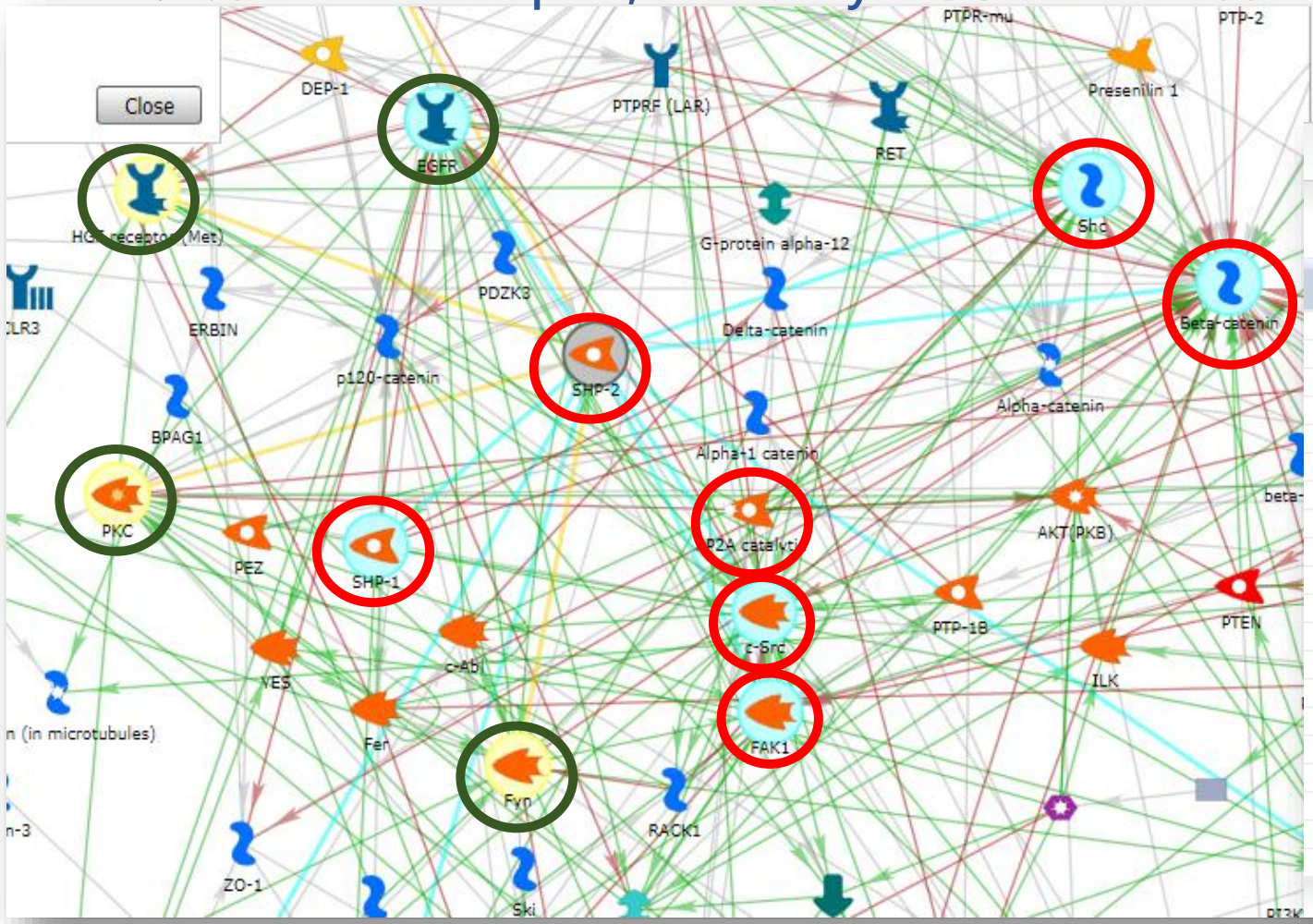


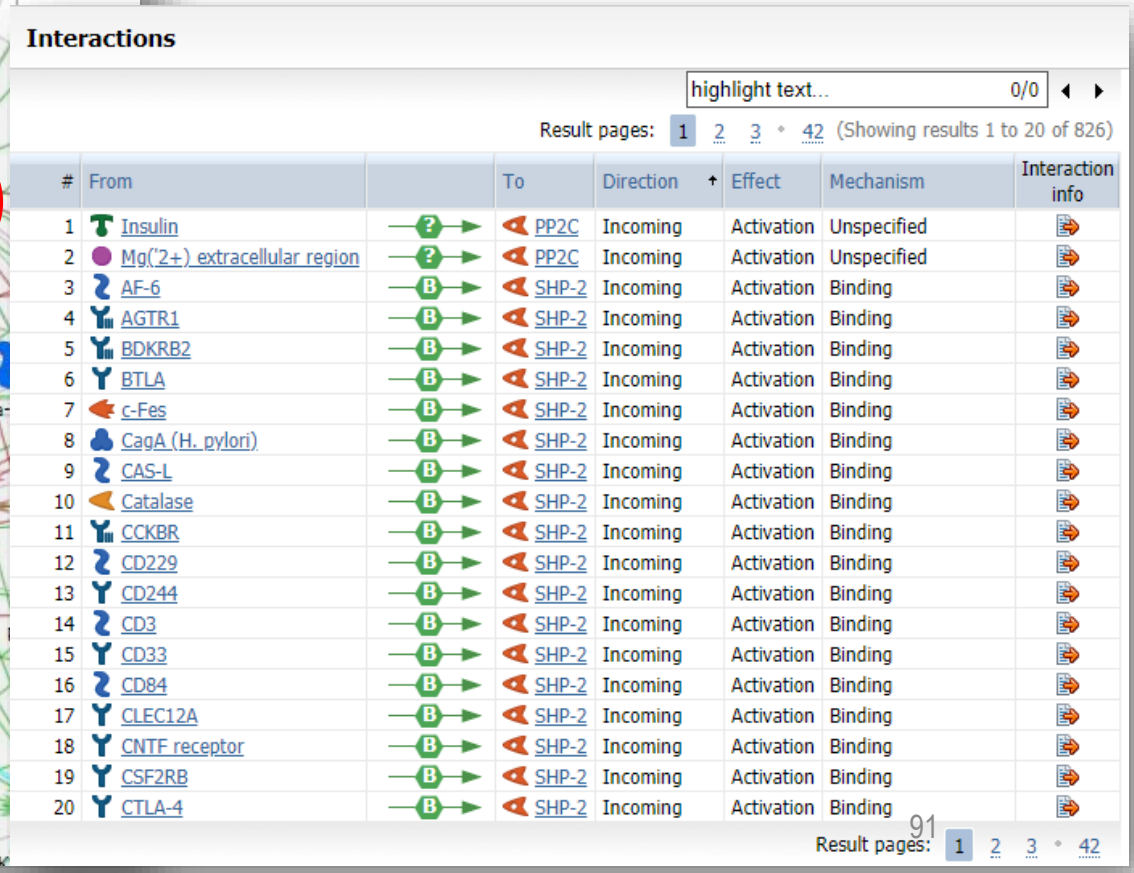
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以 SHP2 (PTPN11) 建構靶點與生物標記的識別與驗證

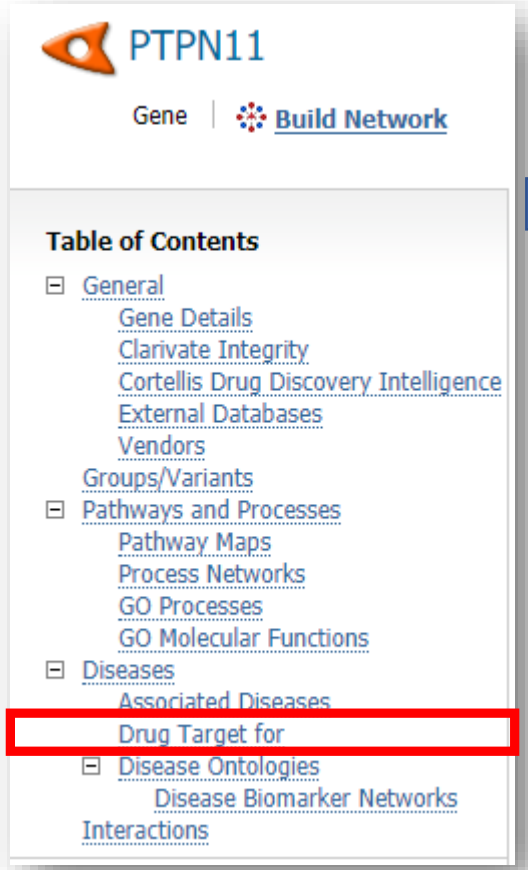
在 Cell adhesion 的過程中。

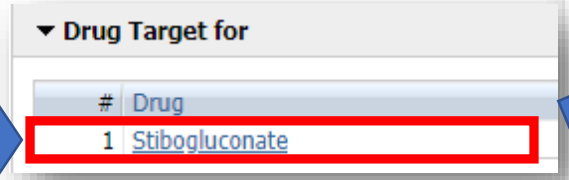
- SHP2 透過去磷酸化作用影響 SHP1, EGFR, c-Src, FAK1 及 beta catenin 的蛋白質作用活性。
- 此外， HGF receptor, PKC 及 Fyn 可能為 SHP2 的上游，並影響SHP2的作用活性。

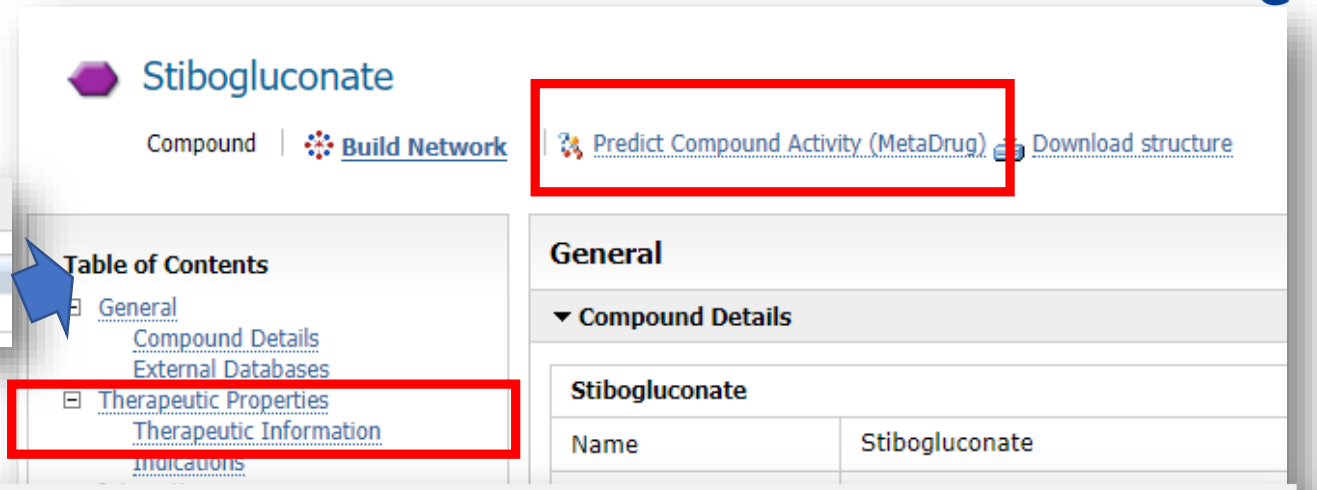


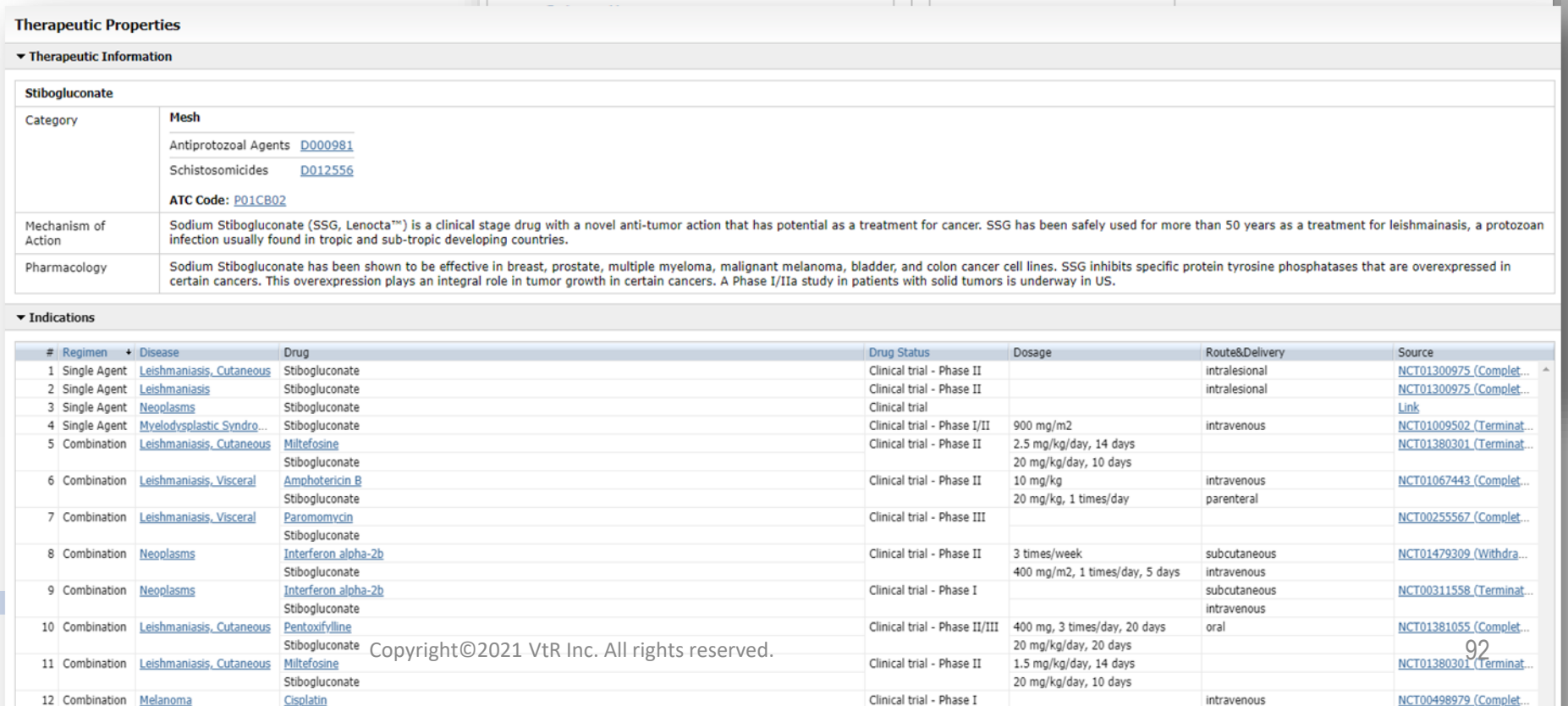


針對SHP2的藥物特性及疾病治療訊息









#	Regimen	Disease	Drug	Drug Status	Dosage	Route&Delivery	Source
1	Single Agent	Leishmaniasis, Cutaneous	Stibogluconate	Clinical trial - Phase II		intralesional	NCT01300975 (Complet...
2	Single Agent	Leishmaniasis	Stibogluconate	Clinical trial - Phase II		intralesional	NCT01300975 (Complet...
3	Single Agent	Neoplasms	Stibogluconate	Clinical trial			Link
4	Single Agent	Myelodysplastic Syndro...	Stibogluconate	Clinical trial - Phase I/II	900 mg/m2	intravenous	NCT01009502 (Terminat...
5	Combination	Leishmaniasis, Cutaneous	Miltefosine	Clinical trial - Phase II	2.5 mg/kg/day, 14 days		NCT01380301 (Terminat...
			Stibogluconate		20 mg/kg/day, 10 days		
6	Combination	Leishmaniasis, Visceral	Amphotericin B	Clinical trial - Phase II	10 mg/kg	intravenous	NCT01067443 (Complet...
			Stibogluconate		20 mg/kg, 1 times/day	parenteral	
7	Combination	Leishmaniasis, Visceral	Paromomycin	Clinical trial - Phase III			NCT00255567 (Complet...
			Stibogluconate				
8	Combination	Neoplasms	Interferon alpha-2b	Clinical trial - Phase II	3 times/week	subcutaneous	NCT01479309 (Withdra...
			Stibogluconate		400 mg/m2, 1 times/day, 5 days	intravenous	
9	Combination	Neoplasms	Interferon alpha-2b	Clinical trial - Phase I		subcutaneous	NCT00311558 (Terminat...
			Stibogluconate			intravenous	
10	Combination	Leishmaniasis, Cutaneous	Pentoxifylline	Clinical trial - Phase II/III	400 mg, 3 times/day, 20 days	oral	NCT01381055 (Complet...
			Stibogluconate		20 mg/kg/day, 20 days		
11	Combination	Leishmaniasis, Cutaneous	Miltefosine	Clinical trial - Phase II	1.5 mg/kg/day, 14 days		NCT01380301 (Terminat...
			Stibogluconate		20 mg/kg/day, 10 days		
12	Combination	Melanoma	Cisplatin	Clinical trial - Phase I		intravenous	NCT00498979 (Complet...

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What is MetaDrug?

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Metadrug預測工具

數據庫挖掘　代謝產物預測　毒性預測　標靶預測　適應症預測　影響到的通路　體學數據分析

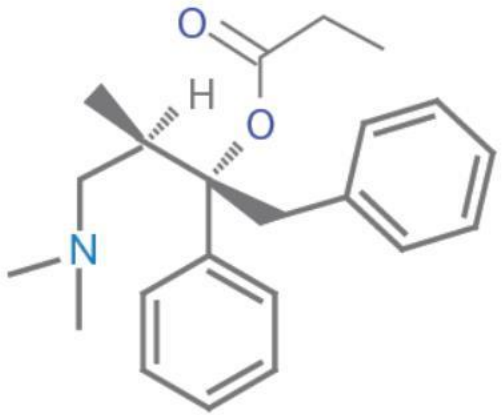
MetaDrug

化合物數據庫

代謝預測工具

毒性預測工具

標靶/
適應症預測



在五分鐘內，
可了解一個化合物
多少訊息?

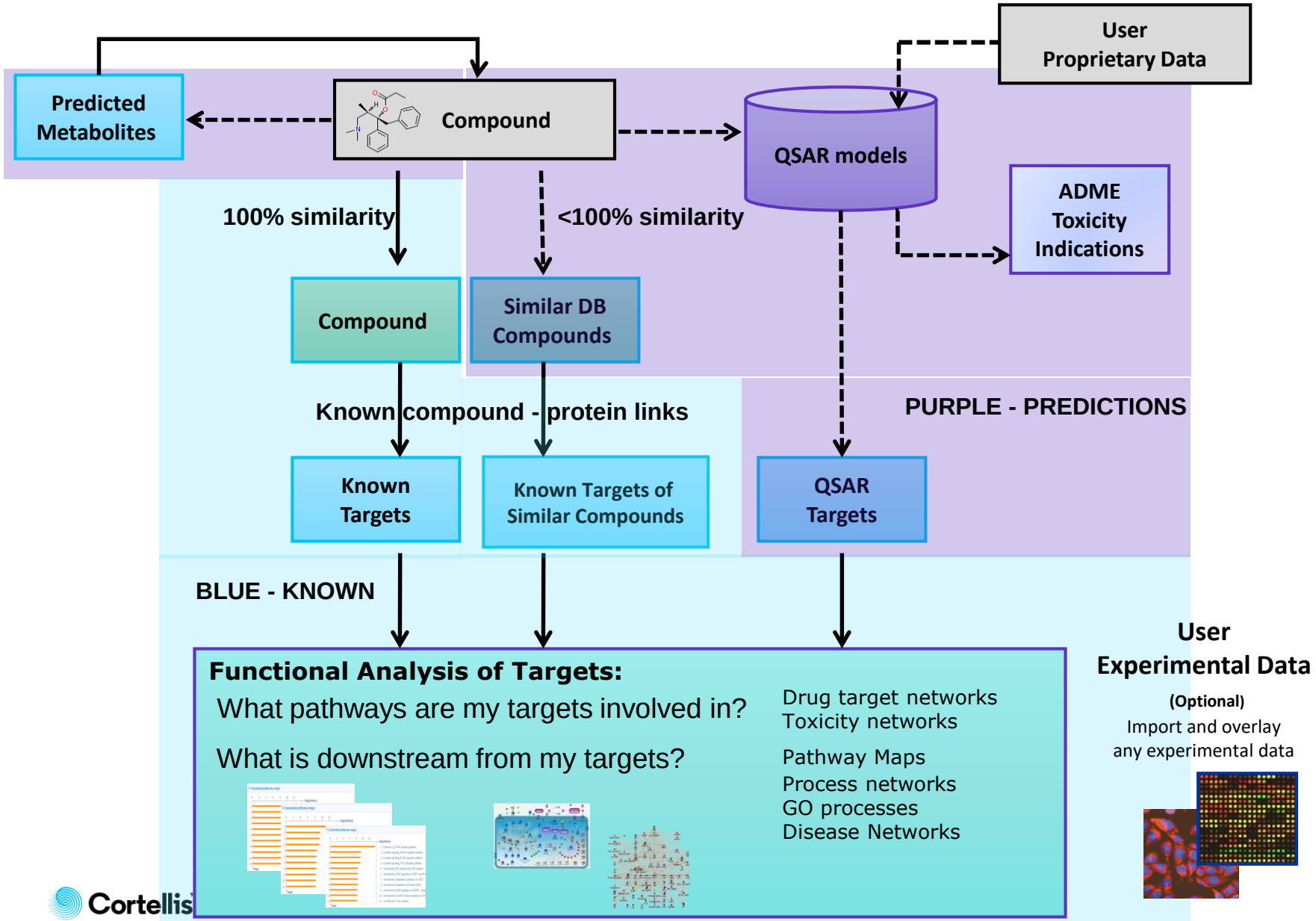
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Metadrug的底層資料

- >70 QSAR 模型，用於預測化合物毒性、藥代動力學特徵、治療活性
- > 160 種代謝規則，用於代謝產物預測
- > 1,600 個經典範式通路圖，涵蓋近200,000 個人類、小鼠、大鼠代謝和信號通路（基於文獻報導的一致性）
- >1,800,000 個蛋白與蛋白、DNA、RNA、代謝物、外源物相互作用
- 數千種疾病生物標記物（Biomarker）
- >800,000 個化合物及其靶標與生物活性資料
- > 5,000 個代謝反應
- > 9,100 個藥物
- >30,000 個內源代謝產物
- 上百萬個基因、蛋白和化合物的別稱（同種異名）
- 人、小鼠、大鼠的蛋白複合物和蛋白家族

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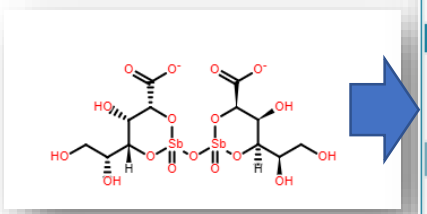
How does MetaDrug work?

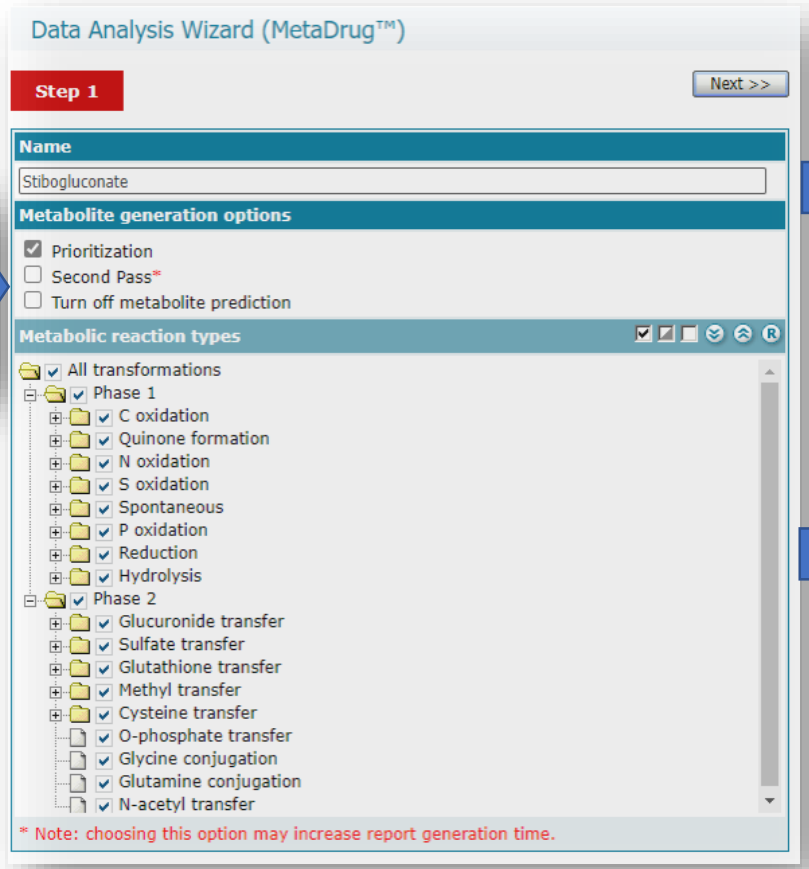


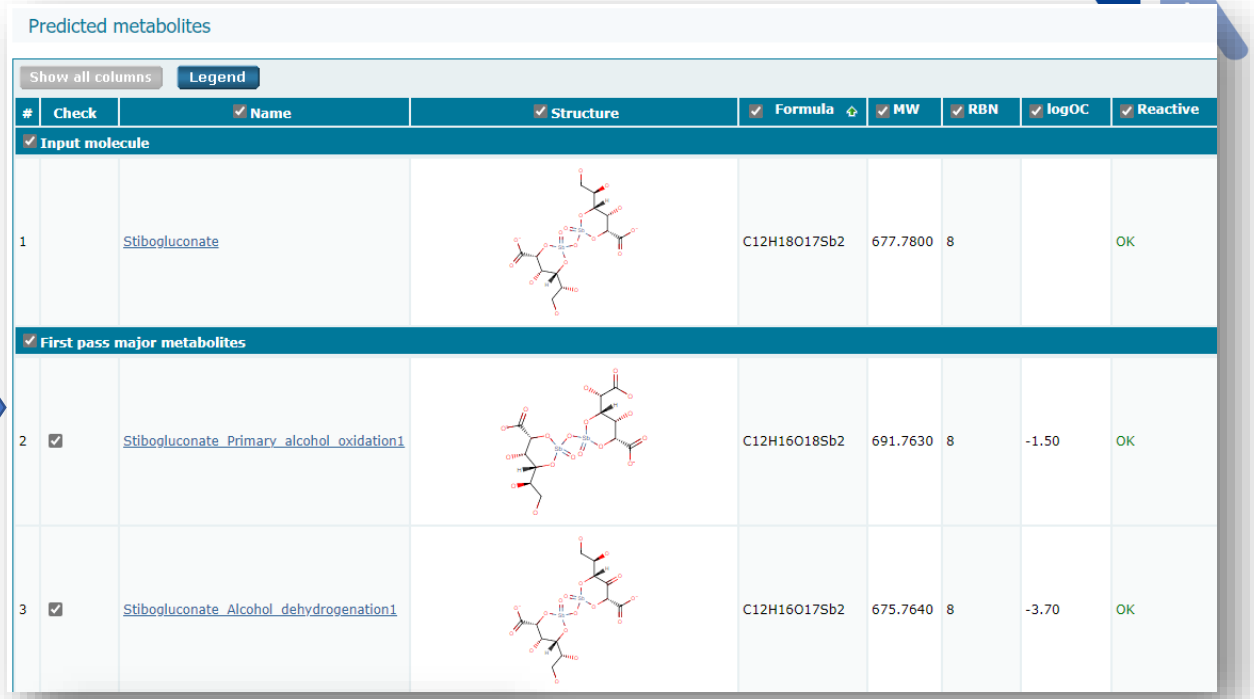
- **A systems pharmacology platform for predicting bioactivity of small molecules.**
- Provides structure-based assessment of compound activity and liability.
- Predict metabolites, ADME Tox, targets and **affected pathways and processes**.

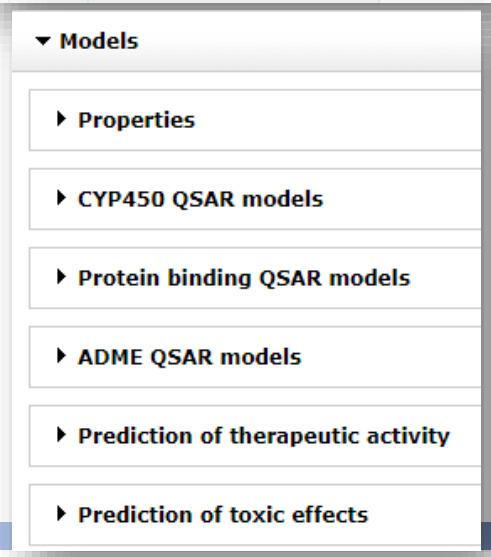
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針對SHP2的藥物活性預測









代謝物活性預測

CYP450 代謝預測

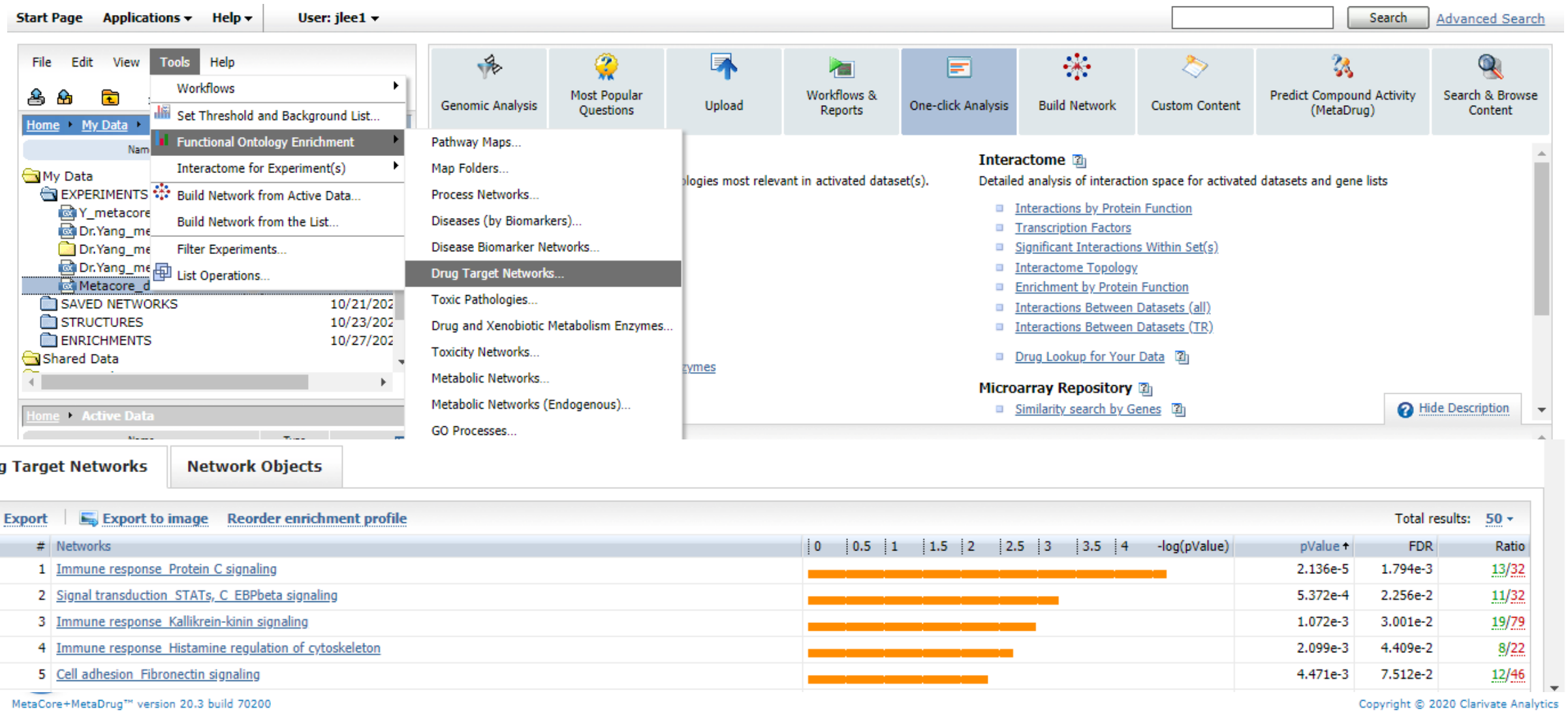
蛋白質結合活性預測

身體代謝吸收活性預測

適應症治療活性預測

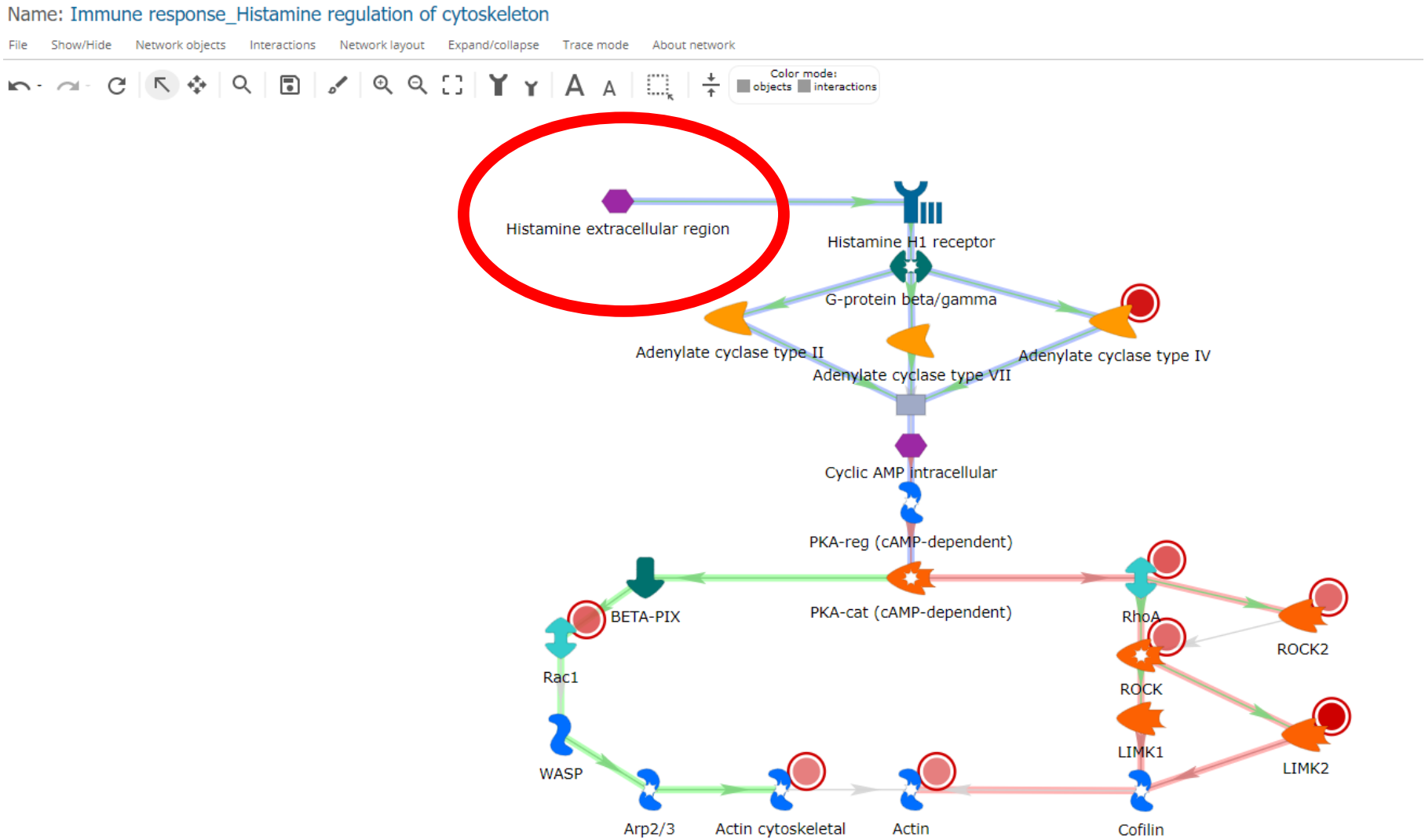
毒性影響預測

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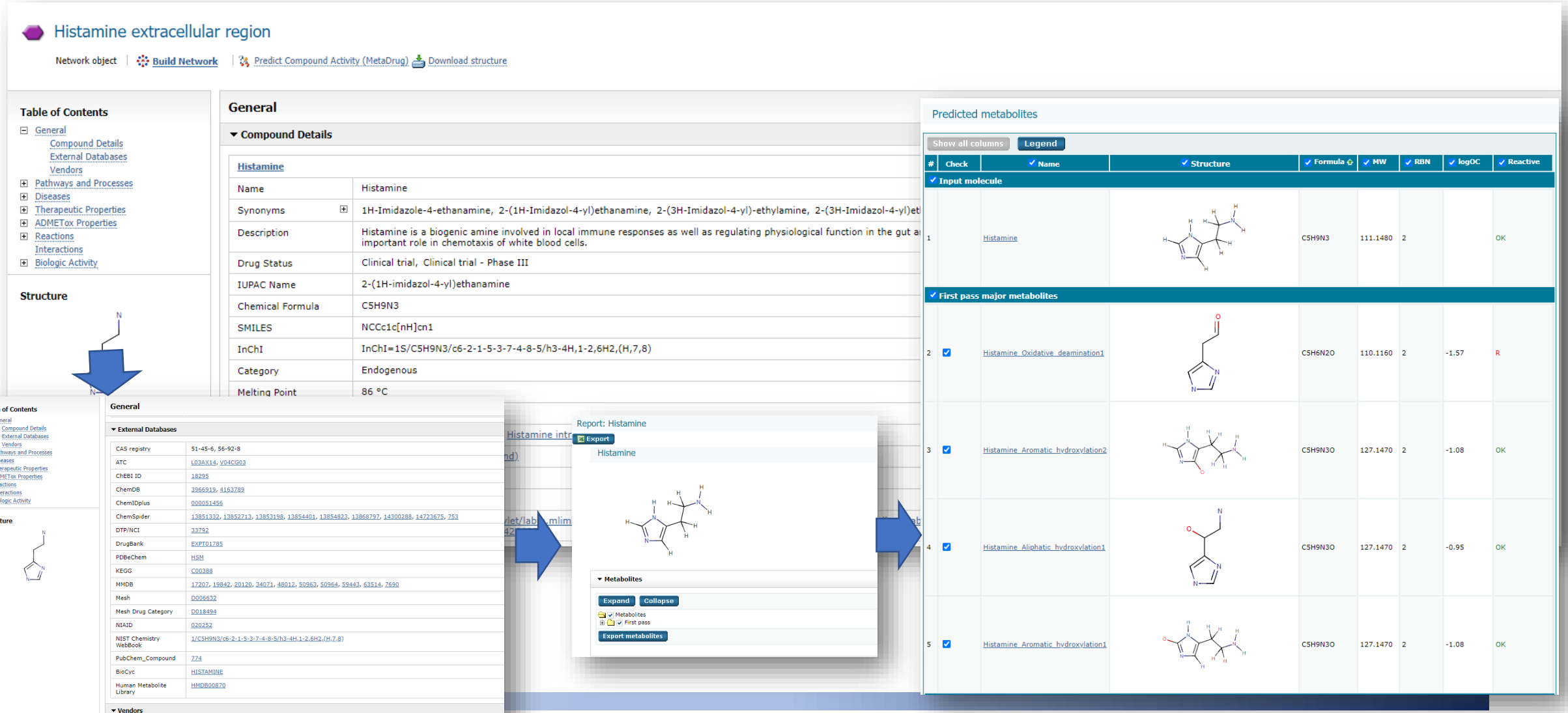
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透過已建立網絡尋找化合物相關資訊



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查看化合物基本資料及代謝物預測



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IV. 化合物活性預測

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上傳化合物結構式進行預測

Data Analysis Wizard (MetaDrug™)

Step 1

Next >>

Name

Histamine

Metabolite generation options

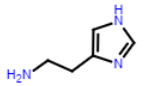
- Prioritization
- Second Pass*
- Turn off metabolite prediction

Metabolic reaction types

- All transformations
  - Phase 1
    - C oxidation
    - Quinone formation
    - N oxidation
    - S oxidation
    - Spontaneous
    - P oxidation
    - Reduction
    - Hydrolysis
  - Phase 2
    - Glucuronide transfer
    - Sulfate transfer
    - Glutathione transfer
    - Methyl transfer
    - Cysteine transfer
    - O-phosphate transfer
    - Glycine conjugation
    - Glutamine conjugation
    - N-acetyl transfer

* Note: choosing this option may increase report generation time.

Preview



Data Analysis Wizard (MetaDrug™)

Step 2

Search type

- Similarity search 0.7 1
- Exact search
- No similarity

Select properties to calculate

- Formula
- MW
- RuleOf5
- RBN
- HBA
- HBD
- logOC
- Reactive

Select QSAR models to calculate*

- CYP450 QSAR models
- Protein binding QSAR models
- ADME QSAR models
- Prediction of therapeutic activity
- Prediction of toxic effects
- Custom QSAR Models

Additional options

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以QSAR model 進行CYP450代謝預測

Report: Histamine

Export

Exact Similarity 0.7 Recalculate

Properties

#	Property	Model description	Value/(TP)
1	Formula	Molecular formula.	C5H9N3
2	HBA	Number of hydrogen bond acceptors.	1
3	HBD	Number of hydrogen bond donors.	3
4	MW	Molecular weight.	111.1480
5	RBN	Number of rotatable bonds.	2
6	Reactive	Identify reactive groups in molecules. OK means that the metabolite does not contain spontaneously reactive groups, R means it does. MetaDrug currently includes 89 rules to predict likely reactive metabolites such as quinones, aromatic and hydroxyl amines, acyl glucuronides, acyl halides, nepoxides, thiophene-S-oxides, furans, phenoxyl radicals, phenols, and aniline radicals.	OK
7	RuleOf5	Lipinski rule of five can be used to indicate whether a molecule is likely to be orally bioavailable. A molecule should not have more than 5 hydrogen bond donors, not more than 10 hydrogen bond acceptors, a molecular weight under 500, and a partition coefficient log P under 5. Rule of five-compliant molecules are marked as OK, non-compliant as Poor. Reference: Lipinski, et al., 2001 (PMID: 11259830).	OK

CYP450 QSAR models

#	Property	Model description	Value/(TP)
1	CYP1A2-inh, prob	Potential to inhibit CYP1A2 at 10 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential inhibitors. Data taken from PubChem Bioassay 1851. Model description: Training set N=9336, Test set N=3113, Sensitivity=0.81, Specificity=0.85, Accuracy=0.87, MCC=0.65.	0.13 (100.00)
2	CYP1A2-sub, prob	Potential to be metabolized by CYP1A2, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate that the compound is a substrate for CYP1A2. Model description: Training set N=309, Test set N=62, Sensitivity=0.71, Specificity=0.91, Accuracy=0.78, MCC=0.60. Reference: Clarivate Analytics.	0.41 (47.13)
3	CYP2B6-sub, prob	Potential to be metabolized by CYP2B6, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate that the compound is a substrate for CYP2B6. Model description: Training set N=228, Test set N=36, Sensitivity=0.90, Specificity=0.81, Accuracy=0.86, MCC=0.72. Reference: Clarivate Analytics.	0.20 (32.53)
4	CYP2C19-inh, prob	Potential to inhibit CYP2C19 at 10 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential inhibitors. Data taken from PubChem Bioassay 1851. Model description: Training set N=9392, Test set N=3149, Sensitivity= 0.80, Specificity=0.79, Accuracy=0.79, MCC=0.59.	0.06 (100.00)
5	CYP2C9-inh, prob	Potential to inhibit CYP2C9 at 10 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential inhibitors. Data taken from PubChem Bioassay 1851. Model description: Training set N=8977, Test set N=2993, Sensitivity=0.64, Specificity=0.88, Accuracy=0.80, MCC=0.54.	0.04 (100.00)
6	CYP2D6-inh, prob	Potential to inhibit CYP2D6 at 10 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential inhibitors. Data taken from PubChem Bioassay 1851. Model description: Training set N=9759, Test set N=3254, Sensitivity=0.62, Specificity=0.92, Accuracy=0.82, MCC=0.59.	0.11 (55.70)
7	CYP2D6-sub, prob	Potential to be metabolized by CYP2D6, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate that the compound is a substrate for CYP2D6. Model description: Training set N=375, Test set N=69, Sensitivity=0.77, Specificity=0.84, Accuracy=0.81, MCC=0.62. Reference: Clarivate Analytics.	0.22 (47.13)
8	CYP3A4-inh, prob	Potential to inhibit CYP3A4 at 10 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential inhibitors. Data taken from PubChem Bioassay 1851. Model description: Training set N=9145, Test set N=3049, Sensitivity=0.74, Specificity=0.83, Accuracy=0.79, MCC=0.57.	0.01 (100.00)
9	CYP3A4-sub, prob	Potential to be metabolized by CYP3A4, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate that the compound is a substrate for CYP3A4. Model description: Training set N=636, Test set N=116, Sensitivity=0.76, Specificity=0.85, Accuracy=0.80, MCC=0.61. Reference: Clarivate Analytics.	0.21 (47.13)
10	sEH-inh, pIC50	Human soluble epoxide hydrolase inhibition, pIC50 (uM). Cutoff is -1.7. The higher the value, the higher the inhibition activity. Reference: Clarivate Analytics. Model description: N=675, R2=0.92, RMSE=0.51.	-2.08 (55.68)

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以QSAR model 進行蛋白質結合與身體代謝吸收預測

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Protein binding QSAR models

#	Property	Model description	Value/(TP)
1	5HT2B-act, prob	Potential to activate 5-hydroxytryptamine (serotonin) receptor 2B at 1 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate active compounds. Training set consists of chemicals and drugs that activate 5HT2B receptor resulting in valvular heart disease. Reference: Chekmarev et al., Chem Res Tox, 2008 (PMID: 18415049). Model description: Training set N=194, Test set N=38, Sensitivity=1.0, Specificity=0.96, Accuracy=0.97, MCC=0.94.	0.20 (28.95)
2	ADR-lig, prob	Potential to bind to Androgen receptor, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential Androgen receptor ligands. Reference: Fang H, Tong W, et al Chem Res Tox 2003 (PMID: 14565775). Model description: Training set N=165, Test set N=32, Sensitivity=1.0, Specificity=1.0, Accuracy=1.0, MCC=1.0.	0.27 (28.95)
3	ESR-lig, prob	Potential to bind to Estrogen receptor at 100 uM or less, range from 0 to 1. Cutoff is 0.5. Values higher than 0.5 indicate potential Estrogen receptor ligands. Training set is based on DSSTox KIERBL data (EPA). Model description: Training set N=164, Test set N=55, Sensitivity=1.0, Specificity=0.87, Accuracy=0.93, MCC=0.86.	0.04 (29.58)
4	PXR-act, prob	Pregnane X receptor activation binary model, range from 0 to 1. Values higher than 0.5 indicate potential PXR activators, values lower than 0.5 are preferable. Reference: Clarivate Analytics. Model description: N=95, R2=0.64, RMSE=0.29.	0.59 (29.66)
5	Pgp-inh, pIC50	Human P-glycoprotein transporter inhibition, pIC50 (uM). Cutoff is -1.7. The higher the value, the higher the inhibition activity. Clarivate Analytics. Model description: N=274, R2=0.85, RMSE=0.4.	-0.94 (29.66)
6	Pgp-sub, prob	Potential to be a substrate of human P-glycoprotein transporter, range from 0 to 1. Cutoff is 0.5. Values closer to 1 indicate potential ligands. Reference: Penzotti, Lamb, et al., 2002 (PMID: 11960484). Model description: N=192, R2=0.65, RMSE=0.3.	0.17 (29.66)
7	SERT-inh, pKi	Human serotonin transporter inhibition, pKi (uM). Cutoff is -1.7. The higher the value, the higher the inhibition activity of the metabolite. Clarivate Analytics. Model description: N=256, R2=0.91, RMSE=0.36.	-0.00 (28.05)
8	hERG-inh, pKi	Human hERG (human ether a-go-go-related gene) channel inhibition , pKi (uM). Cutoff is -1.7. The higher the value, the higher the inhibition activity. Lower values are preferable. Reference: Clarivate Analytics. Model description: N=196, R2=0.93, RMSE=0.23.	-0.81 (32.35)

ADME QSAR models

#	Property	Model description	Value/(TP)
1	BBB, log ratio	Blood brain barrier penetration model. The data is expressed as log values of the ratio of the metabolite concentrations in brain and plasma. Cutoff is -0.3. Larger values indicate that the metabolite is more likely to enter the brain. Reference: Clarivate Analytics. Model description: N=107, R2=0.89, RMSE=0.26.	-0.26 (29.66)
2	G-LogP	Lipophilicity, log of compound octanol-water distribution. Cutoffs are -0.4 to 5.6. Values greater than 5.6 correspond to overly hydrophobic compounds. Reference: Syracuse Research, PHYSPROP database. Model description: N=13474, R2=0.95, RMSE=0.21.	0.13
3	Prot-bind, %	Human serum protein binding, %. Cutoff is 50%. A value of more than 95% is highly bound, less than 50% is a low binding metabolite. Reference: Thummel and Shen, 2001 in Goodman & Gilman's The Pharmacological Basis of Therapeutics. Model description: N=265, R2=0.909, RMSE=10.11.	22.68 (32.35)
4	Prot-bind, log t	Affinity to human serum albumin, log value of the retention time. Cutoff is 0. Positive values correspond to higher protein binding, negative values to lower protein binding. An acceptable level of binding is project dependent. The model is based on retention times of compounds assayed by HPLC using an immobilized HSA column. Values are expressed as log values of the retention time. Reference: Colmenarejo, Alvarez-Pedraglio, et al., 2001 (PMID: 11728183). Model description: N=95, R2=0.904, RMSE=0.2.	-0.59 (29.66)
5	WSol, log mg/L	Water solubility at 25��C, log mg/L. Cutoffs are from 2 to 4. An acceptable level of solubility is project dependent. Reference: Syracuse Research, PHYSPROP database. Model description: N=2871, 2=0.91, RMSE=0.54.	4.39

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Prediction of therapeutic activity

#	Property	Model description	Value/(TP)
1	Allergy	Potential antiallergic activity. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs. Model description: Training set N=258, Test set N=47, Sensitivity= 0.87, Specificity=0.88, Accuracy=0.87, MCC=0.74. Reference: Clarivate Analytics.	0.79 (37.40)
2	Alzheimer	Potential activity against Alzheimer's disease. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs, drug candidates in clinical trials and preclinical compounds with in vivo activity. Model description: Training set N=261, Test set N=44, Sensitivity= 0.91, Specificity=0.82, Accuracy=0.86, MCC=0.73. Reference: Clarivate Analytics.	0.87 (37.69)
3	Angina	Potential antianginal activity. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs, drug candidates in clinical trials and preclinical compounds with in vivo activity. Model description: Training set N=546, Test set N=95, Sensitivity= 0.90, Specificity=0.93, Accuracy=0.92, MCC=0.83. Reference: Clarivate Analytics.	0.55 (35.25)
4	Arthritis	Potential activity against arthritis. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs, drug candidates in clinical trials and preclinical compounds with in vivo activity. Model description: Training set N=460, Test set N=77, Sensitivity= 0.98, Specificity=0.94, Accuracy=0.96, MCC=0.92. Reference: Clarivate Analytics.	0.11 (100.00)
5	Asthma	Potential activity against asthma. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs, drug candidates in clinical trials and preclinical compounds with in vivo activity. Model description: Training set N=366, Test set N=63, Sensitivity= 0.92, Specificity=0.86, Accuracy=0.89, MCC=0.78. Reference: Clarivate Analytics.	0.64 (33.33)
6	Bacterial	Potential antibacterial activity. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs. Model description: Training set N=530, Test set N=97, Sensitivity= 0.87, Specificity=0.90, Accuracy=0.89, MCC=0.77. Reference: Clarivate Analytics.	0.81 (33.33)
7	Cancer	Potential activity against cancer. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs. Model description: Training set N=886, Test set N=167, Sensitivity= 0.89, Specificity=0.83, Accuracy=0.86, MCC=0.72. Reference: Clarivate Analytics.	0.90 (37.50)
8	Depression	Potential activity against depression. Cutoff is 0.5. Values higher than 0.5 indicate potentially active compounds. Training set consists of approved drugs. Model description: Training set N=335, Test set N=62, Sensitivity= 0.93, Specificity=0.82, Accuracy=0.87, MCC=0.75. Reference: Clarivate Analytics.	0.74 (32.00)

Report: Histamine

Export

Exact Similarity 0.7 Recalculate

Prediction of toxic effects

#	Property	Model description	Value/(TP)
1	AMES	Potential to be mutagenic (AMES positive), range from 0 to 1. A value of 1 is AMES positive (mutagenic), and a value of 0 is AMES negative (non-mutagenic). Cutoff is 0.5. Values close to zero are preferable. The AMES assay is based upon the reversion of mutations in the histidine operon in the bacterium Salmonella enterica sv Typhimurium. Reference: Young, Gombar, et al., 2002 (DOI: 10.1016/S0169-7439(01)00181-2). Model description: N=1780, R2=0.69, RMSE=0.29.	0.35 (35.44)
2	Anemia	Potential for causing anemia. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing anemia in vivo. Model organisms: human. Model description: Training set N=324, Test set N=51, Sensitivity= 0.82, Specificity=0.90, Accuracy=0.86, MCC=0.72. Reference: Clarivate Analytics.	0.31 (37.88)
3	Carcinogenicity	Potential for inducing carcinogenicity in rats and mice. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing carcinogenicity in vivo. Model organisms: mouse, rat. Reference: ISSCAN data. Model description: Training set N=1210, Test set N=185, Sensitivity= 0.96, Specificity=0.90, Accuracy=0.93, MCC=0.86.	0.95 (37.88)
4	Carcinogenicity Mouse Female	Potential for inducing carcinogenicity in female mice. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing carcinogenicity in vivo. Model organisms: female mice. Reference: ISSCAN data. Model description: Training set N=640, Test set N=94, Sensitivity= 0.90, Specificity=0.93, Accuracy=0.92, MCC=0.83.	0.77 (32.35)
5	Carcinogenicity Mouse Male	Potential for inducing carcinogenicity in male mice. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing carcinogenicity in vivo. Model organisms: mouse male. Reference: ISSCAN data. Model description: Training set N=584, Test set N=93, Sensitivity= 0.91, Specificity=0.88, Accuracy=0.89, MCC=0.78.	0.90 (32.35)
6	Carcinogenicity Rat Female	Potential for inducing carcinogenicity in female rats. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing carcinogenicity in vivo. Model organisms: female rat. Reference: ISSCAN data. Model description: Training set N=667, Test set N=120, Sensitivity= 0.90, Specificity=0.96, Accuracy=0.93, MCC=0.86.	0.95 (37.88)
7	Carcinogenicity Rat Male	Potential for inducing carcinogenicity in male rats. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing carcinogenicity in vivo. Model organisms: male rat. Reference: ISSCAN data. Model description: Training set N=715, Test set N=117, Sensitivity= 0.92, Specificity=0.88, Accuracy=0.90, MCC=0.79.	0.94 (32.35)
8	Cardiotoxicity	Potential for inducing cardiotoxicity. Cutoff is 0.5. Values higher than 0.5 indicate potentially toxic compounds. Training set consists of chemicals and drugs causing cardiotoxicity in vivo. Model organisms: mouse, rat, human. Model description: Training set N=143, Test set N=30, Sensitivity= 0.80, Specificity=1.00, Accuracy=0.90, MCC=0.82. Reference: Clarivate Analytics.	0.45 (32.35)
		Growth inhibition of MCF7 cell line (human caucasian breast adenocarcinoma), pGI50. Cutoff is 6. Values from 6 to 8 correspond to a toxic metabolite, values less than 6 are preferable, values less than 3 are more	4.69

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再回到分子及路徑機制分析

Report: Histamine

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Possible targets for input molecule

Check all | Uncheck all | Invert all | Group proteins by class

#	Check	Type	Target	Interactions	Database compound	Similarity, %	Input molecule	Link Info
1	☑		Carbonic anhydrase IV		Histamine	100.00	Histamine	
2	☑		Carbonic anhydrase VII		Histamine	100.00	Histamine	
3	☑		CAH15		Histamine	100.00	Histamine	
4	☑		Carbonic anhydrase XIV		Histamine	100.00	Histamine	
5	☑		Histamine H4 receptor		Histamine	100.00	Histamine	
					4-Methylhistamine	89.09		
					N-alpha-Methylhistamine	87.50		
					(S)-alpha-Methyl-histamine	83.05		
					2-(1H-Imidazol-4-yl)-1-methyl-ethylamine	83.05		
					(R)-alpha-Methyl-histamine	83.05		
					[(1S)-2-(3H-imidazol-4-yl)-1-methyl-ethyl]amine	83.05		
					2-Methylhistamine	79.03		
					N1-Methylhistamine	77.78		
					3-(3H-imidazol-4-yl)propylamine	73.33		
6	☑		Carbonic anhydrase VB (mitochondrial)		Histamine	100.00	Histamine	
7	☑		Endothelin-1		Histamine	100.00	Histamine	
8	☑		Carbonic anhydrase IX		Histamine			
9	☑		rEV131		Histamine			
10	☑		Carbonic anhydrase I		Histamine			
					[2-(1H-Imidazol-4-yl)-ethyl]-urea			
					N-[2-(1H-Imidazol-4-yl)-ethyl]-guanidine; dihydroc...			
11	☑		Histamine H2 receptor		Histamine			
					4-Methylhistamine			
					N-alpha-Methylhistamine			
					Beta-Methylhistamine			
					[(1S)-2-(3H-imidazol-4-yl)-1-methyl-ethyl]amine			
					(R)-alpha-Methyl-histamine			
					2-(1H-Imidazol-4-yl)-1-methyl-ethylamine			
					(S)-alpha-Methyl-histamine			
					[2-(1H-Imidazol-4-yl)-ethyl]-dimethyl-amine			
					2-(3-methylimidazol-4-yl)ethylamine			

Enrichment Analysis

Enrichment analysis is a useful tool for suggesting the compound-affected processes, side effects and potential indications. Click here for details.

- Pathway Maps
- Process Networks
- Disease Biomarker Networks
- Drug Target Networks
- Toxicity Networks
- Metabolic Networks
- GO Processes
- GO Molecular Functions
- GO Localizations

MetaCore

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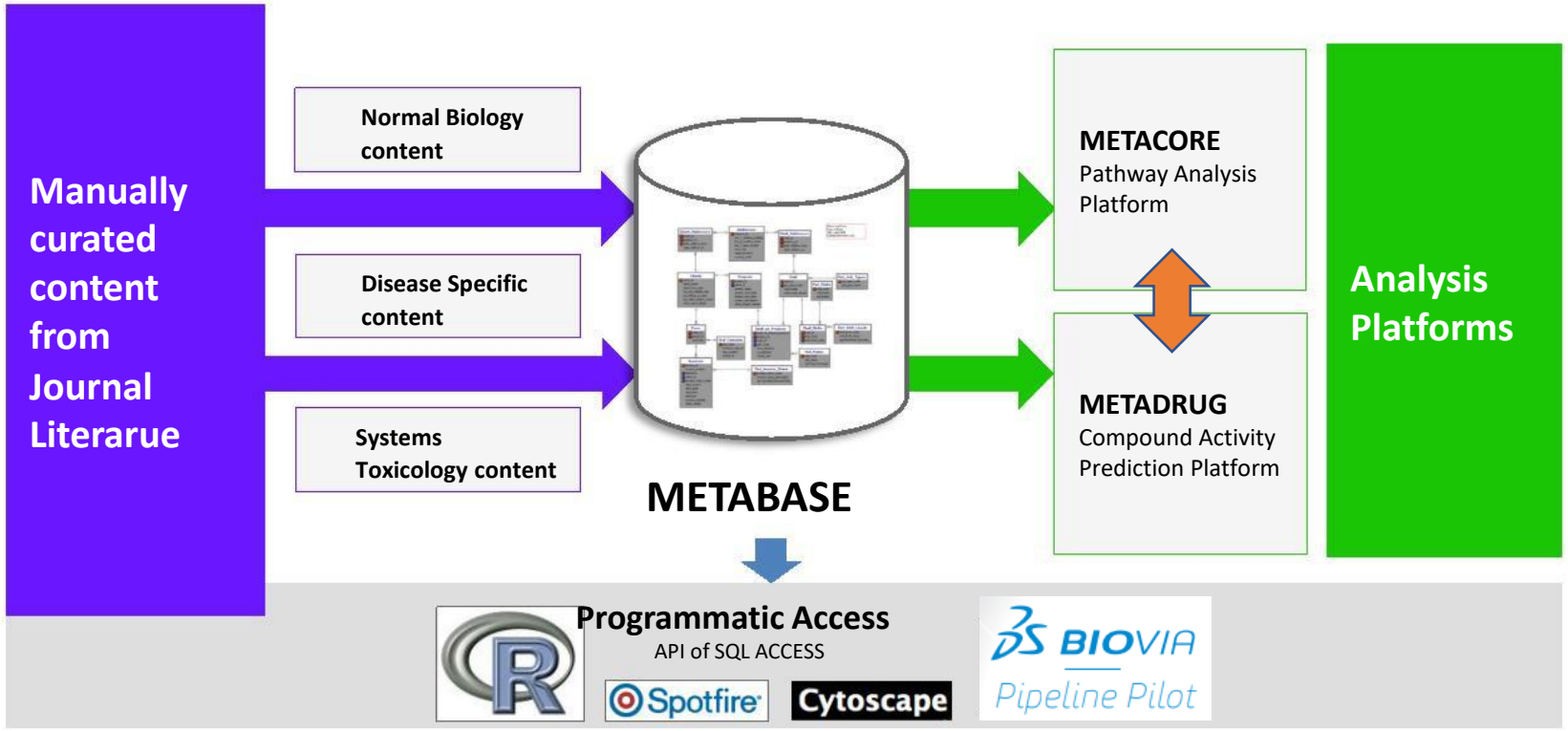
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Live demo

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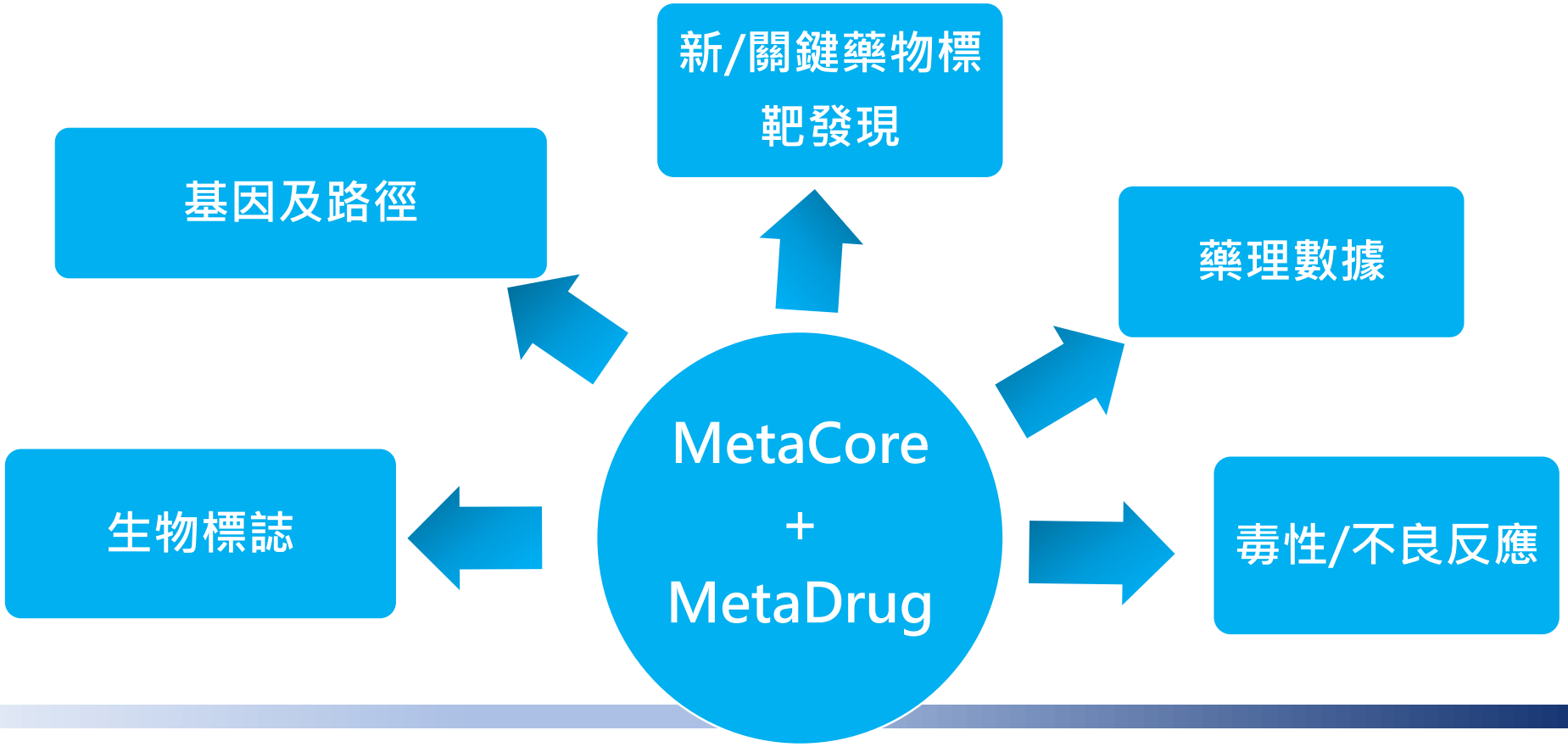
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快速獲取知識，提升新藥開發效率。



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From Virtual to Real… and back

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