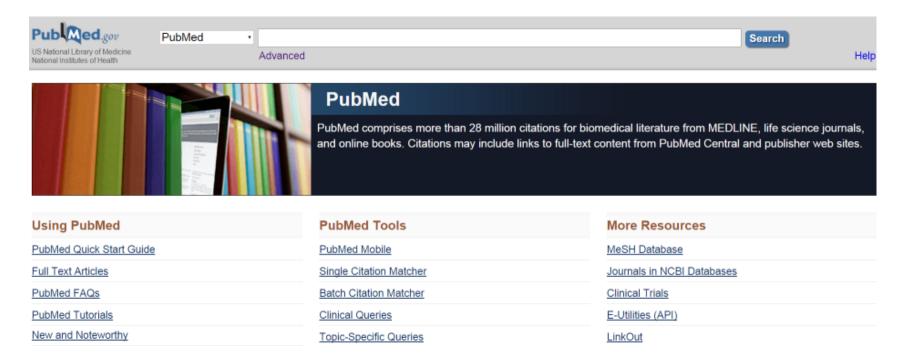
# 美国生物医学文献检索系统 PubMed

黄利辉 医学信息研究所 2019.11.14

## **PubMed**

### 文献是获取知识最基本的来源

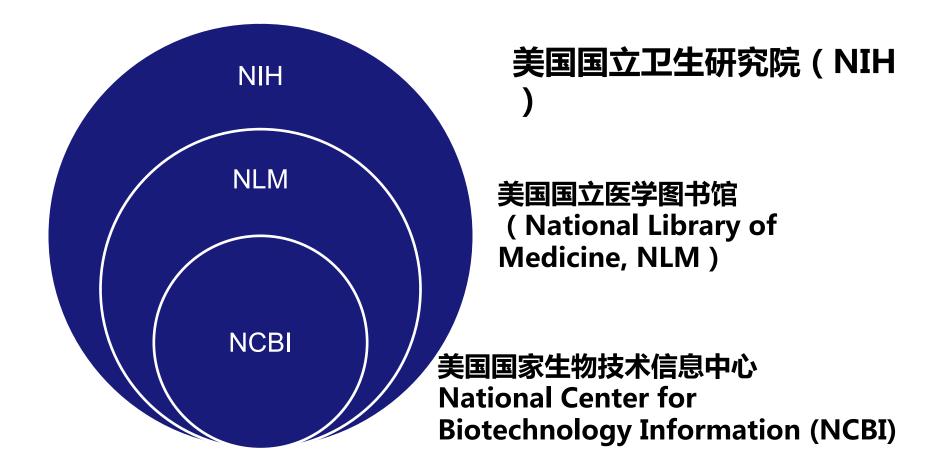


如果说我比别人看得要远一点,那是因为我站在巨人的肩上 ——牛顿

# 一、认识PubMed

首选: Google Chrome浏览器

地址: pubmed.gov



https://www.ncbi.nlm.nih.gov/pubmed/

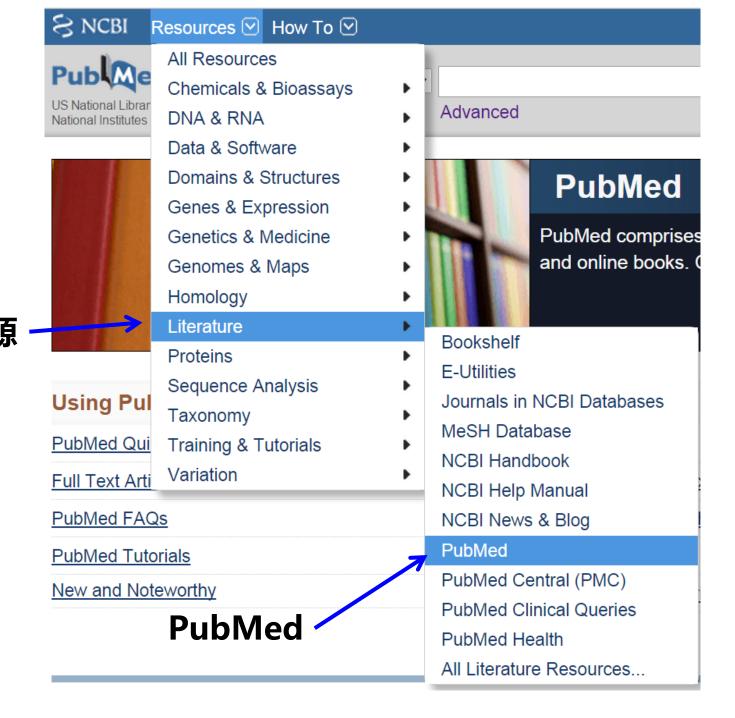




Gore said
"PubMed is
FREE"

on Jun 26 1997

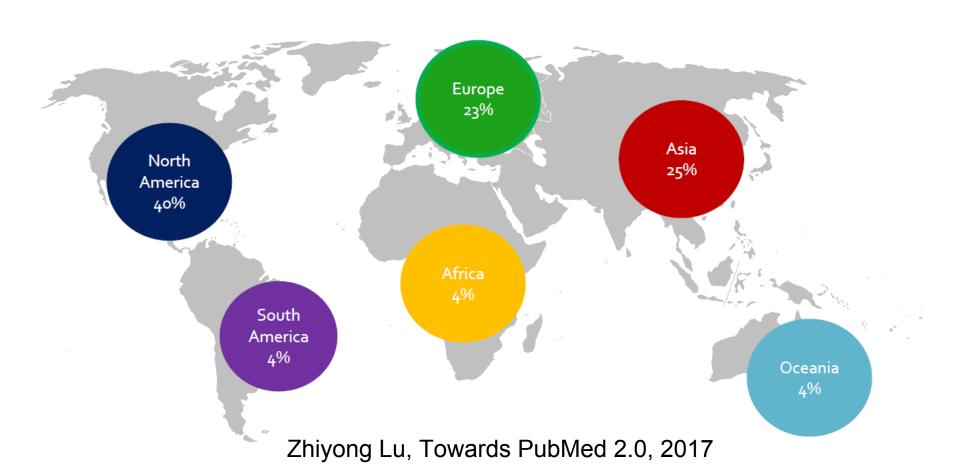
Albert Arnold Gore, Jr 45th vice president of the United States



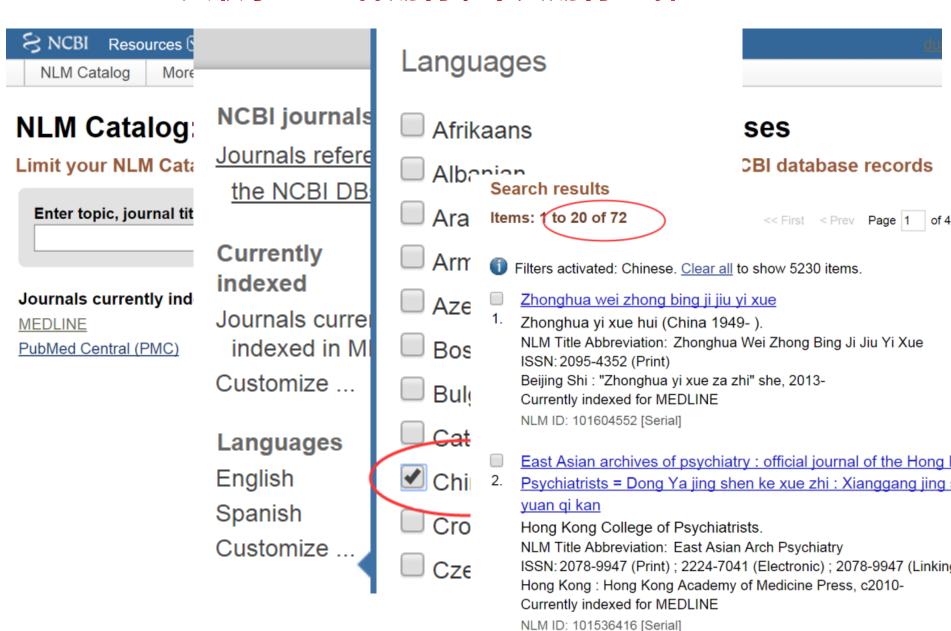
### **PubMed Daily Usage**

- > 2.5 million users daily
- > ~ 3 million searches
- > 9 million page views

# PubMed每日使用量 全球分布



### MEDLINE共收录5230种期刊,中文期刊72种



# 二、医学主题词是什么?如何通过主题词检索文献?

# 投稿时...

### ■《中华医学系列杂志》稿约

- ▶关键词:论著需标引2~5个。
- ▶请尽量使用美国国立医学图书馆编辑的最新版医学主题词表(MeSH)内所列的词。
- ▶如果最新版MeSH中尚无相应的词:
  - 可选用直接相关的几个主题词进行组配。
  - 可根据树状结构表选用最直接的上位主题词。
  - 必要时,可采用习用的自由词,并排列于最后。



# 医学主题词(MeSH)

### Medical Subject Headings

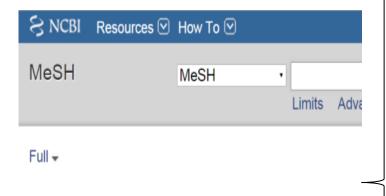
- ■主题词 ( headings )
  - ▶描述文献重点讨论实质内容,对自然语言进行规范化处理的词语。
  - ▶目前共**2.5**万多个,每年更新一次,满足医学科学发展
- ■副主题词 ( subheadings )
  - >是对主题词起限定作用的一类词汇,增强专指性
  - ▶目前共83个,诊断、治疗、流行病学、并发症...
- ■主题词和关键词(Keywords)的区别?

# 特点一:若干同义词的合并词/规范词

- **■例1:胃癌** 
  - > Stomach Cancer
  - > Stomach Tumor
  - > Stomach Tumour



- Receptor-Like Protein Tyrosine Phosphatases, Class 3
- A subclass of receptor-like protein tryosine phosphatases that contain a single and multiple extracellular fibronectin III-like domains. Year introduced: 2008(2002)



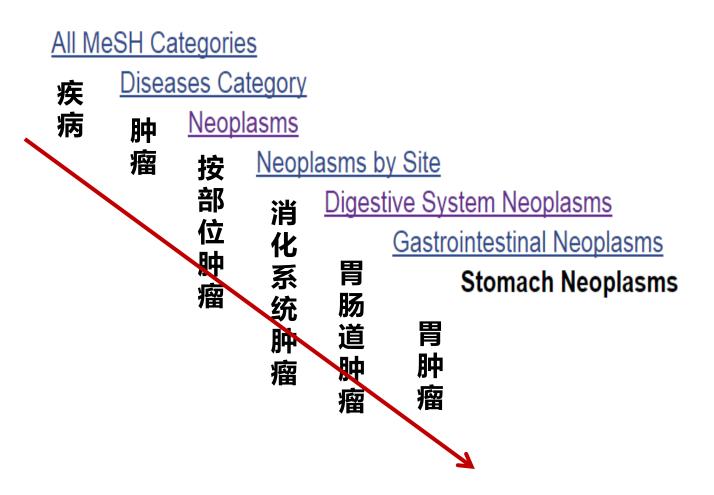
Stomach Neoplasms

Tumors or cancer of the STOMACH.

### Entry Terms:

- Neoplasm, Stomach
- Stomach Neoplasm
- Neoplasms, Stomach
- Gastric Neoplasms
- Gastric Neoplasm
- · Neoplasm, Gastric
- Neoplasms, Gastric
- Cancer of Stomach
- Stomach Cancers
- Gastric Cancer
- · Cancer, Gastric
- Cancers, Gastric
- Gastric Cancers
- Stomach Cancer
- · Cancer, Stomach
- Cancers, Stomach
- Cancer of the Stomach
- · Gastric Cancer, Familial Diffuse

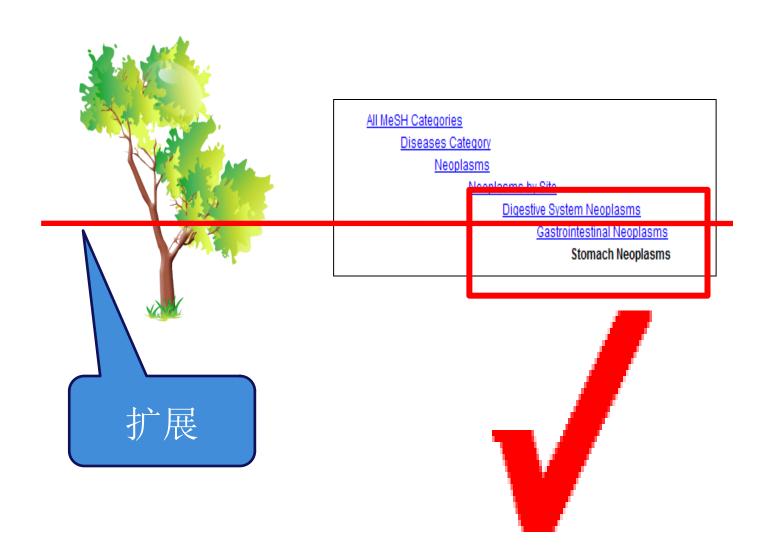
# MeSH词表 层级结构,或树状结构



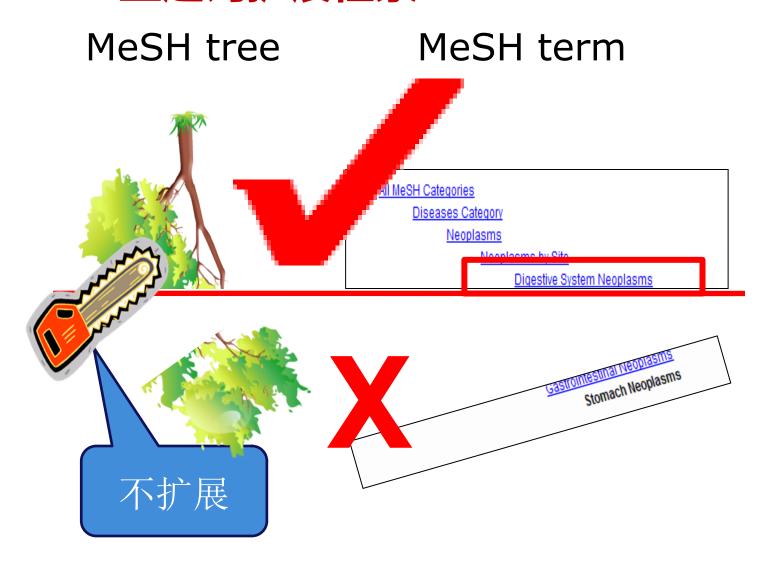
# 技巧1:主题词扩展检索

MeSH tree

MeSH term



# 主题词扩展检索



# 技巧2:主题词加权检索

Format: Abstract -

理解:主题词是如何标注到文章里的

Nature. 2016 Nov 24;539(7630):479. doi: 10.1038/nature.2016.20988.

### CRISPR gene-editing tested in a person for the first time.

Cyranoski D.

#### Comment in

Boost visas for foreign entrepreneurs. [Nature. 2017]

PMID: 27882996 DOI: 10.1038/nature.2016.20988

[Indexed for MEDLINE]

根据文章的实质内容,标注5-10 个主题词

从中再选出3-5个最能表明文章 核心内容的,加上\*,作为主要主 题词 Mesh Major Topic **Publication type, MeSH terms** 

**Publication type** 

News

#### MeSH terms

CRISPR-Cas Systems/genetics\*

China

Clinical Trials as Topic\*

Competitive Behavior

Gene Editing\*/trends

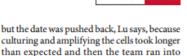
Humans

Neoplasms/genetics

Neoplasms/therapy\*

Translational Medical Research/trends

**United States** 



The researchers removed immune cells from the recipient's blood and then disabled a gene in them using CRISPR-Cas9, which combines a DNA-cutting enzyme with a molecular guide that can be programmed to tell the enzyme precisely where to cut. The disabled gene codes for the protein PD-1, which normally puts the brakes on a cell's immune response: cancers take advantage of that function to proliferate.

China's October holidays.

Lu's team then cultured the edited cells. increasing their number, and injected them back into the patient, who has metastatic nonsmall-cell lung cancer. The hope is that, without PD-1, the edited cells will attack and defeat the cancer.

Lu says that the treatment went smoothly, and that the participant will get a second injection, but declined to give details because of patient confidentiality. The team plans to treat ten people in total; each will receive either two, three or four injections. It is primarily a safety trial, and participants will be monitored for six months to determine whether the injections are causing serious adverse effects. Lu's team will also watch them beyond that time to see if they seem to be benefiting from the treatment.

Other oncologists are excited about CRISPR's entry onto the cancer scene. "The technology to be able to do this is incredible," says Naiyer Rizvi of Columbia University Medical Center in New York City. Antonio Russo of Palermo University in Italy notes that antibodies that neutralize PD-1 have successfully kept lung cancer in check, boding well for a CRISPR-enabled attack on the protein. "It's an exciting strategy," he says. "The rationale is strong."

But Rizvi questions whether this particular trial will succeed. The process of extracting, genetically modifying and multiplying cells is "a huge undertaking and not very scalable", he says. "Unless it shows a large gain in efficacy, it will be hard to justify moving forward." He doubts it will be superior to the use of antibodies, which can be expanded to unlimited quantities in the clinic. Lu says that this question is being evaluated in the trial, but that it's too early to say which approach



Gene editing could improve the ability of immune cells (spherical) to attack cancer.

BIOTECHNOLOGY

## CRISPR gene editing tested in a person

Trial could spark biomedical duel between China and US.

BY DAVID CYRANOSKI

Chinese group has become the first to inject a person with cells that contain ✓ Ligenes edited using the revolutionary CRISPR-Cas9 technique.

On 28 October, a team led by oncologist Lu You at Sichuan University in Chengdu delivered the modified cells into a patient with aggressive lung cancer as part of a clinical trial at the West China Hospital, also in Chengdu.

Earlier clinical trials using cells edited with a different technique have shown promise at treating disease. The emergence of CRISPR, which is simpler and more efficient than other techniques, will probably accelerate the race to get gene-edited cells into the clinic, says Carl June, who specializes in immunotherapy at the University of Pennsylvania in

Philadelphia and led one of the earlier trials.

"I think this is going to trigger 'Sputnik 2.0', a biomedical duel on progress between China and the United States, which is important since competition usually improves the end product," he says.

Iune is also the scientific adviser for a planned US trial that will use CRISPR to target three genes in cells extracted from participants, with the goal of treating various cancers. He expects the trial to start early next year. In March 2017, a group at Peking University in Beijing hopes to start three clinical trials using CRISPR against bladder, prostate and renal-cell cancers. Those trials do not yet have approval or funding.

Lu's trial received ethical approval from a hospital review board in July. Injections into participants were supposed to begin in August

### **Digestive System Neoplasms**

Tumors or cancer of the DIGESTIVE SYSTEM.

Year introduced: 1980

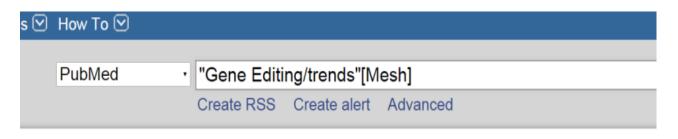
PubMed search builder options

Subheadings:

### 副主题词

analysis	economics	physiology
anatomy and histology	embryology	physiopathology
☐ blood	enzymology	prevention and control
blood supply	epidemiology	psychology
cerebrospinal fluid	ethnology	□ radiotherapy
chemical synthesis	etiology	☐ rehabilitation
chemically induced	genetics	secondary
☐ chemistry	☐ history	secretion
classification	immunology	statistics and numerical data
complications	legislation and jurisprudence	surgery
□ congenital	metabolism	☐ therapy
□ cytology	microbiology	☐ transmission
☐ diagnosis	mortality	☐ transplantation
diagnostic imaging	nursing	ultrastructure
☐ diet therapy	organization and administration	urine
drug effects	parasitology	veterinary
☐ drug therapy	pathology	□ virology
Restrict to MeSH Major Topic.		L-1-10
• •	加权检索	
Do not include MeSH terms found belo	<b>坛屏</b> 检索	

# 技巧3:综述性、趋势性文献:研究前沿



Format: Summary - Sort by: Publication Date - Per page: 20 -

### 组配 副主题词 Trends

Send to ▼

#### Search results

- Emerging Role of CRISPR/Cas9 Technology for MicroRNAs Editing in Cancer
- Research.

Aquino-Jarquin G.

Cancer Res. 2017 Dec 15;77(24):6812-6817. doi: 10.1158/0008-5472.CAN-17-2142. Epub 2017 Dec 5. Review.

PMID: 29208606 Similar articles

- CRISPR Editing Technology in Biological and Biomedical Investigation.
- White MK, Kaminski R, Young WB, Roehm PC, Khalili K.
   J Cell Biochem. 2017 Nov:118(11):3586-3594. doi: 10.1002/icb.26099. Epub 2017 Jul 4.

# 特点二:不断更新变化

- ■例:精准医学
  - > Precision Medicine
  - >来源于个体化医学

### MeSH是不断更新和演化的

### Individualized Medicine

Clinical, therapeutic and diagnostic approaches to optimal disease management based on individual variations in a patient's genetic and environmental profile.

Year introduced: 2010

**2010**年,"Individualized Medicine"被收录到美国国立医学图书馆的医学主题词表(MeSH),其含义是指基于患者遗传与环境特征的个体差异,实现最佳的疾病诊断与治疗。

2016年,更名为"Precision Medicine",仅强调 genetic profile!

#### **Precision Medicine**

Clinical, therapeutic and diagnostic approaches to optimal disease management based on individual variations in a patient's genetic profile.

Year introduced: 2010

"Precision Medicine""一统江湖"

Entry Terms:

- Medicine, Precision
- Medicines, Precision
- Individualized Medicine
- Medicine, Individualized
- Personalized Medicine
- Medicine, Personalized
- Precision-Medicine

"Precision Medicine"主题词树状结构

All MeSH Categories

Analytical, Diagnostic and Therapeutic Techniques and Equipment Category

作为一种治疗措施

**Therapeutics** 

Precision Medicine

All MeSH Categories

<u>Disciplines and Occupations Category</u>

**Health Occupations** 

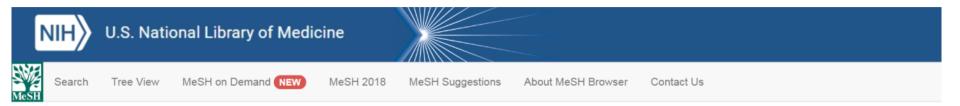
作为一门医学学科

Medicine

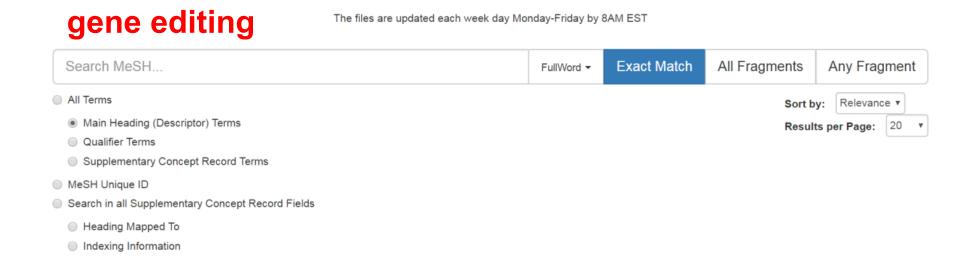
Clinical Medicine

Precision Medicine

### https://meshb.nlm.nih.gov/



### Medical Subject Headings 2019



### Gene Editing MeSH Descriptor Data 2019

Details

Qualifiers

MeSH Tree Structures

Concepts

 MeSH Heading
 Gene Editing

 Tree Number(s)
 E05.393.420.270

 Unique ID
 D000072669

Scope Note Genetic engineering or molecular biology techniques that involve DNA REPAIR mechanisms for incorporating site-specific modifications into a cell's

genome.

Entry Term(s) Genome Editing

Previous Indexing Genetic Engineering (2005-2016)

See Also CRISPR-Associated Protein

CRISPR-Cas Systems

Mutagenesis, Site-Directed

Public MeSH Note 2017 History Note 2017

 Date Established
 2017/01/01

 Date of Entry
 2016/07/08

 Revision Date
 2018/01/16

Gene Editing MeSH Descriptor Data 2019

Details

Qualifiers

MeSH Tree Structures

Concepts

**Allowable Qualifiers** 

classification (CL)

economics (EC)

ethics (ES)

history (HI)

instrumentation (IS)

legislation & jurisprudence (LJ)

methods (MT)

standards (ST)

statistics & numerical data (SN)

trends (TD)
veterinary (VE)

# Gene Editing MeSH Descriptor Data 2019

Details

Qualifiers

MeSH Tree Structures

Concepts

```
Investigative Techniques [E05]
```

Genetic Techniques [E05.393]

Genetic Engineering [E05.393.420]

Directed Molecular Evolution [E05.393.420.175] •

DNA Shuffling [E05.393.420.238]

Gene Editing [E05.393.420.270]

Genetic Therapy [E05.393.420.301] •

Genetic Enhancement [E05.393.420.451]

Metabolic Engineering [E05.393.420.526]

Protein Engineering [E05.393.420.601]

Sex Preselection [E05.393.420.890]

# 检索技巧举例

# 例:基因编辑技术治疗肿瘤的文献

### ■分析检索要点

- ▶基因编辑(技术、手段)
- ▶肿瘤(治疗)

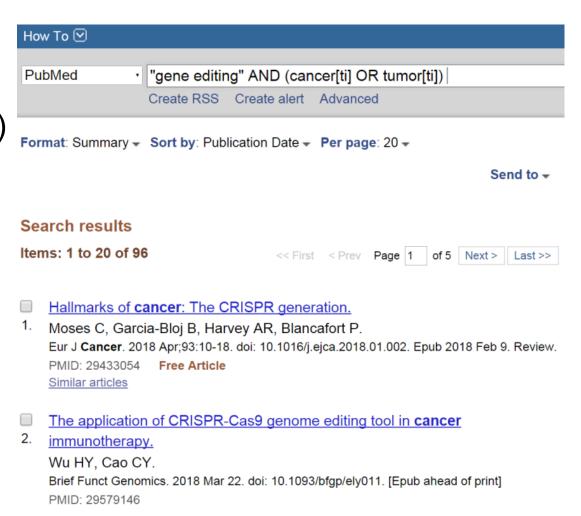
### ■简单检索

- ▶常用布尔逻辑运算符
  - AND OR NOT
- ▶常用检索符
  - 截词检索\*, combin\*=combining OR combined OR combination
  - 词组检索"","stem cell",两词必须在一起
  - 字段检索[], "stem cell"[ti], "stem cell"[tiab]

# 例:基因编辑技术治疗肿瘤 简单检索

### ■简单检索

"gene editing" AND (cancer[ti] OR tumor[ti])





intitle:gene-editing intitle:CCR5





全部

图片

新闻 视频

贴物

更多

设置

工具

找到约 126 条结果 (用时 0.38 秒)

intitle:gene-editing

#### Google 学术: intitle:gene-editing intitle:CCR5

Gene editing of CCR5 in autologous CD4 T cells of ... - Tebas - 被引用次数: 946

... of primary CD4+ T-cells by gene editing of CCR5 ... - Li - 被引用次数:94

Editing CCR5: a novel approach to HIV gene therapy - Cornu - 被引用次数: 26

#### Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected ...

https://www.nejm.org/doi/full/10.1056/nejmoa1300662 - 翻译此页

作者: P Tebas - 2014 - 被引用次数: 943 - 相关文章

2014年3月6日 - Original Article from The New England Journal of Medicine — Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected with HIV.

#### Gene Editing of CCR5 in Hematopoietic Stem Cells in a Nonhuman ...

www.bloodjournal.org/content/124/21/4802 ▼ 翻译此页

作者: CW Peterson - 2014 - 被引用次数: 1 - 相关文章

Abstract. Background: Hematopoietic stem cell (HSC) transplantation remains the only clinically observed path to functional cure of HIV infection. To better ...

#### (PDF) Gene editing of CCR5 in autologous CD4 T cells of persons ...

https://www.researchgate.net/.../260561883\_Gene\_editing\_of\_CCR5\_in\_aut... - 翻译此页 2019年2月3日 - Background: CCR5 is the major coreceptor for human immunodeficiency virus (HIV). We investigated whether site-specific modification of the ...



百度为您找到相关结果约650个

▽搜索工具

#### 专家:编辑CCR5基因不能抗艾滋病,还可能存在非常严重的副作用

2018年11月26日 - 抛开伦理和审查问题,通过Crispr/cas9技术敵除CCR5基因能否达到抗艾滋目 前也仍然是一个问题

https://www.ithome.com/0/397/0... - - 百度快照

#### 修改CCR5基因天生免疫艾滋病毒,基因编辑技术如此成熟了? - 出国...

2018年11月30日 - 但是这次做的是CCR5基因的编辑。很早之前科学家们就发现有些人似乎对 艾滋病病毒免疫,检测结果是他们的基因组中CCR5基因比一般人少了32个"字母",也...

麻省国际出国看病 v - 百度快照

#### 从基因编辑婴儿谈CRISPR-Cas9和CCR5\_生物科技\_健康—线资讯

2018年11月27日 - 这对双胞胎的一个基因(CCR5)经过CRISPR-Cas9基因编辑。这使她们出生后 即能天然抵抗艾滋病。这是世界首例免疫艾滋病的基因编辑婴儿。也意味着中国在基因...

■ 健康一线视频网 マ - 百度快照

#### 贺建奎现身说抱歉 CCR5基因编辑婴儿试验数据被泄露有何危险 深圳...

2018年11月28日 - 贺建奎对"基因编辑婴儿"事件引发的争议表示歉意随后进行主题为"利用 CRISPR/Cas9技术进行局、猴、人胚胎的CCR5基因编辑"的演讲。27日大会第一天未… 森 深圳热线 ~ - 百度快服

#### 基因编辑CCR5闹剧之余,我们谈谈如何做好趋化因子的多色流式, 贺建奎



#### 深圳市科技创新委员会:从未资助"CCR5基因编辑"项目

2018年11月27日 - 二、经核查,我委从未立项资助"CCR5基因编辑"、"HIV免疫基因CCR5胚胎 基因编辑安全性和有效性评估"等自由探索项目,亦未资助南方科技大学贺建奎、覃... •• 环球网 = - 百度快照

#### 贺建奎现身说抱歉 CCR5基因编辑婴儿试验数据被泄露有何危险 深圳...



2018年11月28日 - 斯蒂芬·奎克是贺建奎在斯坦福的导师,更是生物学领域首屈一指的"大亨"。除了斯坦福大学生物工程学教授的...

⇒ 深圳热线 - - 百度快照



intitle:基因编辑 intitle:CCR5 site:gov.cn

0

百度一下

网页

资讯 贴吧 知道

视频 音乐

图片 地图

文库 更多»

时间不限 ▼ 所有网页和文件 ▼ gov.cn ▼

×清除

#### 人类首次基因编辑婴儿诞生 带来的是希望还是恐惧?-临澧县人民政府

2018年11月27日 - 即使这次<mark>基因编辑</mark>试验很完美,但是缺少正常CCR5基因的人也会面临其他病毒威胁(如西尼罗河病毒)和死于流感的风险。穆苏努鲁说,有很多方法可以预防艾滋病... www.linli.gov.cn/item/... ▼ - <u>百度快</u>照

#### 深圳市科技创新委员会关于贺建奎基因编辑项目有关情况的声明-通知...

2018年11月26日 - 二、经核查,我委从未立项资助"CCR5基因编辑"、"HIV免疫基因CCR5胚胎基因编辑安全性和有效性评估"等自由探索项目,亦未资助南方科技大学贺建奎、覃... stic.sz.gov.cn/xxgk/tz... ▼ - 百度快照

#### 基因编辑婴儿、科学伦理不能承受之重

2018年11月27日 - 上海交大生物医学教授指出、将基因编辑技术直接用于胎儿的科学基础很不牢靠。 敲除CCR5基因后,虽然会防止人体感染HIV病毒,但会对人的免疫系统和骨骼生长... www.stcsm.gov.cn/xwzx/... \* V3 - 百度快服

#### 2020年治愈HIV?细数4类最具潜力的HIV疗法-科研讲展-资讯-CPI

www.cpi.gov.cn/publish... ▼ - 百度快照



2018年5月9日 - 具有CCR5基因突变的个体缺乏CCR5蛋白的一部分,使得HIV无法与之结合。利用基因治疗理论上有可能编辑DNA,引入这种突变来阻止HIV。美国Sangamo Therapeutics公司...

#### 基因编辑引专家"愤怒" 科技日报:一次疯狂的冒进

2018年11月27日 - 报道称,贺建奎的团队采用CRISPR/Cas9基因编辑技术,修改的是CCR5基因,而CCR5基因是HIV病毒入侵机体细胞的主要辅助受体之一。 中山大学从事生命科学研... kij.bozhou.gov.cn/cont... \* - 百度快照

#### 本周「科技创享汇」热议:基因编辑,是科技进步还是潘多拉魔盒打开?



2018年12月12日 - 这一次贺建奎的试验,就是通过 CRISPR 基因编辑技术,敲除了两个女婴体内的 CCR5 基因。换句换说,两名婴儿...

www.sipac.gov.cn/dept/... ▼ V1 - 百度快照



#### № 基因编辑技术 图文 百度文库

基民協等技术 广告音楽 でも思想 でもなわれ であるため、 CMMのだらなられる物をおりがいた CMMは10年的日本の CMMは10年の CMMは10年 ★★★★★ 评分:5/5 43页

2016年10月8日 - 基因编辑技术 - 基因编辑技术 产生背景 定义及原理 分类及比较 CRISPR的优点及在植物育种上的应用 CRISPR基...

② 百度文库 ▼ V3

 基因编辑\_ppt
 评分:4.5/5
 18页

 基因编辑技术的概念和原理汇总...ppt
 评分:5/5
 41页

 基因编辑技术和原理 ppt
 评分:5/5
 22页

 更多文库相关文档>>
 22页

#### № 基因编辑技术和原理 图文 百度文库



★★★★★ 评分:5/5 16页

2017年9月11日 - 基因编辑技术和原理 - ? 基因编辑技术指能够让人类 对目标基因进行"编辑",实现对特定DNA片段的敲除、加入...

百度文库 ▼ ▼3 - 百度快照

#### ■ 基因编辑技术和原理讲述 图文 百度文库



2018年10月18日 - 基因编辑技术和原理讲述 - 基因编辑技术和原理 李 做 什么是基因编辑技术? 基因编辑是指对基因组进行定点修饰...

② 百度文库 ▼ V3 - 百度快照

#### № 基因编辑技术的概念和原理 图文 百度文库



2016年6月8日 - 基因编辑技术的概念和原理 - 基因编辑技术的概念和原理 什么是基因编辑技术? 基因编辑是指对基因组进行定点...

図 百度文库 ▼ V3 - 百度快照



### Gene Editing of CCR5 in Autologous CD4 T Cells of ... 翻译此页

2014-9-3 · new england journal of medicine The established in 1812 march 6, 2014 vol. 370? no. 10

gene editing news

china hiv baby

china gene editing babies

Cited by: 957 Author: Pablo Tebas, David Stein, Winson W. Tan...

Gene Editing of CCR5 in Autologous CD4 T Cells of Persons Infected with ...

Publish Year: 2014 位置: 8600 Rockville Pike, Bethesda, MD

wenku.baidu.com,百度文库,专业资料,自然科学,生物学▼

2014-3-6 · CCR5 is the major coreceptor for human immunodeficiency virus (HIV). We investigated whether site-specific modification of the gene ("gene editing") — in this case, the infusion of autologous CD4 T cells in which the CCR5 gene was rendered permanently dysfunctional by a ... https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4084652

#### Editing CCR5: A Novel Approach to HIV Gene Therapy ... 翻译此页

Cited by: 10 Author: Tatjana I. Cornu, Claudio Mussolino, Kristi...

Publish Year: 2015

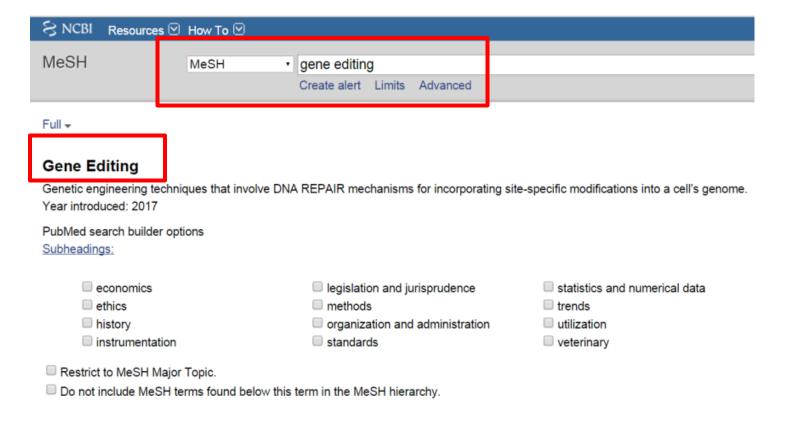
A limited number of people harbor a genomic 32-bp deletion in the CCR5 gene (CCR5∆32), ... we review the current promise and limitations of CCR5 gene editing with engineered nucleases, including factors ... Cornu T.I., Mussolino C., Bloom K., Cathomen T. (2015) Editing CCR5: A Novel Approach to HIV Gene Therapy. In: Berkhout B., Ertl H ...

https://link.springer.com/chapter/10.1007/978-1-4939-2432-5 6 ▼

# 例:基因编辑技术治疗肿瘤 主题检索

### ■ MeSH主题词检索

- ▶查询要点有无主题词
- >组配,表达语义关系





Summary 

20 per page 

Send to: 

Sen

#### Search results

#### Neoplasms

New abnormal growth of tissue. Malignant neoplasms show a greater degree of anaplasia and have the properties of invasion and metastasis, compared to benign neoplasms.

Year introduced: /diagnosis was NEOPLASM DIAGNOSIS 1964-1965

#### Hereditary Breast and Ovarian Cancer Syndrome

Autosomal dominant HEREDITARY CANCER SYNDROME in which a mutation most often in either BRCA1 or BRCA2 is associated
with a significantly increased risk for breast and ovarian cancers.
Year introduced: 2012

#### Early Detection of Cancer

Methods to identify and characterize cancer in the early stages of disease and predict tumor behavior.
 Year introduced: 2009

#### National Cancer Institute (U.S.)

4. Component of the NATIONAL INSTITUTES OF HEALTH. Through basic and clinical biomedical research and training, it conducts and

MeSH	MeSH	•	
		Limits	Advanced

Full + Send to: -

#### Neoplasms

New abnormal growth of tissue. Malignant neoplasms show a greater degree of anaplasia and have the properties of invasion and metastasis, compared to benign neoplasms.

Year introduced: /diagnosis was NEOPLASM DIAGNOSIS 1964-1965

PubMed search builder options

#### Subheadings:



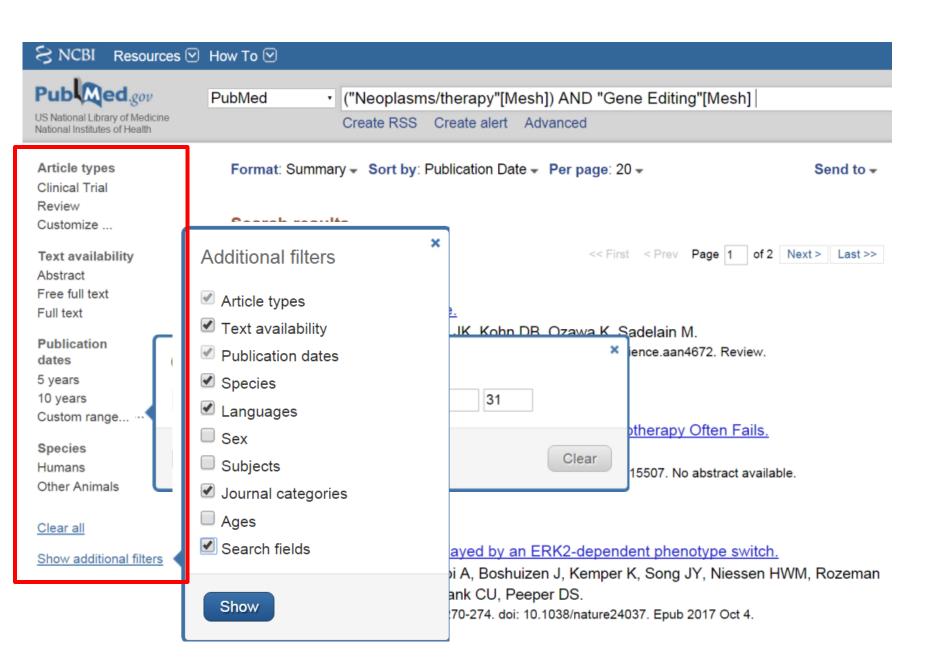
#### 高级检索中把两个检索AND起来



#### History

#### Download history Clear history

Search	Add to builder	Query	Items found	Time
<u>#15</u>	Add	Search "Neoplasms/therapy"[Mesh] Sort by: PublicationDate	1312420	22:06:08
<u>#11</u>	Add	Search "Gene Editing"[Mesh] Sort by: PublicationDate	<u>1181</u>	22:01:29



Format: Abstract -

Send to

Cell. 2017 May 18;169(5):945-955.e10. doi: 10.1016/j.cell.2017.04.035.

### Modeling Rett Syndrome Using TALEN-Edited MECP2 Mutant Cynomolgus Monkeys.

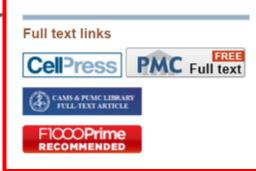
 $\frac{\text{Chen Y}^1, \text{Yu J}^2, \text{Niu Y}^3, \text{Qin D}^4, \text{Liu H}^2, \text{Li G}^5, \text{Hu Y}^4, \text{Wang J}^6, \text{Lu Y}^7, \text{Kang Y}^3, \text{Jiang Y}^8, \text{Wu K}^8, \text{Li S}^2, \text{Wei J}^9, \text{He J}^9, \text{Wang J}^6, \text{Lu Y}^7, \text{Kang Y}^3, \text{Jiang Y}^8, \text{Wu K}^8, \text{Li S}^2, \text{Wei J}^9, \text{He J}^9, \text{Wang J}^6, \text{Liu X}^2, \text{Liu X}^2, \text{Liu Y}^2, \text{Si C}^3, \text{Bai R}^9, \text{Zhang K}^2, \text{Liu J}^2, \text{Huang S}^9, \text{Chen Z}^9, \text{Wang S}^9, \text{Chen X}^2, \text{Bao X}^{10}, \text{Zhang Q}^{10}, \text{Li F}^2, \text{Geng R}^2, \text{Liang A}^2, \text{Shen D}^5, \text{Jiang T}^{11}, \text{Hu X}^4, \text{Ma Y}^9, \text{Ji W}^{12}, \text{Sun YE}^{13}.$ 

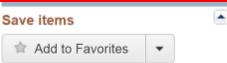
#### Author information

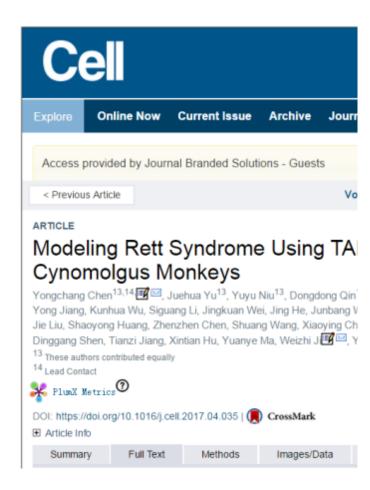
#### Abstract

**Gene-editing** technologies have made it feasible to create nonhuman primate models for human genetic disorders. Here, we report detailed genotypes and phenotypes of TALEN-edited MECP2 mutant cynomologies









#### Modeling Rett Syndrome Using TALEN-Edited MECP2 Mutant Cynomolgus Monkeys

Yongchang Chen, <sup>1,3,12,13,14,\*</sup> Juehua Yu, <sup>2,13</sup> Yuyu Niu, <sup>1,3,12,13</sup> Dongdong Qin, <sup>5,13</sup> Hailiang Liu, <sup>2,13</sup> Gang Li, <sup>8</sup> Yingzhou Hu, <sup>5</sup> Jiaojian Wang, <sup>7</sup> Yi Lu, <sup>8</sup> Yu Kang, <sup>1,3,12</sup> Yong Jiang, <sup>9</sup> Kunhua Wu, <sup>9</sup> Siguang Li, <sup>2</sup> Jingkuan Wei, <sup>1,3</sup> Jing He, <sup>1,3</sup> Junbang Wang, <sup>2</sup> Xiaojing Liu, <sup>2</sup> Yuping Luo, <sup>2</sup> Chenyang Si, <sup>1,3,12</sup> Raoxian Bai, <sup>1,3</sup> Kunshan Zhang, <sup>2</sup> Jie Liu, <sup>2</sup> Shaoyong Huang, <sup>1,3</sup> Zhenzhen Chen, <sup>1,3</sup> Shang Wang, <sup>1,3</sup> Xiaoying Chen, <sup>2</sup> Xinhua Bao, <sup>10</sup> Qingping Zhang, <sup>10</sup> Fuxing Li, <sup>2</sup> Rui Geng, <sup>2</sup> Aibin Liang, <sup>2</sup> Dinggang Shen, <sup>8</sup> Tianzi Jiang, <sup>7,11</sup> Xintian Hu, <sup>5</sup> Yuanye Ma, <sup>1,3</sup> Weizhi Ji, <sup>1,3,12,\*</sup> and Yi Eve Sun<sup>2,4,\*</sup> <sup>1</sup> Yunnan Kev Laboratory of Primate Biomedicine Research. Institute of Primate Translational Medicine. Kunming University of Science and

Technology, Kunming 650500, China

2 Translational Stem Cell Research Center, Tongii Hospital, Tongii University School of Medicine, Shanghai 200065, China

<sup>3</sup>Yunnan Provincial Academy of Science and Technology, Kunming 650051, China

<sup>4</sup>Department of Psychiatry and Biobehavioral Sciences, UCLA Medical School, Los Angeles, CA 90095, USA

<sup>5</sup>Key Laboratory of Animal Models and Human Disease Mechanisms of the Chinese Academy of Sciences & Yunnan Province,

Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming 650223, China

Department of Radiology and BRIC, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA

<sup>7</sup>Key Laboratory for NeuroInformation of the Ministry of Education, School of Life Science and Technology, University of Electronic Science and Technology of China, Chengdu 625014, China

Department of Medical Imaging, the First Affiliated Hospital, Kunming Medical University, Kunming 650032, China

<sup>9</sup>The First People's Hospital of Yunnan Province and The Affiliated Hospital of Kunming University of Science and Technology, Kunming 650032, China

<sup>10</sup>Department of Pediatrics, Peking University First Hospital, Beijing 100034, China

<sup>11</sup>National Laboratory of Pattern Recognition, Brainnetome Center, Institute of Automation, Chinese Academy of Sciences, Beijing 100190, China

12 Kunming Enovate Institute of Bioscience, Kunming 650000, China

<sup>13</sup>These authors contributed equally

14Lead Contact

\*Correspondence: chenyc@lpbr.cn (Y.C.), wji@lpbr.cn (W.J.), ysun@mednet.ucla.edu (Y.E.S.) http://dx.doi.org/10.1016/j.cell.2017.04.035

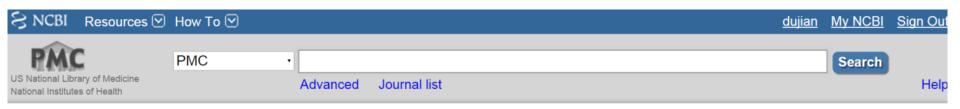
#### SUMMARY

Gene-editing technologies have made it feasible to create nonhuman primate models for human genetic disorders. Here, we report detailed genotypes and phenotypes of TALEN-edited MECP2 mutant cynomolgus monkeys serving as a model for a neurodevelopmental disorder, Rett syndrome (RTT), which is caused by loss-of-function mutations in the human MECP2 gene. Male mutant monkeys were embryonic lethal, reiterating that RTT is a disease of females. Through a battery of behavioral analyses, including primate-unique eye-tracking tests, in combination with brain imaging via MRI, we found a series of physiological, behavioral, and structural abnormalities resembling clinical manifestations of RTT. Moreover, blood transcriptome profiling revealed that mutant monkeys resembled RTT patients in immune gene dysregulation. Taken together, the stark similarity in phenotype and/or endophenotype between monkeys and patients suggested that gene-edited RTT founder monkeys

#### INTRODUCTION

Rett syndrome (RTT) is a progressive neurodevelopmental disorder that mostly manifests in girls with a morbidity rate of 1:10,000–1:15,000 (Amir et al., 1999). Almost 95% of RTT is believed to be caused by mutations of an X-linked gene methyl-CpG-binding protein 2 (MECP2) (Rett, 1966; Amir et al., 1999; Schanen et al., 1998). MECP2 mutations are most often embryonic lethal for boys, except for very few, who are born with severe encephalopathy leading to death before 2 years of age (Schanen et al., 1998). RTT girls seem to have normal development for up to 6–18 months but manifest a series of symptoms associated with intellectual disability, loss of acquired language, and compromised cognitive, social, and motor skills, etc. (Hagberg et al., 1983).

As RTT is a monogenic disorder, genetic modification technologies have made it possible to develop animal models for further study. RTT animal models were first generated in mice and recently in rats (Chen et al., 2001; Guy et al., 2001; Stearns et al., 2007; Ricceri et al., 2008; Yang et al., 2013; Veeraragavan et al., 2016). It is interesting that RTT-related neurological phenotypes mostly occur in adult male rodents, which is different from the human disease (Lombardi et al., 2015; Patterson et al., 2016; Chen et al., 2001; Glaze, 2004; Guy et al., 2001). It is therefore



Journal List > HHS Author Manuscripts > PMC5540256



Cell. Author manuscript; available in PMC 2017 Aug 2.

Published in final edited form as:

Cell. 2017 May 18; 169(5): 945-955.e10.

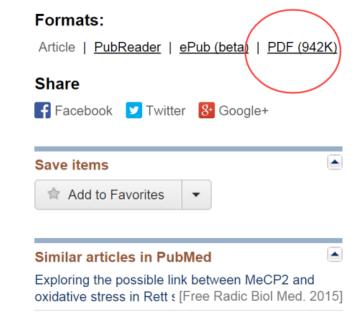
doi: 10.1016/j.cell.2017.04.035

PMCID: PMC5540256 NIHMSID: NIHMS882923

PMID: 28525759

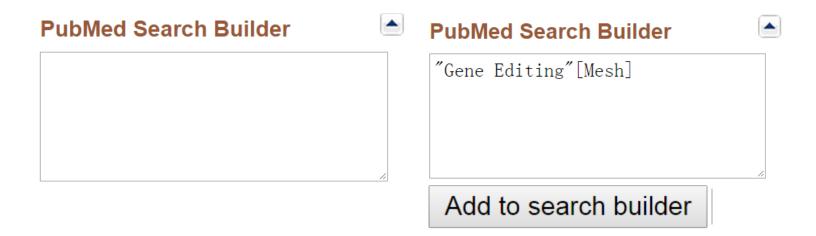
### Modeling Rett Syndrome Using TALEN-Edited *MECP2*Mutant Cynomolgus Monkeys

Yongchang Chen, 1,3,12,13,14,\* Juehua Yu, 2,13 Yuyu Niu, 1,3,12,13 Dongdong Qin, 5,13 Hailiang Liu, 2,13 Gang Li, 6 Yingzhou Hu, 5 Jiaojian Wang, 7 Yi Lu, 8 Yu Kang, 1,3,12



### 总结:MeSH检索两步走

第一步:检索主题词,构建检索策略

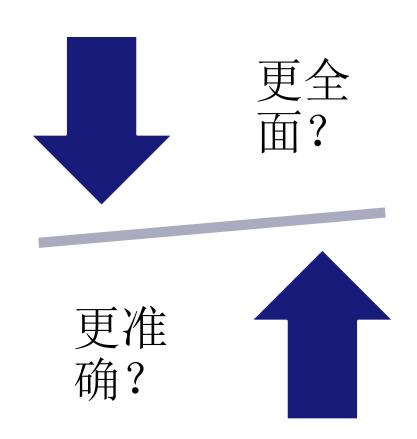


第二步:检索论文





### 主题词检索的优点



主题词检索, PubMed: 选择文章实质内容标注

关键词检索, Baidu:文章全文本标注

### 检索心血管疾病会检索出来痔疮?

#### 主题树

#### 心血管疾病

心脏病(+152) 妊娠并发症, 心血管(+1) 血管疾病(+216) 心血管畸形(+44) 心血管感染(+5)

#### 主题树

心血管疾病

#### 血管疾病

动脉瘤(+14)

血管瘤病(+4)

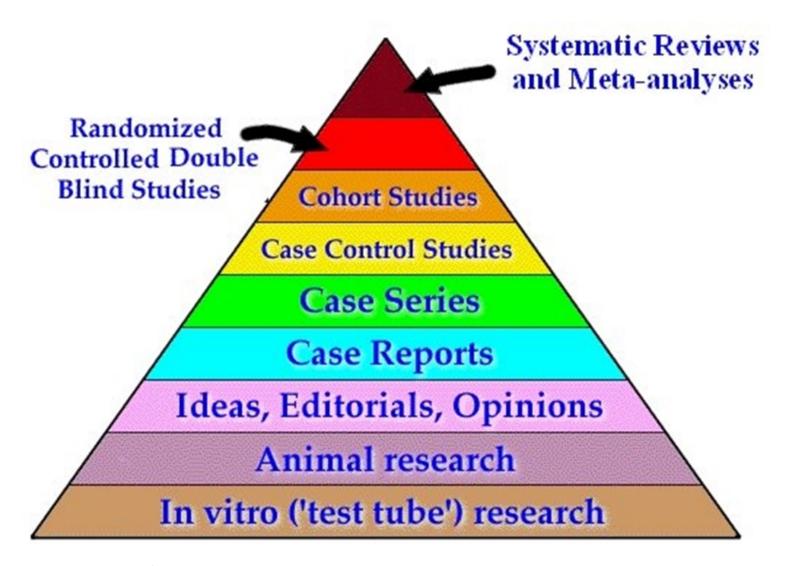
血管性水肿(+1)

主动脉疾病(+8) 动脉闭塞性疾病(+18) 动静脉畸形(+3) 动脉炎(+5) 脑血管障碍(+66) 筋膜间隔综合征(+2) 糖尿病血管病变(+2) 肝静脉闭塞性疾病 充血 高血压(+4) 低血压(+2) 肺静脉闭塞性疾病 视网膜静脉闭塞 弯刀综合征 脾梗死 上腔静脉综合征 毛细血管扩张(+3)

### 例:近5年褥疮护理的英文系统综述

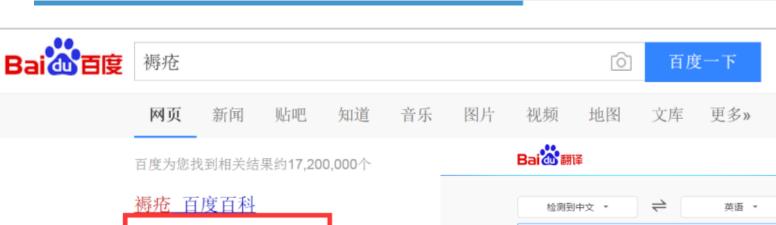
- ■褥疮/护理
- ■近5年
- ■英文
- ■系统综述 (Systematic Review )
  - ➤系统综述,是一种全新的文献综合方法,指针对某一具体临床问题(如:病因、诊断、治疗、预后),系统全面的搜集已发表或未发表的临床研究,采用临床流行病学严格评价文献的原则和方法,筛选出符合质量标准的文献进行定量或定性合并,得出可靠的综合结论。

### 循证医学证据金字塔



注:图片来源(http://library.downstate.edu/EBM2/2100.htm)

### 褥疮:英文



压疮又称压力性溃疡、褥疮,是由于局部组织组织溃烂坏死。皮肤压疮在康复治疗、护理中 病因 临床表现 诊断 治疗

baike.baidu.com/ - - >

#### 褥疮 互动百科



褥疮-褥疮(又称压疮,压<sup>36</sup> 灾住反应万至外养病房 于受压和缺乏脂肪组织 www.baike.com/wiki/



骶、肩胛、枕、肘和足跟等处。





#### 压力性溃疡 AND • 加权检索 ■ 扩展检索 扩展 ↑发送到检索框 选择副主题词 AL 按摩疗法 添加 >> BL血液 CF 脑脊髓液 扩展 CI 化学诱导 ○ 不扩展 CL 分类 CN 先天性 << 取消 CO 并发症(+) 全部取消 DH 膳食疗法

**主题词**:压力性溃疡

英文名称: Pressure Ulcer

#### 主题词:

压力性溃疡

#### 英文名称:

Pressure Ulcer

#### 款目词:

Bedsore(褥疮); Decubitus Ulcer(褥疮); Pressure Sore(受压溃疡)

#### 树状结构号:

C17. 800. 893. 665

#### 历史注释:

2006 (1963)

#### 主题词详解:

An ulceration caused by prolonged pressure on the SKIN and TISSUES when one stay in one position for a long period of time, such as lying in bed. The bony areas of the body are the most frequently affected sites which become ischemic (ISCHEMIA) under sustained and constant pressure.



Full -Send to: -

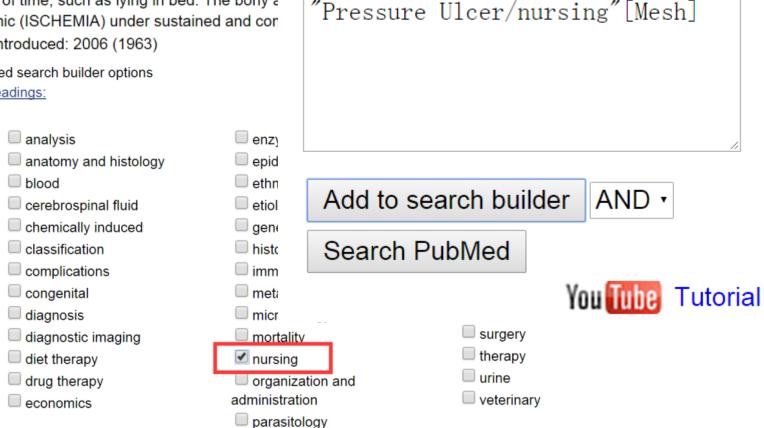
PubMed Search Builder

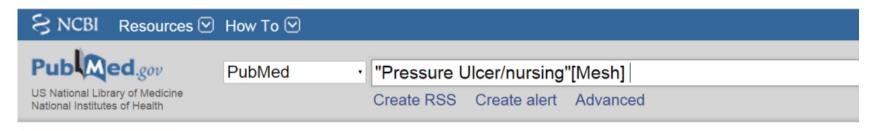
#### Pressure Ulcer

An ulceration caused by prolonged pressure or period of time, such as lying in bed. The bony a ischemic (ISCHEMIA) under sustained and con Year introduced: 2006 (1963)

PubMed search builder options

Subheadings:





# Article types Clinical Trial Review Systematic Reviews Customize ...

Text availability Abstract Free full text Full text

Publication dates 5 years 10 years Custom range...

Species
Humans
Other Animals

Format: Summary - Sort by: Publication Date - Per page: 20 -

Send to ▼

#### Search results

- Healthy Skin Wins: A Glowing Pressure Ulcer Prevention Program That Can
- Guide Evidence-Based Practice.

Martin D, Albensi L, Van Haute S, Froese M, Montgomery M, Lam M, Gierys K, Lajeunesse R, Guse L, Basova N.

Worldviews Evid Based Nurs. 2017 Dec;14(6):473-483. doi: 10.1111/wvn.12242. Epub 2017 Jul 29.

PMID: 28755424 Similar articles

Getting evidence-based pressure ulcer prevention into practice: a process

Article types

clear

clear

clear

Format: Summary - Sort by: Publication Date - Per page: 20 -

Send to ▼

Clinical Trial Review

✓ Systematic Reviews

Customize ...

Text availability

Abstract

Free full text

Full text

Publication dates

√ 5 years

10 years

Custom range...

Species

Humans

Other Animals

Languages

Chinese

✓ English

Customize ...

Clear all

Search results

Items: 1 to 20 of 25

<< First < Prev Page 1 of 2 Next > Last >>

Filters activated: Systematic Reviews, published in the last 5 years, English. Clear all to show 2452 items.

- Healthy Skin Wins: A Glowing Pressure Ulcer Prevention Program That Can
- Guide Evidence-Based Practice.

Martin D, Albensi L, Van Haute S, Froese M, Montgomery M, Lam M, Gierys K, Lajeunesse R, Guse L, Basova N.

Worldviews Evid Based Nurs. 2017 Dec;14(6):473-483. doi: 10.1111/wvn.12242. Epub 2017 Jul 29.

PMID: 28755424 Similar articles

- Getting evidence-based pressure ulcer prevention into practice: a process
- 2. evaluation of a multifaceted intervention in a hospital setting.

Sving E, Fredriksson L, Gunningberg L, Mamhidir AG.

J Clin Nurs. 2017 Oct;26(19-20):3200-3211. doi: 10.1111/jocn.13668. Epub 2017 Mar 21.

PMID: 27875015

J Clin Nurs. 2017 Oct;26(19-20):3200-3211. doi: 10.1111/jocn.13668. Epub 2017 Mar 21.

Getting evidence-based pressure ulcer prevention into practice: a process evaluation of a multifaceted intervention in a hospital setting.

Sving E<sup>1,2,3</sup>, Fredriksson L<sup>2</sup>, Gunningberg L<sup>3</sup>, Mamhidir AG<sup>3,4</sup>.

Author information



CAMS & FUNC LIBRARY
FULL-TEXT ARTICLE

Save items

#### JCN Journal of Clinical Nursing

ORIGINAL ARTICLE

Journal of Clinical Nursing

Getting evidence-based pressure ulcer prevention into practice: a process evaluation of a multifaceted intervention in a hospital setting

Eva Sving, Lennart Fredriksson, Lena Gunningberg and Anna-Greta Mamhidir

Aims and objectives. To describe registered nurses', assistant nurses' and first-line managers' experiences and perceptions of a multifaceted hospital setting intervention focused on implementing evidence-based pressure ulcer prevention.

Background. Pressure ulcer prevention is deficient. Different models exist to support implementation of evidence-based care. Little is known about implementation processes.

Design. A descriptive qualitative approach.

Method. Five focus-group nurse interviews and five individual first-line manager interviews were conducted at five Swedish hospital units. Qualitative content analysis was used.

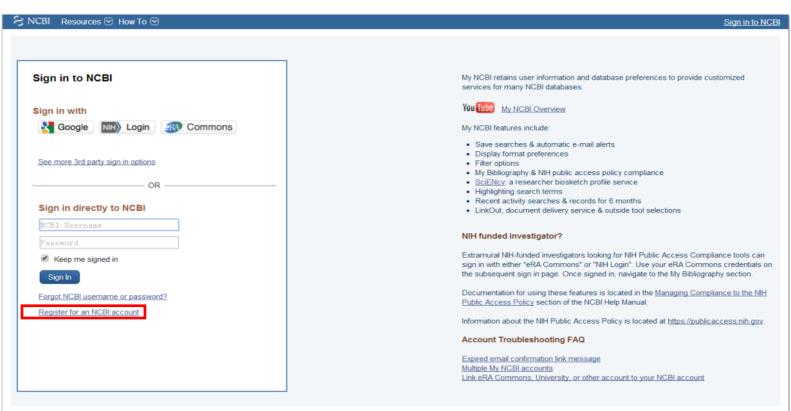
What does this paper contribute to the wider global clinical community?

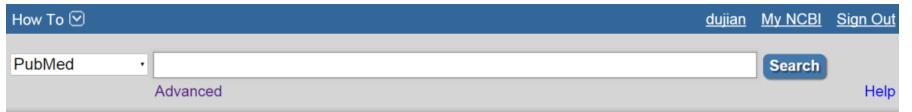
 Implementation of evidencebased pressure ulcer prevention needs to be carefully planned to achieve a shared understanding among nurses and first-line managers regarding the care provided and how it can be improved.

# 三、如何追踪最新文献?如何筛选权威重要文献?

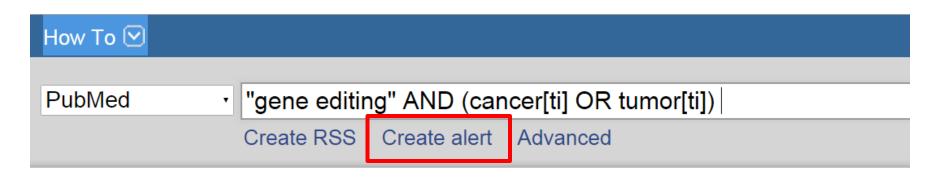
### My NCBI







### 1、追踪最新文献,自动邮箱发送



Format: Summary - Sort by: Publication Date - Per page: 20 -

Send to -

Search results

#### My NCBI » Saved Searches

#### Your PubMed search

Name of saved search:		"gene editing" AND (cancer[ti] OR tumor[ti]					
Search terms:	"gene	editing"	AND	(cancer[ti]	OR	tumor[ti])	
						T1	/.

Test search terms

#### Would you like e-mail updates of new search results?

- No, thanks.
- Yes, please.

E-mail:	: windowsdujian@163.com ( <u>change</u> )			
Schedul	e:			
Fr	equency:	Weekly •		
W	hich day?	Saturday •		

### 每周六,把最新文献发 到我的邮箱

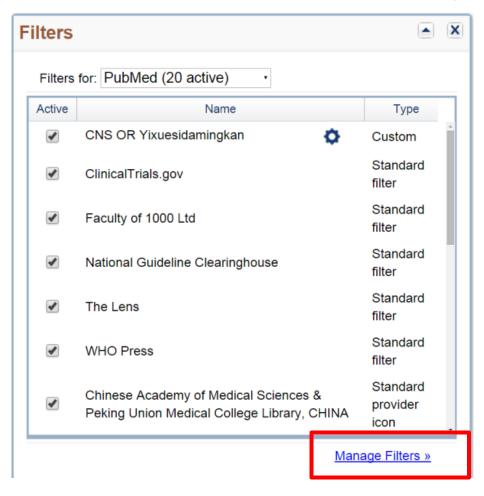
### 2、设置个性化文献过滤器(Filters)



dujian My NCBI Sign Out

#### My NCBI

Customize this page | NCBI Site Preferences | Video Overview | Help



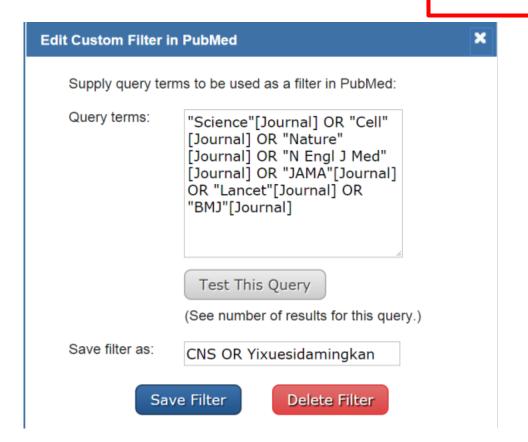


#### My NCBI » Filters

#### You are managing filters for: PubMed

Your PubMed filter list

Create custom filter

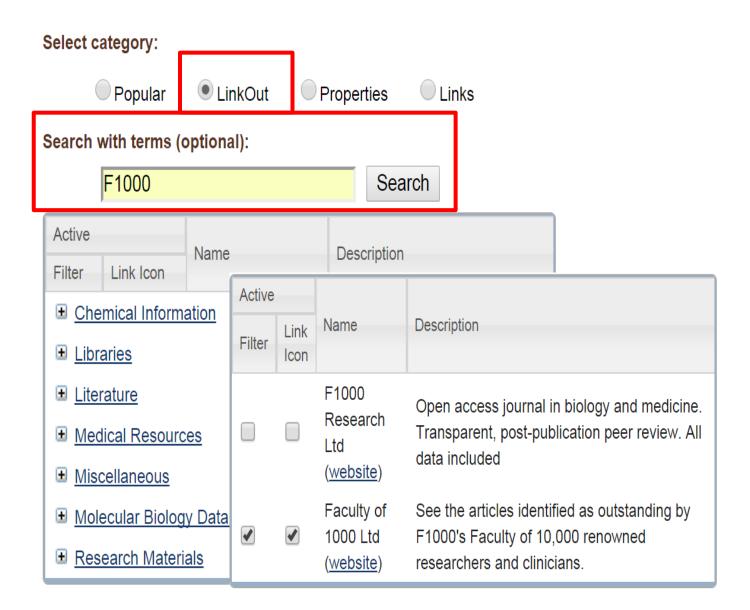


Science
Nature
Cell
N Engl J Med
JAMA
Lancet
BMJ

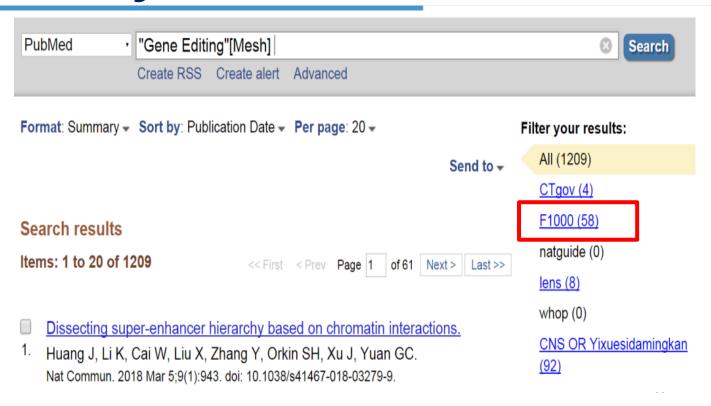


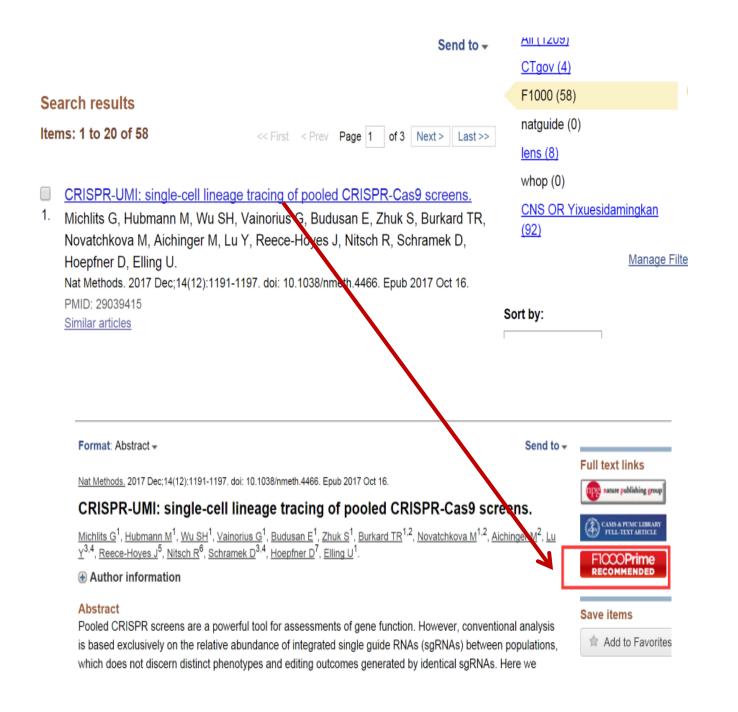
### 如何链接专家推荐出来的重要文献?

**Browse/Search for PubMed Filters** 



### Faculty of 1000: 论文被专家推荐

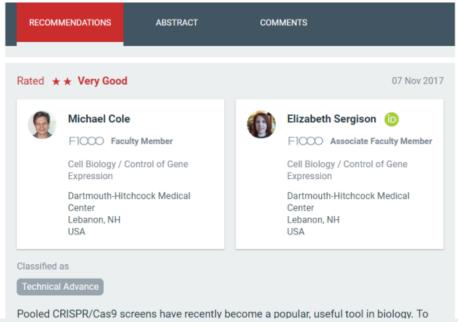




#### CRISPR-UMI: single-cell lineage tracing of pooled CRISPR-Cas9 screens.



2位专家推荐了这篇论 文,认为这是一项重要 的技术讲步。



Cite this Recommendation: Copy to clipboard

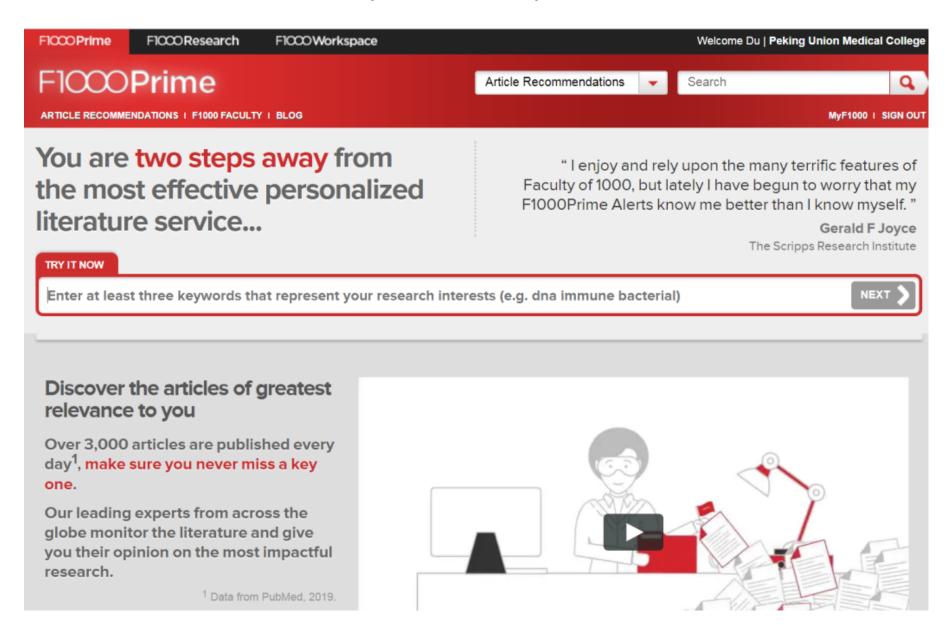




Cole M and Sergison E: F1000Prime Recommendation of [Michlits G et al., Nat Methods 2017 14(12):1191-1197]. In F1000Prime, 07 Nov 2017; 10.3410/f.732002228.793538509

> sensitivity to etoposide and found that their method was reproducible and sensitive. The authors then performed a screen to identify genes involved in iPSC (induced pluripotent stem cell) reprogramming. They identified known genes and a few novel ones. Overall, CRISPR-UMI is a more informative way to perform pooled CRISPR screens.

#### https://f1000.com/prime



### 专家为何认为这篇文章重要?

- Faculty Members also tag the article with the following classifications, if appropriate:
  - Changes Clinical Practice: the article recommends a complete, specific and immediate change in practice by clinicians for a defined group of patients
  - > Confirmation: validates previously published data or hypotheses
  - Controversial: challenges established dogma
  - Good for Teaching: key article in field and/or well written
  - > Interesting Hypothesis: presents new model
  - > New Finding: presents original data, models or hypotheses
  - > Novel Drug Target: suggests new targets for drug discovery
  - > Refutation: disproves previously published data or hypotheses
  - ➤ Technical Advance: introduces a new practical/theoretical technique, or novel use of an existing technique

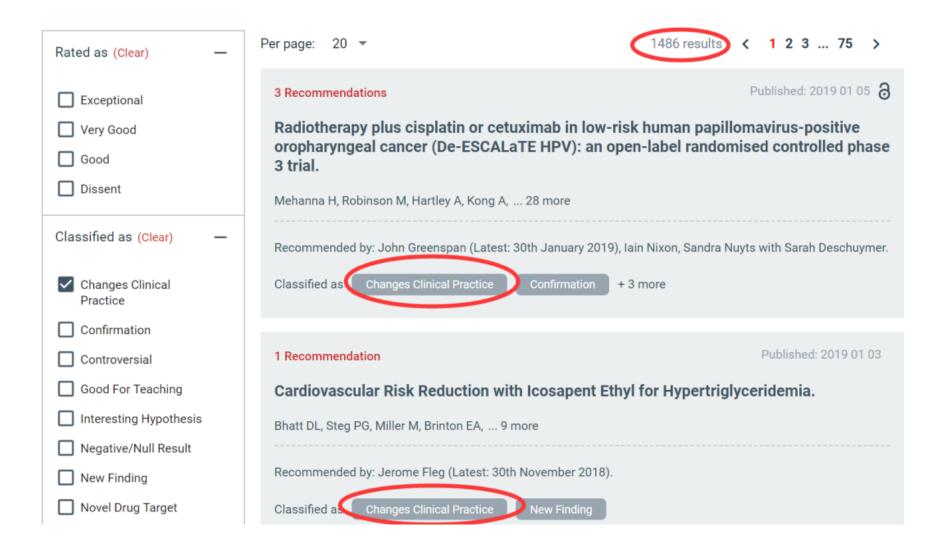
#### F1000Prime Recommendations

Discover the articles of greatest importance and impact in your field, as selected by our Faculty of leading researchers.

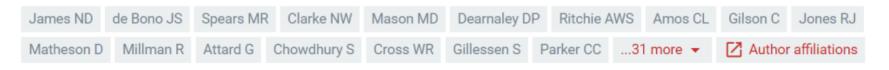
AND N	Article published Reset					
FILTER ~	From to Present to					
	Classifications Reset					
	Changes Clinical Practice	Confirmation	Controversial	Good For Teaching		
	☐ Interesting Hypothesis	Negative/Null Result	New Finding	☐ Novel Drug Target		
	Refutation	☐ Technical Advance	General Interest			
	Article type Reset					
	Clinical Trial: Non-Randomized	Clinical Trial: Randomized	Review/Commentary	Systematic Review/Meta- analysis		

Faculties and Sections: Reset	44个					
All Biology Medicine						
All Faculties						
Anesthesiology & Pain Management	Biochemistry	Bioinformatics, Biomedical Informatics & Computational Biology	Biotechnology			
Cancer Biology	Cardiovascular Biology	Cardiovascular Disorders	Cell Biology			
Chemical Biology	Critical Care & Emergency Medicine	Dermatology	Developmental Biology			
Diabetes & Endocrinology	Ecology	Evolutionary Biology	Gastroenterology & Hepatology			
Gastrointestinal Biology	Genomics & Genetics	Hematology	Immunology			

### 能改变临床实践的工作?

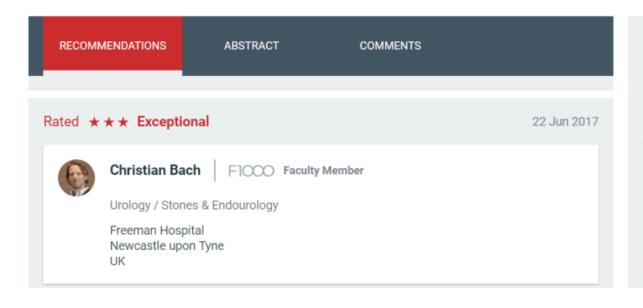


### Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy.



PUBLISHED: 2017 07 27

CITE AS: N Engl J Med. 2017 07 27; 377(4):338-351 https://doi.org/10.1056/NEJMoa1702900



Related articles	
Published on: 2013 Jan 10	
Abiraterone in metastatic prostate cancer without previous chemotherapy.	
Ryan CJ. et al.	
	>

**This article changes clinical practice** - ADT plus Abiraterone and Prednisolone should be given to men with locally advanced or metastatic prostate cancer rather than ADT alone.

This groundbreaking work will change the standard of care for patients who receive longterm androgen-deprivation therapy (ADT), as the data clearly prove that the combination with abiraterone is superior to ADT alone.

Disclosures 对于局部晚期前列腺癌,ADT应该和另外两种药联合应 None declared 用,而不是单用ADT

Cite this Recommendation: Copy to clipboard 

新方案!

Bach C: F1000Prime Recommendation of [James ND et al., N Engl J Med 2017 377(4):338-351]. In F1000Prime, 22 Jun 2017; 10.3410/f.727682848.793533364

#### 撰写论文时参考,引用

### 课程要点小结

#### ■善用主题词检索

- ■文献太多,如何精炼?
  - ▶最新文献
  - ▶综述文献,Review文献类型,/trends副主题词
  - ▶权威期刊文献
    - 医学四大名刊
    - 领域权威期刊(影响因子大于?)
  - ▶专家推荐文献(Faculty of 1000)
  - > 主题词加权检索
  - > . . .

### 实习题

一、通过主题词检索途径查询基因编辑技术治疗肿瘤的相关文献

二、通过主题词和关键词检索途径查询近5年褥疮护理的英文 系统综述类文献

三、注册自己的My NCBI账户,添加权威期刊、F1000等过滤器

## 谢谢! Q & A