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基本資料

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學經歷

國立中興大學/植物病理系/學士 (1973~1977)

國立中興大學/植病研究所/碩士 (1977~1979)

新竹工研院/化工所生物技術組/副研究員(1981~1987)

University of Maryland at Baltimore(美國)/醫學院生化系(Molecular Biology)/博士(1987~1993)

美國馬利蘭大學醫學院/醫學系暨榮民醫學中心/博士後研究員(1993~1994)

高雄醫學大學/生物化學研究所/副教授(1994~2001)

高雄醫學大學附設醫院/醫研部分生室/主任(2001~2006)

高雄醫學大學/生物化學研究所/代理所長(2003/08~2004/01; 2004/08~2005/01)

高雄醫學大學研究發展處學術研究組長/主任(2008~2009)

現職

高雄醫學大學/醫學研究所/教授 (2016~迄今)

高雄醫學大學/生物化學科/所/教授 (2001~迄今)

國立中山大學生物科學系合聘教授 (2009~迄今)

國立屏東科技大學達人學院合聘教授 (2021~迄今)

專長

分子生物、細胞生物、微生物遺傳

Centrosome biology, Cell cycle spindle checkpoints, Genome-Wide 新基因搜尋

蛋白-蛋白交互作用及訊息傳遞:特別注重腦癌和大腸直腸癌症相關基因暨疾病之探討 研究方向

- 1. 應用酵母菌雙混交系統(yeast two-hybrid)、搜尋 Genome-wide 之 novel genes
- 2. 細胞中心體(centrosome)、著絲點(kinetochores)、中節(centromere)的結構蛋白 in mitosis and meiosis 及其調控機制
- 3. 嵌連中心體蛋白和線粒體電子傳遞鏈蛋白在中心體成熟和雙極紡錘體形成的作用機制



- 4. 人類腦腫瘤(brain tumor), 先天小腦症(microcephaly), 神經發育, 神經退化相關基因暨癌基因之 signaling pathways (Wnt; Hh pathways) 研究
- 5. 功能性分析 GSKIP 及其他 GKS3 結合蛋白在 GSK3 參與 Alzheimer's disease 之研究
- 6. 熱帶醫學整合型研究計畫--恙蟲病原立克次體(Orientia tsutsugamushi)進入哺乳類細胞的早期訊息機轉
- 7. To identify novel targets involved in centrosome regulation and mitotic check point control by validated human kinases (e.g. GSK3, Aurora family) and phosphatases with shRNAs
- 8. Functional analysis of GSKIP and other GSK3 binding proteins involve in regulation of Alzheimer's disease
- 9. 開發蜘蛛膜下出血 (subarachnoid hemorrhage)之動物模式與信訊傳遞之路徑及其藥物治療 開發的可能性
- 10. 使用集成大數據分析策略開發以生物標記物指引之抗癌藥物--研發以β-catenin 不同磷酸化 位點作為關鍵合成致死標的物之 APC 缺失型大腸直腸癌的新型藥物(1/3; 2/3;3/3)
- 11. 探索自噬和上皮-間質可塑性 (epithelial to mesenchymal plasticity): 一種新型 BMX 化合物 作為膠質母細胞瘤治療靶點之機制

Ongoing projects (近期計畫):

- 1. Investigation of novel agents for targeting different phosphorylation sites of β -catenin as a critical synthetic lethal target in APC-deficient colorectal cancer 109-111-2320-B-037 -012 -) 1/3; 2/3; 3/3 MOST,整合型計畫
- 2. 功能性分析細胞週期在有絲分裂進行中,中心體調控蛋白和粒線體分裂蛋白 Drp1 的對話 趨動粒線體自噬參與中心體功能和雙極紡錘體形成的作用機制 110 學年度高雄醫學大學「前 瞻重點研究計畫」(KMU-DK(A)111006)
- 3. Joining centrosomal proteins and mitochondrial electron transport chain proteins play the roles for centrosome maturation and bipolar spindle assembly (107-109-2320-B-037 -027) 1/3; 2/3; 3/3
- Functional insights of interplay between human Ninein and AIBp in regulating centrosome and spindle pole organization via GSK3beta, Aurora A and Polo-like kinase 1. (104-2320-B-037-030-MY3) 1/3; 2/3; 3/3
- 5. Functional study on the roles of GSKIP-inactivated GSK3 β to regulating β -catenin, cyclin D1 and Drp1 functions in CCI/chemotherapy-induced neuropathic pain. (104-2314-B-039-054-MY2)
- 6. Functional characterization of GSKIP in embryonic and neurodevelopment via cell based assay and gene knock-out animal model (approved three years by KMU key project, 2018-2019)
- Functional insights of crosstalk between centrosome regulatory proteins and Drp1
 phosphorylation-mediated mitochondrial fission drives mitophagy involved in the bipolar spindle
 assembly during mitosis. Pending for MOST 2022-2024

Brief summary of lab results:

Prof. Yi-Ren Hong received his Ph. D degree in Biochemistry and Molecular Biology from University of Maryland at Baltimore (UMAB, USA). After a successful completion of one year post-doctor at Veteran Hospital & UMAB (USA), he joined the Kaohsiung Medical University and is a professor of Biochemistry since 2001 and then became Joint professor, Dept. of Biological Science, Sun Yat-Sen University (Kaohsiung, Taiwan) since 2009. His Specialties include molecular biology, cell biology, microbial genetics and research focus on cell cycle spindle checkpoints, genome-wide new gene search, protein-protein interaction, brain tumors, neuron degenerative diseases. Ongoing projects include: 1. Characterization and functional analysis of AIBp mediates both Aurora kinase A and Polo-like kinase in cell cycle progressing. 2. Functional analysis of GSKIP and other GSK3 binding proteins involved in regulation of Alzheimer's disease. 3. GSK3 regulates Bcl2L12 and Bcl2L12A anti-apoptosis signaling in glioma and is inhibited by LiCl. He has been accredited with many high impact research publications and has been honored an outstanding scientist and a proud teacher for past two decades. He is a member of ASMBM (USA), ASCB (USA) and CSCMB (Taiwan) and is the recipient of many awards in research domain from CSCMB (Taiwan). In the past several years, Dr. Hong's lab uses human glycogen synthesis kinase 3b as a bait in the yeast two-hybrid system, and we have explored many GSK3b interaction proteins, such as dynamin-like protein, human ninein(hNinein), CGI-99, CABYR variants and one novel protein, GSK3b interaction protein (GSKIP), Astrin, AIBP (Chen, Hwang, et al., 2000; Chen, Howng, et al., 2000; Hong, et al., 2000; Chen, et al., 2003; Howng, Sy, et al., 2004; Howng, Hsu, et al., 2004; Hsu, et al., 2005; Lin, et al., 2006; Chou, et al., 2006, Cheng, et al., 2007; 2008, Howng, et al., 2010; Lieu, et al., 2010, Tang, et al., 2011). Particularly, his lab had cloned and demonstrates the function of GSKIP. The function of GSKIP is similar to that of FRAT/GBP, and our results indicate that GSKIP and GSKIPtide may act as an inhibitor of GSK3b (Biochemistry, 2006). In fact, dysregulation of GSK3 is linking to several prevalent pathological conditions, such as diabetes and/or insulin resistance, and Alzheimer's disease. Therefore, much effort is currently directed to understand the function and control of GSK3 and to diminish the deleterious impact of GSK3 under abnormal conditions. Actually, GSKIP shares a homology with the GID and also acts as a negative regulator of GSK3b, like GID and FRAT/GBP. Hence, his lab has recently proposed to focus on GSKIP in Wnt signaling pathway. Wnt signaling is involved in virtually every aspect of embryonic development and also controls homeostatic self-renewal in a number of adult tissues. Germline mutations in the Wnt pathway cause several hereditary diseases, and perturbations in Wnt signaling promote both human degenerative diseases and cancer. Recently, his lab also extends their researching aims about physiological definition of GSKIP, not only in Wnt pathway, but Hedgehog (Hh) pathway and GSK3b-mediated tau (microtubule-associated protein) dynamics as well. Altogether, the identification of the GSKIP and GSKIPtide as GSK3b inhibitors for drug discovery in Wnt/non-Wnt signaling pathway is important for understanding the molecular basis of these neurological cancers and advanced progression. One is three-year grant from NHRI (The interactions with phosphorylation of hNinein, Astrin and CENP-E in centrosome/spindle function); the other one is three-year grant from

NSC (Early signaling events involved in the entry of scrub typhus-Orientiatsutsugamushi rickettsia into mammalian cells). Therefore, in the next three year (2009-2012) the elucidation of hNinein, Astrin, CENP-E and its associated proteins in centrosomes, kinetochores and spindle checkpoint will help us to understand the molecular events of the centrosome and the regulation of shape, cell locomotion, cell division and disease, with a particular focus on the origin of cancer. In addition, his lab also foresee to achieve the identification of early signaling events involved in the entry of O. tsutsugamushi into mammalian cells is crucial to the understanding of the pathogenic properties of the scrub typhus agents as well as to the therapeutically drug discovery against O. tsutsugamushi infection. His lab hopes to exterminate the scrub typhusinfected by O. tsutsugamushi in Taiwan. Finally, another NSC grant entitled: Functional analysis of GSKIP and other GSK3 binding proteins involve in regulation of Alzheimer's disease also to be approved (Oct. 2009-Sept. 2012). His lab also extends the researching aims about physiological definition of GSKIP, not only in Wnt pathway, but insulin pathway and GSK3β-mediated microtubule dynamics as well. Overall, Dr. Hong's lab is productive and is able to carry out multifaceted research tasks. Almost every approved research grant in his lab, bring up solid results and contributes good publications, especially in the centrosome biology filed. Two centrosome proteins, Ninein and AIBp serve as major contributions from this lab. Therefore, in this proposal, his aimed atcontinuously investigating how AIBp interacts with Aurora A and Plk1 to regulate hNinein in centrosome maturation during G2/M transition. His lab also plain to explore whether GSK3βinteracts with and phosphorylates AIBp, hNinein and p150glued which further mediates crosstalk between Aurora A and Plk1. His lab claims to propose a model to demonstrate that functional interplay of three kinases, GSK3β, Aurora A and Plk1via AIBp, hNinein, p150glued and γ-tubulin in centrosome maturation during G2/M transition and ensuing nucleation in spindle formation. In this proposal, his lab aiming at (1) Delineating whether AIBp as second Bora intermediates crosstalk between Aurora A and Plk1 signaling during G/M transition (2) Investigating whether AIBp coordinates CEP215/CEP192/Aurora A/Plk1 during centrosome maturation and further microtube nucleation. Eventually, this study may prove detail of AIBp involves in regulating centrosome and spindle functions that may be of biological importance as well as for drug discovery of cancer therapy and neuronal disease.

More recently, NSC call for the pre-proposal of NSC grant of Top 100 blazer research project

Title: Functional insights of GSKIP knockout from cell biology and animal models - implicating PKA/GSKIP/GSK3/Drp1 axis in neuronal disorders (2013 NSC pending)

GSKIP has been identified as smallest AKAP, and retains both PKA and GSK3 binding domains [1]. The GSK3β binding of GSKIP is linked to neurite outgrowth [2, 3], but no physiological significance was found for its PKA binding. In this proposal, we attempt to identify that PKA, GSKIP, GSK3 and Drp1 may form a working

complex, which provides a spatial-temporal controlling of mitochondrial dynamics against oxidative stress as shown in model. Our preliminary data had showed that by comparing overexpressed GSKIP with the two defective mutants, Drp1 Ser637 phosphorylation was enhanced 7~8-fold in the GSKIPwt group compared to both defective mutant groups. Moreover, we also reported that GSK3β-mediated phosphorylation at Ser693 of Drp1 is important in controlling mitochondrial morphology under oxidative stress [4]. Thus, we will also evaluate whether GSKIP has a possible physiological role conferring acquired resistance to H₂O₂-induced apoptosis by coordinating both the activation of PKA-mediated Drp1 phosphorylation at Ser637 and tethering GSK3β-mediated Drp1 recruitment. In fact, mitochondria are constantly fusing and dividing with each other, forming large, reticular networks. In humans, mitochondrial fission is regulated by Fis1 and Drp1. Several studies have indicated that Drp1 is essential for proper embryonic development. Drp1 knockout (KO) mice exhibit abnormal brain development and die around embryonic day 12.5. In neural specific Drp1 knockout mice, brain size is reduced and apoptosis is increased. Synapse formation and neurite growth are also impaired [5]. Wakabayashi et al demonstrated that neural specific knockout Drp1 resulted in the appearance of large mitochondria in Purkinje cells and prevented neural tube formation [6]. Drp1 KO leads to early embryonic death and defective neurodevelopment [5, 6]; in addition, GSK3ß KO resulted in developmental defeats due to hepatic apoptosis or cardiac patterning [7] and PKA KO caused embryonic lethal, spinal neural tube and long-term memory defects [8]. Therefore, we assumed GSKIP KO may have a role in affecting normal brain function and may confer vulnerability to neuronal disorders. In our hypothesized model, we suspected on that GSKIP is one of the major regulators of Drp1 Ser637 phosphorylation. Also, GSKIP is pre-required for Drp1 phosphorylation via distinct GSK3ß and PKA binding domains, conferring neuroprotection under H₂O₂ induced-oxidative stress. GSKIP KO is expected to also be important in neurodevelopment though its role requires further elucidation and currently was carried out in our laboratory. A better understanding of the molecular basis of the PKA/GSK3/GSKIP/Drp1 axis in the both PKA and GSK3 signaling pathways will be helpful for drug discovery in neuronal diseases such as Alzheimer's disease (AD) and schizophrenia. To address these scientific interests, in this pre-proposal, four specific aims were setup as follow:

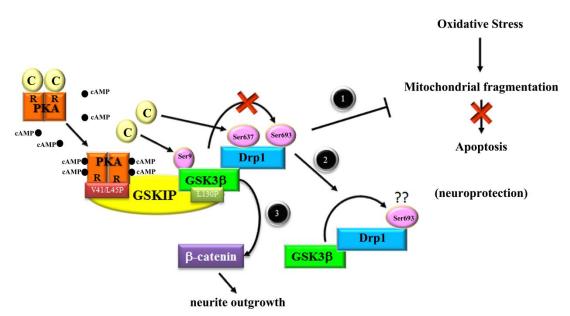
Specific Aims

1. To explore whether PKA/GSKIP/GSK3/Drp1 may form a local complex in spatial-temporal controlling of mitochondrial functions.

- 2. To determine whether GSKIP tethering GSK3 can be used as platform for quick screening the GSK3 interacting proteins in addition to Drp1, such as tau and p53.
- 3. To examine the functional consequences posterior to GSKIP knockout in neuronal disorders.
- 4. To delineate molecular basis of the PKA/GSK3/GSKIP/Drp1 axis in the PKA and GSK3 signaling pathways for drug discovery of neuronal diseases, such as AD and schizophrenia.

Significance

Based on our three previous publications [2-4] and a recent paper published in Nature Cell Biology [9], we propose that it is more likely GSKIP plays vital role in unopposed fusion triggers mitochondrial elongation, enabling mitochondria to resistant autophagic degradation, apoptosis and prevent cell death. A better understanding of the molecular basis of the PKA/GSK3/GSKIP/Drp1 axis in the PKA and GSK3 signaling will provide a footstool for drug discovery to combat neuronal disorders.



Model. A model illustrating the physical interaction of GSKIP, GSK3, PKA RII, and Drp1; status 1, While activating c-AMP signaling, GSKIP wt contributes neuroprotection from hydrogen peroxide-induced apoptosis, which includes three major events: a. PKA binds GSKIP wt and facilitates GSK3 Ser9 phosphorylation, b. GSKIP negatively regulates GSK3 activity (by protein-protein interaction), c. GSKIP –mediates Drp1 phosphorylation at Ser637 by PKA (note: a novel pathway for GSK3 anchoring was identified in this study); status 2. When both GSKIP and PKA signaling are unable to inhibit GSK3 activity, GSK3 may act as an anchoring protein

kinase to phosphorylate Drp1 at Ser693, Alternatively, GSKIP, as an inhibitor of GSK3β through L130, mediates β-Catenin during differentiation.

References

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- [5] Ishihara, N.; Nomura, M.; Jofuku, A.; Kato, H.; Suzuki, S. O.; Masuda, K.; Otera, H.; Nakanishi, Y.; Nonaka, I.; Goto, Y.; Taguchi, N.; Morinaga, H.; Maeda, M.; Takayanagi, R.; Yokota, S.; Mihara, K. Mitochondrial fission factor Drp1 is essential for embryonic development and synapse formation in mice. *Nature cell biology* **11:**958-966; 2009.
- [6] Wakabayashi, J.; Zhang, Z.; Wakabayashi, N.; Tamura, Y.; Fukaya, M.; Kensler, T. W.; Iijima, M.; Sesaki, H. The dynamin-related GTPase Drp1 is required for embryonic and brain development in mice. *The Journal of cell biology* **186**:805-816; 2009.
- [7] Kaidanovich-Beilin, O.; Woodgett, J. R. GSK-3: Functional Insights from Cell Biology and Animal Models. *Frontiers in molecular neuroscience* **4:**40; 2011.
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- [9] Gomes, L. C.; Di Benedetto, G.; Scorrano, L. During autophagy mitochondria elongate, are spared from degradation and sustain cell viability. *Nature cell biology* **13:**589-598; 2011.

執行之專題研究計畫(2006~迄今,包含9個三年期 MOST 多年型計畫)

- 1. PI3K 與 Rho family 訊號傳遞路徑在腦血管收縮之對話(1/3; 2/3; 3/3) (NSC93-95) (主持人,多年型)
- 2. 人類 ninein 及其相關基因蛋白質在細胞中心體功能之研究(1/3; 2/3; 3/3) (NSC94-96) (主持人, 多年型).
- 3. Wnt、Hedgehog 及 Snail-E-cadherin 訊息傳遞路徑受 GSK3/GSKIP 及其相關聯蛋白調控在腦瘤中的對話 (1/3; 2/3; 3/3) (NSC97-99, 2008-2011) (共同主持人,多年型).
- 4. 人類 Ninein, Astrin 及 CENP-E 三者間之相互作用,在中心體、著絲點及紡錘絲功能性及磷酸 化調控之探討 (1/3 -3/3) (NHRI, IRG, 3 年計畫, from 2009-1-1 to 2011-12-31) (主持人,多年型).
- 5. 熱帶醫學整合型研究計畫--恙蟲病原立克次體(Orientia tsutsugamushi)進入哺乳類細胞的早期 訊息機轉(1/3; 2/3; 3/3) (NSC97-99, 2008-2011) (主持人,多年型).
- 6. 高雄醫學大學環境醫學頂尖研究中心計劃--中心體蛋白缺失、染色體不穩定和異倍體形成在口腔癌的研究(1.1ab-14; 6-3 教育部).
- 7. 98-100 探討一個天然存在的 GSK3beta 結合蛋白, GSKIP, 其參與負調控 GSK3beta 之訊息 傳遞---揭開其內生性抑制 GSK3beta 之生理功能 (1/3; 2/3; 3/3) (NSC98-100, 2009-2012) (主持人,多年型).
- 8. 98-100 功能性分析 GSKIP 及其他 GKS3 結合蛋白在 GSK3 參與 Alzheimer's disease 之研究 (1/3; 2/3; 3/3) (NHRI 98-100, 2009-2012) (主持人,多年型).
- 9. 101-103 在細胞週期中 AIBp 調控 Aurora A and Plk1 的特性化及功能性探討 101-2320-B-037 -036 -MY3
- 10. 104~106 功能性探討人類 Ninein 與 AIBp 之相互作用,經由 GSK3beta、Aurora A 及 Polo-like kinase 1 之對話,參與調控中心體及紡錘點組合的形成 (MOST-MY3).
- 11. 107-109 嵌連中心體蛋白和線粒體電子傳遞鏈蛋白在中心體成熟和雙極紡錘體形成的作用機制 (MOST 1/3; 2/3;3/3).
- 12. 109-111 使用集成大數據分析策略開發以生物標記物指引之抗癌藥物--研發以 β -catenin 不同磷酸化位點作為關鍵合成致死標的物之 APC 缺失型大腸直腸癌的新型藥物(1/3; 2/3; 3/3 整合型計畫).
- 13. 112 探索自噬和上皮-間質可塑性:一種新型 BMX 化合物作為膠質母細胞瘤治療靶點之機制 (國科會產學合作研究計畫).
- 14. 112 探討細胞有絲分裂期中,粒線體分裂蛋白形成 Phospho-Drp1-637/Fis1/Mid49 信息傳遞 cluster 嵌合紡錘體組裝檢查點異常及多重紡錘絲的形成和凋亡 (高雄醫學大學前瞻重點研究計畫).

Honor, Awards

Jan 24-26, 2024 第 29 屆細胞及分子生物新知研討會 Ken-Ting, Taiwan.

Dec. 20, 2023 2023 mini-symposium on GBM (召集人暨座長) Kaohsiung, Taiwan.

April 14-15, 2023 第 10 屆人道及國際外科 poster award first prize (1/104) (柯慧君) Kaohsiung, Taiwan.

March 18-19, 2023 第 37 屆生物醫學聯合學術年會 Taipei.

April 20, 2022 高醫大醫學院腫瘤微環境研究新知研討會壁報論文競賽佳作(Conference on Advances in Tumor Microenvironment) Kaohsiung, Taiwan. (林昕儀)

March 25-27, 2022 第 36 屆生物醫學聯合學術年會 陽明交通大學(陽明校區) Taipei, Taiwan. I-Shou University, Kaohsiung, Taiwan. Oct 20, 2021 Virus, Cell (organelles), Life--my humble Opinion (Savage offered exposure)-病毒 細胞 (胞器) 生命:漫談生物醫學與 科技- 野人獻曝; 中正大學演講 Oct. 16, 2021 高醫大研究傑出教師獎 (研究經費獎 of 2020) May 15-16, 2021 第 35 屆生物醫學聯合學術年會. Taipei, Taiwan. Cancelled due.to pandemic Covid-19. Dec 3, 2020 2020 台灣神經外科醫學會年會-登美腦瘤文教基金會得獎-優選獎 (蔡政宇) Oct. 13-16, 2020. 109年度大學生暑期研究計畫壁報論文競賽-優等獎(蔡昀蓉) April 30, 2020 108 學年度高雄醫學大學醫學院年度學生壁報論文 (2020 Student Poster Contest, College of Medicine, KMU) poster award 第一名 (蔡政宇) Feb, 5-7, 2020 27th symposium on recent advances in cellular and molecular biology. Ken-Ting, Taiwan. 44th FEBS Congress July 6-11, 2019, Krakow, Poland. July 2019 March 2019 2019 Kaohsiung International Cancer Symposium & poster award (柯慧君) 第 34 屆生物醫學聯合學術年會 Taipei. & poster award (柯慧君) March 2019 107年鹿港帝寶秋季鄉土教育講座 - 2018/9/29 漫談生物醫學科技 Sept. 2018 July 2018 7-11 July, 11th FENS Forum of Neuroscience, Berlin, Germany. March 2018 第33屆生物醫學聯合學術年會 Taipei. Yeast meeting, 3/24-25/2018, Taipei March 2018. July 9-13, Federation of European Microbiological Societies (FEMS) Congress July 2017 Valencia, Spain 2017 June 2017 Prof. Yi-Ren Hong received The 2017 Albert Nelson Marquis Lifetime Achievement Award as a result of his hard work and dedication to his profession. May 2017 臺灣人體生物資料庫(Taiwan Biobank)科學應用審查委員 Jan. 2017 24th symposium on recent advances in cellular and molecular biology. Ken-Ting, Taiwan Oct. 2016 KMU Outstanding research award of year (paper of 2016) Oct. 2016 考選部牙醫師「生物化學」題庫建置召集人 (coordinator & convener) July 2016 10th FENS Forum in 2016, July 2-6, Copenhagen, Denmark. Jan. 2016 23th symposium on recent advances in cellular and molecular biology. Ken-Ting, Taiwan. July 2015 40th FEBS Congress July 4-9, 2015, Berlin, Germany. July 1, 2015 Invited speaker in NSYSU: Multiple-tasks of GSK3beta with a novel partner GSKIP (II) Invited speaker in Chang Gung University Hospital (Kaohsiung): Multiple-tasks June 12, 2015 of GSK3beta with a novel partner GSKIP (II) reviewer on The Wellcome Trust and Royal Society for a Sir Henry Dale Feb-March, 2015 Fellowship 15th IUBMB International Congress & 24 th FAOBMB-TSMBM.International Oct. 2014 Conference. Oct. 21-26, Taipei, Taiwan. July-2014 指導醫學系學生許晉豪 獲財團法人健康科學文教基金會暨先靈葆雅獎助 April 2014 Annual meeting of ASBMB of Biochemistry and Molecular Biology. April 26-30, San Diego, CA, USA. Poster and as a judge of 18th Annual Undergraduate Student Research Poster Competition. Jan. 2014 22th symposium on recent advances in cellular and molecular biology. Oral presentation referee. Ken-Ting, Taiwan. Dec. 2013 2013 Annual Meeting of the American Society for Cell Biology. December 14-18, New Orleans, LA, USA. July 2013 Federation of European Biochemical Societies CONGRESS 2013 "Mechanisms in Biology" July, 6th - 11th 2013, St. Petersburg, Russia. Jan. 2013 21th symposium on recent advances in cellular and molecular biology. Poster award (周佳樺/生化/生科博) Nov. 2012 中山大學演講: The Collegial Education and Research -my humble Opinion (Savage offered exposure). Nov. 1, 2012 Sept. 2012 高醫大演講: The Collegial Education and Research -my humble Opinion (Savage offered exposure). Sept. 28, 2012.

亞洲名人錄 "Who Is Who in Asia".

Sept. 2012

Sept. 2012	16 th Congress of the European Federation of Neurological Societies, EFNS				
Luna 2012	Stockholm, Sweden. Sept. 8-11, 2012				
June. 2012	輔英演講: The Collegial Education and Research -my humble Opinion. ESP with Cultural Differences: terminology vs. mother tongue. June 5, 2012.				
April 2012	ASBMB of Biochemistry and Molecular Biology. April 21-25, San Diego, CA,				
	USA. Poster and as a judge of 16 th Annual Undergraduate Student Research				
E 1 2012	Poster Competition (大會評審)				
Feb. 2012	20 th symposium on recent advances in cellular and molecular biology. Oral presentation referee, Kaohsiung.				
Dec. 2011	輔英演講: Multi-faceted of GSK3beta with a novel partner GSKIP in disease				
	signaling				
Oct. 2011	7 Th International Congress on Vascular Dementia, Riga, Latvia. Oct. 20-23, 2011.				
Oct. 2011	高醫大研究傑出教師獎(研究經費 of 2010)				
June 2011	4 Th Congress of European Microbiologist, Geneva, Switzerland. June 26-30,				
March 2011	2011. 10th International Conference on AD/PD Barcelona, on March 9 - 13, 2011				
Oct. 2010-2016	考選部牙醫師「生物化學」題庫建置審查委員				
Oct. 2010	高醫大研究傑出教師獎 (研究經費 of 2009)				
Sept. 2010	12th IUBMB Conference and 21st FAOBMB Conference: "The molecules of life:				
•	from discovery to biotechnology" September 26 – October 1, 2010 Melbourne,				
	Australia. (accompany with 周佳樺/生化生科博;林敬智/博後)				
July. 2010	7th FENS Forum in 2010, July 3-7. Amsterdam, The Netherlands.				
Mar. 2010	成大.中山應邀演講: Multiple-tasks of GSK3beta with a novel partner GSKIP.				
Dec. 2009	49 th ASCB, Dec. 5-9. San Diego, CA, USA				
Oct. 2009	高醫大研究傑出教師獎(研究論文 of 2008)				
May 2009	高醫大醫學院研究生論文生醫組競賽第二名 (2/30). Poster award, Ranking 2 nd among thirty (許珈旖 生化碩)				
March 2009	among unity (日 加河 王 [5]) 24 th joint annual conference of biomedical sciences. Poster award. (周佳樺/生化/				
Waten 2009	生科博)				
March 2009	9th International Conference on AD/PD, Prague, CZ. Mar. 11-15. 2009.				
June 2008	第五屆林榮耀教授學術基金會研究論文獎 (鄭大山/生化/醫研博)				
June 2008	高醫大醫學院研究生論文競賽佳作. Poster award (徐夢妤 生化碩)				
Feb. 2008	Keystone symposia on molecular and cellular biology (Wnt/beta-catenin				
	signaling in development and disease (B8). Feb. 17-22, Keystone, Colorado.				
Jan. 2008	16 th symposium recent advances in cellular and molecular biology. Poster award				
Jan. 2007	(周佳樺/生化碩)				
Jan. 2007	15 th symposium recent advances in cellular and molecular biology. Poster award (林敬智/生化/生科博. 鄭大山/生化/醫研博)				
Dec. 2006	46 th ASCB, Dec.9-13. San Diego, CA, USA.				
June 2006	IUBMB International Congress & 11 th FAOBMB Congress. June 18-23, Tyoko,				
	Japan. (accompany with 林敬智/生化/生科博. 鄭大山/生化/醫研博)				
Jan. 2006	14th symposium recent advances in cellular and molecular biology. Section II,				
	chairperson (大會評審)				
Jan. 2006	14 th symposium recent advances in cellular and molecular biology. Poster award				
X 1 2007	(鄭大山/生化/醫研博)				
July 2005	30 th FEBS Congress & 9 th Congress of Biochemistry and Molecular Biology. July 12-7, Budapest.				
March 2005	20 th joint annual conference of biomedical sciences. Poster award (魏碩/中山生				
Waten 2003	科).				
June 2004	ASBMB Congress & IUBMB Congress of Biochemistry and Molecular Biology.				
	June 12-16, Boston, MA, USA				
March 2003	18 th joint annual conference of biomedical sciences. Poster award. (鄭大山/生化				
	醫研博)				
Jan. 2003	11th symposium recent advances in cellular and molecular biology. Poster award.				
	(劉貴玄/生化/醫研博)				
March 2002	17 th joint annual conference of biomedical sciences. Poster award (2 poster: 鄭				
	大山/生化碩;陳昶翰/生化/醫研博).				

Jan. 2002	10 th symposium on recent advances in cellular and molecular biology. Oral presentation referee (大會評審)				
Dec. 2001	世界名人錄 Yi-Ren Hong's profile is included in the "Who Is Who" in the world directory				
Oct. 2001	年度教學優良教師 of year 2000 (醫學院); Outstanding teaching award of year 2000				
Dec. 2001	Yi-Ren Hong's profile is included in the "Who Is Who" in the world directory				
Oct. 2001	6 th World Congress on Advances in Oncology and the 4th International				
Oct. 2001	Symposium on Molecular Medicine. Crete, Greece				
Jan. 2001	9 th symposium on recent advances in cellular and molecular biology. Poster presentation referee				
July 2000	JBC (USA) travel grant: Human ninein, a centrosome associated protein interacts with Glycogen synthase kinase 3. 18 th International Congress of				
1. 1. 2000	Biochemistry and Molecular Biology. July 16-20, Birmingham, UK				
March 2000	15 th joint annual conference of biomedical sciences. Tumor Biology II, Chairman				
Jan. 2000	8 th symposium on recent advances in cellular and molecular biology. Poster presentation referee				
Jan. 1998	6 th symposium on recent advances in cellular and molecular biology. Poster presentation referee				
May 1997	Ann Meeting Formos Med Assoc, Poster award: Studies with the yeast				
Way 1997	two-hybrid system, site-directed mutagenesis and random mutagenesis for NADPH oxidase p67-phox C-terminal SH3 domain.				
May 1997	Yeast Hybrid Systems Symposiun and Workshop, NHRI. Organizer & Coordinator.				
April 1997	12 th joint annual conference of biomedical sciences Proteins and Peptides, Chairman				
1990-93	Research assistantship of University of Maryland at Baltimore (UMAB)				
1989-90	ITRI scholarship				
1987-89	Government Abroad Scholarship (25 th National Science Council) & ITRI supported				
1977-79	Scholarship sponsored by the Ministry of Education				

社會服務:

1. Reviewer of

Cells (2020-2024); Spandodis publications (2017-2024, more than 10 times); Cell cycle (2021); Cancer Lett (2021); Cancers (2021), Frontiers in oncol (2021); Cancer Management and Research (2021); Translational Psychiatry (2020); BioFactors (2020); Cancer Commun. (2020); Cytoskeleton World Journal of Biological Chemistry (2014-2022). Int. J Oncol (2017-2022). Onco Letters (2016-2022). 2. The Wellcome Trust (UK) for Sir Henry Dale Fellowship expert peer reviewer (WT107661RR) (2015). 6. Editorial Board Member of The Open Enzyme Inhibition Journal (2007~); Research and Reports in Biochemistry (2011~); Chief Editor of International Journal of Biochemistry Research & Review (2013~); Academic Editor of Journal of Biochemistry International (2013~); Editorial Board Member of the World Journal of Biological Chemistry (WJBC, 2014~2019); Oncology letters (2019~); IRB member & reviewer of KMUH (2002-2015) °

- 2. Editorial Board Member of Oncology let (2019~); International Journal of Biochemistry: Academic editor (2013~); Journal of Biochemistry International (2013~); Research and Reports in Biochemistry (2011~); The Open Enzyme Inhibition Journal. (2007~);
- 3. IRB member & reviewer of KMUH (since 2002)
- 4. 經濟部工業局自強工業科學基金會"遺傳工程班"籌備人暨講座教授 (since 2002)
- 5. 考選部牙醫學門生物化學命題 選題 委員兼召集人 (2006; 2011; 2017-)
- 6.97年度國科會大專學生參與專題研究計畫研究創作獎審查 (2008)
- 7.98年度大起學校院系所評鑑委員兼召集人(2009~)
- 8. 經濟部學研聯合研究計畫審查(2009)
- 9. 經濟部工業局"農業生技產業化技術推廣計畫-生物技術研發成果產業化創意應用競賽"審查

10. 科月四十系列講座意義務講師(2010)

研究成果:論文期刊發表

研究成果目錄:(一) publications: 論文及著述

- Yang JX, Chuang YC, Tseng JC, Liu YL, Lai CY, Lee AY, Huang CF, Hong YR, Chuang TH (2024) Tumor promoting effect of PDLIM2 downregulation involves mitochondrial ROS, oncometabolite accumulations and HIF-1α activation. J Exp Clin Cancer Res. Jun 17;43(1):169. doi: 10.1186/s13046-024-03094-9. PMID: 38880883; PMCID: PMC11181580. (IF=11.4)
- 2. Nian-Siou Wu, I-Chu Ma, Yi-Fan Lin, Huey-Jiun Ko, Joon-Khim Loh & **Yi-Ren Hong*** (2023) The mystery of phospho-Drp1 with four adaptors in cell cycle: when mitochondrial fission couples to cell fate decisions, Cell Cycle, DOI: 10.1080/15384101.2023.2289753. (IF= 4.3) 本人為通訊作者.
- 3. Thu-Ha Tran, Ming Kao, Hsiao-Sheng Liu, **Yi-Ren Hong,** Yeu Su* and Chi-Ying F. Huang*Repurposing thioridazine for inducing immunogenic cell death in colorectal cancer via eIF2α/ATF4/CHOP and secretory autophagy pathwaysTran et al. Cell Communication and Signaling (2023) 21:184 https://doi.org/10.1186/s12964-023-01190-5. (IF= 8.2)
- 4. Tseng JC, Yang JX, Lee CY, Lo CF, Liu YL, Zhang MM, Huang LR, Liu KJ, Wang CC, Huang CF, Hong YR, Tsou LK, Chuang TH*. Induction of Immune Responses and Phosphatidylserine Exposure by TLR9 Activation Results in a Cooperative Antitumor Effect with a Phosphatidylserine-targeting Prodrug. Int J Biol Sci. 2023 May 11;19(9):2648-2662. doi: 10.7150/ijbs.81683. (IF= 9.2)
- 5. Cheng CT, Lai JM, Chang PM, **Hong YR**, Huang CF, Wang FS* Identifying essential genes in genome-scale metabolic models of consensus molecular subtypes of colorectal cancer. PLoS One. 2023 May 19;18(5):e0286032. doi: 10.1371/journal.pone.0286032. (IF= 3.7)
- 6. Cheng-Yu Tsai, Huey-Jiun Ko, Shean-Jaw Chiou, Xin-Yi Lin, Tsung-Hsien Chuang, Jiin-Tsuey Cheng, Yu-Feng Su, Joon-Khim Loh* & **Yi-Ren Hong***. GSKIP modulates cell aggregation through EMT/MET signaling rather than differentiation in SH-SY5Y human neuroblastoma cells. J. Cell Commun. Signal. (2023). https://doi.org/10.1007/s12079-023-00752-z. (IF= 4.1)本人為通訊作者.
- 7. Ko HJ, Chiou SJ, Tsai CY, Loh JK, Lin XY, Tran TH, Hou CC, Cheng TS, Lai JM, Chang PM, Wang FS, Su CL, Huang CF, **Hong YR***. BMX, a specific HDAC8 inhibitor, with TMZ for advanced CRC therapy: a novel synergic effect to elicit p53-, β-catenin- and MGMT-dependent apoptotic cell death. Cell Commun Signal. 2022 Dec 27;20(1):200. (IF= 8.4)本人為通訊作者.
- 8. Ho CJ, Tsai CY, Zhu WH, Pao YH, Chen HW, Hu CJ, Lee YL, Huang TS, Chen CH, Loh JK, Hong YR*, Wang C (2022) Compound cellular stress maximizes apoptosis in glioblastoma. Cell Cycle 21(11):1153-1165. (IF= 5.173)本人為通訊作者.

- 9. Wu NS, Lin YF, Ma IC, Ko HJ, **Hong YR*** (2022) Many faces and functions of GSKIP: a temporospatial regulation view. Cell Signaling 97:11039. (IF= 4.85)本人為通訊作者..
- 10. Jen-Chih Tseng, Jing-Xing Yang, Yi-Ling Liu, Yu-Wen Su, Alan Yueh-Luen Lee, Ya-Wen Chen, Ko-Jiunn Liu, Yunping Luo, Yi-Ren Hong, Tsung-Hsien Chuang (2022), Sharpening up tumor microenvironment to enhance the efficacy of immune checkpoint blockade on head and neck cancer using a CpG-oligodeoxynucleotide. Cancer Immunol Immunother 71(5):1115-1128. (IF=6.630).
- 11. Jing-Xing Yang, Jen-Chih Tseng, Guann-Yi Yu, Yunping Luo, Chi-Ying F Huang, **Yi-Ren Hong**, Tsung-Hsien Chuang * (2022) Recent Advances in the Development of Toll-like Receptor Agonist-based Vaccine Adjuvants for Infectious Diseases. Pharmaceutics. 14(2):423. (IF=6.525).
- 12. Tsai CY, Chiou SJ, Ko HJ, Lai YL, Lin CY, Wang YH, Wang C, Cheng JT, Kwan AL, Loh JK, Hong YR* (2022) The evolution and physiological role of composite-type GSKIP in mitochondria and Wnt signaling pathways. PLoS ONE 17(1): e0262138. (IF=3.240). 本人為通訊作者.
- 13. Chihuei wang, Yen-Chun Wang, Li-Ting Wang, Ta-I Hung, **Yi-Ren Hong,** Chung-Hwan Chen, and Cheng-Jung Ho (2022) Severe cellular stress drives apoptosis through a dual control mechanism independently of p53. Cell Death Discovery 8(1):282. (IF= 7.109).
- 14. Cheng CT, Wang TY, Chen PR, Wu WH, Lai JM, Chang PM, **Hong YR**, Huang CF, Wang FS*.Computer-Aided Design for Identifying Anticancer Targets in Genome-Scale Metabolic Models of Colon Cancer. Biology (Basel). 2021 Oct 29;10(11):1115. (IF=5.168).
- 15. Chiou, S.-J.; Ko, H.-J.; Hwang, C.-C.; **Hong, Y.-R***. The Double-Edged Sword of Beta2-Microglobulin in Antibacterial Properties and Amyloid Fibril-Mediated Cytotoxicity. Int. J. Mol. Sci. 2021, 22, 6330. (IF=6.208). 本人為通訊作者.
- 16. Tsai, C.-Y.; Ko, H.-J.; Chiou, S.-J.; Lai, Y.-L.; Hou, C.-C.; Javaria, T.; Huang, Z.-Y.; Cheng, T.-S.; Hsu, T.-I.; Chuang, J.-Y.; Kwan, A.-L.; Chuang, T.-H.; Huang, C.-Y.F.; Loh, J.-K.; **Hong, Y.-R***. NBM-BMX, an HDAC8 Inhibitor, Overcomes Temozolomide Resistance in Glioblastoma Multiforme by Downregulating the β-Catenin/c-Myc/SOX2 Pathway and Upregulating p53-Mediated MGMT Inhibition. Int. J. Mol. Sci. 2021, 22, 5907. (IF=6.208). 本人為通訊作者.
- 17. Tsai, C.-Y.; Ko, H.-J.; Huang, C.-Y.F.; Lin, C.-Y.; Chiou, S.-J.; Su, Y.-F.; Lieu, A.-S.; Loh, J.-K.; Kwan, A.-L.; Chuang, T.-H.; **Hong, Y.-R***. Ionizing Radiation Induces Resistant Glioblastoma Stem-Like Cells by Promoting Autophagy via the Wnt/β-Catenin Pathway. Life 2021, 11, 451. (IF=3.251). 本人為通訊作者.
- 18. Ko, H.-J.; Tsai, C.-Y.; Chiou, S.-J.; Lai, Y.-L.; Wang, C.-H.; Cheng, J.-T.; Chuang, T.-H.; Huang, C.-Y.F.; Kwan, A.-L.; Loh, J.-K.; **Hong, Y.-R***. The Phosphorylation Status of Drp1-Ser637 by PKA in Mitochondrial Fission Modulates Mitophagy via PINK1/Parkin to Exert Multipolar Spindles Assembly during Mitosis. Biomolecules 2021, 11, 424. (IF=6.064.) 本人為通訊作者.

- 19. Daniel J. Klionsky* et. al..... among including **Yi-Ren Hong** Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). Autophagy. 2021, Volume 17, Issue 1, 1-382. (IF=13.391)
- 20. Chi-ShiuanWu,Shan-YingWu,Hsin-ChihChen,Chien-AnChu,Han-HsuanTang,Hsiao-ShengLiu,Yi-RenHong,Chi-YingF.Huang, Guan-Cheng Huang, Chun-Li SuChi-Shiuan Wu, Shan-Ying Wu, Hsin-Chih Chen, Chien-An Chu, Han-Hsuan Tang, Hsiao-Sheng Liu, Yi-Ren Hong, Chi-Ying Huang, Guan-Cheng Huang, Chun-Li Su* Curcumin functions as an MEK inhibitor to induce a synthetic lethal effect on KRAS mutant colorectal cancer cells receiving targeted drug regorafenib. The Journal of Nutritional Biochemistry. J Nutr Biochem 2019 Dec; 74:108227.. (IF=6.117)
- 21. HJ Ko†, SJ Chiou†, YH Wong†, YH Wang, YL Lai, CH Chou, CH Wang, JK Loh, AS Lieu, JT Cheng, YT Lin, PJ Lu, MJ Fann, CYF Huang*, and **Yi-Ren Hong*** (2019, Oct).

 GSKIP-Mediated Anchoring Increases Phosphorylation of Tau by PKA but Not by GSK3beta via cAMP/PKA/GSKIP/GSK3/Tau Axis Signaling in Cerebrospinal Fluid and iPS Cells in Alzheimer Disease. Journal of Clinical Medicine,8(10):1751. (IF=4.964) 本人為通訊作者
- 22. Cheng-Wei Chu, Huey-Jiun Ko, Chia-Hua Chou, Tai-Shan Cheng, Hui-Wen Cheng, Yu-Hsin Liang, Yun-Ling Lai, Chen-Yen Lin, Chihuei Wang, Joon-Khim Loh, Jiin-Tsuey Cheng, Shean-Jaw Chiou, Chun-Li Su, Chi-Ying F. Huang and Yi-Ren Hong*. Thioridazine Enhances P62-Mediated Autophagy and Apoptosis Through Wnt/β-Catenin Signaling Pathway in Glioma Cells. Int. J. Mol. Sci. 2019, 20(3), 473; https://doi.org/10.3390/ijms20030473 (IF=6.208)
- 23. Chou CH, Yang MC, Hsiao BX, Wang YH, Liu HF, Chiou SJ, Chuang YC, Yang CN, Lieu AS, Loh JK, Howng SL, Chou AK, Tseng CN, Cheng JT, Hong YR*. The origin of GSKIP, a multifaceted regulatory factor in the mammalian Wnt pathway. Biochim Biophys Acta Molecular Cell Research. 2018 Aug;1865(8):1046-1059. (IF=5.011)
- 24. Chu CW, Yang MC, Chou CH, Huang WS, Hsiao BX, Wang YT, Chiou SJ, Loh JK, Hong YR*. GSK3β mediated Ser156 phosphorylation modulates a BH3 like domain in BCL2L12 during TMZ induced apoptosis and autophagy in glioma cells. Int J Mol Med. 2018 Aug;42(2):905-918. (IF=5.314)
- 25. Rong-Hwa Jan, Chia-Jung Chen, Yi-Ren Hong, Yu-Li Lin* & Li-Kuang Chen* A surface antigen of Orientia tsutsugamushi activates human monocyte-derived dendritic cells via nuclear factor-kB & p38 mitogen-activated protein kinase pathways. Indian J Med Res 148, August 2018, pp 215-224. (IF= 5.274)
- 26. Li-Kwan Chang, Jian-Ying Chung, **Yi-Ren Hong**, Takaya Ichimura, MitsuyoshiNakao and Shih-Tung Liu* Activation of Sp1-mediated transcription by Rta of Epstein–Barr virus via an interaction with MCAF1. Nucleic Acids Research, 2017, Vol. 45, No. 8 5009. (IF =19.120)
- 27. Ming Chang Yang, Shang Tao Chien, Tzu Feng Yang, Shih Yi Lin, Tai Min Lee, **Yi Ren Hong***Downregulation of nuclear and cytoplasmic Chibby is associated with advanced cervical cancer
 ONCOLOGY LETTERS 14: 6632-6644, 2017. (IF =3.111)

- 28. Chung-Lung Cho, Ya-Zhe Lee, Chao-Neng Tseng, Joshua Cho, Yuan-Bin Cheng, Kuo Wei Wang, Han-Jung Chen, Shean-Jaw Chiou, Chia-Hua Chou, Yi-Ren Hong* Hexane fraction of Pluchea indica root extract inhibits proliferation and induces autophagy in human glioblastoma cells.
 BIOMEDICAL REPORTS 7: 416-422, 2017
- 29. Weng CH, Chung FP, Chen YC, Lin SF, Huang PH, Kuo TB, Hsu WH, Su WC, Sung YL, Lin YJ, Chang SL, Lo LW, Yeh HI, Chen YJ, **Yi-Ren Hong**, Chen SA, Hu YF*. Pleiotropic Effects of Myocardial MMP-9 Inhibition to Prevent Ventricular Arrhythmia. Sci Rep. 2016 Dec 14;6:38894. (IF =5.228)
- 30. Shean-Jaw Chiou*, Chan-Chi Wang, Yan-Shen Tseng, Yen-Jung Lee, Shih-Chieh Chen, Chi-Hsien Chou, Lea-Yea Chuang, **Yi-Ren Hong**, Chi-Yu Lu, Chien-Chih Chiu, and Michel Chignard "A novel role for β2-microglobulin: a precursor of antibacterial chemokine in respiratory epithelial cells" Scientific Reports. 2016, Sci Rep. 2016 Aug 9;6:31035. (IF =5.228)
- 31. Tsai MH, Chang CH*, Tsai RK*, **Yi-Ren Hong**, Chuang TH, Fan KT, Peng CW, Wu CY, Hsu WL, Wang LS, Chen LK, Yu HS Cross-regulation of Pro-inflammatory Cytokines by Interleukin-10 and MiR-155 in Orientia tsutsugamushi-infected Human Macrophages Prevents Cytokine Storm. J Invest Dermatol. 2016 Jul;136(7):1398-407. (IF =6.915)
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