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學 歷

- 國立成功大學基礎醫學研究所 博士 (2010/07)
- 高雄醫學大學藥學系 學士 (2003/06)

學術經歷

- 高雄醫學大學天然藥物研究所助理教授 (2015/02-)
- 國立成功大學基礎醫學研究所 專案助理教授 (2013/08-2015/01)
- 國立成功大學藥理學研究所 博士後研究 (2010/09-2013/07)
- 英國牛津大學 訪問研究學者 (2008/11-2009/10)

研究興趣

- 細胞的鈣離子相關訊息是調節許多基本生命功能的重要機制，包括基因表現、細胞生長分化及肌肉收縮。許多研究顯示鈣離子訊息失調會導致許多人類疾病，包括引起癌細胞的移動及擴散轉移現象過度活躍。癌細胞的移動及擴散轉移是影響癌症病患存活的最重要因素，而在細胞的移動及轉移能力的背後，細胞骨架(cytoskeleton)的動態重組是一重要關鍵。本研究室針對細胞鈣離子訊息及細胞骨架調控為研究標的，以研發具有抑制癌細胞轉移能力的活性天然物。
- 近年開始關注化學治療引發神經病變的緩解天然藥物開發。藉由研究團隊合作建構的成熟影像基礎之高通量細胞影像藥物篩選平台，並結合動物模式及細胞模式，開發高潛力新穎神經保護天然物，以應用於神經保護活性的植物新藥開發，用於避免或改善癌症病患接受化學治療時所引起的神經毒性症狀，改善病患生活品質。
- 藉由與其他天然物化學及藥物化學研究團隊的合作，結合本實驗室建立之活細胞鈣離子影像觀測平台、高解析度細胞影像分析及高通量細胞影像藥物篩選平台，可針對活性天然物及小分子藥物庫進行篩選；搭配細胞研究模式及動物試驗研究以驗證藥理機轉及療效，以發展有治療潛力之活性天然物。

研究專長

- 天然藥物之治療活性研究
- 細胞骨架調控相關訊息傳遞研究
- 細胞離子平衡調節和人類疾病機轉及治療探討
- 化學治療引發周邊神經病變的緩解藥物開發
- 生醫影像技術、細胞生物學、分子生物學

論文著作

1. **Chen YF**, Chen LH, Shen MR*. (2018) The distinct role of STIM1 and STIM2 in the regulation of store-operated Ca^{2+} entry and cellular function. *Journal of Cellular Physiology*. 2018 Oct 14. doi: 10.1002/jcp.27532. (SCI)

利用具有不同第一型及第二型鈣離子感應蛋白 (STIM1 & STIM2) 表現量的子宮頸癌細胞株及人類子宮頸癌檢體為研究模式，搭配先進活體細胞光學影像實驗，例如：高感度胞內鈣離子流動觀測、高解析度全內反射顯微影像實驗及獨特影像重組及分析技術等，發現STIM1及STIM2分別調控子宮頸癌細胞的不同功能，並證明STIM1 所調控鈣離子流入對於影響癌細胞移動及侵犯的過程的重要性。

2. Chen YW, **Chen YF**, Chiu WT, Chen HC, Shen MR*. (2017) STIM1-dependent Ca^{2+} signaling regulates podosome formation to facilitate cancer cell invasion. *Scientific Reports*. 7(1):11523. (SCI)

探討內質網鈣離子感應蛋白STIM1對癌細胞移動及侵犯作用的影響，發現STIM1可藉由調控actomyosin細胞骨架系統，加強細胞侵犯性結構-足體環的穩定性及完整性，進而促進細胞外基質降解及癌細胞的侵犯活性。此機制可應用於研發治療藥物以抑制癌細胞轉移。

3. Chiang WF, Cheng TM, Chang CC, Pan SH, Changou CA, Chang TH, Lee KH, Wu SY, **Chen YF**, Chuang KH, Shieh DB, Chen YL, Tu CC, Tsui WL, Wu MH*. (2018) Carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) promotes EGF receptor signaling of oral squamous cell carcinoma metastasis via the complex N-glycosylation. *Oncogene*. 37(1):116-127. (SCI)

探討癌胚抗原相關細胞黏附分子6 (Carcinoembryonic antigen-related cell adhesion molecule 6 ; CEACAM6)在調控表皮生長因子接受器訊息傳遞的機制及在口腔癌治療的應用。

4. Chen YF, Chen LH, Yeh YM, Wu PY, **Chen YF**, Chang LY, Chang JY, Shen MR. * (2017) Minoxidil is a potential neuroprotective drug for paclitaxel-induced peripheral neuropathy. *Scientific reports* 7:45366. (SCI)

利用研究團隊已建構成熱之影像基礎之高通量藥物篩選平台結合動物行為及細胞機制模式，發現具有生髮活性的minoxidil為一高潛力的新穎神經保護劑，除了具有緩解化學治療藥物太平洋紫杉醇引起的周邊神經病變的藥理活性，對於紫杉醇的抗癌活性也具有加成作用。

5. **Chen YF**, Hsu KF, Shen MR*. (2016) The store-operated Ca^{2+} entry-mediated signaling is important for cancer spread. *Biochimica et Biophysica Acta-Molecular Cell Research*. 1863(6 Pt B):1427-35. (SCI)

由內質網鈣離子感應蛋白STIM所啟動的”鈣池調控鈣離子流入(store-operated calcium entry; SOCE)”是調控上皮細胞內鈣離子恆定的主要機制。此論文全方位地介紹癌細胞SOCE機制如何影響癌細胞的細胞移動及癌轉移，並提出專一性抑制癌細胞中STIM1的下游鈣離子訊息的具體可能策略，整合論點以支持癌細胞SOCE機制作為癌症輔助治療標的。

6. Chen YW, **Chen YF**, Chen YT, Chiu WT, Shen MR*. (2016) The STIM1-Orai1 pathway of store-operated Ca^{2+} entry controls the checkpoint in cell cycle G1/S transition. *Scientific Reports*. 6:22142. (SCI)

研究內質網鈣離子感應蛋白STIM1對細胞生長的調控，發現STIM1下游的鈣離子訊息可影響週期素蛋白cyclin E表現量及週期素依賴激酶CDK2活性，進而調節細胞週期的G1/S期轉換而影響癌細胞增生。抑制STIM1活性及其下游的鈣離子訊息可阻止細胞週期前進，引起細胞生長休止及細胞自噬或細胞凋亡的現象。此機制可應用於研發治療藥物以抑制癌細胞生長。

7. Chen LH, Sun YT, **Chen YF**, Lee MY, Chang LY, Chang JY, Shen MR*. (2015) Integrating image-based high-content screening with mouse models identifies 5-hydroxydecanoate as a neuroprotective drug for paclitaxel-induced neuropathy. *Molecular Cancer Therapeutics*. 14:2206-14. (SCI)

化學治療引起的周邊神經病變是一項在癌症病患常見的副作用。其造成的症狀不只傷害癌症病人的生活品質，也容易使病人提早中斷癌症治療，然而目前卻無有效的臨床藥物治療方針可避免此嚴重效應。本研究成功建構以影像基礎之高通量藥物篩選平台(image-based high content drug-screening platform)並結合動物行為及細胞機制模式，並由藥物庫篩選開發一高潛力的新穎神經保護劑5-hydroxydecanoate，具有緩解化學治療藥物太平洋紫杉醇引起的周邊神經病變的藥理活性。

8. Chen YT#, **Chen YF**#, Chiu WT, Liu KY, Liu YL, Chang JY, Chang HS, Shen MR*. (2013) Microtubule-associated histone deacetylase 6 supports the calcium store sensor STIM1 in mediating malignant cell behaviors. *Cancer Research*. 73:4500-4509. (#equal contribution as the 1st author) (SCI)

深入解析內質網鈣離子感應蛋白STIM1的上游活化機制，發現微管骨架蛋白的結構及其蛋白後修飾作用對於STIM1的胞內移動與後續鈣離子相關訊息路徑活化皆扮演重要的調控角色。研究成果顯示癌細胞的鈣離子感應蛋白STIM1相關鈣離子訊息調控路徑可應用於癌症輔助治療或癌症病人的生物標誌，及作為藥物研發或篩選的標的。

9. **Chen YF**, Chen YT, Chiu WT, Shen MR*. (2013) Remodeling of calcium signaling in tumor progression. *Journal of Biomedical Science*. 17;20:23. (invited review article) (SCI)

全方位地介紹癌細胞內鈣離子失衡現象如何影響細胞癌化過程及各種指標性癌細胞惡性功能(如：細胞移動及癌轉移)，亦詳細列舉可能參與其中的鈣離子調控分子，並整合論點以支持癌細胞的鈣離子訊息調控路徑作為癌症輔助治療或癌症病人的生物標誌的應用潛力。

10. Chen YT, **Chen YF**, Chiu WT, Wang YK, Chang HC, Shen MR*. (2013) The ER Ca²⁺ sensor STIM1 regulates actomyosin contractility of migratory cells. *Journal of Cell Science*. 126:1260-1267. (SCI)

探討內質網鈣離子感應蛋白STIM1對癌細胞移動的影響，發現STIM1可藉由調控actomyosin細胞骨架系統，影響細胞的生物力學現象，進而促進癌細胞的移轉活性。此機制可應用於研發治療藥物以抑制癌細胞轉移。

11. **Chen YF**[#], Chiu WT[#], Chen YT, Lin PY, Huang HJ, Chou CY, Chang HS, Tang MJ, Shen MR*. (2011) Calcium store sensor STIM1-dependent signaling plays an important role in cervical cancer growth, migration and angiogenesis. *Proceedings of the National Academy of Sciences USA*. 108:15225-15230. ([#]equal contribution as the 1st author) (SCI)

探討內質網鈣離子感應蛋白STIM1對癌細胞增生、移動及腫瘤血管新生的影響。利用具有不同內質網鈣離子感應蛋白STIM1表現量或功能性的癌細胞株，搭配先進活體細胞光學影像實驗，解析胞內鈣離子恆定失調為細胞癌化過程的重要指標現象。以免疫螢光染色技術分析子宮頸癌病患的癌組織，發現子宮頸癌臨床檢體之鈣離子感應蛋白STIM1表現量和病人預後程度有關；在細胞株實驗發現上皮細胞生長因子 (EGF) 可誘發內質網鈣離子感應蛋白STIM1對細胞膜鈣離子通道的活化作用，繼而引發細胞外鈣離子大量流入細胞；而此胞外鈣離子流入對於子宮頸癌細胞之生長及移行扮演相當重要的調控角色；且在活體動物研究中發現阻斷STIM1下游鈣離子訊息傳遞可抑制腫瘤生長及血管新生。

12. **Chen YF**, Chou CY, Ellory JC, Shen MR*. (2010) The emerging role of KCl cotransport in tumor biology. *American Journal of Translational Research*. 2:345-355. (invited review article) (SCI)

針對鉀氯離子共同運輸蛋白(KCl cotransporters)對癌症侵犯及轉移的重要性及獨特調控機制進行全方位的介紹與分析。

13. **Chen YF**, Chou CY, Wilkins RJ, Ellory JC, Mount DB, Shen MR*. (2009) Motor protein-dependent membrane trafficking of KCl cotransporter-4 is important for cancer cell invasion. *Cancer Research*. 69:8585-8593. (SCI)

探討第四型鉀氯離子共同運輸蛋白(KCl cotransporter-4)對癌症侵犯及轉移的重要性及獨特調控機制。從人類子宮頸癌及卵巢癌的臨床檢體，發現癌細胞中的第四型鉀氯離子共同運輸蛋白(KCC4)表現量和癌細胞侵犯、轉移及癌症病人的預後表現有一致的趨勢。在癌細胞株實驗配合先進光學影像技術發現，第一型類胰島素生長因子 (IGF-1) 及上皮生長因子 (EGF) 會促進侵犯性癌細胞中的KCC4從胞器 (如:內質網及高爾基氏體) 運送到前端 (leading edge) 的細胞膜上；KCC4於此處和細胞骨架結合蛋白ezrin相互作用以調控細胞骨架結構，而促進癌細胞的侵犯及轉移能力。此研究成果可應用為癌症病人的預後生物標誌，也可作為預防癌細胞轉移的治療標的。

14. Hsu YM, **Chen YF**, Chou CY, Tang MJ, Chen JH, Wilkins RJ, Ellory JC, Shen MR*. (2007) KCl cotransporter-3 down-regulates E-cadherin/beta-catenin complex to promote epithelial-mesenchymal transition. *Cancer Research*. 67:11064-11073. (SCI)

探討第三型鉀氯離子共同運輸蛋白(KCl cotransporter-3)藉由調控上細皮胞-間質細胞形態轉

換特性(epithelial-mesenchymal transition)之獨特調控機制而促進癌症侵犯及轉移，並可應用於預防癌細胞轉移的治療標的。

15. Hsu KF, Huang SC, Shiau AL, Cheng YM, Shen MR, **Chen YF**, Lin CY, Lee BH, Chou CY*. (2007) Increased expression level of squamous cell carcinoma antigen 2 and 1 ratio is associated with poor prognosis in early-stage uterine cervical cancer. *International Journal of Gynecological Cancer*. 17:174-181. (SCI)

探討不同亞型的鱗狀上皮細胞癌抗原 (squamous cell carcinoma antigen)表現量可影響子宮頸癌病患的預後情形。此研究成果可應用為癌症病人的預後生物標誌。

16. Hsu YM, Chou CY, Chen HH, Lee WY, **Chen YF**, Lin PW, Alper SL, Ellory JC, Shen MR*. (2007) IGF-1 upregulates electroneutral K-Cl cotransporter KCC3 and KCC4 which are differentially required for breast cancer cell proliferation and invasiveness. *Journal of Cellular Physiology*. 210:626-636. (SCI)

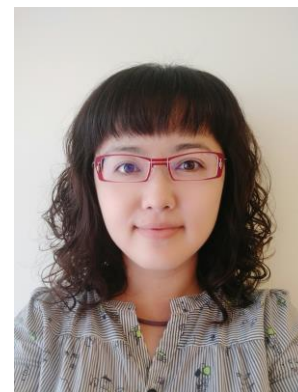
研究第三型及第四型鉀氯離子共同運輸蛋白(KCl cotransporter-3 & KCl cotransporter -4)對於乳癌細胞增生及侵犯作用的各別重要角色。

17. Shen MR, Hsu YM, Hsu KF, **Chen YF**, Tang MJ, Chou CY*. (2006) Insulin-like growth factor 1 is a potent stimulator of cervical cancer cell invasiveness and proliferation that is modulated by alphavbeta3 integrin signaling. *Carcinogenesis*. 27:962-971. (SCI)

探討第一型類胰島素生長因子(insulin-like growth factor 1; IGF-1)藉由調控細胞黏附蛋白活性而影響子宮頸癌細胞的增生及侵犯性。

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RESEARCH INTERESTS

My research interest is to uncover the remodeling of ion homeostasis during cancer progression and to explore the novel functions of ion transport systems in the regulation of tumor malignancy. With this research interest, my research work also focuses on the development of the novel pharmacological approaches targeting ion transport in human cancer.

EDUCATION

- 2004/09-2010/07 **Ph.D. in Basic Medical Sciences**
National Cheng Kung University, Tainan, Taiwan
- 1999/09-2003/06 **B.S. in Pharmacy**
Kaohsiung Medical University, Kaohsiung, Taiwan

RESEARCH EXPERIENCE

- 2015/02~ **Assistant Professor**
Graduate Institute of Natural Products, College of Pharmacy,
Kaohsiung Medical University, Kaohsiung, Taiwan
- 2013/08-2015/01 **Project Assistant Professor**
Institute of Basic Medical Sciences, College of Medicine,
National Cheng Kung University, Tainan, Taiwan
- 2010/09-2013/07 **Postdoctoral Research Fellow**
Department of Pharmacology, College of Medicine,
National Cheng Kung University, Tainan, Taiwan
- 2008/11-2009/10 **Visiting Researcher**
Department of Physiology, Anatomy, and Genetics,
University of Oxford, Oxford, UK

HONORS & AWARDS

- 2018 Outstanding Teaching Award, Kaohsiung Medical University, Kaohsiung, Taiwan
(106 學年度教學優良教師)
- 2017 Outstanding Student Mentoring Award, Kaohsiung Medical University, Kaohsiung, Taiwan
(105 學年度績優導師)
- 2015 Outstanding Research Award, Kaohsiung Medical University, Kaohsiung, Taiwan
(2015 年研究績優教師 優秀論文獎)
- 2013 Invited talk, 37th World Congress of the International Union of Physiological Sciences
(2013 IUPS meeting), Birmingham, UK, July 2013.
- 2013 Outstanding Research Paper Award, Laser Medicine Education, and Research Foundation,
Taiwan (2013 年雷射醫學文教基金會優秀論文獎)
- 2010 Award of Outstanding Thesis by Tien-Te Lee Biomedical Foundation, Taiwan
(第 6 屆永信李天德醫藥科技獎—傑出論文獎)
- 2010 Awarded member of Bio-Inspired Sensing & Bio-Inspired Actuation Summer Institute at
the University of Illinois at Urbana-Champaign, Champaign, IL, U.S.A., by Taiwan
National Science Council and U.S. National Science Foundation Joint Program
- 2007 Graduate students study abroad scholarship by National Science Council, Taiwan
(國科會千里馬計畫補助博士生赴國外研究)

BOARD CERTIFICATION

- 2003 Professional Pharmacist License (Taiwan Pharmacist Board Licensure Exam)
- 2003 Certificate of Chinese Herbal Medicine
Kaohsiung Medical University, Kaohsiung, Taiwan

PUBLICATION

1. **Chen YF**, Chen LH, Shen MR*. (2018) The distinct role of STIM1 and STIM2 in the regulation of store-operated Ca²⁺ entry and cellular function. *Journal of Cellular Physiology*. 2018 Oct 14. doi: 10.1002/jcp.27532. [Epub ahead of print] (SCI)
2. Chen YW, **Chen YF**, Chiu WT, Chen HC, Shen MR*. (2017) STIM1-dependent Ca²⁺ signaling regulates podosome formation to facilitate cancer cell invasion. *Scientific Reports*. 7(1):11523. (SCI)
3. Chiang WF, Cheng TM, Chang CC, Pan SH, Changou CA, Chang TH, Lee KH, Wu SY, **Chen YF**, Chuang KH, Shieh DB, Chen YL, Tu CC, Tsui WL, Wu MH*. (2018) Carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) promotes EGF receptor signaling of oral squamous cell carcinoma metastasis via the complex N-glycosylation. *Oncogene*. 37(1):116-127. (SCI)
4. Chen YF, Chen LH, Yeh YM, Wu PY, **Chen YF**, Chang LY, Chang JY, Shen MR*. (2017) Minoxidil is a potential neuroprotective drug for paclitaxel-induced peripheral neuropathy. *Scientific reports* 7:45366. (SCI)

5. **Chen YF**, Hsu KF, Shen MR*. (2016) The store-operated Ca²⁺ entry-mediated signaling is important for cancer spread. *Biochimica et Biophysica Acta-Molecular Cell Research*. 1863(6 Pt B):1427-35. (SCI)
6. Chen YW, **Chen YF**, Chen YT, Chiu WT, Shen MR*. (2016) The STIM1-Orai1 pathway of store-operated Ca²⁺ entry controls the checkpoint in cell cycle G1/S transition. *Scientific Reports*. 6:22142. (SCI)
7. Chen LH, Sun YT, **Chen YF**, Lee MY, Chang LY, Chang JY, Shen MR*. (2015) Integrating image-based high-content screening with mouse models identifies 5-hydroxydecanoate as a neuroprotective drug for paclitaxel-induced neuropathy. *Molecular Cancer Therapeutics*. 14:2206-14. (SCI)
8. Chen YT[#], **Chen YF**[#], Chiu WT, Liu KY, Liu YL, Chang JY, Chang HS, Shen MR*. (2013) Microtubule-associated histone deacetylase 6 supports the calcium store sensor STIM1 in mediating malignant cell behaviors. *Cancer Research*. 73:4500-4509. (**#equal contribution as the 1st author**) (SCI)
9. **Chen YF**, Chen YT, Chiu WT, Shen MR*. (2013) Remodeling of calcium signaling in tumor progression. *Journal of Biomedical Science*. 17;20:23. (**invited review article**) (SCI)
10. Chen YT, **Chen YF**, Chiu WT, Wang YK, Chang HC, Shen MR*. (2013) The ER Ca²⁺ sensor STIM1 regulates actomyosin contractility of migratory cells. *Journal of Cell Science*. 126:1260-1267. (SCI)
11. **Chen YF**[#], Chiu WT[#], Chen YT, Lin PY, Huang HJ, Chou CY, Chang HS, Tang MJ, Shen MR*. (2011) Calcium store sensor STIM1-dependent signaling plays an important role in cervical cancer growth, migration and angiogenesis. *Proceedings of the National Academy of Sciences USA*. 108:15225-15230. (**#equal contribution as the 1st author**) (SCI)
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