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# Reaxys & Reaxys Medicinal Chemistry

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Science & Technology Policy Research and Information Center





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## OUR SHARED PURPOSE

TO ACCELERATE  
SCIENCE TO  
IMPROVE HEALTH

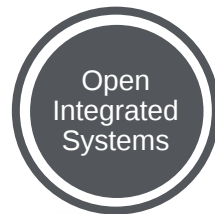
A Knowledge & Information  
Analytics Company



## OUR PROMISE

Partners in propelling research  
and innovation forward to  
transform the way you bring  
new medicines to the world

## OUR KEY DIFFERENTIATORS



**140+**

years of scientific  
knowledge curated as  
semantically rich content to  
enable tomorrow's medical  
breakthroughs

**RELX**

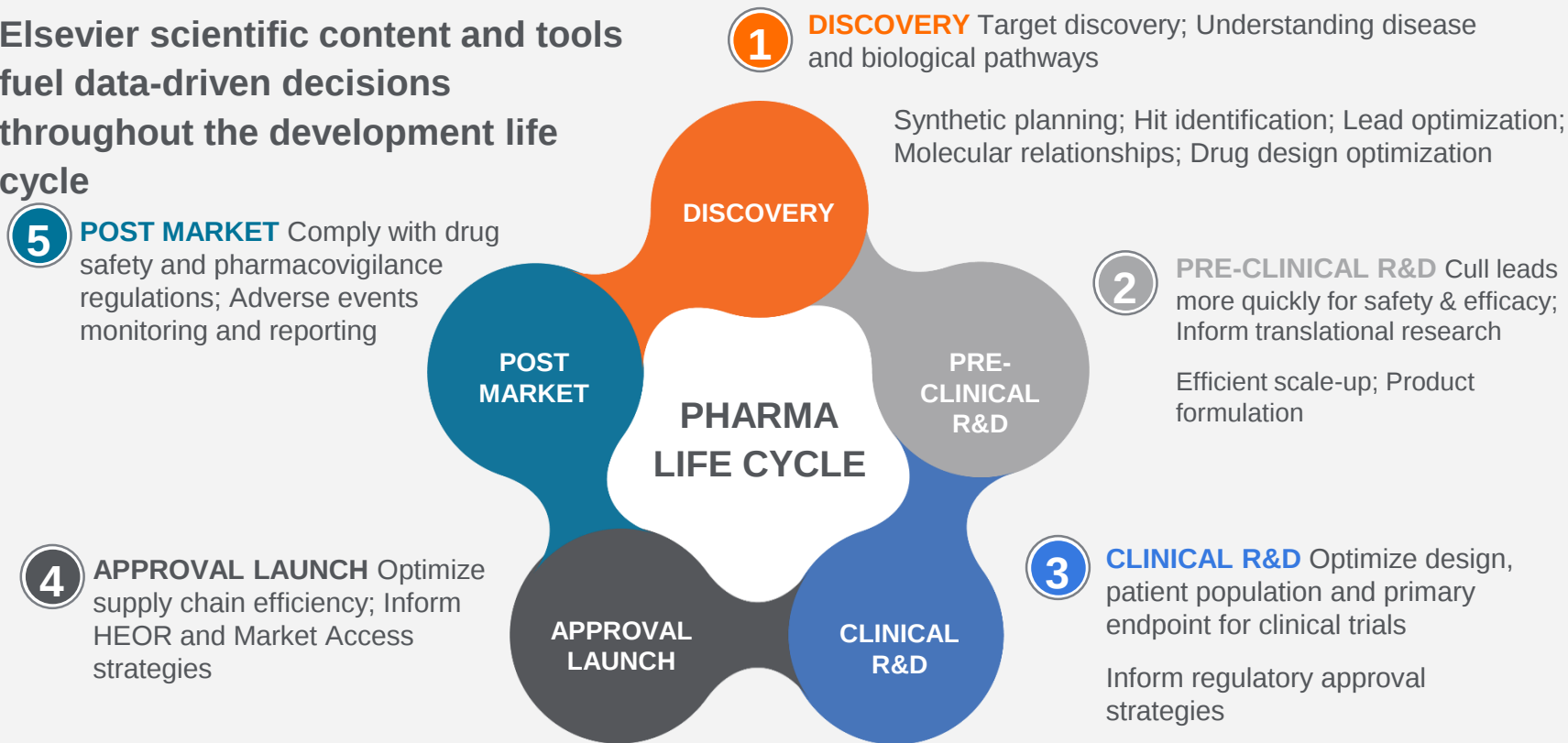
**\$1.4bn**  
on technology annually

**~30,000**  
employees

Serving customers in  
**180+**  
**countries**

Partnering with  
**90%**  
of top Pharma  
companies

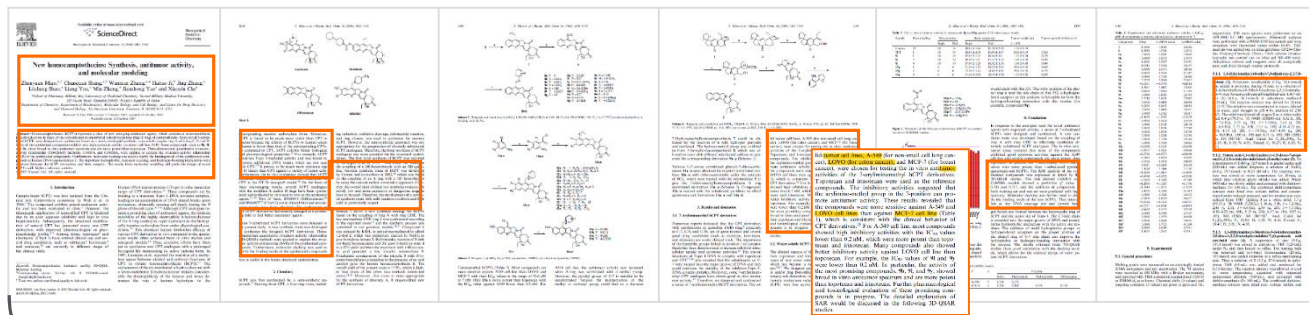
# Elsevier scientific content and tools fuel data-driven decisions throughout the development life cycle



# Agenda

1. Why should you log in to Reaxys?
2. Quick Search (Search by text)
3. Structure Search
4. Query Builder (e.g. Natural compounds searches)
5. Synthesis Planer
6. Structural Activity Relationship (<sup>New!</sup>RMC module) (e.g. Real pharmaceutical case)

# Reaxys索引的內容—文獻內容



Reaxys提煉了文獻的書目資訊，摘要，題錄，並用不同角度的索引詞對文獻內容進行描述。

bibliographic

New homocamptothecins: Synthesis, antitumor activity, and molecular modeling Cited 23 times

Miao, Zhenyuan; Sheng, Chunqun; Zhang, Wannian; Ji, Haitao; Zhang, Jing; Shao, Luecheng; You, Liang; Zhang, Min; Yao, Jianzhong; Che, Xiaoyin - *Bioorganic and Medicinal Chemistry*, 2008, vol. 16, # 3, p. 1493 - 1510

Abstract Index Terms Substances (324) Reactions (78) Full Text

## Abstract

Homocamptothecins (hCPTs) represent a class of new emerging antitumor agents, which contains a seven-membered  $\beta$ -hydroxylactone in place of the conventional six-membered  $\alpha$ -hydroxylactone ring (E ring) of camptothecins. Some novel 7-substituted hCPTs were designed and synthesized based on a newly developed synthetic route which couples ring A with ring C, E and D. Most of the synthesized compounds exhibit very high cytotoxic activity on tumor cell line A549. Some compounds, such as 9b, 9l, and 9y, show broad in vitro antitumor spectrum and are more potent than topotecan. Three-dimensional quantitative structure-activity relationship (3D-QSAR) methods, CoMFA and CoMSIA, were applied to explain the structure-activity relationship (SAR) of the synthesized compounds. Furthermore, molecular docking was used to clarify the binding mode of the synthesized compounds to human DNA topoisomerase I. The important hydrophobic, base-pair stacking, and hydrogen-bonding interactions were observed between the hCPT derivatives and their receptor. The results from molecular modeling will guide the design of novel hCPTs with higher antitumor activity.

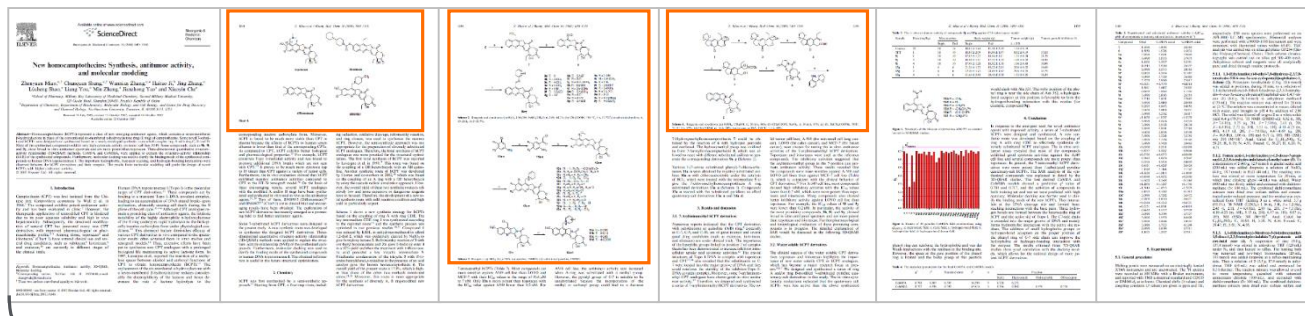
## Index terms

EMTREE drug term: 10 methyl 11 chloro 7 (pyridiniummethyl)homocamptothecin chloride, 7 (2 bromophenyl)iminomethylmethoxyphenyl)iminomethylhomocamptothecin, 7 (2 methylphenyl)iminomethylhomocamptothecin, 7 (2,4 dichlorophenyl)dichlorophenyl)iminomethylhomocamptothecin, 7 (3 chloro 4 fluorophenyl)iminomethylhomocamptothecin, 7 (3 chloro 4 fluorophenyl)iminomethylhomocamptothecin, 7 (3 methylphenyl)iminomethylhomocamptothecin, 7 (3,4 dichlorophenyl)iminomethylphenyl)iminomethylhomocamptothecin, 7 (3,5 dichlorophenyl)iminomethylhomocamptothecin, 7 (3,5 dimethylphenyl)chlorophenyl)iminomethylhomocamptothecin, 7 (4 cyanophenyl)iminomethylhomocamptothecin, 7 (4 methylphenyl)iminomethylphenyl)iminomethylhomocamptothecin, antineoplastic agent, camptothecin derivative, irinotecan, topotecan, unclassified drug  
EMTREE medical term: animal experiment, animal model, antineoplastic activity, article, colon cancer, comparative molecule protein binding, drug structure, drug synthesis, human, human cell, hydrogen bond, hydrophobicity, male, molecular docking, tumor cell line

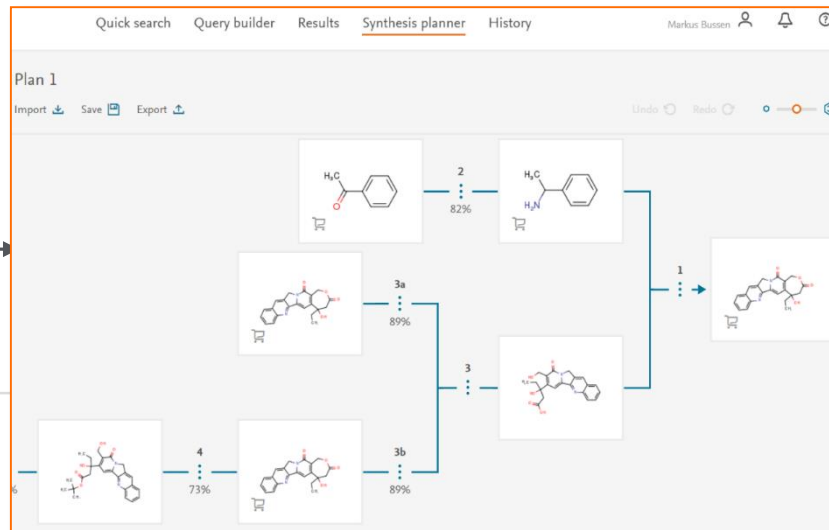
Author keywords: 3D  
Reaxys Index Terms: **tumor cell line** homocamptothecins, Molecular docking hydrophobic surface

Manual [digital] Indexing

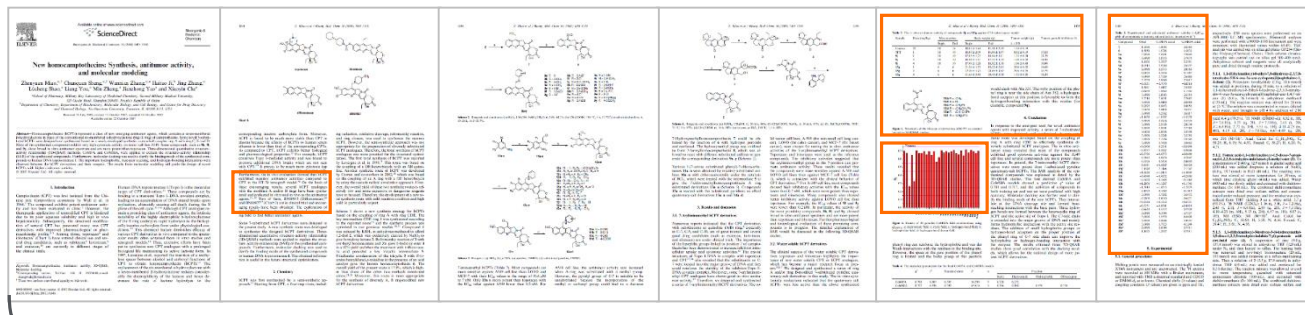
# Reaxys索引的內容—結構與反應



Reaxys的反應記錄，抽提了所有相關的資料，包括收率，催化劑，溶劑，反應類型等



# Reaxys索引的內容—文獻中的資料



Reaxys的物性記錄，抽提了超過500中不同的物性實驗資料，生物活性資料，環境資料，以及譜圖資料等等

Reaxys interface showing search results for **camptothecin** (C20H14N2O4, 348.358, 6075662, 7689-03-4). The interface includes a sidebar with filters and analysis options, and a main results area with various data categories.

**Filters and Analysis**

- By Structure
- Measurement pX
- Highest Clinical Phases
- Targets
- Parameters
- Substance Classes
- Molecular Weight
- Availability
- Availability in other databases
- Available Data
- Document Type
- Publication Year

**Results for camptothecin**

- Identification
- Bioactivity (All)
- Spectra - 139
- Preparations - 221
- Reactions - 1,112
- Targets - 142
- Documents - 3,556

**camptothecin**

- Identification
- Druglikeness
- Bioactivity (All)
- Physical Data - 132
- Spectra - 139
- Other Data - 1,527

# What is Reaxys?

- 化學研究不可缺少之「數據」資料庫
- 從化學相關論文及專利萃取有用必要的「數據」

## Reaxys®



**>118 Million**  
有機、無機及有  
機金屬物質  
**>500 Million**  
公開實驗數據  
(物性、光譜、  
生物活性等)

**>49 Million**  
化學反應(反應條件、  
溶劑、催化劑及產  
率等)

**>54 M 文獻記錄**  
**>16,000 期刊，專利**  
涉及有機化學，材料  
化學，生物醫藥，地  
球科學，工程等多種  
領域

## Reaxys® Medicinal Chemistry



**>20,000 藥物作用標的**  
**>33 M 生物活性資料點**  
結構活性關係資料  
動物活體細胞研究  
細胞外療效  
藥物動力學  
毒性資料  
安全性資料

# Reaxys core philosophy “Using information” not “searching for information”



Delivering lists of references that may be relevant to a query...

The screenshot displays a chemical reaction between acetic acid and aspirin, followed by a table of similar reactions and a list of references.

**Chemical Reaction:**

CC(=O)O.CC(=O)Oc1ccc(cc1)OC(=O)c2ccccc2>>CC(=O)Oc1ccc(cc1)OC(=O)c2ccccc2

**Find Similar Reactions**

| Yield | Conditions                                                                                                                                                                                           |
|-------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 90.8% | Stage #1: 3-(diethylamino) With O-benzotriazol-1-yl-luronium tetrafluoroborate in acetonitrile at 20°C for 3h<br>Stage #2: acetic acid in a<br>Stage #3: acetic acid in d<br>Experimental Procedures |

**Physical Data - 532**

| Dissociation Exponent (pK) | Dissociation Group | Relevance |
|----------------------------|--------------------|-----------|
| 3.48                       | RCOO-H             | 25        |
| 3.47                       |                    | 25        |
| 3.55                       | COOH               | 10        |
| 3.8                        | COOH               | 25        |

**References:**

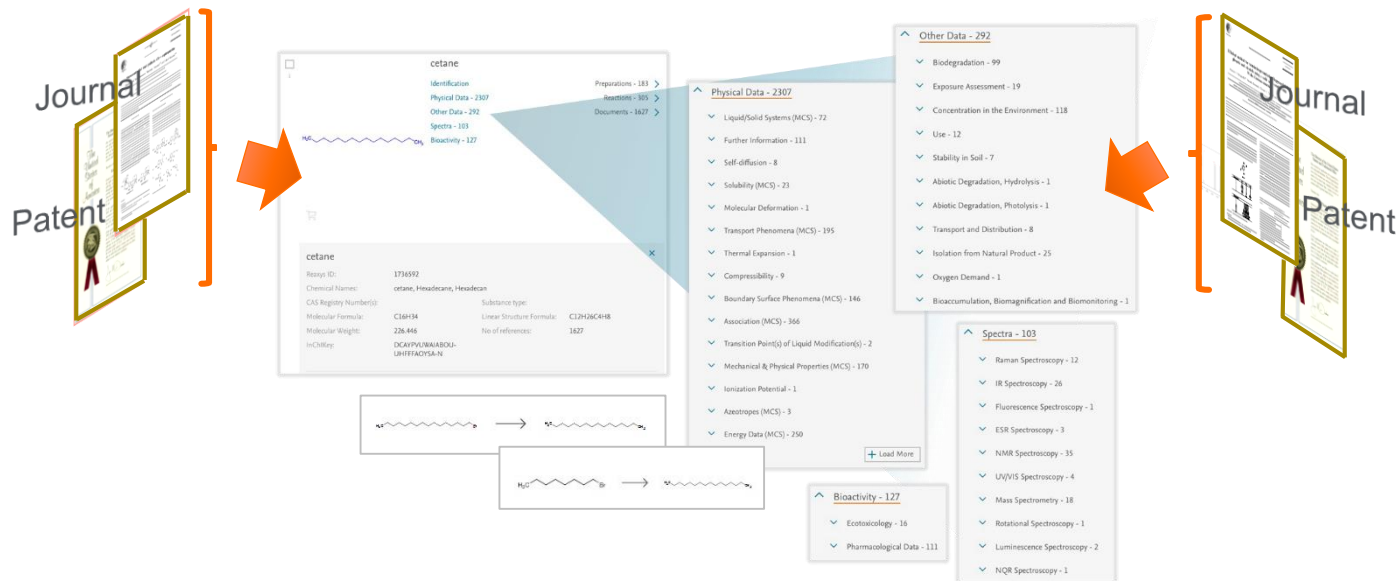
- ☐ Lyophilized **aspirin** with trehalose may decrease the incidence of gastric injuries in healthy dogs Cited 1 times  
Lin, Lee-Shuan; Kayasuga, Yoko; Shimohata, Nobuyuki; +6 others - Journal of Veterinary Medical Science, 2012, vol. 74, # 11, p. 1511 - 1516  
Abstract Index Terms Full Text
- ☐ Incidence of **aspirin** resistance in the patient group of a university hospital in Korea Cited 6 times  
Lee, Young Kyung; Kim, Han-Sung; Park, Ji-Young; +1 other - Korean Journal of Laboratory Medicine, 2008, vol. 28, # 4, p. 251 - 257  
Abstract Index Terms Full Text
- ☐ Increased platelet expression of glycoprotein IIIa following **aspirin** treatment in **aspirin**-resistant but not **aspirin**-sensitive subjects Cited 3 times  
Floyd, Christopher N.; Goodman, Timothy; Becker, Silke; +7 others - British Journal of Clinical Pharmacology, 2014, vol. 78, # 2, p. 320 - 328  
Abstract Index Terms Full Text

Deliver relevant answers on the spot:

- References ranked by relevance
- Reactions with experimental details
- Substances with extensive properties

# Reaxys的資料結構

- 從多個資料來源將化合物及反應彙整到1筆紀錄
- 並且保留資料來源的連結



# How do you get access to Reaxys

Go to <http://reaxys.com>

Reaxys®

Quick search

Query builder <sup>New</sup>

Results

Synthesis planner

History

Alerts

Ryan Huang  

Search for 184475-35-2

Import 

Search Reaxys

184475-35-2

×

Find >

Documents, e.g. published by Schrock

AND

 Draw

Content Overview | Latest update: 11. September 2019 >

118M

 Substances

49M

 Reactions

59M

 Documents

37M

 Bioactivities

1.5M

 Targets

# 免費帳號申請

Reaxys<sup>®</sup>

[Quick search](#) [Query builder](#) <sup>New</sup> [Results](#) [Synthesis planner](#) [History](#) [Alerts](#)

Ryan Huang



Search for 184475-35-2

Your IP: 198.176.125.21 X

## Create account

First Name

Last Name

Email address

Password

Confirm password

- ☒ Remember me on this computer  
(Do not use on a shared computer!)
- ☐ Stay informed about Elsevier products and services
- ☐ I have read and agree to the [Registered User Agreement](#)

Register >

- 儲存、管理搜尋結果
- 被動接收更新內容

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# Quick Search

Reaxys®

Quick search

Query builder <sup>New</sup>

Results

Synthesis planner

History

Alerts

Ryan Huang



Search for 184475-35-2

Import

Search Reaxys

184475-35-2



Find >

Documents, e.g. published by Schrock

AND



Draw

For **Quick Search**,  
1. Enter a search phrase  
2. Draw a structure

- 物質名稱, Gefitinib
- 反應名稱, Wittig Reaction
- 物質理化性質, Solubility of Gefitinib
- 物質的圖譜, NMR of Gefitinib
- 分子式, C<sub>22</sub>H<sub>24</sub>ClFN<sub>4</sub>O<sub>3</sub>
- 反應類型, Substitution
- 關鍵字, Iressa

Content Overview | Latest update: 11. September 2019 >

118M

Substances

49M

Reactions

59M

Documents

37M

Bioactivities

1.5M

Targets

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# Quick Search - 範例一

The screenshot displays the Reaxys Quick Search interface. At the top, the Reaxys logo is on the left, and navigation links for Quick search, Query builder, Results, Synthesis planner, History, and Alerts are in the center. A user profile for Ryan Huang is on the right. Below the navigation bar, a search bar contains the text "Search for gefitinib" with an "Import" button to its right. A dropdown menu titled "Search Reaxys" is open, showing a list of suggestions: "gefitinib", "Chemical Names", "gefitinib", and "gefitinib hydrochloride". A "Find" button is to the right of the dropdown. Below the search bar, a large red text box contains the text: "\* First generation of EGFR Tyrosine kinase inhibitor". At the bottom of the page, a "Content Overview" section shows statistics: 118M Substances, 49M Reactions, 59M Documents, 37M Bioactivities, and 1.5M Targets. The latest update is noted as 11. September 2019.

Reaxys

Quick search Query builder<sup>New</sup> Results Synthesis planner History Alerts

Ryan Huang

Search for **gefitinib** Import

Search Reaxys

gefitinib

Find

Chemical Names

gefitinib

gefitinib hydrochloride

\* First generation of EGFR Tyrosine kinase inhibitor

Content Overview | Latest update: 11. September 2019

118M 49M 59M 37M 1.5M

Substances Reactions Documents Bioactivities Targets

# Quick Search – Preview Page

Reaxys®

Quick search Query builder <sup>New</sup> Results Synthesis planner History Alerts

Ryan Huang  

Results for gefitinib

New  Edit 

搜尋新物質

修正搜尋

前往搜尋結果

預覽3筆資訊

|                                                                                   |        |            |                                                                                                                                                                                                                                                                                                                       |                                                                                                     |                |
|-----------------------------------------------------------------------------------|--------|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|----------------|
|  | 380    | Substances | Structure :  as drawn<br>Edit in Query Builder  Create Alert       | Preview Results  | View Results > |
|  | 22,353 | Documents  | Titles, Abstracts, Keywords : "gefitinib"<br>Edit in Query Builder  Create Alert                                                                    | Preview Results  | View Results > |
|  | 18     | Reactions  | Reaction Query :  as drawn<br>Edit in Query Builder  Create Alert  | Preview Results  | View Results > |
|  | 7      | Targets    | Structure :  as drawn<br>Edit in Query Builder  Create Alert       | Preview Results  | View Results > |

# Results Page

重新搜尋

Reaxys®

Quick search Query builder <sup>New</sup> Results Synthesis planner History Alerts

Ryan Huang

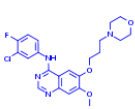
380 <sup>New</sup> Filters

0 selected Limit To Exclude Export Preparations

Sort by No of References ↓ Grid Heatmap

380 Substances out of 6,886 Documents, containing 179 Reactions, 1,100 Targets

**1**

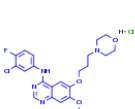


**gefitinib**  
C22H24N4ClFO3 446.909 8949523 184475-35-2

Identification Bioactivity (All) Spectra - 74  
Druglikeness Physical Data - 95 Other Data - 3,181

Preparations - 83 >  
Reactions - 127 >  
Targets - 1,078 >  
Documents - 6,861 >

**2**

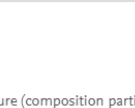


**Gefitinib hydrochloride**  
C22H24ClFN4O3\*ClH 483.37 14998854 184475-55-6

Identification Bioactivity (All) Spectra - 1  
Druglikeness Physical Data - 1

Preparations - 1 >  
Reactions - 2 >  
Targets - 3 >  
Documents - 6 >

**3**



**Reaxys ID: 28938758**  
28938758

Identification Documents - 5 >

mixture (composition partially given)

# Hands on #1

1. 請試著創造帳號並登入
2. 以Quick Search功能搜尋以下物質的溶解度

- Morphin

- $C_{17}H_{19}NO_3$

- CAS # 57-27-2

- Roxanol

**Pentoxifylline**

# Structure Search



# Reaxys中Marvin JS結構編輯器使用

Structure editor ChemAxon's MarvinJS ☐

Create structure template from name >

選擇工具，橡皮，鍵定義，鍵，正負電子

重複基團，R基團，R基團連結端，反應定義工具

元素週期表以及常用原子

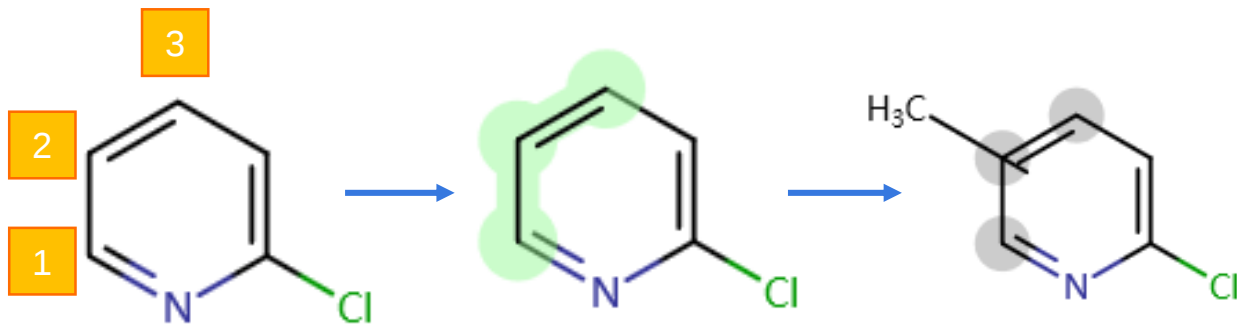
A: 原子屬性定義工具

常見的環

The screenshot shows the MarvinJS structure editor interface. The top bar includes the text 'Structure editor ChemAxon's MarvinJS' and a dropdown menu. Below this is a toolbar with various icons for editing chemical structures. The main workspace is a large white area with the MarvinJS logo and 'by ChemAxon' text. On the right side, there is a vertical toolbar containing a periodic table of elements, with the letter 'A' above it. On the left side, there is a vertical toolbar with various icons for editing chemical structures. At the bottom, there is a horizontal toolbar with various icons for editing chemical structures. Annotations with orange arrows point to specific toolbars and icons, explaining their functions in Chinese. The periodic table on the right is labeled '元素週期表以及常用原子' (Periodic table and common atoms). The 'A' above it is labeled 'A: 原子屬性定義工具' (A: Atomic property definition tool). The left toolbar is labeled '選擇工具，橡皮，鍵定義，鍵，正負電子' (Select tool, eraser, bond definition, bond, positive/negative charge). The bottom toolbar is labeled '重複基團，R基團，R基團連結端，反應定義工具' (Repeat group, R group, R group connection end, reaction definition tool). The bottom horizontal toolbar is labeled '常見的環' (Common rings).

## 不定位取代鍵的使用

- 不定位取代鍵：
  - 在選定的原子上進行基團的連結
  - 可以使用在鏈上，也可以使用在環上



**繪製要求：**

希望1, 2, 3C上存在  
一個NH<sub>2</sub>

**繪製步驟：**

1. 用選擇工具選擇1, 2, 3號C原子,
2. 添加不定位取代, 系統預設添加CH<sub>3</sub>
3. 將CH<sub>3</sub>換成NH<sub>2</sub>

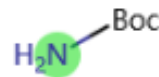
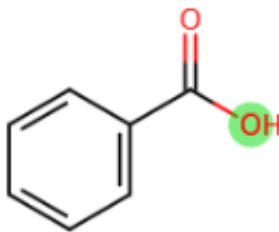
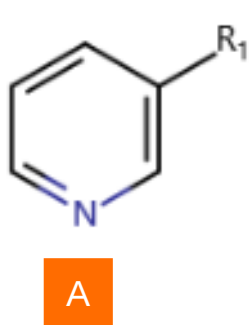
## Not List的應用

- 案例:
  - 定義某位點上不能發生F, Cl, Br, I取代

The image shows a software interface for defining atom lists. On the left, a vertical list contains the following elements: H, C, N, O, S, F, P, Cl, Br. The main window, titled "Periodic table", displays a periodic table with the elements F, Cl, Br, and I highlighted in orange. Below the periodic table, there are two checkboxes: "Atom list" (unchecked) and "NOT list" (checked). An arrow points from the highlighted elements in the periodic table to a chemical structure of pyridine (a six-membered ring with one nitrogen atom). The text "NOT[F, Cl, Br, I]" is written next to the pyridine structure, indicating that these elements are not allowed for substitution at that position.

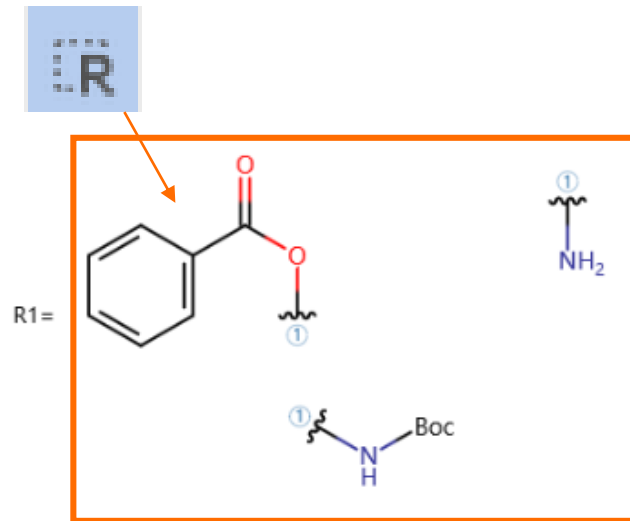
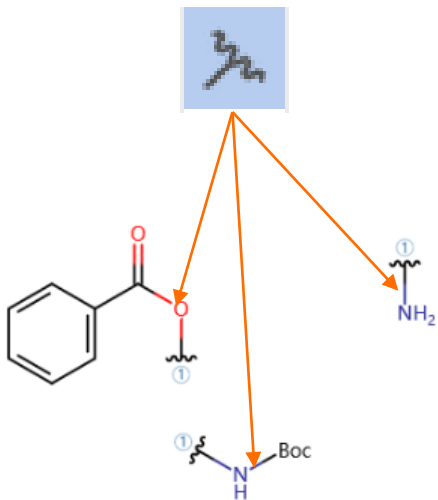
## 自訂R基團

- 案例
  - 定義一個結構A
  - R1分別是下面的這些結構，結構中綠色原子與A結構相連接

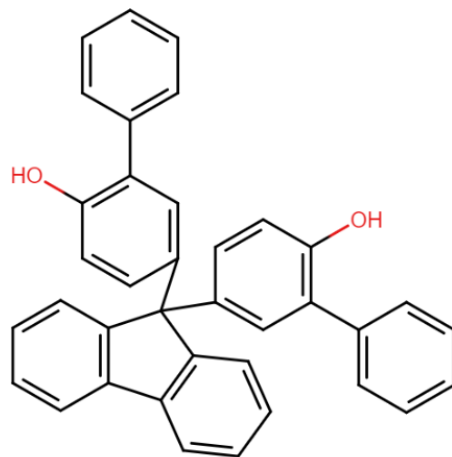


## 繪製方法

- 定義步驟：
  - 使用R基團末端定義工具定義綠色原子
  - 使用R基團定義工具，選擇全部片段，即可完成R1的定義



# Hands on #2



# Query Builder: 查詢範例

- ① 多條件查詢 (天然物、抗菌活性、分子式)
- ② 排除雜訊 (History Crosslink)

# Query Builder查詢範例1(1/4)

## 查詢範例：

是從天然物中萃取出來的化合物，分子式帶有30個碳並具有抗菌效果

- Molecular formular/Natural product/Substance basic index

The screenshot displays the Query Builder interface. At the top, there are icons for Import, Save, Reset form, and Delete. Below these are tabs for Structure, Molecular Formula (highlighted with a red circle), CAS RN, and Doc. Index. A search bar is located at the top right. On the right side, there is a 'Search properties' panel with tabs for Fields, Forms, and History. Under the Fields tab, a list of properties is shown: Reaxys, Basic Indexes, Identification, Chemical Name, Element Symbols, Molecular Formula (highlighted with a red circle), and Molecular Weight. In the main workspace, a 'Molecular Formula' panel is open, showing a dropdown menu with options: 'ends with', 'is' (selected), 'contains', and 'starts with'. The 'is' option is highlighted with a red circle.

- ① 點擊右方的Identification>Molecular Formula
- ② 因為不知道其他成分，選擇"is"，再輸入「C30\*」

## Query Builder查詢範例1(2/4)

The screenshot displays the Query Builder interface. At the top, there is a search bar with the text "Search properties" and "Natural" entered. Below this, a list of search results is shown, including "Isolation from Natural Product" and "Natural Product". In the main query construction area, a dropdown menu is open, showing logical operators: "AND", "OR", "NOT", and "PROXIMITY". The "AND" operator is selected. The query structure shows a condition "Molecular Formula" with the value "C30\*" and another condition "Isolation from Natural Product". The interface also includes buttons for "Import", "Save", "Reset form", and "Delete" at the top left, and a "Search" button at the top right.

\* 可使用關鍵字查詢篩選條件

- ③ 在右上方Find search and fields and form 輸入"Natural"，點擊「Isolation from Natural Product」
- ④ 在左方的運算子選擇AND，內容可不輸入

## Query Builder查詢範例1(3/4)

The screenshot displays the Query Builder interface. The main query area contains three conditions connected by 'AND' operators:

- Molecular Formula is C30\*
- Isolation from Natural Product is Isolation from Natural Product
- Substance Basic Index is antimicrobi\*

The right-hand panel, titled 'Search properties', shows a list of search categories. The 'Basic Indexes' category is expanded, and 'Substance Basic Index' is selected and circled in red. The top search dropdown menu is also open, showing 'Reactions', 'Substances', and 'Documents', with 'Substances' circled in red.

- ⑤ 點擊右方Basic Indexes>「Substance Basic Index」
- ⑥ 輸入“antimicrobi\*”
- ⑦ 因為要找化合物，所以在右上的Search選擇Substance

# Query Builder查詢範例1(4/4)

The screenshot displays the Reaxys Query Builder interface. On the left, a sidebar titled '876' contains a 'Filters and Analysis' menu with options: 'By Structure', 'Substances Classes', 'Molecular Weight', 'Availability', 'Available Data', 'Document Type', and 'Publication Year'. The main area shows '876 Substances' out of 8,094 Documents containing 7,885 Reactions. A 'Back to Query Builder' button is at the top left of the main area. Below the header, a section indicates '0 selected' with an 'Options' dropdown. A chemical structure of Oleanolic acid is shown with a '1' in a box next to it. To the right of the structure, the name 'Oleanolic acid' is listed along with its molecular formula  $C_{30}H_{48}O_3$  and CAS numbers 456,709, 2228570, and 508-02-1. Below the name, a list of data types is provided: 'Hit Data - 27', 'Identification', 'Physical Data - 319', 'Spectra - 234', 'Bioactivity - 1,148', and 'Other Data - 869'. On the far right, a column shows the number of documents for each category: 'Preparations - 171', 'Reactions - 1,451', and 'Documents - 2,065'. At the bottom, a 'Hit Data - 27' button is visible.

## 查詢結果畫面：

分子式，化學名，測試項目，合成方法，衍生物的合成方法等都可以得到確認，如果有其他條件，可透過左方的篩選功能縮小範圍。

# Hands on #3

- 試著搜尋以下物質：
  - 知道是天然產物
  - 分子量知道是348.453
  - 有一組NMR的數據
- 检索策略
  - Query Builder, 添加天然產物選項
  - 分子量設定為 $\geq 348$ , 且 $\leq 349$ , 避免一些誤差
  - 若有明確結構, 可以同時添加結構片段, 或在後期進行篩選
  - 有圖譜數據的話, 可以直接添加圖譜數據

# Hands on #3 衍生範例

- $^{13}\text{C}$  NMR (DMSO- $d_6$ , 150 MHz)  $\delta$  173.5, 157.8, 153.4, 150.1, 148.1, 145.9, 131.6, 130.4, 130.2, 129.2, 128.7, 128.1, 127.8, 120.1, 96.9, 73.6, 65.6, 50.8, 30.2, 7.8

**Tips:** 設定圖譜數據中，包含173, 153, 130, 可以將上述的圖譜找到，  
設定173其實是尋找173.0-173.9的圖譜

# Query Builder

- 添加天然物萃取模組

Reaxys®

Quick search   Query builder   Results   Synthesis planner   History

Search in:   Reactions >   Targets >   Substances >   Documents >

Import   Save   Reset form   Delete all

Structure   Molecular Formula   CAS RN   TI, AB & KW

◇ Isolated from Natural...   ☐ Find any   **Hide fields ^**   ☐ is   ☐ Isolated from Natural Source   ☐

**1** Find search fields and forms  
natural

**2** ◇ Isolated from Natural Source

**3**

**Tips :**

- 按照1, 2, 3步驟，添加天然產物的搜索條件
- 這種模式下的搜尋結果，一定是天然產物

# Query Builder

- 添加分子量模組

Search in: [Reactions >](#) [Targets >](#) [Substances >](#) [Documents >](#)

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

1 Find search fields and forms  
Molecular

2 Molecular Formula

3

Isolated from Natural... ☐ Find any Hide fields ^

is Isolated from Natural Source

AND

Molecular Weight  $\geq$  348

AND

Molecular Weight  $\leq$  349

Molecular Weight

Fragment Molecular Formula

Molecular BINs

Molecular Deformation

# Query Builder

- 添加NMR模組

1

Search in: Reactions > Substances > Documents >

Import Save Reset form Delete all

Structure Molecular Formula CAS RN TI, AB & KW

|          |   |                                    |    |
|----------|---|------------------------------------|----|
| is       | ▼ | Nucleus (NMR Spectroscopy)         | EQ |
| is       | ▼ | Coupling Nuclei                    | EQ |
| is       | ▼ | Solvents (NMR Spectroscopy)        | EQ |
| =        | ▼ | Temperature (NMR Spectroscopy), °C | EQ |
| =        | ▼ | Frequency (NMR Spectroscopy), MHz  | EQ |
| contains | ▼ | 173                                | EQ |

2

Find search fields and forms

NMR

NMR Spectroscopy

3

# Synthesis Planner

# 建構合成路徑(1/3)

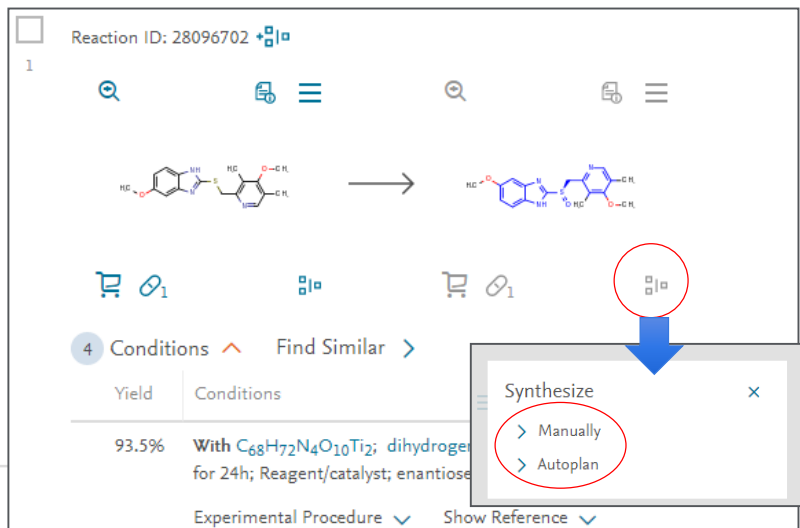
**Synthesis Planner:** 可透過逆合成分析建構合成路徑

- 畫面上可同時提供多種合成方式，便利比較評估
- 也可於化合物查詢結果頁面進入Synthesis Planner

## 查詢範例：Omeprazole的合成

從反應查詢結果進入Synthesis Planner。

- ① 點擊 ，將該化合物作為起始點
- ② 可選擇使用Manually或Autoplan啟動Synthesis Planner
  - Manually: 手動逐步建立合成路徑
  - Autoplan: 顯示Reaxys建議合成路徑



The screenshot displays the Synthesis Planner interface. At the top, it shows 'Reaction ID: 28096702'. Below this is a chemical reaction scheme. A red circle highlights the 'Synthesize' button (represented by a small icon of a flask and a plus sign). A blue arrow points from this button to a dropdown menu titled 'Synthesize'. This menu contains two options: '> Manually' and '> Autoplan', both of which are circled in red. Below the reaction scheme, there is a table with columns 'Yield' and 'Conditions'. The table shows a yield of 93.5% and conditions: 'With C<sub>68</sub>H<sub>72</sub>N<sub>4</sub>O<sub>10</sub>Ti<sub>2</sub>; dihydrogen for 24h; Reagent/catalyst; enantiose'. At the bottom, there are links for 'Experimental Procedure' and 'Show Reference'.

# 建構合成路徑(2/3)

## Autoplan

- 自動規劃5種合成路徑
- 反應產率顯示於路徑上，點擊可顯示實驗步驟

Reaxys<sup>®</sup> Weiwei Cheng

Quick search Query builder Results Synthesis planner History

Synthesis Planner Edit

Autoplan 1 5

Plan 1  
Plan 2  
Plan 3  
Plan 4  
Plan 5

Import Save Export Undo Redo

Reaction scheme showing two chemical structures connected by a reaction arrow labeled 1 and 93.5%.

Show conditions  
Hide preparation  
Add preparations  
Remove preparation

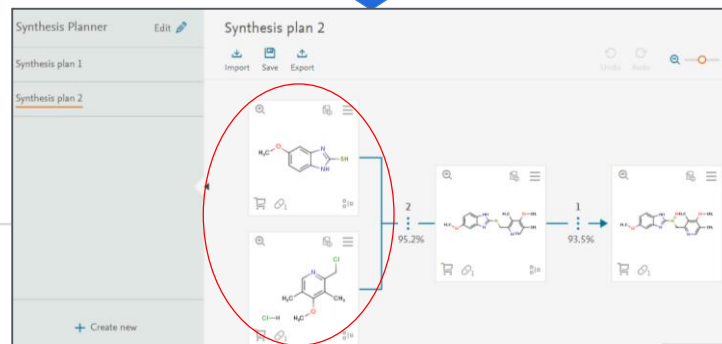
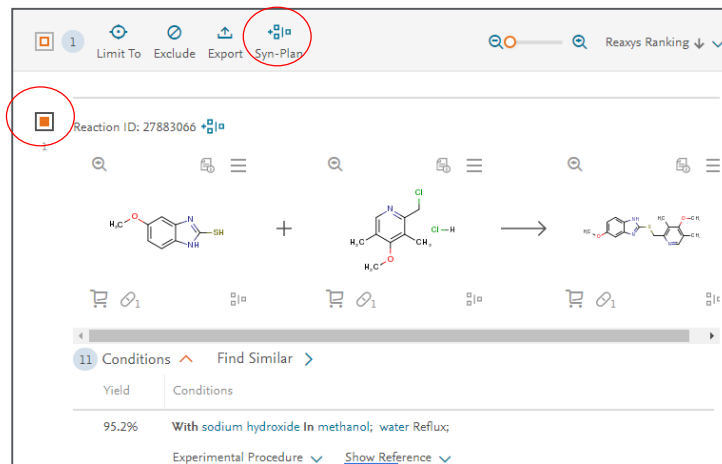
Conditions

| Yield   | Conditions                                                                                                                                                                                                 | Reference                                                                                                                                |
|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| 93.5%   | With $C_{68}H_{72}N_4O_{10}Ti_2$ ; dihydrogen peroxide In water; ethyl acetate at 0°C; for 24h; Reagent/catalyst; enantioselective reaction;<br>Experimental Procedure                                     | Talsi, Evgenii P.; Bryliakov, Konstantin P. - Catalysis Today, 2017, vol. 279, p. 84 - 89<br>Full Text Cited 1 times Details<br>Abstract |
| 86%     | With N-methyl-6-aza-5 $\beta$ ,6 $\beta$ -epoxy-cholestane-3 $\beta$ -tert-butyl/diphenylsilyloxy tetrafluoroborate In dichloromethane at -70 - 20°C; for 3h; Inert atmosphere; enantioselective reaction; | Zhou, Guobin; Guan, Yueqing - Heterocyclic Communications, 2016, vol. 22, # 1, p. 17 - 19<br>Full Text Details Abstract                  |
| 93 % ee | With tert.-butylhydroperoxide In water; toluene at -20°C; for 12h                                                                                                                                          | RATIOPHARM GMBH - US2008/319195, 2008, A1                                                                                                |

# 建構合成路徑(3/3)

## Manually

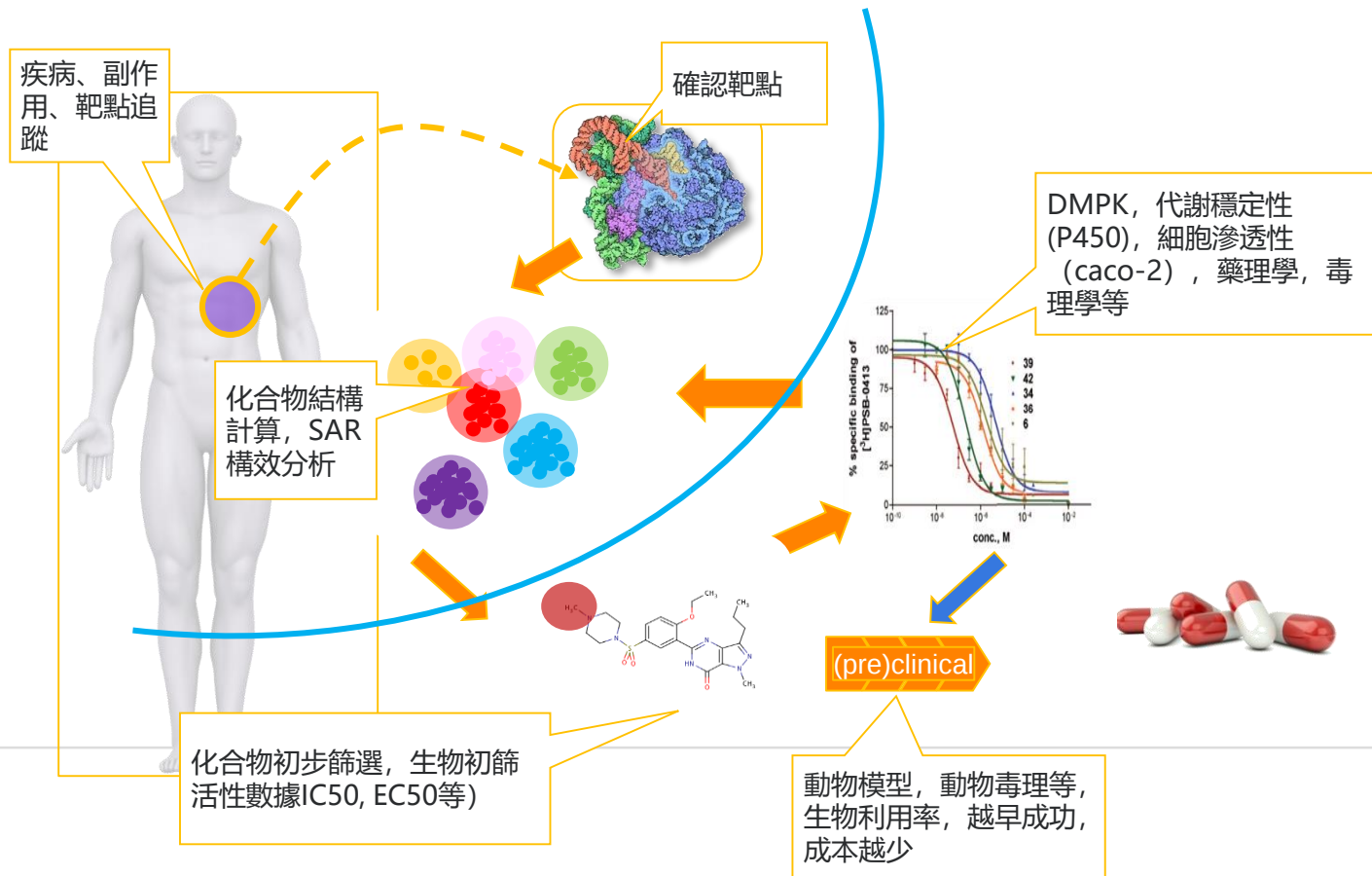
- 選擇要加入的反應，按下Syn-Plan
- 反應直接加入於合成路徑



# Structure Activity Relationship



# Reaxys/RMC如何輔助小分子藥物設計流程



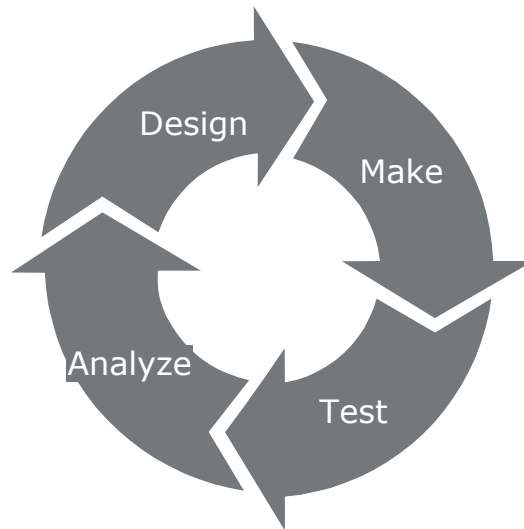
# The design, make, test and analyze cycle lies at the core of drug design



**Drug  
target**

Chemical starting point (Hit) found through HTS, DEL, fragment screening or prior knowledge

- Weakly active
- Target unselective
- Toxicity risk
- Low metabolic stability



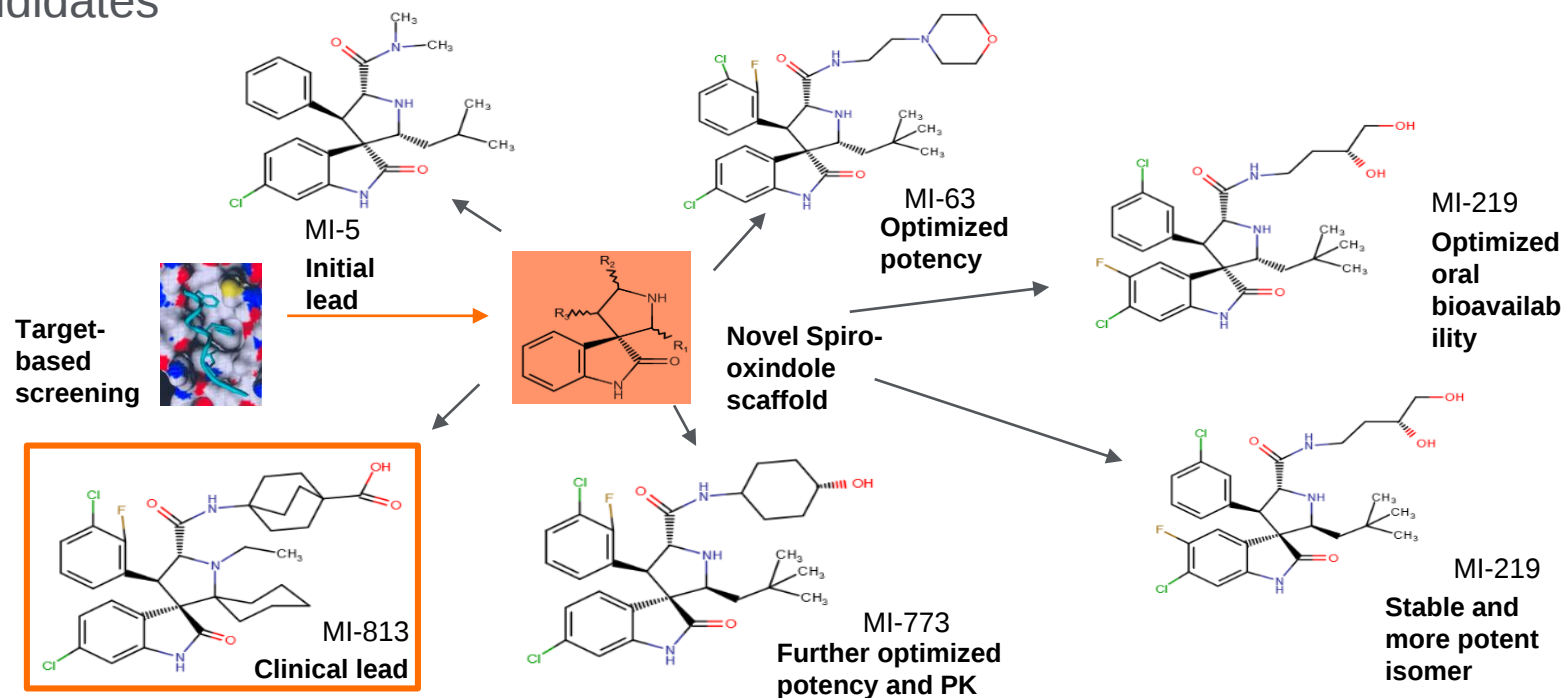
Candidate drug

- Highly potent
- Effective in *in vitro* & *in vivo* models
- Metabolically stable
- No toxicity issues

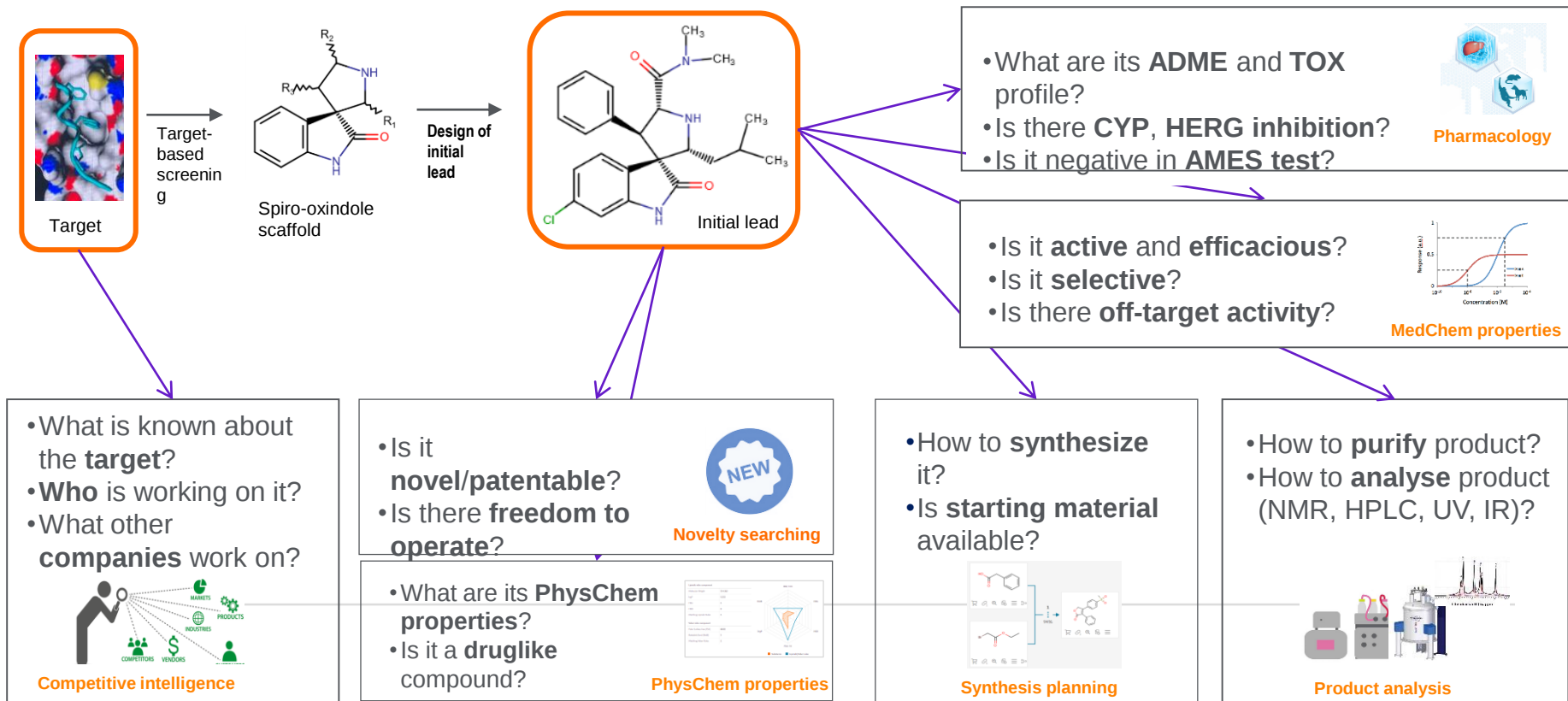
~3  
years

- Multiple of DMTA cycles & hand-overs between multiple labs
- Each cycle between 4-8 weeks

Rational drug design begins with screening against a “druggable” target that is associated with disease state and developing libraries of potential drug candidates



Researchers need to address a number of questions when developing a new drug candidate (competitive landscape, novelty search, synthesis planning, building blocks..)



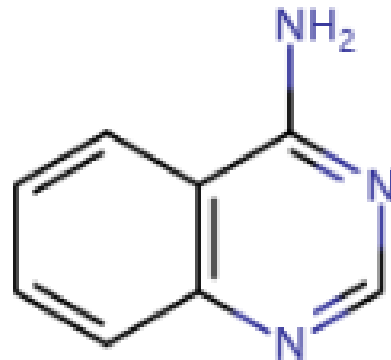
# Reaxys + RMC

## Use Case #2

## 學名藥廠由已知(專利過期)母核結構進行 "Me TOO" "Me BETTER" Project

**Challenge:** a general scaffold has good activity at the EGFR receptor, we need to identify:

- 可以作用在EGFR上、所有含有母核結構的已知化合物，找出所有的IC50 data
- 找出影響活性的可能官能基
- 設計新的結構
- 進行專利評估



Query builder allows the user to setup comprehensive search strategy defining the structure, target and bioactivity

The screenshot displays the Reaxys Query Builder interface. At the top, the Reaxys logo is on the left, and navigation links for Quick search, Query builder (underlined), Results, Synthesis planner, and History are in the center. On the far right are links for Sign in and a help icon. Below the navigation bar is a toolbar with icons for Import, Save, Reset form, and Delete all. To the right of these are icons for Structure, Molecular Formula, CAS RN, and Doc. Index. A Search button with a dropdown arrow is also present. The main workspace contains three query clauses, each with a collapse icon (diamond) and a close icon (X):

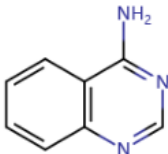
- Structure**: Contains a text input field with the placeholder "Create Structure / Reaction Drawing".
- AND**: A connector button between the first and second clauses.
- Target Name**: Contains a dropdown menu set to "is" and a text input field containing "Target Name".
- AND**: A connector button between the second and third clauses.
- Measurement Parameter**: Contains a dropdown menu set to "is" and a text input field containing "Measurement Parameter".

On the right side of the interface is a sidebar titled "Find search fields and forms" with a search icon. It has three tabs: Fields (selected), Forms, and History. Under the Fields tab, a list of search fields is shown, including MedChem, Target Name, Substance Action on Target, Substance Effect, Measurement pX, Target Nature, Target Mutant/Chimera Details, Target Transfection, and Substance RN. Each field has a collapse icon (diamond) and a refresh icon (circular arrow).

Search for all derivatives of the general structure by selecting from the filter options

Reaxys® Quick search Query builder Results Synthesis planner History Sign in ?

Structure editor Create structure template from name >



Search this structure as:

- ☒ As drawn
  - ☒ As substructure
    - ☐ On all atoms
    - ☐ On heteroatoms
  - ☐ On heteroatoms
  - ☐ Similar
- ☒ Tautomers
- ☐ Stereo
- ☐ Additional ring closures
- ☐ Related Markush
  - ☐ Salts
  - ☐ Mixtures
- ☐ Isotopes
- ☐ Charges
- ☐ Radicals

+ More options

Clear Cancel Transfer to query >

Define the target as EGFR

◇ Target Name

is



Target Name



Target Name



3576280



> Targets

18,839,700

> protein

15,203,250

> binding protein

10,076,444

> heterocyclic compound binding protein

3,260,624

> nucleic acid binding protein

1,264,051

> DNA binding protein

1,064,053

> structure-specific DNA binding protein

147,781

> double-stranded DNA binding protein

147,137

> Epidermal growth factor receptor (EGFR (Epidermal growth factor receptor))

62,930

> Epidermal growth factor receptor [human] (EGFR)

59,040

☐ Epidermal growth factor receptor [dog] (EGFR)

2

☐ Epidermal growth factor receptor [Mus musculus] (Egfr)

3,723

Selected search items:

Epidermal g... [human]

Epidermal g... or [dog]

Epidermal g... usculus]

Epidermal g... vegicus]

More

Clear selected

Transfer

Add the measurement parameter as IC50 and run the search

◇ Measurement Parameter ✕

is ▼ Measurement Parameter

ic50 🔍

Reaxys® Quick search Query builder Results Synthesis planner History Sign in ?

Import Save Reset form Delete all Structure Molecular Formula CAS RN Doc. Index

**Search Substances** ▶ ▼

◇ Structure ✕

On all atoms

**AND**

◇ Target Name ✕

is ▼ Target Name

Epidermal growth factor receptor [human];Epidermal growth factor receptor 🔍

**AND**

◇ Measurement Parameter ✕

is ▼ Measurement Parameter

ic50 🔍

Find search fields and forms 🔍

Fields Forms History

Reaxys ^

- Basic Indexes ▼
- Identification ▼
- Physical Properties ▼
- Spectra ▼
- MedChem ^
- ◇ Target Name 🔍
- ◇ Substance Action on Target 🔍
- ◇ Substance Effect 🔍
- ◇ Measurement pX 🔍
- ◇ Target Nature 🔍
- ◇ Target Mutant/Chimera Details 🔍
- ◇ Target Transfection 🔍

Reaxys provides 8,311 substances matching the criteria defined by the user in their search strategy

Review substance results & switch to Heatmap view:

Reaxys

Quick search Query builder Results Synthesis planner History

Sign in

8,311

Filters and Analysis

By Structure

Measurement pX

Highest Clinical Phases

Targets

Parameters

Substance Classes

Molecular Weight

Availability

Availability in other databases

Available Data

Document Type

Publication Year

Patent Assignee

8,311 Substances out of 886 Documents, containing 13,013 Reactions, 150 Targets

Reaxys - 8,311

0 selected Limit To Exclude Export

Sort by No of References

Heatmap

1

gefitinib

C22H26ClFN4O3 446.909 8949523 184475-35-2

Identification Bioactivity (All) Other Data - 2,446 Preparations - 55 >

Druglikeness Physical Data - 53 Reactions - 85 >

Bioactivity (Hit Data) Spectra - 45 Targets - 1,028 >

Documents - 2,934 >

2

lapatanib

C28H26ClFN4O4S 581.067 10502247 231277-92-2

Identification Bioactivity (All) Other Data - 1,010 Preparations - 53 >

Druglikeness Physical Data - 24 Reactions - 121 >

Bioactivity (Hit Data) Spectra - 26 Targets - 687 >

Documents - 1,576 >

3

erlotinib

C22H23N3O4 393.442 8798958 183321-74-6

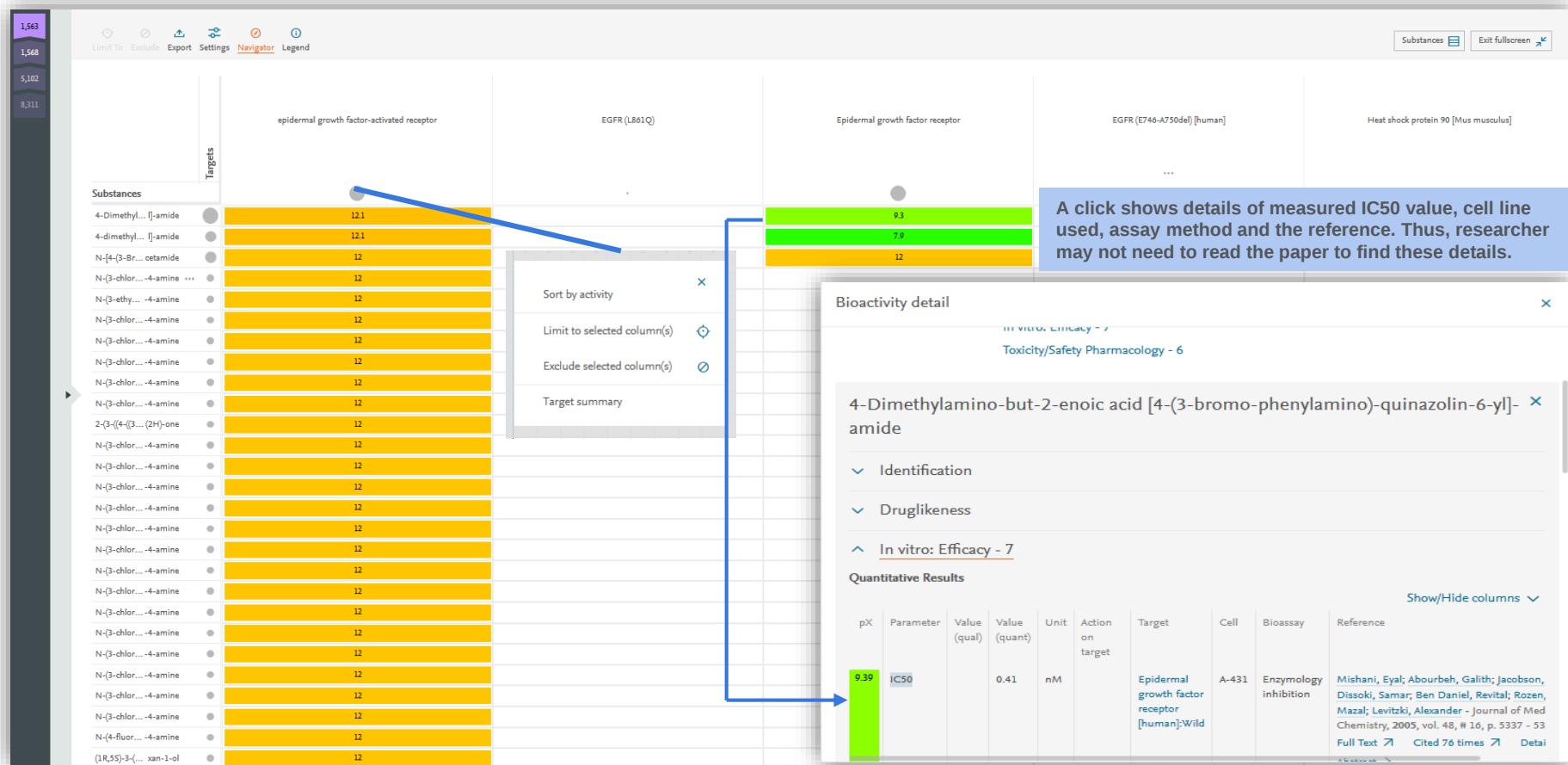
Identification Bioactivity (All) Other Data - 2,403 Preparations - 35 >

Druglikeness Physical Data - 41 Reactions - 88 >

Bioactivity (Hit Data) Spectra - 39 Targets - 997 >

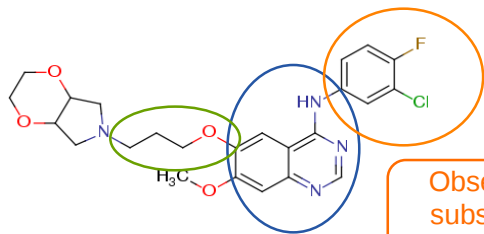
Documents - 790 >

# Heatmap view allows for the rapid assessment of the substance and target interactions

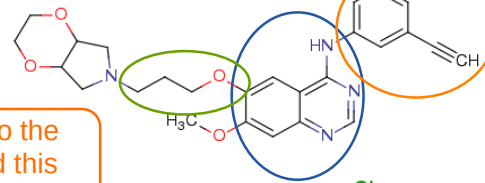


# SAR analysis: What structures give high and low activity?

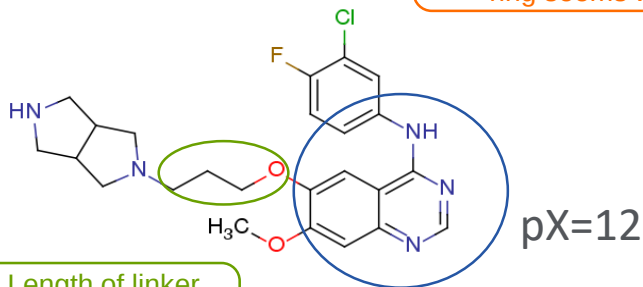
Observation 1: Core ring as defined is present in all



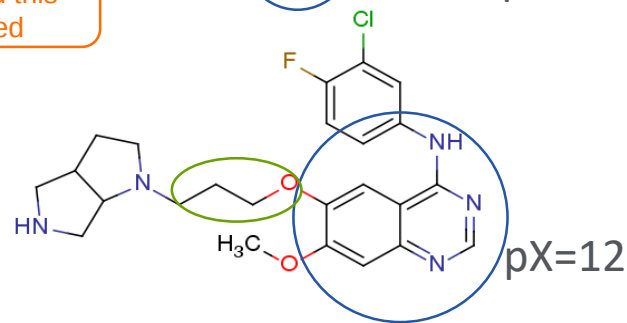
Observation 3: Changes to the substituent pattern around this ring seems well tolerated



pX=12

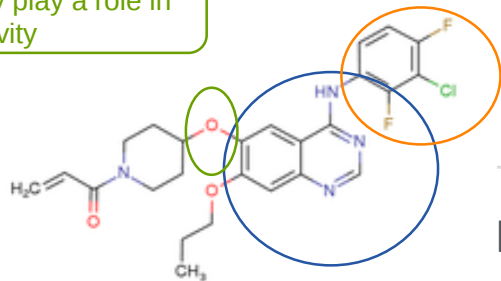


pX=12

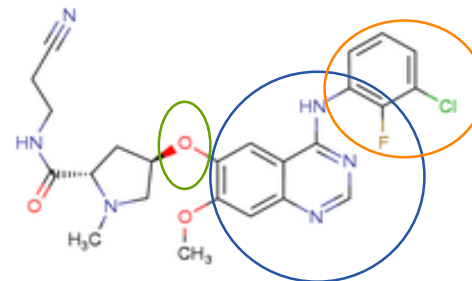


pX=12

Observation 2: Length of linker from the core may play a role in bioactivity

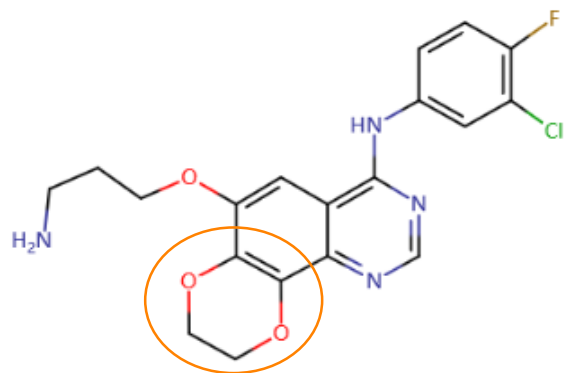
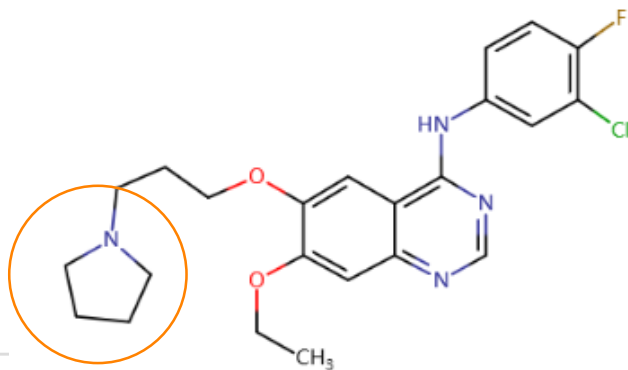
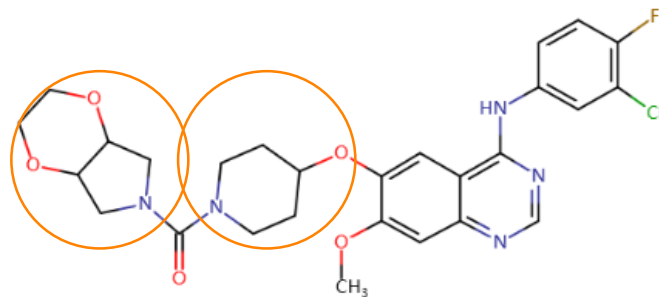
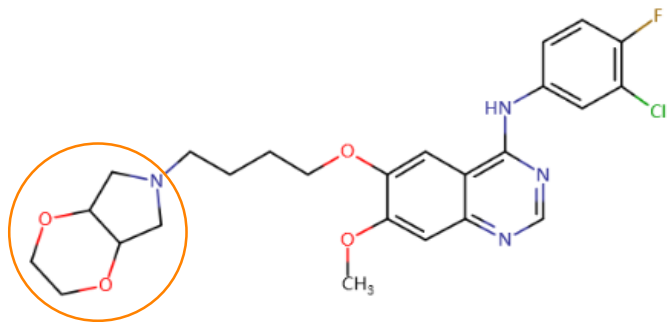


pX=9



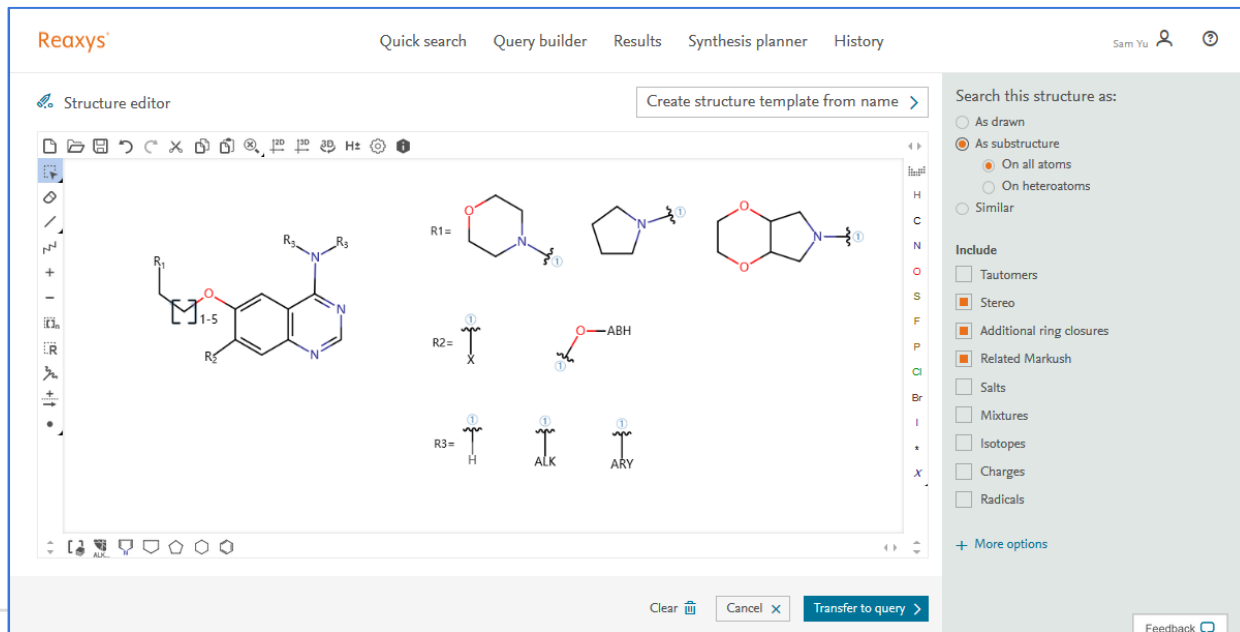
pX=9

Based on SAR observations researchers could potentially design some new compounds



However, before synthesising the new molecules the researcher might want to check if the molecules are patented or not. This will help prevent wastage of time, effort & money

Markush search functionality coupled with powerful structure editor allows researcher to define the R-groups, control the length of side chains etc. thus enabling the researcher to define and search for patent related information



37 Markush structures are obtained from the search and the 3 examples provided show the structure to be similar to the proposed new compounds, thus further analysis on their coverage and claim need to be conducted

Reaxys® Quick search Query builder Results Synthesis planner History Sam Yu

37 Substances out of 28 Documents, containing 11 Reactions, 0 Targets

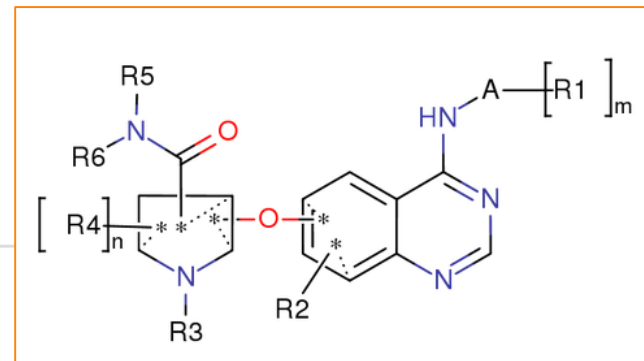
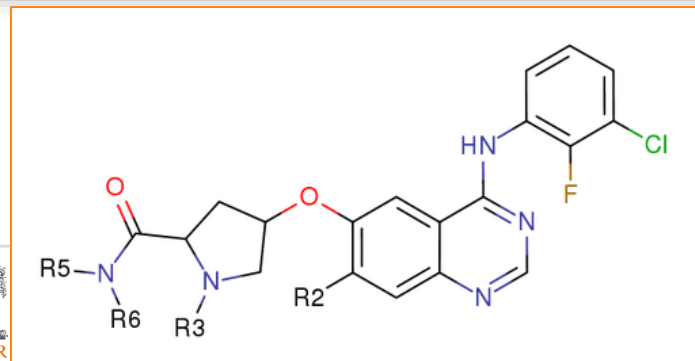
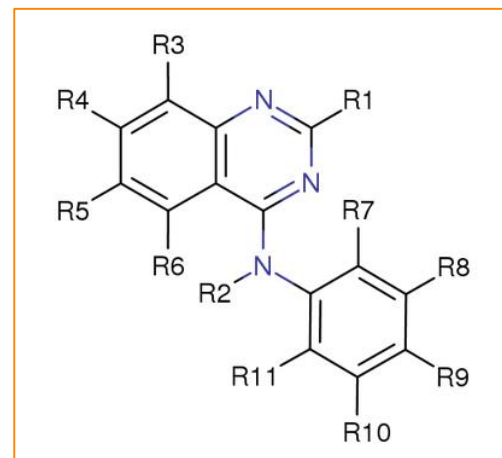
Filters and Analysis

- By Structure
- Measurement pX
- Highest Clinical Phases
- Targets
- Parameters
- Substance Classes
- Molecular Weight
- Availability
- Availability in other databases
- Available Data
- Document Type
- Publication Year

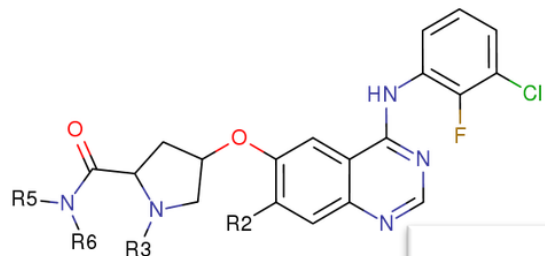
1 Reaxys ID: 11329531  
11329531  
Identification  
Other Data - 3

2 Reaxys ID: 11334491  
11334491  
Identification  
Other Data - 4

3 Reaxys ID: 12250782  
12250782  
Identification



This particular compound is quite similar to the proposed structure and we can see that it has been claimed in an AstraZeneca patent



Reaxys ID: 12250782  
12250782

Identification

Documents - 1 >

**Identification**

Reaxys ID: 12250782

Chemical Names:

CAS Registry Number(s):

Molecular Formula:

Molecular Weight:

InChIKey:

Substance Label - 1

| Location in Patent | Reference                                                                                                                 |
|--------------------|---------------------------------------------------------------------------------------------------------------------------|
| Claim 24           | ASTRAZENECA AB; ASTRAZENECA UK LIMITED - WO2005/30757, 2005, A1<br><a href="#">Full Text</a> <a href="#">Show details</a> |



Reaxys 收錄期刊及專利資料，協助您搜尋整理好的化學反應、文獻、化合物及其特性與實驗數據，並輕鬆與他人分享

Reaxys 化學資料庫為國研院科政中心免費提供全國大專院校使用

## 學習影片 常用文件



Reaxys 實用技巧 - 廖志中老師分享

影片長度: 13:57

瀏覽次數: 160

高雄中山大學廖志中老師分享，如何使用 Reaxys 尋找並匯出海洋生物的次級代謝物詳細資料並整理



New Reaxys Exporting

影片長度: 2:51

瀏覽次數: 79

逐步地指導您輸出所搜的資料，此功能在使用上非常簡單容易上手



ELSEVIER

Help us with simple clicks!

<https://zh.surveymonkey.com/r/2019twtraining>

Contact us if you need technical support  
[r.huang@elsevier.com](mailto:r.huang@elsevier.com)

