大蒜來源的I類新藥ZYZ-802治療老年癡呆的成藥性研究和開發

Discovery and development of the novel compound ZYZ-802 from garlic for the treatment of Alzheimer's disease

申請實體：　澳門科技大學藥學院、中药质量研究国家重点实验室

項目負責人：　朱依諄 講座教授、澳门注册西医师

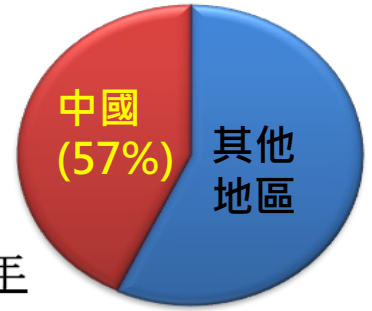
子課題負責人：　Prof. Erwin Neher

謝瑩 副教授

背景與立論依據

AD — 世界第三大殺手僅次於心腦血管疾病和腫瘤

- 與老年相關的神經退行性疾病(港澳地區)
- 神经退行性疾病是一種退化性腦部疾病，腦部功能隨年紀逐漸衰退，最後失去自我照顧能力。最普遍的腦退化症包括Alzheimer's disease ，多數發生在老人身上。
- 65歲以上患病率: 10% ；80歲以上患病率: 20%
- 現時全球1500萬名腦退行性疾病病人中，有約几萬名患者在港澳地區<養和醫院明報健康網>



但 AD 到目前為止沒有非常有效的藥

- 到目前為止FDA也僅批准5個 AD 新藥
- 抗炎治療成為 AD 的一個新希望
- 利用中藥良好特色，篩選創新中藥活性成份甚至單體，以研發創新及副作用較小的抗神經退行疾病的新化合物是良好的研究方向

治疗AD新策略

- S-Propargyl-Cysteine ZYZ-802
- ZYZ-802的抗AD作用
- ZYZ-802的抗炎作用
- 本團隊H2S醫學系列研究合計被引用4069次

但 AD 到目前為止沒有非常有效的藥
到目前為止FDA也僅批准5個 AD 新藥

DRUG NAME	DRUG TYPE AND USE	HOW IT WORKS	COMMON SIDE EFFECTS
Namenda® (memantine)	N-methyl D-aspartate (NMDA) antagonist prescribed to treat symptoms of moderate to severe AD	Blocks the toxic effects associated with excess glutamate and regulates glutamate activation	Dizziness, headache, constipation, confusion
Razadyne® (galantamine)	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD	Prevents the breakdown of acetylcholine and stimulates nicotinic receptors to release more acetylcholine in the brain	Nausea, vomiting, diarrhea, weight loss, loss of appetite
Exelon® (rivastigmine)	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD	Prevents the breakdown of acetylcholine and butyrylcholine (a brain chemical similar to acetylcholine) in the brain	Nausea, vomiting, diarrhea, weight loss, loss of appetite, muscle weakness
Aricept® (donepezil)	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate, and moderate to severe AD	Prevents the breakdown of acetylcholine in the brain	Nausea, vomiting, diarrhea
Cognex® (tacrine)	Cholinesterase inhibitor prescribed to treat symptoms of mild to moderate AD	Prevents the breakdown of acetylcholine in the brain	Hepatotoxicity , Nausea, vomiting, diarrhea

抗炎治療成為 AD 的一個新希望

Therapeutic, manufacturer	Mechanism	Published clinical or preclinical assessment	Ongoing or recently completed clinical trials
Masitinib, AB Science	Mast cell inhibitor	**Phase II**: slowing of cognitive decline when used as **adjunct** therapy to standard of care	Phase III
p40 antibody [such as ustekinumab (Stelara), Janssen or briakinumab (ABT-874), Abbott Laboratories	Proinflammatory cytokine inhibitor	Decreases in soluble Aβ and cognitive impairment (164)	N/A
CHF5074, Chiesi Pharmaceuticals/CereSpir	Microglial modulator	Phase II for MCI: improvements in several cognitive measures (162), decreases in CSF levels of TNF-α and sCD40L	Phase II

Journal of Alzheimer's Disease 60 (2017) S151–S160
DOI 10.3233/JAD-170374
IOS Press

Review

Chinese Medicine: A Hope for Neurodegenerative Diseases?

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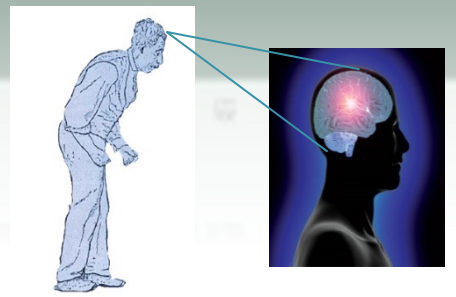
[a]*State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Macau, China*
[b]*School of Pharmacy, Macau University of Science and Technology, Macau, China*

Accepted 12 May 2017

Abstract. With the increase in the proportion of aged population due to the rapid increase of life expectancy, the worldwide prevalence rate of multiple neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and Huntington's disease has been increased dramatically. The demographic trend toward an older population has drawn the attention to new drug discovery and treatment on age-related diseases. Although a panel of drugs and/or therapies are currently available for treating the neurodegenerative diseases, side effects or insufficient drug efficacy have been reported. With the long history in prescription of Chinese medicine or natural compounds for modulating aged-related diseases, emerging evidence was reported to support the pharmacological role of Chinese medicine in ameliorating the symptoms, or interfering with the pathogenesis of several neurodegenerative diseases. This review brings evidence about today's trends and development of a list of potential neuroprotective herbal compounds from both the traditional and modern pharmacological point of view. With future projections, the potential hope and implication of using Chinese medicine as an alternative source for novel drug discovery for neurodegenerative diseases is proposed.

Keywords: Aging, α-synuclein, Alzheimer's disease, amyloid-β, autophagy, Chinese medicine, disease proteins, leonurine, neurodegenerative diseases, Parkinson's disease



利用中藥良好特色，篩選創新中藥活性成份甚至單體，以研發創新及副作用較小的抗神經退行疾病的新化合物是良好的研究方向

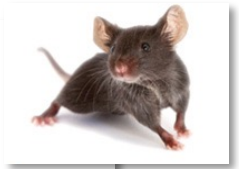
Law & Zhu, *JAD* 2017

治疗AD新策略

抗炎

血管新生

离子通道



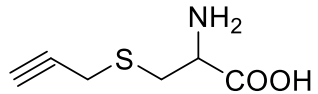
免疫调节

Law & Zhu, *JAD* 2017

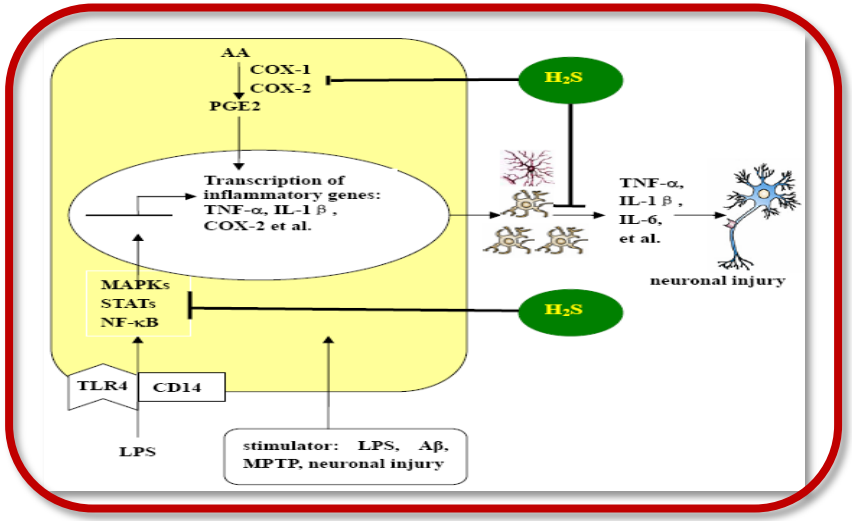
立論依據

S-Propargyl-Cysteine

ZYZ-802

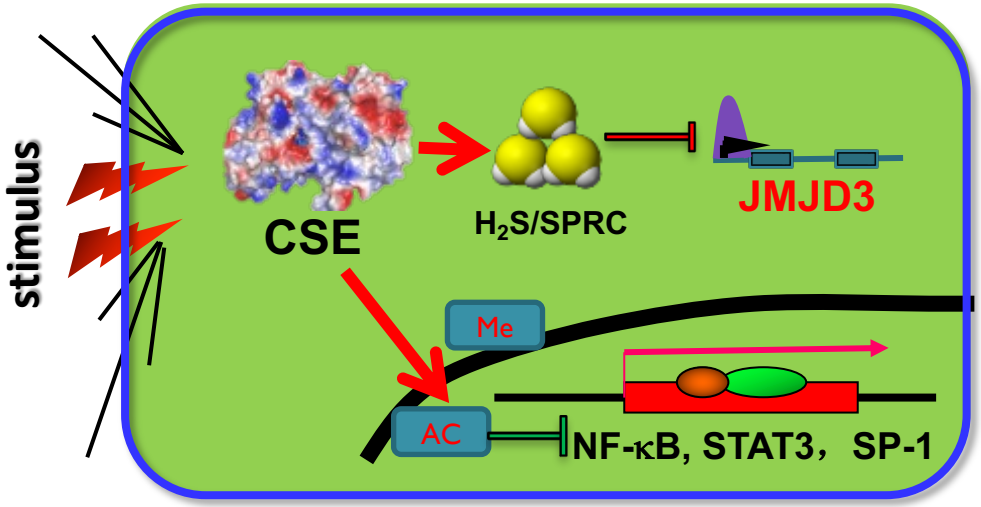


ZYZ-802的抗AD作用



Gong, ...Zhu, *JAD* 2011

ZYZ-802的抗炎作用



Wu et al. ***Cell Mol Immunol***. 2018
Wu et al. ***Antioxid Redox Signal***. 2018
Miao et al. ***Antioxid Redox Signal.*** 2017
Liu et al. ***Bio Pharmaco.*** 2017
Wu et al. ***Redox biology.*** 2016
Hu et al. ***Antioxid Redox Signal***. 2016
Xin et al. ***Antioxid Redox Signal***. 2016
Shen et al. ***Antioxid Redox Signal***. 2015
Pan et al. ***Antioxid Redox Signal***. 2012
Wang et al. ***Antioxid Redox Signal***. 2010

立論依據

同期發表的專題評論文章

Cardiovascular Research

www.elsevier.com/locate/cardiores

Editorial

Something is rotten in the state of angiogenesis — H_2S as gaseous stimulator of angiogenesis

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Received 4 July 2007; accepted 18 July 2007
Available online 25 July 2007

See article by Cai et al. [7] (pages 29–40) in this issue.

The research on a new class of signaling molecules, later named gaseous transmitters or gasotransmitters, started in 1986 with the discovery that the so-called endothelium-derived relaxing factor (EDRF) is identical to nitric oxide [1]. This finding was later awarded with the Nobel Prize and

CBS and CSE is partly tissue specific; some organs express both enzymes, whereas vascular H_2S is mostly generated by CSE and released from vascular smooth muscle cells, apart from a minor non-enzymatic reaction [3]. In aqueous solutions, about one third of H_2S remains non-dissociated at physiologic pH. The effects of H_2S on the cardiovascular system are manifold. Smooth muscle relaxation and hence vasodilatation is induced by H_2S through opening of K_{ATP} channels [3,4], an effect that can be antagonized by pre-incubation with K_{ATP} channel blockers. In the heart, H_2S induces coronary vasodilatation at low concentrations [5]. This effect is eliminated at higher concentrations, where H_2S has negative inotropic effects [5]. Furthermore, H_2S and CSE have been associated with the pathogenesis of hypertension. In spontaneously hypertensive rats, CSE expression is decreased, while exogenous administration attenuated the development of hypertension [6].

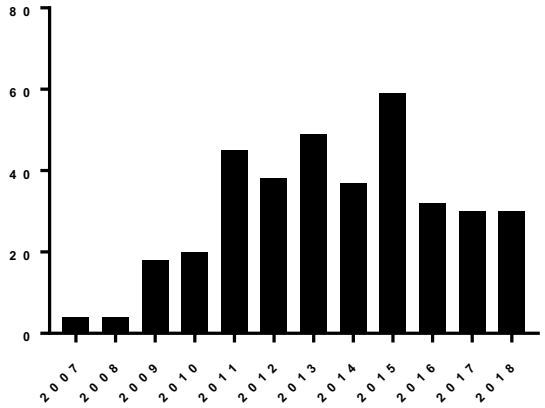
In this issue of *Cardiovascular Research* Cai et al. describe a novel, pro-angiogenic effect of H_2S [7], thereby joining the company of NO and CO as angiogenic factors [8–10]. At first sight, this seems a redundant action, but it is not. Gasotransmitters interact with each other, e.g. NO donors have previously been shown to increase the expression of CSE and the release of H_2S [3]. In the current study, the authors used the H_2S donor NaHS to assess its role during angiogenesis. In summary, the authors showed that H_2S at physiologic concentrations induces in vitro and in vivo angiogenesis, promoting endothelial cell proliferation, adhesion, and migration, whereas higher but still non-toxic concentrations yielded no such effects. Since the effects of the gasotransmitters are so closely related, this study further tried

identified. Another common feature of these 3 known gasotransmitters is their toxic effects in higher concentrations. Despite their toxicity, they are endogenously produced in significant amounts; the toxic effect level of e.g. H_2S is only twice as high as the concentrations in brain tissue, demanding a delicate regulating mechanism to maintain physiological levels [2].

H_2S is endogenously generated from L-cysteine by two distinct enzymes, cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE), which are responsible for the majority of H_2S in mammalian tissue. The expression of

H_2S促血管新生作用是一種新穎的心血管保護機制。

單篇被引用374次



此論文發表後歷年引用情況

關於促血管新生的研究共被引1192次

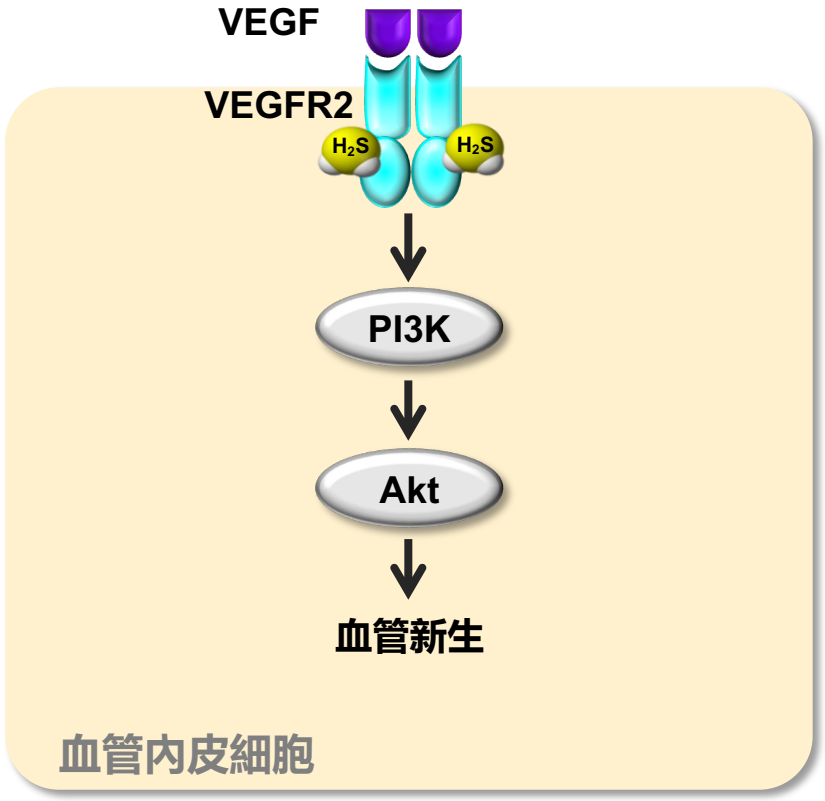
19個國家的141個實驗室證實了我們觀察到的H_2S促血管新生效應。

Cell 2018
Circulation 2013
J Cell Mol Med 2008
J Am Soc Nephrol 2014

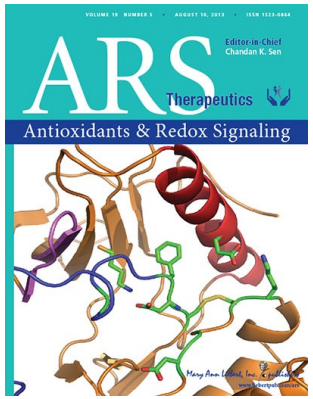
本團隊H_2S醫學系列研究合計被引用4069次

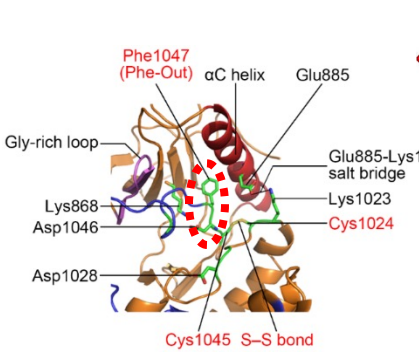
立論依據

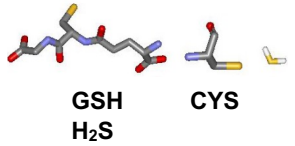
VEGFR2中含有H_2S“分子开关”



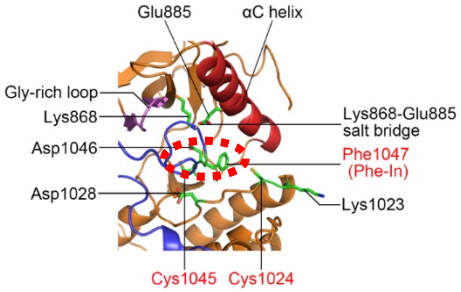
VEGF:血管内皮細胞生長因數
VEGFR2：血管内皮細胞生長因數受體-2







抑制态



激活态

突变相关Cys位点阻断了H_2S效应 *Antioxid & Redox Signal. 2013*

立論依據

水溶性藥物輸送難點：

1.包封率低

2.突釋嚴重

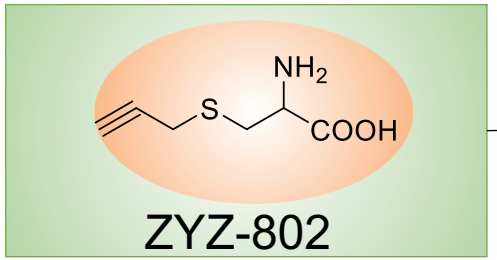
3.難以實現長效釋放

水溶性藥物緩控釋策略：

1.包被在納米載體中

2.共價接枝于聚合物

3.製備成微球製劑



ZYZ-802

缓控释输送体系：

1. 二氧化硅纳米粒
2. 聚合物胶束
3. PLGA微球

釋放周期爲**2天~一個月**的ZYZ-802緩釋製劑

製備方法優化：

- 物理吸附
- 化学结合
- 物理包载

理化性质表徵：

分子量與結構表徵、粒徑、電勢、穩定性

藥物包載與釋放：

載藥量、包封率、藥物釋放動力學

朱依谆, et al. CN104069068A

朱依谆, et al. CN108066286A

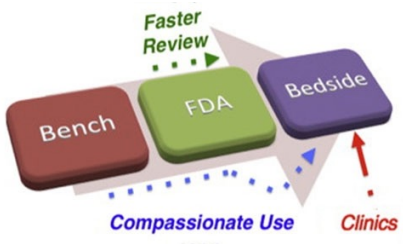
Cabral H, et al. *Chemical Reviews* **2018**

Kakkar A, et al. *Nature Reviews Chemistry* **2017**

Möller K, et al. *Chemistry of Materials* **2016**

Ramazani F, et al. *International J. of Pharmaceutics* **2016**

研究目標

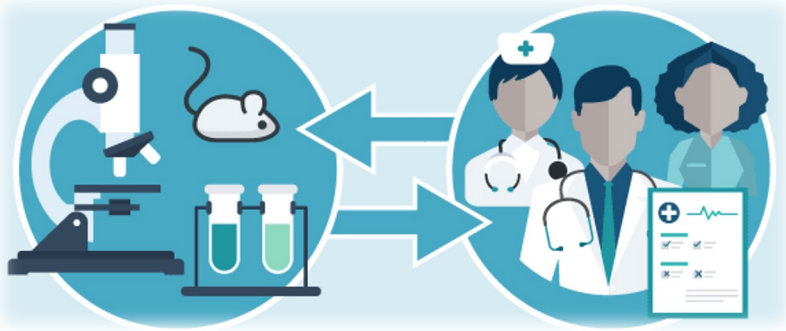


科學技術發展基金
FDCT

1. 完成ZYZ-802長效緩釋劑，並進行藥代動力學-藥效學研究以及安全性評估。

2. 在老年癡呆動物模型上，從行為、形態、生化、蛋白等多層面，探討ZYZ-802對阿爾茨海默症的保護作用，為其臨床轉化提供實驗證據。

3. 從整體、器官、組織、細胞與分子和硫化氫的分子開關等多層次闡述其作用原理：抗炎免疫調節、血管新生、神經元保护和離子通道等。

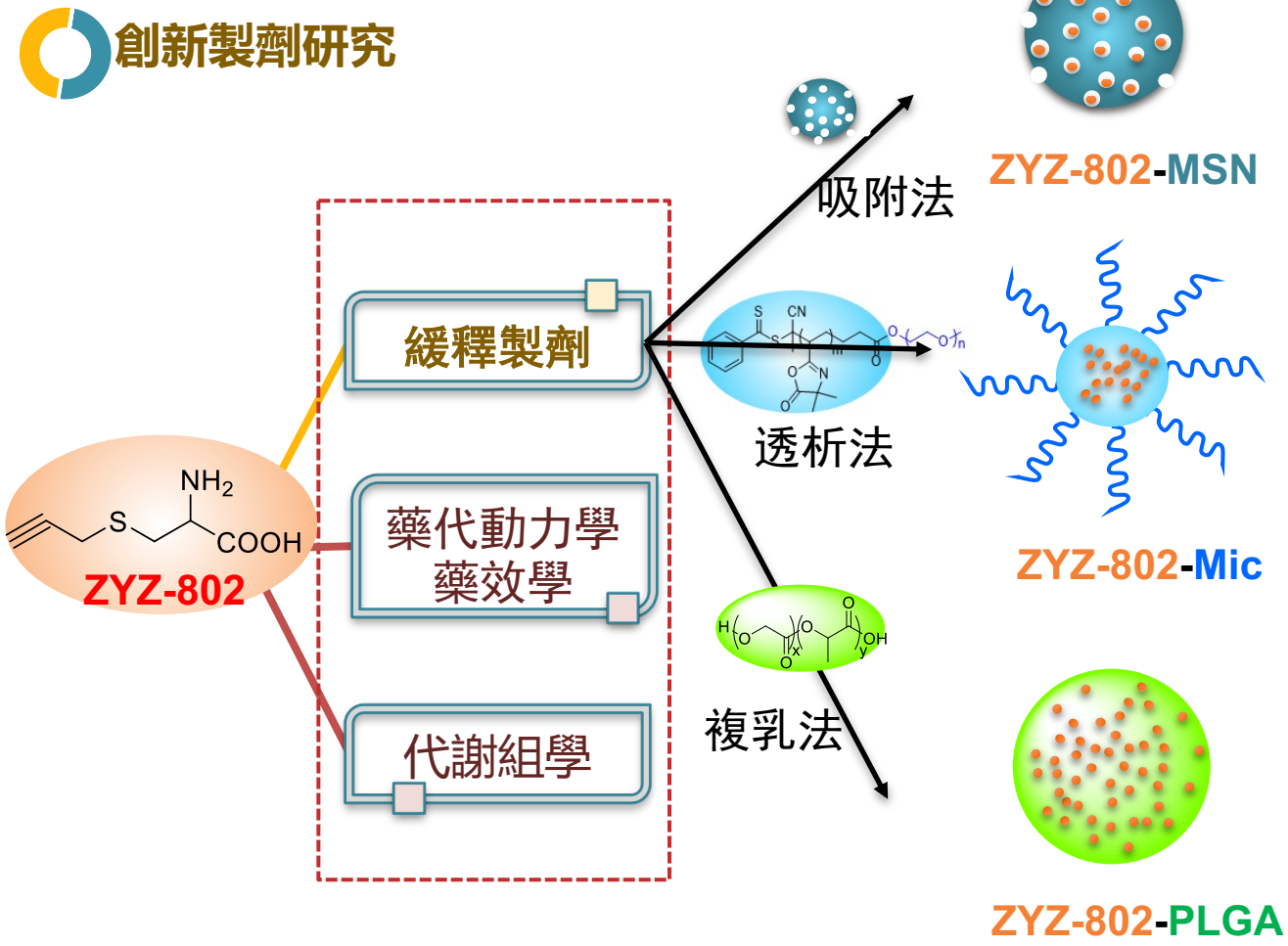


二 研究內容與方法

1. ZYZ-802製劑與PK-PD研究
2. 治療AD的藥效與安全性實驗
3. 創新機制研究

ZYZ-802製劑與PK-PD研究

創新製劑研究



二氧化矽納米粒

- 高載藥量（>70 wt%）
- 可生物降解
- 解吸附控制藥物釋放

聚合物膠束

- 共價接枝，高穩定性
- 可生物降解
- 化學鍵水解和擴散雙重機理控制藥物釋放

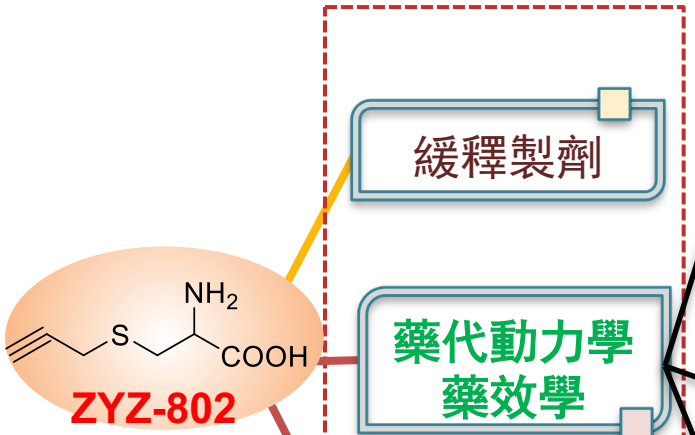
PLGA微球

- 注射劑中最長效的劑型，可有效釋放1~3個月
- 可生物降解
- 基質溶蝕控制藥物釋放

ZYZ-802缓释制剂将维持更为稳定的血药浓度，减少用药次数，从而显著提高病人的依从性

ZYZ-802製劑與PK-PD研究

創新製劑PK研究

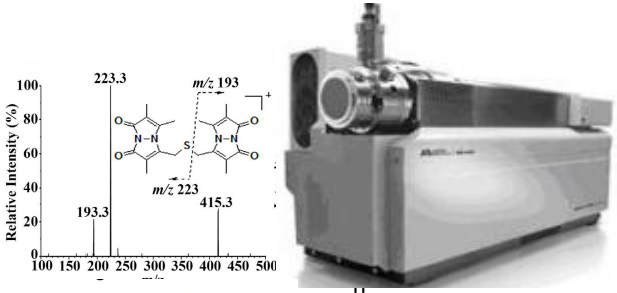


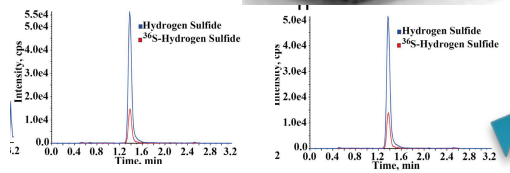
緩釋製劑

藥代動力學
藥效學

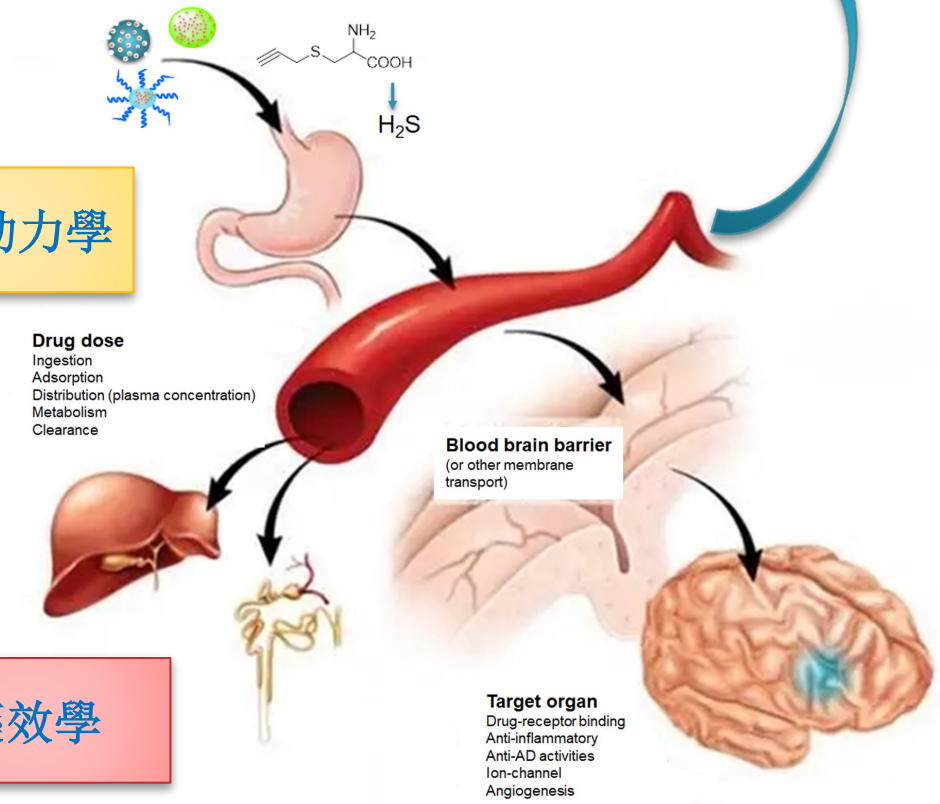
代謝組學

檢測ZYZ-802藥物濃度
檢測H2S濃度





藥物動力學

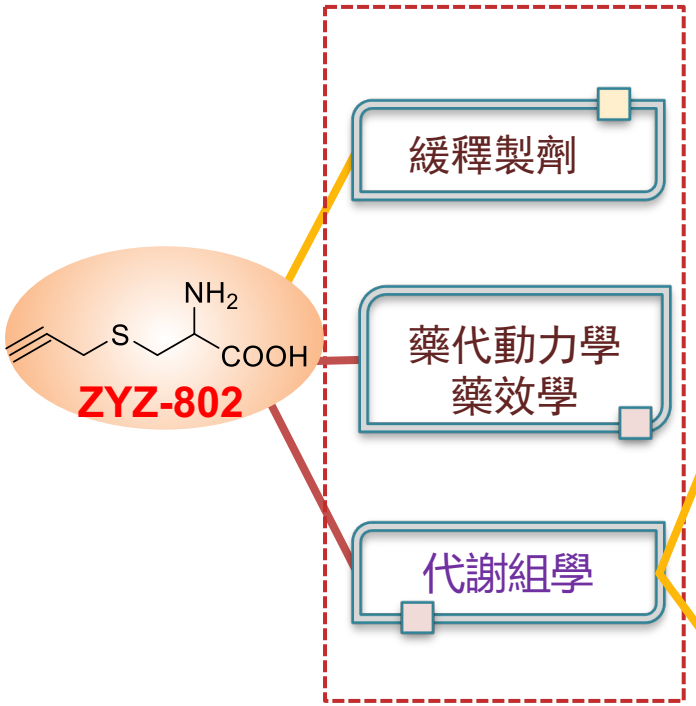


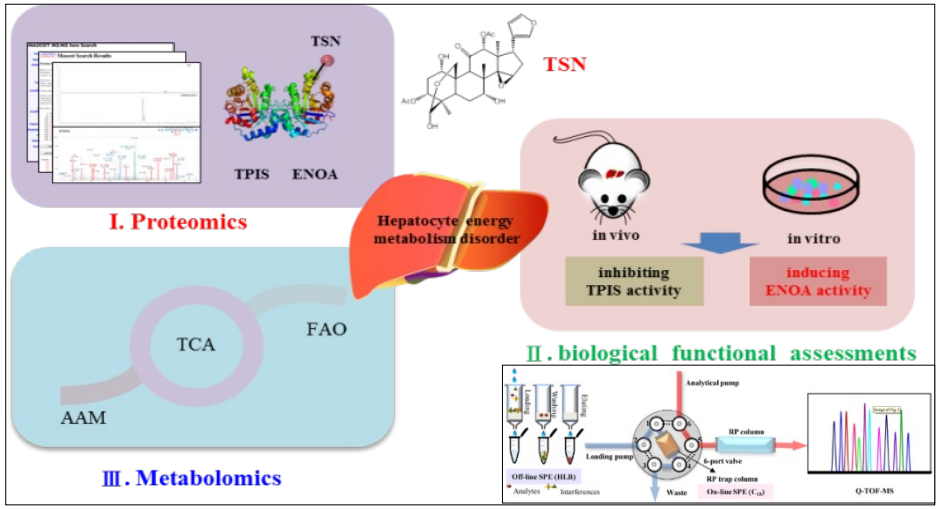
藥效學

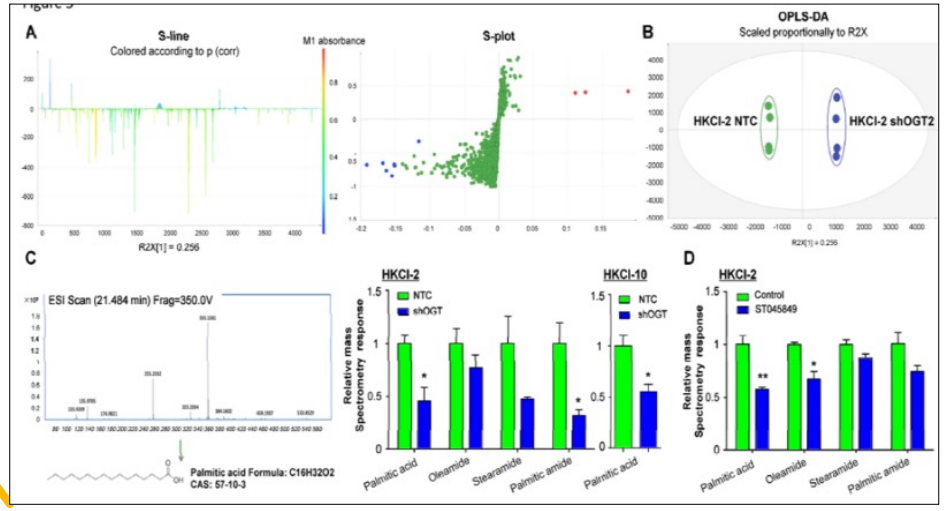
Pharmacokinetics | Pharmacodynamics

ZYZ-802製劑與PK-PD研究

生物分析

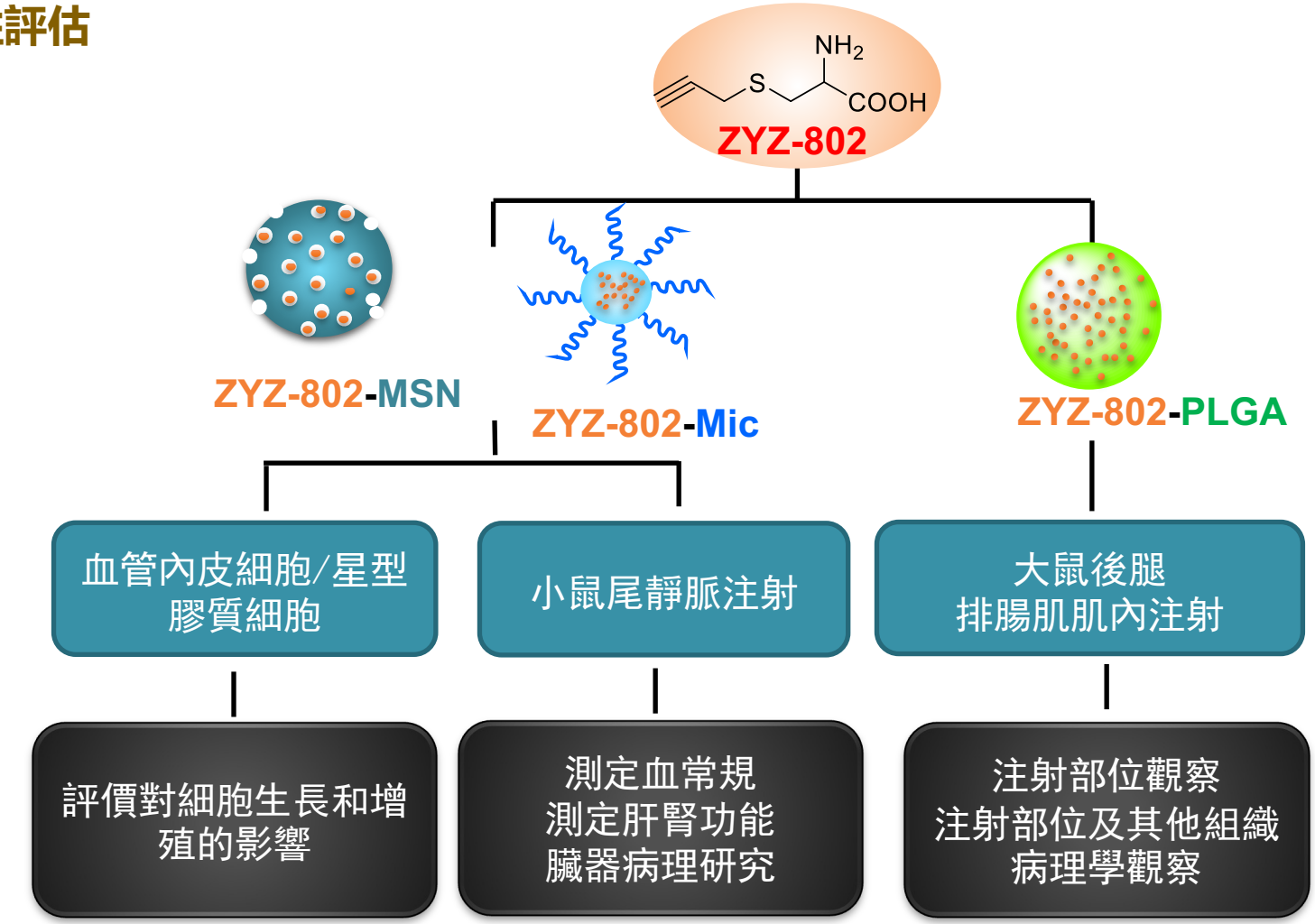






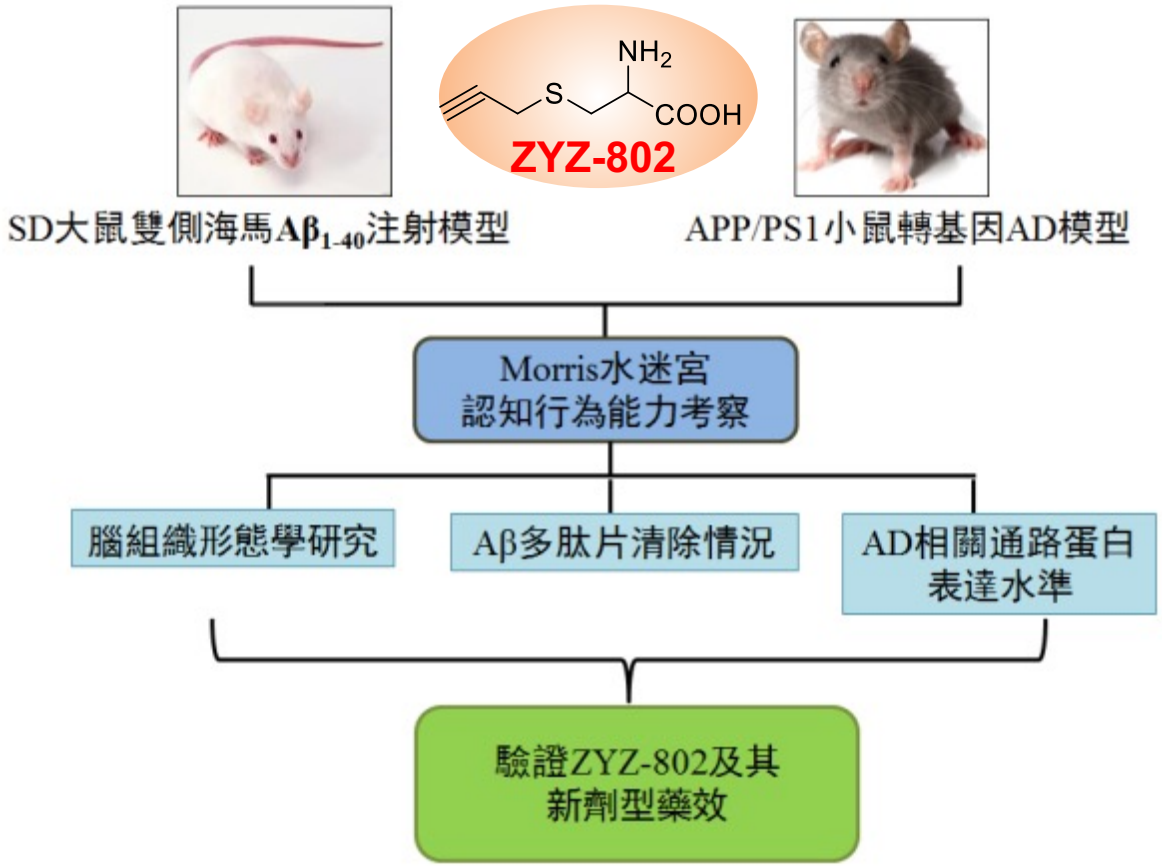
治療AD的藥效與安全性實驗

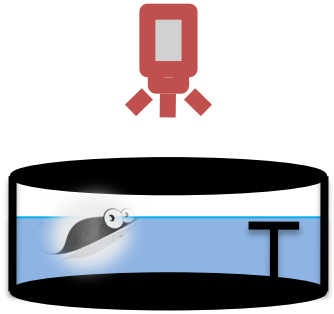
安全性評估

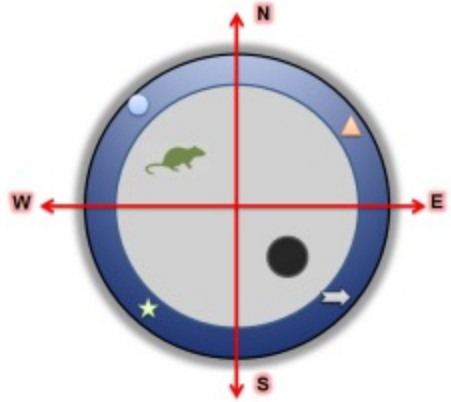


治療AD的藥效與安全性實驗

藥效評估

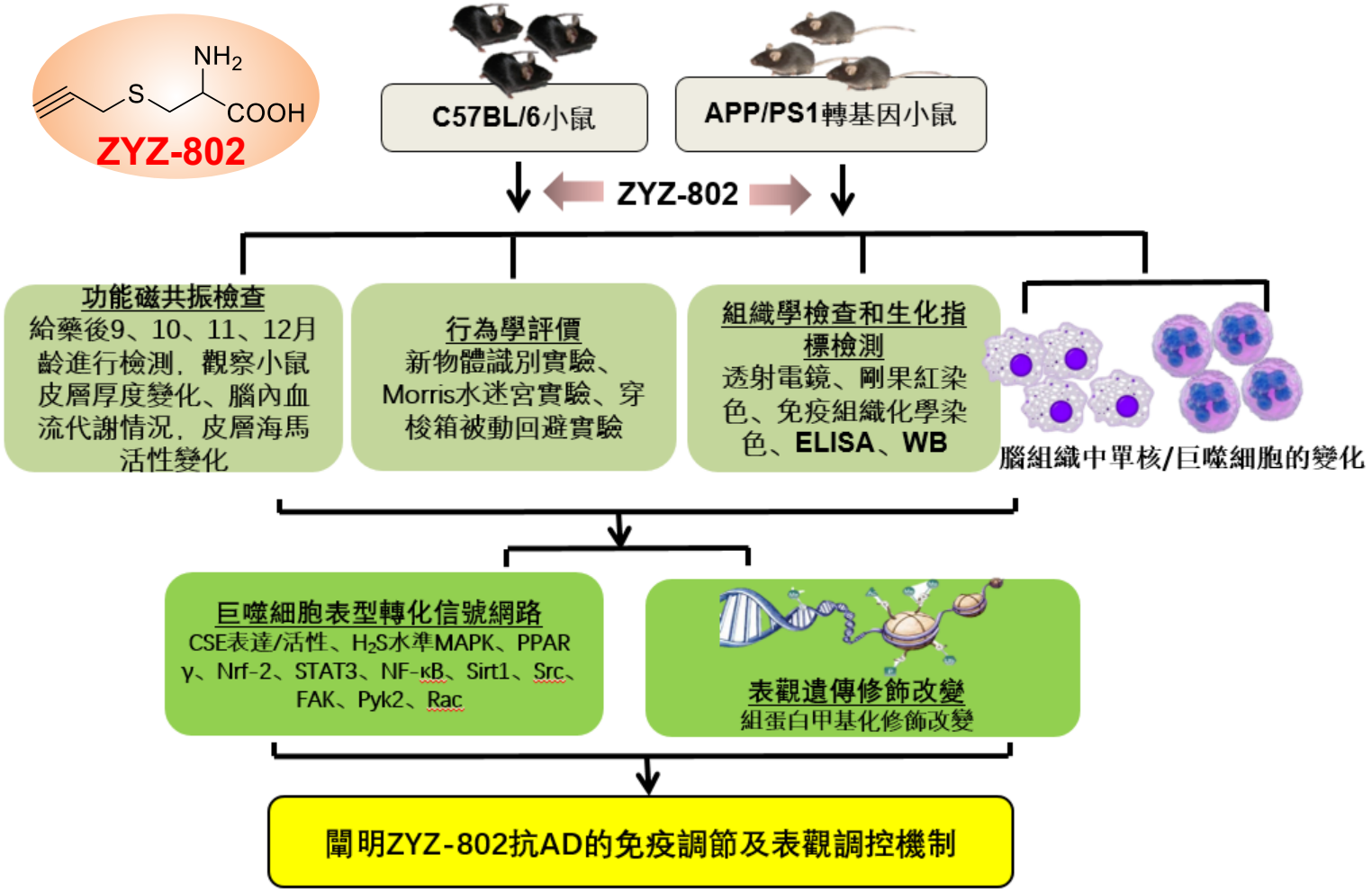






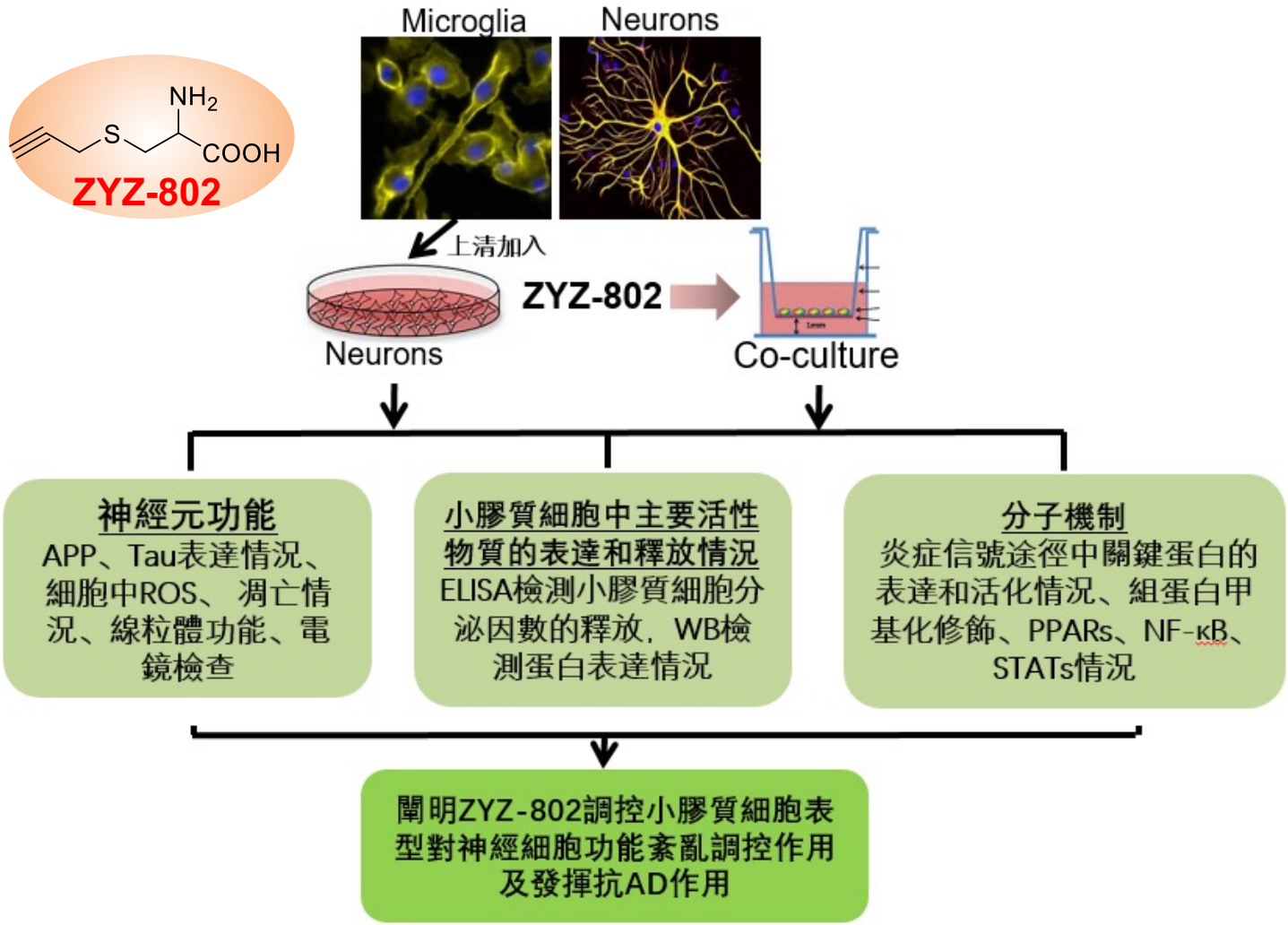
創新機制研究

ZYZ-802抗AD的免疫調節和表觀調控機制



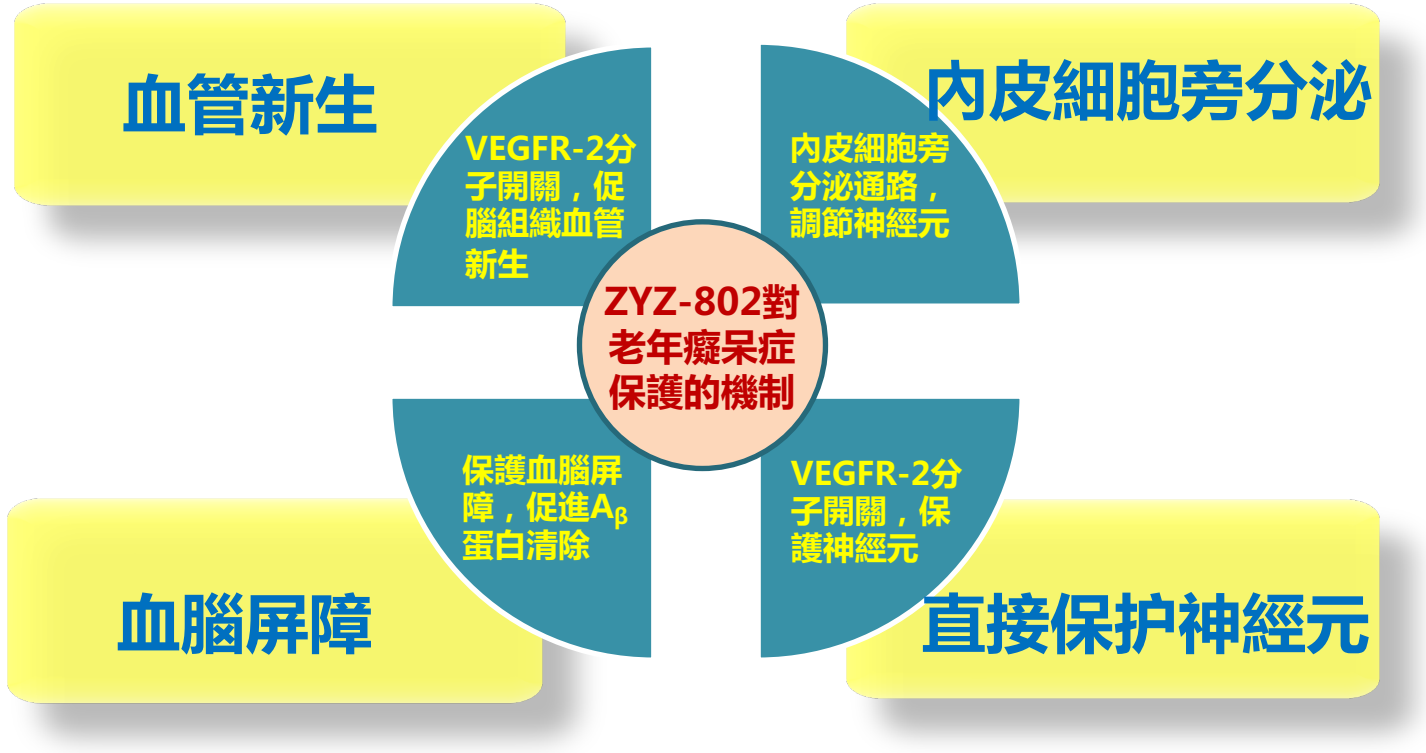
創新機制研究

ZYZ-802神經元細胞和小膠質細胞保護機制



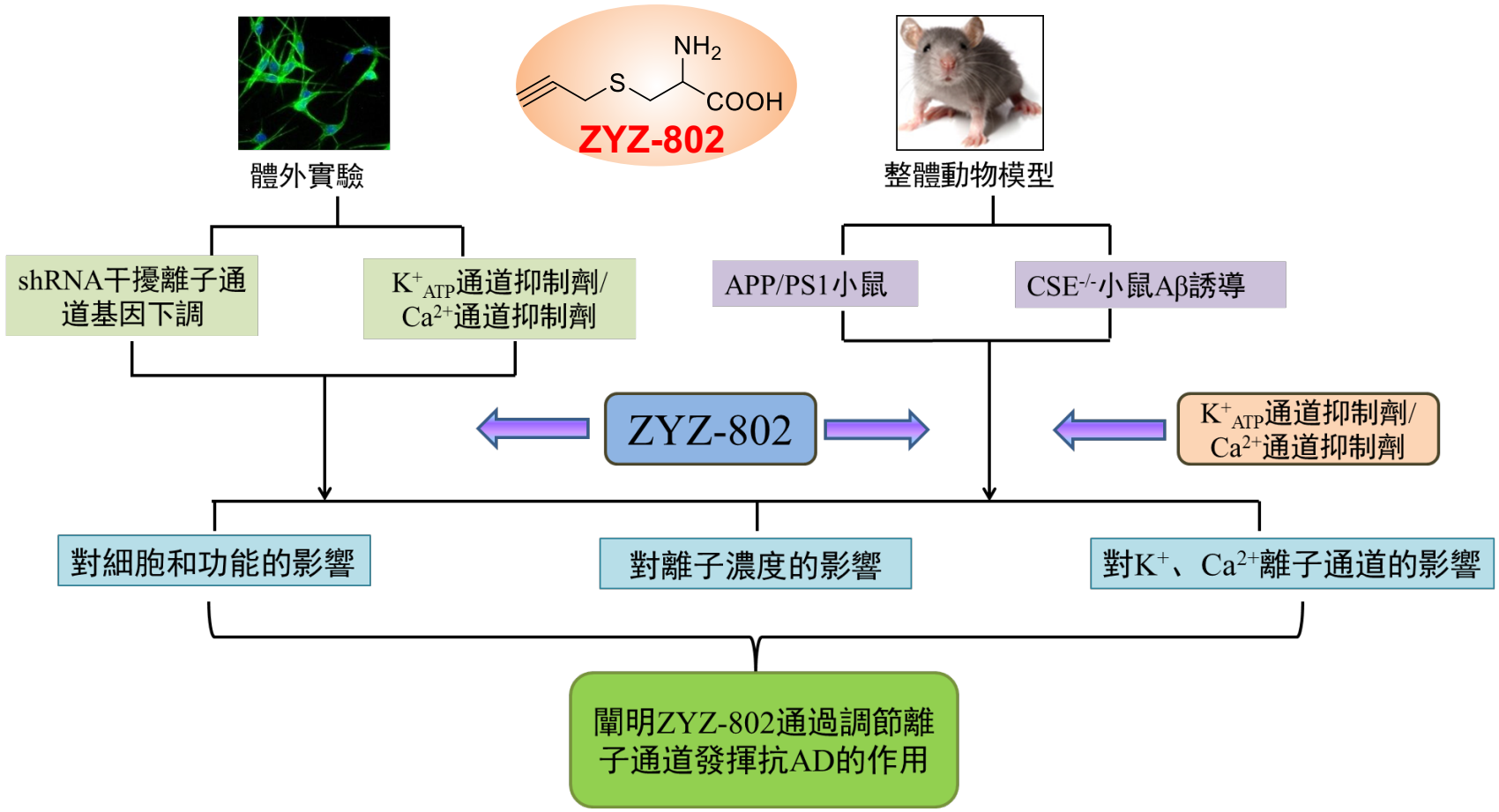
創新機制研究

ZYZ-802神促進小鼠腦內血管新生改善腦內缺氧機制



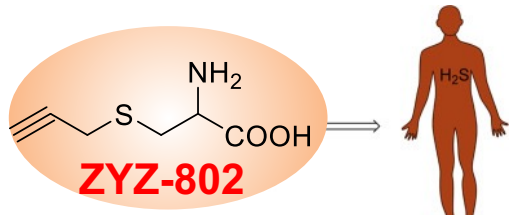
創新機制研究

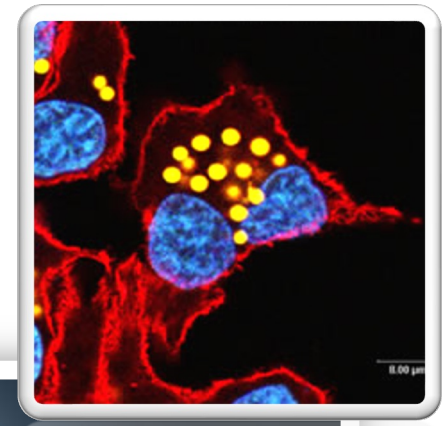
ZYZ-802离子通道的调节作用機制



三 項目創新性

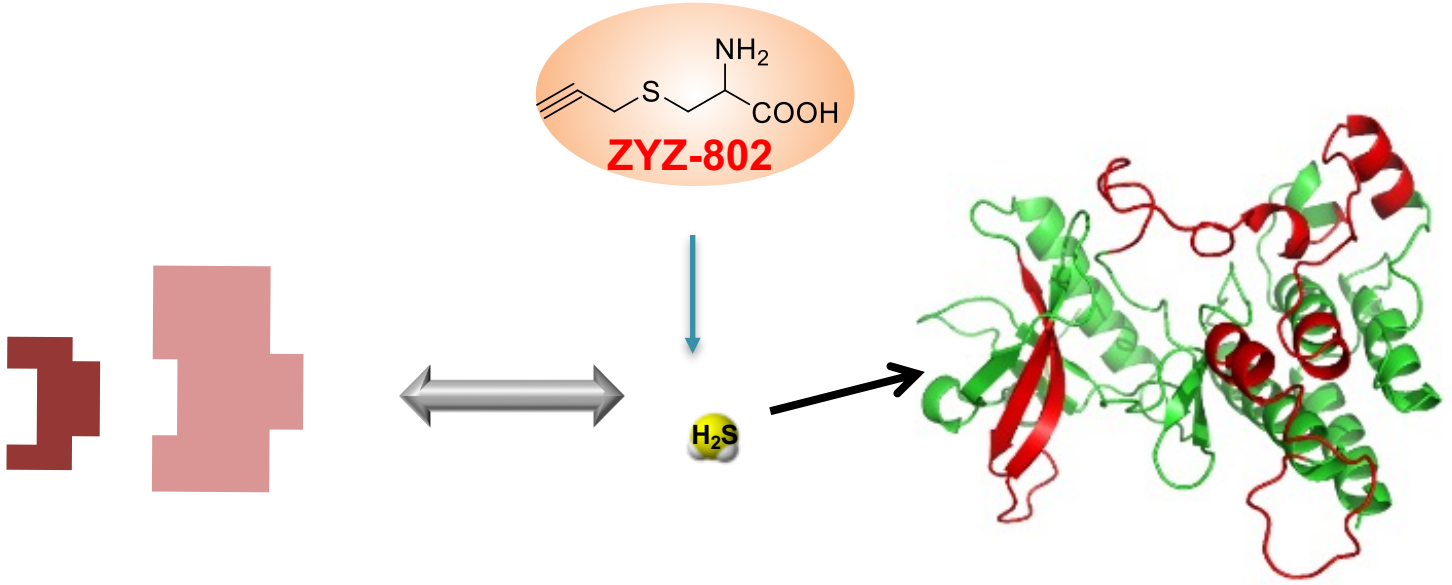
如何長效、緩釋的藥物輸送，實現H2S供體臨床轉化？





項目創新性

細胞如何感知氣體分子H_2S？



經典的配體-受體結合方式：

基於空間構象匹配的對接

H_2S分子極微小:

不足以形成與蛋白分子對接的空間構象

四 研究基礎

根據CFDA藥品申報資料目錄，本項目已完成有關藥學研究資料情況

	原料藥	全部完成
1	基本資訊	√
2	生產資訊	√
3	特性鑒定	√
4	原料藥的品質控制	√
5	對照品	√
6	包裝材料和容器	√
7	穩定性	√

	製劑	大部分完成
1	劑型及產品組成	*
2	產品開發	待完善
3	生產	待完善
4	原輔料的控制	待完善
5	製劑的品質控制	待完善
6	對照品	待完善
7	穩定性	待完善

	其他資料	基本完成
1	非临床研究资料综述	√
2	主要藥效學試驗資料及文獻資料	√ （新製劑部分待補充）
3	安全藥理學的試驗資料及文獻資料	√（部分機制研究待補充）
4	單次給藥毒性試驗資料及文獻資料	√
5	重複給藥毒性試驗資料及文獻資料	√
6	遺傳毒性試驗資料及文獻資料	√
7	生殖毒性試驗資料及文獻資料	√
8	非臨床藥代動力學試驗資料及文獻資料	√

***注：2項新專利已從澳門申請**

（1）一種載S-炔丙基半胱氨酸的微球製劑及其製備方法，中國專利號201910725731 5；

（2）載S-炔丙基半胱氨酸的介孔二氧化矽製劑及其製備方法，中國專利號201910726249 3

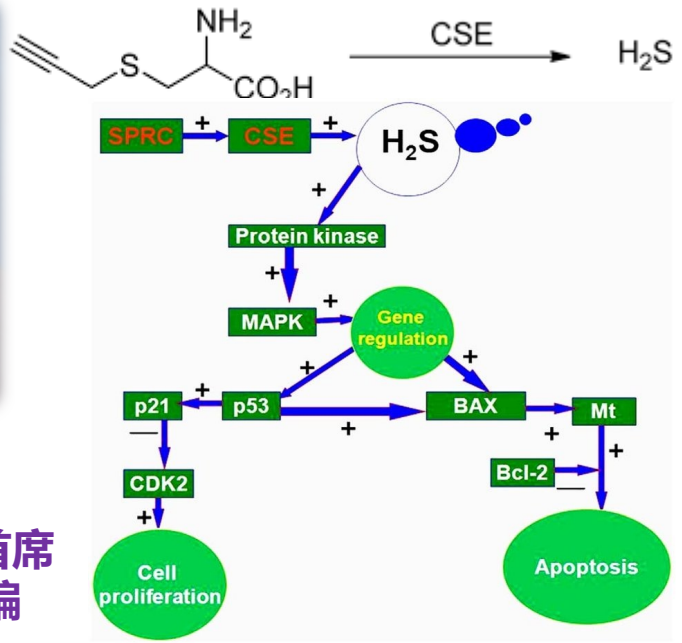
研究基礎

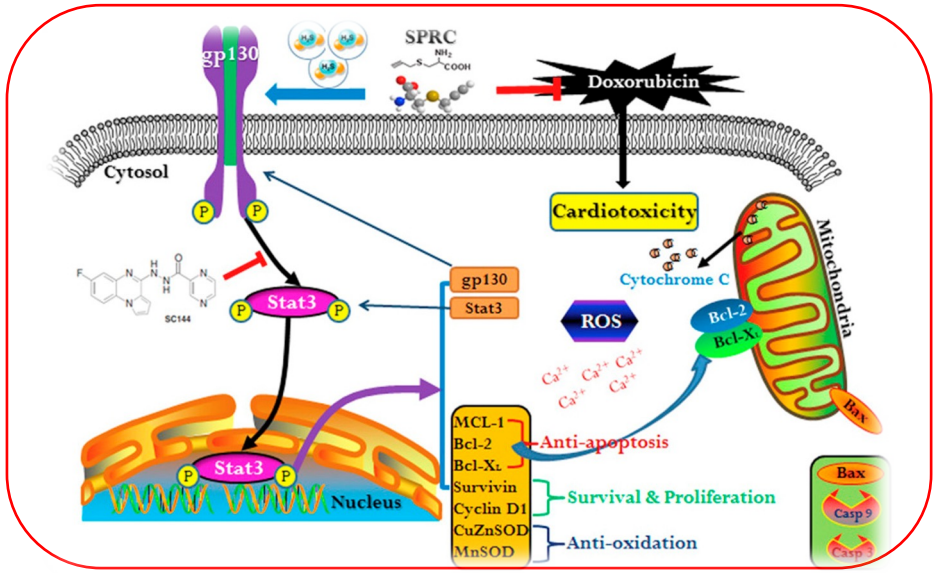
H_2S供體藥效和機制實驗平臺

ZYZ-802原創人

已有进入中美临床研究（I期和II期）的新药（first-in-class）成功经验

朱依諄
講座教授
杰青，长江, 973首席
2届的*JAD*副主编





朱依諄教授致力於氣體信號分子H_2S對神經系統的作用

- 氣體信號分子H_2S成藥性困難，而ZYZ-802作為H_2S的新型供體為成藥性提供了可能。
- ZYZ-802項目曾作為國家一類新藥在國家“十一五”計劃“重大新藥創制”的平臺孵化藥物（2009ZX09301），前期基礎上對ZYZ-802進行了原料药中試優化放大、臨床前藥代動力學及和長期毒性等成藥性研究。

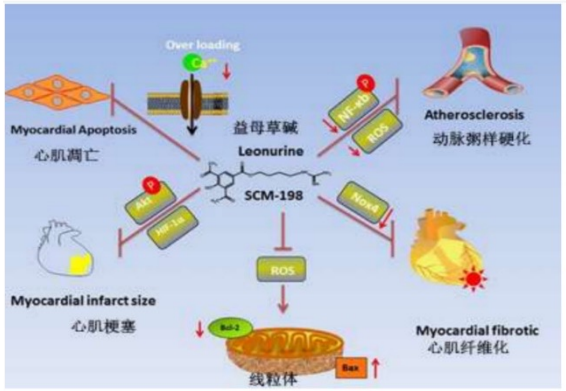
研究基础

原创新药获得国家CFDA 2 个I.1 类新药临床批文，FDA 临床研究也即将开始。

临床批件

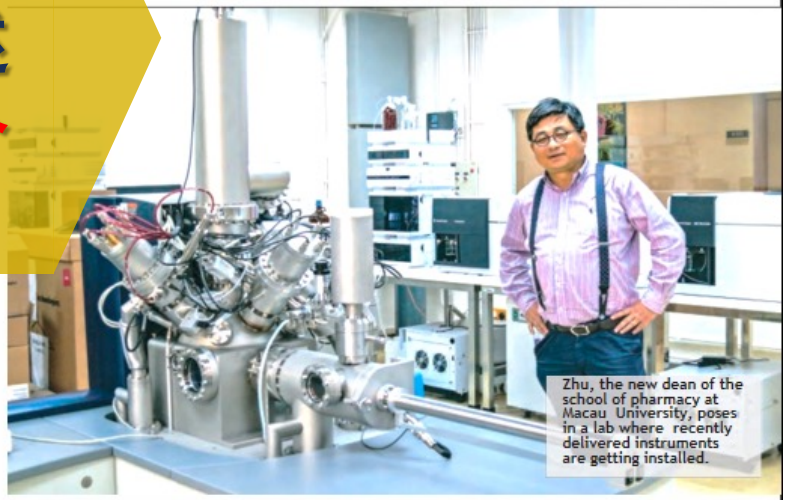
美国化学会的新闻期刊《C&EN》2017年4月出版3页纸的专题新闻报道描述朱教授的新药发现是一个巨大的突破。

科学网 ···



降脂原理示意图：益母草碱通过抑制氧化应激和新靶点NOX-4保护心脏和减少动脉粥样硬化

本报讯（通讯员孙国根记者黄辛）复旦大学特聘讲座教授朱依谆团队在国家重大新药创制的连续资助下，发现从中药益母草中提取并化学合成的单体 -- 益母草碱（又名SCM-198）除对血管保护和脑中风治疗


Zhu, the new dean of the school of pharmacy at Macau University, poses in a lab where recently delivered instruments are getting installed.

DRUG DEVELOPMENT

Chinese professors turn entrepreneurial

Spurred by increased funding and clearer guidelines, academics aim to develop commercial drugs

JEAN-FRANÇOIS TREMBLAY, C&EN HONG KONG

Jianmin Fang is a professor of molecular medicine at Shanghai's Tongji University who for decades has been studying the mechanisms by which tumors develop. Fang also has two companies in Yantai in Northeast China. One, RemeGen, he founded in 2008 to develop biological drugs for cancers and other diseases. It now employs 250 people. The other provides manufacturing services to RemeGen and other drug firms.

In Beijing, Xiaodong Wang is the founder of the National Institute of Biological Sciences, a government lab that conducts basic life sciences research and employs 700 people. On the side, Wang is founder and director of BeiGene, an oncology drug research firm he launched in 2010. BeiGene has several drug candidates being tested on patients in China and other countries.

Fang and Wang are pioneers who started their companies before it was fashionable for Chinese academics to do so. China has long been fertile ground for entrepreneurs wanting to set up drug discovery firms. But among the hundreds of biotechs that have sprung up across the country in the past 15 years, few were launched by academics. Many, if not most, are led by Chinese-born entrepreneurs who worked in the U.S. biotech sector.

But more and more academics are launching their own companies nowadays. In a shift, the institutions they work for are encouraging them to do so, and the government is supplying financing.

Although professor-CEOs remain less common in China than in the West, the country is quickly catching up as it aims to make science and innovation play a more important role in economic development. The main driver for any academic to start his or her own drug firm is the desire to develop new treatments for patients rather than advance science for its own sake. "Papers push the boundaries of knowledge, but the new knowledge has to become a treatment," Fang says. "Science has to translate into a medical solution."

After receiving his Ph.D. in biology from Dalhousie University, Fang did a postdoc at Harvard Medical School, where he studied tumor biology and angiogenesis, or blood vessel growth, in tumors. The insights he accumulated over the years led him to launch RemeGen, which is now developing several drug candidates. One, an anti- body drug conjugate, is undergoing Phase II clinical trials in China for the treatment of breast and gastric cancers.

Fang says he could have successfully launched RemeGen in the U.S., but being based in China will benefit a greater numbe of patients. "China's FDA has not approved many biological drugs, so the need is huge from the patients' perspective," he says.

At Shanghai Institute of Materia Medica (SIMM), a state pharmaceutical research la that also trains students, several academics are developing commercial drug candidates Jian Ding, a professor and former director o SIMM, went so far as to create a biotech firm in 2011 to conduct drug development for scientists at SIMM. The company, HaiHe Pharmaceutical, now also works wit academics and biotech firms not associated with the institute.

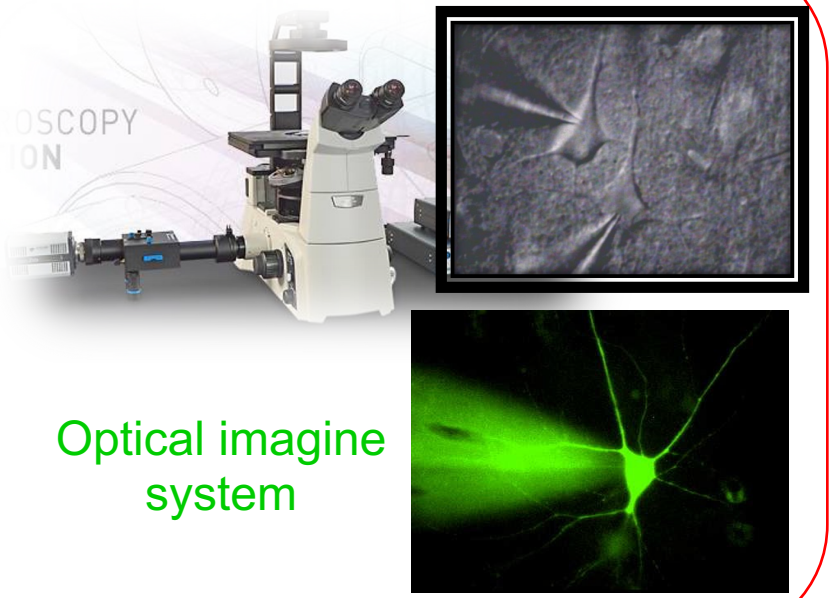
A focus of HaiHe is developing treatment for cancers that are prevalent in China, say Ying Huang, the company's

CREDIT: JEAN-FRANÇOIS TREMBLAY/C&EN

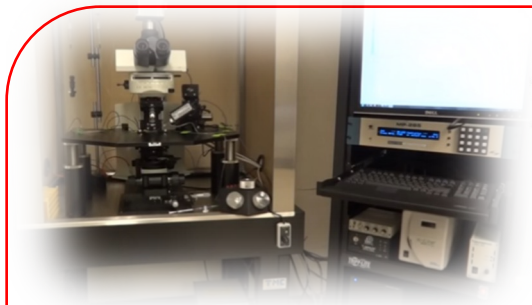
研究基礎

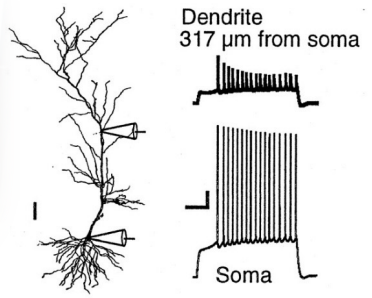
離子通道
實驗平臺

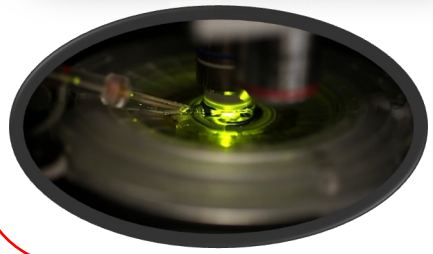
Erwin Neher
诺奖获得者



Optical imagine system







Electrophysiology system

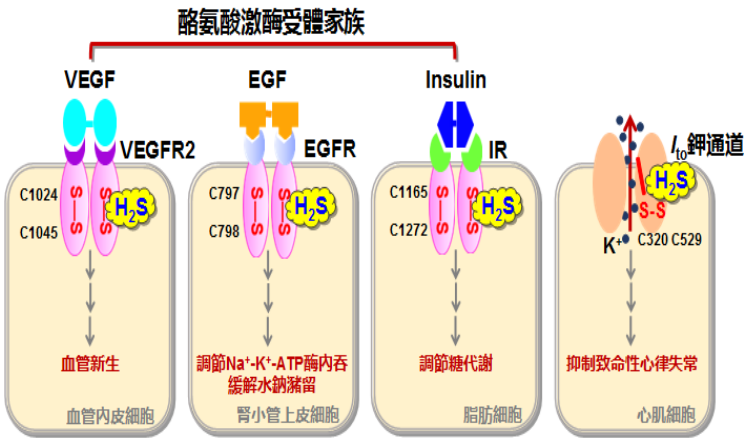
Neher教授的实验室，专注于以世界尖端生物物理学实验技术研究神经退行性疾病、心血管系统疾病和免疫系统相关疾病，并利用相关技术研究开发针对特殊靶点的新一代高效特异性药物。

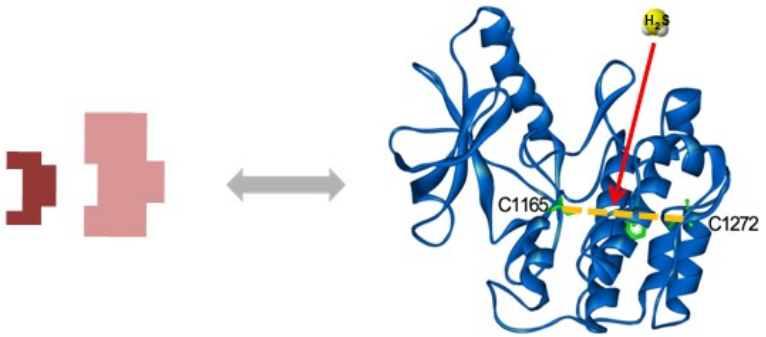
于海杰
助理教授

研究基礎

H_2S靶分子及其分子開關實驗平臺

朱依純， 杰青，
长江特聘教授





經典的配體-受體結合方式：
基於空間構象匹配的對接

未發現表觀遺傳學修飾

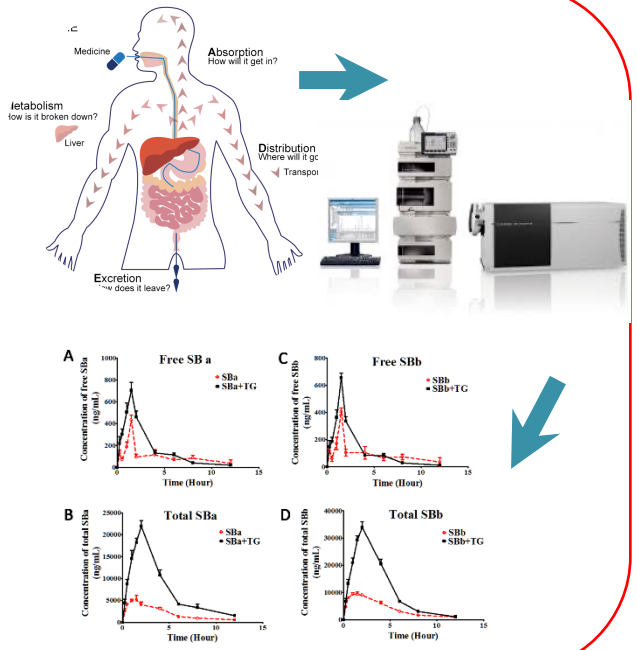
朱依純教授致力於氣體信號分子H_2S靶分子的尋找併發現了H_2S作用的二硫鍵分子開關。

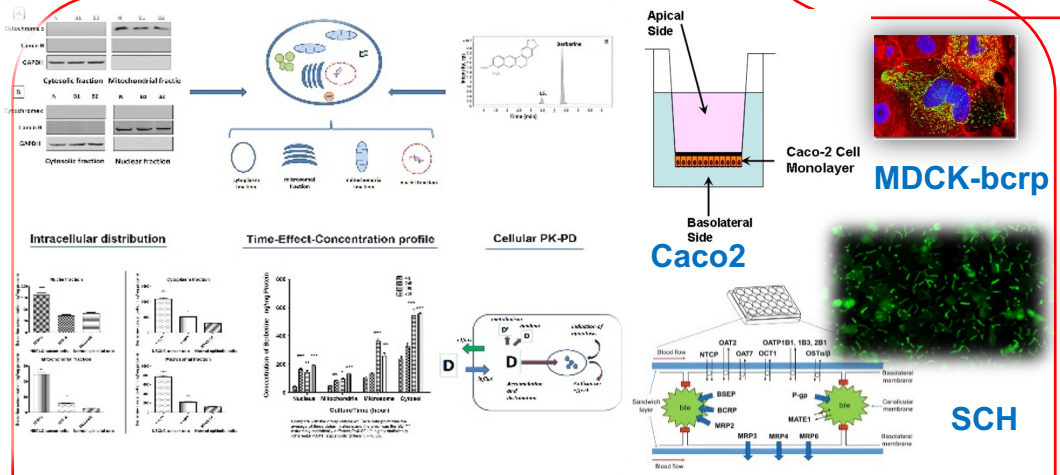
- 發現H_2S在血管內皮細胞中的靶分子VEGFR2及其胞內激酶活性區的C1045-C1024分子開關。
- 發現多個含有H_2S作用分子開關的酪氨酸激酶，為H_2S在體內具有多種重要的生物學功能提供了機制上的解釋。

4 研 究 基 礎

藥代動力學與藥效學實驗平臺

謝瑩
副教授





細胞藥代動力學

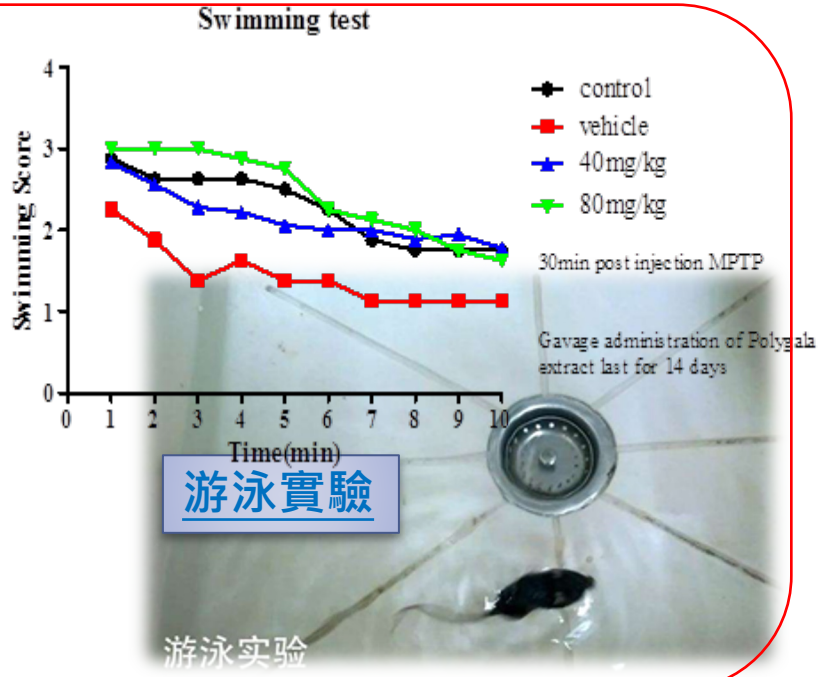
轉運蛋白研究

謝瑩副教授的團隊专注于以結合現代分析技術和組學技術研究藥物代謝動力學和藥效機制，特別是代謝綜合徵疾病研究，并利用相关技术研究开发中藥中高效低毒药物。

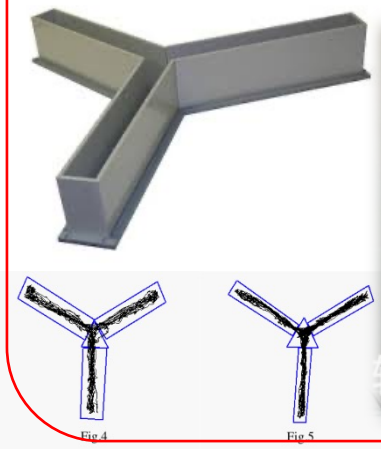
研究基礎

AD動物模型
實驗平臺

Betty Law
副教授



Y-迷宮



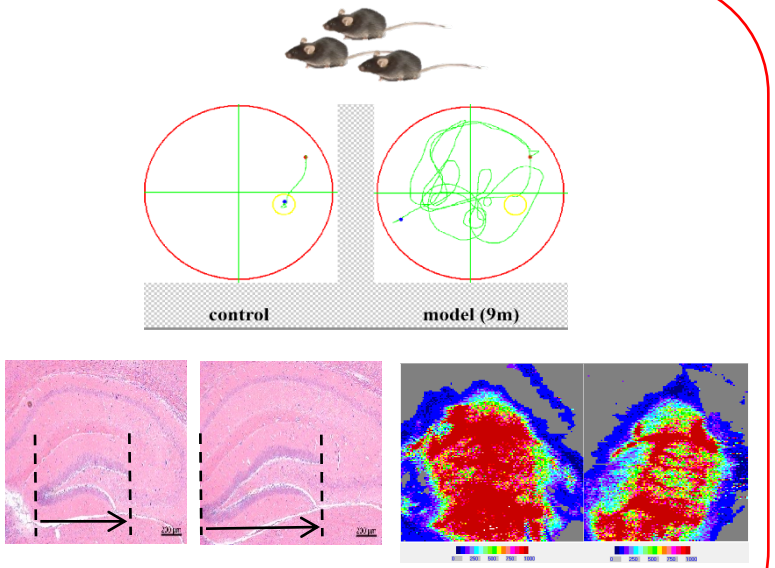
轉棒實驗

主要從事神經退行性疾病尤其是行為學模型和藥理研究，建立了完整的相關動物模型。在中藥和有效成份抗AD和PD研究有所很好的積累。

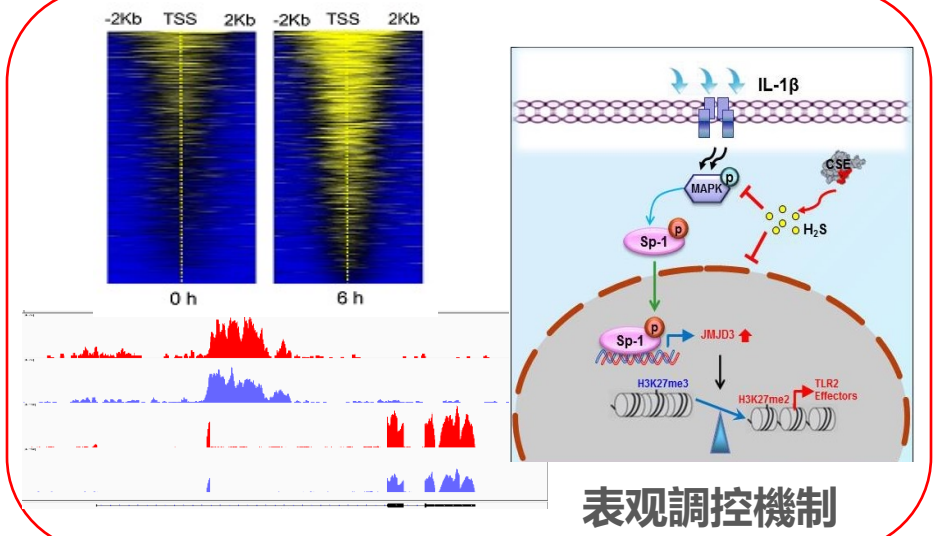
研究基礎

药效及免疫和表觀調控機制平台

劉新華
副研究員



藥效評價



表观調控機制

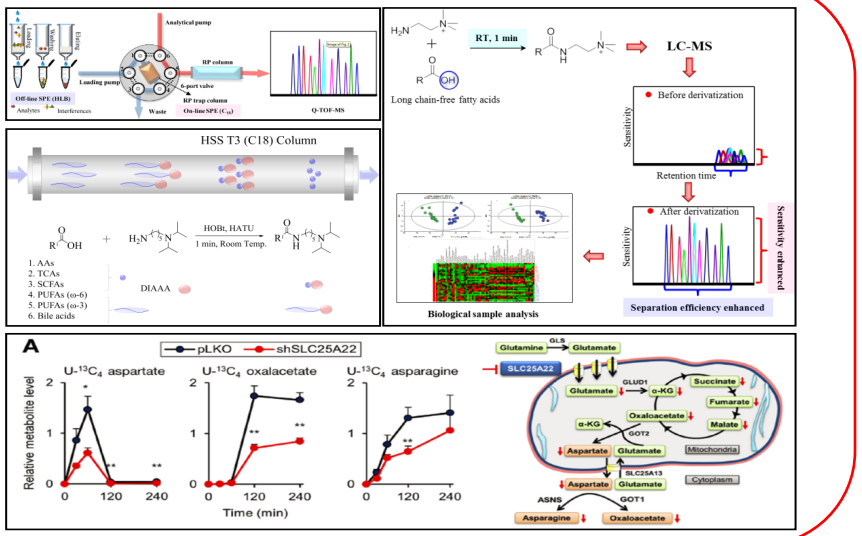
目前主要從事**分子藥理**研究，表觀遺傳學在心腦血管疾病，**免疫性疾病及神經系統疾病**過程的調控作用，深入挖掘**調控AD靶點**及潛在機制研究。

研究基礎

代謝組學和蛋白组学實驗平臺

伍建林
副教授

LC-SPE-MS/NMR

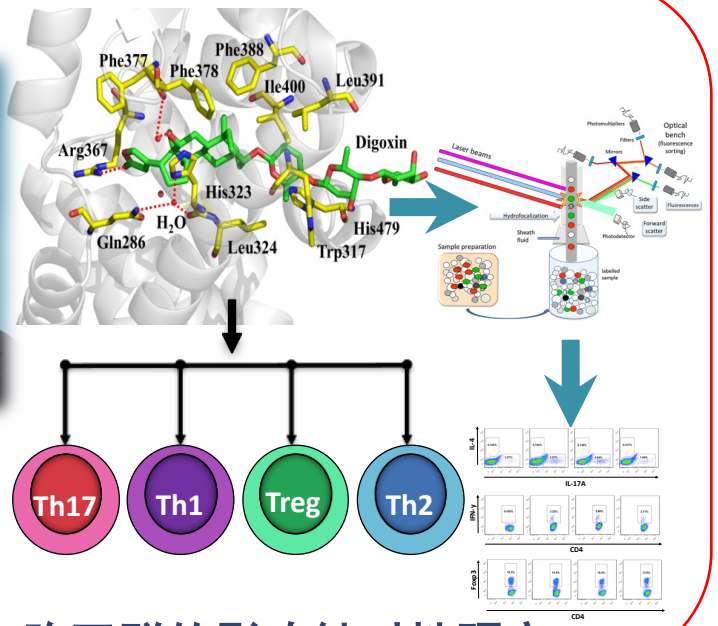


目前主要從事基於**LC、SPE、MS**和**NMR**的代謝組學、代謝流和蛋白組學整合分析方法研究神經退行性疾病、呼吸道疾病、腫瘤病理機制及藥物作用機制的分析新方法和新技術等。

研究基礎

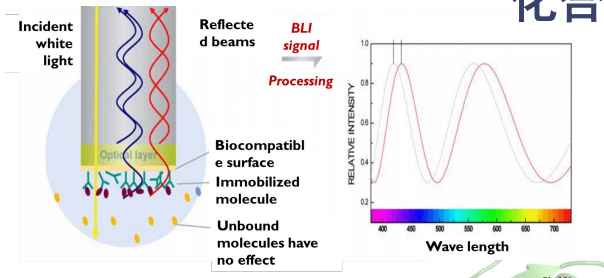
免疫炎症
药理
實驗平臺

李婷
副教授

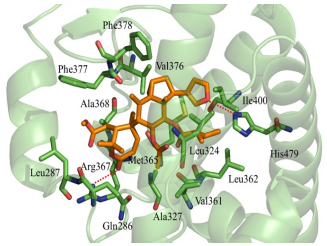


T细胞亚群的影响针对性研究

化合物與靶蛋白



霸蛋白发现

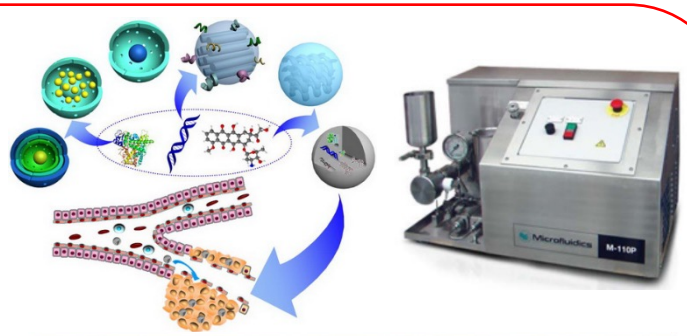


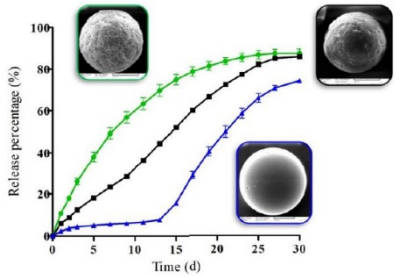
李婷副教授的團隊專注於炎症和沒有的藥理機制研究，特別是新靶點的發現研究，在免疫和炎症的新藥研究做出了卓有成效的研究。

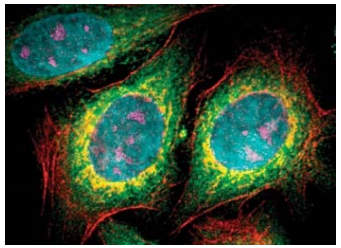
研究基礎

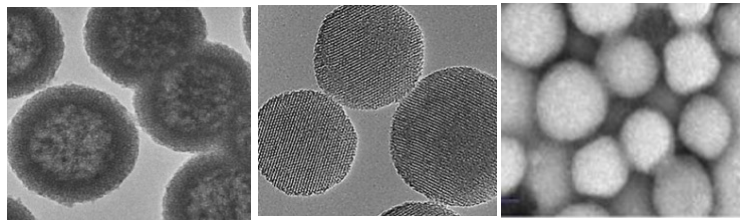
新型緩控釋製劑平臺

王晓琳
助理教授







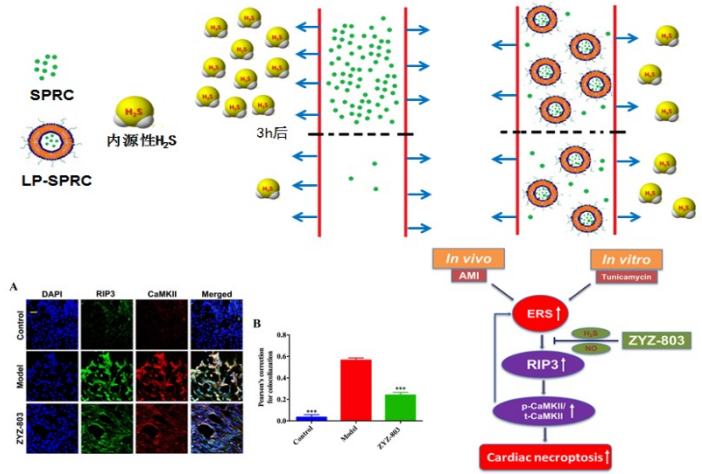


研究方向爲多功能納米藥物/基因輸送系統、長效微球製劑、多孔矽製劑、生物材料用于藥物的靶向、智能化輸送以实现心脑血管等疾病的精准治療。

研究基礎

活性小分子
重點實驗室
平臺

茅以誠
副教授



目前主要從事硫化氫氣體信號小分子藥物的作用機制研究及其新劑型設計、開發與改造。

五 预算分析

1,500万MOP

预期成果：

完成临床前申报的资料，争取进入临床研究和实现产业化

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Review

Chinese Medicine: A Hope for Neurodegenerative Diseases?

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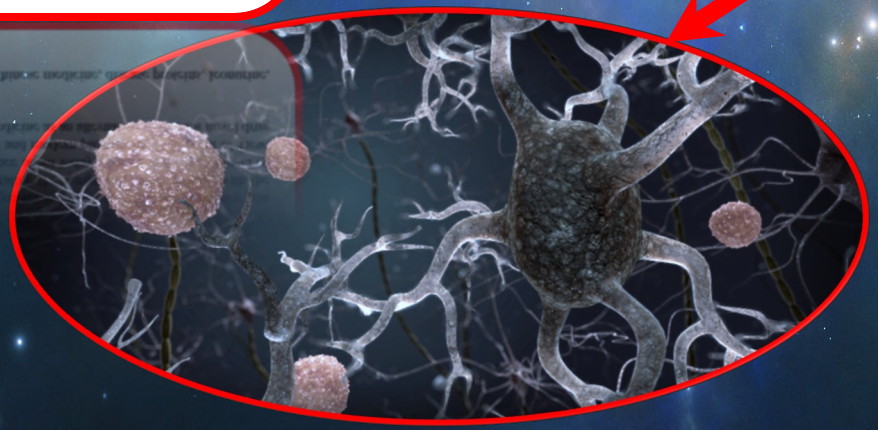
Abstract. With the increase in the proportion of aged population due to the rapid increase of life expectancy, the worldwide prevalence rate of multiple neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and Huntington's disease has been increased dramatically. The demographic trend toward an older population has drawn the attention to new drug discovery and treatment on age-related diseases. Although a panel of drugs and/or therapies are currently available for treating the neurodegenerative diseases, side effects or insufficient drug efficacy have been reported. With the long history in prescription of Chinese medicine or natural compounds for modulating aged-related diseases, emerging evidence was reported to support the pharmacological role of Chinese medicine in ameliorating the symptoms, or interfering with the pathogenesis of several neurodegenerative diseases. This review brings evidence about today's trends and development of a list of potential neuroprotective herbal compounds from both the traditional and modern pharmacological point of view. With future projections, the potential hope and implication of using Chinese medicine as an alternative source for novel drug discovery for neurodegenerative diseases is proposed.

Keywords: Aging, α-synuclein, Alzheimer's disease, amyloid-β, autophagy, Chinese medicine, disease proteins, leonurine, neurodegenerative diseases, Parkinson's disease

Chinese Medicine : A hope for Neurodegenerative Disease?

Yes!!!



THANKS