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爱思唯尔生命科学客户顾问

今天的内容

- 文献检索的原理简介
- Reaxys数据库**文献**检索的技巧
  - Keytruda 相关信息检索
  - 中枢神经系统常见肿瘤分子病理学及靶向治疗
- Reaxys数据库**专利**检索技巧
  - NASH(Nonalcoholic steatohepatitis)治疗相关的专利检索
  - CD137相关的生物药专利
- Reaxys Medicinal Chemistry**数据**检索技巧
  - 如何通过靶点筛选小分子抑制剂

文献信息检索的挑战

1. 使用什么‘检索词汇’进行检索？
2. 为什么‘检索词汇’输入后，得到了‘这个结果’？
3. 检索结果如何更便捷的查看？

1. 怎么检索不到？这么检索这么少？怎么检索这么多？
2. 如何缩小范围？如果扩大范围？
3. 如何分类，如何整理？

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什么是检索词汇

Free text

标题

Non-oncogenic Acute Viral Infections Disrupt Anti-cancer Responses and Lead to Accelerated Cancer-Specific Host Death

作者关键词

Index term

摘要

SUMMARY

In light of increased cancer prevalence and cancer-specific deaths in patients with infections, we investigated whether infections alter anti-tumor immune responses. We report that acute influenza infection of the lung promotes distal melanoma growth in the dermis and leads to accelerated cancer-specific host death. Furthermore, we show that during influenza infection, anti-melanoma $CD8^+$ T cells are shunted from the tumor to the infection site, where they express high levels of the inhibitory receptor programmed cell death protein 1 (PD-1). Immunotherapy to block PD-1 reverses this loss of anti-tumor $CD8^+$ T cells from the tumor and decreases infection-induced tumor growth. Our findings show that acute non-oncogenic infection can promote cancer growth, raising concerns regarding acute viral illness sequelae. They also suggest an unexpected role for PD-1 blockade in cancer immunotherapy and provide insight into the immune response when faced with concomitant challenges.

正文核心词汇

discordant

anti-tumor

programmed cell death protein 1

Influenza infection

Cell Reports
Report

OPEN ACCESS
CellPress

Non-oncogenic Acute Viral Infections Disrupt Anti-cancer Responses and Lead to Accelerated Cancer-Specific Host Death

Frederick J. Kohlhapp,[1,2,11] Erica J. Huelsmann,[3,11] Andrew T. Lasek,[3,11] Jason M. Schenkel,[4,11] Jevgenijs Lucics,[3,5] Joseph R. Broucek,[6] Josef W. Goldufsky,[7] Tasha Hughes,[8] Janet P. Zayas,[3] Hubert Dolubizno,[3] Ryan T. Sowalsky,[3] Regina Kühnar,[3] Sarah Burd,[7] John C. Kubasiak,[6] Arman Nabatiyan,[3,5] Sh'Rae Marshall,[1] Praveen K. Bommareddy,[1] Shengguo Li,[1] Jenna H. Newman,[1] Claude E. Monken,[1,2] Sasha H. Shafikhani,[3] Amanda L. Marzo,[3,5] Jose A. Guevara-Patino,[9] Ahmed Lasfar,[1,9] Paul G. Thomas,[10] Edmund C. Lattime,[1,2] Howard L. Kaufman,[1,2] and Andrew Zloza[1,2,12,*]

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SUMMARY

In light of increased cancer prevalence and cancer-specific deaths in patients with infections, we investigated whether infections alter anti-tumor immune responses. We report that acute influenza infection of the lung promotes distal melanoma growth in the dermis and leads to accelerated cancer-specific host death. Furthermore, we show that during influenza infection, anti-melanoma $CD8^+$ T cells are shunted from the tumor to the infection site, where they express high levels of the inhibitory receptor programmed cell death protein 1 (PD-1). Immunotherapy to block PD-1 reverses this loss of anti-tumor $CD8^+$ T cells from the tumor and decreases infection-induced tumor growth. Our findings show that acute non-oncogenic infection can promote cancer growth, raising concerns regarding acute viral illness sequelae. They also suggest an unexpected role for PD-1 blockade in cancer immunotherapy and provide insight into the immune response when faced with concomitant challenges.

INTRODUCTION

Our current understanding of immunity relies principally on studies in which a single type of challenge or re-challenge is made to the immune system. Such work has been instrumental in deconstructing complicated immune cell functions and intricate molecular signaling networks. However, the immune system is often tasked with responding to multiple concomitant challenges, and how one type of challenge dictates the immune response to another is not well understood.

The majority of the work thus far on concomitant challenges has been done in the context of pathogenic co-infections, and findings in this field are discordant (Kenney et al., 2015; Mueller et al., 2007; Osborne et al., 2014; Stelekati et al., 2014). Further, although infections and cancers are two of the most common human maladies and cancer patients are at increased risk of infections, very little information is available regarding the consequences of concomitant non-oncogenic infection and cancer; thus, this subject is a matter of ongoing debate (Cooley et al., 2005; Kohler et al., 1990; Wong et al., 2010). Case studies performed in the late 19th century report cancer regression in the context of infection-like reactions (e.g., in response to Coley's toxin), and recent work proposes that anti-tumor T cell populations can be expanded as a by-product of infection (Coley, 1891; Garrett, 2015; Iwagawa et al., 2014). However, emerging epidemiological studies report an increased prevalence of cancers and increased cancer [illegible] tion (Attié et al., 2014; Fox et al., 2010; Crum-Cianflone et al., 2009; Huang et al., 20[illegible]; Su et al., 2011; Swaminathan et al., 2015).

Therefore, toward advancing the scientific understanding of immunity in the context of multiple concomitant challenges, we investigated the effect of acute, non-oncogenic,

Cell Reports 17, 957–968, October 18, 2016 © 2016 The Author(s). 957

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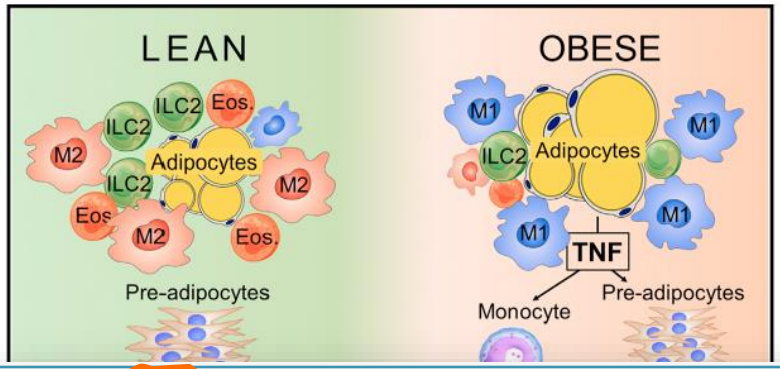
什么是同义词

Report

Cell Reports

PD-1 Is Involved in the Dysregulation of Type 2 Innate Lymphoid Cells in a Murine Model of Obesity

Graphical Abstract



Authors

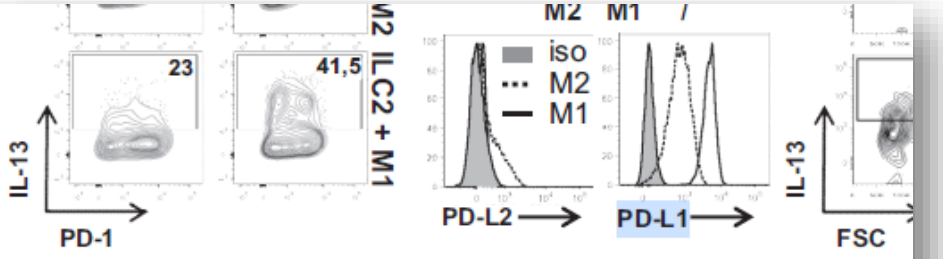
Guillaume Oldenhove, Elodie Boucquey, Anaelle Taquin, ..., Kevin Englebert, Louis Boon, Muriel Moser

Correspondence

guillaume.oldenhove@ulb.ac.be

In Brief

The function of ILC2s is compromised during obesity. Here, Oldenhove et al.



correlation between PD-1 expression, ILC2 dysfunction, and consequently impaired beige adipocyte function (Figures 1E and S3). By contrast, KLRG1 was expressed by all ILC2s in both lean and obese mice, and ICOS was slightly upregulated in a minor population of ILC2s, regardless of PD-1 expression (Figure 1D).

M1-type Macrophages Express PD-L1 and Inhibit ILC2 Function *In Vitro*

We next examined whether the expression of the PD-L1 was also regulated in the visceral adipose tissue during chronic inflammation. The data in Figure 2A show that MHCII$^+$ CD64$^+$ cells, which mainly represent macrophages (Tamoutounour et al., 2012), displayed increased levels of PD-L1 in WT obese mice. Of note, two s were noted in the adipose tissue of HFD-fed mice: of live macrophages increased by more than 50%

1 PD-1 Is Involved in the Dysregulation of Type 2 Innate Lymphoid Cells in a Murine Model of Obesity

Oldenhove G., Boucquey E., Taquin A., Acolty V., Bonetti L., Ryffel B., Le Bert M., Englebert K., Boon L., Moser M.

Cell Reports 2018 25:8 (2053-2060.e4) Cited by: 5

Embase MEDLINE ^Abstract vIndex Terms >View Full Text

Abstract:

Recent observations clearly highlight the critical role of type 2 innate lymphoid cells in maintaining the indirectly by sustaining a Th2-prone environment enriched in eosinophils and alternatively activated individuals. In this work, we identify the PD-1-PD-L1 pathway as a factor leading to ILC2 destabilization triggering interleukin-33 (IL-33)-dependent PD-1 expression on ILC2s and recruiting and activating PD- homeostasis. The function of ILC2s is compromised during obesity. Here, Oldenhove et al. show that 2 innate responses, and promoted tissue homeostasis. PD-1 may therefore represent a target for imm

1 PD-1 Is Involved in the Dysregulation of Type 2 Innate Lymphoid Cells in a Murine Model of Obesity

Oldenhove G., Boucquey E., Taquin A., Acolty V., Bonetti L., Ryffel B., Le Bert M., Englebert K., Boon L., M

Cell Reports 2018 25:8 (2053-2060.e4) Cited by: 5

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Drug Terms

interleukin 1 receptor like 1 protein, interleukin 33, messenger RNA, **programmed death 1 ligand 1**, trans

Disease Terms

obesity

Other Terms

adipose tissue, animal cell, animal experiment, animal model, article, bone marrow cell, cell differentia eosinophil count, glucose tolerance, in vitro study, intra-abdominal fat, lipid diet, **lymphoid cell**, macro expression, protein function, upregulation

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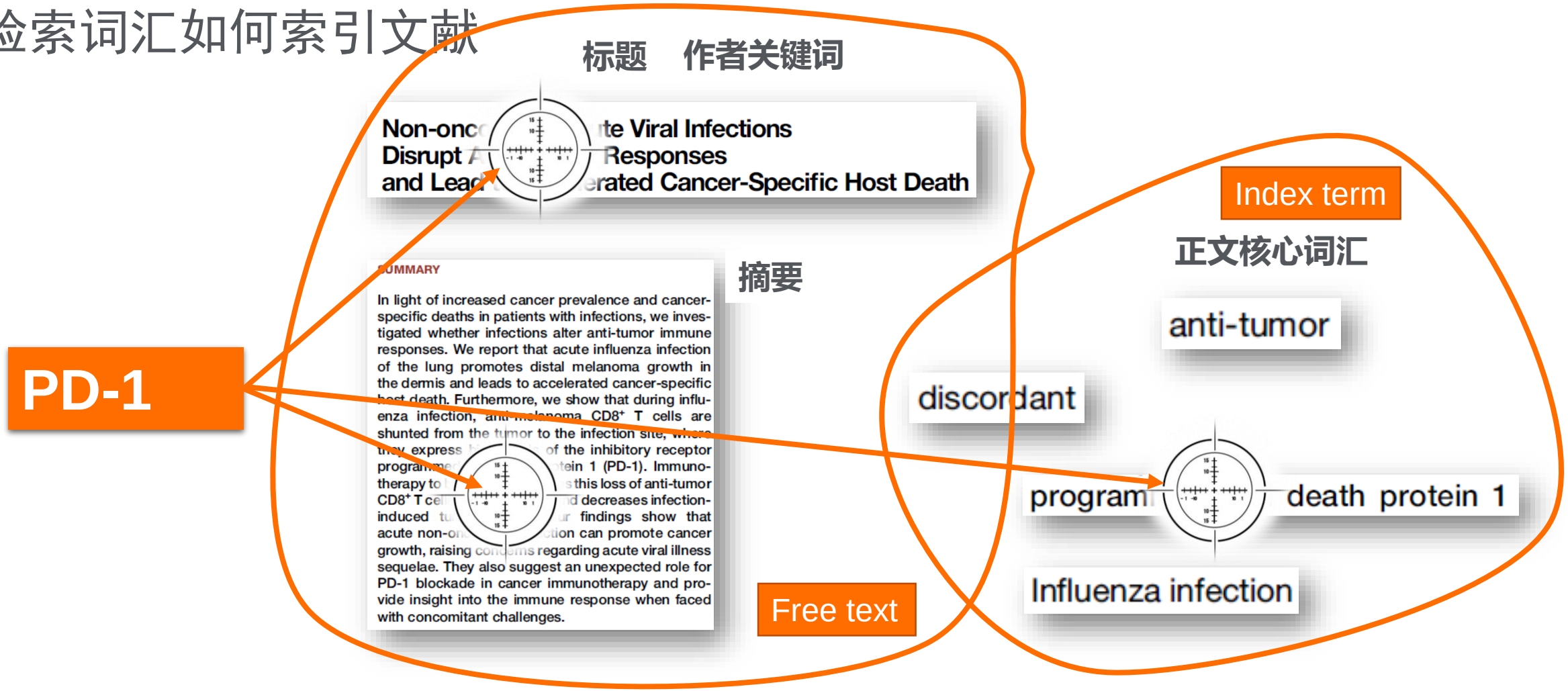
检索词汇如何索引文献

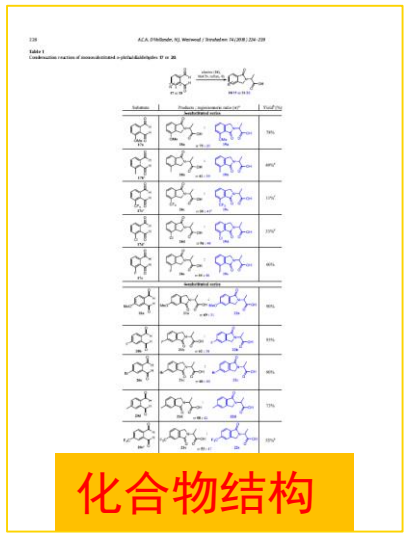


- ‘free text’ 匹配是进行词汇的一致性匹配，不做扩展
- ‘index term’ 匹配是会包含同义词和下位词的匹配

检索词汇，进行‘free text’命中文献，进行‘index term’命中文献，再去重呈现结构

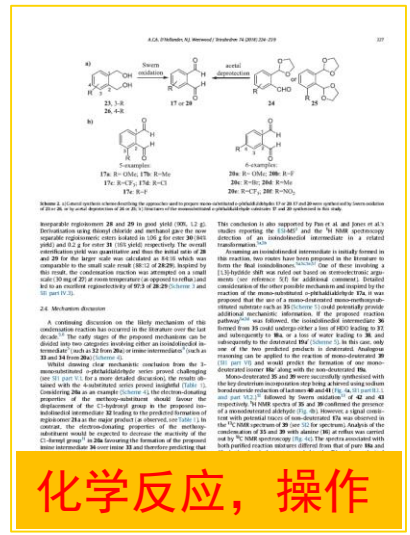
一篇全文期刊中的内容

标题摘要

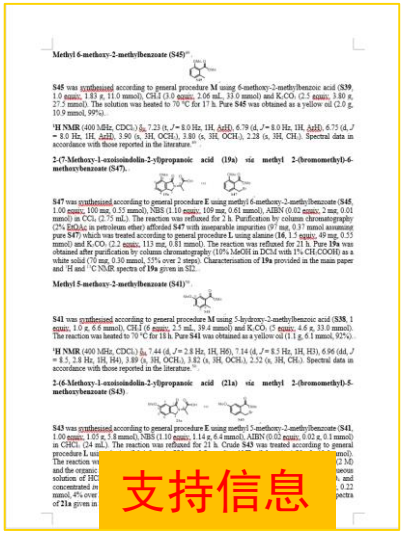


化合物结构

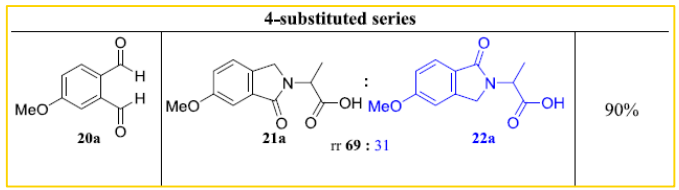
数据，原文关键词（含同义词）

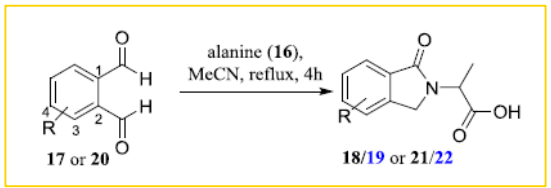


化学反应，操作



支持信息



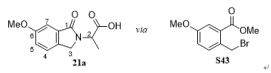


21a: **Mp:** 194–196 °C; **IR** ν_{max} cm^{-1} (thin film) 3370 (O–H stretch), 1730 (C=O stretch), 1636 (C=O stretch), 1493 (C=C stretch), 1456 (C–H bend), 1447 (C–H bend), 1196 (C–O stretch), 1022, 770; **^{1}H NMR** (500 MHz, CD_3OD) δ_H 7.48 (d, J = 8.5 Hz, 1H, H4), 7.29 (d, J = 2.5 Hz, 1H, H7), 7.19 (dd, J = 8.5, 2.5 Hz, 1H, H5), 5.00 (q, J = 7.5 Hz, 1H, CH), 4.54 (d, J = 17.0 Hz, 1H, H3), 4.48 (d, J = 17.0 Hz, 1H, H3), 3.86 (s, 3H, OCH_3), 1.61 (d, J = 7.5 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, CD_3OD) δ_C 174.8 (COOH), 171.0 (C1), 161.6 (C6), 135.8 (C3a), 134.3 (C7a), 125.2 (C4), 121.0 (C5), 107.4 (C7), 56.1 (OCH_3), 51.2 (CH), 48.1 (C3), 15.9 (CH_3); **HRMS** (ES^+) m/z calculated for $C_{12}H_{14}NO_4$ $[M+H]^+$: 236.0917; found: 236.0921. See SI1 part IX for experimental procedure and SI2 for ^{1}H and ^{13}C NMR spectra.

22a: **Mp:** 191–193 °C; **IR** ν_{max} cm^{-1} (thin film) 3229 (O–H stretch), 1717 (C=O stretch), 1628 (C=O stretch), 1611 (C=C stretch), 1558 (C=C stretch), 1506 (C=C stretch), 1447 (C–H bend), 1435 (C–H bend), 1298 (C–N stretch), 1206 (C–O stretch), 1086, 1026, 845, 775; **^{1}H NMR** (500 MHz, CD_3OD) δ_H 7.68 (d, J = 8.5 Hz, 1H, H7), 7.13 (d, J = 2.0 Hz, 1H, H4), 7.04 (dd, J = 8.5, 2.2 Hz, 1H, H6), 4.98 (q, J = 7.5 Hz, 1H, CH), 4.57 (d, J = 17.0 Hz, 1H, H3), 4.50 (d, J = 17.0 Hz, 1H, H3), 3.88 (s, 3H, OCH_3), 1.60 (d, J = 7.5 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, CD_3OD) δ_C 174.8 (COOH), 171.0 (C1),164.9 (C5), 146.2 (C3a), 125.6 (C7), 125.4 (C7a), 116.3 (C6), 108.8 (C4), 56.2 (OCH_3), 50.9 (CH), 48.4 (C3), 15.9 (CH_3); **HRMS** (ES^+) m/z calculated for $C_{12}H_{14}NO_4$ $[M+H]^+$: 236.0917; found: 236.0921. See SI1 part IX for experimental procedure and SI2 for ^{1}H and ^{13}C NMR spectra.

inseparable regioisomers **28** and **29** in good yield (90%, 1.2 g). Derivatisation using thionyl chloride and methanol gave the now separable regioisomeric esters isolated in 1.06 g for ester **30** (84% yield) and 0.2 g for ester **31** (16% yield) respectively. The overall esterification yield was quantitative and thus the initial ratio of **28** and **29** for the larger scale was calculated as 84:16 which was comparable to the small scale result (88:12 of **28**:**29**). Inspired by this result, the condensation reaction was attempted on a small scale (30 mg of **27**) at room temperature (as opposed to reflux) and led to an excellent regioselectivity of **97**:**3** of **28**:**29** (Scheme 3 and SI1 part IV.3).

2-(6-Methoxy-1-oxoisoindolin-2-yl)propanoic acid (21a) ***via*** **methyl 2-(bromomethyl)-5-methoxybenzoate (S43)**



S43 was synthesised according to general procedure **E** using methyl 5-methoxy-2-methylbenzoate (**S41**, 1.00 equiv, 1.05 g, 5.8 mmol), NBS (1.10 equiv, 1.14 g, 6.4 mmol), AIBN (0.02 equiv, 0.02 g, 0.1 mmol) in $CHCl_3$ (24 mL). The reaction was refluxed for 21 h. Crude **S43** was treated according to general procedure **L** using alanine (**16**, 1.5 equiv, 775 mg, 8.7 mmol) and NEt_3 (2.2 equiv, 1.78 mL, 12.8 mmol). The reaction was refluxed for 2 h. Crude **21a** was basified using an aqueous solution of NaOH (2 M) and the organic impurities were extracted with DCM. The aqueous layer was acidified using an aqueous solution of HCl (1 M). The organics were extracted with DCM, combined, dried over $MgSO_4$ and concentrated *in vacuo*. Pure **21a** was obtained after trituration in MeCN as a white solid (51 mg, 0.22 mmol, 4% over 2 steps). Characterisation of **21a** provided in the main paper and ^{1}H and ^{13}C NMR spectra of **21a** given in SI2.

文献中包含的内容：

一些关键的概念

Supporting Information中的内容

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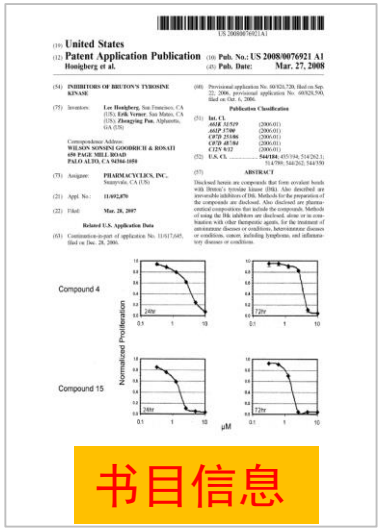
一篇典型的药物方面专利原文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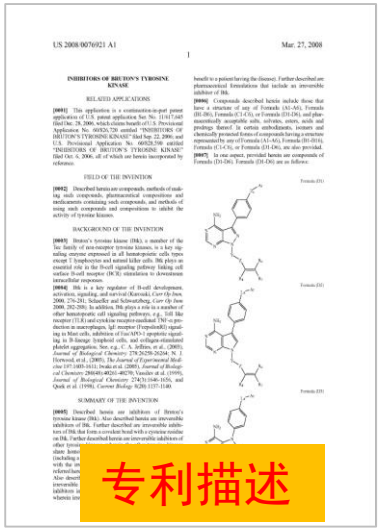
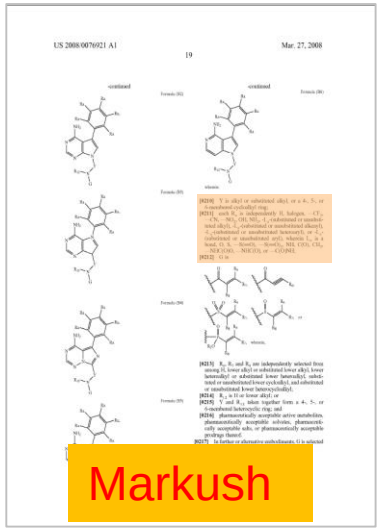
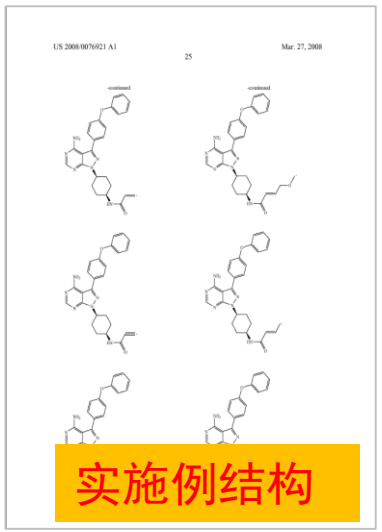
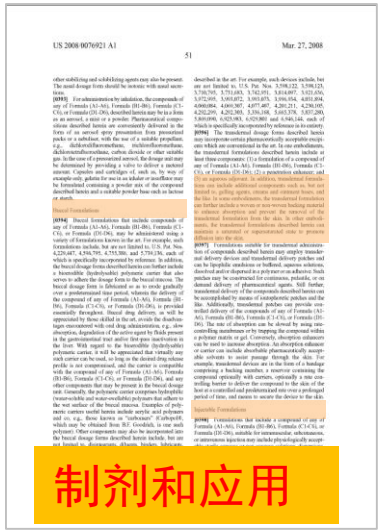
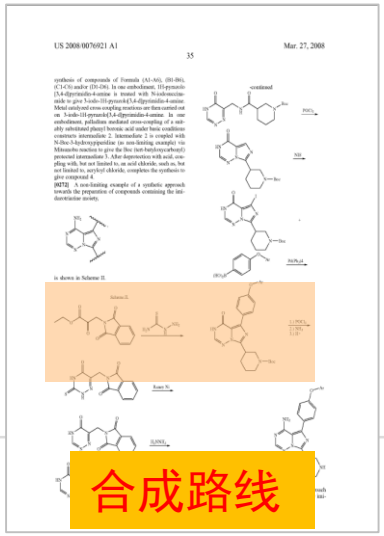
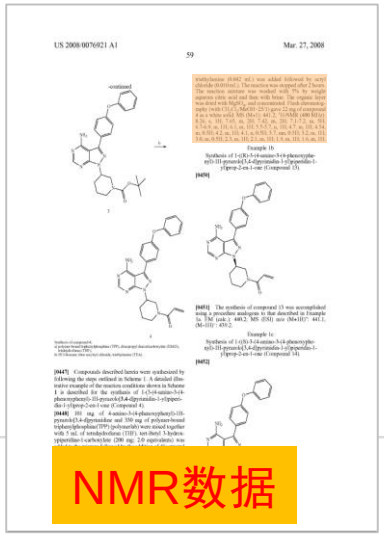

专利描述


Markush


实施例结构


制剂和应用


合成路线


NMR数据


IC50数据

典型药物专利中的内容：

1. 书目内容
2. 专利描述
3. Markush结构及实施例
4. 反应合成路线
5. 实施例的实验室据
6. 实施例的应用数据

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今天的内容

- 文献检索的原理简介
- Reaxys数据库**文献**检索的技巧
  - Keytruda 相关信息检索
  - 中枢神经系统常见肿瘤分子病理学及靶向治疗
- Reaxys数据库**专利**检索技巧
  - NASH(Nonalcoholic steatohepatitis)治疗相关的专利检索
  - CD137相关的生物药专利
- Reaxys Medicinal Chemistry**数据**检索技巧
  - 如何通过靶点筛选小分子抑制剂

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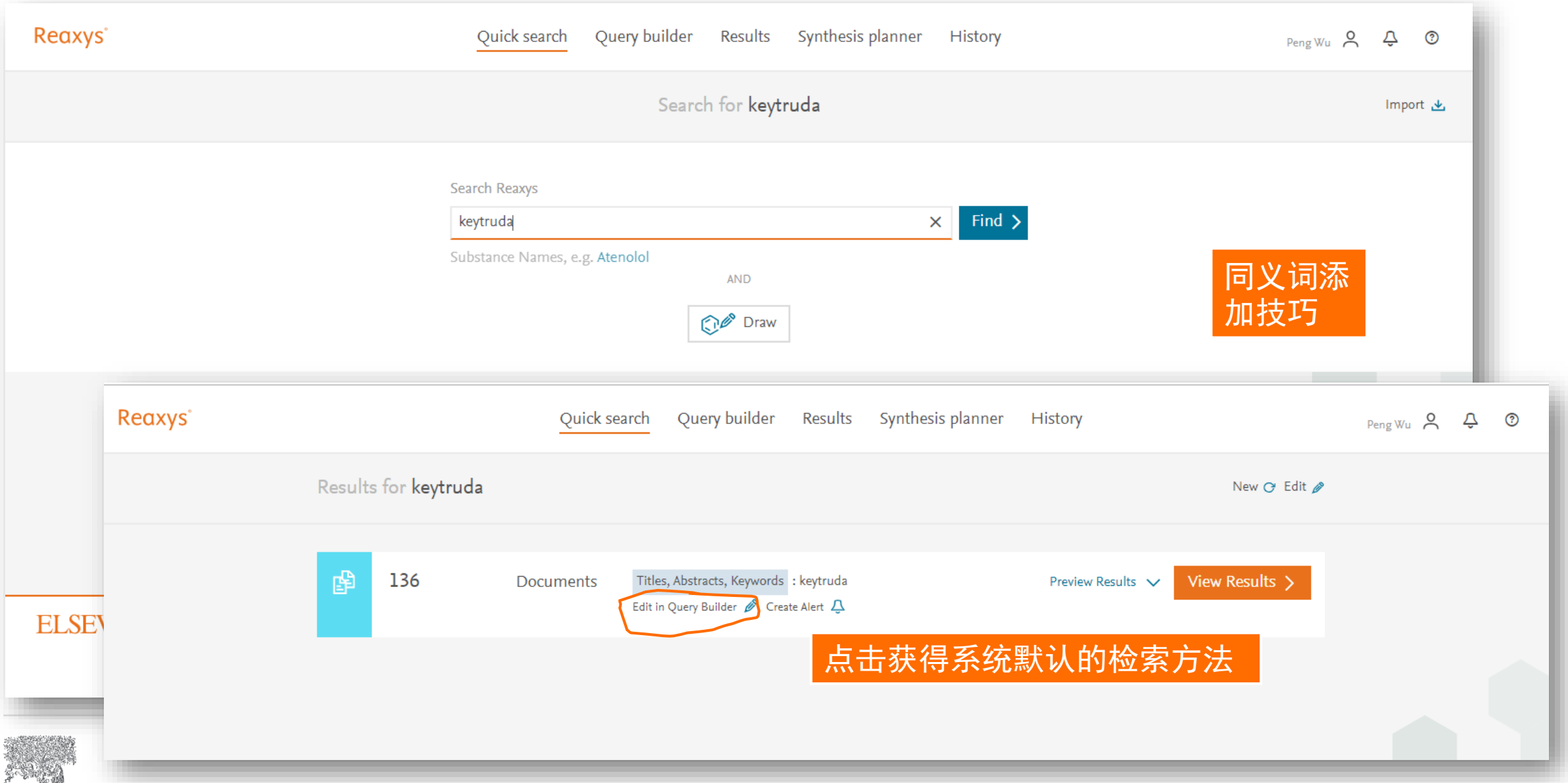
Case 1： Keytruda 相关信息检索
Case 2： 中枢神经系统常见肿瘤分子病理学及靶向治疗

Case 1：Keytruda相关信息检索



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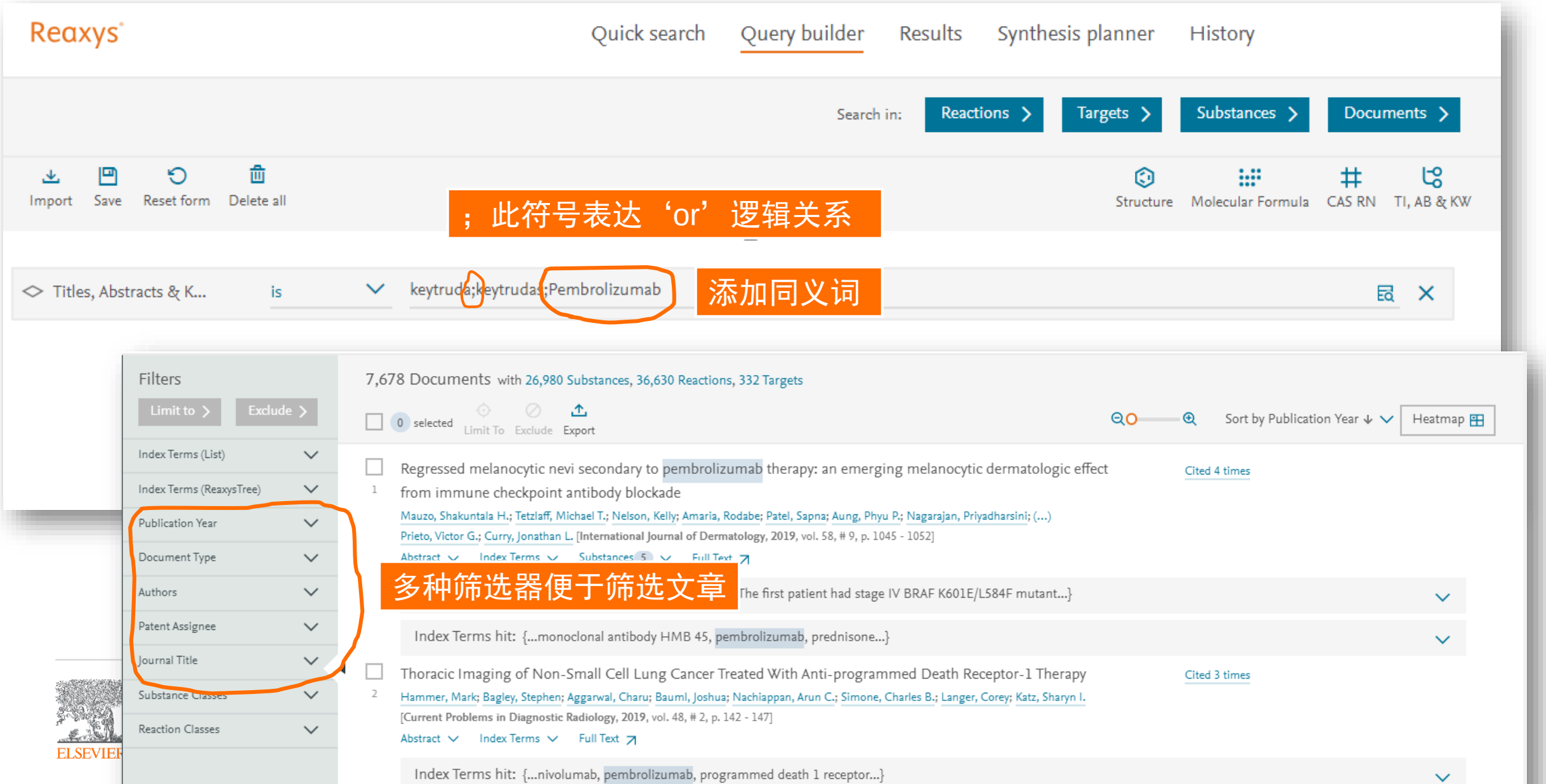
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Query builder
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Synthesis planner
History
Search in:
Reactions
Targets
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Documents
Import
Save
Reset form
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Structure
Molecular Formula
CAS RN
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Index Terms (ReaxysTree)
Publication Year
Document Type
Authors
Patent Assignee
Journal Title
Substance Classes
Reaction Classes
7,678 Documents with 26,980 Substances, 36,630 Reactions, 332 Targets
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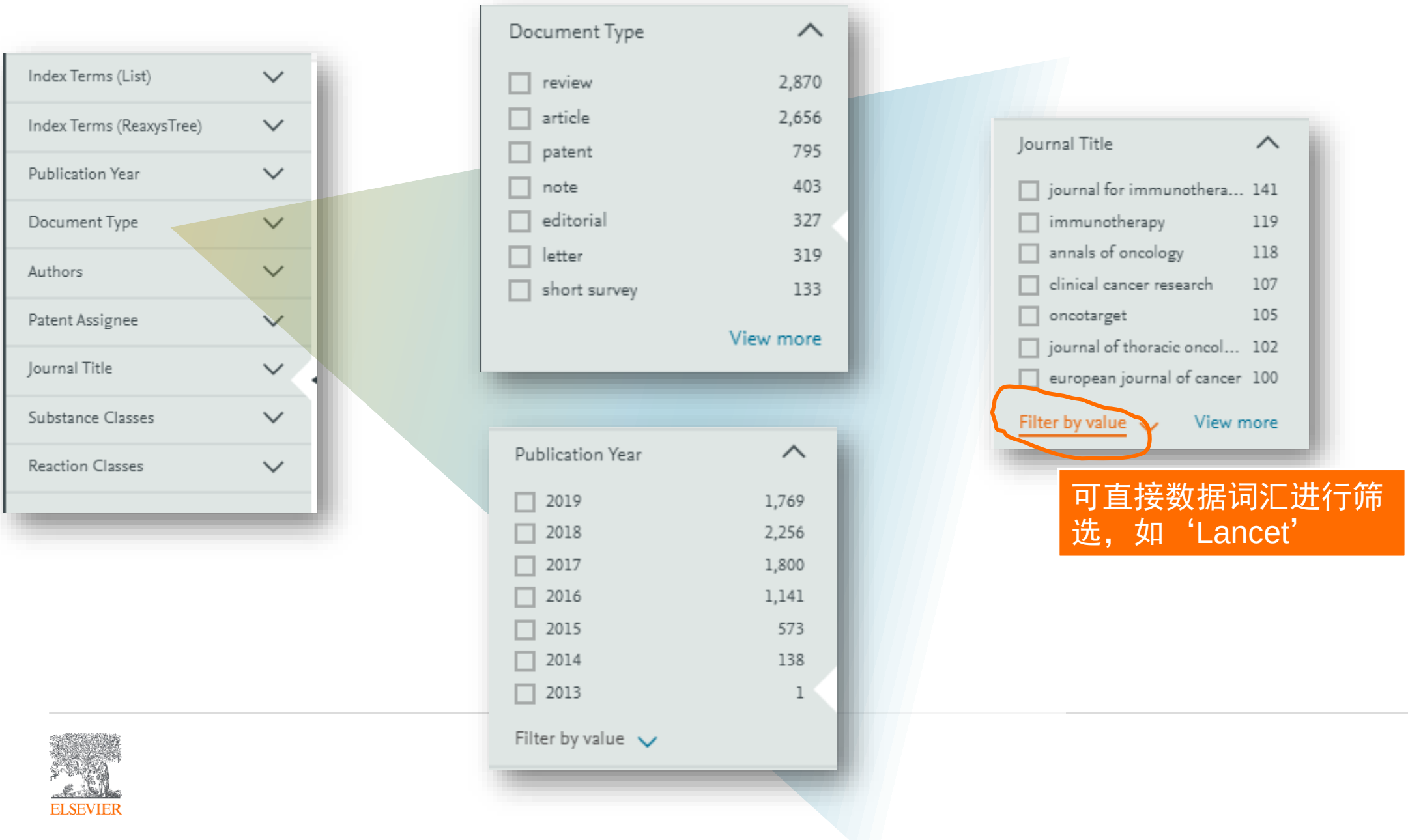
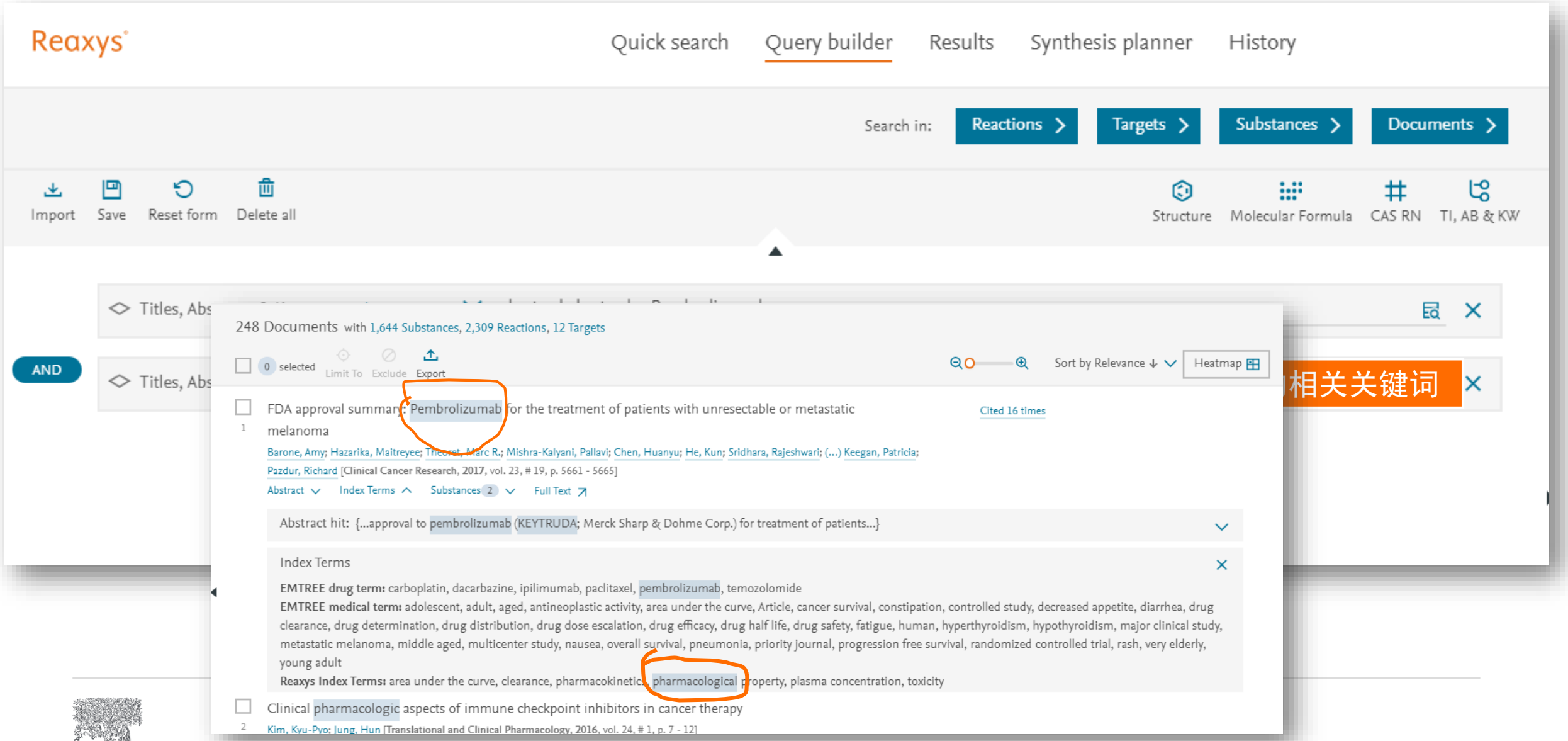
多种筛选器便于筛选文章
1
Regressed melanocytic nevi secondary to pembrolizumab therapy: an emerging melanocytic dermatologic effect from immune checkpoint antibody blockade
Cited 4 times
Mauzo, Shakuntala H.; Tetzlaff, Michael T.; Nelson, Kelly; Amaria, Rodabe; Patel, Sapna; Aung, Phyu P.; Nagarajan, Priyadharsini; (...)
Prieto, Victor G.; Curry, Jonathan L. [International Journal of Dermatology, 2019, vol. 58, # 9, p. 1045 - 1052]
Abstract
Index Terms
Substances 5
Full Text
The first patient had stage IV BRAF K601E/L584F mutant...}
Index Terms hit: {...monoclonal antibody HMB 45, pembrolizumab, prednisone...}
2
Thoracic Imaging of Non-Small Cell Lung Cancer Treated With Anti-programmed Death Receptor-1 Therapy
Cited 3 times
Hammer, Mark; Bagley, Stephen; Aggarwal, Charu; Bauml, Joshua; Nachiappan, Arun C.; Simone, Charles B.; Langer, Corey; Katz, Sharyn I.
[Current Problems in Diagnostic Radiology, 2019, vol. 48, # 2, p. 142 - 147]
Abstract
Index Terms
Full Text
Index Terms hit: {...nivolumab, pembrolizumab, programmed death 1 receptor...}

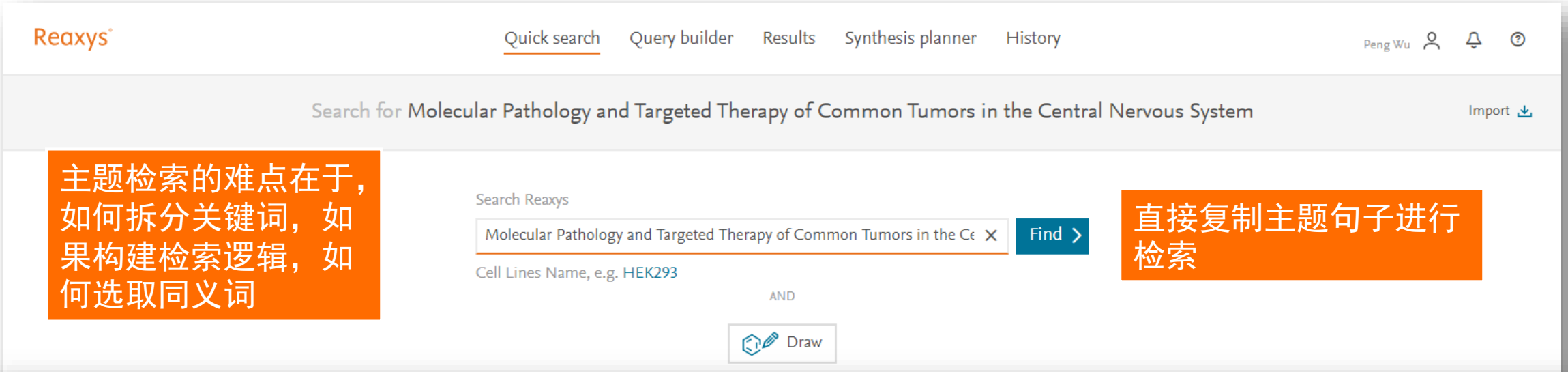

Index Terms (List)
Index Terms (ReaxysTree)
Publication Year
Document Type
Authors
Patent Assignee
Journal Title
Substance Classes
Reaction Classes
Document Type
review 2,870
article 2,656
patent 795
note 403
editorial 327
letter 319
short survey 133
View more
Publication Year
2019 1,769
2018 2,256
2017 1,800
2016 1,141
2015 573
2014 138
2013 1
Filter by value
Journal Title
journal for immunothera... 141
immunotherapy 119
annals of oncology 118
clinical cancer research 107
oncotarget 105
journal of thoracic oncol... 102
european journal of cancer 100
Filter by value
View more
可直接数据词汇进行筛选，如‘Lancet’

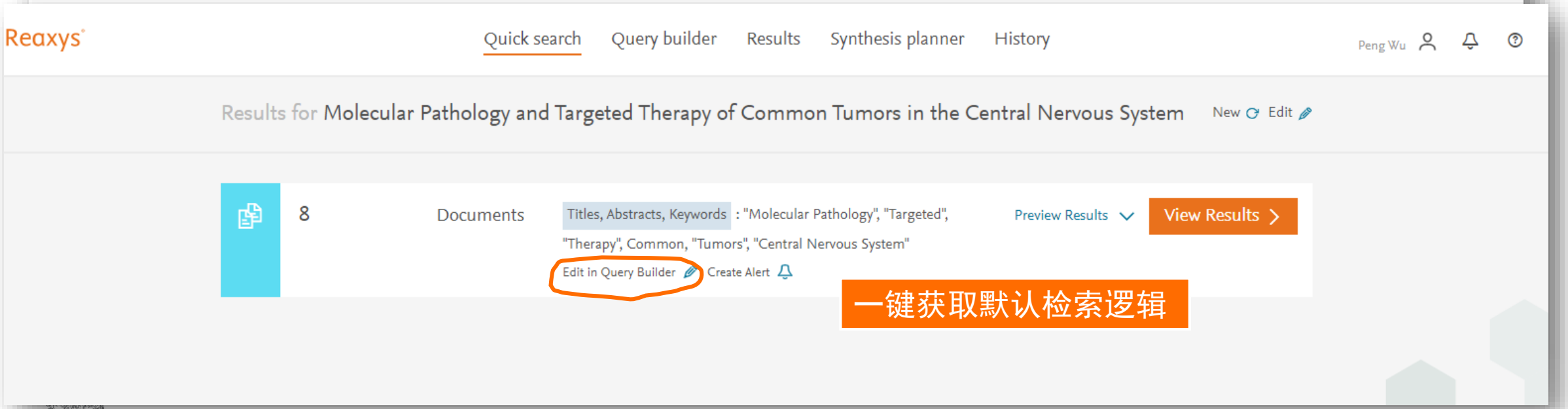
ELSEVIER


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
Titles, Abs
AND
Titles, Abs
248 Documents with 1,644 Substances, 2,309 Reactions, 12 Targets
0 selected
Limit To
Exclude
Export
Sort by Relevance
Heatmap
相关关键词
FDA approval summary: Pembrolizumab for the treatment of patients with unresectable or metastatic melanoma
Cited 16 times
Barone, Amy; Hazarika, Maitreyee; Theoret, Marc R.; Mishra-Kalyani, Pallavi; Chen, Huanyu; He, Kun; Sridhara, Rajeshwari; (...) Keegan, Patricia; Pazdur, Richard [Clinical Cancer Research, 2017, vol. 23, # 19, p. 5661 - 5665]
Abstract
Index Terms
Substances 2
Full Text
Abstract hit: {...approval to pembrolizumab (KEYTRUDA; Merck Sharp & Dohme Corp.) for treatment of patients...}
Index Terms
EMTREE drug term: carboplatin, dacarbazine, ipilimumab, paclitaxel, pembrolizumab, temozolomide
EMTREE medical term: adolescent, adult, aged, antineoplastic activity, area under the curve, Article, cancer survival, constipation, controlled study, decreased appetite, diarrhea, drug clearance, drug determination, drug distribution, drug dose escalation, drug efficacy, drug half life, drug safety, fatigue, human, hyperthyroidism, hypothyroidism, major clinical study, metastatic melanoma, middle aged, multicenter study, nausea, overall survival, pneumonia, priority journal, progression free survival, randomized controlled trial, rash, very elderly, young adult
Reaxys Index Terms: area under the curve, clearance, pharmacokinetics, pharmacological property, plasma concentration, toxicity
Clinical pharmacologic aspects of immune checkpoint inhibitors in cancer therapy
Kim, Kyu-Pyo; Jung, Hun [Translational and Clinical Pharmacology, 2016, vol. 24, # 1, p. 7 - 12]

ELSEVIER

Case 2：中枢神经系统常见肿瘤分子病理学及靶向治疗





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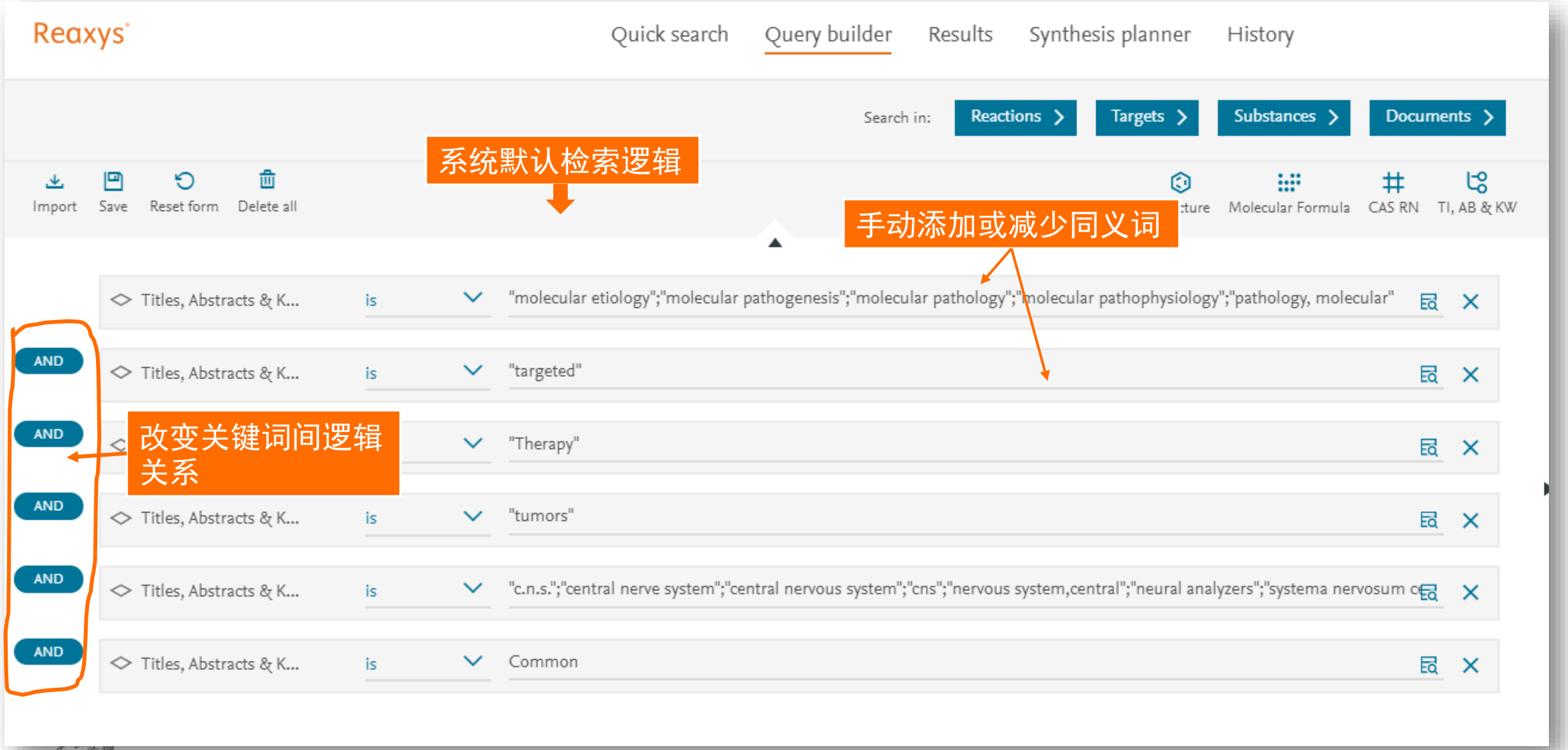
手动调节，控制检索文献的范围，精确度



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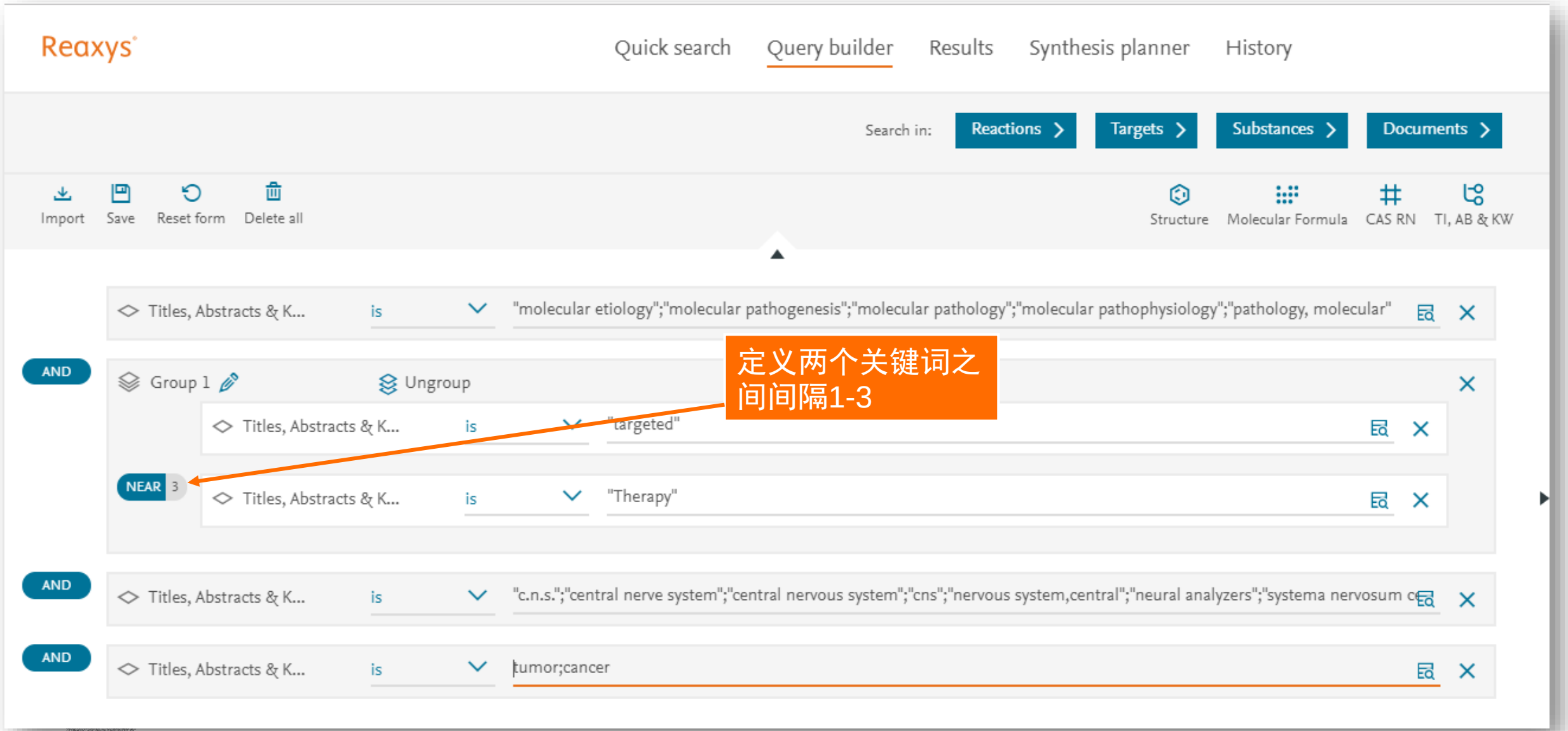
Reaxys
Quick search
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Results
Synthesis planner
History
Search in:
Reactions
Targets
Substances
Documents
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Reset form
Delete all
Structure
Molecular Formula
CAS RN
TI, AB & KW
Titles, Abstracts & K...
is
"molecular etiology";"molecular pathogenesis";"molecular pathology";"molecular pathophysiology";"pathology, molecular"
AND
Group 1
Ungroup
Titles, Abstracts & K...
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"targeted"
NEAR 3
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is
"c.n.s.";"central nerve system";"central nervous system";"cns";"nervous system,central";"neural analyzers";"systema nervosum ce
AND
Titles, Abstracts & K...
is
tumor;cancer
定义两个关键词之间间隔1-3

ELSEVIER

27 Documents with 39 Substances, 0 Reactions, 1 Targets

结果集也被扩大

0 selected Limit To Exclude Export

Sort by Publication Year Heatmap

儿童高级别胶质瘤的分子发病机制及治疗意义

1 Molecular pathogenesis and therapeutic implications in pediatric high-grade gliomas

Juratli, Tareq A.; Qin, Nan; Cahill, Daniel P.; Filbin, Mariella G. [**Pharmacology and Therapeutics, 2018**, vol. 182, p. 70 - 79]

Abstract Index Terms Substances 10 Full Text

Abstract

High-grade gliomas (HGG) are the most common malignant brain tumors in the pediatric population and account for a large subset of all pediatric central nervous system neoplasms. The management of pediatric HGG continues to be challenging, with poor outcome in many cases despite aggressive treatments. Consequently, parallel research efforts have been focused on identifying the underlying genetic and biological basis of pediatric HGG in order to more clearly define prognostic subgroups for treatment stratification as well as identify new treatment targets. These cutting-edge advances have revolutionized pediatric neuro-oncology and have revealed novel oncogenic vulnerabilities that are being therapeutically leveraged. Promising treatments – including pathway-targeting small molecules as well as epigenetic therapy – are being evaluated in clinical trials, and recent genomic discoveries in rare glioma subgroups have led to the identification of additional new potentially-actionable alterations. This review summarizes the current state of knowledge about the molecular characterization of pediatric HGG in correlation to the revised World Health Organization (WHO) classification, as well as provides an overview of some targeted treatment approaches in the modern clinical management of high-grade gliomas.

Index Terms

Author keyword: Brain tumor, CNS, Epigenetics, IDH, Pediatric glioma, Targeted therapy
EMTREE drug term: histone H3
EMTREE medical term: anaplastic ganglioglioma, antiangiogenic activity, cancer patient, cancer prognosis, cancer staging, cancer survival, carcinogenesis, child, childhood cancer, disease association, gene mutation, gene targeting, genetic code, glioblastoma, glioma, human, malignant transformation, missense mutation, molecular pathology, molecularly targeted therapy, outcome assessment, overall survival, pleomorphic xanthoastrocytoma, pontine glioma, priority journal, Review, somatic mutation, world health organization
Reaxys Index Terms: Permeability, acetylation, domain boundary, maximum tolerated dose, methylation, separation method, transfer reaction

2 Epithelioid hemangioendothelioma as a model of YAP/TAZ-driven cancer: Insights from a rare fusion sarcoma Cited 3 times

Lamar, John M.; Nehru, Vijeyaluxmy Motilal; Weinberg, Guy [**Cancers, 2018**, vol. 10, # 7, art. no. 229]

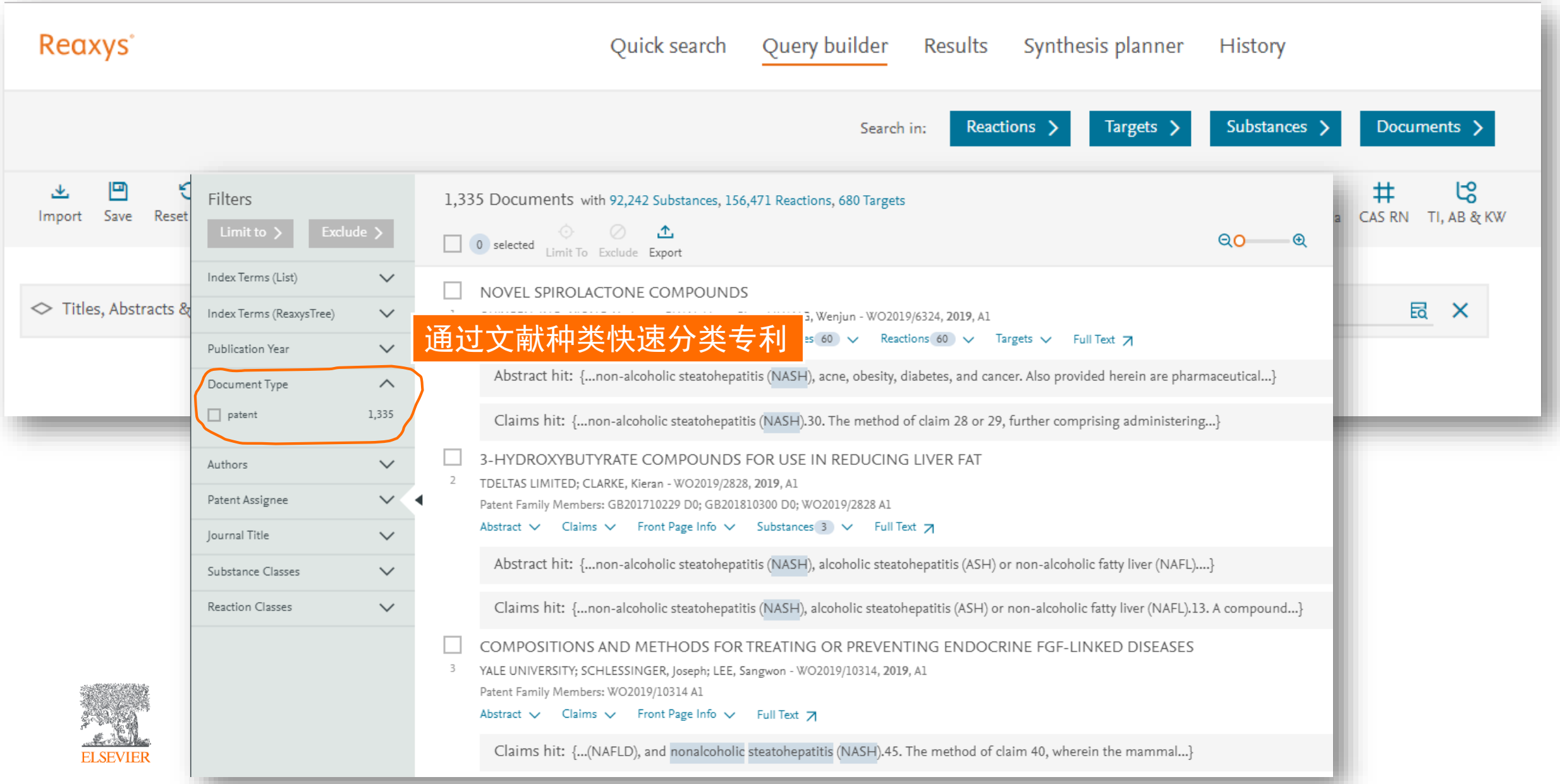
ELSEVIER

Reaxys专利检索技巧

Case 3:　NASH(Nonalcoholic steatohepatitis)治疗相关的专利

Case 4：　CD137相关的生物药专利

Case 3： NASH(Nonalcoholic steatohepatitis)治疗相关的专利



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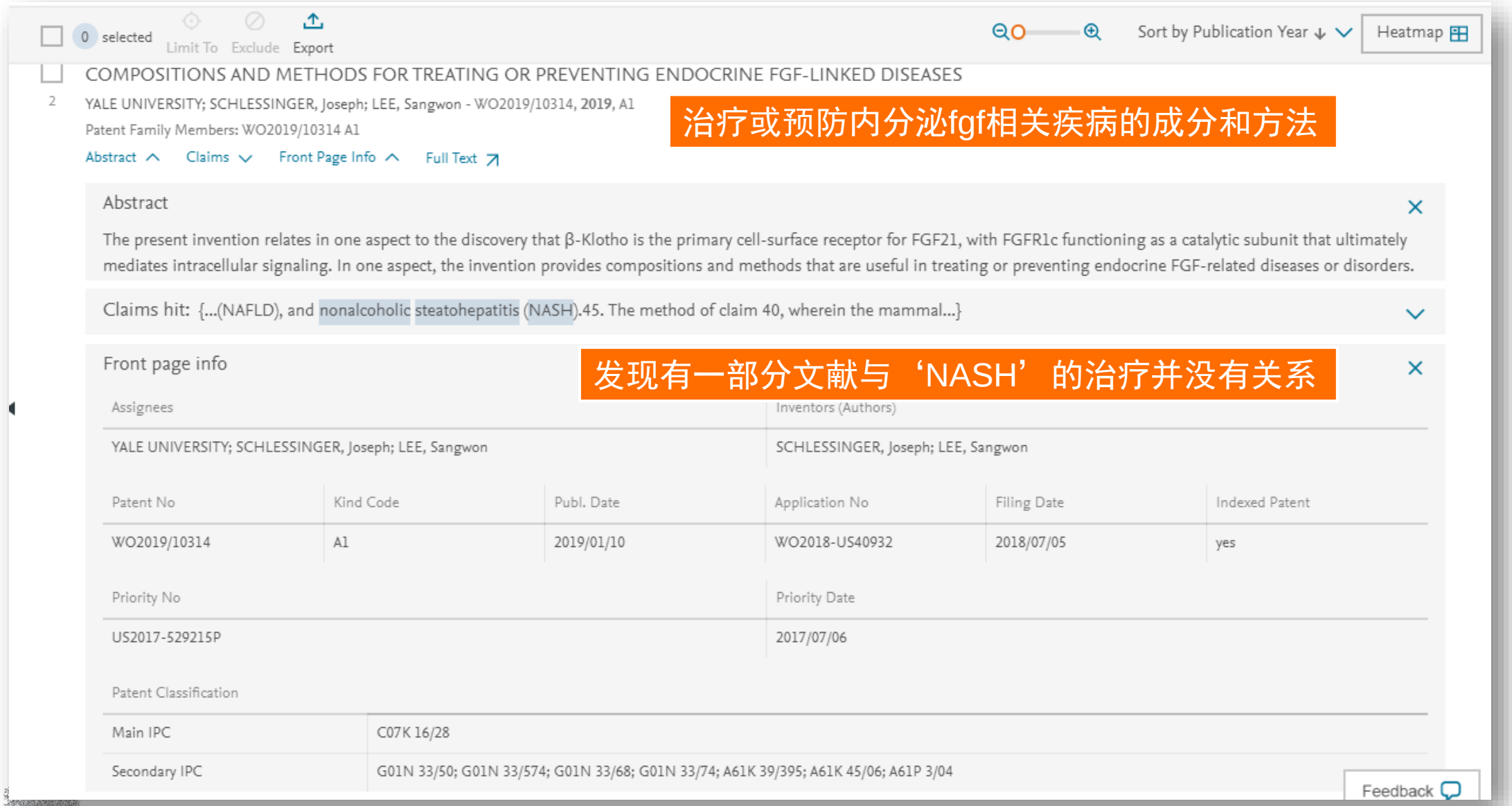
0 selected
Limit To
Exclude
Export
Sort by Publication Year
Heatmap
COMPOSITIONS AND METHODS FOR TREATING OR PREVENTING ENDOCRINE FGF-LINKED DISEASES
2
YALE UNIVERSITY; SCHLESSINGER, Joseph; LEE, Sangwon - WO2019/10314, 2019, A1
Patent Family Members: WO2019/10314 A1
治疗或预防内分泌fgf相关疾病的成分和方法
Abstract
Claims
Front Page Info
Full Text
Abstract
The present invention relates in one aspect to the discovery that β-Klotho is the primary cell-surface receptor for FGF21, with FGFR1c functioning as a catalytic subunit that ultimately mediates intracellular signaling. In one aspect, the invention provides compositions and methods that are useful in treating or preventing endocrine FGF-related diseases or disorders.
Claims hit: {...(NAFLD), and nonalcoholic steatohepatitis (NASH).45. The method of claim 40, wherein the mammal...}
Front page info
发现有一部分文献与‘NASH’的治疗并没有关系
Assignees
Inventors (Authors)
YALE UNIVERSITY; SCHLESSINGER, Joseph; LEE, Sangwon
SCHLESSINGER, Joseph; LEE, Sangwon
Patent No
Kind Code
Publ. Date
Application No
Filing Date
Indexed Patent
WO2019/10314
A1
2019/01/10
WO2018-US40932
2018/07/05
yes
Priority No
Priority Date
US2017-529215P
2017/07/06
Patent Classification
Main IPC
C07K 16/28
Secondary IPC
G01N 33/50; G01N 33/574; G01N 33/68; G01N 33/74; A61K 39/395; A61K 45/06; A61P 3/04
Feedback

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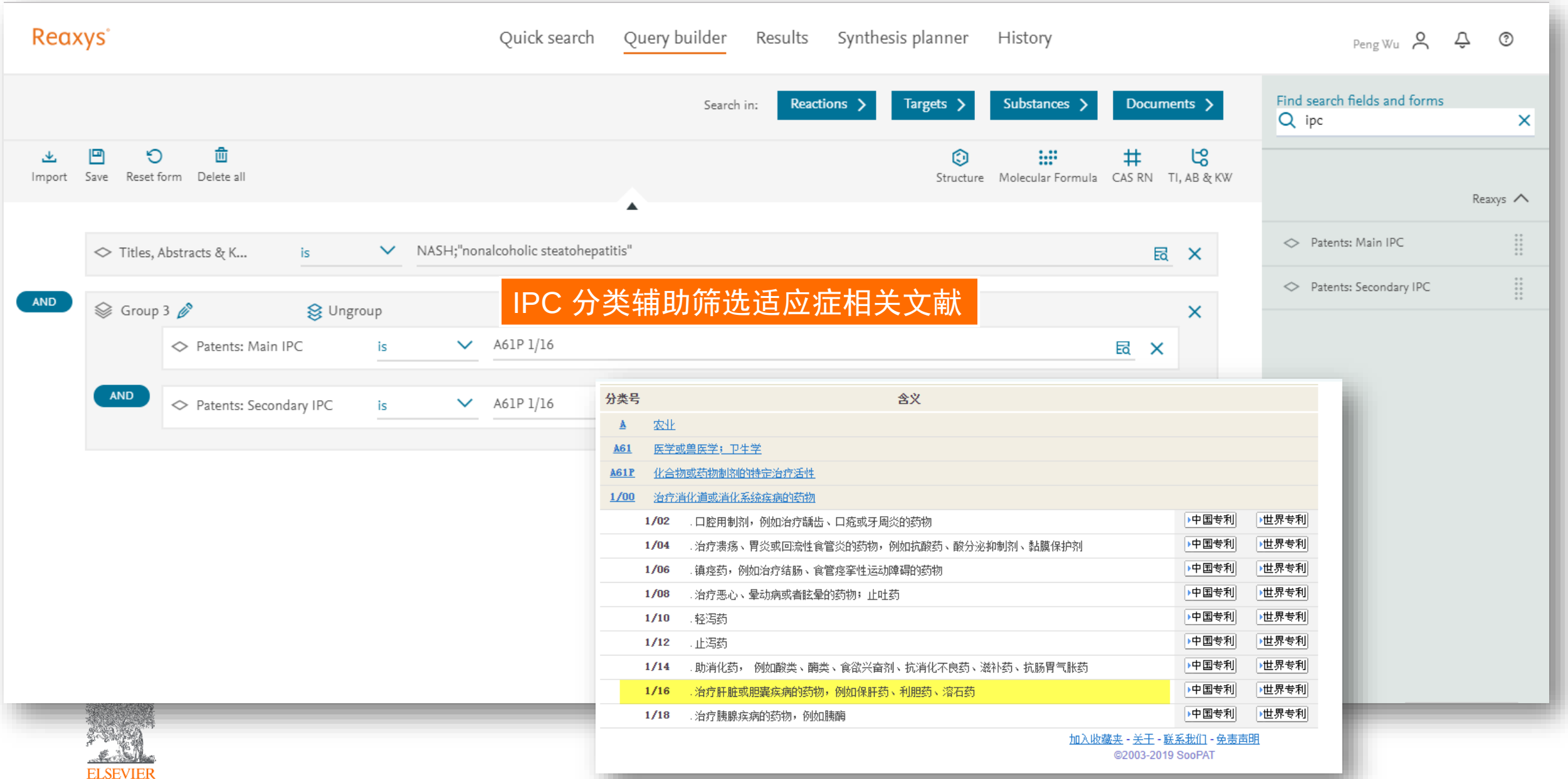
Reaxys
Quick search
Query builder
Results
Synthesis planner
History
Peng Wu
Search in:
Reactions
Targets
Substances
Documents
Import
Save
Reset form
Delete all
Structure
Molecular Formula
CAS RN
TI, AB & KW
Find search fields and forms
ipc
Reaxys
Patents: Main IPC
Patents: Secondary IPC
Titles, Abstracts & K...
is
NASH;"nonalcoholic steatohepatitis"
AND
Group 3
Ungroup
IPC 分类辅助筛选适应症相关文献
Patents: Main IPC
is
A61P 1/16
AND
Patents: Secondary IPC
is
A61P 1/16
分类号
含义
A 农业
A61 医学或兽医学；卫生学
A61P 化合物或药物制剂的特定治疗活性
1/00 治疗消化道或消化系统疾病的药物
1/02 .口腔用制剂，例如治疗龋齿、口疮或牙周炎的药物
1/04 .治疗溃疡、胃炎或回流性食管炎的药物，例如抗酸药、酸分泌抑制剂、黏膜保护剂
1/06 .镇痉药，例如治疗结肠、食管痉挛性运动障碍的药物
1/08 .治疗恶心、晕动病或者眩晕的药物；止吐药
1/10 .轻泻药
1/12 .止泻药
1/14 .助消化药， 例如酸类、酶类、食欲兴奋剂、抗消化不良药、滋补药、抗肠胃气胀药
1/16 .治疗肝脏或胆囊疾病的药物，例如保肝药、利胆药、溶石药
1/18 .治疗胰腺疾病的药物，例如胰酶
中国专利
世界专利
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©2003-2019 SooPAT

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Case 4：检索2019年2月，与CD137相关的，人用药，含抗原或抗体的医药配置品（生物药类专利）

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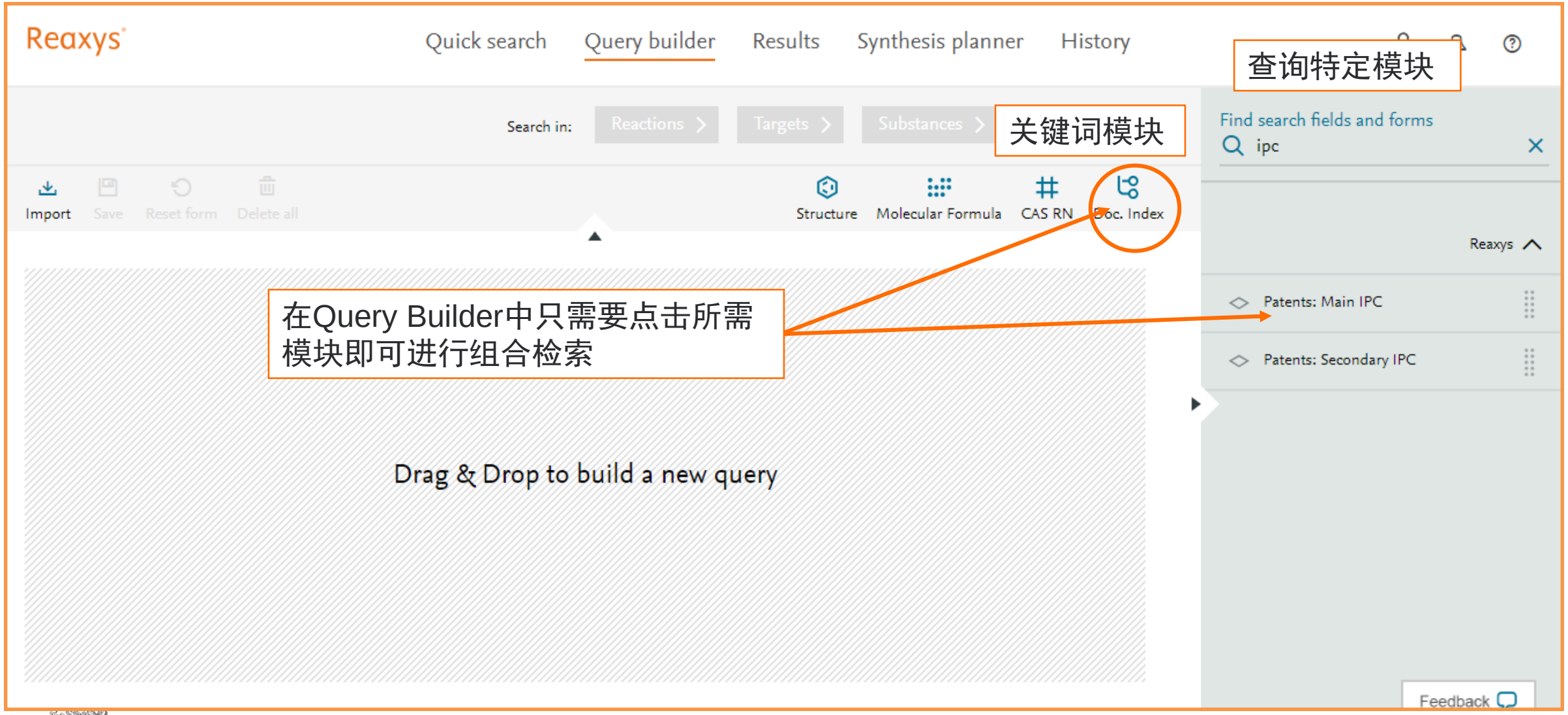
组合模块构建


Reaxys
Quick search
Query builder
Results
Synthesis planner
History
查询特定模块
Search in:
Reactions
Targets
Substances
关键词模块
Find search fields and forms
ipc
Import
Save
Reset form
Delete all
Structure
Molecular Formula
CAS RN
Doc. Index
Reaxys
在Query Builder中只需要点击所需模块即可进行组合检索
Patents: Main IPC
Patents: Secondary IPC
Drag & Drop to build a new query
Feedback

检索结果

2 METHODS AND COMPOSITIONS FOR PREPARING GENETICALLY ENGINEERED CELLS

JUNO THERAPEUTICS, INC.; BONYHADI, Mark L. WO2019/32929, **2019**, A1

Patent Family Members: WO2019/32929 A1

Abstract Claims Front Page Info Full Text

Claims hit: {...of CD28, CD137 (4-1-BB), OX40, or ICOS.42. The method of claim 41, wherein...}

Assignees			Inventors (Authors)
JUNO THERAPEUTICS, INC.; BONYHADI, Mark L.			BONYHADI, Mark L.
Patent No	**Kind Code**	**Publ. Date**	**Application No**
WO2019/32929	A1	2019/02/14	WO2018-US46151
Priority No			**Priority Date**
US2017-543359P			2017/08/09
Patent Classification			
Main IPC	A61K 39/00		
Secondary IPC	C12N 5/0783		

公开日期
授权状况

IPC
分类

Claims

CLAIMS

WHAT IS CLAIMED:

1. A method for genetically engineering
(a) incubating an input composition, un
T cells, wherein the stimulating conditi
or more intracellular signaling domains
(b) introducing a nucleic acid encoding
incubating.
2. A method for genetically engineering
population of T cells comprising naive-
the stimulating conditions comprises th
or more intracellular signaling domains
the incubating the input composition under stimulating conditions is performed prior to, during and/or subsequent to introducing a nucleic acid encoding a
receptor.
3. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 3 days.
4. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 4 days.
5. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 5 days.
6. The method of claim 1 or claim 2, wherein the incubating is carried out for at least 6 days.
7. A method for stimulating T cells, the method comprising:
(a) incubating, under stimulating conditions, an input composition comprising T cells comprising a culture-initiating amount of naive-like T cells or a CD8+
stimulated composition, wherein the stimulating conditions comprise the presence of a stimulatory reagent capable of activating one or more intracellular si
components of a TCR complex and/or one or more intracellular signaling domains of one or more costimulatory molecules, thereby generating a stimulated
(b) introducing into the stimulated cell composition a nucleic acid encoding a genetically engineered recombinant receptor, wherein the method thereby gen
cells expressing the genetically engineered recombinant receptor.

ation of T cells com
ains of one or more
the introducing is
for between 2 and 6
ains of one or more

专利‘Claim’部分的摘取和可索引，对于生物药类专利的检索非常有利。

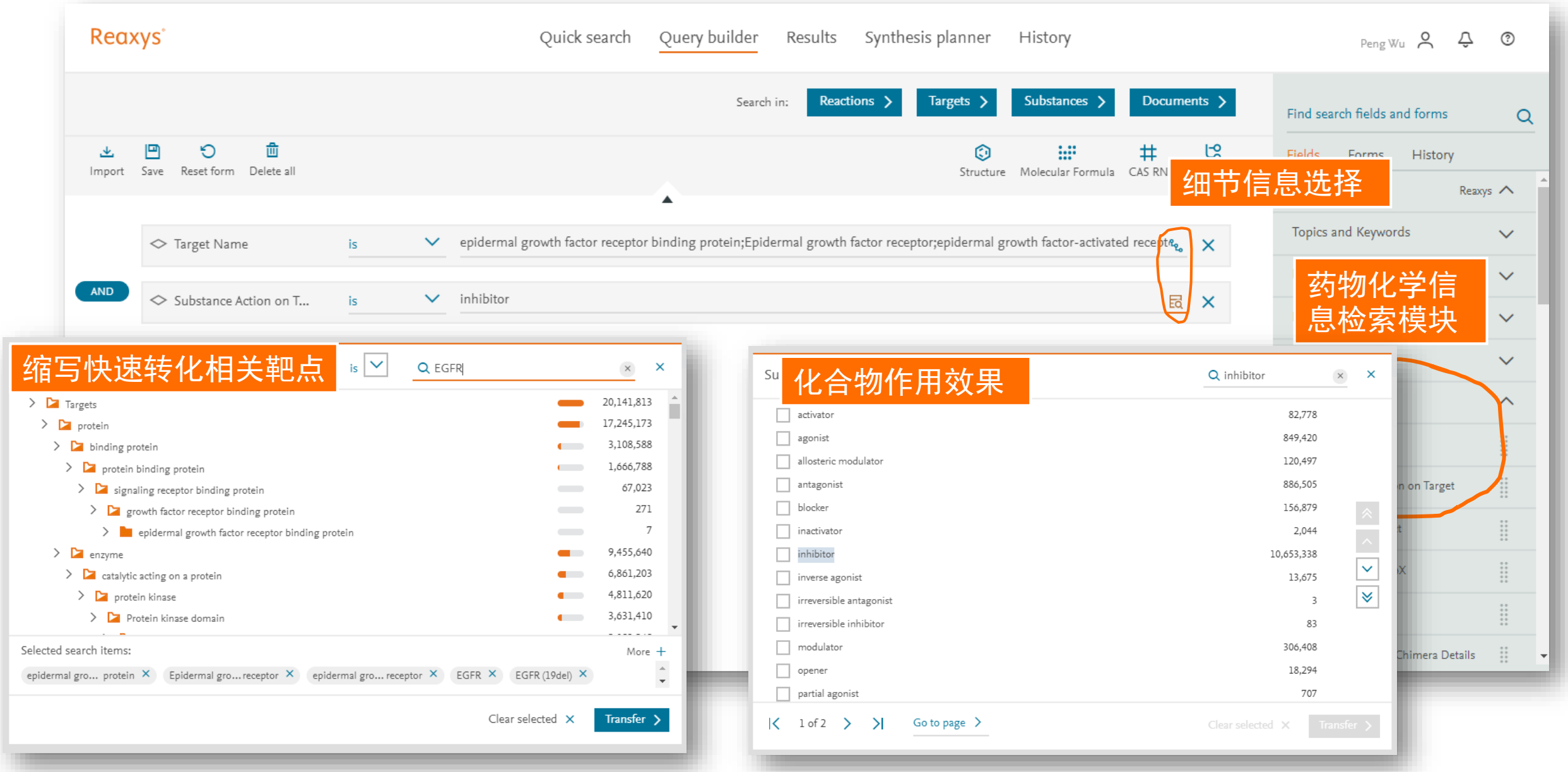
通常生物药类的专利，不具有结构式，且专利标题和摘要一般会撰写得比较简单，造成了生物药类专利检索的困难

ELSEVIER

Reaxys Medicinal Chemistry模块应用

Case 5: 如何通过靶点筛选小分子抑制剂

Case 5: 如何通过靶点筛选小分子抑制剂



Reaxys

Quick search | Query builder | Results | Synthesis planner | History

Peng Wu

71.40 K Query

Filters

Limit to > Exclude >

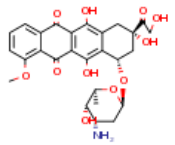
- By Structure
- Measurement pX
- Highest Clinical Phases
- Targets
- Parameters
- Substance Classes
- Molecular Weight
- Number of Fragments
- Availability
- Availability in other databases
- Available Data
- Do
- Pu
- Patent Assignee
- LogP
- H Bond Donors

71,403 Substances out of 2,922 Documents, containing 102,517 Reactions, 375 Targets

0 selected | Limit To | Exclude | Export | Preparations

Sort by No of References | Grid | Heatmap

1



doxorubicin

$C_{27}H_{29}NO_{11}$ 543.527 1445814 23214-92-8

Identification | Bioactivity (All) | Other Data - 6,037

Druglikeness | Physical Data - 164

Bioactivity (Hit Data) | Spectra - 239

Preparations - 68 >

Reactions - 364 >

Targets - 393 >

Documents - 27,491 >

doxorubicin

- Identification
- Druglikeness
- Bioactivity (Hit Data)
- Bioactivity (All)
- Physical Data - 164
- Spectra - 239

生物活性数据

Bioactivity (All)

- In vitro: Efficacy - 12410
- In vivo: Animal Model - 2116
- Metabolism - 756
- Pharmacokinetic - 995
- Toxicity/Safety Pharmacology - 12536

pX	Parameter	Value (qual)	Value (quant)	Unit	Action on target	Cell	Bioassay	Effect
14.9	IC50	=	1.3E-09	µM	Inhibitor	MMA cell line		
13.2	IC50		6.19E-08	µM		OVCAR-3 cell line	In Vitro (others)	antiprolifera agent
12.3	GI50	=	3E-07	µg/mL		NCI-H460 cell line		

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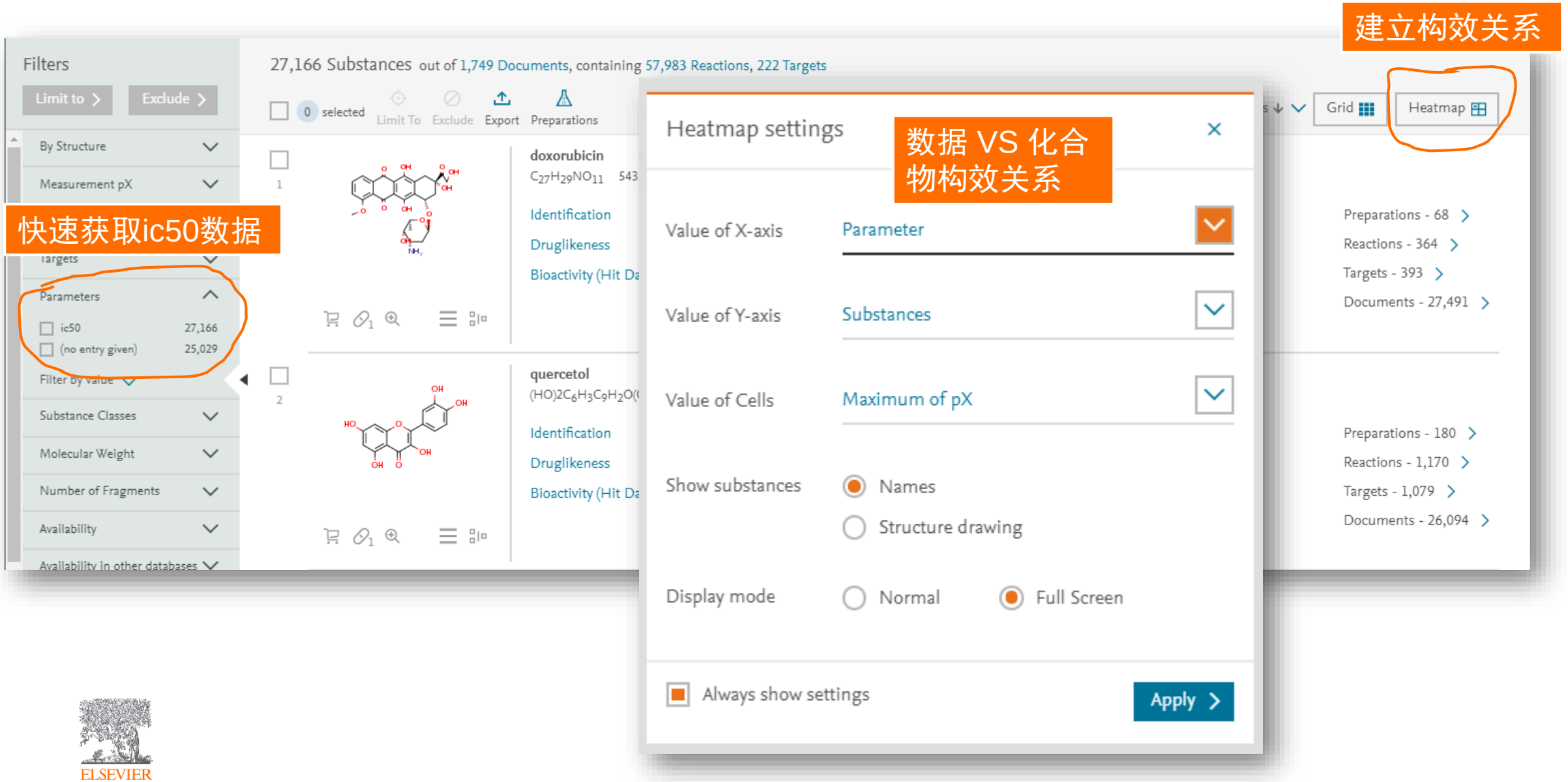
建立构效关系

快速获取ic50数据

数据 VS 化合物构效关系



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Limit To | Exclude | Export | Settings | Navigator | Legend

Substances | Exit Full Screen

导出结果

ic50

Parameter

Substances

staurosporine — 12.8

4-[(3-chloro-4... nazoline — 12.7

6,7-dimetho... -4-amine

4-Dimethyla... l]-amide

(1R,5S)-3-(3-((...xan-1-ol

N-(4-fluorop... -4-amine

N-(3-chloro-... -4-amine

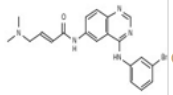
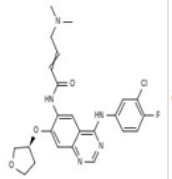
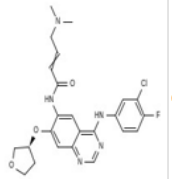
N-(3-chloro-... -4-amine

N-(3-chloro-... -4-amine

N-(3-chloro-... -4-amine

N-(3-chloro-... -4-amine

N-(3-chloro-... -4-amine

	A	B	C	D	E	F	G	H	I	J	K	L
1	Structure: Image	SMILES	CAS Registry Number	Chemical Name	Molecular Formula	Molecular Weight	Target Name	Target, Subunit, Species	Substance Action on Tar	Bioassay Category	Medchem: Measuremen	Unit
9		CN(C)C\C=C\C(=O)NC1=		4-Dimethylamino-but-2	C20H20BrN5O	426.316	Epidermal growth factor	Epidermal growth factor	Inhibitor	In Vitro (Efficacy)	IC50	nM
16		CN(C)CC=CC(=O)NC1=(		4-[(3-chloro-4-fluoroph	C24H25ClFN5O3	485.946	epidermal growth factor	epidermal growth factor	Inhibitor	In Vitro (Efficacy)	IC50	nM
17		CN(C)CC=CC(=O)NC1=(		4-[(3-chloro-4-fluoroph	C24H25ClFN5O3	485.946	epidermal growth factor	epidermal growth factor	Inhibitor	In Vitro (Efficacy)	IC50	nM

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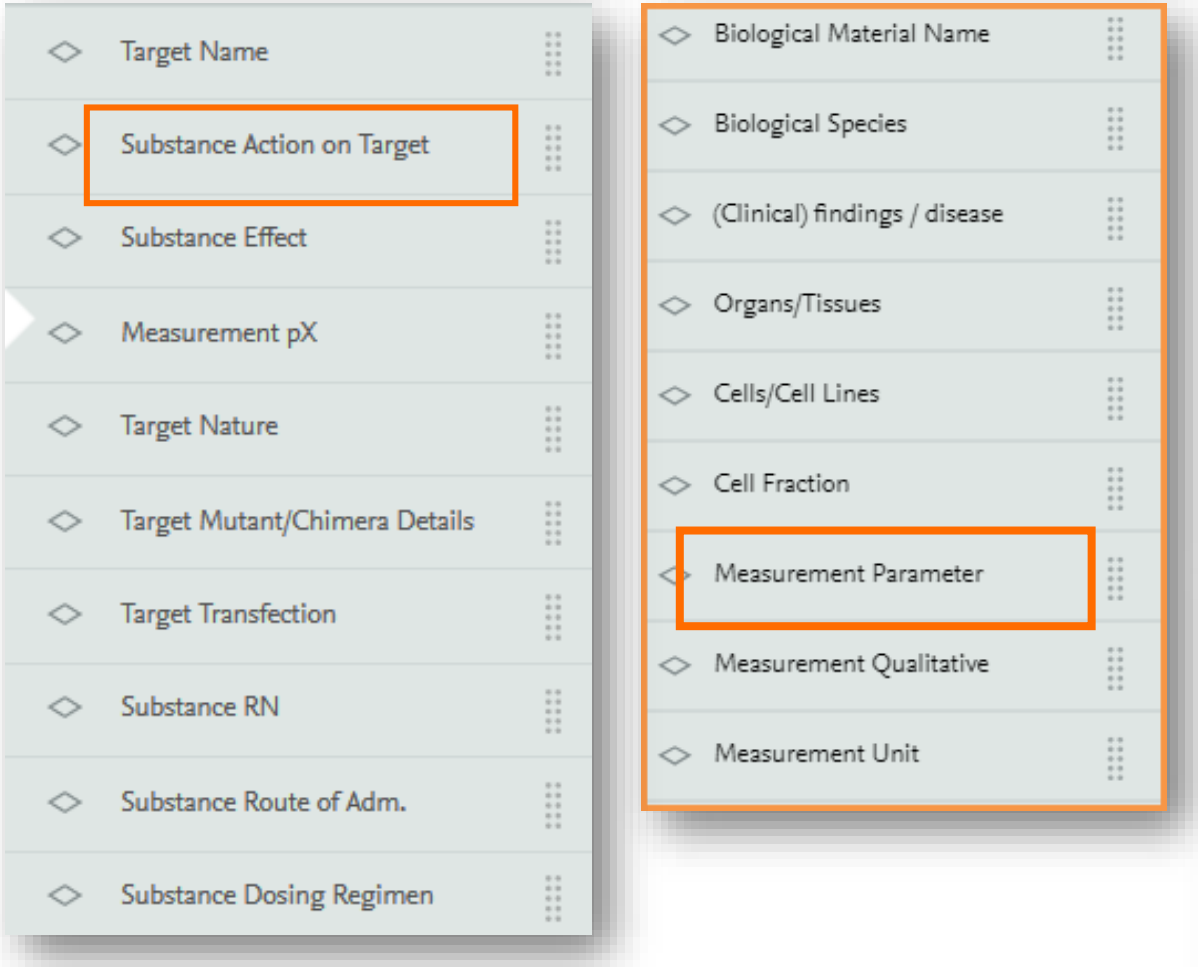
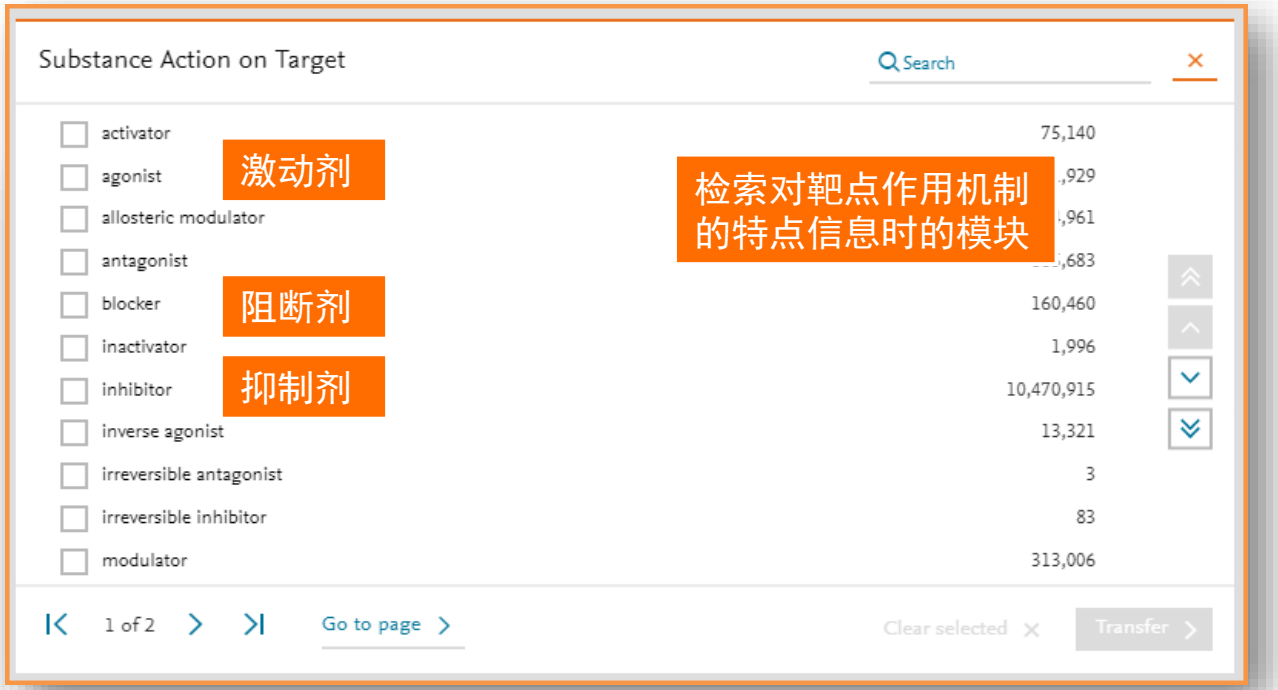
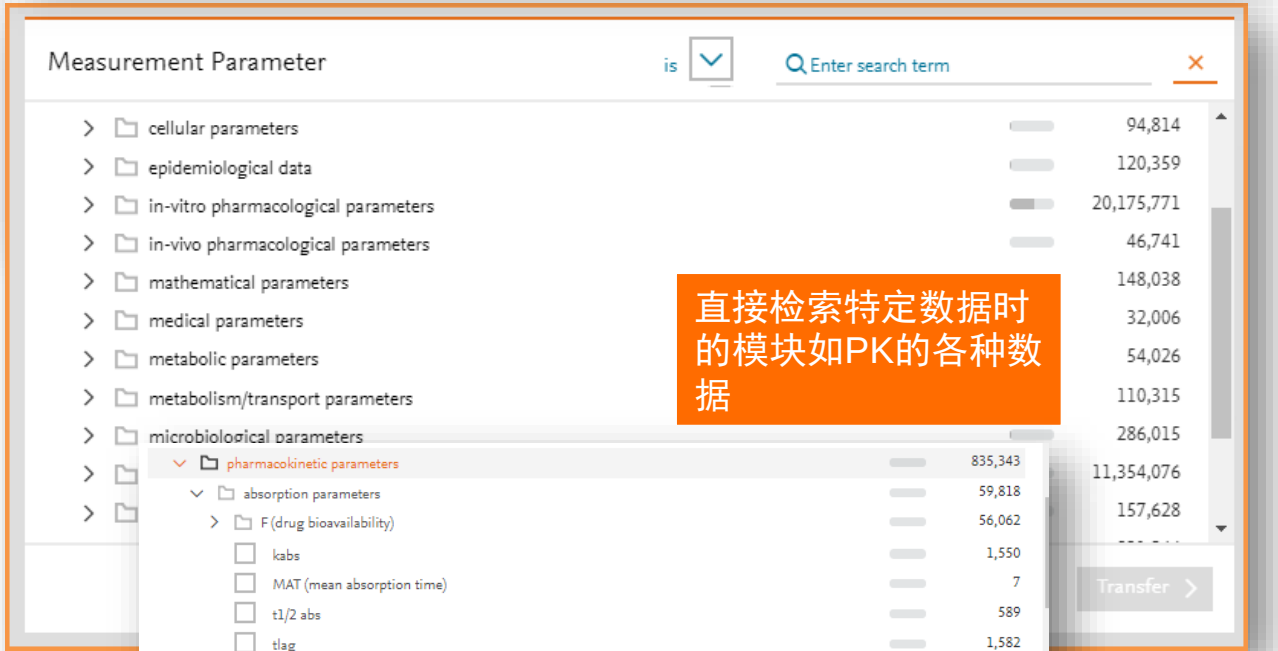
RMC-特定的信息检索方法



各种分类细致的信息检索模块，快捷锁定对应结果





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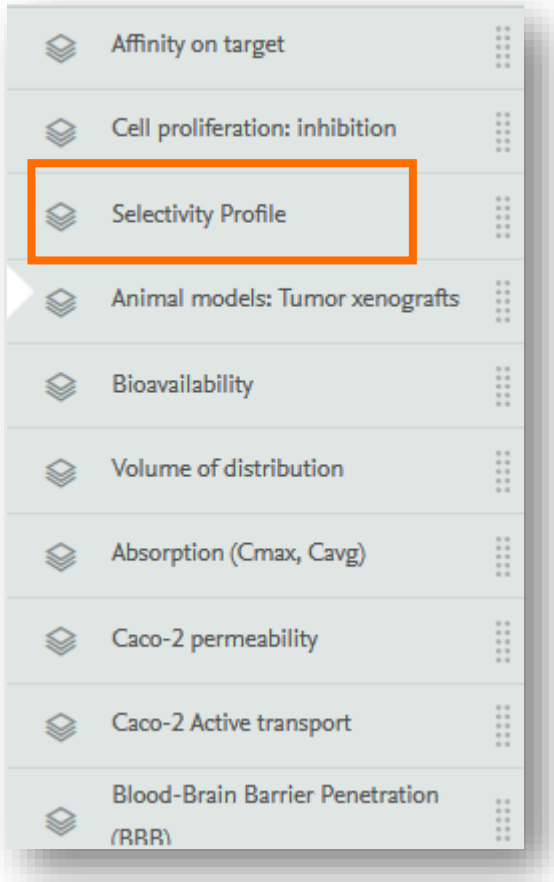
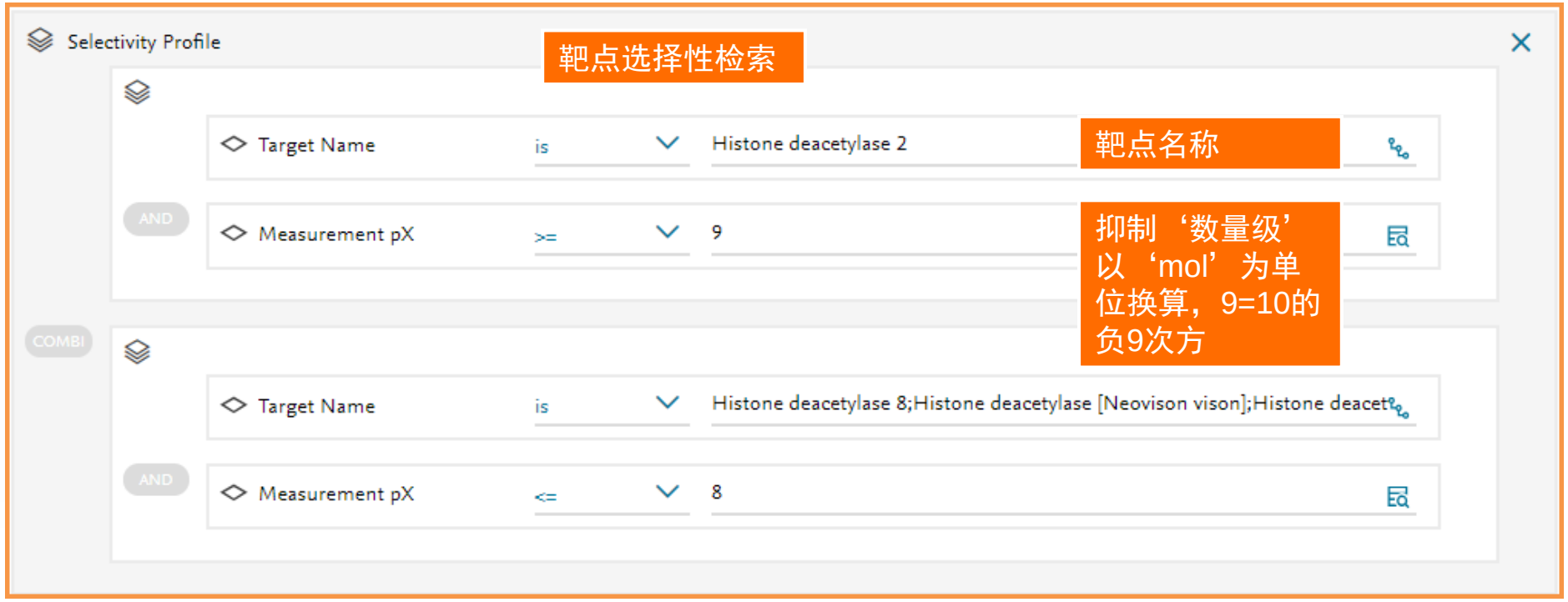
RMC-组合信息便捷检索



预设的组合检索模块，便捷检索综合信息，如对于不同亚型的同类靶点，差异抑制性



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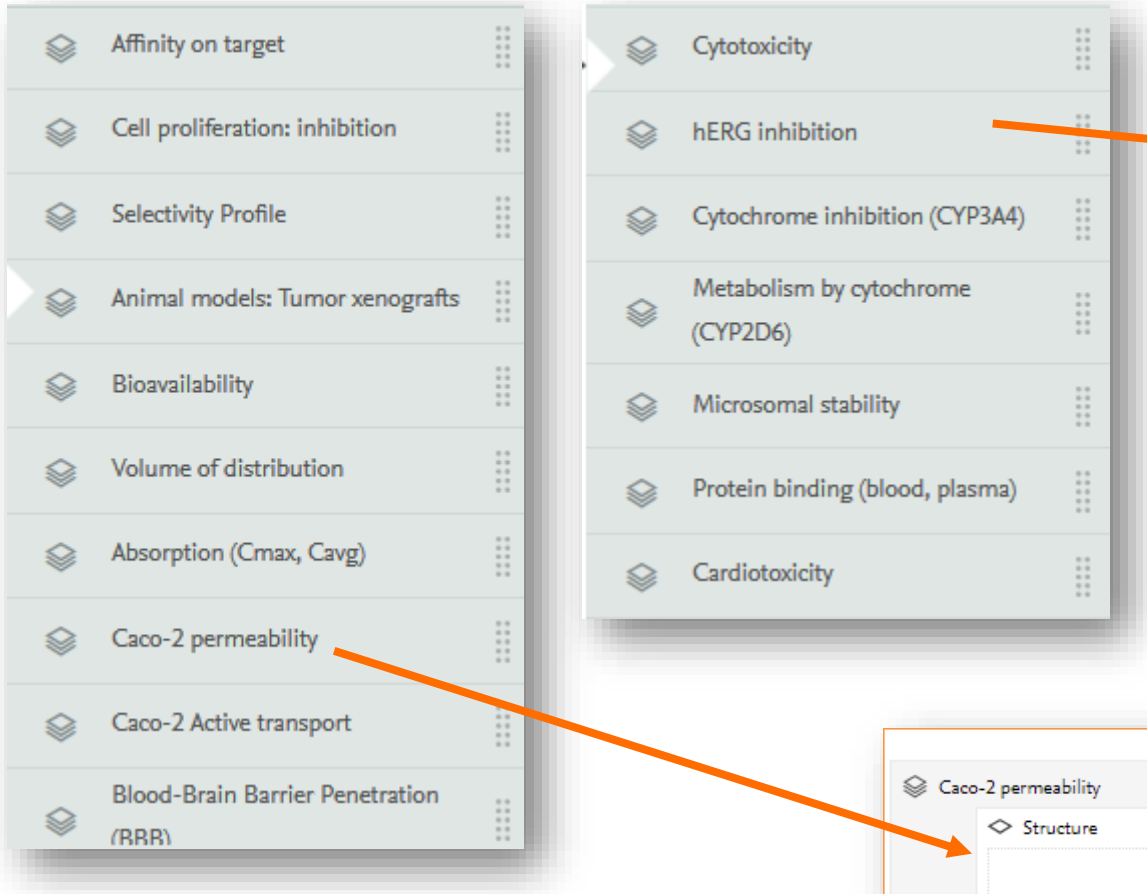
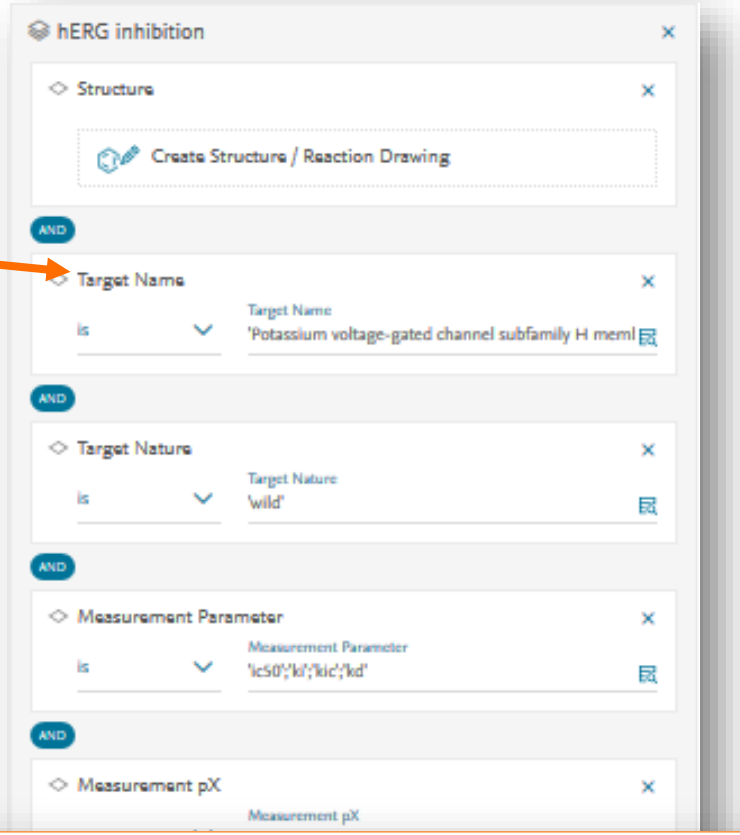
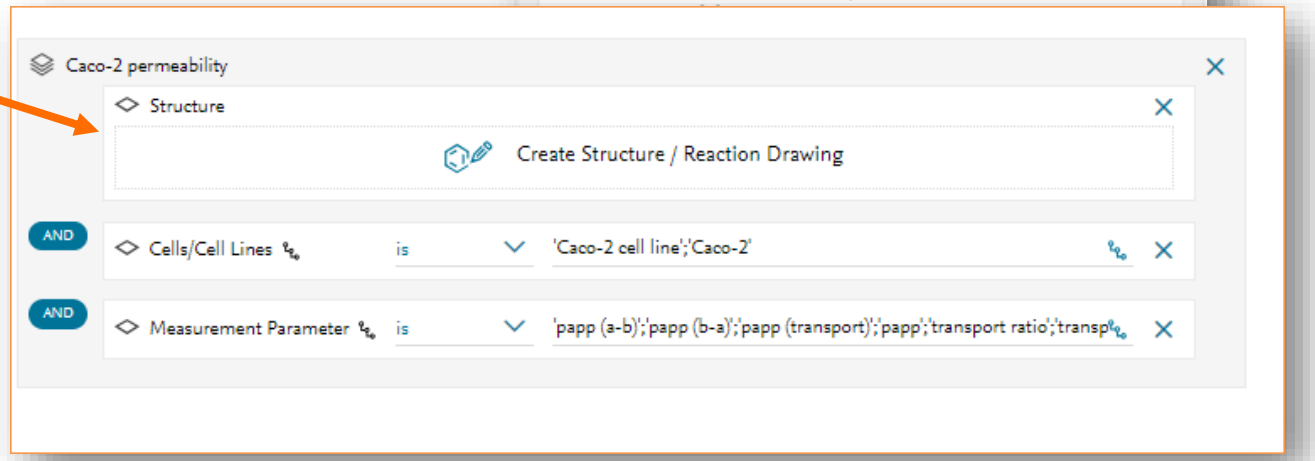
RMC-组合信息便捷检索







只需要特定结构即可初步快速检索特殊信息

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Thank you