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專長說明：

鈣離子訊息、活細胞分子造影、光遺傳學、癌症抗化性與轉移

研究興趣：

1. 鈣離子訊息對癌症抗化性與轉移之調控
2. 烹飪油煙誘發肺癌形成之機制探討
3. 缺氧環境引發三陰性乳癌轉移與腎臟纖維化之機制探討

近五年代表作：

1. Lai, Y.S., Chan, T.W., Nguyen, T.M.H., Lin, T.C., Chao, Y.Y., Wang, C.Y., Hung, L.Y., Tsai, S.J. and ***Chiu, W.T.**** (2024 Mar) Store-operated calcium entry inhibits primary ciliogenesis via the activation of Aurora A. FEBS Journal 291(5):1027-1042.
2. Chang, H.A., Ou Yang, R.Z., Su, J.M., Nguyen, T.M.H., Sung, J.M., Tang, M.J. and ***Chiu, W.T.**** (2023 Oct) YAP nuclear translocation induced by HIF-1α prevents DNA damage under hypoxic conditions. Cell Death Discovery 9(1):385.
3. Lin, Y.S., Huang, W.H., Hsu, K.F., Tang, M.J.* and ***Chiu, W.T.**** (2023 Sep) Reversion of chemoresistance by endocannabinoid-induced ER stress and autophagy activation in ovarian cancer. American Journal of Cancer Research 13(9):4163-4178.
4. Sun, C.C., Lee, S.Y., Chen, L.H., Lai, C.H., Shen, Z.Q., Chen, N.N., Lai, Y.S., Tung, C.Y., Tzeng, T.Y., ***Chiu, W.T.**** and Tsai, T.F.* (2023 Jun) Targeting Ca^{2+}-dependent pathways to promote corneal epithelial wound healing induced by Cisd2 deficiency. Cellular Signalling 109:110755.
5. Lin, T.C.#, Chung, P.J.#, Shen, C.A., Nguyen, T.M.H., Lin, Y.S., Lin, S.C., Hsiao, S.C.*, and ***Chiu, W.T.**** (2023 Jun) Depletion of intracellular Ca^{2+} induces FOXM1 SUMOylation and accumulation on the inner nuclear membrane affecting G2/M transition. European Journal of Cell Biology 102(2):151332.
6. Lai, Y.S.#, Chang, C.C.#, Chen, Y.Y., Lin, T.C., Nguyen, N.T., Xu, J., Chen, Y.C., Chang, Y.F., Chang, Y.F., Wang, C.Y., Chen. P.S., Lin, S.C., Peng, I.C., Tsai, S.J., and ***Chiu, W.T.**** (2023 Jun) Optogenetically engineered Ca^{2+} oscillation-mediated DRP1 activation promotes mitochondrial fission and cell death. Journal of Cell Science 136(12):jcs260819.
7. Nguyen, T.M.H., Lai, Y.S., Chen, Y.C., Lin, T.C., Nguyen, N.T. and ***Chiu, W.T.**** (2023 Apr) Hypoxia-induced YAP activation and focal adhesion turnover to promote cell migration in mesenchymal TNBC cells. Cancer Medicine 12(8):9723-9737.
8. Cheng, H.F.#, ***Chiu, W.T.***#, Lai, Y.S., Truong, T.T., Lee, P.Y. and Huang, C.C.* (2023 Jan) High-frequency noncontact low-intensity pulsed ultrasound modulates Ca^{2+} dependent transcription factors contributing to cell migration. Ultrasonics 127:106852.
9. Truong, T.T.[#], ***Chiu, W.T.***[#], Lai, Y.S., Huang, H., Jiang, X. and Huang, C.C.* (2022 Mar) Ca^{2+} signaling-mediated low-intensity pulsed ultrasound-induced proliferation and activation of motor neuron cells. *Ultrasonics* 124:106739.
10. Lin, Y.S., Lin, Y.H., Nguyen Thi, M, Hsiao, S.C. and ***Chiu, W.T.**** (2022 Jan) STIM1 controls the focal adhesion dynamics and cell migration by regulating SOCE in osteosarcoma. *Int J Mol Sci* 23(1):162.
11. Sun, C.C., Lee, S.Y., Kao, C.H., Chen, L.H., Shen, Z.Q., Lai, C.H., Tzeng, T.Y., Su Pang, J.H., ***Chiu, W.T.**** and Tsai, T.F.* (2021 Oct) Cisd2 plays an essential role in corneal epithelial regeneration. *EBioMedicine* 73:103654.
12. Lai, Y.S., Chang, Y.H., Chen, Y.Y., Xu, J., Yu, C.S., Chang, S.J., Chen, P.S., Tsai, S.J. and ***Chiu, W.T.**** (2021 Jun) Ca^{2+}-regulated cell migration revealed by optogenetically engineered Ca^{2+} oscillations. *J Cell Physiol* 236(6):4681-4693.
13. Huang, H.K., Lin, Y.H., Chang, H.A., Lai, Y.S., Chen, Y.C., Huang, S.C., Chou, C.Y. and ***Chiu, W.T.**** (2020 Feb) Chemoresistant ovarian cancer enhances its migration abilities by increasing store-operated Ca^{2+} entry-mediated turnover of focal adhesions. *J Biomed Sci* 27(1):36.

林世杰 *(Shih-Chieh Lin, Ph.D.)*

國科會年輕學者養成計畫得主

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研究興趣：

利用各種生物資訊工具探勘各式公用生物訊息資料庫，藉此衍生新穎研究方向、降低研究成本及試誤學習之時間，再結合細胞生物及分子生物學，用以探討疾病生成之致病機制以及開發可能的治療方向

研究方向：

1. 探討子宮內膜異位症之致病機轉以及發展新穎之治療方法。
2. 研究前列腺癌第二代雄激素阻斷治療藥物生成抗藥性機制及發展可能之治療方法。
3. 研究 mRNA 3'端未轉譯區(3'-untranslated region)之轉換於疾病生成的影響為何。
4. 研究男性不孕之致病機轉及其臨床診斷之運用。

近五年代表作：

1. **Shin-Chih Lin**#, Yu-Sheng Cheng#, Yi-Syuan Lin, Hui-Kuan Lin, Thi My Hang Nguyen, Wen-Tai Chiu, Ya-Chuan Tsai, Hsing-Yi Chen, Tsung-Yen Lin, Shih-Chieh Lin*. The Long noncoding RNA lncZBTB10 facilitates AR function by S-palmitoylation to promote prostate cancer progression and abiraterone resistance. British Journal of Cancer 2025 Feb 16. doi: 10.1038/s41416-025-02938-1.
2. Yi-Syuan Lin, Ya-Chuan Tsai, Chia-Jung Li, Tzu-Tang Wei, Bo-Wen Lin, Ya-Na Wu, Shang-Rung Wu, Shin-Chih Lin, **Shih-Chieh Lin***. Overexpression of NUDT16L1 sustains proper function of mitochondria and leads to ferroptosis insensitivity in colorectal cancer. Redox Biology 2024 Nov;77:103358.
3. Shin-Chih Lin, Ya-Chuan Tsai, Ying-Lan Chen, Yun-Chen Huang, Hui-Kuan Lin, Yi- Syuan Lin, Yu-Sheng Cheng, Hsing-Yi Chen, Chia-Jung Li, Tsung-Yen Lin, **Shih-Chieh Lin***. Un-methylation of NUDT21 represses docosahexaenoic acid biosynthesis contributing to enzalutamide resistance in prostate cancer. Drug Resist Updat. 2024 Nov;77:101144.
4. Yu-Sheng Cheng, Hsing-Yi Chen, Yu-Chiao Lin, Yi-Syuan Lin, Yi-Chun Yeh, Yi-Hsuan Yeh, Yung-Hsuan Cheng, Yung-Ming Lin, Han-Yu Weng, Tsung-Yen Lin, **Shih-Chieh Lin***. The MAEL expression in mitochondria of human spermatozoa and the association with asthenozoospermia. Andrology, 2023 Oct;11(7):1286-1294.
5. **Shih-Chieh Lin**, Wan-Ning Li, Shin-Chih Lin, Haun-Tzu Hou, Ya-Chuan Tsai, Tin-Chien Lin, Meng-Hsing Wu, Shaw-Jenq Tsai. Targeting YAP1 ameliorates progesterone resistance in endometriosis. Human Reproduction, 2023 Jun, 38(6):1124-1134.
6. Hsiu-Chi Lee, Chien-Hui Ou, Yun-Chen Huang, Pei-Chi Hou, Chad J Creighton, Yi- Syuan Lin, Che-Yuan Hu, **Shih-Chieh Lin***. YAP1 overexpression contributes to the development of enzalutamide resistance by induction of cancer stemness and lipid metabolism in prostate cancer. Oncogene 2021 Apr;40 (13):2407-2421

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專長說明：

腫瘤生物學 (Tumor biology)

研究興趣:

1. Microenvironment in tumor development 腫瘤微環境與癌症發展之分子機制探討
2. Regulation of extracellular vesicle in cancer progression 癌症發展過程中細胞外囊泡之角色與調節
3. Pancreatic cancer and urothelial carcinoma 胰臟癌、泌尿道上皮癌

近五年代表作:

1. **Chu-An Wang†**, Ya-Chin Hou†, Yi-Kai Hong, Yu-Jing Tai, Chieh Shen, Pei-Chi Hou, Jhao-Lin Fu, Cheng-Lin Wu, Siao Muk Cheng, Daw-Yang Hwang, Yung-Yeh Su, Yan-Shen Shan*, Shaw-Jenq Tsai*. Intercellular TIMP-1-CD63 signaling directs the evolution of immune escape and metastasis in KRAS mutated pancreatic cancer cells. *Mol Cancer* 24, 25 (2025).
2. Yu-Ying Chao, Ruei-Ci Lin, Ping Jui Su, **Chu-An Wang**, Ting-Yuan Tu, Ya-Chin Hou, Yi-Tzui Tsai, I-Chen Peng, Shaw-Jenq Tsai, Yan-Shen Shan, Chia-Yih Wang. Melanophilin-induced primary cilia promote pancreatic cancer metastasis. Cell Death & Disease. 2025 Jan 16;16(1):22.
3. Yi-Chia Hsieh, Tsung-Han Cheng, **Chu-An Wang**, Che-Yuan Hu, Wen-Horng Yang, Chien-Hui Ou, Hau-Chern Jan. Increased ratio of red cell distribution width to lymphocyte percentage as a novel preoperative marker for unfavorable survival outcomes in upper tract urothelial carcinoma. *Biomedical Reports.* 2024 Dec 10;22(2):32.
4. Lian-Chung Yu*, **Chu-An Wang***, Che-Yuan Hu, Kun-Che Lin, Chien-Hui Ou, Hau-Chern Jan. Preoperative systemic inflammation response index enhances the prognostic value of tumor multifocalityin upper tract urothelial carcinoma. *Oncol Lett.* 2024 Jul 15;28(3):436.
5. **Chu-An Wang**, Chien-Feng Li, Rho-Chi Huang, Yo-Hua Li, Jing-Ping Liou, Shaw-Jenq Tsai. Suppression of Extracellular Vesicle VEGF-C-mediated Lymphangiogenesis and Pancreatic Cancer Early Dissemination By a Selective HDAC1/2 Inhibitor. *Mol Cancer Ther.* 2021 Sep;20(9):1550-1560.
6. **Chu-An Wang** and Shaw-Jenq Tsai. Regulation of lymphangiogenesis by extracellular vesicles in cancer metastasis. *Exp Biol Med (Maywood)***.** 2021 Jun 18;15353702211021022.
7. Wan-Ning Li, Kuei-Yang Hsiao, **Chu-An Wang**, Ning Chang, Pei-Ling Hsu, Chung-Hsien Sun, Shang-Rung Wu, Meng-Hsing Wu, Shaw-Jenq Tsai. Extracellular vesicle-associated VEGF-C promotes lymphangiogenesis and immune cells infiltration in endometriosis. *PNAS* October 13, 2020 117 (41) 25859-25868
8. **Chu-An Wang**, Yi-Hern Chang, Pei-Chi Hou , Yu-Jing Tai **,** Wan-Ning Li, Pei-Ling Hsu, ShangRung Wu, Wen-Tai Chiu, Chien-Feng Li , Yan-Shen Shan , Shaw-Jenq Tsai. DUSP2 regulates extracellular vesicle-VEGF-C secretion and pancreatic cancer early dissemination. *J Extracell Vesicles.* 2020 Apr 4;9(1):1746529.

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專長說明：

宿主微生物交互作用(Host-Pathogen Interactions)、自噬作用(Autophagy)、免疫學(Immunology)、細胞生物學(Cell Biology)

研究興趣:

1. 細胞內脂多醣結合之蛋白及其角色。
   Role of intracellular lipopolysaccharide (LPS)-interacting proteins
2. 細胞內脂多醣和細菌外膜囊泡在外泌體產生中的角色及其對敗血症的影響。
   Role of intracellular LPS and bacterial outer membrane vesicles in exosomes production and the implications in sepsis
3. 外泌體在細胞間通訊中造成 A 群鏈球菌致病機制的角色。
   Role of exosomes in intercellular communications for the pathogenesis of group A Streptococcus
4. 皮膚免疫於登革致病機轉中的角色及影響。
   Role of skin immunity in dengue pathogenesis and the implications

近五年代表作:

1. **Cheng YL***, Mello-Vieira J, Covarrubias-Pinto A, Gonzalez A, Kuncha SK, Kew C, Zhang K, Afzal AM, Diab N, Borchert S, Chen W, Huang TC, Hornef MW, Hübner CA, Hensel M, Dikic I*. Intracellular lipopolysaccharide regulates ER remodeling upon bacterial infection. 2025. https://www.biorxiv.org/content/10.1101/2024.07.25.605133v1
2. Su MSW, Lee CJ, **Cheng YL,** Chiang-Ni C, Hsieh YC, Liao CC, Wu JJ*. Group A Streptococcal peroxide response regulator aids in bacterial defense against host innate and nutritional immunity. 2025, **Submitted.**
3. **Cheng YL**[#], Su MSW[#], Liao CC[#], Hsieh YC, Lu SL, Omori H, Noda T, Chu YL, Chen CL, Lin YS*, Wu JJ*. Inhibition of mitochondrial ROS turns LC3-associated phagocytosis to autophagy upon resveratrol treatment for group A *Streptococcus* clearance in endothelial cells. 2024, **Submitted.** (# equal contribution, Co-first author)
4. Kew C, Huang W, Prieto-Garcia C, Willoughby M, Meier-Credo J., Tietgen M., Torres SG, Klatt S, Ho-Xuan H, **Cheng YL**, Stolz A, Antebi A, Fleming I, Göttig S and Dikic I*. Acinetobacter baumannii derived outer membrane vesicles induce glutamine deprivation to promote pathogenesis. **Sci Adv**, 2024, **Revised.**
5. Kew C, Prieto-Garcia C, Bhattacharya A, Tietgen M, Mello-Vieira J, Klatt S, **Cheng YL,** Rathore R, Fleming I, Tan MW, Göttig S, Kempf VAJ, Dikic I*. The aryl hydrocarbon receptor and FOS mediate cytotoxicity induced by *Acinetobacter baumannii*. **Nat Comm**, 2024, 15:7939.
6. Su MSW[#], **Cheng YL**[#], Lin YS*, Wu JJ*. Interplay between Group A Streptococcus and Host Innate Immune Responses. *Microbiol. Mol. Biol. Rev*, 7:e0005222, 2024. (# equal contribution, Co-first author). doi: 10.1128/mmbr.00052-22.
7. Shin D, Bhattacharya A, **Cheng YL**, Alonso MC, Medipour AR, van der Heden van Noort GJ, Ovaa H, Hummer G, Dikic I*. (2020) Bacterial OTU deubiquitinases regulate substrate ubiquitination upon *Legionella* infection. *eLife* 9:e58277. doi: 10.7554/eLife.58277.
8. **Cheng YL**, Kuo CF, Lu SL, Omori H, Wu YN, Hsieh CL, Noda T, Wu SR, Anderson R, Lin CF, Chen CL, Wu JJ*, Lin YS*. (2019) Group A streptococcus induces LAPosomes via SLO/β1 integrin/NOX2/ROS pathway in endothelial cells that are ineffective in bacterial killing and suppress xenophagy. *mBio* 10(5):e02148-19. doi: 10.1128/mBio.02148-19.
9. **Cheng YL**, Wu YW, Kuo CF, Lu SL, Liu FT, Anderson R, Lin CF, Liu YL, Wang WY, Chen YD, Zheng PX, Wu JJ*, Lin YS*. (2017) Galectin-3 inhibits galectin-8/parkin-mediated ubiquitination of group A streptococcus. *mBio* 8(4):e00899-17. doi: 10.1128/mBio.00899-17.
10. Lu SL, Kawabata T, **Cheng YL**, Omori H, Hamasaki M, Kusaba T, Iwamoto R, Arimoto H, Noda T, Lin YS, Yoshimori T*. (2017) Endothelial cells are intrinsically defective in xenophagy of *Streptococcus pyogenes*. *PLoS Pathog.* 13(7):e1006444. doi: 10.1371/journal.ppat.1006444.
11. Chen YD[#], Fang YT[#], **Cheng YL**, Lin CF, Hsu LJ, Wang SY, Anderson R, Chang CP, Lin YS*. (2017) Exophagy of annexin A2 via RAB11, RAB8A and RAB27A in IFN-γ-stimulated lung epithelial cells. *Sci Rep.* 7(1):5676. doi: 10.1038/s41598-017-06076-4. [#]Equal contribution

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研究興趣:

結構生物學實驗室

本實驗室主要利用 X 射線蛋白質結晶學 (X-ray protein crystallography) 與單分子冷凍電子顯微鏡 (Single-particle cryo-EM)，解析生物大分子的分子結構，藉此闡述分子結構與功能間的關係與機轉。研究主題聚焦在與核酸共同作用的蛋白質的功能探討，鑽研的生物問題涉及基因組的穩定性、基因調控、RNA 代謝、RNA 修飾…等。

本團隊目前主要的研究主題為人類粒線體基因組 (mtDNA) 的降解機制。受到損傷的 mtDNA 需要即時的被清除以維持其完整性與功能，若否，則突變將累積在其中，造成粒線體功能下降，此與老化、神經退化性疾病，急慢性發炎相關疾病呈正相關。人類的粒線體中有一負責降解受損 mtDNA 的複合體，在此稱之為 mtDNA 降解體 (mtDNA degradation machinery)。此複合體包含了 DNA 聚合酶γ，DNA 解旋酶 Twinkle 與核酸外切酶 MGME1，但這些分子是如何組成 mtDNA 降解體、個別的功能是如何執行與調控，均有許多未解之謎。本實驗室希望藉由了解 mtDNA 降解體運作的結構機轉，闡明受損 mtDNA 的清除機制，並進一步了解其與相關疾病發展的關係，以期對細胞老化及相關疾病的治療上，有所助益。

另外，我們還有兩個 RNA 結合蛋白—RNA 甲基轉移酶 NSUN 及 RNA 解旋酶 DDX 的蛋白質功能研究，這些計畫拓展了本團隊的研究範疇，使我們跨足於轉錄組功能領域，加強了本團隊對基礎分子生物學的研究深度。

近五年代表作:

1. Chiu, H.P., Shen, C.H., Wu, J.K., Mao, E.Y.C., Yen, H.Y., Chang, Y.P., **Wu, C.C.*** and Fan, H.F.* (2024) Nuclease-induced stepwise photodropping (NISP) to precisely investigate single-stranded DNA degradation behaviors of exonucleases and endonucleases. *Nucleic Acids Res.*, 52, e97. doi: 10.1093/nar/gkae822.

2. Mao, E.Y.C., Yen, H.Y., **Wu, C.C.*** (2024) Structural basis of how MGME1 processes DNA 5' ends to maintain mitochondrial genome integrity. *Nucleic Acids Res.* 52, 4067-4078. doi: 10.1093/nar/gkae186.

3. **Wu, C.C.**, Lin, J.L.J., Yuan H.S.* (2020) Structures, Mechanisms, and Functions of His-Me Finger Nucleases. *Trends Biochem Sci* 45(11):935-946. doi: 10.1016/j.tibs.2020.07.002.

4. **Wu, C.C.**, Lin, J.L.J., Yang-Yen, H.F., and Yuan, H.S.* (2019) A unique exonuclease ExoG cleaves between RNA and DNA in mitochondrial DNA replication. *Nucleic Acids Research* 47:5405-5419. doi: 10.1093/nar/gkz241.

余建泓 *(Yu Chien-Hung, Ph.D.)*

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研究興趣：

密碼子是將遺傳訊息傳遞到胺基酸以至於蛋白質的橋樑，也是分子生物學的中心法則的核心。絕大部分的胺基酸可以被兩個以上的同義密碼子表達，但是這些同義密碼子的使用頻率並不相同，我們稱這種現象為密碼子使用偏移。有趣的是，密碼子使用偏移存在於幾乎所有已知的基因體中，但是為什麼這種現象會在長久的演化過程中被保留下來，並不清楚。 我們之前的研究結果顯示，密碼子的使用偏移雖然不改變胺基酸的序列，卻可以調控蛋白質的摺疊以及調控信使核醣核酸與蛋白質的表達量。在臨床上，隨著定序技術的進步，越來越多的疾病也被發現是與序列中同義密碼子的突變有關。未來實驗室的研究將運用分子生物學、生物化學、遺傳學以及生物資訊學的方法，來探討為什麼密碼子使用偏移會影響基因表達的機制。也希望透過更深入了解密碼子使用偏移的機制，可以發展出治療同義密碼子突變相關疾病的方法。

近五年代表作：

1. Zhou, Z., Dang, Y., Zhou, M., Li, L., **Yu, C.H.**, Fu, J., Chen, S., and Liu, Y. (2016) Codon usage is an important determinant of gene expression levels largely through its effects on transcription. *Proc. Natl. Acad. Sci. U.S.A.*, 113, E6117-E6125.

2. **Yu, C.H.***, Dang, Y.*, Zhou, Z*., Wu, C., Zhao, F., Sachs, M.S., and Liu, Y. (2015) Codon usage influences the local rate of translation elongation to regulate co-translational protein folding. *Mol. Cell*, 59, 744-754. (*co-first authors) (Cover article and highlighted in TIBS)

3. **Yu, C.H.** and Olsthoorn, R.C. (2015) Monitoring ribosomal frameshifting as a platform to screen anti-riboswitch drug candidates. *Methods Enzymol.*,550, 385-393.

4. **Yu, C.H.** and Olsthoorn, R.C. (2014) Stimulation of ribosomal frameshifting by RNA G-quadruplex structures. *Nucleic Acids Res.*, 42, 1887-1892.

5. **Yu, C.H.** Luo J., Iwata-Reuyl, D., and Olsthoorn, R.C. (2013) Exploiting preQ1 riboswitches to regulate ribosomal frameshifting. *ACS Chem. Biol.*, 8, 733-740.

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研究興趣：

1. 去結合蛋白運用於血小板凝聚與癌細胞轉移之研究
2. 三環毒素與其結合受体之研究
3. 翼狀螺旋轉錄因子與其致病突變蛋白之研究
4. A 群鏈球菌的致命因子熱原性外毒素 B 之研究
5. 中草藥有療效成份之分離（鯊魚軟骨、冬蟲夏草、巴西洋菇）

近五年代表作：

1. Wang, C.-C., Houng, H.-C. , Kuo, C.-F., Lin, Y.-S., Wu, J.-J., Lin. M.-T., Liu, C.-C., Chen, C.-Y., Huang, W., and Chuang, W.-J. (2009) "Solution Structure and Backbone Dynamics of Streptopain: Insight into Diverse Substrate Specificity", J. Biol. Chem., 284, 10957-10967.

2. Chen, C.-Y., Liu, Y.-C., Hsieh Y.-H., Shiu, J.-H., Chen, Y.-C., Tang, M.-J., Lo, Szecheng J., and Chuang, W.-J. (2009) "Effect of D to E Mutation of the RGD Motif in Rhodostomin on its Activity, Structure, and Dynamics: Importance of the Interactions Between the D Residue and Integrin", Proteins, 76, 808-821.

3. Anangi, R., Chen, C.-C., Lin Y.-W., Cheng, Y.-R., Cheng, C.-H., Chen, Y.-C., Chu, Y.-P., and Chuang, W.-J. (2010) “Expression in Pichia pastoris and Characterization of APETx2, a Specific Inhibitor of Acid Sensing Ion Channel 3”, Toxicon, 56, 1388-1397.

4. Chu, Y.-P., Chang, C.-H., Shiu, J.-H., Chang, Y.-T., Chen, C.-Y., and Chuang, W.-J. (2011) “Solution Structure and Backbone Dynamics of the DNA-Binding Domain of FOXP1: Insight into its Domain Swapping”, Protein Science, 20, 908-924.

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研究興趣：

- The epigenome of human diseases.
- Regulatory mechanisms of methylcytosine deposition in DNA and in RNA.

近年代表作：

1. Chang CJ*, **Huang PH*#**, Chen SY, Su PC, Ding LY, Hou YC, Hung MN, Chen KL, Wu YN, Wu SR, Lin FC, Lu PJ, Wu HY, Chen YJ, Chang CH, Chang CP, Hwang DY, Wang YC#, Shan YS#. Macrophage activation determines muscle wasting in pancreatic cancer. (***In Revision***, 2025). (*, first; #, corresponding authors)
2. Chen SY, Fang YH, Huang CY, Wu JH, Shan YS, Liu YW and **Huang PH**. Transcriptome-wide RNA 5-methylcytosine profiles of human iPSCs and iPSC-derived cardiomyocytes. ***Scientific Data***, 2024 Dec 18;11(1):1378.
3. Ding LY, Chang CJ, Chen SY, Chen KL, Li YS, Wu YC, Hsu TY, Ying HY, Wu HY, Hughes MW, Wang CY, Chang CH, Tang MJ, Chuang WJ, Shan YS, Chang CJ, and **Huang PH**. Stromal Rigidity Stress Accelerates Pancreatic Intraepithelial Neoplasia Progression and Chromosomal Instability via Nuclear Protein Tyrosine Kinase 2 Localization. ***Am J Pathol***. 2024 Jul;194(7):1346-1373.
4. Fang YH, Wang SPH, Liao IC, Tsai KJ, **Huang PH**, Yang PJ, Yen CJ, Liu PY, Shan YS, Liu YW. HLA-E^{high} /HLA-G^{high} /HLA-II^{low} human iPSC-derived cardiomyocytes exhibit low immunogenicity for heart regeneration. ***Adv Healthc Mater***. 2023 Nov;12(29):e2301186.
5. Cheng HC, **Huang PH**, Lai FJ, Jan MS, Chen YL, Chen SY, Chen WL, Hsu CK, Huang W, Hsu LJ. Loss of fragile WWOX gene leads to senescence escape and genome instability. ***Cell Mol Life Sci***. 2023 Oct 28;80(11):338.
6. Chen SY and **Huang PH**. Enrichment of mRNA and bisulfite-mRNA library preparation for next-generation sequencing. ***J Vis Exp***. 2023 Jul 7:(197).
7. Chen SY, Chen KL, Ding LY, Yu CH, Wu HY, Chou YY, Chang CJ, Chang CH, Wu YN, Wu SR, Hou YC, Lee CT, Chen PC, Shan YS, and **Huang PH**. RNA bisulfite sequencing reveals NSUN2-mediated suppression of epithelial differentiation in pancreatic cancer. ***Oncogene***. 2022;41(22):3162-3176.
8. Ding LY, Hou YC, Kuo IY, Hsu TY, Tsai TC, Chang HW, Hsu WY, Tsao CC, Tian CC, Wang PS, Wang HC, Lee CT, Wang YC, Lin SH, Hughes MW, Chuang WJ, Lu PJ, Shan YS, **Huang PH**. Epigenetic silencing of AATK in acinar to ductal metaplasia in murine model of pancreatic cancer. ***Clin Epigenetics***. 2020 Jun 17;12(1):87.
9. Wang HC, Lin YL, Hsu CC, Chao YJ, Hou YC, Chiu TJ, **Huang PH,** Tang MJ, Chen LT, Shan YS. Pancreatic stellate cells activated by mutant KRAS-mediated PAI-1 upregulation foster pancreatic cancer progression via IL-8. ***Theranostics***. 2019 Sep 23;9(24):7168-7183.

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專長與研究興趣:

病菌宿主交互作用(pathogen-host interaction)

代表作:

1. Hui-Chen Hsieh, I-Hsiang Huang, Shao-Wen Chang, Po-Lin Chen, Yu-Cheng Su, Shuying Wang, Wei-Jiun Tsai, Ping-Hung Chen, Raffi V. Aroian, and **Chang-Shi Chen**. PRMT-7/PRMT7 activates HLH-30/TFEB to guard plasma membrane integrity compromised by bacterial pore-forming toxins. ***Autophagy***. 2024 Feb 19:1-24.

2. Sin-Tian Wang, Cheng-Ju Kuo, Chih-Wen Huang, Tzer-Min Lee, Jenn-Wei Chen, and **Chang-Shi Chen**. OmpR coordinates the expression of virulence factors of enterohemorrhagic *Escherichia coli* in the alimentary tract of *Caenorhabditis elegans*. ***Molecular Microbiology***. 2021 Jul;116(1):168-183.

3. Cheng-Rung Huang, Cheng-Ju Kuo, Chih-Wen Huang, Yu-Ting Chen, Bang-Yu Liu, Chung-Ta Lee, Po-Lin Chen, Wen-Tsan Chang, Yun-Wen Chen, Tzer-Min Lee, Hui-Chen Hsieh, and **Chang-Shi Chen**. Host CDK1 and formin mediate microvillar effacement induced by enterohemorrhagic *Escherichia coli*. ***Nature Communications***. 2021 Jan 4;12(1):90.

4. Chia-En Tsai, Fang-Jung Yang, Ching-Han Lee, Yen-Ping Hsueh, Cheng-Ju Kuo, and **Chang-Shi Chen.** The conserved regulator of autophagy and innate immunity hlh-30/TFEB mediates tolerance of enterohemorrhagic *Escherichia coli* in *Caenorhabditis elegans*. ***Genetics***. 2021 Mar 3;217(1):1-17.

5. Daniel J. Klionsky, and **Chang-Shi Chen,** et. al. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). ***Autophagy*.** 2021 Feb 8:1-382.

6. Cheng-Ju Kuo, Ya-Chu Hsu, Sin-Tian Wang, Bang-Yu Liou, Serene Boon-Yuean Lim, Yi-Wei Chen, and **Chang-Shi Chen.** IGLR-2, a leucine-rich repeat domain containing protein, is required for the host defense in *Caenorhabditis elegans*. ***Front Immunol***. 2020 Nov 30;11:561337.

7. Cheng-Ju Kuo, Sin-Tian Wang, Chia-Mei Lin, Hao-Chieh Chiu, Cheng-Rung Huang, Der-Yen Lee, Geen-Dong Chang, Ting-Chen Chou, Jenn-Wei Chen, and **Chang-Shi Chen**. A multi-omic analysis reveals the role of fumarate in regulating the virulence of Enterohemorrhagic *Escherichia coli*. ***Cell Death Dis*.** 2018 Mar 7;9(3):381.

8. Huan-Da Chen, Cheng-Yuan Kao, Bang-Yu Liu, Shin-Whei Huang, Cheng-Ju Kuo, Jhen-Wei Ruan, Yen-Hung Lin, Cheng-Rung Huang, Yu-Hung Chen, Horng-Dar Wang, Raffi V. Aroian, and **Chang-Shi Chen**. HLH-30/TFEB-mediated autophagy functions in a cell-autonomous manner for epithelium intrinsic cellular defense against bacterial pore-forming toxin in *C. elegans*. ***Autophagy*.** 2017 Feb;13(2):371-385.

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專長說明：

PROTAC/PhosTAC/Induced Proximity/Chemical Biology/Targeted Protein Degradation/Targeted Protein Dephosphorylation/Drug Discovery/Functional Genomics

研究興趣:

我們的研究主要聚焦在與人體疾病相關的蛋白質修飾。許多人類疾病已經發現與不正常的蛋白質修飾相關，例如癌症及神經退化疾病。然而，我們對於這些不正常的蛋白質修飾與疾病的關聯性仍有許多未知，且現有的工具仍無法有效調控。利用化學生物學鄰近誘導的最新技術，我們將研發新的小分子、胜肽或催化型藥物模組，例如蛋白質降解或磷酸化標靶嵌合體(PROTAC/PhosTAC)等雙功能分子等，讓我們能專一標靶特定蛋白質並進行細胞內修飾，以了解不同轉譯後修飾對其蛋白質功能的影響及其與疾病的關聯性。

近五年代表作:

1. Yu-Yu Chen*, Dong-Ting Ke*, Yen-Chun Lee*, Chun-Hsin Yeh, Yu-Ching Ko, Meng-Han Tu, Chien-Hung Yu, Zhenyi Hu, **Po-Han Chen**[#]. TogoPhosTAC: A Ready-To-Go and Adaptable Targeted Protein Dephosphorylation System. Research Square, preprint (2025)(*co-first author)([#]correspondence)
2. Zhenyi Hu*, **Po-Han Chen***, Wenxue Li*, Mackenzie Krone, Sijin Zheng, Jacques Saarbach, Ines Urquizo Velasco, John Hines, Yansheng Liu, Craig M. Crews. EGFR targeting PhosTACs as a dual inhibitory approach reveals differential downstream signaling. ***Science Advances*** (2024)(*co-first author)
3. Zhenyi Hu*, **Po-Han Chen***, Wenxue Li, Todd Douglas, John Hines, Yansheng Liu, and Craig M Crews. Targeted dephosphorylation of tau by phosphorylation targeting chimeras (PhosTACs) as a therapeutic modality. ***Journal of the American Chemical Society*** (2023) (*co-first author)
4. Alexander R Kovach, Kristianne M Oristian, David G Kirsch, Rex C Bentley, Changde Cheng, Xiang Chen, **Po-Han Chen**, Jen-Tsan Ashley Chi, and Corinne M Linardic. Identification and targeting of a HES1-YAP1-CDKN1C axis in fusion-negative rhabdomyosarcoma. ***Molecular Oncology*** (2022)
5. **Po-Han Chen***, Zhenyi Hu*, Elvira An, Ifunanya Okeke, Sijin Zheng, Xuanmeng Luo, Angela Gong, Saul Jaime-Figureroa, and Craig M Crews. Modulation of phosphoprotein activity by phosphorylation targeting chimeras (PhosTACs). ***ACS Chemical Biology*** (2021) 16, 12, 2808-2815 (*co-first author)
6. **Po-Han Chen**, and Jen-Tsan Chi. Unexpected zinc dependency of ferroptosis – what is in a name? ***Oncotarget*** (2021) 12(12):1126
7. Chao-Chieh Lin, Wen-Hsuan Yang, Yi-Tzu Lin, Xiaohu Tang, **Po-Han Chen**, Chien-Kuang Ding, Dan Chen Qu, James V. Alvarez and Jen-Tsan Chi. EMT-driven DDR2 expression in breast cancer regulates ferroptosis through the Hippo pathway. ***Oncogene*** (2021) 40(11):2018-2034
8. Wen-Hsuan Yang, Chao-Chieh Lin, Jianli Wu, Pei-Ya Chao, Kuan Chen, **Po-Han Chen**, and Jen-Tsan Chi. The Hippo pathway effector YAP promotes ferroptosis via the E3 Ligase SKP2. ***Molecular Cancer Research*** (2021) 19(6):1005-1014
9. **Po-Han Chen***, Jianli Wu*, Yitong Xu, Chien-Kuang Cornelia Ding, Alexander A. Mestre, Chao-Chieh Lin, Wen-Hsuan Yang, and Jen-Tsan Chi. Zinc transporter ZIP7 is a novel determinant of ferroptosis. ***Cell Death and Disease*** (2021) 12(2):1-12 (*co-first author)
10. Katherine K. Slemmons, Michael D. Deel, Yi-Tzu Lin, Kristianne M. Oristian, Nina Kuprasertkul, Katia C. Genadry, **Po-Han Chen**, Jen-Tsan Ashley Chi, and Corinne M. Linardic. A method to culture human alveolar rhabdomyosarcoma cell lines as rhabdospheres demonstrates an enrichment in stemness and notch signaling. ***Biology Open*** (2021) 10(2):bio050211

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專長說明：

Immunology, Cardiovascular and renal diseases, Disease animal models, Tissue fibrosis

研究興趣:

1. IL-1 family cytokines and inflammatory diseases
2. Dynamic regulation of immune cell populations in tissue injury
3. Development of therapeutics for treating inflammatory diseases
4. Animal models of cardiovascular and kidney diseases
5. Endothelial-to-mesenchymal transition in tissue repair and fibrosis

近五年代表作:

1. Yamagishi R, Kamachi F, Nakamura M, Yamazaki S, Kamiya T, Takasugi M, Cheng Y, Nonaka Y, Yukawa-Muto Y, Thuy L, Harada Y, Arai T, Loo TM, Yoshimoto S, Ando T, Nakajima M, Taguchi H, Ishikawa T, Akiba H, Miyake S, Kubo M, Iwakura Y, Fukuda S, **(Chen WY)**, Kawada N, Rudensky A, Nakae S, Hara E, Ohtani N*. Gasdermin D-mediated release of IL-33 from senescent hepatic stellate 2 cells promotes obesity-associated hepatocellular carcinoma. ***Science Immunology*** 2022 Jun 24;7(72):eabl7209.
2. Kuo CF+, **(Chen WY)**+, Yu HH, Tsai YH, Chang YC, Chang CP, Tsao Nina*. IL-33/ST2 axis plays a protective effect in Streptococcus pyogenes infection through strengthening of the innate immunity. ***International Journal of Molecular Sciences***. 2021 Sep 29;22(19):10566.
3. **(Chen WY)***, Wu YH, Tsai TH, Li RF, Lai AC, Li LC, Yang JL, Chang YJ*. Group 2 innate lymphoid cells contribute to IL-33-mediated alleviation of cardiac fibrosis. ***Theranostics.*** 2021, 11(6):2594-2611. (*co-correspondence)
4. Tzeng YR, Lee CH, (**Chen WY)**, Yang JL, Tzeng HT*. Inhibition of plasminogen activator inhibitor-1 blocks programmed death ligand 1 endocytosis and improves the response of melanoma cells to immune checkpoint blockade. ***Journal of Investigative Dermatology***. 2021, 141(11):2690-2698.e6.
5. Lu SW, Pan HC, Hsu YH, Chang KC, Wu LW, **(Chen WY)**, Chang MS*. IL-20 antagonist suppresses PD-L1 expression and prolongs survival in pancreatic cancer models. ***Nature Communications.*** 2020, 11(1):4611.
6. Wu YH, Lai AC, Chi PY, Thio CL, **(Chen WY)**, Tsai CH, Lee YL, Lukacs NW, Chang YJ*. Pulmonary IL-33 orchestrates innate immune cells to mediate RSV-evoked airway hyperreactivity and eosinophilia. ***Allergy.*** 2020, 75(4):818-830.
7. Sung HY, (**Chen WY**), Huang HT, Wang CY, Chang SB, Tzeng SF. Downregulation of interleukin-33 expression in oligodendrocyte precursor cells impairs oligodendrocyte lineage progression. ***Journal of Neurochemistry.*** 2019, 150(6):691-708.
8. Weng YH^{+}, (**Chen WY**)$^{+}$, Lin YL, Wang JY*, and Chang MS*. Blocking IL-19 signaling ameliorates allergen-induced airway inflammation. ***Frontiers in Immunology***. 2019, 19:968 (+co-first author)
9. Li LC, Yang JL, Lee WC, Chen JB, Lee CT, Wang PW, Vaghese Z, (**Chen WY**)*. Palmitate aggravates proteinuria-induced cell death and inflammation via CD36-inflammasome axis in the proximal tubular cells of obese mice. ***American Journal of Physiology-Renal Physiology.*** 2018, 315(6) F1720-F1731 (*correspondence)
10. (**Chen WY**)*****, Yang JL, Wu YH, Li LC, Li RF, Chang YT, Dai LH, Wang WC, Chang YJ*. IL-33/ST2 axis mediates hyperplasia of intrarenal urothelium in obstructive renal injury. ***Experimental and Molecular Medicine***. 2018, 50(4):1-11. (*co-correspondence)

鄭宏祺 *(Cheng, Hung-Chi, Ph.D.)*

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研究興趣：

1. 癌症轉移所需之粘著分子(Adhesion molecules; 包含纖連蛋白[fibronectin])及胞外基質(extracellular matrix)與腫瘤微環境的研究
2. 阻斷懸浮癌細胞fibronectin及內皮細胞dipeptidyl peptidase IV(DPP IV)間粘著反應來抑制癌症轉移，包括結合位點胜肽抑制劑、植化素抑制劑、癌症疫苗、特異巡弋標靶轉移癌細胞
3. 探討懸浮癌細胞表面fibronectin多聚體之組裝的分子機制進而研發抗癌轉移小分子藥物
4. CD26 (DPP IV) 在癌症免疫學及免疫治療上之重要性與應用

近五年代表作：* means corresponding author

1. Chih-Wei Chen, Cheng-Han Yang, Yuan-Ho Lin, Ya-Chin Hou, Tain-Junn Cheng, Sheng-Tsung Chang, Yu-Hua Huang, Shang-Ting Chung, Chung-Ching Chio, Yan-Shen Shan, **Hung-Chi Cheng***, and Wen-Tsan Chang* **(2021, Apr)**. The Fibronectin Expression Determines the Distinct Progressions of Malignant Gliomas via Transforming Growth Factor-Beta Pathway. ***International Journal of Molecular Sciences***, 22(7), 3782. (2019 JCR IF=4.556) (Rank=48/177(27.12%) Chemistry, Multidisciplinary)
2. Hong-Yi Chang, Chi-Hua Lee, Yi-Syuan Li, Jing-Tong Huang, Sheng-Hui Lan, Yi-Fang Wang, Wu-Wei Lai, Yi-Ching Wang, Yan-Ju Lin, Hsiao-Sheng Liu, **Hung-Chi Cheng* (2020, Nov)**. MicroRNA-146a suppresses tumor malignancy via targeting vimentin in esophageal squamous cell carcinoma cells with lower fibronectin membrane assembly. ***Journal of Biomedical Science***, 27(1):102. (2019 JCR IF= 5.762) (Rank=17/139(12.23%) Medicine, Research and Experimental)
3. Li-Tzu Huang, Chen-Lung Tsai, Shin-Huei Huang, Ming-Min Chang, Wen-Tsan Chang, Li-Hsin Cheng and **Hung-Chi Cheng* (2020, Nov)**. Depleting RhoA/Stress Fiber-Organized Fibronectin Matrices on Tumor Cells Non-Autonomously Aggravates Fibroblast-Driven Tumor Cell Growth. ***International Journal of Molecular Sciences***, 21(21), 8272. (2019 JCR IF=4.556) (Rank=48/177(27.12%) Chemistry, Multidisciplinary)
4. Tsung-Cheng Lin, Cheng-Han Yang, Li-Hsin Cheng, Wen-Tsan Chang, Yuh-Rong Lin and **Hung-Chi Cheng* (2019, Dec)**. Fibronectin in Cancer: Friend or Foe. ***Cells***, 9(1), 27. (2019 JCR IF=4.366) (Rank=70/195(35.9%), Cell biology).
5. Yu-Shiuan Wang, Hong-Tai Tzeng, Chung-Han Tsai, **Hung-Chi Cheng**, Wu-Wei Lai, Hsiao-Sheng Liu, Yi-Ching Wang (2018, Nov). VAMP8, a vesicle-SNARE required for RAB37-mediated exocytosis, possesses a tumor metastasis suppressor function. ***Cancer Letters***, 28; 437: 79-88. (2019 JCR IF=7.360) (Rank=30/244(12.29%), Oncology)
6. Po-Lin Tseng, Wei-Hsuan Wu, Tsung-Hui Hu, Chih-Wei Chen, **Hung-Chi Cheng**, Chien-Feng Li, Wen-Hui Tsai, Hui-Ju Tsai, Meng-Che Hsieh, Jiin-Haur Chuang and Wen-Tsan Chang.(2018, Feb). Decreased succinate dehydrogenase B in human hepatocellular carcinoma accelerates tumor malignancy by inducing the Warburg effect. ***Scientific Reports***, 15; 8(1):3081. (2019 JCR IF=3.998) (Rank=17/71(23.94%), Multidisciplinary Sciences)
7. Rong-Jane Chen, Hsiao-Che Kuo, Li-Hsin Cheng, Yu-Hsuan Lee, Wen-Tsan Chang, Bour-Jr Wang, Ying-Jan Wang, **Hung-Chi Cheng* (2018, Jan)**. Apoptotic and Nonapoptotic Activities of Pterostilbene against Cancer. ***International Journal of Molecular Sciences***, 19, 287. (2019 JCR IF=4.556) (Rank=48/177(27.12%) Chemistry, Multidisciplinary).
8. Tsung-Cheng Lin, Ying-Chih Liao, Wen-Tsan Chang, Cheng-Han Yang, Li-Hsin Cheng, Megan Cheng, **Hung-Chi Cheng* (2018, Jun)**. The Establishment of a Lung Colonization Assay for Circulating Tumor Cell Visualization in Lung Tissues. ***The Journal of Visualized Experiments***, (136), e56761, (2019 JCR IF=1.163) (Rank=45/71 (63.4%) Multidisciplinary Sciences).
9. Ya-Ting Wang, Jocelyn Chen, Chou-Wei Chang, Jayu Jen, Tzu-Yu Huang, Chun-Ming Chen, Roger Shen, Suh-Yuen Liang, I-Cheng Cheng, Shuenn-Chen Yang, Wu-Wei Lai,Kuang-Hung Cheng, Tao-Shih Hsieh, Ming-Zong Lai, **Hung-Chi Cheng**, Yi-Ching Wang, and Ruey-Hwa Chen **(2017, Aug)**. Ubiquitination of tumor suppressor PML regulates prometastatic and immunosuppressive tumor microenvironment. ***Journal of Clinical Investigation***, 127(8):2982-2997. (2019 JCR IF=11.864) (Rank=3/139 (2.16%) Medicine, Research and Experimental)
10. Yi-Ching Wang, Hong-Tai Tzeng, Chung-Han Tsai, Yi-Ting Yen, **Hung-Chi Cheng**, Yi-Chieh Chen, Shih-Wen Pu, Yu-Shiuan Wang, Yan-Shen Shan, Yau-Lin Tseng, Wu-Chou Su, Wu-Wei Lai and Li-Wha Wu **(2017, May)**. Dysregulation of Rab37-Mediated Cross-talk between Cancer Cells and Endothelial Cells via Thrombospondin-1 Promotes Tumor Neovasculature and Metastasis. ***Clinical Cancer Research***, 23(9):2335-2345. (2019 JCR IF=10.107) (Rank=18/244 (7.38%) Oncology)
11. Ying-Jan Wang, Jing-Fang Lin, Li-Hsin Cheng, Wen-Tsan Chang, Ying-Hsien Kao, Ming-Min Chang, Bour-Jr Wang and **Hung-Chi Cheng* (2017, Mar)**. Pterostilbene prevents AKT-ERK axis-mediated polymerization of surface fibronectin on suspended lung cancer cells independently of apoptosis and suppresses metastasis. ***Journal of Hematology & Oncology***, 10(1):72. (2019 JCR IF=11.059) (Rank=3/76 (3.95%) Hematology)
12. Chung-Han Tsai, **Hung-Chi Cheng**, Yu-Shiuan Wang, Pinpin Lin, Jayu Jen, I-Ying Kuo, Ying-Hua Chang, Pao-Chi Liao, Ruey-Hwa Chen, Wei-Chien Yuan, Han-Shui Hsu, Muh-Hwa Yang, Ming-Ta Hsu, Chu-Yi Wu, Yi-Ching Wang. **(2014, Sep)**. Small GTPase Rab37 targets tissue inhibitor of etalloproteinase 1 for exocytosis and thus suppresses tumor metastasis. ***Nature communications***,5:4804. (2019 JCR IF=12.121) (Rank=6/71 (8.45%) Multidisciplinary Sciences)

劉卜慈 (*Pu Ste Liu. Ph.D.*)

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專長說明：

免疫學、免疫代謝體學、代謝症候群、腫瘤免疫學

研究興趣:

1. 探討訓練免疫在肥胖和肥胖所引發動脈粥狀硬化的機轉
2. 解構粒線體調控腫瘤巨噬細胞免疫反應及功能之機轉

近五年代表作:

1. **Liu PS***, Chen YT, Li XY, Hsueh PC, Tzeng SF, Shi PZ, Xie X, Parik S, Fendt S-M, Ho PC*. CD40 signal rewires fatty acid and glutamine metabolism for stimulating macrophage anti-tumorigenic functions. *Nature Immunology, 2023, 24, 452-62.*

2. Raines LN, Zhao H, Wang Y, Chen H-Y, Gallart-Ayala H, Hsueh P-C, Cao W, Koh Y, Alamonte-Loya A, **Liu PS**, Ivanisevic J, Lio C-WJ, Ho P-C, Huang SC-C. PERK is a critical metabolic hub for immunosuppressive function in macrophages. *Nature Immunology, 2022, 23, 431–445.*

3. Yu YR, Imrichova H, Wang H, Chao T, Xiao Z, Gao M, Rincon-Restrepo M, Franco F, Genolet R, Cheng WC, Jandus C, Coukos G, Jiang YF, Lo-casale JW, Zippelius A, **Liu PS**, Tang L, Bock C, Vannini N, Ho PC. Disturbed mitochondrial dynamics in CD8 + TILs reinforce T cell exhaustion. *Nature Immunology, 2021, 21, 1540–1551.*

4. Xie X, **Liu PS**, Percipalle P. Analysis of global transcriptome changes in mouse embryonic fibroblasts after dsDNA and dsRNA viral mimic stimulation. *Frontiers in Immunology, section Molecular Innate Immunity, 2019, 17, April.*

王憶卿 (*Wang, Yi-Ching. Ph.D.*)

藥理學研究所　講座教授兼所長　分機：5502　Email: ycw5798@mail.ncku.edu.tw

專長與研究興趣:

肺癌分子機制與轉譯研究：

1. 腫瘤微環境 (tumor microenvironment) 研究。
   A、免疫查核點 (immune checkpoint) 之轉譯後修飾分析 (post-translational modifications)。
   B、癌細胞與免疫細胞傳輸系統 (protein trafficking) 與訊息傳遞分析。
   C、細胞 exocytosis 與分泌體 (secretomics) 研究。
2. 癌症生物學 (cancer biology) 研究。
   A、轉錄調控與訊息傳遞分析。
   B、抗藥性與腫瘤轉移機轉探討。
   B、抗癌藥物與抗體開發。

近五年代表作:

1. Hsieh HC, Young MJ, Chen KY, Su WC, Lin CC, Yen YT, Hung JJ*, **Yi-Ching Wang***. **2025**. Inhibition of USP24 augments T-cell anti-tumor immunity by destabilizing PD-1. ***Science Advances*** DOI: 10.1126/sciadv.adt4258.
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3. Kuo WT, Kuo IY, Hsieh HC, Wu ST, Su WC, **Yi-Ching Wang***. **2024**. Rab37 mediates trafficking and membrane presentation of PD-1 to sustain T cell exhaustion in lung cancer**.** ***J Biomed Sci.*** 7;31(1):20.
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研究興趣:

1. 基因體醫學於癌症治療策略之應用

本實驗室運用次世代定序技術(Next generation sequencing, NGS)及基因體巨量生物資訊分析來解構癌症病患的全基因圖譜，並結合基礎研究及臨床醫學技術，全面探尋可能之基因變異及其致病機轉，從中找到疾病之預測及防治之道，以應用於預測病患癌症復發狀況、提供新治療建議與找到臨床可用的預測指標。

2. 神經保護藥物開發

癌症化學治療容易伴隨嚴重的神經損傷副作用，但目前仍無有效的方針可避免此嚴重效應。本研究團隊已建立高通量神經保護劑篩選平台，由不同分子藥庫篩選出對抗化療副作用之神經保護先導藥物(lead compounds)，已進入臨床前試驗，進一步進行化學結構及藥物活性之最佳化研究，預期大幅提升癌症病人生活品質。

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研究興趣：

1. **癌症基因的研究:**

探討DNA損傷修復和細胞自嗜 (autophagy) 相互調控之分子機制。

2. **抗癌藥物的研究:**

研發新穎的奈米化存活素標靶藥物 (anti-BIRC5/Survivin nano-drugs)。

3. **乳癌的研究:**

探討荷爾蒙療法 (endocrine therapy) 於雌性激素受體陽性之乳癌其抗藥性誘發之機制、研發在雌激素受體陽性乳癌治療上能取代 Tamoxifen 的新藥物。

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研究興趣：

1. Exploring the cellular and molecular mechanisms of long-term synaptic plasticity, metaplasticity, and structural plasticity.
2. Studying the cellular and molecular mechanisms that contribute to neurological disorders, such as stress-related psychiatric disorders, drug addiction, pain, autism spectrum disorders, and neurodevelopmental disorders.
3. Investigating the cellular and molecular mechanisms that regulate adult neurogenesis, including its developmental processes and associated cognitive functions.
4. Interrogating the gut-to-brain neural circuits and molecular signaling for memory encoding and mood regulation.

研究方法：電氣生理學、蛋白化學、神經化學、分子生物學、光遺傳學

近五年代表作：

1. Lin YT, Chen CC, Huang CC, Nishimori K, **Hus KS.*** (2017) Oxytocin stimulates hippocampal neurogenesis via oxytocin receptor expressed in CA3 pyramidal neurons. Nat. Commun. 8:537.
2. Lin YT, Hsieh TY, Tsai TC, Chen CC, Huang CC, **Hsu KS.*** (2018) Conditional deletion of hippocampal CA2/CA3a oxytocin receptor impairs the persistence of long-term social recognition memory in mice. J. Neurosci. 38(5):1218-1231.
3. Yang CY, Yu TH, Wen WL, Lin P, **Hus KS.*** (2019) Conditional deletion of CC2D1A reduces hippocampal synaptic plasticity and impairs cognitive function through Rac1 hyperactivation. J. Neurosci. 39(25):4959-4975.
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研究興趣：探討人類新陳代謝疾病 (Insulin resistance、糖尿病及其引起之併發症等) 之分子病理機轉。主要研究主題為：

1.胰島素抵抗和β細胞缺陷

2.週邊組織血清素系統在代謝體內平衡扮演的角色

3.RNA編輯對人類代謝疾病之影響

4.代謝疾病與情緒障礙之間的相關性

研究方法: 細胞培養、基因轉殖、細胞和分子生物學技術及動物模式

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專長與研究興趣:

動物行為學：以果蠅為動物模式探討老年痴呆症的分子機制，主要利用乙型－澱粉樣蛋白（beta amyloid)轉基因果蠅去了解乙型－澱粉樣蛋白在疾病過程中如何造成學習與記憶喪失及細胞死亡

細胞影像學：研究細胞是如何釋放及接受傳導物質，主要用分泌型細胞株探討傳導物質釋放的分子調控機理。

近五年代表作:

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10. Chiang HC, Wang L, Xie Z, Yau A, Zhong Y. PI3 kinase signaling is involved in Abeta-induced memory loss in Drosophila. *Proc Natl Acad Sci U S A.* 2010 107(15):7060-5.
11. Chiang HC, Iijima K, Hakker I, Zhong Y. Distinctive roles of different beta-amyloid 42 aggregates in modulation of synaptic functions. *FASEB J.* 2009 23(6):1969-77.

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研究興趣:

(1) 神經退化性疾病 Alzheimer's disease 之病理機制探討

(2) 憂鬱症與失智症相關性研究

近五年代表作:

1. Chun-Lin Su, Chun-Wei Su, **Ya-Hsin Hsiao**, Po-Wu Gean (2016). Epigenetic regulation of BDNF in the learned helplessness-induced animal model of depression. Journal of Psychiatric Research 76, 101-10.

2. Hui-Chi Hung*, **Ya-Hsin Hsiao***, Po-Wu Gean (2015). Sonic hedgehog signaling regulates amygdalar neurogenesis and extinction of fear memory. European Neuropsychopharmacology 25(10):1723-32.

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研究興趣:

腫瘤轉移及抗藥性：

轉移性的癌細胞較惡性並且具有抗藥性而成為癌症主要的死因，存在循環系統中的轉移性細胞不僅能夠抗失巢凋亡，也能躲過免疫偵測而達成轉移的目的，然而存在腫瘤微環境中的一群訊號分子，能特異性的啟動腫瘤轉移侵犯到血管的機制，而癌細胞如何滲透及特異性的植入遠端組織，其中的相關分子及機轉尚未釐清，並且高度與轉移復發及病人存活率相關。

研究議題及策略：

一般而言，有關癌轉移的研究皆聚焦在原位癌或是已經轉移成功的組織中，然而循環系統中的微環境其重要性在轉移過程中常被忽略，如何調控腫瘤細胞在無依存的微環境存活及促進遠端轉移仍然未知。我們使用細胞及動物模式，並且根據其臨床相關性，來研究細胞激素，包括 PGE2, ANGPTL4 及 PTX3 如何調控頭頸癌及大腸直腸癌的抗失巢凋亡、轉移及抗藥性，這些主要議題的探討將能應用於相關癌症的治療及抗藥性，研究結果將能釐清發炎因子 COX-2 如何影響 ANGPTL4 及 PTX3 的活化與促進腫瘤轉移的關係，以及 COX-2 抑制劑，例如希樂葆及阿斯匹靈對於在癌正轉移預防的效果評估。

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1. Shieh JM, Chang TW, Wang JH, Liang SP, Kao PL, Chen LY, Yen CJ, Chen, YJ, Chang WC and **Chen BK** (2023) RNA-binding protein-regulated fibronectin is essential for EGFR-activated metastasis of head and neck squamous cell carcinoma. *FASEB J* **37**, e23206
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5. Muhammad Irham L, Chou WH, Wang YS, Adikusuma W, Sung-Ching Wong H, Aryani Perwitasari D, Huang WC, **Chen BK***, Yang HI and Chang WC (2020) Evaluation for the Genetic Association between Store-Operated Calcium Influx Pathway (STIM1 and ORAI1) and Human Hepatocellular Carcinoma in Patients with Chronic Hepatitis B Infection. *Biology (Basel)* **9,** E388 (*: correspondence)
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專長說明： 臨床心臟病學，腫瘤心臟病學，幹細胞，心臟再生研究

研究興趣:

1. 幹細胞再生醫學研究

心肌細胞一旦受損，幾乎是無法再生。利用幹細胞進行心肌細胞再生，是目前研究趨勢之一。本研究團隊發展出低免疫源性「人類誘導性多能幹細胞」，進行再生醫學臨床前研究。另外，本團隊也利用小動物以及大動物心肌梗塞模式，探討心肌再生的機制。最終的目標是經由完整的臨床前試驗，逐一解決目前心臟再生醫療的困境，以期將心臟再生醫療帶入臨床，用以治療病患。

2. 腫瘤心臟病學研究

癌症治療引起的心臟毒性是臨床上嚴峻課題，但目前仍無有效的方法可治療或是避免此嚴重副作用。本研究團隊利用「人類誘導性多能幹細胞分化成心肌細胞」建立心肌細胞之研究平台，以及小動物以及大動物模式，進行致病機轉與臨床前試驗的研究。

研究方法：心臟電氣生理學、細胞和分子生物學技術、人類誘導性多能幹細胞模式、小動物以及大動物人類疾病模式

近五年代表作:

1. Fang, Y.H., Wang, S.P.H., Liao, I.C., Tsai, K.J., Huang, P.H., Yang, P.J., Yen, C.J., Liu, P.Y., Shan, Y.S., **Liu, Y.W.*** (2023) HLA-E^{high} /HLA-G^{high} /HLA-II^{low} Human iPSC-Derived Cardiomyocytes Exhibit Low Immunogenicity for Heart Regeneration. *Advanced Healthcare Materials* 12(29):e2301186. doi: 10.1002.
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專長說明：

奈米修飾技術、病毒學、細胞工程、高分子設計與合成

研究興趣:

有鑒於 2015 年 10 月美國食品藥物管理局(US Food and Drug Administration)通過第一例臨床病毒治療(virotherapy)，但侷限於腫瘤局部注射方式(intra-tumoral injection)，導致無法廣泛使用於腫瘤治療。我們團隊透過多種化學修飾方法與奈米技術來改善病毒治療無法用於全身循環的問題。目前也用於免疫檢查點抑制劑(immune checkpoint inhibitor)與 mRNA。

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7. Liao, Z.X., Huang, K.Y., Kempson I.M., Li, H.J., **Tseng, S.J.***, and Yang, P.C.* (2020) Nanomodified strategies to overcome EGFR-tyrosine kinase inhibitors resistance in non-small cell lung cancer. *Journal of Controlled Release* 324:482-492.

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專長說明: 磁振造影技術、生醫影像分析

研究興趣: 各項磁振神經影像技術(magnetic resonance imaging, MRI)如功能性磁振造影(functional MRI)、擴散磁振造影(diffusion MRI)、磁振頻譜與創新掃描技術，並將上述磁振造影技術應用至臨床前動物造影以及臨床的腦影像研究。研究主題包含：(1) 解析發育過程中的腦神經纖維連結；(2) 發展小動物磁振造影技術；(3) 探討失智症患者的大腦神經纖維微結構與功能網路連結。結合磁振神經影像處理分析技術，促使我們能夠探討腦的功能與微結構網路連結情形。

近五年代表作:

1. Hsieh, Y. L.[#], **Huang, S. M.**[#], Yu, S., Chao, T. N., Chiang, C. W., Kan, Y. Y, Chang, Y. S., Kuo, L. W.*, and Yu, H. S.* Chronic blue light exposure induced spatial anxiety in an adolescent mouse model: *Per2* upregulation and altered brain resting-state functional activity. *NeuroImage*, 2025. (Accepted). doi: 10.1016/j.neuroimage.2025.121259 ([#]Equal contribution)
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5. **Huang, S. M.**[#], Wu C. Y.[#], Lin Y. H., Hsieh, H. H., Yang H. C., Chiu, S. C., Peng, S. L.* (2022) Differences in brain activity between normal and diabetic rats under isoflurane anesthesia: A resting-state functional MRI study. *BMC Medical Imaging*, 22:136. doi: 10.1186/s12880-022-00867-6 ([#]Equal contribution)
6. Altunkaya, S.[#], **Huang, S. M.**[#], Hsu, Y. H., Yang, J. J., Lin C. Y., Kuo, L. W., Tu, M. C.* (2022) Dissociable Functional Brain Networks Associated with Apathy in Subcortical Ischemic Vascular Disease and Alzheimer's Disease. *Frontiers in Aging Neuroscience*, 13:717037. doi: 10.3389/fnagi.2021.717037 ([#]Equal contribution)

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研究興趣：

(1) Underlying Mechanisms for the Methamphetamine- and ketamine-induced Toxicity

(2) Signaling Pathways and Molecular Mechanisms for Cocaine-related Learning, Memory, Retrieval and Reconsolidation

(3) Effects of Stress on Motivation, Cognitive Functions and the respective underpinnings (CNS, Endocrine, and Immune System)

(4) Biological Mechanisms of Social Support and Conformity

近五年代表作：

1. L-H. Sun, W-Y. Tzeng, Y-H. Wang, W-T. Deng, **L. Yu** (Correspondence Author), Chianfang G. Cherng, 2019, Relevance of number and physiological status of conspecifics in preventing stress-induced decreases in newly proliferated cells and neuroblasts. Psychopharm, 236:3329–3339.
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專長與研究興趣:

1. 有機磷中毒及解毒機制
2. 成癮藥物中毒致死機制
3. 癲癇猝死機制
4. 神經細胞與膠細胞交互作用參與中風後誘發中樞神經調控循環反應異常之機理
5. 表關基因修飾於上呼吸道消化癌之角色

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1. Chuang YC, Chen SD, Lin TK, Chang WN, Lu CH, Liou CW, Chan SHH, **Chang AYW.** Transcriptional upregulation of nitric oxide synthase II by nuclear factor-κB promotes apoptotic neuronal cell death in the hippocampus following experimental status epilepticus. *Journal of Neuroscience Research,* 2010, 88:1898-1907.
2. Chou JLJ, Wu CHY, Tsai CY, **Chang AYW**, Chan SHH. Proteomic investigation of a neural substrate intimately related to brain death. *Proteomics*, 2011, 11:239-248.
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12. Chen CH, **Chang AYW**, Li SH, Tsai HT, Shiu LY, Su LJ, Wang WL, Chiu TJ, Luo SD, Huang TL, Chien CY. Suppression of Aurora-A-FLJ10540 signaling axis prohibits the malignant state of head and neck cancer. *Molecular Cancer*. 2015, 14:83. doi: 10.1186/s12943-015-0348-7.

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研究興趣：

We employed molecular, cellular and mechanobiological approach to study pathophysiological mechanisms of cancer, organ fibrosis and keloid. Microenvironment of fibrosis tissue is constituted by complex interactions of parenchymal, mesenchymal cells, vascular and inflammatory cells. We used advanced technology of confocal microscope co-axis with atomic force microscope to assess single fiber stiffness in normal and fibrotic tissues. We also applied single cell RNA sequence (scRNAseq) and spatial transcriptomics for unveiling pathological mechanism. We are currently developing technology for conceptual breakthrough in assessment of structural characteristics of single collagen fiber under physiological and pathophysiological conditions, including:

1. Exploration of mechanobiological landscape (mechanomics) of the tissue and organ.
2. Combination of spatial transcriptomics with mechanomics for fibrosis studies.

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6. Wu LY, Han CL, Lin HH, Tang MJ. Ha-Ras^{V12}-Induced Multilayer Cellular Aggregates are Mediated by Rac1 Activation Rather than YAP Activation. Biomedicines 10(5), 977, 2022.
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8. Kuo CH, Lee GH, Wu HL, Huang JY and Tang MJ. Breaking the symmetry of cell contractility drives tubulogenesis via CXCL1 polarization. Proc. Natl. Acad. Sci. (In press) 2024

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研究興趣：

1. 神經退化性疾病之基因轉殖大小動物模式建立
2. microRNA 於神經退化性疾病的影響
3. microRNA 對神經保護功能的調控機制
4. 應用基因治療於人類遺傳性疾病的探討
5. 胚胎發育及胚胎幹細胞的研究

高影響力代表作：

1. Chan SC, Tung CW, Lin CW, Tung YS, Wu PM, Cheng PC, Chen CM, **Yang SH*.** 2023. miR-196a provides antioxidative neuroprotection via USP15/Nrf2 regulation in Huntington's disease. **Free Radic Biol Med.** 209(Pt 2):292-300.
2. Yang HI, Huang PY, Chan SC, Tung CW, Cheng PC, Chen CM, **Yang SH*.** 2022. miR-196a enhances polymerization of neuronal microfilaments through suppressing IMP3 and upregulating IGF2 in Huntington's disease. **Mol Ther Nucleic Acids.** 30: 286-299.
3. Tung CW, Huang PY, Chan SC, Cheng PH, **Yang SH*.** 2021. The regulatory roles of microRNAs toward pathogenesis and treatments in Huntington's disease. **J Biomed Sci.** 28(1):59.
4. Yusuf IO, Chen HM, Cheng PH, Chang CY, Tsai SJ, Chuang JI, Wu CC, Huang BM, Sun HS, **Yang SH*.** 2019. Fibroblast growth factor 9 activates anti-oxidative functions of Nrf2 through ERK signalling in striatal cell models of Huntington's disease. **Free Radic Biol Med.** 130:256-266.
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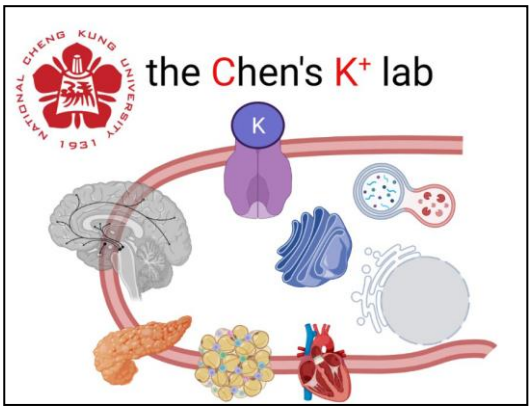
專長與研究興趣:

I express my interest in K^+ channels, as I plan to spend my academic life continuing to understand how K^+ channels are trafficked in the cell and facilitate communication among organs, including the brain, pancreas, adipose tissue and heart (as seen in the logo I designed on the left).



近五年代表作：

1. L.C. Ho, Y. H. Chen, T.Y. Wu, L.Z. Kao, S.Y. Hung, H.H. Liou, **P.C. Chen**, P.J. Tsai, H.K, Lin, Y. C. Lee, H.H. Wang, Y.S. Tsai (2023, Nov). Phosphate burden induces vascular calcification through a NLRP3-caspase 1-mediated pyroptotic pathway. *Life Sciences*, 332:122123 (PMID: 37742736)

2. C. T. Lee, W. H. Tsai, C. C. Chang, **P. C. Chen**, C. S. J. Fann, H. K Chang, S. Y. Liu, M. Z. Wu, P. C. Chiu, ,W. M. Hsu, W. S. Yang, L. P. Lai, W. Y. Tsai, S. B. Yang , P.L. Chen (2023, Nov). Genotype-phenotype correlation in Taiwanese children with diazoxide-unresponsive congenital hyperinsulinism. Frontiers in Endocrinology, 14:1283907 (PMID:38033998)

3. Y.Y. Kuo, H.Y. Tsai, Y.M. Kuo, S.F. Tzeng, P.S. Chen, P. H. Hsu, Y.T. Lin, **P.C. Chen*** (2023, Sep). Glibenclamide promotes FGF21 secretion in interscapular BAT and attenuates depression-like behaviors in male mice with HFD-induced obesity. *Life Sciences*, 328:121900 (PMID:37391066)

4. Y.H. Chen, Y.Y. Kuo, Y.Q. You, Y.T. Lin, **P.C. Chen*** ((2023, March). Endonuclease VIII-like 1 deficiency potentiates nigrostriatal dopaminergic neuron degeneration in a male mouse model of Parkinson's disease. *Journal of Neurochemistry*, 165:741-755 (PMID:36840377)

5. C.H. Lin, Y.C. Lin, SB Yang, **P.C. Chen*** (2022, April). Carbamazepine promotes surface expression of mutant Kir6.2-A28V ATP-sensitive potassium channels by modulating Golgi retention and autophagy. *Journal of Biological Chemistry*,*298*:101904 (PMID:35398096)

6. H.Y. Cho, **P.C. Chen**, T.H. Chuang, M.C. Yu, S.N. Wu (2022, March). Activation of voltage-gated Na+ current by GV-58, a known activator of Cav channels. *Biomedicines*, 10:721 (PMID:35327523)

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8. Y.Y. Lam, S.F. Tsai, **P.C. Chen**, Y.M. Kuo, Y.W. Chen (2021, Aug). Piloglitazone rescues high-fat diet-induced depression-like phenotypes and hippocampal astrocytic deficits in mice. *Biomed Pharmacother*. 140: 111734. (PMID: 34022606)

9. Y.Y. Kuo, J.K. Lin, Y.T. Lin, J.C. Chen, Y.K. Kuo, P.S. Chen, S.N. Wu, **P.C. Chen*** (2020, Aug). Glibenclamide restores dopoaminergic reward circuitry in obese mice through interscapular brown adipose tissue. *Psychoneuroendocrinology*, 118:104712. PMID:32479969

顏賢章 *(Shian-Jang Yan, Ph.D.)*

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研究興趣：

1. 為何不同類型功能的細胞使用相同的基因組涉及表觀遺傳過程（epigenetics process)。這些過程必須受到嚴格的監管， 以防止不適當的細胞行為可能導致的人類疾病如癌症和過早老化。
2. 本實驗室利用遺傳、 生化、 分子和細胞生物、 藥理、 和高解析度即時成像技術，並結合果蠅和哺乳動物系統上有效的 遺傳學工具，研究抗老及抗癌的機制。
3. 我們的工作側重於信號傳遞 (signaling transduction pathways) 和染色質因子 (chromatin factors） 之間的網路 (network)，研究表觀遺傳的信號傳遞和染色質因子網路與環境疾病之間的連接。隨著我們更加地瞭解表觀遺傳機制，希望可以 提供新的方法及藥物以預防治療癌症和老年疾病。
4. 我們利用果蠅研究奈米銀對活體生物的影響及其細胞與分子機制。奈米銀是在日常生活中被廣泛使用的材質，主要因為奈米銀有殺菌的效果，然而這樣的應用對活體生物的安全性及作用機制有待進一步探討。

近五年代表作：

1. Che-Wei Chang, Yu-Hshun Chin, Meng-Syuan Liu, Yu-Chia Shen, **Shian-Jang Yan*** (2024, Sep). High sugar diet promotes tumor progression paradoxically through aberrant upregulation of pepck1. **Cellular and Molecular Life Sciences,** 81:396, 1-14. Basel, Switzerland. Scopus Citations=1. 5 year IF=7.7. R/C=44/313, BIOCHEMISTRY & MOLECULAR BIOLOGY
2. Po-Jen Wu, **Shian-Jang Yan*** (2022, Oct). HP1a-mediated heterochromatin formation promotes antimicrobial responses against Pseudomonas aeruginosa infection. ***BMC Biology,*** 20(1):234, 1-16. London, United Kingdom. Scopus Citations=2. 5 year IF=5.4. R/C=15/109, BIOLOGY.
3. Bin-Hsu Mao, Yi-Kai Luo, Bour-Jr Wang, Chun-Wan Chen, Fong-Yu Cheng, Yu-Hsuan Lee, **Shian-Jang Yan***, Ying-Jan Wang* (2022, Jan). Use of an in silico knowledge discovery approach to determine mechanistic studies of silver nanoparticles-induced toxicity from in vitro to in vivo. ***Particle and Fibre Toxicology,*** 19(1):6, 1-25. London, United Kingdom. Scopus Citations=19. 5 year IF=8.8. R/C=5/106, TOXICOLOGY.
4. Che-Wei Chang, Yu-Chia Shen, and **Shian-Jang Yan*** (2021, Dec). HP1a-mediated heterochromatin formation inhibits high dietary sugar-induced tumor progression. ***Cell Death & Disease,*** 12(12):1130, 1-12. London, United Kingdom. Scopus Citations=4. 5 year IF=8.6. R/C=33/205, CELL BIOLOGY.
5. Chia-Jung Yu[#], Dian W. Damaiyanti[#], **Shian-Jang Yan**, Chih-Hsing Wu, Ming-Jer Tang, Dar-Bin Shieh, Peter P. Liu and Ping-Yen Liu (2021, Dec). The Pathophysiologic Role of Gelsolin in Chronic Kidney Disease: Focus on Podocytes. ***International Journal of Molecular Sciences,*** 22(24):13281, 1-13. Basel, Switzerland. Scopus Citations=3. 5 year IF=5.6. R/C=66/313, BIOCHEMISTRY & MOLECULAR BIOLOGY.
6. Zi-Yu Chen, Yu-Chen Su, Fong-Yu Cheng, **Shian-Jang Yan***, and Ying-Jan Wang* (2021, Dec). Lifetime bioaccumulation of silver nanoparticles accelerates functional aging by inactivating antioxidant pathways, an effect reversed by pterostilbene. ***Environmental Science-Nano,*** 8, 3774-3791. London, United Kingdom. Scopus Citations=6. 5 year IF=6.7. R/C=63/358, ENVIRONMENTAL SCIENCES.
7. DJ Klionsky...**Shian-Jang Yan**...et al. (2021, Jan). Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). ***Autophagy,*** 17(1), 1-382. Scopus Citations=1672. 5 year IF=16.8. R/C=13/205, CELL BIOLOGY.
8. Guan-Rong Lai, Yi-Fen Lee, **Shian-Jang Yan***, Huei-Ju Ting* (2020, May). Active vitamin D induced gene-specific hypomethylation in prostate cancer cells developing vitamin D resistance. ***American Journal of Physiology-Cell Physiology***, 318(5), C836-C847. Bethesda, United States of America. Scopus Citations=9. 5 year IF=5.2, R/C=8/85, PHYSIOLOGY.
9. Zi-Yu Chen†, Nian-Jhen Li, Fong-Yu Cheng, Jian-Feng Hsueh, Chiao-Ching Huang, Fu-I Lu, Tzu-Fun Fu, **Shian-Jang Yan†**, Yu-Hsuan Lee*, and Ying-Jan Wang* (2020, Apr). The Effect of the Chorion on Size-Dependent Acute Toxicity and Underlying Mechanisms of Amine-Modified Silver Nanoparticles in Zebrafish Embryos. ***International Journal of Molecular Sciences***, 21(8):2864, 1-20. Basel, Switzerland. Scopus Citations=58. 5 year IF=5.6. R/C=66/313, BIOCHEMISTRY & MOLECULAR BIOLOGY.
10. Rong-Jane Chen, Yu-Ying Chen, Mei-Yi Liao, Yu-Hsuan Lee, Zi-Yu Chen, **Shian-Jang Yan**, Ya-Ling Yeh, Li-Xing Yang, Yen-Ling Lee, Yuan-Hua Wu*, Ying-Jan Wang* (2020, Mar). The Current Understanding of Autophagy in Nanomaterial Toxicity and Its Implementation in Safety Assessment-Related Alternative Testing Strategies. ***International Journal of Molecular Sciences***, 21(7):2387, 1-24. Basel, Switzerland. Scopus Citations=59. 5 year IF=5.6. R/C=66/313, BIOCHEMISTRY & MOLECULAR BIOLOGY.

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研究興趣：

1. Circuit-based approach of gut-brain axis
2. Gut microbiota in the regulation of emotion
3. Gut-derived metabolites in the regulation stress response and innate defensive behavior

近五年代表作 (* corresponding author)：

1. Lai TT, Tsai YH, Liou CW, Fan CH, Hou YT, Yao TH, Chuang HL, **Wu WL***. The gut microbiota modulate locomotion via vagus-dependent glucagon-like peptide-1 signaling. ***npj Biofilms and Microbiomes*.** 2024 Jan 16;10(1):2. PMID: 38228675.
2. Lai TT, Liou CW, Tsai YH, Lin YY, **Wu WL***. Butterflies in the gut: the interplay between intestinal microbiota and stress. ***Journal of Biomedical Science*.** 2023 Nov 28;30(1):92. PMID: 38012609.
3. Liou CW, Cheng SJ, Yao TH, Lai TT, Tsai YH, Chien CW, Kuo YL, Chou SH, Hsu CC, **Wu WL***. Microbial metabolites regulate social novelty via CaMKII neurons in the BNST. ***Brain, Behavior, and Immunity.*** 2023 Oct;113:104-123. PMID: 37393058.
4. Liou CW*, Yao TH, **Wu WL***. Intracerebroventricular delivery of gut-derived microbial metabolites in mice. ***Journal of Visualized Experiments*.** 2022 Jun 2;(184). PMID: 35723471.
5. Wu JT, Sun CL, Lai TT, Liou CW, Lin YY, Xue JY, Wang HW, Chai LMX, Lee YJ, Chen SL, Chang AYW, Hung JH, Hsu CC, **Wu WL***. Oral short-chain fatty acids administration regulates innate anxiety in adult microbiome-depleted mice. ***Neuropharmacology*.** 2022 Aug 15;214:109140. PMID: 35613660.
6. Needham BD*, Funabashi M, Adame MD, Wang Z, Boktor JC, Haney J, **Wu WL**, Rabut C, Ladinsky MS, Hwang SJ, Guo Y, Zhu Q, Griffiths JA, Knight R, Bjorkman PJ, Shapiro MG, Geschwind DH, Holschneider DP, Fischbach MA, Mazmanian SK*. A gut-derived metabolite alters brain activity and anxiety behavior in mice. ***Nature*.** 2022 Feb;602(7898):647-653. PMID: 35165440.
7. **Wu WL***, Adame MD, Liou CW, Barlow JT, Lai TT, Sharon G, Schretter CE, Needham BD, Wang MI, Tang W, Ousey J, Lin YY, Yao TH, Abdel-Haq R, Beadle K, Gradinaru V, Ismagilov RF, Mazmanian SK. Microbiota regulate social behavior via stress response neurons in the brain. ***Nature*.** 2021 Jul;595(7867):409-414. PMID: 34194038.
8. **Wu WL***, Cheng SJ, Lin SH, Chuang YC, Huang EY, Chen CC*. The Effect of ASIC3 Knockout on Corticostriatal Circuit and Mouse Self-grooming Behavior. ***Frontiers in Cellular Neuroscience.*** 2019 Mar 12;13:86. PMID: 30930747.
9. Needham BD, Tang W, **Wu WL***. Searching for the gut microbial contributing factors to social behavior in rodent models of autism spectrum disorder. ***Developmental Neurobiology***. 2018 May;78(5):474-499. PMID: 29411548.
10. Lee YK*, Mehrabian P, Boyajian S, **Wu WL**, Selicha J, Vonderfecht S, Mazmanian SK*. The Protective Role of Bacteroides fragilis in a Murine Model of Colitis-Associated Colorectal Cancer. ***mSphere***. 2018 Nov 14;3(6):e00587-18. PMID: 30429227.

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專長說明： 脂蛋白代謝；非酒精性脂肪肝；宿主代謝與病毒感染；病毒致病機轉

研究興趣:

1.探討載脂蛋白對代謝性疾病及病毒感染的影響

2.研究壓力誘導載脂蛋白 J 伴護蛋白對於脂肪代謝的影響

3.開發緩解細胞內脂肪異位沈積的多肽

近五年代表作:

1. Shuangdi Duan, Nong Qin, Jiayi Pi, Pei Sun, Yating Gao, Lamei Liu, Zenghui Li, Ya Li, Liyang Shi, Qiang Gao, Ye Qiu, Songqing Tan, Chun-Hsiang Wang, Tzu-Ying Chen, Sin-Tian Wang, Kung-Chia Young, **Hung-Yu Sun***. Antagonizing apolipoprotein J chaperone promotes proteasomal degradation of mTOR and relieves hepatic lipid deposition. Hepatology, 2023; 78(4):1182-1199
2. Pin-Nan Cheng, **Hung-Yu Sun**, I-Che Feng, Sin-Tian Wang, Yen-Cheng Chiu, Hung-Chih Chiu, Shih-Chieh Chien, Kung-Chia Young. Reversibility of some oxidative stress markers in chronic hepatitis C patients after receiving direct-acting antiviral agents. J Virus Erad. 2023;9(1):100318.
3. Shuangdi Duan, Jiayi Pi, Chun-Hsiang Wang, Yi-Chou Hou, Chung-Ying Andy Lee, Cheng-Jui Lin, Liyang Shi, Kung-Chia Young, **Hung-Yu Sun***. Assessment of ELISA-based method for the routine examination of serum indoxyl sulfate in patients with chronic kidney disease. Heliyon. 2022;8(12):e12220.
4. Cong Wang, Xue Li, Binbin Xue, Changping Yu, Luoling Wang, Rilin Deng, Hui Liu, Zihao Chen, Yingdan Zhang, Suping Fan, Chaohui Zuo, **Hung-Yu Sun**, Haizhen Zhu, Jianli Wang, and Songqing Tang. RasGRP1 promotes the acute inflammatory response and restricts inflammation-associated cancer cell growth. Nat Commun. 2022;13(1):7001.
5. Pin-Nan Cheng, **Hung-Yu Sun**, I-Che Feng, Yen-Cheng Chiu, Sin-Tian Wang, Dyoness Charmaine Tan, Hung-Chih Chiu, Shih-Chih Chien, Kung-Chia Young. Interdependence of glycemic and lipid modulation in cured chronic hepatitis C patients by direct-acting antiviral agents. J Microbiol Immunol Infect. 2022;S1684-1182(22)00095-0.
6. Shu-Fang Hsieh, **Hung-Yu Sun**, Sin-Tian Wan, Sin-Syue Li, Ya-Ting Hsu, Kung-Chia Young. Plasma lipid profiling increased cardiometabolic risks in acute myeloid leukaemia patients pre- and postchemotherapy. J. Biomed. Lab. Sci. 2022;34(2).
7. **Hung-Yu Sun**, Tzu-Ying Chen, Yu-Ching Tan, Chun-Hsiang Wang, Kung-Chia Young. Sterol O-acyltransferase 2 chaperoned by Apolipoprotein J facilitates hepatic lipid accumulation following viral and nutrient stresses. Commun Biol. 2021;4(1):564.
8. Li Y, Wang X, Han Y, **Sun HY**, Hilborn J, Shi L. Click chemistry-based biopolymeric hydrogels for regenerative medicine. Biomed Mater. 2021;16;16(2):022003.
9. Pinals RL, Ledesma F, Yang D, Navarro N, Jeong S, Pak JE, Kuo L, Chuang YC, Cheng YW, **Sun HY**, Landry MP. Rapid SARS-CoV-2 Spike Protein Detection by Carbon Nanotube-Based Near-Infrared Nanosensors. Nano Lett. 2021;10;21(5):2272-2280.
10. Tsai P, Lin TY, Cheng SL, **Sun HY**, Chen SF, Young KC. Differential dynamics of hepatic protein expressions with long-term cultivated hepatitis C virus infection. J Microbiol Immunol Infect. 2020;53(5):715-723.
11. Lin YM, **Sun HY**, Chiu WT, Su HC, Chien YC, Chang HA, Chong LW, Chang HC, Young KC, Bai CH, Tsao CW. Etifoxine, a TSPO Ligand, Worsens Hepatitis C-Related Insulin Resistance but Relieves Lipid Accumulation. Biomed Res Int. 2019; 3102414.
12. Lai HH, Li CW, Hong CC, **Sun HY**, Chiu CF, Ou DL, Chen PS. TARBP2-mediated destabilization of Nanog overcomes sorafenib resistance in hepatocellular carcinoma. Mol Oncol. 2019;13(4):928-945.
13. Tsai P, Lin CC, **Sun HY**, Lee JC, Chang TT, Young KC. Viral dynamics of persistent hepatitis C virus infection in high-sensitive reporter cells resemble patient's viremia. J Microbiol Immunol Infect. 2018;51(4):446-455.
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發明專利: 一種應用於抑制細胞內脂質積累的多肽及其合成方法(2022)，發明人: **孫宏羽**、秦儂、莊詠鈞、鄭又瑋(專利編號: ZL 2021 1 0245720.4，已授權)

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專長說明：

Peripheral nerve neurophysiology, peripheral nerve regeneration, chronic neuroinflammation, stem cell biology, tissue engineering, neuromodulation and electrical stimulation, difficult wound and pathological scar

研究興趣:

1. Regenerative medicine: peripheral nerve regeneration, electrical stimulation, neuromodulation, wound healing and tissue regeneration, flap angiogenesis
2. Scar research: pathogenesis and treatment of keloids and hypertrophic scars
3. Stem cell research: adipose stem cells, neural stem cells, vascular stem cells
4. Medical device development: electrical stimulator, pain modulator, AIoT, smart wound sensor

近五年代表作:

1. Woo-Youl Maeng, Yerim Lee, Szu-Han Chen, Kyung Su Kim, Daeun Sung, Wan-Ling Tseng, Gyu-Nam Kim, Young-Hag Koh, **Yuan-Yu Hsueh***, Jahyun Koo*. 3D printed biodegradable hydrogel-based multichannel nerve conduits mimicking peripheral nerve fascicules. Mater Today Bio. 2025 Jan 23:31:101514.
2. Yuan-Shuo Hsueh, Szu-Han Chen, Wan-Ling Tseng, Sheng-Che Lin, De-Quan Chen, Chih-Chung Huang, **Yuan-Yu Hsueh***. Leptin deficiency leads to nerve degeneration and impairs axon remyelination by inducing Schwann cell apoptosis and demyelination in type 2 diabetic peripheral neuropathy in rats. Neurochemistry International. 2025 Jan:182:105908.
3. Yi-Syuan Shin#, Kuo-Shu Hung, Chung-Te Tsai, Meng-Hsuan Wu, Chih-Lung Lin, **Yuan-Yu Hsueh***. Validation of multispectral imaging-based tissue oxygen saturation detecting system for wound healing recognition on open wounds. Journal of Biomedical Optics, 2024 Aug 29(8):086004-1~13.
4. Szu-Han Chen#, Yu-Wen Lin#, Wan-Ling Tseng, Wei-Tso Lin, Sheng-Che Lin, **Yuan-Yu Hsueh***. Ultrahigh frequency transcutaneous electrical nerve stimulation for neuropathic pain alleviation and neuromodulation. Neurotherapeutics 2024 Feb 16;21(3):e00336.
5. Jyun-Yuan Huang, Tzyy-Yue Wong, Ting-Yuan Tu, Ming-Jer Tang, Hsi-Hui Lin, **Yuan-Yu Hsueh***. Assessment of Tilapia Skin Collagen for Biomedical Research Applications in Comparison with Mammalian Collagen. Molecules. 2024 Jan 13;29(2):402.
6. Chia-Bao Chu, Chao-Chun Yang, **Yuan-Yu Hsueh**, Po-Chuan Chen, Yi-Kai Hong, Yu-Yun Kuo, Shaw-Jenq Tsai. Aberrant expression of IL-17A in mast cells contributes to the pathogenesis of hidradenitis suppurativa. Br J Dermatol. 2023 Nov 16;189(6):719-729.
7. Szu-Han Chen#, Chia-Ching Wu, Wan-Ling Tseng, Fu-I Lu, Ya-Hsin Liu, Shau-Ping Lin, Sheng-Che Lin, **Yuan-Yu Hsueh***. Adipose-derived stem cells modulate neuroinflammation and improve functional recovery in chronic constriction injury of the rat sciatic nerve. Front Neurosci. 2023 Jun 29;17:1172740.
8. Ming-Wei Hsu#, Szu-Han Chen, Wan-Ling Tseng, Kuo-Shu Hung, Tzu-Chun Chung, Sheng-Che Lin, Jahyun Koo and **Yuan-Yu Hsueh***. Physical processing for decellularized nerve xenograft in peripheral nerve regeneration. Front. Bioeng. Biotechnol. 2023 May 30; 11:1217067.
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研究興趣：

結合X-ray 結構生物學 (Crystallogrpahy) 及蛋白質溶液小角度散射 (Small-Angle Scattering) 的技術，去探討蛋白質的三度空間結構和功能，以及蛋白和蛋白質、蛋白質和核酸之間的交互作用。目前的研究主題為：

1. 探討A型鏈球菌 (Group A Streptococcus) 毒力因子的結構基礎以及調控網絡，理解這些分子對於A型鏈球菌的細胞內發病機制的結構以及作用模式。
2. 探討困難艱梭桿菌 (*Clostridium difficile*) 分選酶的結構與功能，以及和受質的特異性結合之作用原理。
3. 探討介白素1家族(Interleukin 1 family) 細胞激素受體之結構彈性與辨認受質功能之關係。
4. 探討登革病毒疫苗研發之結構基礎。

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研究興趣：

1.先天免疫系統之調控 (Molecular mechanisms of Innate Immunity)

2.病菌與宿主先天免疫系統互動機制 (Interactions between pathogens and the host innate immune system)

3.細胞訊息傳遞 (Signal transduction)

近五年代表作：

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研究興趣：

細胞自噬是一個演化上高度保存的溶酶體依賴系統，在真核生物中用以調節細胞的蛋白質和細胞器的衡定。此系統已被證明能控制不同的細胞功能，包括誘導細胞死亡，免疫激活作用，消除病原體和癌症的產生。我的研究興趣主要是探討細胞自噬作用如何調節肝癌腫瘤免疫和治療的相關應用，以及在登革熱病毒感染中的角色。實驗室目前主要方向為:

1. 外源凝集素誘導的細胞自噬作用在肝癌治療和化療抗性的探討
2. 細胞自噬作用在調節肝癌相關巨噬細胞功能和腫瘤免疫的角色
3. 細胞自噬相關蛋白和登革熱病毒蛋白的相互作用

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研究興趣：

病毒感染引起人類許多疾病，嚴重者甚至造成死亡。想要有效的治療、預防及控制病毒感染引起的疾病，首先必須瞭解病毒的致病機制。我實驗室的研究以動物模型來探討病毒致病機制，應用分子病毒學的方法，找出病毒致病的基因，並深入探討其機轉。同時也研究病毒感染後與宿主的互動，宿主的那一些分子會促進病毒感染，進而加重疾病的嚴重程度，其機轉又為何，期望能提供訊息，幫助臨床醫師更有效的治療、預防及控制病毒感染引起的疾病。目前實驗室研究神經性之病毒如疱疹病毒及新生兒腸病毒(coxsackievirus B3、enterovirus D68 及 enterovirus A71) 的致病機轉，發展腸病毒疫苗。實驗室也與成大眼科醫師合作尋找治療視網膜剝離的藥物。

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研究興趣：

腸道為人體中細菌數目最多的部位，腸道菌會以各種方式影響到人體的各種生理運作; 例如免疫系統發育、代謝、老化、中樞神經運作等等。實驗室以過去針對腸道致病菌如腸出血性大腸桿菌及艱難梭狀桿菌的研究為起點，擴展研究的焦點到腸道微生物相與這些致病菌之間的相互作用、與人體之間的相互作用。我的研究興趣主要為以系統生物學方法研究這些致病菌基因的功能、對於這些致病菌的作用機轉及腸道微生物相與感染間的相互作用。

實驗室目前主要方向為:

1. 腸出血性大腸桿菌致病基因的篩檢及其作用機制探討
2. 艱難梭狀桿菌元噬菌體調控毒素基因表現機制探討
3. 口腔厭氧菌導致細胞發炎及癌症發生嚴重程度機制探討
4. 腸道菌相相關之研究

近五年代表作：

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8. Correlation Between Pathogenic Determinants Associated with Clinically Isolated Non-Typhoidal *Salmonella*. Ouali BEF*, Chiou TH*, **Chen JW***, Lin IC, Liu CC, Chiang YC, Ho TS, Wang HV. Pathogens. 2021 Jan 15;10(1):74.
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10. Effects of *Acanthamoeba castellanii* on the dissolved oxygen and the microbial community under the experimental aquatic model. Tsai CM, **Chen JW**, Lin WC. Exp Parasitol. 2020 Nov;218:107985.
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研究興趣:

登革病毒感染是以節肢動物傳播的病毒疾病中主要的原因之一。截至目前為止，尚無針對登革病毒的抗病毒藥物或治療方法獲得許可。病毒蛋白中的非結構性蛋白 1 (NS1) 在登革病毒感染中扮演重要角色；細胞內的角色有幫助病毒複製和病毒顆粒的產生，細胞外的角色則是參與在血漿滲漏與免疫逃避。因此，我的研究興趣專注於非結構性蛋白 1 的致病機制與發展具潛力的臨床應用。

主要研究方向為：

- 非結構性蛋白 1 在調控細胞內環境恆定的角色。
- 非結構性蛋白 1 的分泌路徑。
- 以非結構性蛋白 1 為基礎，發展有效且可廣泛應用的次單位疫苗與治療性抗體。

近五年代表作:

1. Tien SM, Chang PC, Lai YC, Chuang YC, Tseng CK, Kao YS, Huang HJ, Hsiao YP, Liu YL, Lin HH, Chu CC, Cheng MH, Ho TS, Chang CP, Ko SF, Shen CP, Anderson R, Lin YS*****, **Wan SW***, Yeh TM*****. Therapeutic efficacy of humanized monoclonal antibodies targeting dengue virus nonstructural protein 1 in the mouse model. PLoS Pathog 2022; 18: e1010469. (*equal contribution as the corresponding author)
2. Huang HJ, Yang M, Chen HW, Wang S, Chang CP, Ho TS, Kao YS, Tien SM, Lin HH, Chang PC, Lai YC, Hsiao YP, Liu YL, Chao CH, Anderson R, Yeh TM, Lin YS*****, **Wan SW***. A novel chimeric dengue vaccine candidate composed of consensus envelope protein domain III fused to C-terminal-modified NS1 protein. Vaccine 2022; 40: 2299-2310. (*equal contribution as the corresponding author)
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8. **Wan SW**, Wu-Hsieh BA, Lin YS, Chen WY, Huang Y, Anderson R. The monocyte-macrophage-mast cell axis in dengue pathogenesis. *J Biomed Sci* 2018; 25:77. (SCI)
9. Chiu YH, Chen MC, **Wan SW**. Sodium hyaluronate/chitosan composite microneedles as a single-dose intradermal immunization system. *Biomacromolecules* 2018; 19:2278-2285. (SCI)

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專長說明：

Viral vector engineering, Recombinant protein expression, Vaccine antigen modification, Serological analysis platform development

研究興趣:

桿狀病毒表現載體系統 (Baculovirus expression vector system) 為真核蛋白表現常用系統之一，其具備真核細胞的轉譯後修飾，並可表現複雜的多體蛋白，目前已有部分流感病毒和 COVID-19 的次單位疫苗利用此系統產出。本實驗室以桿狀病毒表現載體系統進行以下研究：

1. **開發潛在傳染疾病的血清診斷系統和疫苗抗原：**利用桿狀病毒及其昆蟲宿主的細胞做為蛋白質表面展示平台，生產病毒或其他傳染性疾病之血清檢驗系統和疫苗。
2. **抗原蛋白或酵素蛋白之質性改造：**利用基因工程改造血清檢測或疫苗之抗原、以及醫療和食品安全檢驗之特用酵素 (specialty enzymes)，提高其蛋白表現、免疫原性、或酵素活性。
3. **病毒載體工程：**利用桿狀病毒能攜帶長片段外源基因，以及容易進入多種細胞之特性，使其做為基因表現和基因治療 (gene therapy) 之載體。

近五年代表作:

1. **Tsai, C.H.***, Ho, Y.H., Sung, T.C., Wu, W.F.[#], and Chen, C.S.[#] (2017) *E. coli* proteome microarrays identified the substrates of ClpYQ protease. *Molecular & Cellular Proteomics* 16(1): 113-120.

2. **Tsai, C.H.***, Wei, S.C., Jan, J.T., Liao, L.L., Chang, C.J., and Chao, Y.C.[#] (2019) Generation of stable influenza virus hemagglutinin through structure-guided recombination. *ACS Synthetic Biology* 8(11): 2472-2482.

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5. Wei, S.C., Hsu, W.T., Chiu, C.H., Chang, F.Y., Lo, H.R., Liao, C.Y., Yang, H.I., Chou, Y.C., **Tsai, C.H.*[#] (co-corresponding)** and Chao, Y.C.[#] (2021) An integrated platform for serological detection and vaccination of COVID-19. *Frontiers in Immunology* 12: 771011.

6. **Tsai, C.H.***, Chuang, Y.C., Tang, C.K., Lin, Y.H., Lin, C.Y., and Wu, Y.L.[#] (2021) Carbohydrate metabolism is a determinant for the host specificity of baculovirus infections. *iScience* 25(1): 103648.

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個人網址：

專長說明：

免疫學、過敏免疫學、微菌叢及益生菌在過敏性疾病的作用、微菌叢研究

研究興趣:

微菌叢在人體免疫功能中扮演重要角色，過敏性疾病和黏膜發炎等代謝相關疾病的免疫功能異常通常與腸道微生物的紊亂有關。因此，探討微菌叢如何調控黏膜免疫發炎已成為預防和治療這些疾病的重點研究課題。本實驗室專注於過敏及黏膜發炎疾病，基於過去開發益生菌蛋白改善過敏性氣喘及研究環境微生物暴露引發過敏性發炎加劇的成果，進一步擴展至黏膜發炎疾病，探討微菌叢與宿主黏膜免疫的相互作用。實驗室主要研究方向：

1. 研究益生菌或有益共生菌在改善過敏及黏膜發炎疾病中的作用機制。
2. 開發控制免疫代謝的策略，以應用於治療過敏及黏膜發炎疾病。
3. 將微菌叢的變化作為疾病的生物標記，並開發微菌叢移植治療過敏及黏膜發炎疾病的方法。

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2. Pei-Chi Chen, Han-Yin Hsu, Yi-Chu Liao, Chia-Chia Lee, Miao-Hsi, Hsieh, Wen-Shou Kuo, Lawrence Shih-Hsin Wu, and Jiu-Yao Wang. Oral administration of Lactobacillus delbrueckii subsp. lactis LDL557 attenuates airway inflammation and changes the gut microbiota in a Der p-sensitized mouse model of allergic asthma. Asian Pac J Allergy Immunol. 2024 May 6. doi: 10.12932/AP-200823-1672. Online ahead of print.
3. Natalia Paramonova, Ilva Trapina, Brigita Gradauskiene (Sitkauskiene), Samanta Plavina, Laura Tamsauskiene, Daina Bastyte, Ingrida Rumba-Rozenfelde, Sandra Tapina, Ieva Stakaitiene, Rasa Ugenskiene, Lawrence Shih-Hsin Wu, Jiu-Yao Wang, Miao-Hsi Hsieh, Pei-Chi Chen, and Nikolajs Sjakste. Genetic Diversity in Bronchial Asthma Susceptibility: Exploring the Role of Vitamin D Receptor Gene Polymorphisms in Varied Geographic Contexts. Int J Mol Sci. 2024 Feb 5;25(3):1943.
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7. Pei-Chi Chen, Miao-Hsi Hsieh, Wen-Shuo Kuo, Lawrence Shih-Hsin Wu, Hui-Fang Kao, Li-Fan Liu, Zhi-Gang Liu, Wen-Yih Jeng, Jiu-Yao Wang. Moonlighting glyceraldehyde-3-phosphate dehydrogenase (GAPDH) protein of Lactobacillus gasseri attenuates allergic asthma via immunometabolic change in macrophages. J Biomed Sci. 2022 Sep 29;29(1):75.
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研究興趣：

1. To investigate the novel function of Chk2 in preventing tumorigenesis.
2. To study the molecular mechanism by which autophagy regulates steroidogenic cell growth and differention.
3. To study the role of primary cilia in controlling cell fate determination.

近五年代表作：

1. Jhih-Siang Syu, Takashi Baba, Jyun-Yuan Huang, Hidesato Ogawa, Chi-Han Hsieh, Jin-Xian Hu, Ting-Yu Chen,Tzu-Chien Lin, Megumi Tsuchiya, Ken-Ichirou Morohashi, Bu-Miin Huang, Fu-l Lu and **Chia-Yih Wang*** (2017) Lysosomal activity maintains glycolysis and cyclin E1 expression by mediating Ad4BP/SF-1 stability for proper steroidogenic cell growth, *Scientific Reports*, Accepted
2. Yi-Ru Shen, Han-Yu Wang, Yung-Che Kuo, Shih-Chuan Shih, Chun-Hua Hsu, Yet-Ran Chen, Shang-Rung Wu, **Chia-Yih Wang***, Pao-Lin Kuo* (2017) SEPT12 Phosphorylation Results in Loss of the Septin Ring/Sperm Annulus, Defective Sperm Motility and Poor Male Fertility, *PLOS Genetics*, Accepted
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11. Takashi Baba, Hiroyuki Otake, Tetsuya Sato, Kanako Miyabayashi, Yurina Shishido, **Chia-Yih Wang**, Yuichi Shima, Hiroshi Kimura, Mikako Yagi, Yasuhiro Ishihara, Shinjiro Hino, Hidesato Ogawa, Mitsuyoshi Nakao, Takeshi Yamazaki, Dongchon Kang, Yasuyuki Ohkawa, Mikita Suyama, Bon-chu Chung, and Ken-ichirou Morohashi (2014) Glycolytic genes as the targets of a nuclear receptor Ad4BP/SF-1, *Nature Communications*, 5,3634,pp1-13
12. **Chia-Yih Wang**, Wei-Yi Chen, Pao-Yen Lai, and Bon-chu Chung (2013) Distinct Functions of Steroidogenic Factor-1 (NR5A1) in the nucleus and the centrosome, *Molecular and Cellular Endocrinology*, 371, 1-2, pp148-153
13. **Chia-Yih Wang**, Yung-Hsin Kao, Pao-Yen Lai, Wei-Yi Chen, and Bon-chu Chung (2013) Steroidogenic Factor-1 (NR5A1) maintains centrosome homeostasis in steroidogenic cells by restricting centrosomal DNA-PK activation, *Molecular and Cellular Biology*, 33, 3, pp476-484

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專長與研究興趣:

1. 細胞外微環境(物理及化學因子)如何調控間質幹細胞之生長及分化
2. 細胞收縮力之調控
3. 細胞骨架的動態及組成對細胞功能的影響

近五年代表作:

1. Wu MC, Yu HW, Chen YQ, Ou MH, Serrano R, Huang GL, **Wang YK**, Ling KH, Fan YJ, Wu CC, del Álamo JC, Chiu A, Chien S, Kuo JC. Early committed polarization of intracellular tension in response to cell shape determines the osteogenic differentiation of mesenchymal stem cells, Acta Biomater, S1742-7061:00709-7, 2022.
2. Tu TY, Shen YP, Lim SH, **Wang YK**. A Facile method for generating a smooth and tubular vessel lumen using a viscous fingering pattern in a microfluidic device. Front Bioeng Biotechnol. 10: 877480, 2022.
3. Liao FC, **Wang YK**, Cheng MY, Tu TY. A Preliminary investigation of embedding in vitro HepaRG spheroids into recombinant human collagen type I for the promotion of liver differentiation. Polymers (Basel). 14: 1923, 2022.
4. Wu KC, Liao KS, Yeh LR, **Wang YK***. Drug Repurposing: The Mechanisms and Signaling Pathways of Anti-Cancer Effects of Anesthetics. Biomedicines. 10: 1589, 2022.
5. Lu HL, Wu KC, Chen CW, Weng HK, Huang BM, Lin TY, Liu MH, So EC, Lin RM, **Wang YK***. Anticancer Effects of Midazolam on Lung and Breast Cancers by Inhibiting Cell Proliferation and Epithelial-Mesenchymal Transition. Life 11:1396, 2021.
6. Lin JW, Huang YM, Chen YQ, Chuang TY, Lan TY, Liu YW, Pan HW, You LR, **Wang YK**, Lin KH, Chiou A, Kuo JC. Dexamethasone accelerates muscle regeneration by modulating kinesin-1-mediated focal adhesion signals. Cell Death Discov 7: 35, 2021
7. Miyagawa T, Chen ZY, Chang CY, Chen KH, **Wang YK**, Liu GS, Tseng CL. Topical application of hyaluronic acid-RGD peptide-coated gelatin/Epigallocatechin-3 Gallat (EGCG) nanoparticles inhibits corneal neovascularization via inhibition of VEGF production. Pharmaceutics 12: 404, 2020.
8. Wu KC, Weng HK, Hsu YS, Huang PJ, **Wang YK***. Aqueous extract of Arctium lappa L. root (burdock) enhances chondrogenesis in human bone marrow-derived mesenchymal stem cells. BMC Complement Med Ther 20: 364, 2020
9. Chiu CY, Chen YC, Wu KW, Hsu WC, Lin HP, Chang HC, Lee YC, **Wang YK**, Tu TY. Simple in-house fabrication of microwell for generating uniform hepatic multicellular cancer aggregates and discovering novel therapeutics. Materials 12:E3308, 2019
10. Wei WC, Bianchi F, **Wang YK**, Tang MJ, Ye H, Clitsch MD. Coincidence detection of extracellular pH and membrane stretch by the Gq coupled receptor OGR1. Curr Biol, 28: 3815-23, 2018
11. Chen YC, Wu KC, Huang BM, So EC, **Wang YK***. Midazolam inhibits chondrogenesis via peripheral benzodiazepine receptor in human mesenchymal stem cells. J Cell Mol Med, 22: 2896-2907, 2018 (Corresponding)
12. Jheng GW, Hur SS, Chang CM, Wu CC, Cheng JS, Lee HH, Chung BC, **Wang YK**, Lin KH, Del Álamo JC, Chien S, Tsai JW. Lis1 dysfunction leads to traction force reduction and cytoskeletal disorganization during cell migration. Biochem Biophys Res Commun. 497:869-875, 2018
13. Hsu CK, Lin HH, Harn HI, **Wang YK**, Ho YT, Chen WR, Lee YC, Shieh SJ, Cheng CM, McGrath J, Tang MJ. Caveolin-1 controls hyperresponsiveness to mechanical stimuli and fibrogenesis-associated RUNX2 activation in keloid fibroblasts. J Invest Dermotol, 138:208-218, 2018

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研究興趣：

Mechanobiology-assisted Tissue Engineering & Regenerative Medicine (MBATERM) lab:

1. 探討不同細胞微環境，如何幫助幹細胞及組織重建
2. 利用力學生物學(mechanobiology)幫助組織工程與再生醫學的研究與治療，了解其相關分子機轉，包含血管、皮膚、中樞與周邊神經、肌肉骨骼系統等
3. 以細胞生物力學了解細胞如何感受環境誘導因子及如何轉化機械刺激成細胞內訊息傳遞
4. 探討幹細胞與組織工程可發明創新治療策略

近五年代表作：

1. Chang W. T., Wu C. C., Lin Y. W, Shih J. Y., Chen Z. C., Wu S.N, Wu C. C, Hsu C. H. Dynamic Changes in miR-21 Regulate Right Ventricular Dysfunction in Congenital Heart Disease-Related Pulmonary Arterial Hypertension. ***Cells.*** 11(3):564. doi: 10.3390/cells11030564.(2022)
2. Yadav A., Huang T. C., Chen S.H., Ramasamy T. S., Hsueh Y. Y , Lin S.P., Lu F. I., Liu Y. H., Wu C. C. Sodium phenylbutyrate inhibits Schwann cell inflammation via HDAC and NFκB to promote axonal regeneration and remyelination. ***J. Neuroinflammation.*** 18, 238 (2021)
3. Chang M. M., Wu S. Z., Yang S. H., Wu C. C., Wang C. Y., Huang B. M.. FGF9/FGFR1 promotes cell proliferation, epithelial-mesenchymal transition, M2 macrophage infiltration and liver metastasis of lung cancer. ***Transl Oncol.*** 14(11):101208. doi: 10.1016/j.tranon.2021.101208 (2021)
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5. Chen, S. H., Wu, C. C., Lin, S. C., Tseng, W. L., Huang, T. C., Yadav, A., Lu, F. I., Liu, Y. H., Lin, S. P. & Hsueh, Y. Y. Investigation of Neuropathology after Nerve Release in Chronic Constriction Injury of Rat Sciatic Nerve. ***Int. J. Mol. Sci***. 22, doi:10.3390/ijms22094746 (2021).
6. Yusuf, I. O., Chen, H. M., Cheng, P. H., Chang, C. Y., Tsai, S. J., Chuang, J. I., Wu, C. C., Huang, B. M., Sun, H. S., Chen, C. M. & Yang, S. H. Fibroblast Growth Factor 9 Stimulates Neuronal Length Through NF-kB Signaling in Striatal Cell Huntington's Disease Models. ***Mol. Neurobiol***. 58, 2396-2406, doi:10.1007/s12035-020-02220-w (2021).
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研究興趣：

實驗室研究方向為探討脊髓損傷、神經病變痛(neuropathic pain)、惡性腦癌的致病機轉與開發新型有效治療。

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28. Wong CE, Lee PH, Huang CC, **Lee JS***. Comments on "The "Hand as Foot" teaching method in neuroanatomy of ventricle system". Asian J Surg. 2022 Apr;45(4):1022-1023 本人為通訊作者
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41. Chiang LJ, Wang CK, Tsai HW, **Lee JS***. Diagnostic dilemma in discriminating between spinal neurenteric cysts and simple arachnoid cysts based on embryogenesis and surgical correlation. World Neurosurg. 2020 Feb;134:489-494

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心血管疾病-致病機轉與治療策略、疾病動物模式。

近五年代表作:

1. **Fan-E Mo*** (2021, Apr) Shear-Regulated Extracellular Microenvironments and Endothelial Cell Surface Integrin Receptors Intertwine in Atherosclerosis. *Front Cell Dev Biol*, 9, 640781.

2. Bor-Chyuan Su, Pei-Ling Hsu, **Fan-E Mo*** (2020, Mar). CCN1 triggers adaptive autophagy in cardiomyocytes to curb its apoptotic activities. *J Cell Commun Signal*, 14(1), 93-100.

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4. Pei-Ling Hsu, Jheng-Sin Chen, Chin-Yung Wang, Hua-Lin Wu, **Fan-E Mo*** (2019, Jun). Shear-induced CCN1 promotes atheroprone endothelial phenotypes and atherosclerosis. *Circulation*, 139(25):2877–2891.

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6. Pei-Ling Hsu, **Fan-E Mo*** (2016, Jun). Matricellular protein CCN1 mediates doxorubicin-induced cardiomyopathy in mice. *Oncotarget*, 7(24), 36698-36710.

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研究興趣：

1. 脊髓受創傷後神經纖維之再生與運動功能復原。
2. 中樞神經系統內星狀膠細胞對疤痕組織形成所扮演的角色。
3. 受創脊髓中血管之新生過程與功能特性。
4. 神經纖維超微結構與可塑性研究。

Dr. Hsu's research has long focused on axonal plasticity in the central nervous system, particularly in the field of axonal regeneration and wound healing after spinal cord injury. He is investigating how non-neuronal cells and matrix molecules regulate axonal regrowth and tissue repair during wound healing. His research will elucidate the mechanism underlying the formation of an astroglial scar in injured spinal cord and the roles of astrocytes in repairing damaged blood vessels during wound healing. His ultimate goal is to better understand how to create a promotive environment that fosters axonal regeneration and recovery of motor function after spinal cord injury.

近五年代表作：

1. Lin, Y.C., Ko, T.L., Shih, Y.H., Lin, M.Y.A.; Fu, T.W., Hsiao, H.S.; **Hsu, J.Y.**, Fu, Y.S., 2011. Human umbilical mesenchymal stem cells promote recovery after ischemic stroke. *Stroke* 42, 2045-2053.

2. **Hsu, J.Y.**, Bourguignon, L.Y., Adams, C.M., Peyrollier, K., Zhang, H., Fandel, T., Cun, C.L., Werb, Z., Noble-Haeusslein, L.J., 2008. Matrix metalloproteinase-9 facilitates glial scar formation in the injured spinal cord. *Journal of Neuroscience* 28, 13467-13477.

3. **Hsu, J.Y**., McKeon, R., Goussev, S., Werb, Z., Lee, J.U., Trivedi, A., Noble-Haeusslein, L.J., 2006. Matrix metalloproteinase-2 facilitates wound healing events that promote functional recovery after spinal cord injury. Journal of Neuroscience 26, 9841-9850. (Selected by the Editor as one of the only 4 articles highlighted with commentaries in the section “This Week in the Journal”)

4. **Hsu, J.Y.**, Stein, S.A., Xu, X.M., 2006. Development of the corticospinal tract in the mouse spinal cord: a quantitative ultrastructural analysis. Brain Research 1084, 16-27.

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研究興趣：

1. Investigating the pathophysiology of Alzheimer's disease and identifying potential therapeutic approaches.
2. Examining the relationship between metabolic disorders and depression to develop effective treatment strategies.
3. Assessing the effect of physical exercise on brain health.

近五年代表作：

1. Zhao ZW, Wang YC, Chen PC, Tzeng SF, Chen PS, and **Kuo YM***. Dopamine D1 receptor agonist alleviates post-weaning isolation-induced neuroinflammation and depression-like behaviors in female mice. *Behavioral and Brain Functions*, 2025 Mar; 21:6.
2. Huang CC, Tsai SF, Liu SC, Yeh MC, Hung HC, Lee CW, Cheng CL, Hsu PL*, **Kuo YM***. Insulin mediates lipopolysaccharide-induced inflammatory responses and oxidative stress in BV2 microglia. *Journal of Inflammation Research*, 2024 Nov; 2:17:7993-8008.
3. Tsai SF, Hsu PL, Yeh MC, Hung HC, Shih MMC, Chung BC, Wang CY, Chang CJ*, **Kuo YM***. High-fat diet-induced increase in glucocorticoids contributes to adipogenesis in obese mice. *Biomedical Journal*, 2024 Jul; 22: 100772.
4. Chang CW, Hsu JY, Lo YT, Liu YH, Mee-Inta O, Lee HT, **Kuo YM***, Liao PC*. Characterization of hair metabolome in 5xFAD mice and patients with Alzheimer's disease using mass spectrometry-based metabolomics. *ACS Chemical Neuroscience*, 2024 Feb; 15(3):527-538.
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6. Hung HC, Tsai SF, Chou HW, Tsai MJ, Hsu PL*, **Kuo YM***. Dietary fatty acids differentially affect secretion of pro-inflammatory cytokines in human THP-1 monocytes. *Scientific Reports*, 2023 Apr; 13:5511.
7. Mee-Inta O, Hsieh CF, Chen DQ, Fan CH, Chiang YY, Liu CC, Sze CI, Gean PW, Wu PC, Yang MS, Huang PS, Wu PC, **Kuo YM***, Huang CC*. High-frequency ultrasound imaging for monitoring the function of meningeal lymphatic system in mice. *Ultrasonics*, 2023 Feb; 131:106949.
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9. Wang TF, Wu SY, Pan BY, Tsai SF, **Kuo YM***. (2022 Jan) Inhibition of nigral microglial activation reduces age-related loss of dopaminergic neurons and motor deficits. *Cells* 11: 481.
10. Tsai SF, Hung HC, Shih MC, Chang FC, Chung BC, Wang CY, Lin YL, **Kuo YM***. High-fat diet-induced increases in glucocorticoids contribute to the development of non-alcoholic fatty liver disease in mice. *FASEB Journal*, 2022 Jan; 36: e22130.
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12. Lkhagvasuren B, Mee-inta O, Zhao ZW, Hiramoto T, Boldbaatar D, **Kuo YM***. Pancreas-brain crosstalk. *Frontiers in Neuroanatomy*, 2021 Jul; 15:691777.
13. Wu SY, Pan BS, Tsai SF, Chiang YT, Huang BM, Mo FE, **Kuo YM***. BDNF reverses aging-related microglial activation. *Journal of Neuroinflammation*, 2020 Jul; 17:210.

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研究興趣：

1.探討癌細胞對化療及標靶藥物產生抗性的機制，增進治療的效果。
2.探討在癌症抗藥性發展過程中，參與其中的發炎反應、細胞死亡機制及自噬作用。

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研究興趣:

血管新生(Angiogenesis)與動物胚胎的發育、傷口的癒合、和女性的月經週期有關。當這個生理過程失衡，會產生許多血管的病變含腫瘤的生長與轉移。近四十年來，已有許多的臨床前實驗證明血管新生和惡性腫瘤的發生和轉移有著密切的相關性，但截至目前為止只有幾種抗血管新生的藥物上市，最大原因是複雜的腫瘤微環境內的各式細胞(含內皮細胞)與腫瘤細胞交互作所致。

目前實驗室的研究方向包括: 1)口腔與食道癌於近年來分居於台灣十大癌症死因第五與第九位，但其致病機制仍不清楚。透過與臨床醫師合作，結合細胞與分子生物，透過轉錄體學、蛋白體甚至於代謝體等多體學的技術，研究腫瘤微環境的交戶作用(含微生物、發炎細胞與血管等細胞)在口腔食道黏膜上皮細胞癌化與轉移所扮演的角色與機轉。2)癌症是無法癒合的傷口，也會利用基因轉殖與剔除的技術探討該基因表現量的改變於皮膚傷口癒合角色的探討與藥物研發。

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研究興趣：

1. **新穎致癌基因 TIAM2 之功能研究及其致癌機制之探討。**TIAM2 是一個非常新穎的基因但是相關的細胞內功能性分析報導仍付之厥如。我們的研究結果發現 TIAM2 是一個腦部特有的表現蛋白，而且僅表現在神經元細胞。重要的是 87%肝癌組織都可檢測到異位性表現的 TIAM2 蛋白，因此 TIAM2 和癌症生成的確有顯著相關性。利用細胞及小鼠動物模式，證實了 TIAM2 大量表現不但增加細胞生長速率，TIAM2 更會使低轉移性細胞株轉化成高侵入性轉移性細胞株。我們利用表現人類 TIAM2S 的轉置基因（TIAM2S-TG）小鼠發現 TIAM2S-TG 顯示出比野生型小鼠高得多的血清素量。而且老化的 TIAM2S-TG 小鼠在多重器官出現高度發炎的現象，甚至自然發展出大腸直腸癌。由於血清素影響免疫力，導致慢性發炎，且血清素調節失常引發人類發炎症性腸道症，我們將利用 TIAM2S-TG 小鼠作為模型來進一步探討 TIAM2S 介導癌化的機制。此外在腦內 TIAM2S 的功能性研究，日前我們的研究率先證實 TIAM2S 在神經細胞中為一個新穎的血清素調解因子，並參與大腦塑化和調解運動行為。
3. **人類第九纖維母細胞生長因子基因表現之調控機制。**人類第九纖維母細胞生長因子(FGF9)是一個高度保留在各個物種且具有促進多種細胞生長的基因。研究顯示 FGF9 在胚胎發育、器官形成、性別發展和維持生命機能上可能扮演重要角色。本實驗室的主題是探討 FGF9 基因表現再各層級之調控機制及其在性別發育上所扮演角色。
4. **生物資訊學。**本實驗室希望有系統的朝向生物資訊學教育推廣、研究發展、及服務等方面努力。目前的研究方向是研究基因體的結構性多行性(CNV)分佈及其在人類疾病的影響、及發展癌症基因體醫學相關之資料庫(TAG)等。

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研究興趣：

由於抗生素濫用，新的抗藥性細菌不斷產生。近年來陸續發現帶有多重抗藥性的"超級細菌"。這類抗藥性細菌出現的速度已超越新型抗生素的研發速度，再加上因為人類旅行日漸便利的推波助瀾，這類細菌也快速的散佈全球。這種狀況已經對於醫學界以抗生素來控制感染性疾病的方式帶來隱憂，也對人類健康造成嚴重威脅。因此，對於致病性細菌發展新的預防以及治療策略刻不容緩。

本實驗室的長程目標就是要發展出新的預防及治療策略以對抗不斷演化的致病性細菌。為達此目標，我們從了解細菌致病的機轉著手。因為在了解了致病性細菌入侵人類的過程中如何和宿主交互作用以逃離免疫系統攻擊及獲得生存所需的養分，將有助於找出可能的切入點。致病性大腸桿菌是最常見的人類致病性細菌之一。而且大腸桿菌也是至今為止，人類研究最多的細菌。因此，我們以致病性大腸桿菌為模型，進行其致病機轉研究。而現今，實驗室以研究造成新生兒腦膜炎的K1莢膜大腸桿菌以及泌尿道致病性大腸桿菌為主。

要引起新生兒腦膜炎，K1莢膜大腸桿菌須先在血流中增殖達到一定數目才能穿越血腦障壁進入中樞神經系統。我們正在研究此細菌如何躲避人類血流中的免疫系統的擊殺而繼續增殖，以及它如何和構成血腦障壁的腦微血管內皮細胞交互作用達到穿越血腦障壁的目的。泌尿道致病性大腸桿菌會感染膀胱以及腎臟。在感染過程中，此菌會入侵到泌尿道上皮細胞、抑制宿主免疫反應以及造成細胞凋亡。實驗室正在研究這些反應的機制。

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Research interest：

磷酸水解酶PP2A一直以來被認為是扮演抑制腫瘤的角色。PP2A完全酶是由三種次單元所組成，包括了催化次單元C、結構次單元A、及多變的調節次單元B。目前至少有四種B調節次單元家族被發現，而PP2A在細胞中具有的多元功能是由於完全酶中多變的B次單元所造成。我們的研究致力於探討B次單元在PP2A抑制腫瘤的分子機制。另一方面，近年來我們也發現含有特定的B次單元(B56γ3)的PP2A扮演促進癌化的的角色，我們的研究顯示含有B56γ3的PP2A促進癌化的一項分子機制是透過正向調節AKT/mTOR/p70S6K訊息路徑的所致，我們接續也以次世代定序分析腫瘤細胞轉錄體來探究含有B56γ3的PP2A在促進癌化角色中的新穎機制。近來，我們也展開對液態液態相位分離(liquid-liquid phase separation)(LLPS)的分子現象的探索。LLPS參與在細胞中的許多必要的現象及活性的調控，我們發現與PP2A有交互作用的分子STOML2及MID1可能具有LLPS的分子特質，因此也致力於探討這些分子的LLPS特質，以及LLPS是否調節這些分子的細胞功能及在疾病的病理的角色。

研究方向：

一、探討PP2A在大腸癌及胰臟癌的癌化中的角色及新穎分子機制。

二、探討STOML2的LLPS特質以及LLPS調節STOML2在粒線體的功能

三、探討MID1的LLPS特質以及MID1凝聚體的細胞功能及在肝癌的角色

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1. Chen C, Lin HW., Huang MF, **Chiang CW**, Lee KH, Phuong NT, Cai ZY, Chang WC and Lin DY. (2024 Jan.4). Sumoylation of SAP130 regulates its interaction with FAF1 as well as its protein stability and transcriptional repressor function. BMC Mol and Cell Biol, 25, 2
2. Hsiao KC, Ruan SY, Chen SM., Lai TY, Chan RH, Zhang YM, Chu CA, Cheng HC, Tsai HW, Tu Y F, Law BK., Chang TT, Chow NH, **Chiang CW .** (2023 Jul). The B56γ3-containing protein phosphatase 2A attenuates p70S6K-mediated negative feedback loop to enhance AKT-facilitated epithelial-mesenchymal transition in colorectal cancer. Cell Commun Signal. 10;21(1):172.
3. Wu PM, Yu WH, **Chiang CW**, Wu CY, Chen JS, Tu YF. (2022 Feb) Novel Variations in the KDM5C Gene Causing X-Linked Intellectual Disability. *Neurology Genetics* 8(1):e646.
4. Law ME, Yaaghubi E, Ghilardi AF, Davis BJ, Ferreira RB, Koh J, Chen S, DePeter SF., Schilson CM, **Chiang CW**, Heldermon CD, Nørgaard P, Castellano RK, and Law BK. (2022 May). Inhibitors of ERp44, PDIA1, and AGR2 induce disulfide-mediated oligomerization of Death Receptors 4 and 5 and cancer cell death. Cancer Lett. 28;534:215604
5. Tu YF, Jiang ST, **Chiang CW**, Chen LC, Huang CC. (2021 Jun). Endothelial-specific insulin receptor substrate-1 overexpression worsens neonatal hypoxic-ischemic brain injury via mTOR-mediated tight junction disassembly. *Cell Death Discov* 29;7(1):150.
6. Wang M, Law ME, Davis BJ, Yaaghubi E, Ghilardi AF, Ferreira RB, **Chiang CW**, Guryanova OA, Kopinke D, Heldermon CD, Castellano RK, Law BK. (2019 Dec). Disulfide bond-disrupting agents activate the tumor necrosis family-related apoptosis-inducing ligand/death receptor 5 pathway. *Cell Death Discov* 10;5:153.
7. Wang CH, Hung PW, **Chiang CW**, Lombès M, Chen CH, Lee KH, Lo YC, Wu MH, Chang WC, Lin DY. (2019 Aug). Identification of two independent SUMO-interacting motifs in Fas-associated factor 1 (FAF1): Implications for mineralocorticoid receptor (MR)-mediated transcriptional regulation. *Biochim Biophys Acta Mol Cell Res* 1866(8):1282-1297.
8. Wang M, Ferreira RB, Law ME, Davis BJ, Yaaghubi E, Ghilardi AF, Sharma A, Avery BA, Rodriguez E, **Chiang CW**, Narayan S, Heldermon CD, Castellano RK, Law BK. (2019 May). A novel proteotoxic combination therapy for EGFR+ and HER2+ cancers. *Oncogene* 38(22):4264-4282.

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專長與研究興趣:

免疫學(DNA疫苗,黏膜與細胞免疫),高等病毒學(反轉錄病毒; 病毒重組與出芽機制),細胞生化學(蛋白交互作用; 蛋白生化與胞膜訊息),分子遺傳學(核酸轉錄與轉訊調控)

病毒生活史需要病毒蛋白與寄主細胞的交互協調作用，這個進程也伴隨著病毒基因的繁殖與表達而形成具感染性的生物體。寄主細胞內有哪些蛋白可被病毒蛋白霸佔借用於病毒組裝及感染呢?又有哪些病毒蛋白可與寄主細胞蛋白互通款曲欺騙寄主的免疫防衛系統呢? 我們能瞭知並利用這些交互作用的機制進而發展抗病毒藥物或疫苗嗎？這些是我實驗室最基本的科學研究訴求。我目前主要的研究方向在瞭解HCV及腸病毒(EV-A71)之宿主交互作用與致病機制:利用蛋白質體學找出對抗或幫助病毒繁殖或致病的寄主蛋白因子，以做治療性疫苗開發。正進行的實驗計畫有:(1)蛋白質體學運用與分析C型肝炎病毒(HCV)核蛋白(Core)在肝細胞及免疫細胞內作用的蛋白網路。(2) 腸病毒(EV71)結構蛋白的宿主蛋白交互作用與致病機制。(3) RT-LAMP與病毒核酸偵測 (4)發展拮抗或偵測病毒的小分子DNA適體(aptamer)。

選擇性代表作:

1. Chen KW, Chen TY, Wang ST, Hou TY, **Wang SW**, Young KC. Establishment of quantitative and recovery method for detection of dengue virus in wastewater with noncognate spike control. J Virol Methods 2023 Apr;314:114687.
2. Wang LC, Yao HW, Chang CF, **Wang SW**, Wang SM, Chen SH. Suppression of interleukin-6 increases enterovirus A71 lethality in mice. J Biomed Sci. 2017 Dec 12;24(1):94.
3. Lai MC, Sun HS, **Wang SW**, Tarn WY. DDX3 functions in antiviral innate immunity through translational control of PACT. FEBS J. 2015 Oct 10. SCI: Impact factor 4.001, Ranking 77/290.
4. Manrique M, Kozlowski PA, Cobo-Molinos A, **Wang SW**, Wilson RL, Martinez-Viedma Mdel P, Montefiori DC, Carville A, Aldovini A. Resistance to infection, early and persistent suppression of simian immunodeficiency virus SIVmac251 viremia, and significant reduction of tissue viral burden after mucosal vaccination in female rhesus macaques. J Virol. 2014 Jan;88(1):212-24. SCI: Impact factor 4.648, Ranking 7/32.
5. Lai MC, **Wang SW**, Cheng L, Tarn WY, Tsai SJ, Sun HS. Human DDX3 interacts with the HIV-1 Tat protein to facilitate viral mRNA translation. PLoS One, 2013 Jul; 8(7):e68665. SCI: Impact factor 3.534, Ranking 8/55.
6. Wang JH, Cheng L, Wang CH, Ling W, **Wang SW***, and Lee GB*. An integrated chip capable of performing sample pretreatment and nucleic acid amplification for HIV-1 detection. Biosensors and Bioelectronics, 2013 Mar, 41: 484-91. SCI: Impact factor 6.451, Ranking 1/27. Co-correspondence.
7. Sun HY, Lin CC, Lee JC, **Wang SW**, Cheng PN, Wu IC, Chang TT, Lai MD, Shieh DB, Young KC. Very low-density lipoprotein/lipo-viro particles reverse lipoprotein lipase-mediated inhibition of hepatitis C virus infection via apolipoprotein C-III. Gut, 2012 Jun 11, Epub ahead of print. SCI: Impact factor 13.319, Ranking 2/74.
8. Yeh MT, **Wang SW**, Yu CK, Lin KH, Lei HY, Su IJ, Wang JR. A single nucleotide in stem loop II of 5'-untranslated region contributes to virulence of enterovirus 71 in mice. PLoS one, 2011; 6(11):e27082. Epub2011Nov.1. SCI: Impact factor 3.534, Ranking 8/55.
9. Lee JW, Liao PC, Young KC, Chen SL, Chang CL, Cheng TS, Lai MD, **Wang SW*.** Identification of hnRNPH1, NF45, and C14orf166 as novel host interacting partners of the mature hepatitis C virus core protein. Journal of Proteome Research, 2011 Oct 7; 10(10):4522-34. Epub 2011 Aug.24. SCI: Impact factor 5.001, Ranking 9/78. Correspondence.
10. Yang ML, Chen YH, **Wang SW**, Huang YJ, Leu CH, Yeh NC, Chu CY, Lin CC, Shieh GS, Chen YL, Wang JR, Wang CH, Wu CL, Shiau AL. Galectin-1 binds to influenza virus and ameliorates influenza pathogenesis. Journal of Virology, 2011 Oct, 85(19):10010-20. Epub 2011 Jul 27. SCI: Impact factor 4.648, Ranking 7/32, Equal contribution to first authors (60%).
11. Ko NY, Lee HC, Hung CC, Tseng FC, Chang JL, Lee NY, Chang CM, Lee MP, Chen BJ, **Wang SW***, Ko WC. Trends of HIV and Sexually Transmitted Infections, Estimated HIV Incidence, and Risky Sexual Behaviors Among Gay Bathhouse Attendees in Taiwan: 2004-2008. AIDS Behavior, 2011 Feb; 15(2):292-7, Correspondence, SCI: Impact factor 3.312, Ranking 2/37

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Research and teaching plan

My major is bacterial genetics, but I also have extensive experiences for overall bacteriology from molecular level to environmental level. By using the knowledge, I challenge to ask right and interesting questions. I was also involved in iGEM team in NCKU, which is an international competition for synthetic biology, because synthetic biology is one of my major as well.

Enterohemorrhagic *E. coli* (EHEC) expressing Shiga toxin is one of infectious bacteria shows a severe symptom. Since the toxin gene is in a prophage region in the EHEC genome, the toxin is expressed when the phage is activated by environmental stress like antibiotic treatment. Then, we are investigating mechanism for the prophage induction, and also challenging to inhibit the phage production to prevent the toxin production. We found some chemical compounds and proteins to inhibit the toxin production. Currently, we are studying the inhibition mechanism, and developing applications of them. Now, phage study is one of hot topic in bacteriology, and many new findings are reported from arms race between bacteria and phage. Besides, I also study for development of new antibiotics, novel cloning method, restriction enzyme for genomic rearrangement, bacterial cell morphology, genomic manipulation, screening for chemical compound etc.

My education trains your social skills like critical thinking, trouble shooting, even attitude and communication. Research is a good model to learn them, so not only final results, but the processes are also important. The most important skill for Master degree is to ask a right question. If you ask wrong question, you will not get right answer. Furthermore, the most important skill for PhD degree is to ask an interesting question. The interesting question will open a novel scientific field. Furthermore, people in my laboratory are coming from different countries and departments. You can enjoy the mixed culture.

Recent selected publications in the last 5 years

1. Matsumoto T*, Hashimoto M*, Huang WC, Teng CH, Niwa T, Yamada M, Negishi T. (2024) Molecular characterization of a carbon dioxide-dependent Proteus mirabilis small-colony variant isolated from a clinical specimen. J Infect Chemother. 30(9):881-886.
2. Hashimoto M**,** Mao BH, Chiou CS, Huang WC, Nyoman Putra Dwija IB, Jeng SL, Wu JJ, Wang MC, Lin WH, Tseng CC, Teng CH. (2022) Association between Escherichia coli with NotI-restriction resistance and urinary tract infections. J Microbiol Immunol Infect. S1684-1182(21)00271-1.
3. Kotaka Y, Hashimoto M, Lee KI, Kato JI. (2023) Mutations identified in engineered Escherichia coli with a reduced genome. Front Microbiol. 14:1189877.
4. Hashimoto M, Mao BH, Chiou CS, Huang WC, Nyoman Putra Dwija IB, Jeng SL, Wu JJ, Wang MC, Lin WH, Tseng CC, Teng CH. (2022) Association between Escherichia coli with NotI-restriction resistance and urinary tract infections. J Microbiol Immunol Infect. 55: 686-694.
5. Hashimoto M, Ma YF, Wang ST, Chen CS, Teng CH. (2021) Iron Acquisition of Urinary Tract Infection Escherichia coli Involves Pathogenicity in Caenorhabditis elegans. Microorganisms. 9(2):310.
6. Matsumoto T*, Hashimoto M*, Teng CH, Hsu PC, Ota Y, Takamizawa M, Kato R, Negishi T. (2020) Molecular characterization of a carbon dioxide-dependent Escherichia coli small- colony variant isolated from blood cultures. Int J Med Microbiol. 310(5):151431.

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研究興趣：

1. 神經免疫與神經退化
2. 小膠質細胞誘發神經毒性;
3. 腦細胞培養開發
4. 膠質細胞與神經細胞的交互作用

選擇性代表作:

1. **Chu CH**, Chen JS, Chan YL, Lu WJ, Huang YT, Mao PC, Sze CI, Sun H.* TIAM2S-positive microglia enhance inflammation and neurotoxicity through soluble ICAM-1-mediated immune priming ***FASEB J. 2023 Nov;37(11):e23242.***
2. Kuo HC, Chen SL, Chiu SC, Lee KF, **Chu CH*** Tolerized Microglia Protect Neurons Against Endotoxin-Induced TNF-α Production via an LBP-Dependent Intracellular p38 MAPK Signaling Pathway ***Inflammation 2023 Oct;46(5):2011-2023.***
3. Kuo HC, Lee KF, Chen SL, Chiu SC, Lee LY, Chen WP, Chen CC, **Chu CH*** Neuron–Microglia Contacts Govern the PGE2 Tolerance through TLR4-Mediated de Novo Protein Synthesis. ***Biomedicines. 2022; 10(2):419.***
4. **Chu CH**, Chen JS, Chuang PC, Su CH, Jan YL, Yang YJ, Chisng YT, Su YY, Gean PW, Sun H.* TIAM2S as a novel key regulator for serotonin level enhances dendritic plasticity and locomotion behaviors ***FASEB J. 2020 Feb;34(2):3267-3288.***
5. **Chu CH**, Wang S, Li CL, Chen SH, Hu CF, Chung YL, Chen SL, Wang Q, Lu RB, Gao HM, Hong JS* Neurons and astroglia govern microglial endotoxin tolerance through macrophage colony-stimulating factor receptor-mediated ERK1/2 signals. ***Brain Behav Immun. 2016 Jul;55:260-72.***
6. **Chu CH**, Chen SH, Wang Q, Langenbach R, Li H, Zeldin D, Chen SL, Wang S, Gao H, Lu RB, Hong JS* PGE2 Inhibits IL-10 Production via EP2-Mediated β-Arrestin Signaling in Neuroinflammatory Condition. ***Mol Neurobiol. 2015 Aug;52(1):587-600.***

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研究興趣：

1. 病毒共感染與宿主調控：研究 SARS-CoV-2、IAV 等如何透過宿主受體與醣基修飾影響感染與共感染機制，進一步探討病毒與癌症交互作用及免疫逃逸機制，並應用多體學技術解析病毒劫持宿主基因與代謝路徑。
2. 醣科學與 RNA 結合蛋白：研究 N-鏈糖基化在癌症、糖尿病與發炎中的調控機制，探討醣基修飾對 RNA 代謝與 AGO2 在核內 RNA 干擾的影響。
3. 癌症與病毒疫苗開發：運用生物資訊與 AI 建模設計單株抗體與疫苗，研究 SARS-CoV-2、IAV、DENV、EBV 在宿主免疫調控中的作用，開發醣基標靶治療與 RNAi 免疫療法 以應用於病毒感染與癌症治療。

選擇性代表作：

1. **Huang HC** and Angeletti D. Monoclonal antibodies lock down SARS-CoV-2 spike. *Trends in Immunology* 2023 Oct 5.
2. **Huang HC**, Wang SH, Fang GC, Chou WC, Liao CC, Sun CP, Jan JT, Ma HH, Ko HY, Ko YA Chiang MT, Liang JJ, Kuo CT, Lee TA, Diego Morales-Scheihing DM, Shen CY, Chen SY, McCullough LD, Cui L, Wernig G, Tao MH, Lin YL, Chang YM, Wang SP, Lai YJ, Li CW. Upregulation of PD-L1 by SARS-CoV-2 promotes immune evasion. *Journal of Medical Virology*. 2023 7.
3. **Huang HC**, Lai YJ, Liao CC, Yang WF, Huang KB, Lee IJ, Chou WC, Wang SH, Wang LH, Hsu JM, Sun CP, Kuo CT, Wang J, Hsiao TC, Yang PJ, Lee TA, Huang W, Li FA, Shen CY, Lin YL, Tao MH, Li CW. Targeting conserved N-glycosylation blocks SARS-CoV-2 variant infection in vitro. *EBioMedicine*. 2021 Dec;74:103712.
4. **Huang HC**, Liao CC, Wang SH, Lee IJ, Lee TA, Hsu JM, Kuo CT, Wang J, Hsieh WC, Chang SJ, Chen SY, Tao MH, Lin YL, Lai YJ, Li CW. Hyperglycosylated spike of SARS-CoV-2 gamma variant induces breast cancer metastasis. *Am J Cancer Res.* 2021 Oct 15;11(10):4994-5005.
5. **Huang HC**, Bi-He Cai, Ching-Shu Suen, Hsueh-Yi Lee, Ming-Jing Hwang, Fu-Tong Liu, Reiji Kannagi BGN/TLR4/NF-κB Mediates Epigenetic Silencing of Immunosuppressive Siglec Ligands in Colon Cancer Cells (2020). *Cells*. 2020, 9, 397.

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研究興趣：

Viral pathogenesis, virus-host cell interaction, diagnostic virology, epidemiology, virulence gene analysis, antigenicity and vaccine development of enterovirus A71, influenza, dengue and SARS-CoV-2 viruses.

近五年代表作：

1. Hung SJ, Hsu YM, Huang SW, Tsai HP, Yang Lee LY, Hurt A, Barr IG, Shih SR, Wang JR*. 2020. Genetic variations on 31 and 450 residues of influenza A nucleoprotein affect viral replication and translation. J. Biomed. Sci. Jan 6;27(1):17.
2. Huang SW, Tsai HP, Hung SJ, Ko WC, Wang JR*. 2020. Assessing the risk of dengue severity using demographic information and laboratory test results with machine learning. PLoS Negl Trop Dis 2020 Dec 23;14(12):e0008960._
3. Cheng YW, Chuang YC, Huang SW, Liu CC, Wang JR*. 2022. An auto-antibody identified from phenotypic directed screening platform shows host immunity against EV-A71 infection. J. Biomed. Sci. 2022 Feb 8;29(1):10.
4. Cheng D, Huang SW, Chin WX, Hung SJ, Tsai HP, Chu JJH, Chao CH, Wang JR*. 2022. Impact of intrahost NS5 nucleotide variations on dengue virus replication. Front. Microbiol. 13:894200.
5. Chao CH, Cheng D, Huang SW, Chuang YC, Yeh TM and Wang JR*. 2022. Serological responses triggered by different SARS-CoV-2 vaccines against SARS-CoV-2 variants in Taiwan. Front. Immunol. 13:1023943.
6. Cheng D, Huang SW, Tsai YH, Lien YY, Wang JR*. 2023. Antigenic mapping of enterovirus A71 from Taiwan and Southeast Asia. Antiviral Res. 212:105569.
7. Hsieh WS, Chao CH, Shen CY, Cheng D, Huang SW, Wang YF, Chen CC, Chen SH, Hsu LJ, Wang JR*. 2024. VP1 Codon deoptimization and high-fidelity substitutions in 3D polymerase as potential vaccine strategies for eliciting immune responses against enterovirus A71. J Virol. Jan 23;98(1):e0155823. doi: 10.1128/jvi.01558-23. Epub 2024 Jan 4.
8. Tsai YY, Cheng D, Huang SW, Hung SJ, Wang YF, Lin YJ, Tsai HP, Chu JJH, Wang JR*. 2024. The molecular epidemiology of a dengue virus outbreak in Taiwan: population wide versus infrapopulation mutation analysis. PLOS NTD: https://doi.org/10.1371/journal.pntd.0012268
9. Hee JR, Cheng D, Chen YH, Wang SH, Chao CH, Huang SW, Ling P, Wan SW, Chang CP, Chu JJH, Yeh TM, Wang JR. 2025. A non-structural protein 1 substitution of dengue virus enhances viral replication by interfering with the antiviral signaling pathway. J Biomed Sci 32, 25 (2025). https://doi.org/10.1186/s12929-024-01116-4.
10. Shen CY, Cheng D, Ruan JW, Wang JR. 2025. Infection of neuronal cells by severe case enterovirus A71 enhances NF-κB activity and increases NF-κB related pro-inflammatory cytokines. J Med Virol 97:e70308. https://doi.org/10.1002/jmv.70308.

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研究興趣：

1. 探討腫瘤抑制蛋白質 WWOX 在癌症發展進程中之角色：我們過去的研究已經證實 WWOX 有調控細胞生長、凋亡、與基因組穩定的作用，將繼續深入探討 WWOX 所影響的細胞訊息傳遞路徑與分子機制。
2. 分析 WWOX 調控細胞生理作用的分子機制。
3. 研究WWOX影響免疫細胞功能之角色。

近五年代表作：

1. Cheng YY, Chou YT, Lai FJ, Jan MS, Chang TH, Jou IM, Chen PS, Lo JY, Huang SS, Chang NS, Liou YT, Hsu PC, Lin YS, and **Hsu LJ**. 2020. *Wwox* deficiency leads to neurodevelopmental and degenerative neuropathies and glycogen synthase kinase 3β-mediated epileptic seizure activity in mice. Acta Neuropathol Commun. 8:6.
2. Huang SS, **Hsu LJ**, Chang NS. 2020. Functional role of WW domain-containing proteins in tumor biology and diseases: insight into the role in ubiquitin-proteasome system. FASEB BioAdv. 2:234-253.
3. Chou YT, Lai FJ, Chang NS, **Hsu LJ**. 2020. *Wwox* deficiency causes downregulation of prosurvival ERK signaling and abnormal homeostatic responses in mouse skin. Front. Cell Dev. Biol. 8:558432.
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6. Hsu CY*, Lee KT, Sun TY, Sze CI, Huang SS*, **Hsu LJ***, Chang NS. 2021. WWOX and its binding proteins in neurodegeneration. Cells 10:1781. (*****contributed equally)
7. Chang YS, Hou SY, Yu SS, Tsai SY, Chen YY, **Hsu LJ**, Tsai PJ, Lin HK, Lin CH, Tsai YS. 2022. Postnatal dexamethasone therapy impairs brown adipose tissue thermogenesis and autophagy flux in neonatal rat pups. Theranostics 12(13):5803-5819.
8. Lin YH, Shih YH, Yap YV, Chen YW, Kuo HL, Liu TY, **Hsu LJ**, Kuo YM, Chang NS. 2022. Zfra inhibits TRAPPC6AΔ-initiated pathway of neurodegeneration. Int J Mol Sci. 23:14510.
9. Cheng HC, Huang PH, Lai FJ, Jan MS, Chen YL, Chen SY, Chen WL, Hsu CK, Huang W, **Hsu LJ**. 2023. Loss of fragile *WWOX* gene leads to senescence escape and genome instability. Cell Mol Life Sci. 80(11):338.
10. Hsieh WS, Chao CH, Shen CY, Cheng D, Huang SW, Wang YF, Chen CC, Chen SH, **Hsu LJ****, Wang JR**. 2024. VP1 codon deoptimization and high-fidelity substitutions in 3D polymerase as potential vaccine strategies for eliciting immune responses against enterovirus A71. J Virol. 98(1):e0155823. (**correspondence)
11. Lin WH, Sheu SM, Wu CF, Huang WC, **Hsu LJ**, Yu KC, Cheng HC, Kao CY, Wu JJ, Wang MC, Teng CH. 2025. O-antigen of uropathogenic *Escherichia coli* is required for induction of neutrophil extracellular traps. J Microbiol Immunol Infect. 58(2):209-218.

張權發 *(Chang, Chuan-Fa, Ph.D.)*

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研究興趣：

1. 利用醣質體蛋白體學方法研究腸病毒 A71 型之致病機轉。
2. 以醣質體及蛋白質體方法尋找癌細胞上新型醣類癌症標記。
3. 研究醣類轉移酵素在癌細胞生長及轉移所扮演的角色。
4. 醣類微矩陣晶片(Carbohydrate Microarray)製作及研究應用。

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專長與研究興趣:

1. 維生素B的生理與病理作用機轉
2. 以斑馬魚模式研究神經功能、行為分析及癲癇疾病模式之建立與應用
3. 以斑馬魚模式探討干擾葉酸代謝對病理性血管新生之影響與治療潛能
4. 斑馬魚癌症及黑色素細胞相關疾病模式之建立與應用

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研究興趣：

代謝致病機轉之探討

肥胖、糖尿病、心血管疾病與癌症占全世界人數多達 15%的比例，而且已經被證實與慢性發炎或代謝疾病有密切的關聯性，亦為全球急欲解決的課題。因此，藉由脂肪細胞(adipocytes)機轉上的探討，以及肥胖及糖尿病等代謝疾病模式的研究，可以釐清慢性發炎及代謝異常在癌症所扮演的重要角色。

個人化腫瘤標誌之搜尋及探討

肝癌及尿路上皮癌為台灣常見的癌症，因此如何藉由準確性高、非侵入性的檢測方式早期發現，並以個人化的方式加以有效的治療為本實驗室研究的目標。實驗室以核酸晶片的資料挑選一些癌症相關之腫瘤標誌作深入探討，如：與氧化壓力相關、與致癌訊息傳遞路徑相關、與 microRNA 相關、及免疫癌症相關之基因…等，以實現個人化醫學檢驗之目標。

砷化物致癌及抗癌之研究

由於砷化物的抗癌機轉為多標的攻陷癌細胞，因此其抗藥性問題不若標靶藥物嚴重。若能釐清其抗癌機轉及副作用，進而合併其他藥物於臨床醫療的使用上，將更有助於提昇其抗癌效果。除此，如何避免其毒性作用以提供臨床治療之參考，亦為重要的臨床課題。

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專長與研究興趣:

1.肝癌發生(hepato-carcinogenesis)與 B 型肝炎病毒感染之關係與分子機轉: B 型肝炎病毒感染是導致肝癌很重要的原因。在癌症發生過程中，細胞常發生基因不穩定性(genomic instability)。因此維持基因的穩定與完整性對於預防癌症發生扮演重要的角色。我們發現 B 型肝炎病毒的表面抗原 pre-S2 突變種會造成基因不穩定性及造成 DNA 損害(DNA damage)。因此我們以 B 型肝炎病毒為 study model，探討慢性 B 型肝炎帶原者在轉變成肝癌的過程中 DNA damage 與 DNA repair 機制的調控及其對 HCC 發生的影響。

2.DNA Repair 之分子病理: DNA Repair (DNA 修復)是細胞內維持 DNA 結構完整及修復 DNA 損害最重要的一個機制。當生物體 DNA 受到環境途變原(environmental mutagens)例如 x-ray，紫外線，以及有毒化學物質等刺激而引起 DNA 結構不正常時，就需靠 DNA Repair 功能來使之恢復正常功能。DNA Repair 功能異常的病人由於 DNA 突變率較高，導致癌症的機率較正常人高出許多。我們主要的研究方向為探討 DNA Repair 的分子機轉及其調控，尤其是近年來才分離出的因子 hHR23 A 及 hHR23B (human homolog of Rad23 A / B)，探討其在 DNA Repair 過程中所扮演的角色。除此之外，我們也利用微矩陣(Microarray)生物晶片技術來探討紫外線等環境途變原所引發的 DNA Repair 分子機轉。同時我們也進一步分析 DNA Repair 不正常病人的細胞株，以了解 DNA Repair 異常所引發的相關病理機制。

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研究興趣:

多潛能幹細胞分化心肌與心血管細胞分化與成熟機制, 微組織力學平台建立結合磁性感測即時偵測系統, 遺傳性心臟病於物化刺激下之分子、功能特徵以及代謝狀況

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研究興趣：

(1) C 型肝炎病毒細胞培養之感染、複製、致病模式與抗病毒藥物

(2) C 型肝炎病毒顆粒之型態與生物特性

(3) 脂肪代謝與病毒感染之相關性

(4) 載脂蛋白 (apolipoproteins)在病毒感染、代謝性疾病、肥胖之影響

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2. Cheng PN, Liu WC, Tsai HW, Wu IC, Chang TT, **Young KC**. Association of intrahepatic cccDNA reduction with the improvement of liver histology in chronic hepatitis B patients receiving oral antiviral agents. J Med Virol. 2011 Feb 83:602-607. (correspondence)
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4. Lee JW, Liao PC, **Young KC**, Chang CL, Chen SSL, Chang TT, Lai, MD, Wang SW. Identification of hnRNPH1, NF45, and C14orf166 as Novel Host Interacting Partners of the Mature Hepatitis C Virus Core Protein. J Proteome Res 2011 Aug 10(10):4522-4534.
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研究興趣：

本實驗室主軸為探討微生物感染之先天免疫代謝機制，建立人類感染性疾病之動物模式，並作為治療藥物(益生菌)篩選之轉譯醫學研究。主軸為：(1)**A群鏈球菌之致病機轉** (2)**困難梭狀桿菌感染之腸炎病理機制** (3)**益生菌之先天免疫代謝調控機制**。

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3. YH Liu, PH Wu, CC Kang, YS Tsai, CK Chou, CT Liang, JJ Wu, YS Lin, SY Wang, CC Liu, and **PJ Tsai***. Group A Streptococcus subcutaneous infection-induced encephalopathy is attenuated by blocking circulating TNF. ***Front. Microbiol.*** 2019. 10:265.
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6. IL Hsu, FH Yeh, YC Chin, CI Cheung, ZC Chia, LX Yang, YJ Chen, TY Cheng, SP Wu, **PJ Tsai***, NY Lee*, MY Liao*, and CC Huang*. Multiplex antibacterial processes and risk in resistant phenotype by high oxidation-state nanoparticles: New killing process and mechanism investigations. ***Chem. Engine. J.*** 2021. 409: 128266. (Cover page)
7. YH Lai#, BY Tsai#, CY Hsu, YH Chen, PH Chou, YL Che, H C, Liu, WC Ko, **PJ Tsai***, and YP Hung*. The role of Toll-like receptor-2 in *Clostridioides difficile* infection: evidence from mouse model to clinical patients. ***Front Immunol.*** 2021. 12:691039.
8. BY Tsai#, YH Lai#, CW Chiu, CY Hsu, YH Chen, YL Chen, **PJ Tsai***, YP Hung*, and WC Ko*. Effect of Doxycycline in Decreasing the Severity of *Clostridioides difficile* Infection in Mice. ***Antibiotics.*** 2022. 11:116.
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12. BY Tsai#, **PJ Tsai#**, CC Lee, CW Chiu, YH Lai, JC Lee, WC Ko, and YP Hung. Association of Single Nucleotide Polymorphisms in Nucleotide-Binding Domain Leucine-Rich Repeat Protein 1 with *Clostridioides difficile* Colonization or Infection. ***Infect Drug Resist.*** 2023. 16:413-421. (equal contribution)
13. CS Chang, SS Yu, LC Ho, SH Chao, TY Chou, AN Shao, LZ Kao, CY Chang, YH Chen, MS Wu, **PJ Tsai***, N. Maeda, and YS Tsai*. Inguinal fat compensates whole body metabolic functionality in partially lipodystrophic mice with reduced PPARγ expression. ***Int J Med Sci.*** 2023.
14. SY Leu, YL Tsang, CC Yang, AN Shao, CY Chang, LC Ho, HK Lin, **PJ Tsai***, JM Sung*, and YS Tsai*. Current insights on NLRP3 inflammasome regulation in metabolic diseases. ***J. Endocrinol.*** 2023.

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專長與研究興趣:

- RNA metabolism
- Post-translational regulation
- Precision oncology

近五年代表作

Refereed Paper (As a first or corresponding author):

1. Hui-Huang Lai, Jie-Ning Li, Ming-Yang Wang, Hsin-Yi Huang, Carlo M. Croce, Hui-Lung Sun, Yu-Jhen Lyu, Jui-Wen Kang, Ching-Feng Chiu, Mien-Chie Hung, Hiroshi I. Suzuki, **Pai-Sheng Chen*** (2018, Feb). HIF-1α promotes autophagic proteolysis of Dicer and enhances tumor metastasis. *Journal of Clinical Investigation*, 2018 Feb 1;128(2):625-643. doi: 10.1172/JCI89212. **(IF 13.3, Ranking 2.1%) *Corresponding Author**
2. Hui-Huang Lai, **Pai-Sheng Chen*** (2018, Aug). Dual mechanism of Dicer downregulation facilitates cancer metastasis. *Molecular & Cellular Oncology*, 24;5(5):e1472056. doi: 10.1080/23723556.2018.1472056. eCollection 2018. **(IF 2.6, Ranking 54.3%) *Corresponding Author**
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4. Hui-Huang Lai, Chih-Wei Li, Chih-Chen Hong, Hung-Yu Sun, Da-Liang Ou, **Pai-Sheng Chen*** (2019, Jan). TARBP2-mediated destabilization of Nanog overcomes sorafenib resistance in hepatocellular carcinoma. *Molecular Oncology*, 2019 Jan 18. doi: 10.1002/1878-0261.12449. [Epub ahead of print]. MOST 107-2320-B-006-068. **(IF 5.0, Ranking 20.8%) *Corresponding Author**
5. Ming-Yang Wang, Hsin-Yi Huang, Yao-Lung Kuo, Chiao Lo, Hung-Yu Sun, Yu-Jhen Lyu, Bo-Rong Chen, Jie-Ning Li, **Pai-Sheng Chen***. (2019, Feb). TARBP2-Enhanced Resistance During Tamoxifen Treatment in Breast Cancer. *Cancers*, 2019, 11(2), 210; doi.org/10.3390/cancers11020210. *US Patent #US 11,435,353 B2 and European Patent Approved #3539541* **(IF 4.5, Ranking 24.2%) *Corresponding Author**
6. **Pai-Sheng Chen**[#], Shao-Chieh Lin, Shaw-Jenq Tsai* (2020, Mar). Complexity in Regulating microRNA Biogenesis in Cancer. *Experimental Biology and Medicine*, 245(5):395-401. doi: 10.1177/1535370220907314. Epub 2020 Feb 19. **(IF 2.8, Ranking 48.7%) [#]First Author**
7. **Pai-Sheng Chen**[#], Wen-Tai Chiu, Pei-Ling Hsu, Shih-Chieh Lin, I-Chen Peng, Chia-Yih Wang, Shaw-Jenq Tsai* (2020, May). Pathophysiological Implications of Hypoxia in Human Diseases. *Journal of Biomedical Science*, 27(1):63. doi: 10.1186/s12929-020-00658-7. **(IF 9.0, Ranking 7.9%) [#]First Author**
8. Jie-Ning Li, Hui-Lung Sun, Ming-Yang Wang, **Pai-Sheng Chen*** (2021, Jul). E-cadherin Interacts With Posttranslationally-Modified AGO2 to Enhance miRISC Activity. *Frontiers in Cell and Developmental Biology*, 9:671244. doi: 10.3389/fcell.2021.671244. eCollection 2021. **(IF 4.6, Ranking 12.8%) *Corresponding Author**
9. Jie-Ning Li, Ming-Yang Wang, Yi-Ting Chen, Yao-Lung Kuo, **Pai-Sheng Chen*** (2021, Dec). Expression of SnoRNA U50A Is Associated with Better Prognosis and Prolonged Mitosis in Breast Cancer. *Cancers*. 13(24):6304. doi: 10.3390/cancers13246304. *European Patent Approve #3540078* **(IF 4.9, Ranking 24.2%) *Corresponding Author**
10. Yu-Yun Shao[#], **Pai-Sheng Chen**[#], Liang-In Lin, Bin-Shyun Lee, Andrew Ling, Ann-Lii Cheng, Chiun Hsu & Da-Liang Ou* (2022, Mar). Low miR-10b-3p associated with sorafenib resistance in hepatocellular carcinoma. *British Journal of Cancer*. doi: 10.1038/s41416-022-01759-w. Online ahead of print. **(IF 8.1, Ranking 14.3%) [#]First Author**
11. Jie-Ning Li, Zhu-Jun Loh, Hui-Wen Chen, I-Ying Lee, Jui-Hung Tsai[*], **Pai-Sheng Chen**[*]. (2024, Oct) SnoRNA U50A mediates everolimus resistance in breast cancer through mTOR downregulation. ***Translational Oncology***, Volume 48, 2024. **(IF 4.5, Ranking 24.2%) *Corresponding Author**
12. Jie-Ning Li, Ming-Yang Wang, Yu-Jhen Lyu, Pownraj Brindangnanam, Mohane Selvaraj Coumar, **Pai-Sheng Chen***. (2024, Oct). A transcription-independent role for HIF-1α in modulating microprocessor assembly. ***Nucleic Acids Research***. 52(19):11806-11821. doi: 10.1093/nar/gkae792. **(IF 16.1, Ranking 1.9%) *Corresponding Author**

Patents

1. Method of Evaluating Drug Resistance and Treatment Effect. **European Patent #EP3539541 B1. Chen Pai-Sheng***, Li Jie-Ning, Kuo Yao-Lung, Wang Ming-Yang. 2020/12 Approved
2. Method of Evaluating Drug Resistance and Treatment Effect. **US Patent #US 11,435,353 B2. Chen Pai-Sheng***, Li Jie-Ning, Kuo Yao-Lung, Wang Ming-Yang. 2022/09 Approved
3. Method and kit for the evaluation of the prognosis of breast cancer. **European Patent #EP3540078. Chen Pai-Sheng***, Li Jie-Ning, Kuo Yao-Lung. 2022/10 Approved

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專長與研究興趣:

微生物體學(Microbiome)、腸道細菌與免疫學、肥胖與代謝疾病

近五年代表作:

1. Chen, H. D., Kao, C. Y., Liu, B. Y., Huang, S. W., Kuo, C. J., Ruan, J. W., Lin, Y. H., Huang, C. R., Chen, Y. H., Wang, H. D., Aroian, R. V. & Chen, C. S. HLH-30/TFEB-mediated autophagy functions in a cell-autonomous manner for epithelium intrinsic cellular defense against bacterial pore-forming toxin in C. elegans. Autophagy. 2017 Feb;13(2):371-385. doi: 10.1080/15548627.2016.1256933.
2. Ruan JW, Statt S, Huang CT, Tsai YT, Kuo CC, Chan HL, Liao YC, Tan TH, Kao CY. Dual-specificity phosphatase 6 deficiency regulates gut microbiome and transcriptome response against diet-induced obesity in mice. Nat Microbiol. 2016 Nov 28;2:16220. doi: 10.1038/nmicrobiol.2016.220.
3. Statt S, Ruan JW, Huang CT, Wu R, Kao CY. Lipidome and transcriptome profiling of pneumolysin intoxication identifies networks involved in statin-conferred protection of airway epithelial cells. Sci Rep. 2015 May 29;5:10624. doi: 10.1038/srep10624.
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專長說明：

臨床生化學、檢驗品管學、血管生物學、心血管疾病機制

研究興趣:

There are two research interests in my lab. First, I have been investigating the functions of macrophages in regulating atherosclerosis and vascular inflammation. The polarization of macrophages significantly alters the progression of cardiovascular disease toward pro- or anti-inflammation. Immunometabolism of macrophages and the microenvironment determine macrophage characteristics, which may provide a therapeutic strategy for treating cardiovascular diseases. Second, the development of laboratory-derived tests, particularly mass spectrometry analysis, is the other research interest in my lab. These works intend to bring new biochemical test platforms applied in precision medicine.

近五年代表作:

1. Shih PC, Lin CH, Chokkalingam U, Prakash E, Kao CN, Chang CF, Lin WL. The Aloe vera acemannan polysaccharides inhibit phthalate-induced cell viability, metastasis, and stemness in colorectal cancer cells. Ecotoxicol Environ Saf. 2024 Nov 18;288:117351.
2. Chi WY, Lee GH, Tang MJ, Chen BH, Lin WL, Fu TF. Disturbed intracellular folate homeostasis impairs autophagic flux and increases hepatocytic lipid accumulation. BMC Biology. 2024 Jul;22 (1): 146
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4. Lin WL, Hung JH and Huang Wenya. Association of the Hepatitis B virus large Surface Protein with Viral Infectivity and Endoplasmic Reticulum Stress-mediated Liver Carcinogenesis (review). Cells. 2020 Sep, 8;9 (9):2052-67.
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7. Lin WL, Guu SY, Tsai CC, Prakash E, Viswaraman M, Chen HB, and Chang CF. Derivation of cinnamon blocks leukocyte attachment by interacting with sialosides. PLoS One. 2015 Jun 15; 10(6):e0130389.
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9. Lin WL, Lin YS, Shi GY, Chang CF, and Wu HL. Lewisy Promotes Migration of Oral Cancer Cells by Glycosylation of Epidermal Growth Factor Receptor. PLoS One. 2015 Mar 23;10(3):e0120162.
10. Lin WL, Chang CF, Shi CS, Shi GY, and Wu HL. Recombinant Lectin-Like Domain of Thrombomodulin Suppresses Vascular Inflammation by Reducing Leukocyte Recruitment via Interacting with Lewis Y on Endothelial Cells. Arterioscler Thromb Vasc Biol. 2013 Oct;33(10):2366-73.
11. Cheng TL, Wu YT, Lai CH, Kao YC, Kuo CH, Liu SL, Hsu YY, Chen PK, Cho CF, Wang KC, Lin WL, Chang BI, Chen CM, Weiler H, Shi GY, and Wu HL. Thrombomodulin Regulates Keratinocyte Differentiation and Promotes Wound Healing. J Invest Dermatol. 2013 Jun;133(6):1638-45.

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研究興趣：

1. **陰道鞭毛蟲系統生物學**：陰道滴蟲是非病毒源的性病中，最盛行的病原體；而且會提高患者感染人類愛滋病毒的危險性。隨著臨床上抗藥株的增加，陰道滴蟲症儼然成為公共衛生上的重大威脅。同時這是目前世界上擁有最多基因數的物種，這個基因的存在，超過人的基因的總數，這對未來研究對人類有致病性的寄生蟲，都是一個最重要的基礎研究。隨著這隻寄生蟲基因體被解開後，讓人更容易勘得其中緣由。我們目前使用基因表達晶片，二維電泳，miRNA 晶片，來觀察鐵離子對該寄生蟲生理上與致病機轉的影響。
2. **多形性膠質母細胞瘤系統生物學**：多形性膠質母細胞瘤 (glioblastoma multiforme; GBM) 是大腦最常見的惡性腫瘤，也是不折不扣的腦癌，如僅使用手術治療，中期存活僅有3-4個月；加上手術後放射治療，可延長至 10 個月；加手術後放療及 BCNU，可將中期存活再延長一點至一年，但是五年存活率一般仍為零。我們目前使用基因表達晶片，二維電泳，miRNA 晶片，array CGH 與大鼠動物模式來探討 GBM 在臨床上致病，癒後等相關之基因表達。並以 Kinase 為主幹，探討 GBM 癌化的訊息傳遞模式。

近五年代表作：

1. Liu, YC (Liu, Yu-Cheng); **Shin, JW (Shin, J. W.)**; Tseng, VS (Tseng, Vincent S.) Discovering indirect gene associations by filtering-based indirect association rule mining. International Journal of Innovative Computing Information and Control. 2011 OCT 7(10):6041-6053
2. Kao, HH (Kao, Hsin-Hsin); Wu, CJ (Wu, Chao-Jung); Won, SJ (Won, Shen-Jeu); **Shin, JW (Shin, Jyh-Wei)**; Liu, HS (Liu, Hsiao-Sheng); Su, CL (Su, Chun-Li) Kinase Gene Expression and Subcellular Protein Expression Pattern of Protein Kinase C Isoforms in Curcumin-treated Human Hepatocellular Carcinoma Hep 3B Cells. PLANT FOODS FOR HUMAN NUTRITION 2011 JUN 66(2):136-142
3. Tai, CH (Tai, Chien-Hsuan); **Shin, JW (Shin, Jyh-Wei)**; Chang, TY (Chang, Tsuey-Yu); Hsiung, SK (Hsiung, Suz-Kai); Lin, CC (Lin, Chun-Che); Lee, GB (Lee, Gwo-Bin) An integrated microfluidic system capable of sample pretreatment and hybridization for microarrays. MICROFLUIDICS AND NANOFLUIDICS 2011 MAY 10(5):999-1009
4. Yeh CY, Shih SM, Yeh HH, Wu TJ, **Shin JW**, Chang TY, Raghavaraju G, Lee CT, Chiang JH, Tseng VS, Lee YC, Shen CH, Chow NH, Liu HS. Transcriptional activation of the Axl and PDGFR-alpha by c-Met through a ras- and Src-independent mechanism in human bladder cancer. BMC Cancer. 2011 Apr 16;11(1):139.
5. Chen PY, Liu HL, Hua MY, Yang HW, Huang CY, Chu PC, Lyu LA, Tseng IC, Feng LY, Tsai HC, Chen SM, Lu YJ, Wang JJ, Yen TC, Ma YH, Wu T, Chen JP, Chuang JI, **Shin JW**, Hsueh C, Wei KC. Novel magnetic/ultrasound focusing system enhances nanoparticle drug delivery for glioma treatment. Neuro Oncol. 2010 Oct;12(10):1050-60. Epub 2010 Jul 27.
6. Wei KC, Huang CY, Chen PY, Feng LY, Wu TW, Chen SM, Tsai HC, Lu YJ, Tsang NM, Tseng CK, Pai PC, **Shin JW**. Evaluation of the prognostic value of CD44 in glioblastoma multiforme. Anticancer Res. 2010 Jan;30(1):253-9.
7. Wang JN, **Shin JW**, Chang TY, Wang JY, Wu JM. Decreased proinflammatory cytokines production in children with complicated parapneumonic pleural effusion after intrapleural fibrinolytic treatment. Inflammation. 2009 Dec;32(6):410-8.
8. Lin WC, Li SC, Lin WC, **Shin JW**, Hu SN, Yu XM, Huang TY, Chen SC, Chen HC, Chen SJ, Huang PJ, Gan RR, Chiu CH, Tang P. Identification of microRNA in the protist Trichomonas vaginalis. Genomics. 2009 May;93(5):487-93. Epub 2009 Feb 3.
9. Liu CJ, Lien KY, Weng CY, **Shin JW**, Chang TY, Lee GB. Magnetic-bead-based microfluidic system for ribonucleic acid extraction and reverse transcription processes. Biomed Microdevices. 2009 Apr;11(2):339-50.

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研究興趣：

1. **棘阿米巴(*Acanthamoeba spp.*)的致病機制與毒力因子：**棘阿米巴角膜炎是自由營生致病性棘阿米巴屬在角膜寄生造成的感染症，嚴重時會造成角膜潰瘍、穿孔、視力甚而整個眼球的喪失。棘阿米巴一旦由眼睛、傷口黏膜感染或經呼吸道吸入肺部，透過血流進入大腦後，引起肉芽腫性阿米巴腦炎。本實驗室自寄生蟲與宿主的交互作用去尋找可能的毒力因子，希望能釐清棘阿米巴破壞角膜上皮細胞及基質的致病機制。
2. **棘阿米巴藥物療程的改良測試與新療程開發**：棘阿米巴的首選治療藥物—聚六亞甲基雙胍(polyhexamethylene biquanide, PHMB)在台灣使用並不普及，臨床上卻已出現數例以此藥物治療無效的案例。目前PHMB對蟲體的作用機制並無詳盡了解，甚而蟲體產生抗藥性的風險評估及蟲體對藥物產生耐受性或是抗藥能力的機轉等相關研究也付之闕如。一旦抗藥蟲株感染發生，後續治療藥物的使用與選擇將無所適從。本實驗室目前正針對此藥物對棘阿米巴的作用進行深入的分析，並同時進行新藥物與療程的測試，期望解決台灣目前對棘阿米巴感染的困境。

近五年代表作：

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專長說明：寄生蟲學、細胞生物學、 系統生物學

研究興趣：

1. 一氧化氮在陰道鞭毛蟲體內的調控角色

本研究室先前證實一氧化氮可延長陰道鞭毛蟲在缺鐵環境之壽命，然而其分子機制仍未知。一氧化氮參與細胞內多個訊號傳遞及細胞反應，如細胞骨架之改變，且在缺鐵狀況下陰道鞭毛蟲會有轉型成偽囊體的過程。因此我們將著重於釐清一氧化氮訊號對細胞轉型的角色為何。

2. 鐵離子媒介之甲硝唑毒殺作用

甲硝唑（metronidaozle）是陰道鞭毛蟲症的首選藥物，然而其抗藥性也不斷被報導。甲硝唑的作用機制仍未知，但已知其毒殺效力與鐵離子或鐵代謝相關。因此本研究室著重於解析鐵與甲硝唑作用之關聯性。其中鐵依賴型細胞死亡（ferroptosis）是否參與甲硝唑的毒殺是我們的研究重點。

3. 原蟲與致病性細菌、病毒之交互作用

陰道鞭毛蟲寄生於陰道，這個環境中充斥著其他微生物，包括細菌與病毒。本研究室探討陰道中益生菌與陰道鞭毛蟲之交互作用，藉此釐清陰道細菌對陰道鞭毛蟲致病力之影響。此外，人類乳突病毒（HPV）感染是造成子宮頸癌的重要因子，且其與陰道鞭毛蟲共感染的機率相當高。然而陰道鞭毛蟲感染是促進或降低癌化是我們好奇的。因此我們會利用系統生物學的方式，探討陰道鞭毛蟲在HPV引起子宮頸癌的過程中究竟扮演什麼角色。

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研究興趣:

我的實驗室主要在整合細胞生物學、生物資訊學、以及分子病理學等方法，來從事腫瘤標誌(Tumor marker)之開發與研究。觀諸現有的腫瘤標誌，以下列兩類在正常細胞中較不會出現：

1.腫瘤胚基因/蛋白(Oncofetal genes/proteins):以甲種胎兒蛋白(Alpha fetal protein; AFP)為代表。這類基因在正常成人細胞中表現量極低或完全不表現。

2.融合基因(Fusion genes):以白血病常見的 bcr/abl、pml/rara 等為代表。此類融合基因在正常細胞不會出現。

我們運用自己開發的生物資訊工具來尋找新的腫瘤胚基因，最後找到了一群與細胞分化、胚胎發育極為相關，而在腫瘤又有表現的新穎基因，目前正積極進行研究，一方面運用病理檢體以及臨床資料，期能找出這些基因的臨床應用，另一方面則使用分子生物及細胞生物的方法，希望對這些基因的功能有進一步的了解。

在基因的功能方面，我們找到了一個新穎基因 LRRC16B，具備 leucine rich region domain，由 XTT、soft agar 以及 Xenograft 等研究顯示該基因可以促進細胞 proliferation 及 transformation。該新穎基因的上下游、調控方式、cell cycle 的影響、在胚胎發育及腫瘤生成所扮演的角色等等，尚有許多待值得深入探討的地方。除此之外，尚有 3 個新穎基因經 chromatin immunoprecipitation 顯示為 Wnt 的 Target genes，並且在肝癌組織中會過量表現，這些基因也值得進一步探討。

在基因的臨床應用方面，我們的生物資訊分析找到了 Lin28B，進一步實驗顯示如果在肝癌病人的血流細胞中偵測到 Lin28B 的 transcripts，則有明顯的早期復發的狀況。Lin28B 與 cancer stem cell 之間的關係，也是一個有趣的課題。

除上述基因之外，尚有若干新穎基因初步看來頗為有趣，將來也會是值得探討的對象。

在融合基因方面，本實驗室分別開發出高通量以及高涵蓋率的方法來偵測融合基因。期望未來能夠發現新穎的融合基因，成為癌症診斷與治療的新標的。

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研究興趣:

1. The role of EBV in Hodgkin lymphoma
2. Anti-tumor immunity for diffuse large B-cell lymphoma
3. Translational studies of diffuse large B-cell lymphoma

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研究興趣：

1. 肝臟病理
2. 肝癌發生機轉及預後因子
3. 病毒性肝炎
4. 血庫學

近五年代表作：

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研究興趣：

1. 消化道病理
2. 大腸直腸癌

近五年代表作：

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