CAS BIOFINDER DISCOVERY PLATFORM™

快速使用指南 (QUICK GUIDE)

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大綱

- CAS BioFinder簡介與界面介紹
- 配體檢索與配体詳情信息（配體與細節概述）
- 骨架檢索與構效關係分析（支架與搜救分析）
- 蛋白/通路/靶點、疾病與生物標誌物（Proteins and Pathways;疾病與生物標記）
- 生物活性預測（Predictive Analytics）

科學資訊管理對新藥研發至關重要

低增長時代的特點對創新的要求極大提升，而在當今的創新環境下，數據管理任務艱巨

- 信息鴻溝會導致創新管線薄弱、研發效率低下，以及意外的知識產權風險
- 由於數據量和數據類型日益複雜，藥物發現流程中，整合和分析關鍵的研發數據資訊，對於迅速做出關鍵決策至關重要。
- 持續的數據管理有助於開發差異化的成果，支撐創新藥物的發現，確保藥物研發成功進入審批階段，並可避免後續智慧財產權問題。

来源：CAS Insights洞察报告 Challenges and opportunities in data for drug discovery | CAS

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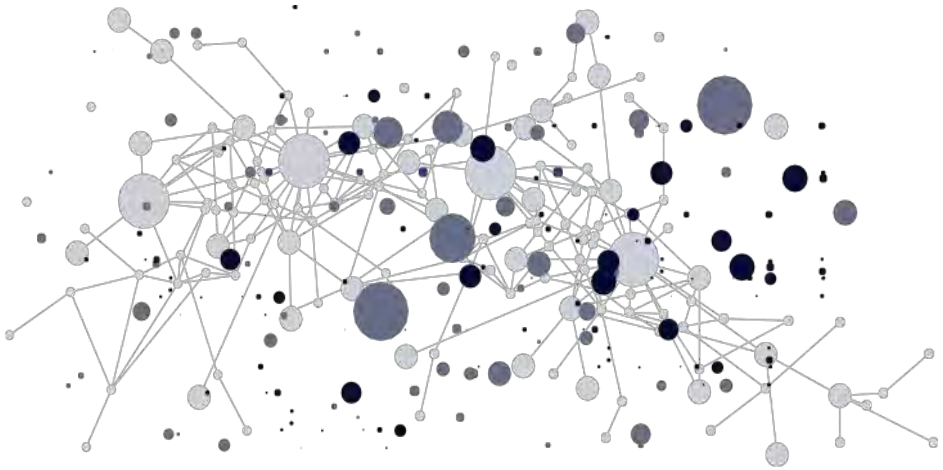
生命科學領域研究離不開重要的數據資訊基礎，但為什麼卻難以加以利用？

缺乏關聯性

生命科學研究和數據分散在各個資料庫、

期刊和專利等眾多互不關聯的資源之中



未一致化

不同資源對相同資訊的描述各不相同，因此很難對數據進行分析和比較

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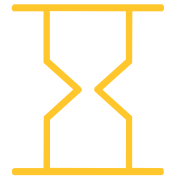
數據問題導致延緩創新進程，增加財務風險

遺漏見解

這些見解能夠為研究人員制定研發戰略提供指導

僅在美國，每年就有5,000到6,000起專利侵權和專利無效的訴訟，法院判定的賠償金額接近 50 億美元[1]。

耗費時間



生命科學數據量每 14 年翻一番[2]

數據科學家將 50%-80% 的時間都花費在收集和整理用於分析模型的數據資訊的瑣碎的工作中[3]

1. Vuleta, B. (2023). 25 Patent Litigation Statistics - High-Profile Feuds about Intellectual Property. LegalJobs. https://legaljobs.io/blog/patent-litigation-statistics/
2. Bornmann, L. et al. (2021). Growth rates of modern science: a latent piecewise growth curve approach to model publication numbers from established and new literature databases. (Humanities and Social Sciences Communications), 8, 224. https://doi.org/10.1057/s41599-021-00903-w
3. Lohr, S. (2014.) For Big-Data Scientists, 'Janitor Work' Is Key Hurdle to Insights. The New York Times. August 17, 2014. https://www.nytimes.com/2014/08/18/technology/for-big-data-scientists-hurdle-to-insights-is-janitor-work.html
4. Genetic Engineering & Biotechnology News Top 25 Biotech Companies of 2019. 5. Pharm Exec's Top 50 Companies 2020.6. Shanghai Ranking's Global Ranking of Academic Subjects 2020.

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利用CAS BioFinder 加速早期藥物研發

預測新型分子可能對生物過程產生的影響

識別與您感興趣的疾病或靶點相關的骨架和分子

發現與您感興趣的疾病相關的生物標誌物

找出哪些候選藥物最有可能成為最安全、最佳的先導化合物

持續開發中的更多內容與功能（序列、抗體、PDC、藥物情報等）

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CAS BioFinder檢索介面

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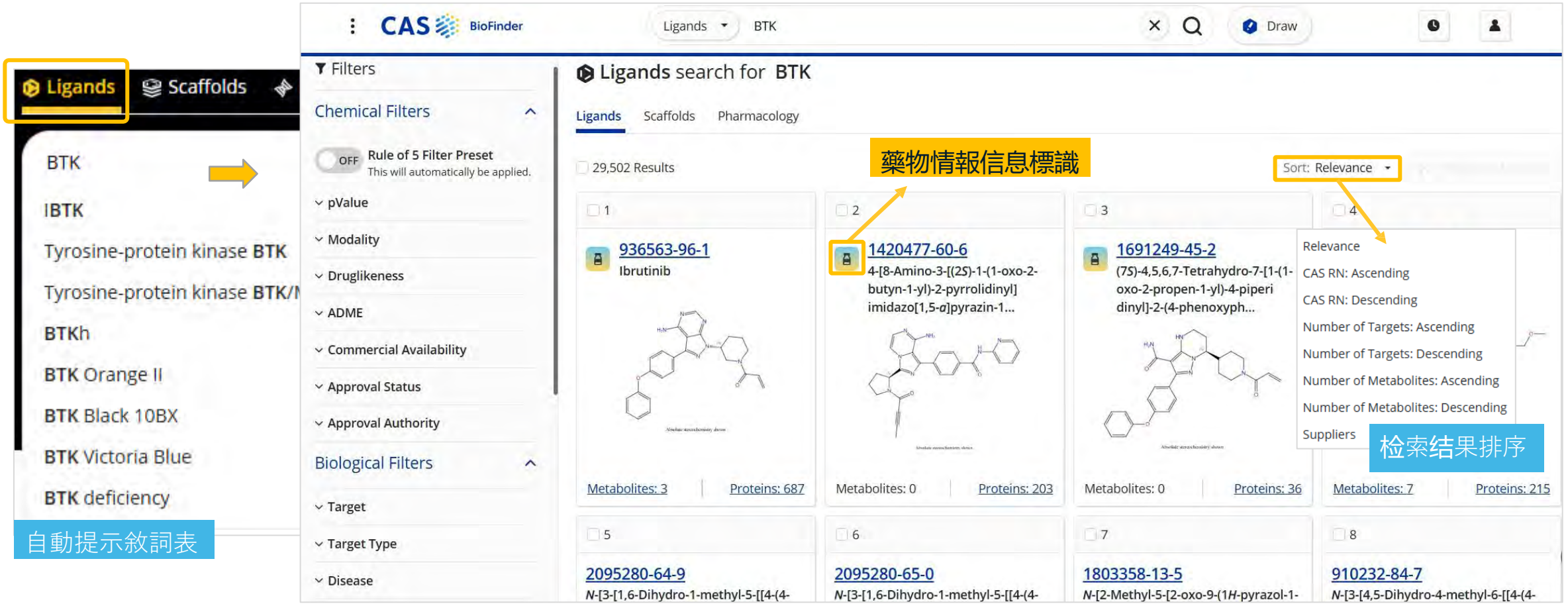
基於靶點、疾病、藥物名稱以及結構，檢索資訊



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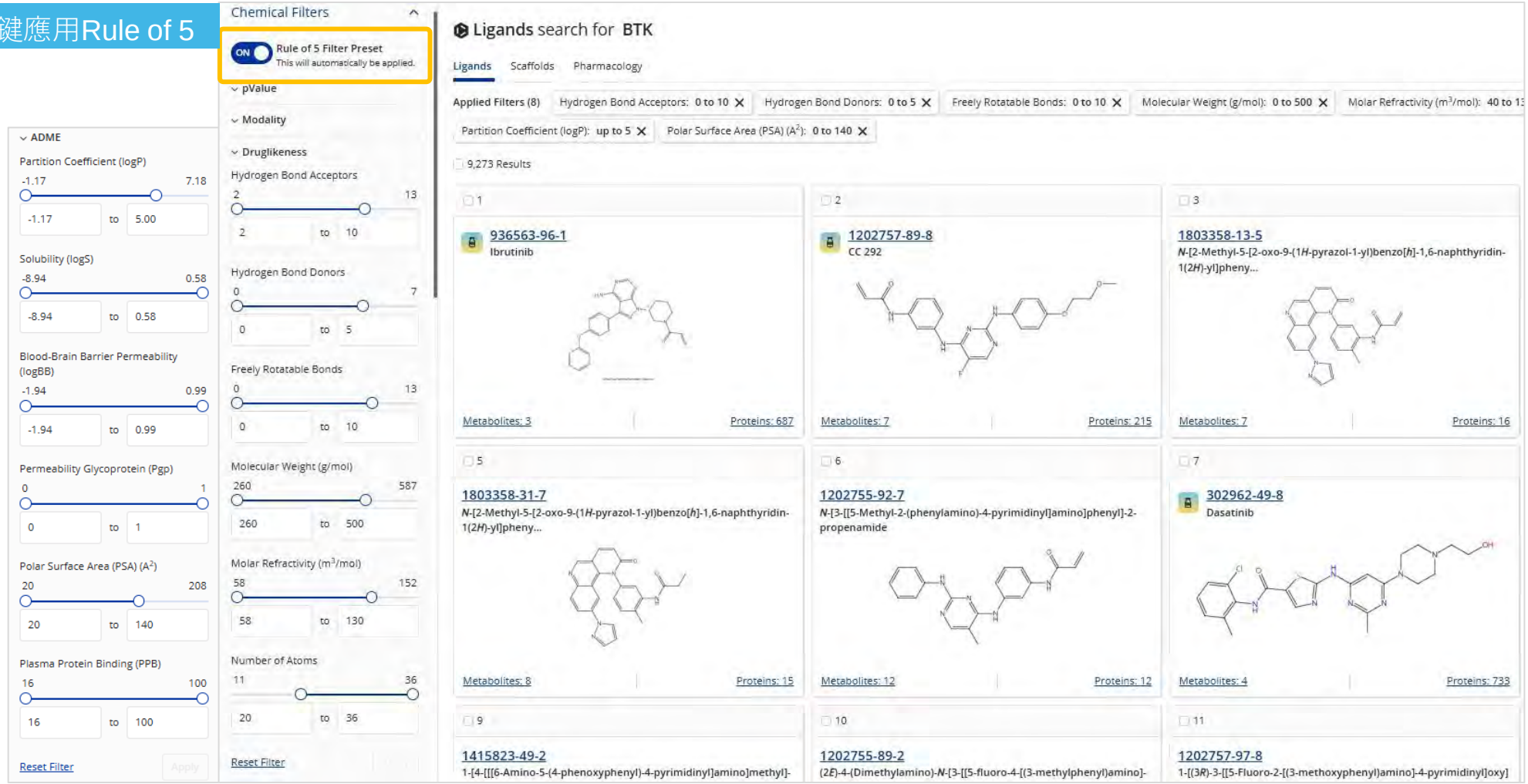
篩選具有類似先導化合物特性的小分子配體

一鍵應用Rule of 5



- 氢键受體<10
- 氢键供體<5
- 自由旋轉键 <10
- 分子量 <500
- 摩尔折射率：
  40-130 m³/mol
- 原子数: 20-70

- logP <5
- 极性表面积：
  0-140 Å²

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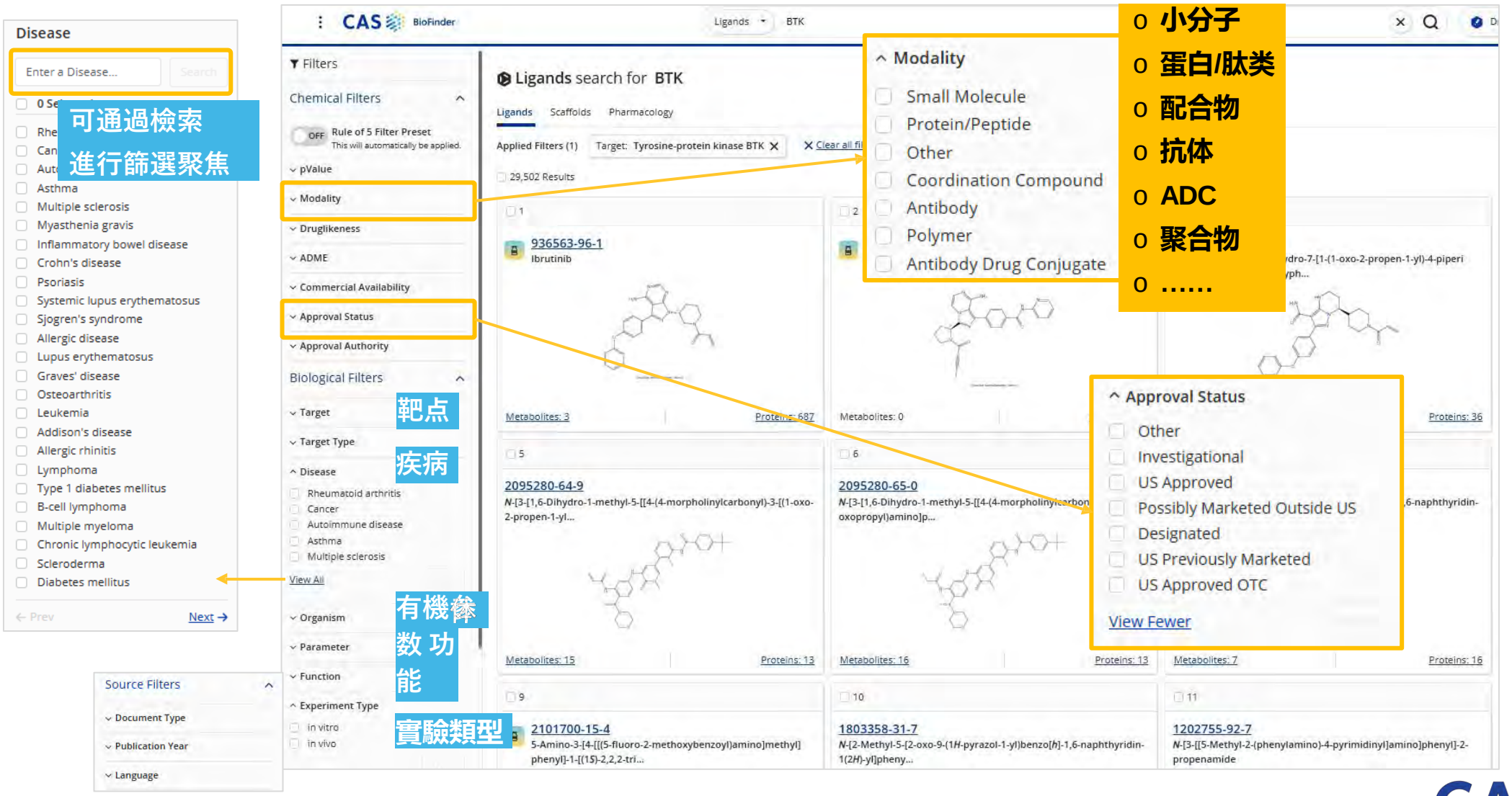
配體檢索結果的縱覽與聚焦



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縱覽配體檢索結果集相關骨架結構與藥理學數據

查看配體檢索結果關聯的骨架結構

數據可視化:

- 柱狀/折線圖：每條柱形/折線節點
- 代表針對不同靶點的測量實驗數量調節圖下方的橫條，可放大圖表的特定區域

可下載表格中的詳細數據

點擊View，可查看原文中的Assay的細節

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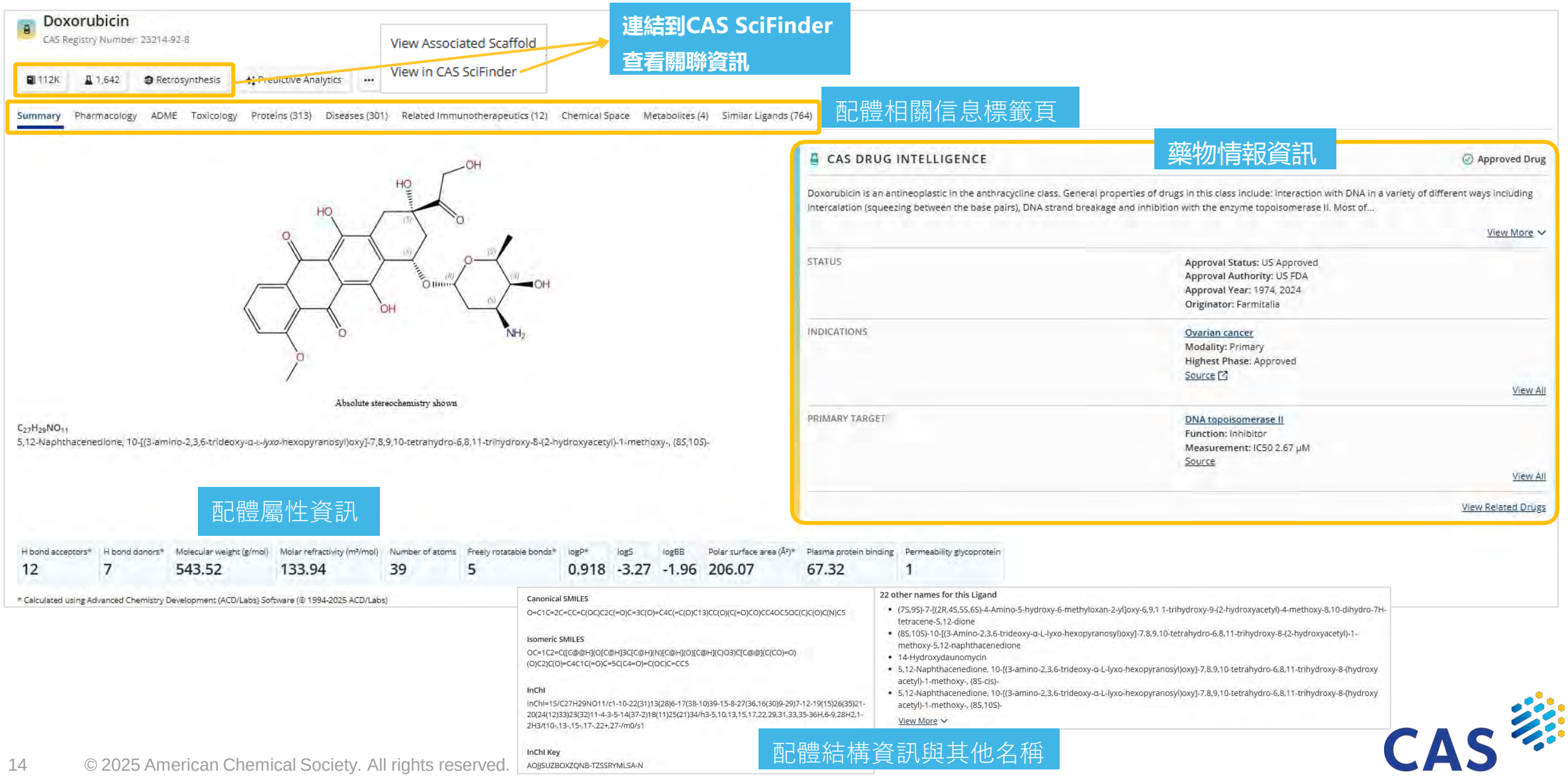
探索配體的詳細資訊



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藥物情報資訊(Drug Intelligence)

CAS DRUG INTELLIGENCE — Approved Drug

Doxorubicin is an antineoplastic in the anthracycline class. General properties of drugs in this class include: interaction with DNA in a variety of different ways including intercalation (squeezing between the base pairs), DNA strand breakage and inhibition with the enzyme topoisomerase II. Most of...

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STATUS

Approval Status: US Approved
Approval Authority: US FDA
Approval Year: 1974, 2024
Originator: Farmitalia

INDICATIONS

Ovarian cancer
Modality: Primary
Highest Phase: Approved
Source

View All

PRIMARY TARGET

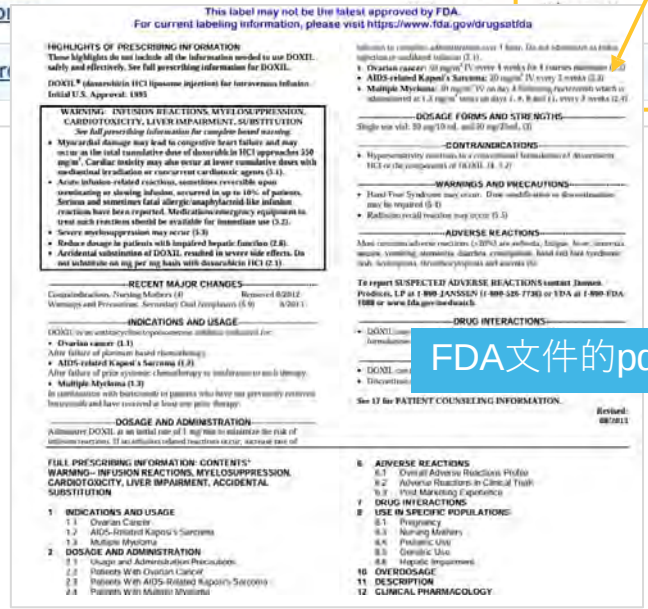
DNA topoisomerase II
Function: Inhibitor
Measurement: IC50 2.67 µM
Source

View All

Indications 相關適應症

所處臨床階段和獲批資訊

Name	Modality	Highest Phase	Source
Ovarian cancer	Primary	Approved	View
AIDS-related Kaposi's sarcoma	Primary	Approved	View
Multiple myeloma	Primary	Approved	View
Locally advanced or unresectable soft tissue sarcoma	Primary	Phase III	View
Kaposi's sarcoma	Primary	Phase II	View
Glioblastoma	Primary	Phase II	View
Lung non-small cell carcinoma			View
Pancreatic ductal adenocarcinoma			View



FDA文件的pdf

Targets 相關靶標

View Related Drugs

Primary Target	Function	Measurement
DNA topoisomerase II	Inhibitor	IC50 2.67 µM
Albumin	Binding Agent	-
DNA gyrase	Inhibitor	-
DNA topoisomerase II	Inhibitor	IC50 2.67 µM
A673	Inhibitor	IC50 200.0 nM
HepG2	Inhibitor	IC50 24.68 µM
Human ovarian cancer cell line	Inhibitor	IC50 0.074 µM

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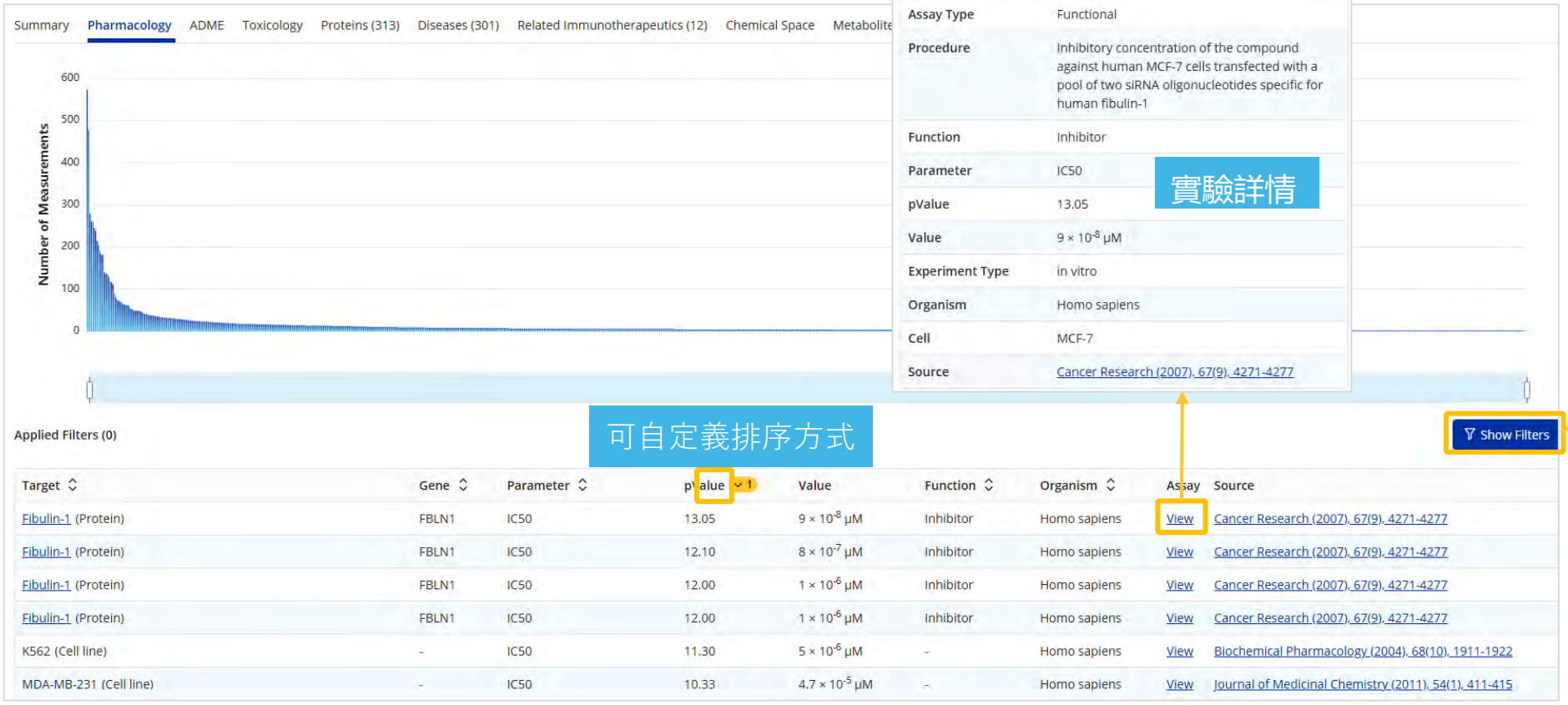
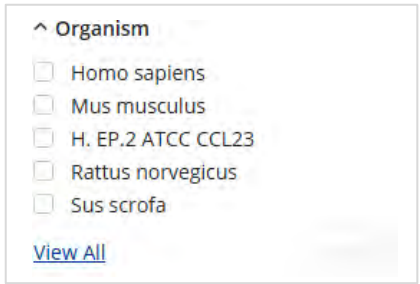
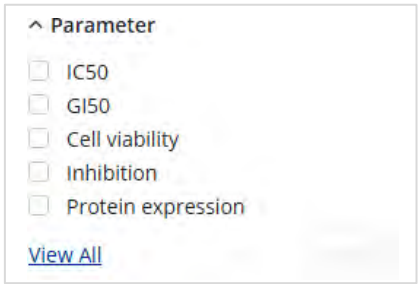
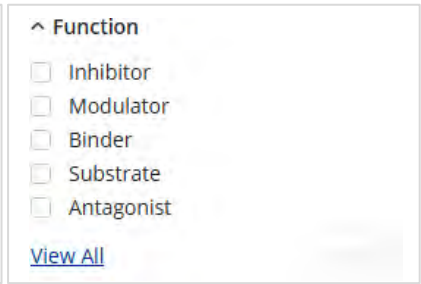
配體藥理學資訊



藥理活性實驗數據篩選項







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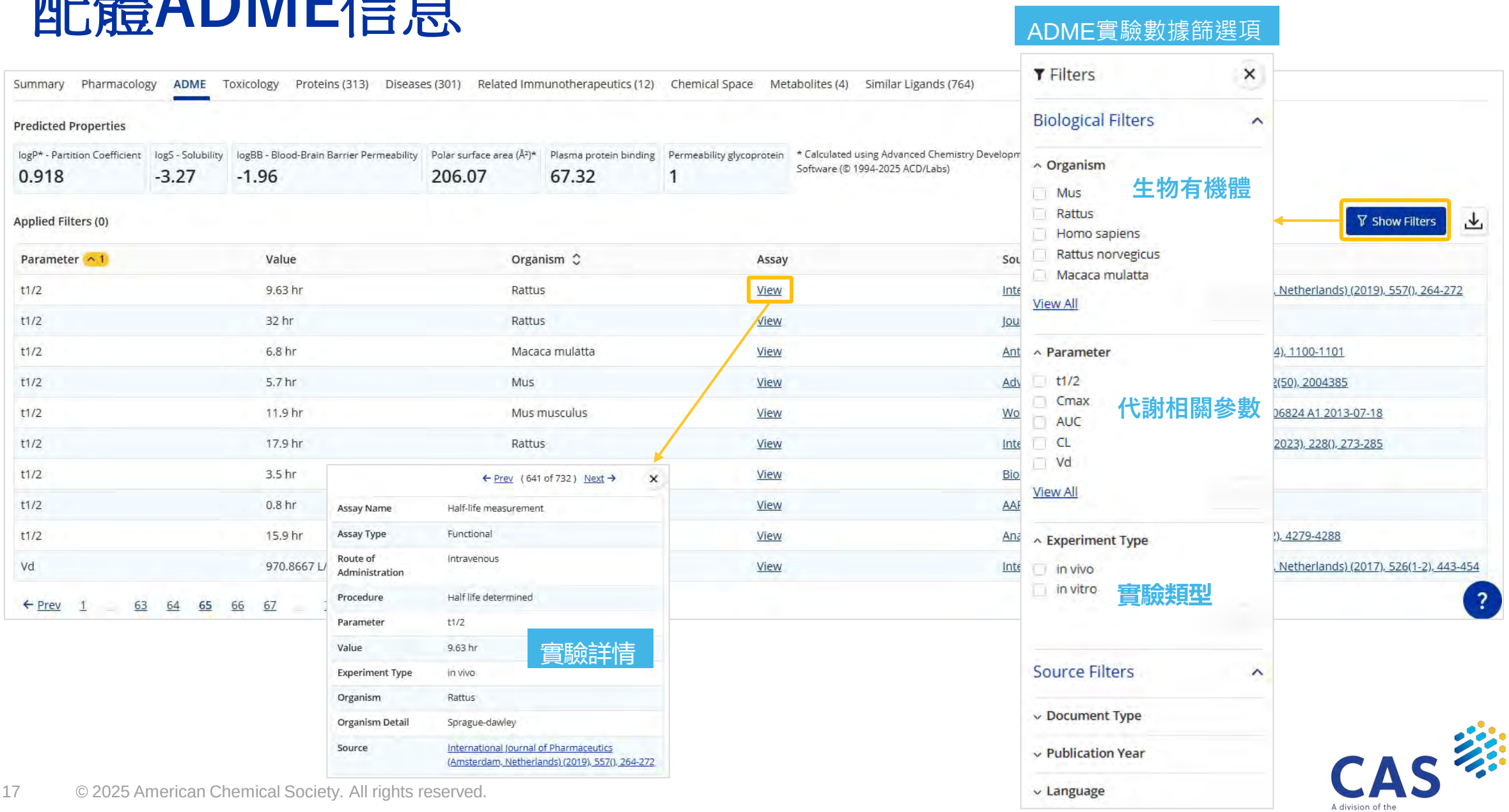
配體ADME信息



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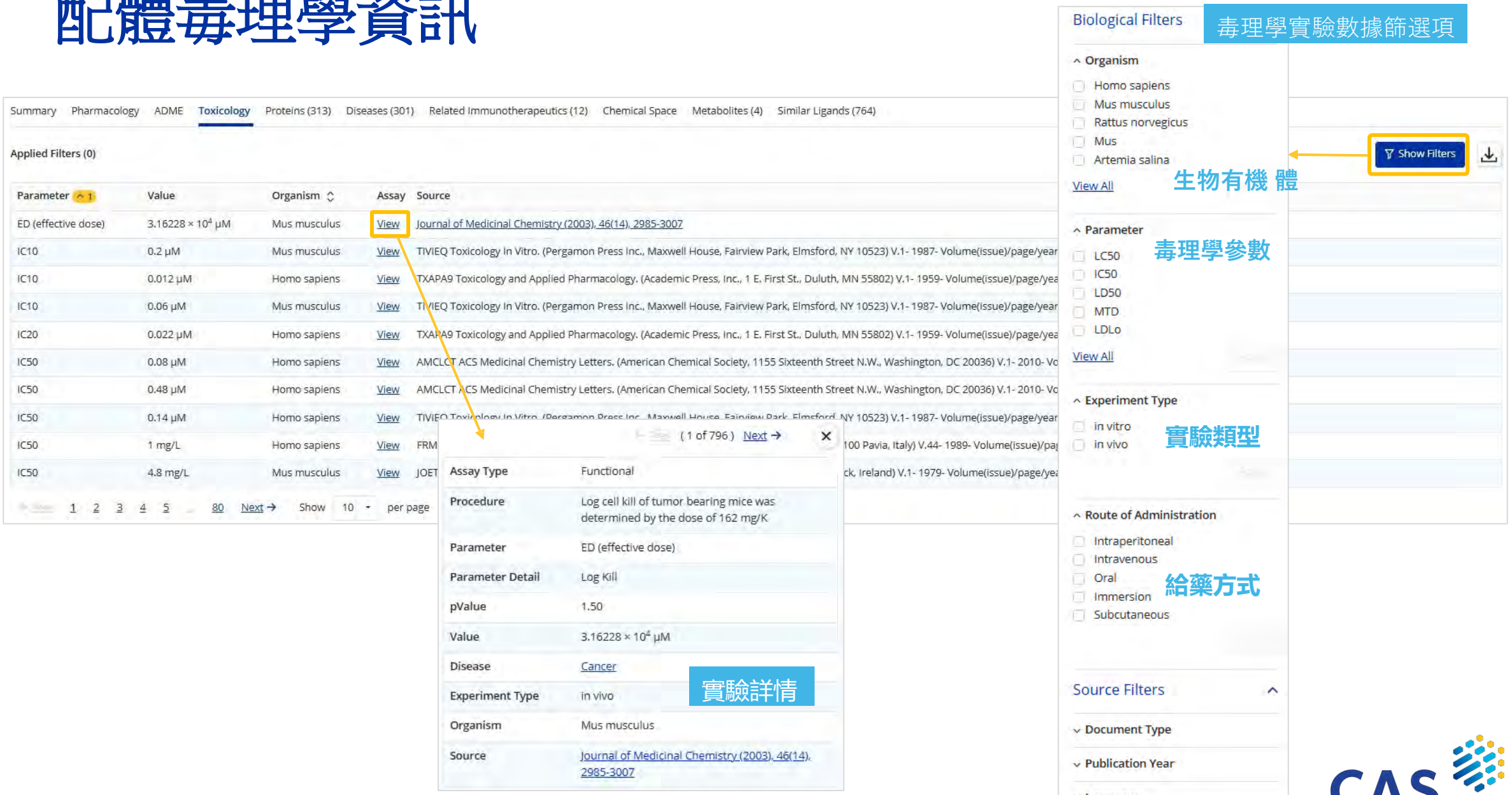
配體毒理學資訊



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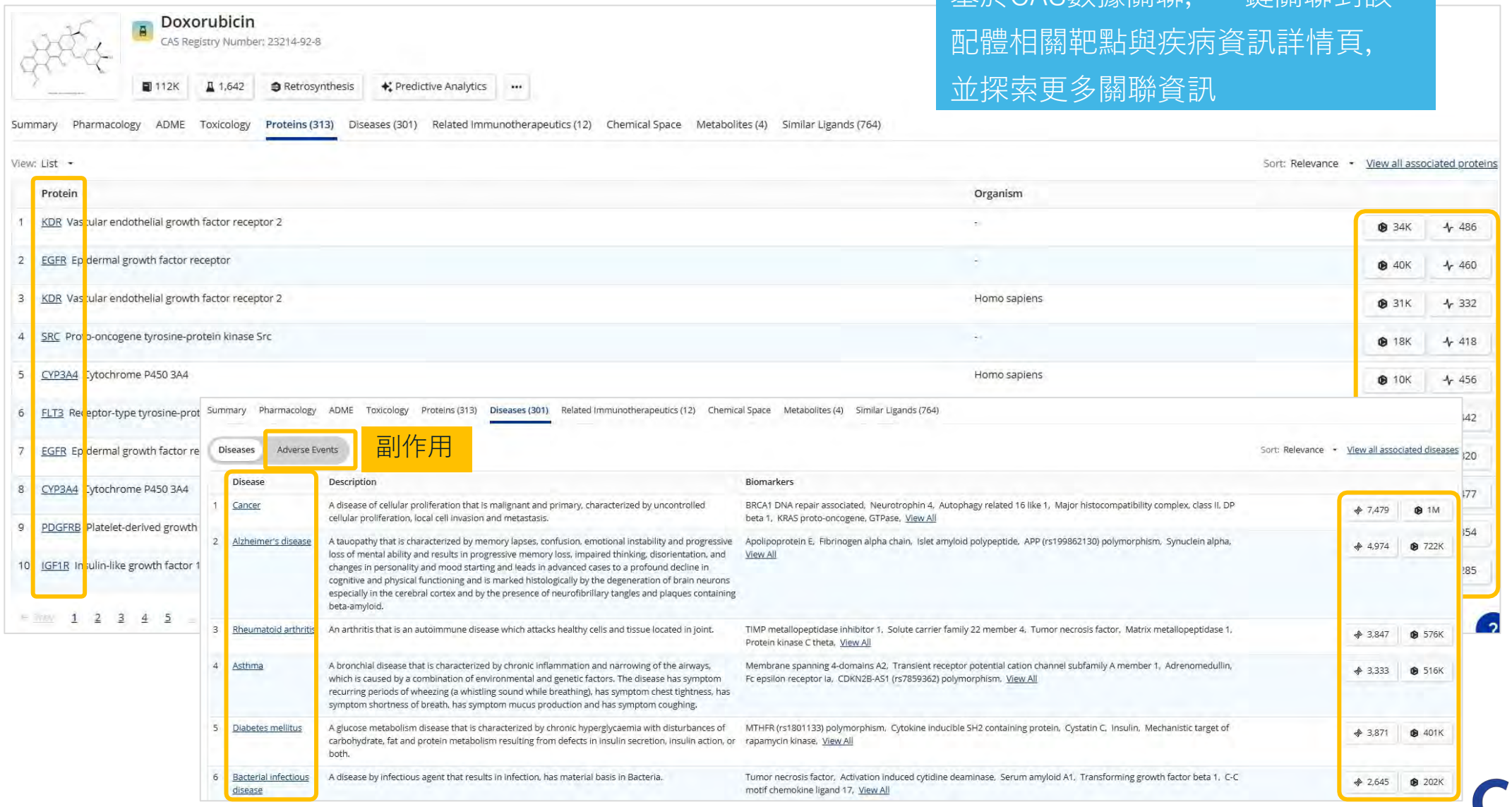
配體相關靶點與疾病資訊

基於CAS數據關聯，一鍵關聯到該配體相關靶點與疾病資訊詳情頁，並探索更多關聯資訊



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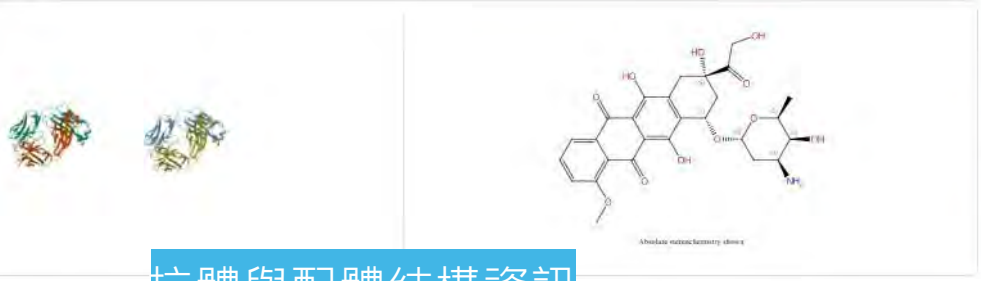
配體相關免疫療法資訊

Summary | Pharmacology | ADME | Toxicology | Proteins (313) | Diseases (301) | **Related Immunotherapeutics (12)** | Chemical Space | Metabolites (4) | Similar Ligands (764)

MAb-DMBA-SIL-Dox



Antibody	Cetuximab
Antigen	Epidermal growth factor receptor (EGFR)
Payload	Doxorubicin
Therapeutic Target	DNA topoisomerase 2-alpha
Drug-Antibody Ratio	5.57
Linker	DMBA-SIL
Method	Site-specific conjugation with the respective EGFR mAb via thiolmaleimide Michael addition.

免疫療法詳情

抗體與配體結構資訊

Trastuzumab-PC4AP-DOX

Antibody	Trastuzumab
Antigen	Receptor tyrosine-protein kinase erbB-2 (ERBB2)
Payload	Doxorubicin
Therapeutic Target	DNA topoisomerase 2-alpha
Drug-Antibody Ratio	2
Linker	Photocaged C4AP
Method	Random conjugation through reduced inter-chain cysteines.

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ADC藥物詳情

Trastuzumab emtansine

CAS Registry Number: 1018448-65-1

1,972 | 8 | Retrosynthesis | Predictive Analytics | ...

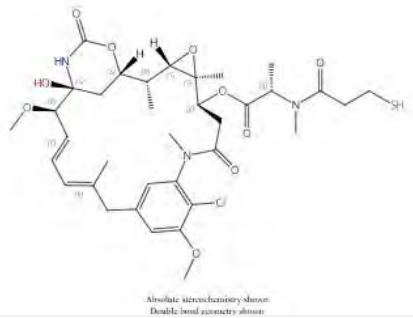
Summary | Pharmacology | ADME | Proteins (2) | Diseases (1)

Antibody	Trastuzumab
Antigen	Receptor tyrosine-protein kinase erbB-2 (ERBB2)
Payload	Mertansine DM1
Therapeutic Target	Microtubule
Drug-Antibody Ratio	3.5
Linker	Succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC)
Method	Random conjugation through nucleophilic lysines.

ADC藥物詳情

抗體3D結構圖

藥物分子結構



CAS DRUG INTELLIGENCE 藥物情報資訊 — Approved Drug

Trastuzumab emtansine (ado-trastuzumab emtansine, trade name Kadcyla) is a combination between a monoclonal antibody and a small-molecule drug. Each molecule of trastuzumab emtansine consists of a single trastuzumab molecule with several molecules of DM1, a cytotoxic maytansinoid, attached. SMCC, or...

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STATUS	**Approval Status:** US Approved **Approval Authority:** US FDA **Approval Year:** 2013 **Originator:** Genentech
INDICATIONS	Breast cancer **Modality:** Primary **Highest Phase:** Approved Source
PRIMARY TARGET	Receptor tyrosine-protein kinase erbB-2 **Function:** Blocker Source

Heavy Chain Sequence

EVQLVESGGGLVQPGGSLRLSCAASGGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYSRWGGDG
FYAMDYDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNV
NHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL
TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL
TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Light Chain Sequence

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYQQHYTTPPTPTFGQG
TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPV
TKSFNRGEC

HCDR1	HCDR2	HCDR3	LCDR2	LCDR1	LCDR3
GFNIKDTY	IYPTNGYT	SRWGGDGFYAMDY	SAS	QDVNTA	QQHYTTPPT

CDR序列

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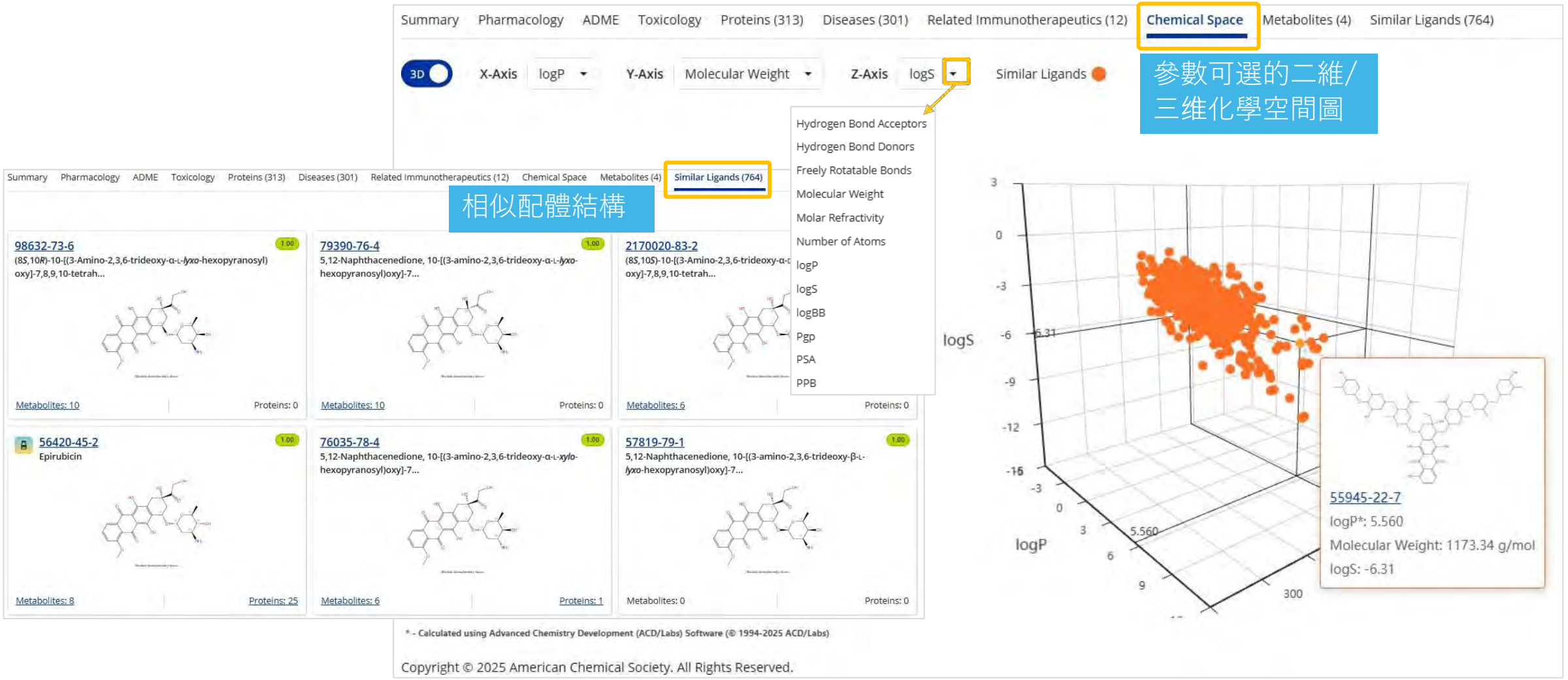
相似配體結構與可視化分析



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探索配體代謝產物

已知代謝產物：Known
預測代謝產物：Confidence Score置信度分值，表示發生該生物轉化的概率

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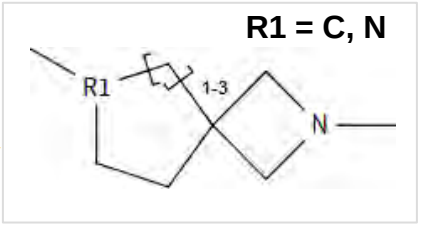
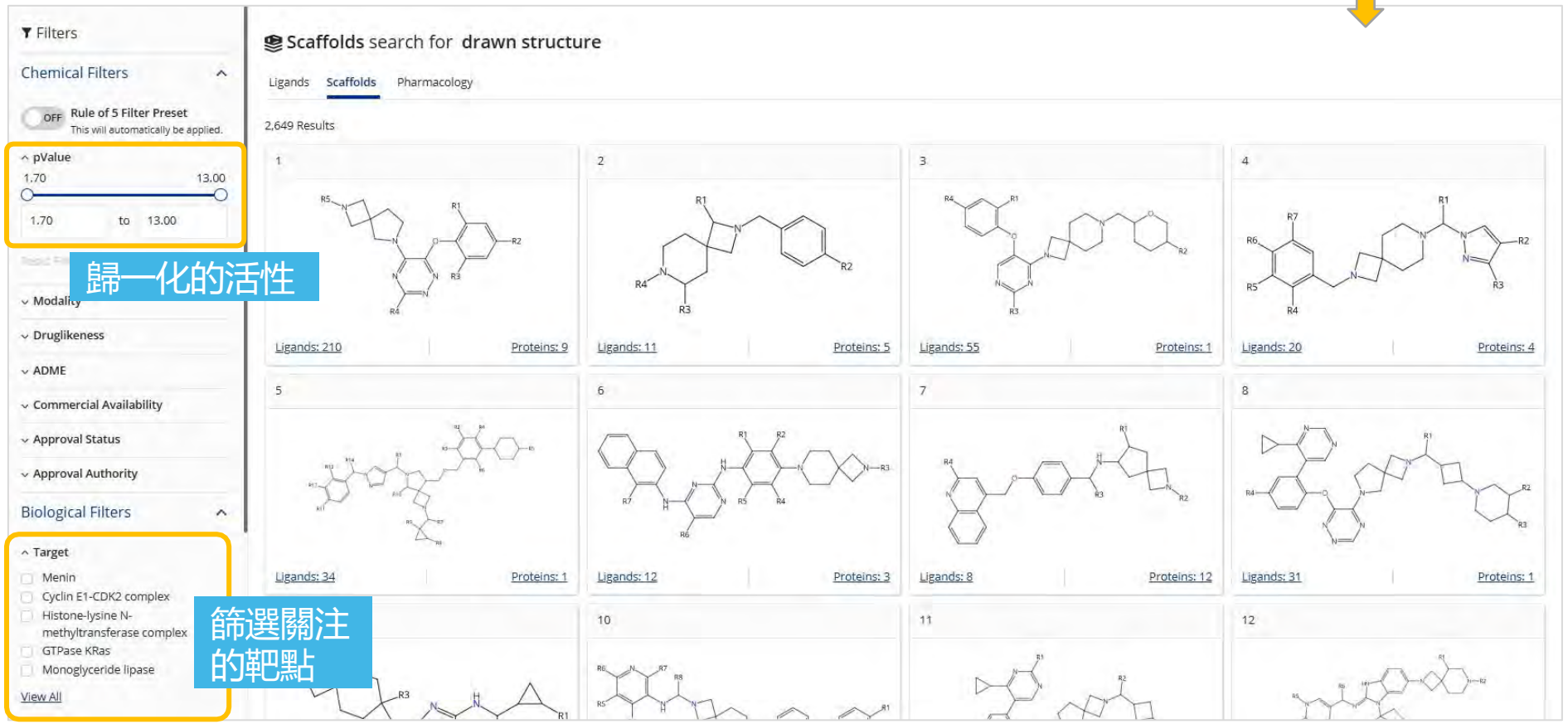
基於靶點或結構片段，探索活性結構骨架

繪製核心結構片段





歸一化的活性

篩選關注的靶點

$$pKa = -\log_{10} Ka$$

$$pIC50 = -\log_{10} IC50$$

IC50越小，pValue越大，抑制活性越高。

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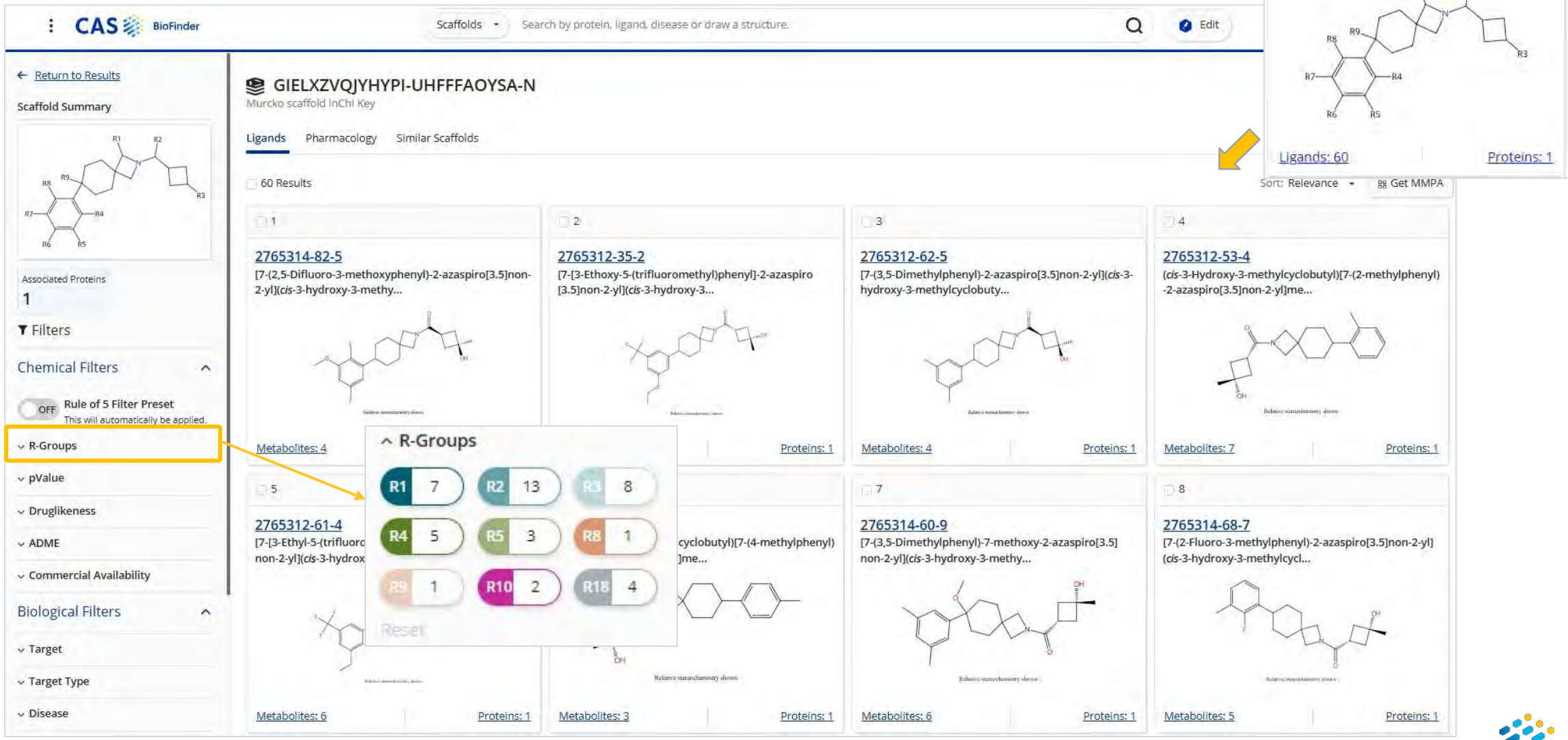
探索目標結構骨架的SAR數據



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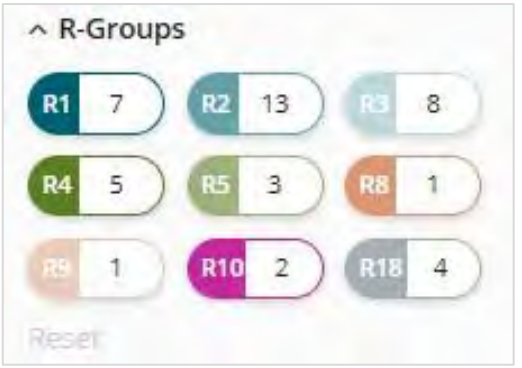
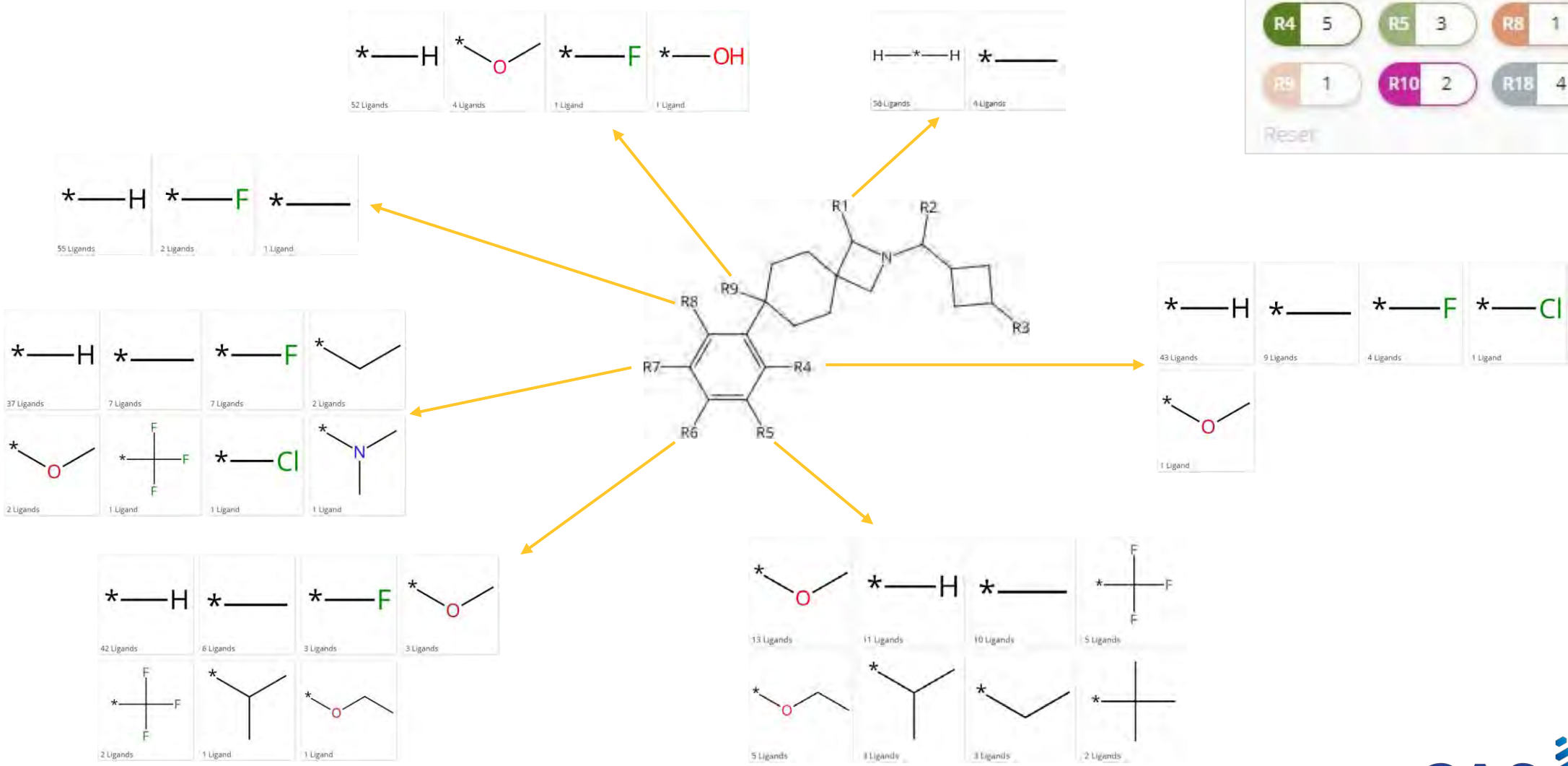
探索目標結構骨架的SAR數據





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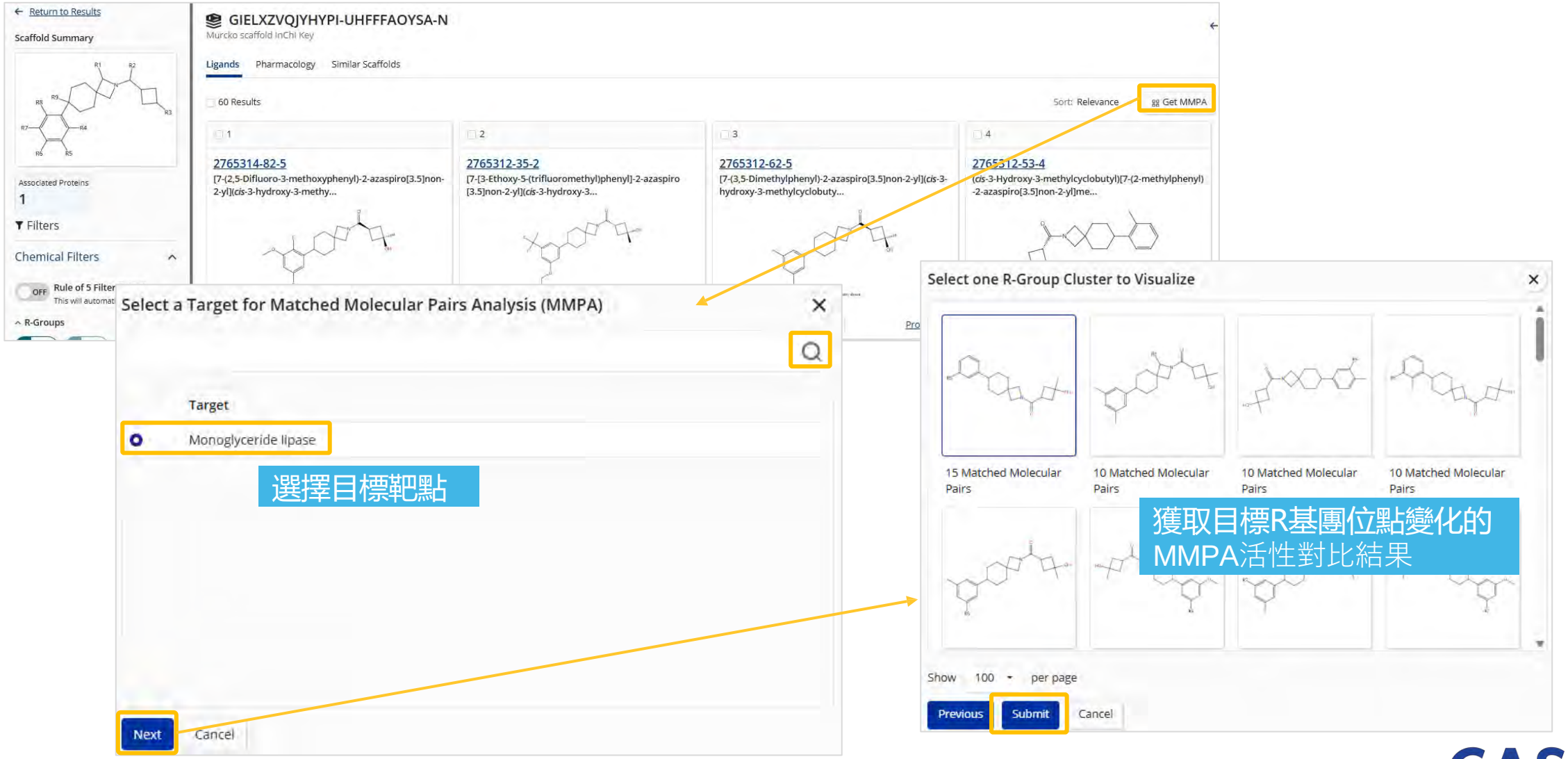
符合分子對分析（MMPA）



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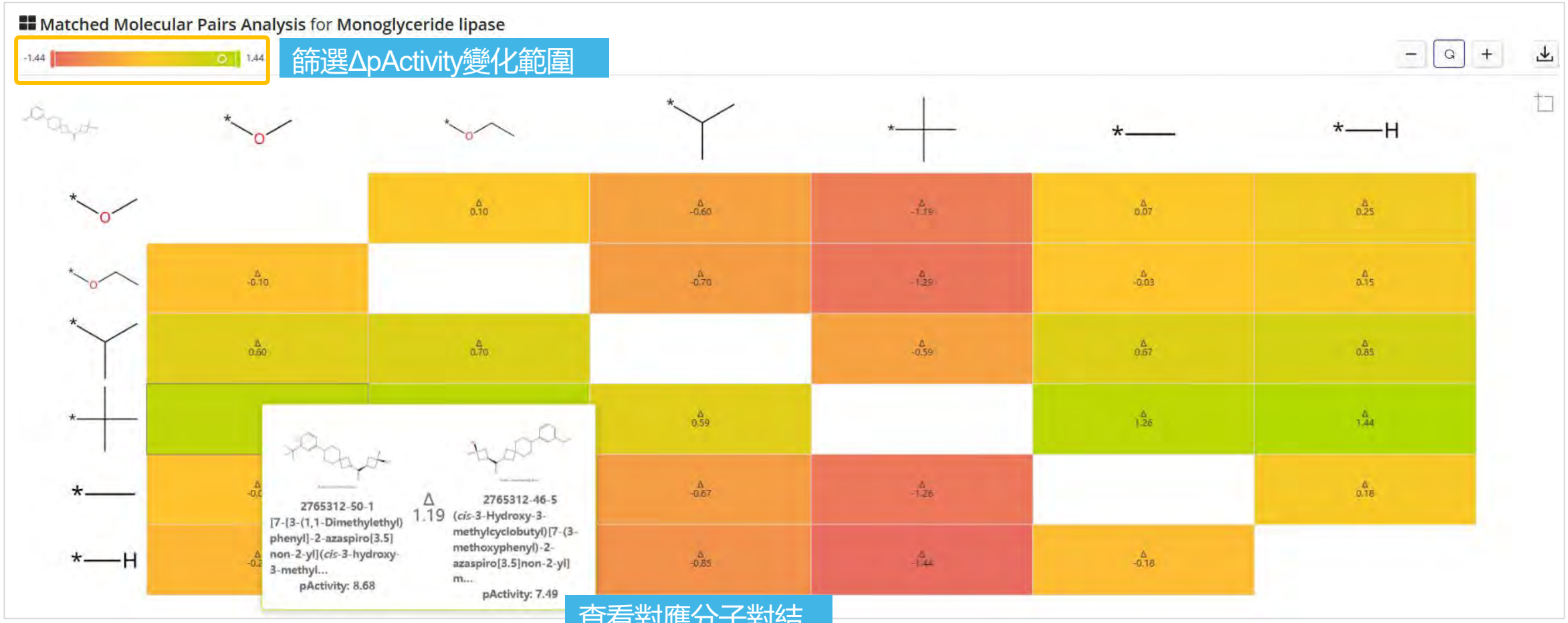
符合分子對分析（MMPA）

快速直觀獲取匹配分子對ΔpActivity熱圖



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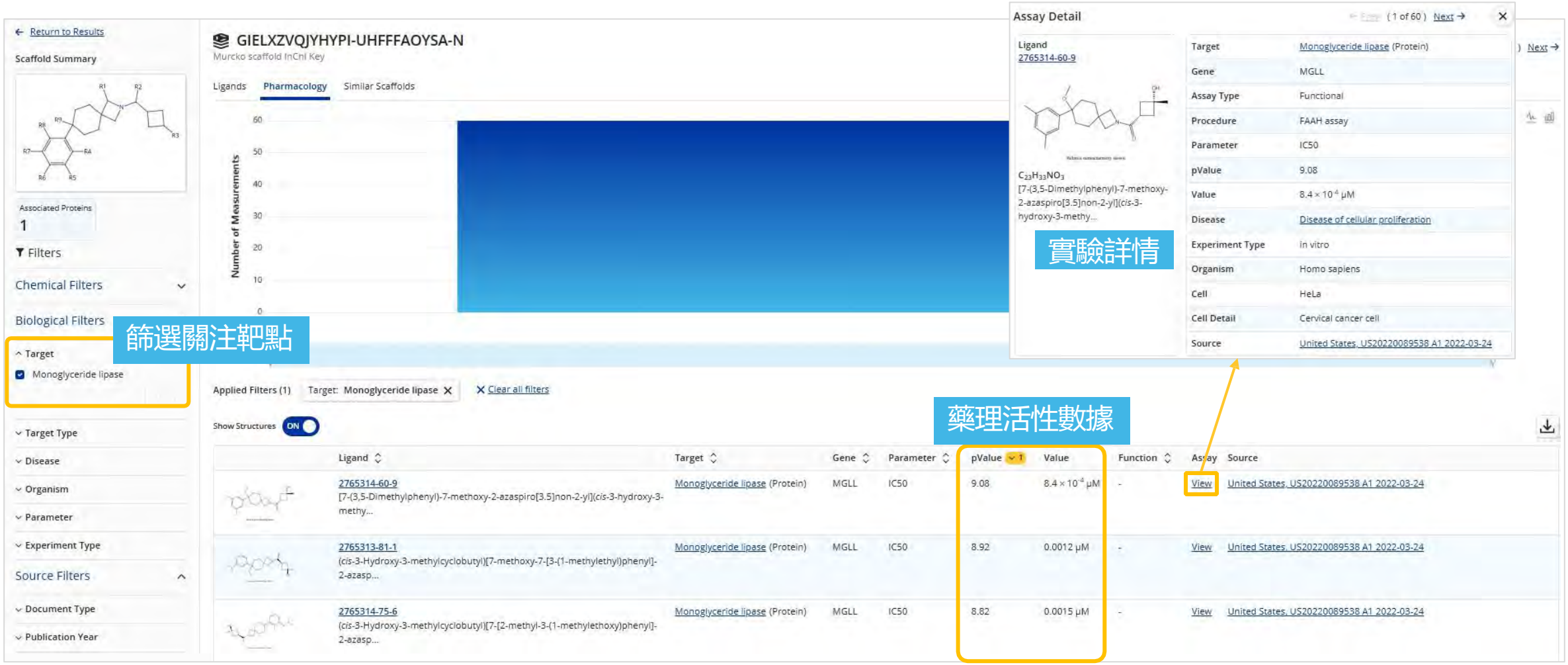
查看同一結構骨架中的配體藥理活性



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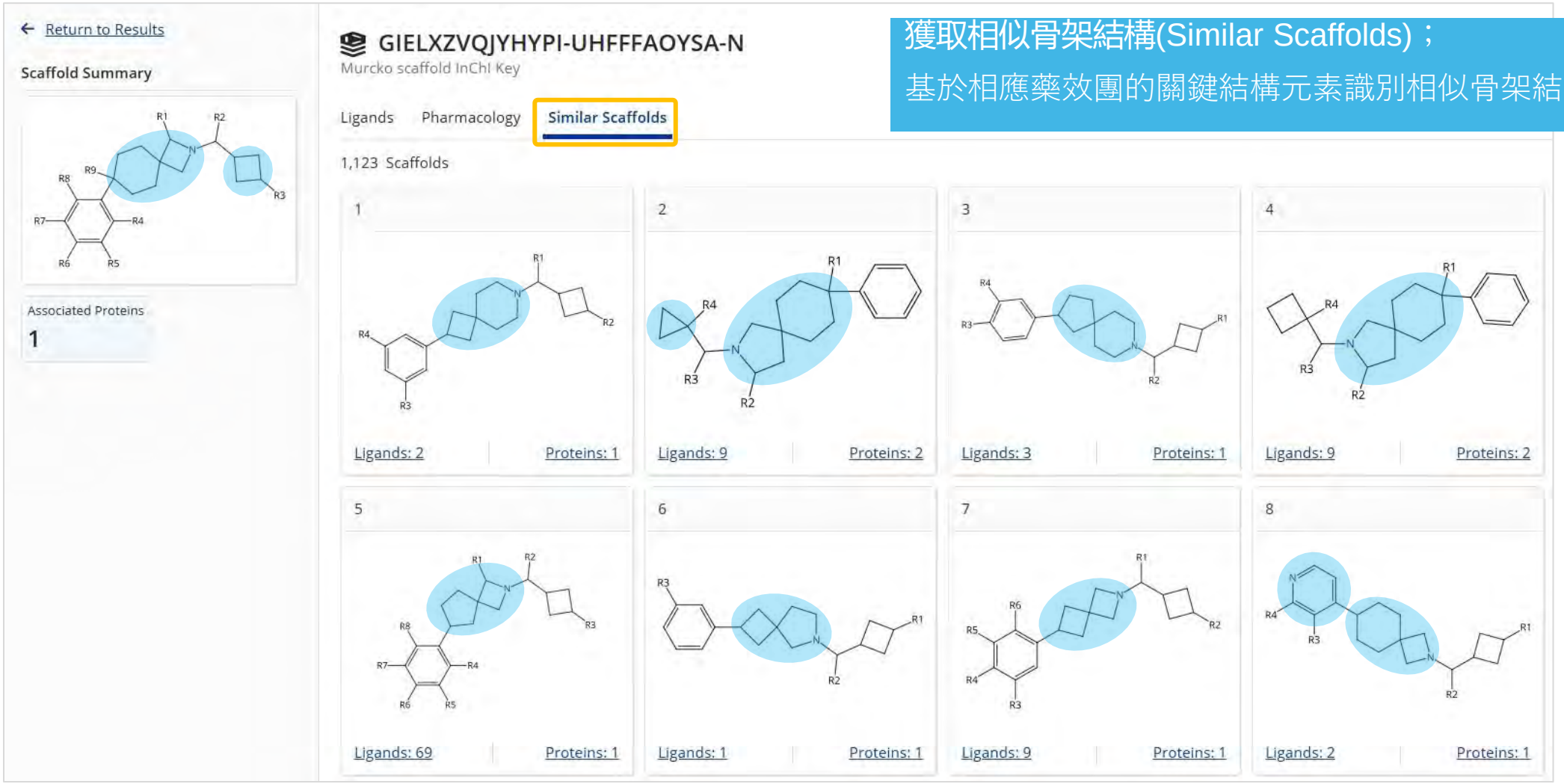
獲取與目標骨架相似骨架結構，啟發新的SAR假設



獲取相似骨架結構(Similar Scaffolds)；

基於相應藥效團的關鍵結構元素識別相似骨架結構

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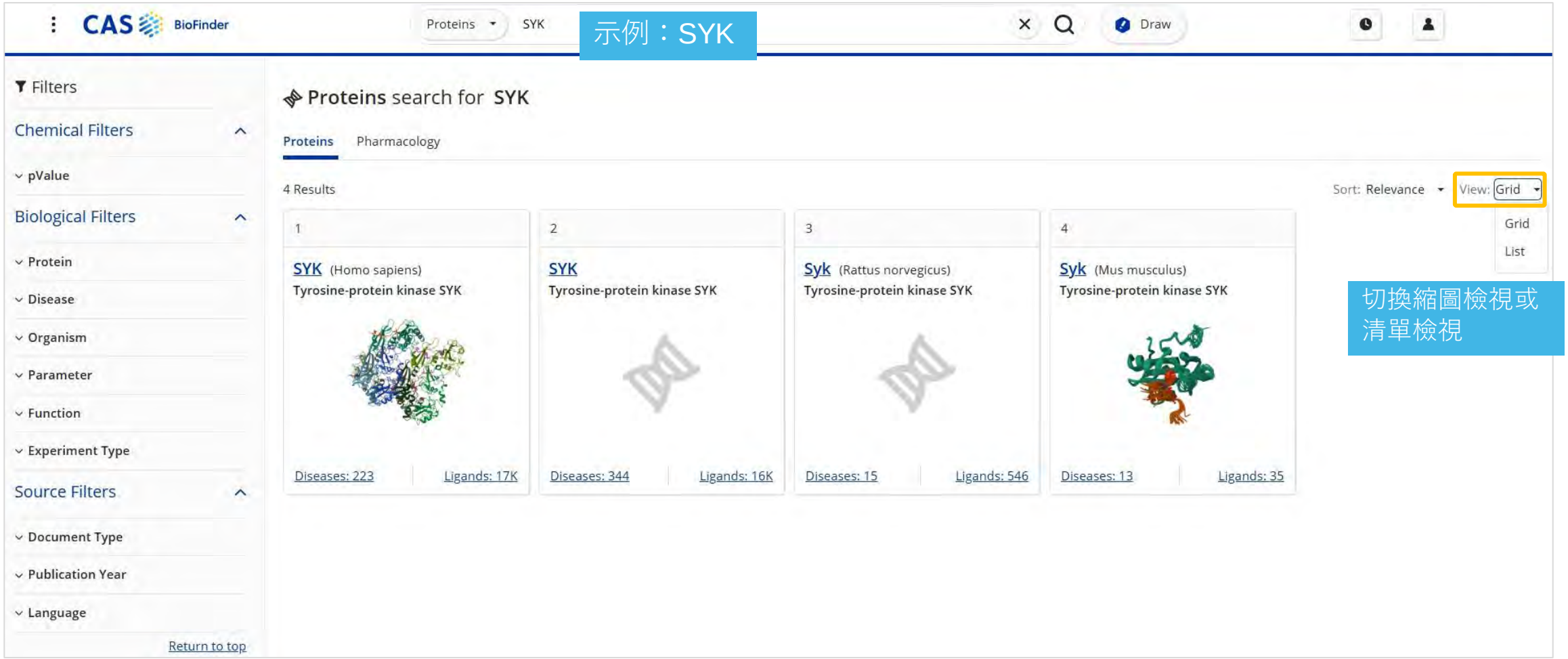
大綱

- CAS BioFinder簡介與檢界面介紹（介紹與介面）
- 配體檢索與配體詳情信息（配體與細節概述）
- 骨架檢索與構效關係分析（支架與搜救分析）
- **蛋白/通路/靶點、疾病與生物標誌物（Proteins and Pathways; 疾病與生物標記）**
- 生物活性預測（Predictive Analytics）

通過靶點、疾病或配體，獲取歸一化的蛋白檢索結果



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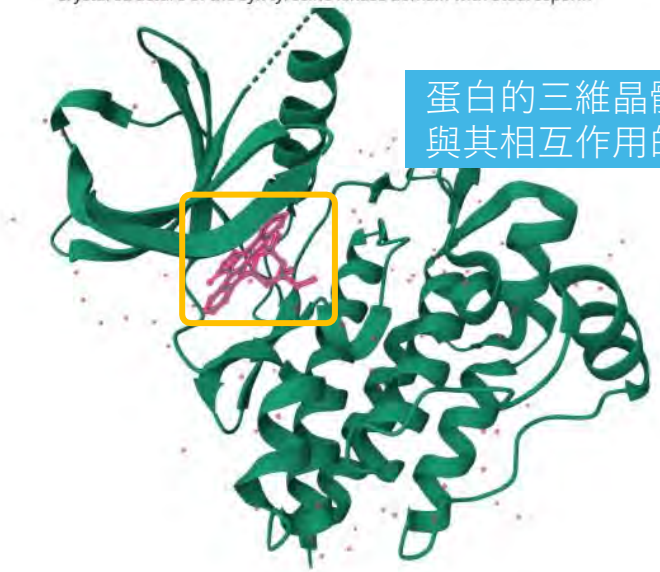
蛋白詳情資訊與立體結構展示

SYK
Tyrosine-protein kinase SYK

Summary | Pharmacology | Ligands (31K) | Diseases (388) | Chemical Space | Pathways

Crystal structure of the syk tyrosine kinase domain with Staurosporin



蛋白的三維晶體結構及
與其相互作用的小分子

STAUROSPORINE
1XBC | Model 1 | Instance ASM_1 | B [auth A] | STU 1

1XBC 下載cif格式結構檔

Homo sapiens
unspecified
Rattus norvegicus
Mus musculus

來源有機體

Organism
Homo sapiens | GET FASTA | Copy Sequence

>P43405-1|Tyrosine-protein kinase SYK|Homo sapiens
MASSGMADSANHLPFFFGNITREEAEDYLVQGGMSDGLYLLRQSRNYLGGFALSVAHGRKAHHYTIERELNGTYAIAGGRTHASPADLCHYHSQESDGLVCLLKKPFNRPQGVQPK
TGPFEDLKENLIREYVKQTWNLQGQALEQAIISQKPQLEKLIATTAHEKMPWFHGKISREESEQIVLIGSKTNGKFLIRARDNNGSYALCLLHEGKVLHYRIDKDKTGKLSIPEGK
KFDTLWQLVEHYSYKADGLLRVLTVPCQKIGTQGNVNFGGRPQLPGSHPATWSAGGIISRIKSYSFPKPGHRKSSPAQGNRQESTVSFNPYEPELAPWAADKGPQREALPMDTEVY
ESPYADPEEIRPKEVYLDRKLLTLEDKELGSGNFGTVKKGYYQMKKVVKTVAVKILKNEANDPALKDELLAEANVMQQLDNPYIVRMIGICEAESWMLVMEMAELGPLNKYLQQNR
HVKDKNIIELVHQVSMGMKYLEESNFVHRDLAARNVLLVTQHYAKISDFGLSKALRADENYYKAQTHGKWPVKWYAPECINYYKFSSKSDVWSFGVLMWEAFSYGQKPYRGMKGSE
VTAMLEKGERMGCPAGCPREMYDLMNLCWTYDVENRPGFAAVELRLRNYYYDVVN

序列詳情

Identifier	Method	Resolution	Chain	Positions	Source
1A81	X-Ray	3.0 Å	A/C/E/G/I/K	9 - 262	PDB
1CSY	NMR	-	A	163 - 265	PDB
1CSZ	NMR	-	A	163 - 265	PDB
1XBA	X-Ray	2.00 Å	A	353 - 635	PDB
1XBB	X-Ray	1.57 Å	A	353 - 635	PDB
1XBC	X-Ray	2.00 Å	A	353 - 635	PDB
3BUW	X-Ray	1.450 Å	A/C	317 - 329	PDB
				349 - 635	PDB

歸一化的靶點名稱
與其他詳情資訊

Synonyms

Spleen associated tyrosine kinase
Spleen tyrosine kinase

External Links and Identifiers

Alliance of Genome Resources: HGNC:11491
CHEMBL: CHEMBL2599
Ensembl gene: ENSG00000165025.15, ENSG00000165025
HGNC: HGNC:11491
NCBI Gene: 6850
OMIM: 600085
Uniprot reviewed: P43405
View Less

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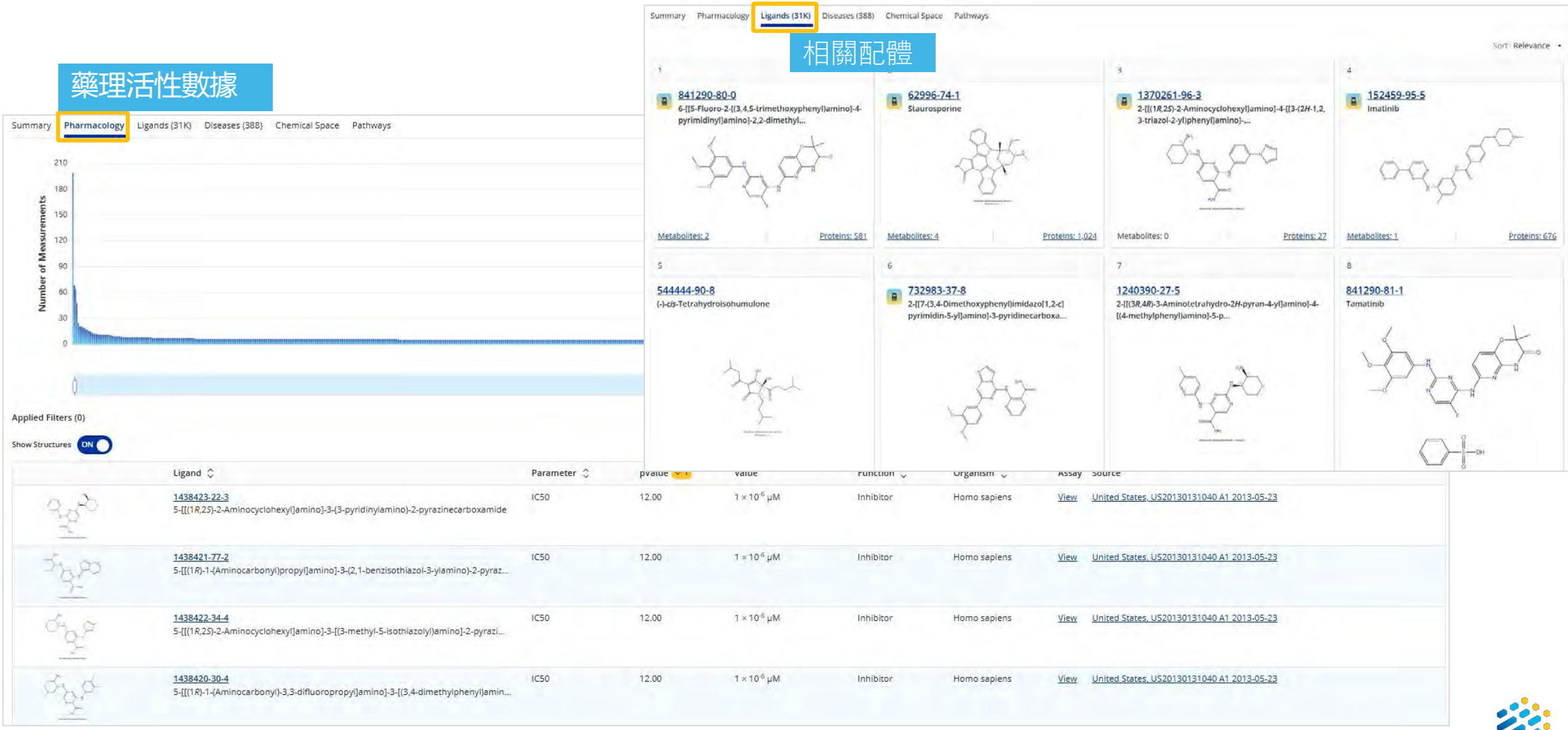
相關配體與藥理活性數據



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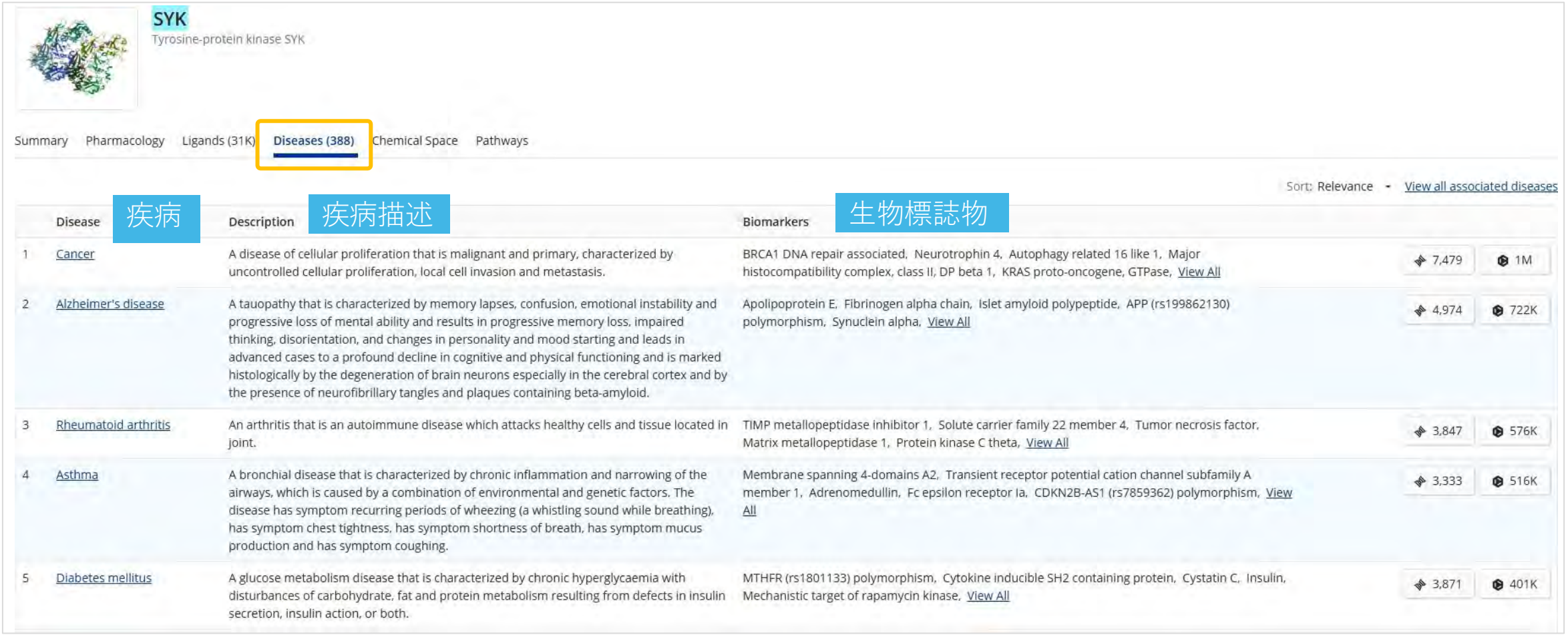
蛋白相關疾病資訊



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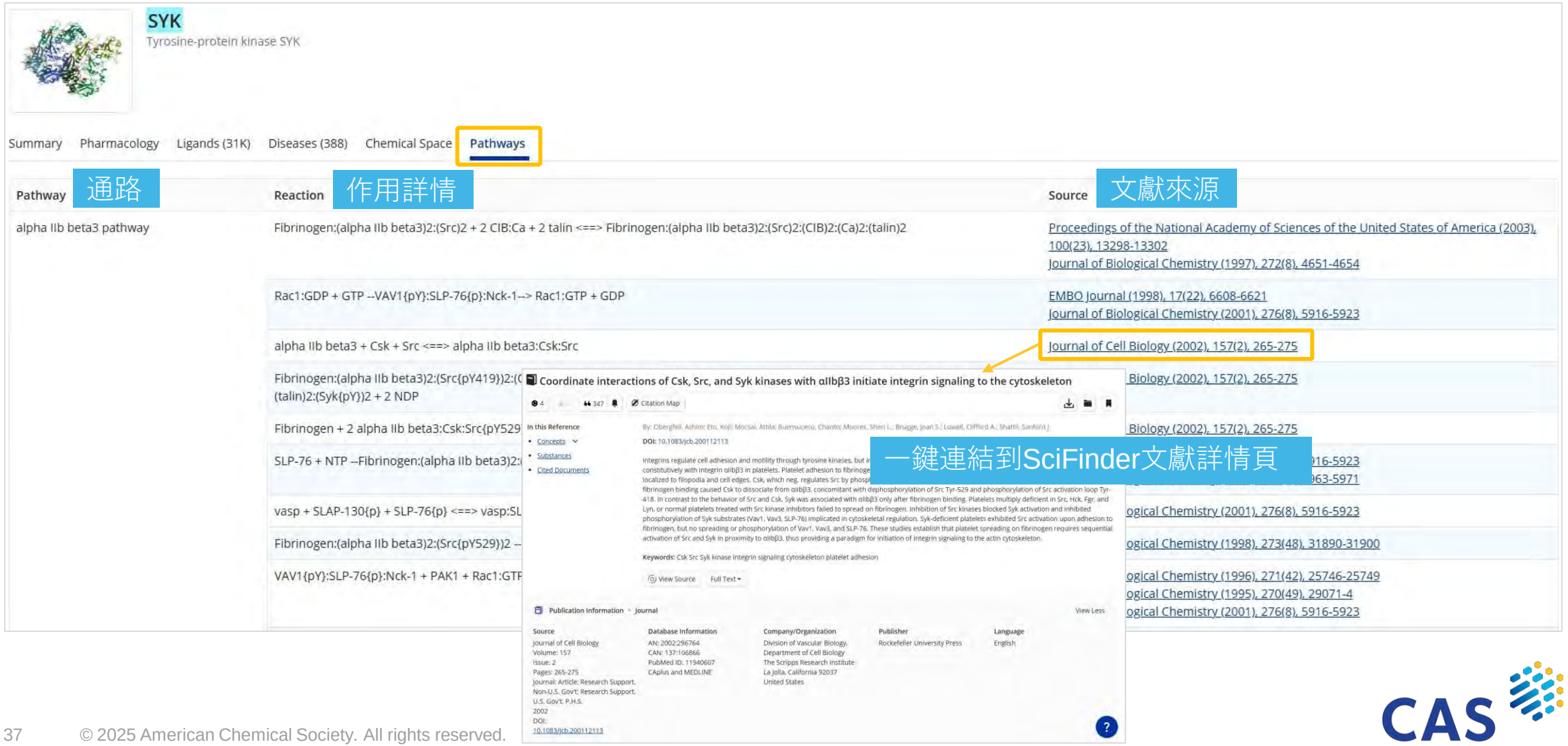
蛋白的生物通路資訊



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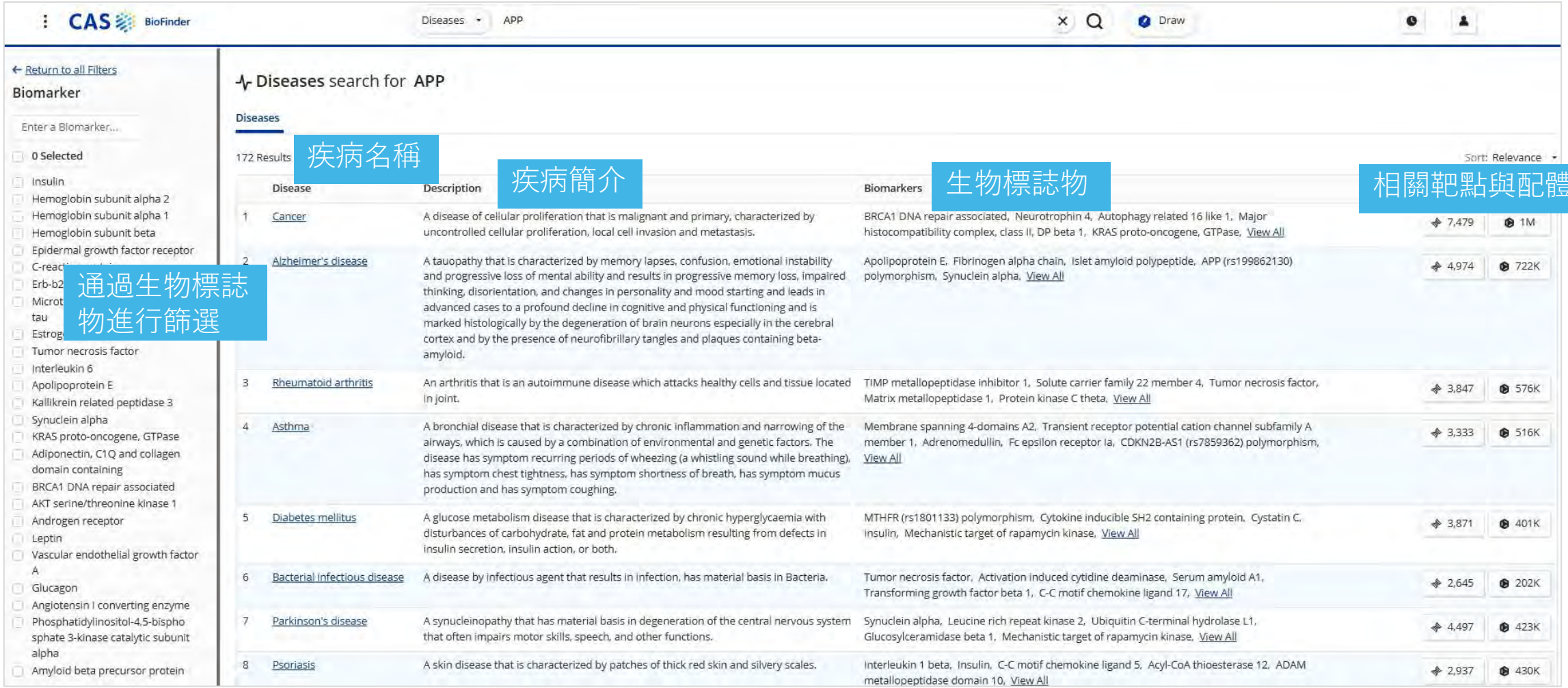
通過疾病名稱、靶點或配體檢索相關疾病資訊



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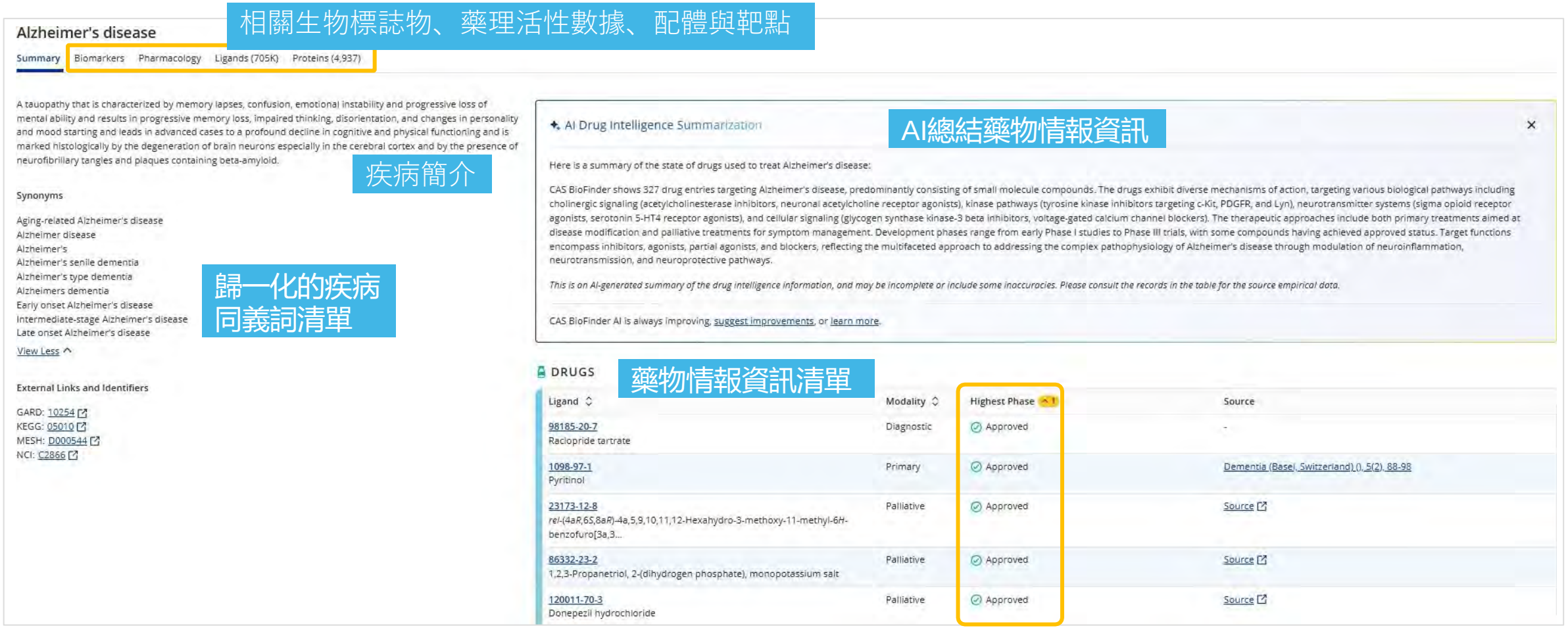
疾病詳情頁與相關藥物資訊



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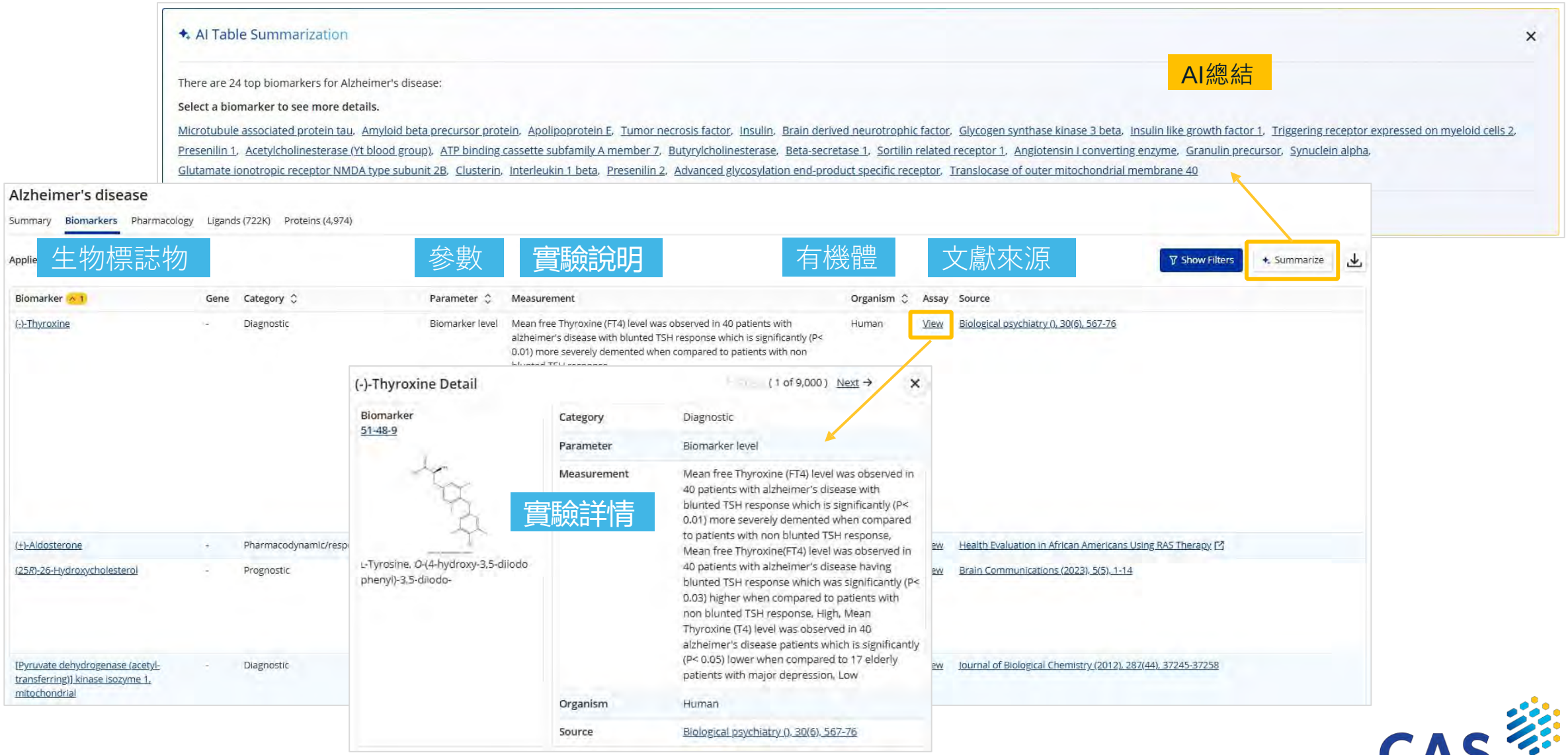
疾病與生物標誌物



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- **生物活性預測（Predictive Analytics）**

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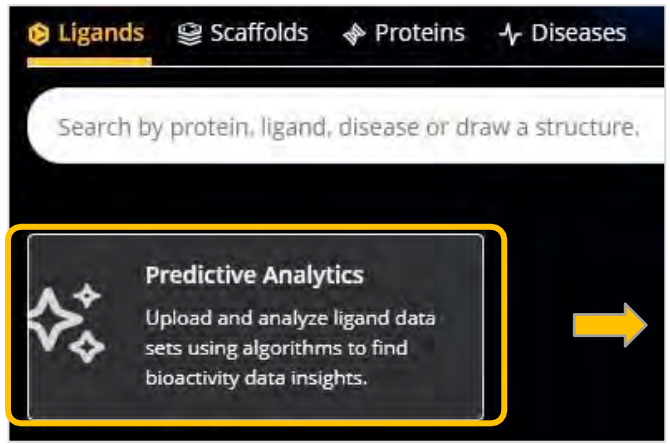
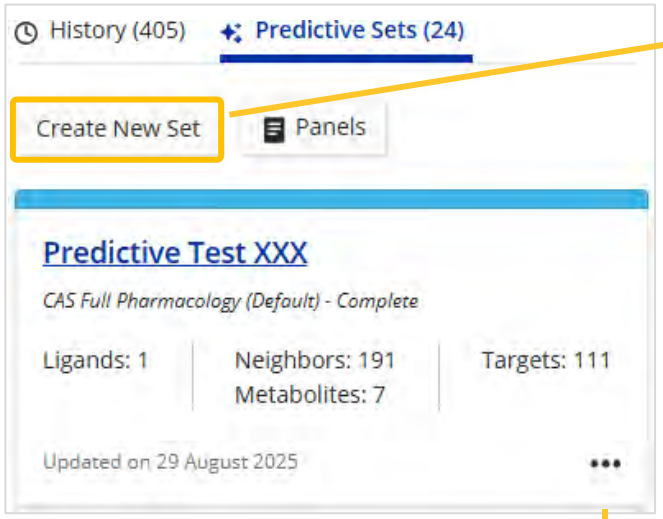
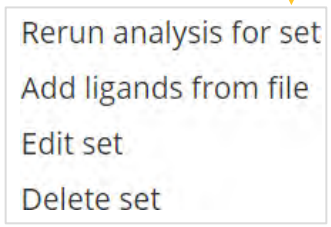
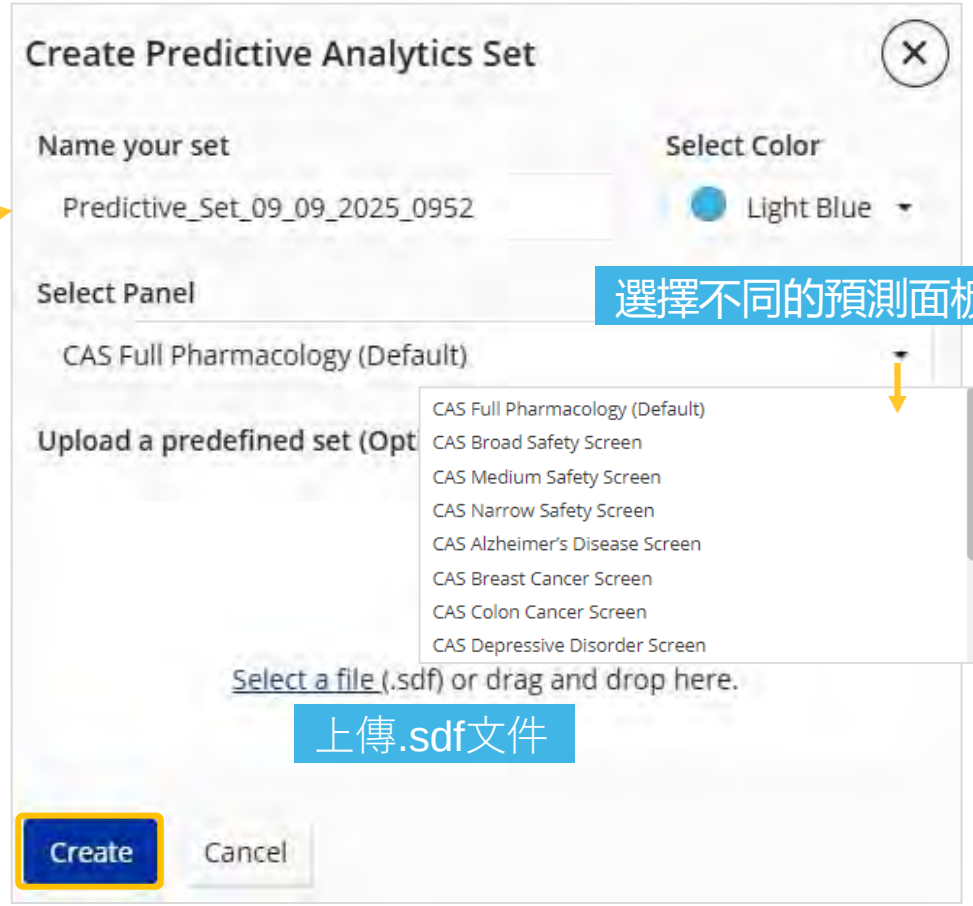
Predictive Analytics：通過演算法預測配體對不同靶點的生物活性數據









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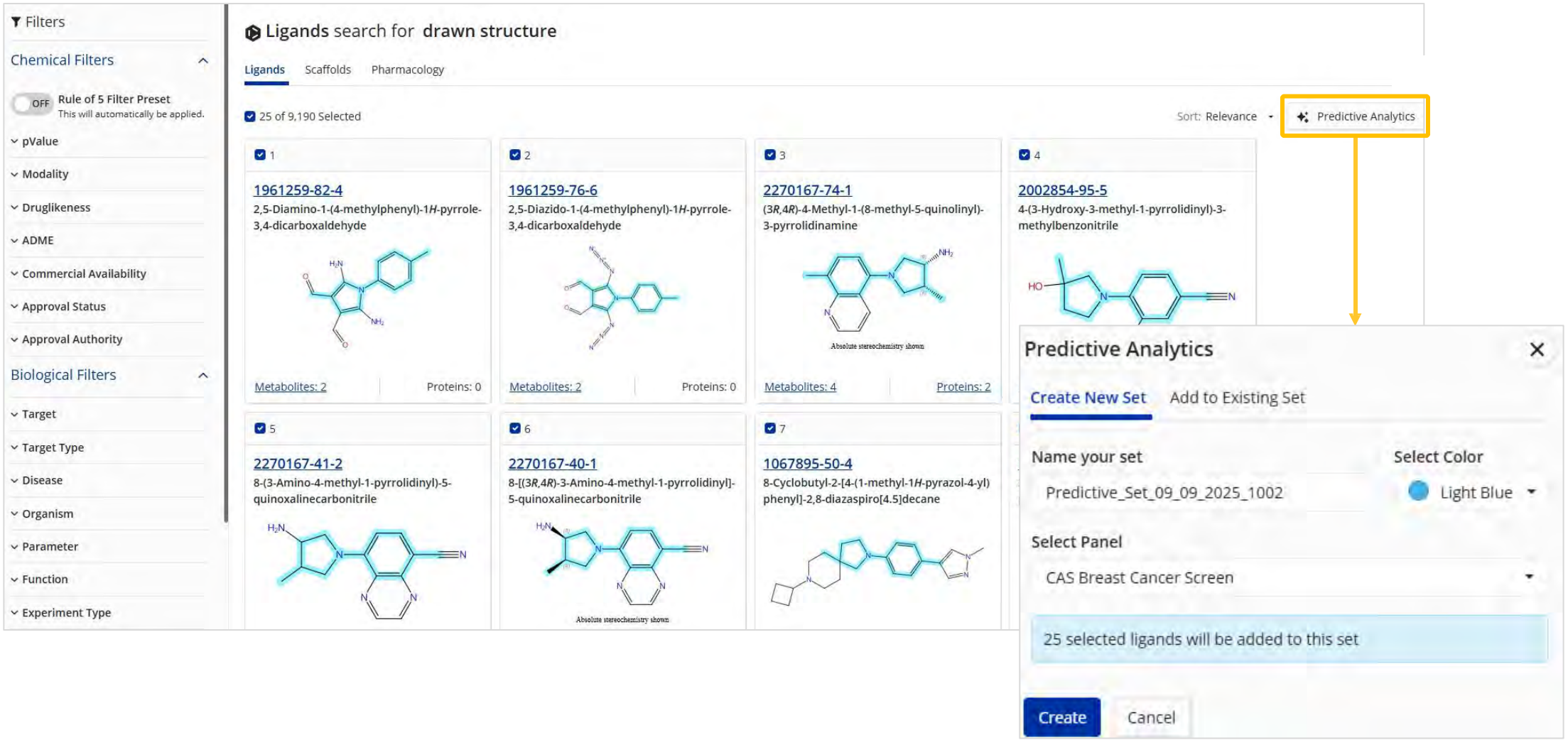
可從檢索結果集中添加配體結構



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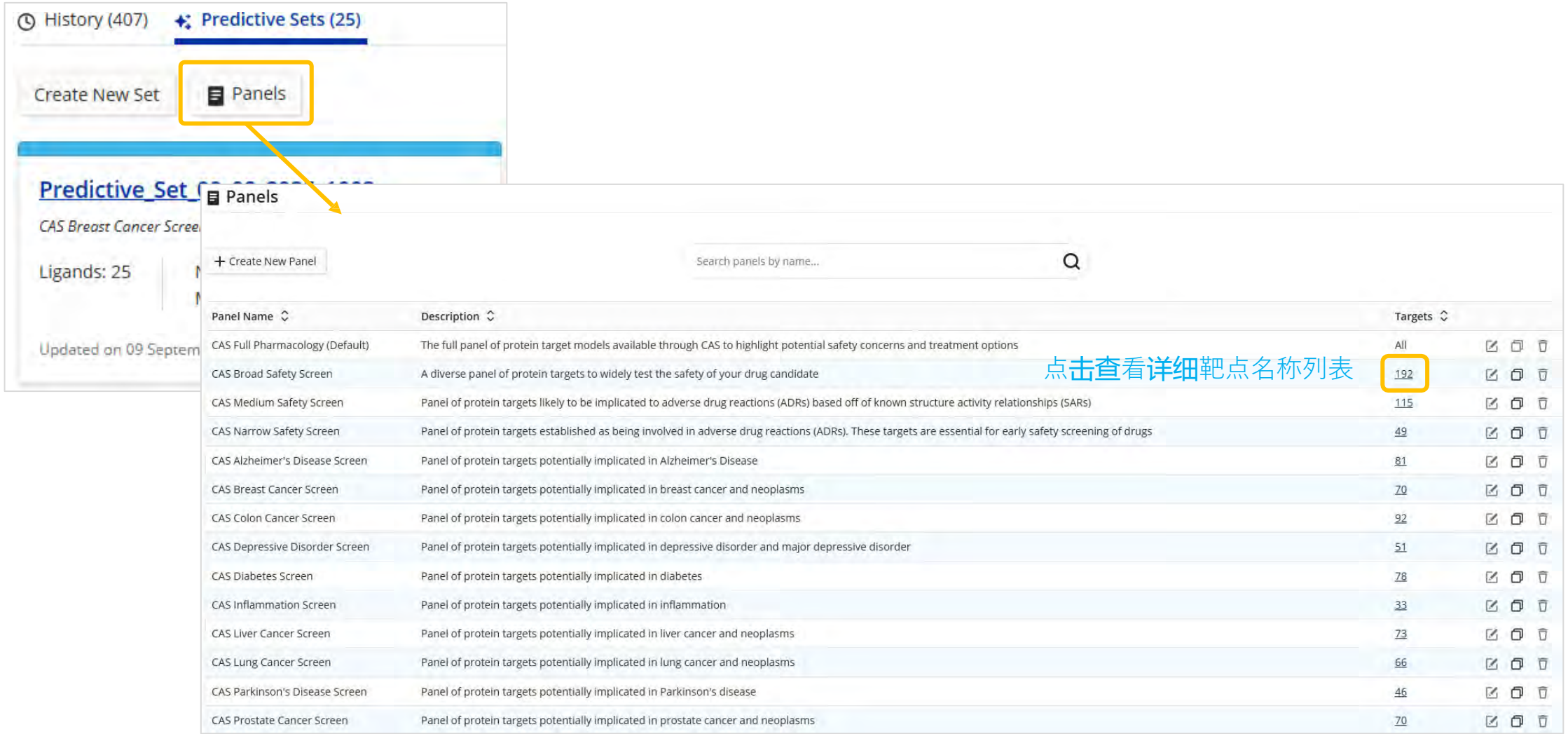
不同的蛋白靶點面板說明



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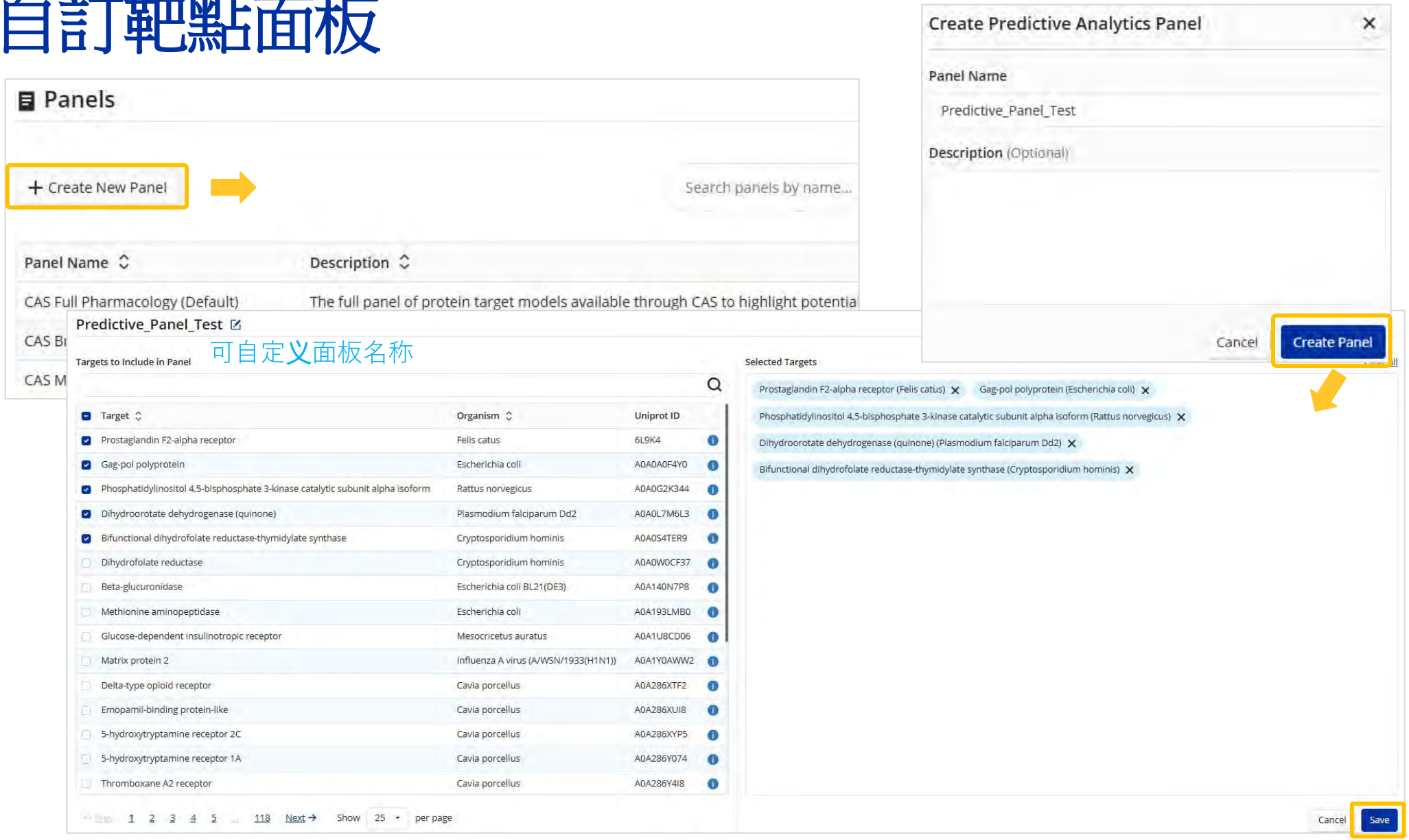
自訂靶點面板



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生物活性預測結果

使用左側篩選功能可對這些數據進行細化分析：

- 活性值(pActivity)
- 置信度分數(Confidence score)
- 靶點(Target)
- 有機體(Organism)

助於探索特定範圍內的pAct, 或有較高可信度的預測資訊。

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總結

配體檢索 (Ligands)

- 基於藥物名稱、CAS RN、結構、靶點、疾病等，獲取配體資訊
- 通過類藥性、ADME、實驗參數、藥物功能、生物有機體等，進行篩選聚焦
- **查看並評估化合物的藥理學、ADME、毒理學和代謝物資訊及可視化展示**

骨架檢索(Scaffolds)

- 基於結構或靶點等資訊，高效獲取相關骨架結構，並通過官能團R-Groups，進行構效關係分
- 通過 SAR 以及MMPA，優化目標骨架或先導化合物的效力和選擇性
- 探索針對關注靶點同一結構骨架中活性最高的配體，獲取相似骨架結構與拓展

蛋白/通路/靶點與疾病檢索(Proteins & Diseases)

- 高效獲取蛋白質通路/靶點與疾病生物標誌物資訊，探索藥物作用機制和適應症

預測配體 與不同靶點的生物活性(Predictive Analytics)

- **預測特定結構針對特定靶點的藥理活性資訊**
- 關注配體的脫靶效應與藥物再利用

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相關資源Learn More

https://biofinder.cas.org/

獲取CAS BioFinder登錄訪問網址

https://www.cas.org/solutions/biofinder-discovery-platform

瞭解更多關於CAS BioFinder的資訊

https://cas-biofinder.zendesk.com/hc/en-us

獲取CAS BioFinder使用說明資訊

獲取更多技術支援與說明，請聯繫：tliu2@acs-i.org

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Between problems and progress are connections that matter

謝謝！

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