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科技部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. YS Cheng, HY Chen, YC Lin, YS Lin, YC Yeh, YH Yeh, YH Cheng, YM Lin, HY Weng, TY Lin, **SC Lin**. The MAEL expression in mitochondria of human spermatozoa and the association with asthenozoospermia. **Andrology**. 2023 Feb 13. doi: 10.1111/andr.13408. Online ahead of print.
2. KC Wei, SF Lai, WL Huang, KC Yang, PC Lai, WJ Wei, TH Chang, YC Huang, YC Tsai, SC Lin, SJ Lin, **SC Lin**. An innovative targeted therapy for fluoroscopy-induced chronic radiation dermatitis. **J Mol Med (Berl)**. 2022 Jan;100(1):135-146
3. HC Lee, CH Ou, YC Huang, PC Hou, CJ Creighton, YS Lin, CY Hu, **SC 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
4. HC Lee, **SC Lin**, MH Wu, SJ Tsai. Inhibiting NTRK2 signaling causes endometriotic lesion regression. **Reproduction** 2021 Jan;161(1):11-19.
5. CY Kao, M Xu ,L Wang ,SC Lin, HJ Lee, L Duraine, HJ Bellen, DS Goldstein, SY Tsai, MJ Tsai. Elevated COUP-TFII expression in dopaminergic neurons accelerates the progression of Parkinson's disease through mitochondrial dysfunction. **PLoS Genet**. 2020 Jun 24;16(6):e1008868.
6. JB Yan, CC Lai, JW Jhu, B Gongol, TL Marin, **SC Lin**, HY Chiu, CJ Yen, LY Wang, IC Peng. Insulin and Metformin Control Cell Proliferation by Regulating TDG-Mediated DNA Demethylation in Liver and Breast Cancer Cells. **Mol Ther Oncolytics** 2020 Jun 24;18:282-294.
7. **SC Lin**, HC Lee, CT Hsu, YH Huang, WN Li, PL Hsu, MH Wu, and SJ Tsai Targeting anthrax toxin receptor 2 ameliorates endometriosis progression. **Theranostics**. 2019; 9(3): 620-632.
8. HC Lee, **SC Lin**, MH Wu, SJ Tsai. Induction of Pyruvate Dehydrogenase Kinase 1 by Hypoxia Alters Cellular Metabolism and Inhibits Apoptosis in Endometriotic Stromal Cells. Reprod Sci. 2019 Jun;26(6):734-744. AL Li, TS Chung, YN Chan, CL Chen, **SC Lin**, YR Chiang, CH Lin, CC Chen , N Ma microRNA expression pattern as an ancillary prognostic signature for radiotherapy. **J Transl Med**. 2018 Dec 5;16(1):341
9. P Li, SY You, C Nguyen, Y Wang, J Kim, D Sirohi, A Ziembiec, DJ. Luthringer, **SC Lin**, T Daskivich, J Wu, MR. Freeman, R Saouaf, D Li, HL. Kim. Genes involved in prostate cancer progression determine MRI visibility. **Theranostics** 2018; 8(7):1752-1765.

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研究興趣及專長：

鈣離子訊息、活細胞分子造影、光遺傳學、癌症抗化性與轉移

近五年代表作：

1. 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.
2. 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.
3. 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.
4. 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.
5. 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.
6. ***Chiu, W.T.***, Vi Tran, T.T., Pan, S.C., Huang, H.K., Chen, Y.C. and Wong, T.W.* (2019 Oct) Cystic fibrosis transmembrane conductance regulator: a possible new target for photodynamic therapy enhances wound healing. *Adv Wound Care* 8(10):476-486.
7. Yang, C.Y., Chang, P.W., Hsu, W.H., Chang, H.C., Chen, C.L., Lai, C.C.*, ***Chiu, W.T.**** and Chen, H.C.* (2019 May) Src and SHP2 coordinately regulate the dynamics and organization of vimentin filaments during cell migration. *Oncogene* 38(21):4075-4094.
8. Chang, Y.J., Lo, Y.L.*, ***Chiu, W.T.****, Huang, C.L., Chang, H.A. and Phan, Q.H. (2018 Dec) Scanned laser pico projection and Stokes-Mueller matrix imaging polarimetry for detecting cancer cells with different cytoskeletal organizations and metastatic potencies. *IEEE Photonics J* 10(6):3901612.
9. Chen, Y.C., ***Chiu, W.T.****, Chang, C., Wu, P.C., Tu, T.Y., Lin, H.P.* and Chang, H.C.* (2018 Oct) Chemo-photothermal effects of doxorubicin/silica-carbon hollow spheres on liver cancer. *RSC Adv* 8:36775-36784.
10. Huang, T.Y., Lin, Y.H., Chang, H.A., Yeh, T.Y., Chang, Y.H., Chen, Y.F., Chen, Y.C., Li, C.C. and ***Chiu, W.T.**** (2018 Jun) STIM1 knockout enhances PDGF-mediated Ca^{2+} signaling through upregulation of the PDGFR–PLCγ–STIM2 cascade. *Int J Mol Sci* 19(6):1799.
11. ***Chiu, W.T.****, Chang, H.A., Lin, Y.H., Lin, Y.S., Chang, H.T., Lin, H.H., Huang, H.S., Tang, M.J. and Shen, M.R. (2018 Feb) Bcl-2 regulates store-operated Ca^{2+} entry to modulate ER stress-induced apoptosis. *Cell Death Discov* 4:37.

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專長說明：

腫瘤生物學

研究興趣:

1. Pancreatic cancer initiation and progression: the interaction of cells within the microenvironment 胰臟癌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

近五年代表作:

1. **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.
2. Wei-Che Tseng, Chi-Yuan Chen, Ching-Yuh Chern , **Chu-An Wang**, Wen-Chih Lee, Ying-Chih Chi, Shu-Fang Cheng, Yi-Tsen Kuo , Ya-Chen Chiu , Shih-Ting Tseng , Pei-Ya Lin, Shou-Jhen Liou, Yi-Chen Li, Chin-Chuan Chen. Targeting HR Repair as a Synthetic Lethal Approach to Increase DNA Damage Sensitivity by a RAD52 Inhibitor in BRCA2-Deficient Cancer Cells. *Int J Mol Sci*. 2021 Apr 23;22(9):4422.
3. **Wang CA** and Shaw-Jenq Tsai. Regulation of lymphangiogenesis by extracellular vesicles in cancer metastasis. *Exp Biol Med (Maywood).* 2021 Jun 18;15353702211021022.
4. 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.
5. **Chu-An Wang**, Yi-Hern Chang , Pei-Chi Hou , Yu-Jing Tai , Wan-Ning Li, Pei-Ling Hsu, Shang-Rung 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. 在細菌感染中細胞內脂多醣及細菌外膜囊泡於內質網自噬作用中之角色及作用機轉。
   Role of intracellular lipopolysaccharide (LPS) and bacterial outer membrane vesicles in ER-phagy during bacterial infection
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. 內質網於登革致病機轉中的角色及影響。
   Role of endoplasmic reticulum in dengue pathogenesis and the implications
4. 細胞自噬作用及LC3相關之吞噬作用於A群鏈球菌感染致病機轉中之角色。
   Role of autophagy and LC3-associated phagocytosis (LAP) in the pathogenesis of group A streptococcal infection

近五年代表作:

1. **Cheng YL**, Zhang K, Kuncha SK, Hensel M, Covarrubias-Pinto A, Gonzalez A, Kew C, Chen W, Diab N, Hornef WM, Dikic I*. Lipopolysaccharides binds to FAM134B triggering ER fragmentation and forming bacteria-containing vacuoles. *Manuscript in preparation.*

2. 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.

3. **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.

4. **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.

5. 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.

6. 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:

本實驗室主要利用 X 射線蛋白質結晶學，並合併冷凍電子顯微鏡，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。本人的研究興趣包括:蛋白質與核酸之間的交互作用、蛋白質構型變化與功能調控、生物大分子複合體的組成、蛋白質與小分子藥物間的交互作用...等。

實驗室目前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此基因組的完整性與功能，若否，則突變容易累積在其中，此與細胞老化及許多神經退化性疾病呈正相關。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)。此複合體涉及了許多粒線體中重要的蛋白質分子，如 DNA polymerase γ，DNA helicase Twinkle 與 exonuclease 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，均仍是未知。本實驗室希望藉由了解 mtDNA 降解體運作的結構機轉，闡明一完整的粒線體 DNA 降解機制，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。

近五年代表作:

1. **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.

2. **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.

3. Chen, S.F., Huang, N.L., Lin, J.H., **Wu, C.C.**, Wang, Y.R., Yu, Y.J., Gilson, M.K.*, and Chan, N.L.* (2018) Structural insights into the gating of DNA passage by the topoisomerase II DNA-gate. *Nature Communications* 9:3085. doi: 10.1038/s41467-018-05406-y.

4. **Wu, C.C.**[1], Baiga, T.J.[1], Downes, M.[1], La Clair, J.J., Atkins, A.R., Richard, S.B., Fan, W., Stockley-Noel, T.A., Bowman, M.E., Noel, J.P.*, and Evans, R.M.* (2017) Structural basis for specific ligation of the peroxisome proliferator-activated receptor delta. *Proceedings of the National Academy of Sciences of the United States of America* 114:E2563-E2570. doi: 10.1073/pnas.1621513114. ([1]These three authors contribute equally to this work)

5. Wang, Y.R., Chen, S.F., **Wu, C.C.**, Liao, Y.W., Lin, T.S., Liu, K.T., Chen, Y.S., Li, T.K., Chien, T.C., and Chan, N.L.* (2017) Producing irreversible topoisomerase II-mediated DNA breaks by site-specific Pt(II)-methionine coordination chemistry. *Nucleic Acids Research* 45:10861-10871. doi: 10.1093/nar/gkx742.

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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：

核糖核酸干擾術（RNAi）是利用小片斷雙股核糖核酸（siRNA）抑制細胞中基因的表現，對研究基因功能或治療病毒感染有相當的價值。本實驗室已經改良以 RNA polymerase III 啟動子表現 shRNA 之質體，建立快速且方便的分析系統篩選極有效的 siRNA 分子，並發展可誘導式之 RNAi 調控系統。利用 RNAi 抑制病毒基因的表現與複製來治療病毒的感染，包括 B 型肝炎病毒、登革熱病毒、腸病毒及鼻咽癌病毒等，並藉由抑制細胞生長與凋亡之相關基因達到腫瘤治療或防止病因性細胞凋亡。

近五年代表作：

1. Cheng TL and Chang WT. (2007) Construction of simple and efficient DNA vector-based short hairpin RNA expression systems for specific gene silencing in mammalian cells. *Methods in Molecular Biology*, 408, 221-39. (invited method)

2. Wu RH, Cheng TL, Lo SR, Hsu HC, Hung CF, Teng CF, Wu MP, Tsai WH, and Chang WT. (2007) A tightly regulated and reversibly inducible siRNA expression system for conditional RNAi-mediated gene silencing in mammalian cells. *Journal of Gene Medicine*, 9, 620-634.

3. Chen CL, Lin CF, Chang WT, Huang WC, Teng CF, and Lin YS. (2008) Ceramide induces p38 MAPK and JNK activation through a mechanism involving a thioredoxin-interacting protein-mediated pathway. *Blood*, 111, 4365-4374.

4. Cheng TL, Teng CF, Tsai WH, Yeh CW, Wu MP, Hsu HC, Hung CF, and Chang WT. (2009) Multi-target therapy of malignant cancers by the head-to-tail tandem array multiple shRNAs expression system. *Cancer Gene Therapy*, 16, 516-531.

5. Cheng TL, Liao CC, Tsai WH, Lin CC, Yeh CW, Teng CF, and Chang WT. (2009) Identification and characterization of mitochondrial targeting sequence and mechanism in human citrate synthase. *Journal of Cellular Biochemistry*, (Proofreaded)

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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.
5. Shiu, J.-H., Chen, C.-Y., Chen, Y.-C., Chang, Y.-T., Chang, Y.-S., Huang, C.-H., and Chuang, W.-J. (2012) ” Effect of P to A mutation of the N-terminal residue adjacent to the RGD motif in rhodostomin on its activity, structure, and dynamics: Importance of dynamic properties in the recognition of integrin ” , Plos One, 7, e28833.
6. Cheng CH, Chen YC, Shiu JH, Chang YT, Chang YS, Huang CH, Chen CY, Chuang WJ. (2012) Dynamics and functional differences between dendroaspin and rhodostomin: Insights into protein scaffolds in integrin recognition. Protein Science,21(12): 1872-84.
7. Chen YC, Cheng CH, Shiu JH, Chang YT, Chang YS, Huang CH, Lee JC, Chuang WJ. (2012) Expression in Pichia pastoris and characterization of Echistatin, a RGD-containing short disintegrin. Toxicon, 60(8):1342-8.

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研究興趣：

- Epigenomes of human malignancies.
- Regulatory mechanisms of methylcytosine deposition in DNA and in RNA.
- Cellular regeneration of pancreas and skeletal muscle.

近年代表作：

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專長與研究興趣:

病菌宿主交互作用(pathogen-host interaction)

近五年代表作:

1. 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.
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12. Yi-Wei Chen, Wen-Chien Ko, **Chang-Shi Chen**, and Po-Lin Chen. Evaluating Virulence and Pathogenesis of Aeromonas Infection in a Caenorhabditis elegans Model. **J Vis Exp.** 2018 Dec 20;(142).
13. Ling-Hsien Tu, Ning-Hsuan Tseng, Ya-Ru Tsai, Yi-Wei Lo, Jien-Lin Charng, Hua-Ting Hsu, Yu-Sheng Chen, Rong-Jie Chen, Ying-Da Wu, Yi-Tsu Chan, **Chang-Shi Chen**, Jim-Min Fang, and Yun-Ru Chen. Rationally designed divalent caffeic amides inhibit amyloid-β fibrillization, induce fibril dissociation, and ameliorate cytotoxicity. **Eur J Med Chem**. 2018 Oct 5;158:393-404.
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15. Cheng-Ju Kuo, Sin-Tian Wang, and **Chang-Shi Chen**. Detection of Enterohemorrhagic Escherichia coli Colonization in Murine Host by Non-invasive In Vivo Bioluminescence System. **J Vis Exp**. 2018 Apr 9;(134).
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17. Chia-Wen Tsai, Rong-Tzong Tsai, Shih-Ping Liu, **Chang-Shi Chen**, Min-Chen Tsai, Shao-Hsuan Chien, Huey-Shan Hung, Shinn-Zong Lin, Woei-Cherng Shyu, and Ru-Huei Fu. Neuroprotective Effects of Betulin in Pharmacological and Transgenic C. elegans Models of Parkinson's Disease. **Cell Transplant.** 2017 Dec;26(12):1903-1918.
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專長說明：

PROTAC/PhosTAC/Bifunctional Molecules/Chemical Biology/Targeted Protein Modification/Drug Discovery/Functional Genomics/Functional Proteomics

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阿茲罕默症，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。搭配生物化學/基因體學/蛋白質體學及化學生物學等領域最新的生物技術，我們將研發新的工具及催化型藥物，例如 PROTAC/PhosTAC 及相關的雙功能分子等，讓我們能專一標靶特定蛋白質，更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:

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2. 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)

3. **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 (*equal contribution)

4. **Po-Han Chen**, and Jen-Tsan Chi. Unexpected zinc dependency of ferroptosis – what is in a name? ***Oncotarget*** (2021) 12(12):1126

5. 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

6. 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

7. **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 (*equal contribution)

8. 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

9. **Po-Han Chen**, Watson Hua-Sheng Tseng, and Jen-Tsan Chi. The intersection of DNA damage response and ferroptosis- a rational for combination therapeutics. ***Biology-Basel*** (2020) 9(8):187

10. Chien-Kuang Cornelia Ding[‡], Joshua Rose[‡], Tianai Sun[‡], Jianli Wu, **Po-Han Chen**, Chao-Chieh Lin, Wen-Hsuan Yang, Kai-Yuan Chen, Hana Lee, Emily Xu, Sarah Tian, Jadesola Akinwuntan, Jinshi Zhao, Ziqiang Guan, Pei Zhou and Jen-Tsan Chi. MESH1 is a cytosolic NADPH phosphatase that regulates ferroptosis. ***Nature Metabolism*** (2020) 2(3):270-277

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12. **Po-Han Chen**, Jimin Hu, Jianli Wu, Duc T. Huynh, Timothy J. Smith, Samuel Pan, Brittany J. Bisnett, Alexander B. Smith, Annie Lu, Brett M. Condon, Jen-Tsan Chi, and Michael Boyce. Gigaxonin glycosylation regulates intermediate filament turnover and may impact giant axonal neuropathy etiology or treatment. ***JCI insight*** (2020) 5(1)

13. **Po-Han Chen**, Jen-Tsan Chi and Michael Boyce. Functional crosstalk among oxidative stress and O-GlcNAc signaling pathways. ***Glycobiology*** (2018) 28(8):556-564

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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)

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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)

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專長與研究興趣:

肺癌分子機制與轉譯研究：

1. 癌症微環境 (tumor microenvironment) 研究。
   A、癌細胞與免疫細胞傳輸系統 (protein trafficking) 與訊息傳遞分析。
   B、細胞 exocytosis 與分泌體 (secretomics) 研究。
2. 癌症幹細胞 (cancer stem cell) 研究。
   A、轉錄調控與訊息傳遞分析。
   B、抗癌藥物與抗體開發。

近五年代表作:

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2. Kuo IY, Yang YE, Yang PS, Tsai YJ, Tzeng HT, Cheng HC, Kuo WT, Su WC, Chang CP*, **Wang YC*. 2021**. Converged Rab37/IL-6 trafficking and STAT3/PD-1 transcription axes elicit an immunosuppressive lung tumor microenvironment. ***Theranostics*** 11(14):7029-7044. (cover article of May 2021 issue)
3. Hsieh CHs, Hsieh HC, Shih FS, Wang PW, Yang LX, Shieh DB*, **Wang YC*. 2021**. An innovative NRF2 nano-modulator induces lung cancer ferroptosis and elicits an immunostimulatory tumor microenvironment. ***Theranostics*** 11(14):7072-7091. (cover article of May 2021 issue)
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6. Jen J, Liu CY, Chen YT, Wu LT, Shieh YC, Lai WW, **Wang YC*. 2018**. Oncogenic zinc finger protein ZNF322A promotes stem cell-like properties in lung cancer through transcriptional suppression of c-Myc expression. ***Cell Death Differ*** 26:1283-1298.
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8. Cho SH, Kuo IY, Lu PF, Tzeng HT, Lai WW, Su WC, **Wang YC*. 2018**. Rab37 mediates exocytosis of secreted frizzled-related protein 1 to inhibit Wnt signaling and thus suppress lung cancer stemness. ***Cell Death Dis*** 9(9):868.
9. Tzeng HT, Tsai CH, Yen YT, Cheng HC, Chen YC, Pu SW, Wang YS, Shan YS, Tseng YL, Su WC, Lai WW, Wu LW* **Wang YC*. 2017**. Dysregulation of Rab37-mediated cross-talk between cancer cells and endothelial cells via thrombospondin-1 promotes tumor neovasculature and metastasis. ***Clin Cancer Res*** 23(9):2335-2345. (highlighs of May 2017 issue)
10. S.-Y. Liao, C.-W. Chiang, C.-H. Hsu, Y.-T. Chen, J. Jen, H.-F. Juan, W.-W. Lai, and **Wang YC*. 2017**. CK1δ/GSK3β/FBXW7α axis promotes degradation of the ZNF322A oncoprotein to suppress lung cancer progression. ***Oncogene*** 36(41):5722-5733.
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12. Jen J, Lin LL, Lo FY, Chen HT, Liao SY, Tang YA, Su WC, Salgia R, Hsu CL, Huang HC, Juan HF, **Wang YC*. 2016**. Oncoprotein ZNF322A transcriptionally deregulates alpha-adducin, cyclin D1 and p53 to promote tumor growth and metastasis in lung cancer. ***Oncogene*** 5;35(18):2357-69.
13. Tang YA, Chen CH, Sun S, Cheng CP, Tseng VS, Hsu HS, Su WC, Lai WW, **Wang YC*. 2015**. Global Oct4 target gene analysis reveals novel downstream PTEN and TNC genes required for drug-resistance and metastasis in lung cancer. ***Nucleic Acids Res*** 43(3):1593-608
14. Tsai CH, Cheng HC, Wang YS, Lin P, Jen J, Kuo IY, Chang YH, Liao PC, Chen RH, Yuan WC, Hsu HS, Yang MH, Hsu MT, Wu CY, **Wang YC*. 2014**. Small GTPase Rab37 targets tissue inhibitor of metalloproteinase 1 for exocytosis and thus suppresses tumor metastasis. ***Nat Commun*** 2014 Sep 3;5:4804.

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研究興趣：

1. Oncogene的致癌機轉研究：

實驗室主要著眼在Src oncoprotein以及EGF receptor如何透過Eps8在細胞內作用而造成細胞不正常地生長與惡化，影響病人預後的能力。

2. 抗癌藥物的研究：

實驗室目前主要在探討細胞致癌機轉，期望經由細胞訊息傳遞的研究找到適合藥物的標靶，來專一性地抑制癌細胞生長。

3. Src/Eps8 在巨噬細胞內參與的免疫功能研究與促癌作用

實驗室發現Src/Eps8表現會受到TLRs的訊息調控。進一步發現。這些蛋白質會參與巨噬細胞的吞噬細菌與殺菌作用。透過此研究得以瞭解這些致癌蛋白在先天免疫的功能以及腫瘤內巨噬細胞如何轉化為M2 type。

近五年代表作：

1. Chen, YJ, MY Hsieh, MY Chang, HC Chen, MS Jan, MC Maa, and **TH Leu***. (2012) Eps8 protein facilitates phagocytosis by increasing TLR4-MyD88 protein interaction in LPS-stimulated macrophages. J Biol Chem 287, 18806-18819.

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3. Hsieh, MY, MY Chang, YJ Chen, YK Li, TH Chuang, GY Yu, CH Cheung, HC Chen, MC Maa, and **TH Leu**.* (2014) The inducible nitric-oxide synthase (iNOS)/Src axis mediates Toll-like receptor 3 tyrosine 759 phosphorylation and enhances its signal transduction leading to interferon-β synthesis in macrophages. J Biol Chem. 289, 9208-9222.

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5. Chen, HC, WC Chien, MY Chang, MY Hsieh, MD Lai, MC Maa, and **TH Leu***. (2015) The iNOS/Src/FAK axis contributes to lithium chloride-mediated macrophage migration. Nitric Oxide. 47, 58-64.

6. Chuang JP, Kao CY, Lee JC, Ling P, Maa MC, **Leu TH***. (2020) EPS8 regulates an NLRP3 inflammasome-independent caspase-1 activation pathway in monosodium urate crystal-treated RAW264.7 macrophages. Biochem Biophys Res Commun. 2020 Sep 24;530(3):487-493. doi: 10.1016/j.bbrc.2020.05.084. Epub 2020 Jun 25.

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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。

3. 鈣離子訊息系統在腫瘤生物學的重要角色

鈣池調控的鈣離子流入(Store-operated calcium entry)為胞內鈣離子濃度調控的主要機制，產生的鈣離子訊息調控在癌症進程，如腫瘤增生、侵襲與轉移扮演極重要的角色。本實驗室研究主軸包括細胞內鈣離子運送蛋白及通道如何被特定生長因子、細胞激素或致癌基因調控，最終影響癌症的發展及進程。

近五年代表作：

1. Hsu YT, Chen LH, Liu YH, Chu SK, Chen TY, Tsai KJ, **Shen MR***, Liu W* (2023). Electrical sympathetic neuromodulation protects bone marrow niche and drives hematopoietic regeneration during chemotherapy. *Small Methods*, e2201300.
2. Chen YF, Wu CH, Chen LH, Lee HW, Lee JC, Yeh TK, Chang JY*, Chou MC, Wu HL, Lai YP, Song JS, Yeh KC, Chen CT, Lee CJ, Shia KS*, **Shen MR*.** (2022) Discovery of potential neuroprotective agents against paclitaxel-induced peripheral neuropathy. *Journal of Medicinal Chemistry*, 65(6):4767-4782.
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4. Yeh YM, Lin PC, Lee CT, Chen SH, Lin BW, Lin SC, Chen PC, Chan RH, **Shen MR*.** (2020) Treatment monitoring of colorectal cancer by integrated analysis of plasma concentration and sequencing of circulating tumor DNA. *Molecular Cancer*, 19:150.
5. Chen LH, Yeh YM, Chen YF, Hsu YH, Wang HH, Lin PC, Chang LY, Lin CK, Chang MS*, **Shen MR*.** (2020) Targeting interleukin-20 alleviates paclitaxel-induced peripheral neuropathy. *Pain*, 161(6):1237-1254.
6. Lin PC, Yeh YM, Lin BW, Lin SC, Chen PC, **Shen MR*.** (2020) Intratumor heterogeneity of MYO18A and FBXW7 variants impact the clinical outcome of stage III colorectal cancer. *Frontiers in Oncology*, 10:588557.
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8. Yeh YM, Hsu SJ, Lin PC, Hsu KF, Wu PY, Su WC, Chang JY, **Shen MR*.** (2017) The c.1085A>G genetic variant of CSF1R gene regulates tumor immunity by altering the proliferation, polarization, and function of macrophages. *Clinical Cancer Research*, 23(20):6021-6030.

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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。

近五年代表作：

1. Cheng SM, Shieh MC, Lin TY and **Cheung CHA***(**2022**); **The "Dark Side" of autophagy on the maintenance of genome stability: Does it really exist during excessive activation?** *Journal of Cellular Physiology* 237(1):178-188

2. Cheng SM, Lin TY, Chang YC, Lin IW, Leung E and **Cheung CHA*** (**2021**); **YM155 and BIRC5 downregulation induce genomic instability via autophagy-mediated ROS production and inhibition in DNA repair**; *Pharmacological Research* 166:105474.

3. **Cheung CHA***, Chang YC, Lin TY, Cheng SM, and Leung E (**2020**). **Anti-apoptotic proteins in the autophagic world: an update on functions of XIAP, Survivin, and BRUCE**; *Journal of Biomedical Science* 27:31.

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5. Chang YC, Kondapuram SK, Yang TH, Syed SB, Cheng SM, Lin TY, Lin TC, Coumar MS, Chang JY, Leung E and **Cheung CHA*** (**2020**); **The SMAC mimetic LCL161 is a direct ABCB1/MDR1-ATPase activity modulator and BIRC5/Survivin expression down-regulator in cancer cells**; *Toxicology and Applied Pharmacology* 401:115080

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7. Huang WT, Tsai YH, Chen SH, Kuo CW, Kuo YL, Lee KT, Chen WC, Wu PC, Chuang CY, Cheng SM, Lin C-H, Leung EY, Chang YC, and **Cheung CHA*** **(2017)**. **HDAC2 and HDAC5 up-regulations modulate survivin and miR-125a-5p expressions and promotes hormone therapy resistance in estrogen receptor positive breast cancer cells**; *Frontiers in Pharmacology* 8:902

8. Sarvagalla S, **Cheung CHA**, Tsai JY, and Coumar MS* **(2016)**. **Disruption of protein-protein interaction: Hot Spot detection, structure-based virtual screening and in vitro testing for anti-cancer drug target-survivin**; *RSC Advances* 6:31947-41959

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研究興趣：

1. 神經突觸可塑性(synpatic plasticity)及結構可塑性(structural plasticity)之調控因子及分子作用機轉之研究。
2. 壓力(Stress)及催產素(Oxytocin)對於神經突觸可塑性及神經元新生作用影響之研究。
3. 個體壓力感受性差異之探討。
4. 記憶形成及遺忘之分子機制探討。

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. Lin YT, **Hus KS.*** (2018) Oxytocin receptor signaling in the hippocampus: role in regulating neuronal excitability, network oscillatory activity, synaptic plasticity and social memory. Prog. Neurobiol. 171:1-14.

4. 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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10. Yu TH, Wu YJ, Chien ME, **Hsu KS**.* (2023) Multisession anodal transcranial direct current stimulation enhances adult hippocampal neurogenesis and context discrimination in mice. J. Neurosci. 43(4):635-646.

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研究興趣：

1. 學習和記憶是神經科學研究的一個重要領域，而扁桃體(Amygdala)之神經細胞和人類之學習和記憶有密切之關聯。目前我們利用一種動物行為模式，即長期增益現象，在老鼠扁桃體腦切片標本中，探討動物學習與記憶形成之細胞機轉，並利用藥理分析找出藥物可用於改善一些記憶不良之病人。
2. 失智症是一種嚴重的退化性疾病可影響一個人的思維和記憶。老人癡呆症是失智症最常見的一種。我們利用兩種基因轉殖鼠作為老人癡呆症的動物模式，探討各種可以惡化或預防老人癡呆症的細胞或分子機制。我們最終的目標是經由生理及藥理實驗找出可防止老人痴呆之藥物。

近五年代表作：

1. Chang CH, ***Gean PW*** (2019) The ventral hippocampus controls stress-provoked impulsive aggression through the ventromedial hypothalamus in the post-weaning socially isolated mice. Cell Reports 28, 1195–1205.
2. Chang CH, Kuek E JW, Su CI, ***Gean PW*** (2020) MicroRNA-206 regulates stress-provoked aggressive behaviors in post-weaning social isolation mice. Mol Ther-Nucleic Acids 20, 812-822.
3. Hung HC, Liu CC, Su CL, ***Gean PW*** (2020) Inhibition of sonic hedgehog signaling suppresses glioma stem-like cells through inducing autophagic cell death. Frontier Oncology 10:1233. doi: 10.3389/fonc.2020.01233
4. Chu CH, Chen JS, Chuang PC, Su CH, Chan YL, Yang YJ, Chiang YT, Su YY, **Gean PW**, Sun HS. (2020) TIAM2S as a novel regulator for serotonin level enhances brain plasticity and locomotion behavior. FASEB J. 34: 3267-3288.
5. Liu CC, Wu CL, Yeh IC, Wu SN, Sze CI, ***Gean PW.*** (2021) Cilostazol eliminates radiation-resistant glioblastoma by re-evoking big conductance calcium-activated potassium channel activity. American J Cancer Research 11(4):1148-1169.
6. Chang CH, Liu YC, Sun CY, Su CL and ***Gean PW**. (2021) Regulation of stress-provoked aggressive behaviors by endocannabinoids. Neurobiology of Stress 15: 100337.
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9. Chang HH, Chang YY, Tsai BC, Chen LJ, Chang AC, Chuang JY, ***Gean PW**, Hsueh YS. (2022) A Selective Histone Deacetylase Inhibitor Induces Autophagy and Cell Death via SCNN1A Downregulation in Glioblastoma Cells. Cancers (Basel) 14(18):4537.
10. Li JY, Yu YJ, Su CL, Shen YQ, *Chang CH, ***Gean PW*** (2023) Modulation of methamphetamine memory reconsolidation by neural projection from basolateral amygdala to nucleus accumbens. Neuropsychopharmacology 48, 478–488.
11. Onanong MI, Hsieh CF, Chen DQ, Fan CH, Chiang YY, Liu CC, Sze CI, **Gean PW**, hing Wu PC, Yang MH, Huang PS, Wu PC, Kuo YM, Huang CC. (2023) High-frequency ultrasound imaging for monitoring the function of meningeal lymphatic system in mice.98 Ultrasonics 131: 106949

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研究興趣：

1. 氧自由基代謝酵素在骨髓性白血病的癌症生物學及抗癌藥物相關研究。

2. 慢性骨髓性白血病的抗癌藥物抗藥性作用機轉研究。

近五年代表作：

1. Ling-Yi Xiao, **Wai-Ming Kan**. (2017) p53 modulates the effect of ribosomal protein S6 kinase1 (S6K1) on cisplatin toxicity in chronic myeloid leukemia cells. Pharmacological Research. (in press).
2. Ling-Yi Xiao, **Wai-Ming Kan** (2017). Poly ADP-ribose polymerase inhibition suppresses cisplatin toxicity in chronic myeloid leukemia cells. Anti-Cancer Drugs, 28(3), 316-321.
3. Ling-Yi Xiao, **Wai-Ming Kan.** (2017) Cyclic AMP (cAMP) confers drug resistance against DNA damaging agents via PKAIA in CML cells. European Journal of Pharmacology, 794:201-208.
4. Yu-Lin Chen, **Wai Ming Kan**. (2015) Down-regulation of superoxide dismutase 1 by PMA is involved in cell fate determination and mediated via protein kinase D2 in myeloid leukemia cells . Biochimica et Biophysica Acta (BBA) - Molecular Cell Research , 1853(10 Pt A):2662-75.
5. **Kan, W. M.**, Chao, C. S., Lin, S. J., Chen, C. H., Feng, J. Y., Lu, F. H., Lin, P. C., & Ho, T. S. (2013). Thanatology for Medical College Students – Cultivation of Medical Humanity.. Journal of Medical Education, 17(3), 97-106. (SCI).

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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。

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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:

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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.

3. Chih-Hua Chang, **Ya-Hsin Hsiao**, Yu-Wen Chen, Yang-Jung Yu, and Po-Wu Gean (2015). Social isolation-induced increase in NMDA receptors in the hippocampus exacerbates emotional dysregulation in mice. Hippocampus 25(4):474-85.

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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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研究興趣：

1. 以動物和細胞培養模式，探討神經滋養因子和抗氧化劑的神經保護作用機轉和相互關係。

2. 探討粒線體損傷在神經退化性疾病中以及褪黑激素的保護作用機轉所扮演的角色。

3. 探討腦溫高低對大腦功能的影響。

近五年代表作：

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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

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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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5. Tsai CY, Chan JYH, Hsu KS, **__Chang AYW,__ Chan SHH. Brain-derived neurotrophic factor ameliorates brain stem cardiovascular dysregulation during experimental temporal lobe status epilepticus. *PLoS One*, 2012, 7:e33527.
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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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5. Chen KY., Lin SH., Cheng SY, Lo TK, Huang HY, Tang MJ, Yang CC. Androgenetic alopecia is associated with increased scalp hardness. J. Eur. Acad. Dermatol. Venere. 2020. Jan 15. Doi: 10.1111/jdv.16194.
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7. 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.
8. Liu GY, Chen SC, Lee GH, Shaiv K, Chen PY, Cheng H, Hong SR, Yang WT, Huang SH, Chang YC, Wang HC, Kao CL, Sun PC, Chao MH, Lee YY, Tang MJ and Lin YC. Precise Control of Microtubule Disassembly in Living Cells. EMBO J. e110472, 2022.

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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. 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.
2. 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.
3. 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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5. Her LS, Lin JY, Fu MH, Chang YF, Li CL, Tang TY, Jhang YL, Chang CY, Shih MC, Cheng PH, **Yang SH*.** 2015. The differential profiling of ubiquitin-proteasome and autophagy systems in different tissues before the onset of Huntington's disease models. **Brain Pathol.** 25(4):481-90.
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專長與研究興趣:

My general interest is to understand metabolic influence on neuronal activity and its contribution to development of disease. ATP sensitive potassium (K_{ATP}) channels are of special interest, because their open probability directly depends on the metabolic state of a cell. K_{ATP} channels are closed at high ATP to ADP ratios and open in response to decreased ATP and increased ADP levels. Hence, few projects have been initiated as follows:

- Effect of NMDA receptor in leptin mediated concert trafficking of ATP sensitive potassium channel (K_{ATP}) and Kv2.1 channel trafficking in pancreatic beta cells and hypothalamic neurons
- To discover the role of voltage gated Kv2.1 channels in MPTP induced nigrostriatal degeneration: relevant to Parkinson's disease
- The role of oxidative DNA damage and repair in striatal neurodegeneration (*In collaboration with Dr. Marcus Calkins in the Graduate Institute of Clinical Medicine*)

近五年代表作:

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2. Y. W., S.L. Shyng*, **P.C Chen*** (2015), Concerted Trafficking Regulation of Kv2.1 and K_{ATP} Channels by Leptin in Pancreatic β-Cells. *J Biol Chem*, 290:29676-29690. "Paper of the Week"
3. M.H. Fu, C.L. Li, H.L. Lin, **P.C. Chen**, M.J. Calkins, Y.F. Chang, P.H. Cheng, S.H. Yang (2015) Stem cell transplantation therapy in Parkinson's disease. *Springerplus*. 4:597. eCollection. Review
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5. G. Martin, **P.C. Chen**, P. Devaraneni, S.L. Shyng, (2013), Pharmacological rescue of trafficking-impaired ATP-sensitive potassium channels. *Front Physiol*. Dec 24;4:386. eCollection.
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7. **P.C. Chen** , E. Olson, Q. Zhou , Y. Kryukova , H. Sampson ,D.Y. Thomas, S.L. Shyng (2013), Carbamazepine as a Novel Small Molecule Corrector of Trafficking-Impaired ATP-Sensitive Potassium Channels Identified in Congenital Hyperinsulinism, *J Biol Chem* 288:20942-20954.
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9. C. Escartin, S. Joon Won, C. Malgorn, G. Auregan G, A.E. Berman , **P.C. Chen**, N. Déglon, J.A. Johnson,S. Won Suh, R.A.Swanson (2011), Nuclear factor erythroid 2-related factor 2 facilitates neuronal glutathione synthesis by upregulating neuronal excitatory amino Acid transporter 3 expression, *J Neurosci*. 31:7392-7401.
10. **P.C. Chen**, C.E. Bruederle, H.Y. Gaisano, S.L. Shyng (2011), Syntaxin 1A regulates processing and endocytic trafficking of pancreatic ATP-sensitive potassium Channels, *Am. J. Physiol. Cell Physiol.* 300*:* C506-C516.
11. F.F. Yan, E.B. Pratt, **P.C. Chen**, F. Wang, W.R. Skach, L.L. David, S.L. Shyng (2010), Role of HSP90 in biognenesis of the β-CELL ATP-sensitive potassium channel complex, *Mol. Biol. Cell.* 21: 1945-1954.

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研究興趣：

本實驗室主要有三個研究方向。一、缺氧誘導因子(HIF-1α)調控基因與癌症抗藥性之研究。細胞因為缺氧會產生種種不同的生理反應或病理變化，包括學習記憶、癌症、心血管疾病、生長遲緩、腦部疾病、肺部疾病等。我們利用生物資訊學的方法，將基因體中會受缺氧誘導因子調控之基因（包括人類、大鼠、小鼠）找尋出來，並研究其在生理、病理上的功能，尤其著重在癌症抗藥性方面的探討，目前以大腸癌及胰臟癌的抗藥性機制為重點；二、研究整個基因體的調控(Gene regulatory network)及細胞分化、去分化及再分化的機轉。表觀基因體調控（epigenomic modification and reprograming）對細胞之命運影響至巨，甚或造成細胞病變。我們利用生物資訊學、功能性基因體學、系統生物學等尖端方法，對此一現象作深入的研究；三、探討子宮內膜異位(endometriosis)成因之分子機制，子宮內膜異位症約佔生殖年齡期婦女人數的10-15%，大部分會導致不孕症的發生，目前有關子宮內膜異位形成之原因，並不清楚。本實驗室過去幾年的研究，在這個領域已有相當不錯的成果，未來將著重在整合性基因功能上的研究。

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2. SC Lin, HC Lee, CT Hsu, YH Huang, WN Li, PL Hsu, MH Wu*, SJ Tsai* Targeting anthrax toxin receptor 2 ameliorates endometriosis progression. **Theranostics**; 9(3): 620-632, 2019. doi: 10.7150/thno.30655
3. JL Fu, KY Hsiao, HC Lee, WN Li, N Chang, MH Wu*, SJ Tsai* Suppression of COUP-TFII upregulates angiogenin and promotes angiogenesis in endometriosis **Hum Reprod** 33 (8): 1517-27, 2018
4. PC Hou, YH Li, SC Lin, SC Lin, JC Lee, PW Lin, JP Liou, JY Chang, CC Kuo, YM Liu, HS Sun, **SJ Tsai*** Hypoxia-induced downregulation of DUSP-2 phosphatase drives colon cancer stemness. **Cancer Res**, 77 (16): 4305-4316, 2017.
5. KY Hsiao, YC Lin, SK Gupta, N Chang, L Yen, H. S Sun*, **SJ Tsai*** Non-coding effects of circular RNA CCDC66 promote colon cancer growth and metastasis. **Cancer Res** 77:2339-2350, 2017. (High cite paper, hot paper)
6. SC Lin, HC Lee, PC Hou, JL Fu, MH Wu, **SJ Tsai*** Targeting hypoxia-mediated YAP1 nuclear translocation ameliorates pathogenesis of endometriosis without compromising maternal fertility. **J Pathol** 242: 476–487, 2017. (Cover story)
7. SC Lin, KY Hsiao, N Chang, PC Hou, **SJ Tsai*** Loss of dual specificity phosphatase-2 promotes angiogenesis and metastasis via upregulation of interleukin-8 in colon cancer. **J Pathol** 241 (5): 638-48, DOI: 10.1002/path.4868, 2017
8. HC Lee, **SJ Tsai*** Hypoxia: endocrine targets of hypoxia-inducible factors. **J Endocrinol**, 234(1):R53-R65, 2017.
9. CW Chien, PC Ho, HC Wu, YL Chang, SC Lin, PW Lin, JC Lee, YJ Chang, HS Sun, **SJ Tsai*** 2016 Targeting TYRO3 inhibits epithelial-mesenchymal transition and increases drug sensitivity in colon cancer. **Oncogene** 12(2):61-77. doi: 10.1080/15476278. 2016
10. SC Lin, CY Kao, HJ Lee, C Creighton, M Ittmann, **SJ Tsai**, S Tsai, and MJ Tsai Dysregulation of miRNAs-COUP-TFII-FOXM1-CENPF axis contributes to the metastasis of prostate cancer. **Nat Commun** 7:11418, 2016
11. KY Hsiao, MH Wu, N Chang, SH Yang, CW Wu, HS Sun, **SJ Tsai*** Coordination of AUF1 and miR-148a to destabilize DNA methyltransferase 1 mRNA under hypoxia in endometriosis. **Mol Hum Reprod** 21:894-904, 2015
12. SC Lin, YH Li, MH Wu, YF Chang, DK Lee, S Tsai, MJ Tsai, and **SJ Tsai*** Suppression of COUP-TFII by proinflammatory cytokines contributes to the pathogenesis of endometriosis. **J Clin Endocrinol Metab** 99(3): E427-37, 2014
13. TM Chen, YH Shih, JT Tseng, MC Lai, Ch Wu, YH Li, **SJ Tsai***, and HS Sun* Overexpression of FGF9 in colon cancer cells is mediated by hypoxia-induced translational activation. **Nucleic Acids Res** 42:2932-44, 2014
14. MH Wu, PC Chuang, YJ Lin, **SJ Tsai*** Suppression of annexin A2 by prostaglandin E_2 impairs phagocytic ability of peritoneal macrophage in women with endometriosis. **Hum Reprod** 28:1045-53, 2013
15. J Qin, SP Wu, F Dai, X Xie, CM Cheng, C J Creighton, A Frolov, Gustavo Ayala4, X Lin, XH Feng, MM Ittmann, **SJ Tsai**, MJ Tsai, S Y Tsai Inhibition of TGF-β-dependent growth barrier by COUP-TFII to promote prostate tumor growth and metastasis. **Nature** 493: 236-240, 2013

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：

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2. 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. 5 year IF=9.14. R/C=4/94, TOXICOLOGY.
3. 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. 5 year IF=9.62. R/C=36/195, CELL BIOLOGY.
4. 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. 5 year IF=6.628. R/C=69/297, BIOCHEMISTRY & MOLECULAR BIOLOGY.
5. 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. 5 year IF=9.35. R/C=29/279, ENVIRONMENTAL SCIENCES.
6. 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. 5 year IF=16.142. R/C=22/195, CELL BIOLOGY.
7. 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. 5 year IF=5.225, R/C=14/81, PHYSIOLOGY.
8. 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. 5 year IF=6.628. R/C=69/297, BIOCHEMISTRY & MOLECULAR BIOLOGY.
9. 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. 5 year IF=6.628. R/C=69/297, BIOCHEMISTRY & MOLECULAR BIOLOGY.
10. Bin-Hsu Mao, Zi-Yu Chen, Ying-Jang Wang* & **Shian-Jang Yan*** (2018, Feb). Silver nanoparticles have lethal and sublethal adverse effects on development and longevity by inducing ROS-mediated stress responses. ***Scientific Reports***, 8(1):2445, 1-16. London, United Kingdom. 5 year IF=5.516. R/C=19/74, MULTIDISCIPLINARY SCIENCES. (Cited 220 times)

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研究興趣：

1.探討腸道微生物對神經疾病與精神失調的影響

2.探討腸道微生物代謝物對神經疾病與精神失調的影響

3.探討腸-腦軸對神經疾病與精神失調的影響

近五年代表作：

- Wu, J.T., Sun, C.L., Lai, T.T., Liou, C.W., Lin, Y.Y., Xue, J.Y., Wang, H.W., Chai, L.M.X., Lee, Y.J., Chen, S.L., Chang, A.Y.W., Hung, J.H., Hsu, C.C., **Wu, W.L.***, 2022. Oral short-chain fatty acids administration regulates innate anxiety in adult microbiome-depleted mice. **Neuropharmacology,** 214, 109140.
- Liou, C.W., Yao, Z.H., **Wu, W.L.***, 2022. Intracerebroventricular delivery of gut-derived microbial metabolites in mice. **Journal of Visualized Experiments : JoVE**, Jun 2;(184). doi: 10.3791/63972.
- Needham, B.D.*, Funabashi, M., Adame, M.D., Wang, Z., Boktor, J., Haney, J., **Wu, W.L.**, Rabut, C., Ladinsky, M.S., Hwang, S.J., Guo, Y., Griffiths, J.A., Knight, R., Bjorkman, P.J., Shapiro, M.G., Geschwind, D.H., Holschneider, D.P., Fischbach, M.A., Mazmanian, S.K.*, 2022. A gut-derived metabolite alters brain activity and anxiety behaviour in mice. **Nature,** 602, 647-653.
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- Ko, J., Isas, J.M., Sabbaugh, A., Yoo, J.H., Pandey, N.K., Chongtham, A., Ladinsky, M., **Wu, W.L.**, Rohweder, H., Weiss, A., Macdonald, D., Munoz-Sanjuan, I., Langen, R., Patterson, P.H., Khoshnan, A., 2018. Identification of distinct conformations associated with monomers and fibril assemblies of mutant huntingtin. **Human molecular genetics,** 27, 2330-2343.
- Needham, B.D., Tang, W., **Wu, W.L.***, 2017. Searching for the gut microbial contributing factors to social behavior in rodent models of autism spectrum disorder. **Developmental Neurobiology,** 78, 474-499.
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- Chan, K.Y., Jang, M.J., Yoo, B.B., Greenbaum, A., Ravi, N., **Wu, W.L.**, Óscar Sánchez-Guardado, L., Lois, C., Mazmanian, S.K., Deverman, B.E.*, Gradinaru, V.*, 2017. Engineered adeno-associated viruses for efficient and noninvasive gene delivery throughout the central and peripheral nervous systems. **Nature Neuroscience,** 20, 1172-1179.

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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

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2. Shuangdi Duan, Nong Qin, Jiayi Pi, Pei Sun, Yating Gao, Lamei Liu, Zenghui Li, Ya Li, Liyang Shi, Qiang Gao, Ye Qiu, Songqing Tan, 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. (Corresponding Author) (Accepted)
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. (Corresponding Author)
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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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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：

擬人小鼠研製與應用

近五年代表作：

1. Ya-Fang Wang, **Chun-Keung Yu***. Animal models of enterovirus 71 infection: applications and limitations. Journal of Biomedical Science 2014, 21:31 (DOI: 10.1186/1423-0127-21-31)
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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)

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BOOK

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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、echovirus 11、enterovirus D68 及 enterovirus A71) 的致病機轉。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。

近五年代表作：

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9. Wang LC et al., (2022) Therapeutics for fulminant hepatitis caused by enteroviruses in neonates 2022) Front. Pharmacol. 13:1014823. doi: 10.3389/fphar.2022.1014823

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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、抑制性化合物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. 艱難梭狀桿菌抑制性化合物的篩檢及其作用機制探討
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. 相關腸道微生物相之研究

近五年代表作：

1. Antimicrobial-resistant Escherichia coli distribution and whole genome analysis of sequence type 131 E. coli isolates in public restrooms in Taiwan. Chang SM, **Chen JW**, Tsai CS, Ko WC, Scaria J, Wang JL. Front Microbiol. 2022 (accepted).
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5. 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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9. Comparative Genomics of Escherichia coli Sequence Type 219 Clones From the Same Patient: Evolution of the IncI1 blaCMY-Carrying Plasmid in Vivo. Kao CY, **Chen JW**, Liu TL, Yan JJ, Wu JJ. Front Microbiol. 2018 Jul 9;9:1518.
10. A multi-omic analysis reveals the role of fumarate in regulating the virulence of enterohemorrhagic Escherichia coli. Kuo CJ, Wang ST, Lin CM, Chiu HC, Huang CR, Lee DY, Chang GD, Chou TC, **Chen JW***, Chen CS*. Cell Death Dis. 2018 Mar 7;9(3):381.
11. Lauric Acid Is an Inhibitor of Clostridium difficile Growth in Vitro and Reduces Inflammation in a Mouse Infection Model. Yang HT*, **Chen JW***, Rathod J, Jiang YZ, Tsai PJ, Hung YP, Ko WC, Paredes-Sabja D, Huang IH. Front Microbiol. 2018 Jan 17;8:2635
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13. Immunization with Recombinant TcdB-Encapsulated Nanocomplex Induces Protection against Clostridium difficile Challenge in a Mouse Model. Liu YW, Chen YH, **Chen JW**, Tsai PJ, Huang IH. Front Microbiol. 2017 Jul 25;8:1411.

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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)
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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.

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3. **Tsai, C.H.***, Wei, S.C., Lo, H.R., and Chao, Y.C.# (2020) Baculovirus as versatile vectors for protein display and biotechnological applications. *Current Issues in Molecular Biology* 34: 231-256.

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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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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
3. **Chia-Yih Wang**, Hui-Ling Tsai, Jhih-Siang Syu, Ting-Yu Chen, Mei-Tsz Su (2016) Primary cilium-regulated EG-VEGF signaling facilitates trophoblast invasion, *Journal of Cellular Physiology*, Accepted
4. Meng-Shao Lai, **Chia-Yih Wang**, Shang-Hsun Yang, Chia-Ching Wu, H. Sunny Sun, Shaw-Jenq Tsai, Jih-Ing Chuang, Yung-Chia Chen, Bu-Miin Huang (2016) The expression profiles of fibroblast growth factor 9 and its receptors in developing mice testes, *Organogenesis* ,Accepted
5. Ting-Yu Chen, Jhih-Siang Syu, Tzu-Chien Lin, Hui-ling Cheng, Fu-l Lu and **Chia-Yih Wang*** (2015) Chloroquine alleviates etoposide-induced centrosome amplification by inhibiting CDK2 in adrenocortical tumor cells, *Oncogenesis*,4,ppe180
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10. **Chia-Yih Wang**, Pao-Yen Lai, Ting-Yu Chen and Bon-chu Chung (2014) NR5A1 prevents centriole splitting by inhibiting centrosomal DNA-PK activation and beta-catenin accumulation, *Cell Communication and Signaling*,12,1,pp55-
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
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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.
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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
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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)
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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).
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7. 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. FGF9 induces neurite outgrowth upon ERK signaling in knock-in striatal Huntington's disease cells. ***Life Sci.*** 267, 118952, doi:10.1016/j.lfs.2020.118952 (2021).
8. Wang, T. Y., Chang, M. M., Li, Y. J., Huang, T. C., Chien, S. & Wu, C. C. Maintenance of HDACs and H3K9me3 Prevents Arterial Flow-Induced Venous Endothelial Damage. ***Front Cell Dev Biol*** 9, 642150, doi:10.3389/fcell.2021.642150 (2021).
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25. Lee, D. Y., Yang, T. L., Huang, Y. H., Lee, C. I., Chen, L. J., Shih, Y. T., Wei, S. Y., Wang, W. L., Wu, C. C. & Chiu, J. J. Induction of microRNA-10a using retinoic acid receptor-alpha and retinoid x receptor-alpha agonists inhibits atherosclerotic lesion formation. ***Atherosclerosis*** 271, 36-44, doi:10.1016/j.atherosclerosis.2018.02.010 (2018).
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研究興趣：

實驗室研究方向為神經發炎、神經損傷與再生，主要探討脊髓損傷與神經病變痛(neuropathic pain)的機制與治療。

近五年代表作：

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12. Wong CE, Wang WH, Lan MY, Lee PH, Huang CC, Su PF, Lee JS*. Predicting the Need for Desmopressin Treatment During Inpatient and After Discharge Following Endoscopic Sellar Surgery. Front Neurol. 2022 Feb 17;13:843646. doi: 10.3389/fneur.2022.843646. 本人為通訊作者
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16. Chang Y, Chi KY, Tai TW, Cheng YS, Lee PH, Huang CC, Lee JS*. Risk factors for postoperative urinary retention following elective spine surgery: a meta-analysis. Spine J. 2021 Nov;21(11):1802-1811. 本人為通訊作者
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21. Wong CE, Lee PH, Huang CC, Chen HW, Tien CH, Huang CY, Lee JS. Teaching NeuroImages: A Ruptured Lumbar Disc Mimicking Spinal Tumor. Neurology. 2021. Jun; 96:e3003-e3004. 本人為通訊作者.
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28. Hsu HJ, Sze J, Wang CK, Lee JS*. Unilateral foot drop caused by thoracic herniated intervertebral disc. Int J Case Rep Images 2019;10:101078Z01HH2019.
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專長與研究興趣:

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.

3. **Fan-E Mo***, Pei-Ling Hsu (2019, Nov). Response by Mo and Hsu to Letter Regarding Article, "Shear-Induced CCN1 Promotes Atheroprone Endothelial Phenotypes and Atherosclerosis". *Circulation*, 140 (20), e768-e769.

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5. Pei-Ling Hsu, Yung-Ching Lin, Hao Ni, and **Fan-E Mo*** (2018, Apr).Ganoderma Triterpenoids Exert Antiatherogenic Effects in Mice by Alleviating Disturbed Flow-Induced Oxidative Stress and Inflammation. *Oxidative Medicine and Cellular Longevity*, vol. 2018, Article ID 3491703.

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

許鍾瑜 *(Jung-Yu Hsu, Ph.D.)*

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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：

- Alzheimer's diseases: 1) Pathophysiology; 2) Biomarker; 3) Treatment strategy
- Exercise & brain function: 1) Neuroinflammation; 2) Autonomic nervous system
- Interaction between metabolic disorders and depression

近五年代表作：

1. 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*. (2023) High-frequency ultrasound imaging for monitoring the function of meningeal lymphatic system in mice. *Ultrasonics* 131:106949.
2. Tsai SF, Hsu PL, Chen YW, Hossain MS, Chen PC, Tzeng SF, Chen PS, **Kuo YM***. (2022) High-fat diet induces depression via astrocyte-mediated hyperactivation of the ventral hippocampal glutamatergic afferents to the nucleus accumbens. *Molecular Psychiatry* 27: 4372-4384.
3. Wang TF, Wu SY, Pan BY, Tsai SF, **Kuo YM***. (2022, January) Inhibition of nigral microglial activation reduces age-related loss of dopaminergic neurons and motor deficits. *Cells* 11: 481.
4. Tsai SF, Hung HC, Shih MC, Chang FC, Chung BC, Wang CY, Lin YL, **Kuo YM***. (2022) High-fat diet-induced increases in glucocorticoids contribute to the development of non-alcoholic fatty liver disease in mice. *FASEB Journal* 36: e22130.
5. Wang TF, Tsai SF, Zhao ZW, **Kuo YM***. (2021) Exercise-induced increase of corticosterone participates in exercise-enhanced adult hippocampal neurogenesis in mice. *Chinese Journal of Physiology*, 64: 186-193.
6. Lkhagvasuren B, Mee-inta O, Zhao ZW, Hiramoto T, Boldbaatar D, **Kuo YM***. (2021) Pancreas-brain crosstalk. *Frontiers in Neuroanatomy* 15:691777.
7. Wu SY, Pan BS, Tsai SF, Chiang YT, Huang BM, Mo FE, **Kuo YM***. (2020) BDNF reverses aging-related microglial activation. *Journal of Neuroinflammation* 17:210.
8. Tsai SF, Liu YW, **Kuo YM***. (2019) Acute and long-term treadmill running differentially induce c-Fos expression in regions- and time-dependent manners in mouse brain. *Brain Structure & Functio*n 224, 2677-2689.
9. Mee-inta O, Zhao ZW, **Kuo YM***. (2019) Physical exercise inhibits inflammation and microglial activation. *Cells* 8, 691.
10. Beh ST, **Kuo YM***, Chang WSW, Wilder-Smith E, Tsao CH, Tsai CH, Chen LT, Liao LD*. (2019) Preventive hypothermia as a neuroprotective strategy for paclitaxel-induced peripheral neuropathy. *Pain*, 160:1505-1521.

陳政義 *(Cheng-Yi Chen, Ph.D.)*

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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。

近五年代表作：

1. Tsai HW, Chen YL, Wang CI, Lin YH, Chu PM, Huang YC, **Chen CY***. Anterior gradient 2 induces resistance to sorafenib via endoplasmic reticulum stress regulation in hepatocellular carcinoma. *Cancer Cell International* 2023 23: 42
2. Li CJ, Tsai HW, Chen YL, Wang CI, Lin YH, Chu PM, Chi HC, Huang YC, **Chen CY***. Cisplatin or Doxorubicin reduces cell viability via the PTPIVA3- JAK2-STAT3 cascade in hepatocellular carcinoma. *Journal of hepatocellular carcinoma* 2023:10 123–138
3. Chen YL, Hsieh CC, Chu PM, Chen JY, Huang YC and **Chen CY***. Roles of protein tyrosine phosphatases in hepatocellular carcinoma progression *ONCOLOGY REPORTS*, 2023 49: 48
4. Cheng CC, Ho AS, Peng CL, Chang JS, Sie ZL, Wang CL, Chen YL, **Chen CY***. Sorafenib suppresses radioresistance and synergizes radiotherapy-mediated CD8+ T cell activation to eradicate hepatocellular carcinoma. *International Immunopharmacology* 112 (2022) 109110
5. Chu PY, Huang WC, Tung SL, Tsai CY, Chen CJ, Liu YC, Lee CW, Lin YH, Lin HY, **Chen CY**, Yeh CT, Lin KH* and Chi HC*. IFITM3 promotes malignant progression, cancer stemness and chemoresistance of gastric cancer by targeting MET/AKT/FOXO3/c-MYC axis. *Cell & Bioscience* 2022 12:124
6. Lin YH, Liu YC, **Chen CY**, Chi HC, Wu MH, Huang PS, Chang CC, Lin TK, Yeh CT, and Lin KH*. LPAL2 Suppresses Tumor Growth and Metastasis of Hepatocellular Carcinoma by Modulating MMP9 Expression. *Cells* 2022, 11, 2610
7. Lin YH, Lim SN, **Chen CY**, Chi HC, Yeh CT * and Lin WR*. Functional Role of Mitochondrial DNA in Cancer Progression. *International journal of molecular sciences*. 2022, 23, 1659
8. Wang CI, Chu PM, Chen YL, Lin YH, **Chen CY***. Chemotherapeutic drug-regulated cytokines might influence therapeutic efficacy in HCC. *International journal of molecular sciences* 2021 Dec 20; 22: 13627
9. Chen TW, Chang KP, Cheng CC, **Chen CY**, Hong SW, Sie ZL, Cheng HW, Yen WC, Huang YL, Liu SC, Wang CI. Characterization of recurrent relevant genes reveals a novel role of RPL36A in radioresistant oral squamous cell carcinoma. *Cancers* 2021 Nov 10; 13: 5623
10. Huang PS, Liao CJ, Huang YH, Yeh TC, **Chen CY**, Tang HC, Chang CC, Lin KH. Functional and clinical significance of dysregulated microRNAs in liver cancer. *Cancers* 2021 Oct 26; 13: 5361
11. Huang PS, Lin YH, Chi HC, Tseng YH, **Chen CY**, Lin TK, Yeh CT, Lin KH. Dysregulated FAM215A stimulates LAMP2 expression to confer drug-resistant and malignant in human liver cancer. *Cells* 2020 Apr 14; 9(4): E961
12. Wu CH, **Chen CY**, Yeh CT, Lin KH. Radiosensitization of hepatocellular carcinoma through targeting aadio-associated microRNA. *Int J Mol Sci*. 2020 Mar 9; 21:1859
13. **Chen CY**, Chen CY, Liu CC, Chen CP. Omega-3 polyunsaturated fatty acids reduce preterm labor by inhibiting trophoblast cathepsin S and inflammasome activation. *Clinical Science.* 2018 Oct 04; 132:2221-2239
14. Chen CP, **Chen CY**, Wu YH, Chen CY. Oxidative stress attenuates FOXO1-enhanced integrin β3 expression and placental cell motility. *Free Radical Biology and Medicine.* 2018 Aug 20;124:189-198

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研究興趣：

My major interest has been focused on the in vitro and in vivo regulation of anti-tumor effects in male reproductive systems by different factors, such as Chinese herbs, neuropeptides, anesthesia drugs and environmental toxicants.

近五年代表作：**(* Corresponding author)**

1. Chang MM, Pan BS, Wang CY, **Huang BM***. 2019. Cordycepin induced unfolded protein response-dependent cell death, and AKT/MAPK mediated drug resistance in mouse testicular tumor cells. Cancer Medicine. 8(8):3949-3964.
2. Ho SY, Wu WS, Lin LC, Wu YH, Chiu HW, Yeh YL, **Huang BM***, Wang YJ*. 2019. Cordycepin enhances radiosensitivity in oral squamous carcinoma cells by inducing autophagy and apoptosis through cell cycle arrest. International Journal of Molecular Sciences, 20(21). pii: E5366. doi: 10.3390/ijms20215366.
3. Kang FC, Wang SC, So EC, Chang MM, Wong KL, Cheng KS, Chen YC, **Huang BM***. 2019. Propofol could increase caspases and MAPKs pathways and suppress Akt pathway to induce apoptosis in MA-10 mouse Leydig tumor cells. Oncology Reports. 41:3565-3574.
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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:

血管新生(Angiogenesis)在人類的生理過程如：胚胎的發育、傷口的癒合、和女性的月經週期有關。而血管新生是一個同時受到血管新生抑制與促進劑之間劑量的抗衡所控制複雜的生理過程。當這個平衡失去控制，將會導致許多病變如腫瘤的生長與蔓延。近三、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不可分的關係，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。長期透過與臨床醫師合作，結合細胞與分子生物，透過高通量的基因體、蛋白體甚至於代謝體等技術探討微環境交戶作用(含發炎細胞浸潤與血管新生)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：

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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研究興趣：

磷酸水解酶PP2A在近來已被認為扮演抑制腫瘤形成的角色。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的多元組合及功能是由於多變的B次單元所造成。我們探討PP2A在抑制腫瘤形成的分子機制，也致力於探討B次單元所扮演的細胞角色。近年來我們也發現PP2A可能扮演促進癌症轉移的証據，目前致力探討其可能的機制及臨床上的意義。另外，我們發現PP2A調控的蛋白質分子有類似液體相位分離(liquid-liquid phase separation)的分子特質，因此，我們也致力於探討液體相位分離的現象及在腫瘤形成的角色。

研究方向：

一、探討PP2A的B56gamma次單元在大腸癌及胰臟癌中的角色及調控癌化的分子機轉。

二、探討PP2A與PI3K/AKT/mTOR/p70S6K訊息路徑之間的交互作用及生理角色。

三、探討蛋白質分子液體相位分離的現象及在癌化的角色。

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8. Tzeng HT, Li TH, Tang YA, Tsai CH, Lu FPJ, Lai WW, **Chiang CW** and Wang YC. (co-corresponding) (2017) Phosphorylation of Rab37 by protein kinase C alpha inhibits the exocytosis function and metastasis suppression activity of Rab37. *Oncotarget* 18;8(65):108556-108570.
9. Liao SY, **Chiang CW** , Hsu CH, Chen YT, Jen J, Juan HF, Lai WW, and Wang YC (2017 Jun 5) CK1δ/GSK3β/FBXW7α axis promotes degradation of the ZNF322A oncoprotein to suppress lung cancer progression. *Oncogene* 12;36(41):5722-5733.

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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.
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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.
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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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專長：微生物遺傳學、微生物基因體學、細胞生物學 、分子生物學

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 always challenge to ask right and interesting questions, and find the answer. I also involve in iGEM team in NCKU, which is an international competition for synthetic biology.

Escherichia coli is common bacteria, and shows various phenotypes, which are non-pathogenic, enterohemorrhagic, uropathogenic and so on. Enterohemorrhagic *E. coli* (EHEC) shows the most severe symptom with Shiga toxin. The toxin gene is in a prophage region in the EHEC genome. Namely, the *E. coli* cell is just a carrier of the prophage, which harbors the major toxin. 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. 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 logical 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.

Recent selected publications in the last 5 years

1. **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.
2. **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.
3. 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.
4. Ueda D, Matsugane S, Okamoto W, **Hashimoto M**, Sato T. (2018) Non-enzymatic pathway with superoxide in intracellular terpenoid synthesis. Angew Chem Int Ed Engl. 57 (32) 10347-10351.
5. **Hashimoto M**, Matsushima H, Suparthana PI, Ogasawara H, Yamamoto H, Teng CH and Sekiguchi J. (2018) Digestion of peptidoglycan near the cross-link is necessary for the growth of *Bacillus subtilis*. Microbiol. 164 (3) 299-307

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研究興趣：

1. 小膠質細胞之免疫記憶調控;
2. 神經發炎與神經退化;
3. 智慧化大腦晶片

The publication (selected):

1. Kuo HC, Chen SL, Chiu SC, **Chu CH*** Tolerized microglia protect neurons against endotoxin-induced TNF-α production via a TLR4-dependent intracellular p38 MAPK signaling pathway ***Submitted.***
2. **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 ***Submitted.***
3. Wang LY[#], **Chu CH**[#], Wang CC[#], Sun H, Chen CA, Hsiao YH* TIAM2S as a novel target to alleviate cognitive deficits in Alzheimer's disease model mice by upregulating BDNF expression and neuroplasticity ***Submitted.***
4. 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.***
5. **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.***
6. **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.***
7. **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.***
8. **Chu CH**, Lo JF, Hu WS, Lu RB, Chang MH, Tsai FJ, Tsai CH, Weng YS, Tzang BS, Huang CY* Histone acetylation is essential for ANG-II-induced IGF-IIR gene expression in H9c2 cardiomyoblast cells and pathologically hypertensive rat heart. ***J Cell Physiol. 2012 Jan;227(1):259-68.***
9. Chen RJ, Wu HC, Chang MH, Lai CH, Tien YC, Hwang JM, Kuo WH, Tsai FJ, Tsai CH, Chen LM, Huang CY, **Chu CH*** Leu27IGF2 plays an opposite role to IGF1 to induce H9c2 cardiomyoblast cell apoptosis via Galphaq signaling. ***J Mol Endocrinol. 2009 Dec;43(6):221-30.***
10. **Chu CH**, Tzang BS, Chen LM, Liu CJ, Tsai FJ, Tsai CH, Lin JA, Kuo WW, Bau DT, Yao CH, Huang CY* Activation of insulin-like growth factor II receptor induces mitochondrial-dependent apoptosis through G(alpha)q and downstream calcineurin signaling in myocardial cells. ***Endocrinology. 2009 Jun;150(6):2723-31.***
11. Cheng YC, Kuo WW, Wu HC, Lai TY, Wu CH, Hwang JM, Wang WH, Tsai FJ, Yang JJ, Huang CY, **Chu CH*** ZAK induces MMP-2 activity via JNK/p38 signals and reduces MMP-9 activity by increasing TIMP-1/2 expression in H9c2 cardiomyoblast cells. ***Mol Cell Biochem. 2009 May;325(1-2):69-77.***
12. **Chu CH**, Huang CY, Lu MC, Lin JA, Tsai FJ, Tsai CH, Chu CY, Kuo WH, Chen LM, Chen LY* Enhancement of AG1024-induced H9c2 cardiomyoblast cell apoptosis via the interaction of IGF2R with Galpha proteins and its downstream PKA and PLC-beta modulators by IGF-II. ***Chin J Physiol. 2009 Feb 28;52(1):31-7.***
13. Chang MH, Kuo WW, Chen RJ, Lu MC, Tsai FJ, Kuo WH, Chen LY, Wu WJ, Huang CY, **Chu CH*** IGF-II/mannose 6-phosphate receptor activation induces metalloproteinase-9 matrix activity and increases plasminogen activator expression in H9c2 cardiomyoblast cells. ***J Mol Endocrinol. 2008 Aug;41(2):65-74.***
14. **Chu CH**, Tzang BS, Chen LM, Kuo CH, Cheng YC, Chen LY, Tsai FJ, Tsai CH, Kuo WW, Huang CY* IGF-II/mannose-6-phosphate receptor signaling induced cell hypertrophy and atrial natriuretic peptide/BNP expression via Galphaq interaction and protein kinase C-alpha/CaMKII activation in H9c2 cardiomyoblast cells. ***J Endocrinol. 2008 May;197(2):381-90.***

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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. Tsai YH, Huang SW, Hsieh WS, Cheng CK, Chang CF, Wang JR*. 2019. VP1 codon-deoptimization and high-fidelity polymerase reverse genetics virus as next generation enterovirus A71 as vaccine candidate. J Virol 93: e02308-18. (*corresponding author)
2. Huang SW, Hung SJ, Wang JR*. 2019. Application of deep sequencing methods for inferring viral population diversity. J Virol Methods 266: 95-102, 2019.
3. Huang SW, Cheng D, Wang JR*. 2019. Enterovirus A71: virulence, antigenicity, and genetic evolution over the years. J. Biomed. Sci. Oct 21;26(1):81.
4. 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.
5. Huang SW, Tai CH, Hsu YM, Cheng D, Hung SJ, Chai KM, Wang YF, Wang JR*. 2020. Assessing application of pseudovirus system for emerging SARS-CoV-2 and re-emerging avian influenza virus H5 subtypes in vaccine development. Biomed. J. 2020 Aug;43(4):375-387.
6. 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.
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8. Huang YL, Lin TM, Wang SY, Wang JR*. 2022. The role of conserved arginine and proline residues in enterovirus VP1 protein. J. Microbiol. Immunol. Infect. 55: 590-597.
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10. 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.
11. 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.
12. 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.

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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 有調控細胞生長與凋亡的作用，將繼續深入探討 WWOX 所影響的細胞訊息傳遞路徑。
2. 分析 WWOX 操控細胞生理作用的分子機制。
3. 研究WWOX調控免疫細胞功能之角色。

近五年代表作：

1. **Hsu LJ**, Chiang MF, Sze CI, Su WP, Yap YV, Lee IT, Kuo HL, and Chang NS. 2016. HYAL-2-WWOX-SMAD4 signaling in cell death and anticancer response. Front. Cell Dev. Biol., 4:141.
2. Chen YD, Fang YT, Chang CP, Lin CF, **Hsu LJ**, Wu SR, Chiu YC, Anderson R, Lin YS. 2017. S100A10 Regulates ULK1 localization to ER-mitochondria contact sites in IFN-γ-triggered autophagy. J. Mol. Biol. 429(1):142-157.
3. **Hsu LJ**, Hong Q, Chen ST, Kuo HL, Schultz L, Heath J, Lin SR, Lee MH, Li DZ, Li ZL, Cheng HC, Armand G, Su WP, and Chang NS. 2017. Hyaluronan activates Smad4/Hyal-2/WWOX signaling and causes bubbling cell death when the signaling complex is overexpressed. Oncotarget 8(12):19137-19155.
4. Chen YD, Fang YT, Cheng YL, Lin CF, **Hsu LJ**, Wang S, Anderson R, Chang CP, and Lin YS. 2017. Exophagy of annexin A2 via RAB11, RAB8A and RAB27A in IFN-gamma-stimulated lung epithelial cells. Sci. Rep. 7(1):5676.
5. Chuang MH, Chang JT, **Hsu LJ**, Jan MS, and Lu FJ. 2017. Antitumor activity of the Chinese medicine JC-001 is mediated by immunomodulation in a murine model of hepatocellular carcinoma. Integr. Cancer Ther. 16(4):516-525.
6. Chou PY, Lai FJ, Chen YA, Sie YD, Kuo HL, Su WP, Wu CY, Liu TY, Wen KY, **Hsu LJ**, Sze CI, and Chang NS. 2019. Strategies by which WWOX-deficient metastatic cancer cells utilize to survive via dodging, compromising, and causing damage to WWOX-positive normal microenvironment. Cell Death Discov. 5:97.
7. 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.
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9. 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.
10. Chen SM, Chieng WW, Huang SW, **Hsu LJ**, Jan MS. 2020. The synergistic tumor growth inhibitory effect of probiotic Lactobacillus on transgenic mouse model of pancreatic cancer treated with gemcitabine. Sci. Rep. 10(1):20319.
11. Chen SM, **Hsu LJ**, Lee HL, Lin CP, Huang SW, Lai CJL, Lin CW, Chen WT, Chen YJ, Lin YC, Yang CC, Jan MS. 2020. *Lactobacillus* attenuate the progression of pancreatic cancer promoted by *Porphyromonas gingivalis* in *K-ras*^{G12D} transgenic mice. Cancers 12(12):E3522.

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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。

近五年代表作：

1. Chen HP, Lee YK, Huang SY, Shih PC, Hsu PC, **Chang CF***. Phthalate exposure promotes chemotherapeutic drug resistance in colon cancer cells. Oncotarget. 2018;9(17): 13167-13180. (*Corresponding author).
2. Wang YF, **Chang CF**, Chi CY, Su IJ, Wang JR. Glycan-Binding Preferences and Genetic Evolution of Human Seasonal Influenza A(H3N2) Viruses during 1999-2007 in Taiwan. PLoS One. 2018;13: e0178927.
3. Lin YP, Lee YL, Hung CY, **Chang CF***, Chen Y. Detection of adulterated drugs in traditional Chinese medicine and dietary supplements using hydrogen as a carrier gas. PLoS One. 2018;13: e0205371.
4. Chen KR, Yu CK, Kung SH, Chen SH, **Chang CF**, Ho TC, Lee YP, Chang HC, Huang LY, Lo SY, Chang JC, Ling P. Toll-Like Receptor 3 Is Involved in Detection of Enterovirus A71 Infection and Targeted by Viral 2A Protease. Viruses. 2018:10: 689.
5. Chuang PK, Hsiao M, Hsu TL, **Chang CF**, Wu CY, Chen BR, Huang HW, Liao KS, Chen CC, Chen CL, Yang SM, Kuo CW, Chen P, Chiu PT, Chen IJ, Lai JS, Yu CDT, Wong CH. Signaling Pathway of Globo-series Glycosphingolipids and β1,3-galactosyltransferase V (β3GalT5) in Breast Cancer. Proc Natl Acad Sci U S A. 2019:116:3518-3523.
6. Chang SC, LinWL, Chang YF, Lee CT, Wu JS, Hsu PH, **Chang CF***. Glycoproteomic Identification of Novel Plasma Biomarkers for Oral Cancer. J. Food Drug Anal. 2019:27:483-493.
7. Tu HC, Lee YP, Liu XY, **Chang CF**, Lin PC. Direct Screening of Glycan Patterns from Human Sera: A Selective Glycoprotein Microarray Strategy. ACS App. Bio Materials. 2019:2: 1286-1297. DOI: 10.1021/acsabm.9b00001.
8. Yen CL, Liao YC, Chen RF, Huang YF, Chung WC, Lo PC, **Chang CF**, Wu PC, Shieh DB, Jiang ST, Shieh CC. Targeted Delivery of Curcumin Rescues Endoplasmic Reticulum-Retained Mutant NOX2 Protein and Avoids Leukocyte Apoptosis. J. Immunol. 2019:202:3394-3403.
9. Tsai YH, Huang SW, Hsieh WS, Cheng CK, **Chang CF**, Wang YF, Wang JR. Enterovirus A71 Containing Codon-Deoptimized VP1 and High-Fidelity Polymerase as Next-Generation Vaccine Candidate. J Virol. 2019:93:e02308-e02318.
10. Lin GY, **Chang CF**, Lan CY. The interaction Between Carbohydrates and the Antimicrobial Peptide P-113Tri is Involved in the Killing of Candida albicans. Microorganisms. 2020:8:299. (4.128, 52/137, Microbiology)
11. Ke LY, Chan HC, Chen CC, **Chang CF**, Lu PL, Chu CS, Lai WT, Shin SJ, Liu FT, Chen CH. Increased APOE glycosylation plays a key role in the atherogenicity of L5 low-density lipoprotein. FASEB J. 2020:34:9802-9813 DOI: 10.1096/fj.202000659R.
12. Chan HC, Ke LY, Lu HT, Weng SF, Chan HC, Law SH, Lin IL, **Chang CF**, Lu YH, Chen CH, Chu CS. An Increased Plasma Level of ApoCIII-Rich Electronegative High-Density Lipoprotein May Contribute to Cognitive Impairment in Alzheimer's Disease. Biomedicines. 2020:8:E542.
13. Lee YK, Chang WC, Prakash E, Peng YJ, Tu ZJ, Lin CH, Hsu PH, **Chang CF***. Carbohydrate ligands for COVID-19 spike proteins. Viruses. 2022:14:330. https://doi.org/10.3390/v14020330.
14. Ko CY, Chu TH, Hsu CC, Chen HP, Huang SC, Chang CL, Tzou SJ, Chen TY, Lin CC, Shih PC, Lin TH, **Chang CF***, Lee YK. Bioinformatics analyses identify the therapeutic potential of ST8SIA6 for colon cancer. J. Pers. Med. 2022:12:401. https://doi.org/10.3390/ jpm12030401.
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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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研究興趣：

1. 登革及新冠病毒感染之致病機轉。

2. 病毒感染之治療及預防。

近五年代表作：

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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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1. YH Liu, YC Chang, LK Chen, PA Su, WC Ko, YS Tsai, YH Chen, HC Lai, CY Wu, YP Hung, and **PJ Tsai***. The ATP-P2X7 signaling axis is an essential sentinel for intracellular *Clostridium difficile* pathogen-induced inflammasome activation. ***Front. Cell & Infect. Microbiol.*** 2018. 8:84.
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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.
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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:

- Function and regulation of non-coding RNAs
- Post-translational modifications
- Cancer biomarker and precision oncology

近五年代表作(Selected Publications Within Five Years)

Refereed Paper (*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***. HIF-1α promotes autophagic proteolysis of Dicer and enhances tumor metastasis. ***J Clin Invest.*** 2018;128(2):625–643. doi:10.1172/JCI89212. (*指導第一作者賴輝寰博士生獲第 28 屆王民寧獎)
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7. Complexity in regulating microRNA biogenesis in cancer. **Pai-Sheng Chen**, Shao-Chieh Lin, Shaw-Jenq Tsai*. ***Exp Biol Med (Maywood).*** 2020 Mar;245(5):395-401. doi: 10.1177/1535370220907314. Epub 2020 Feb 19.
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Seminar Invitation:

9. **Pai-Sheng Chen***. A noncanonical HIF-1alpha pathway for metastasis control. 第 13 屆海峽兩岸細胞生物學學術研討會 2018/07/18-22 **(Invited speaker)**

Book Chapter:

10. **Pai-Sheng Chen***. Regulation of Selective Proteolysis in Cancer. ***The Ubiquitin/Proteasome System.*** In production. Matthew Summers, editor, IntechOpen, London, UNITED KINGDOM. ISBN 978-953-51-7766-1 **(Invited book chapter)**

Conference Paper:

11. Chih-Wei Li, Hui-Huang Lai, Da-Liang Ou, **Pai-Sheng Chen*.** Role of TARBP2 in regulating sorafenib resistance of hepatocellular carcinoma cells. 2017 The 32rd Joint Annual Conference of Biomedical Science
12. Jie-Ning Li, Yao-Lung Kuo, Wen-Hui Ku, Yu-Jhan Lu, Ming-Yang Wang, **Pai-Sheng Chen***. Membrane-anchored E-cadherin/Ago2 complex promote non-canonical miRNA biogenesis of miR-451a. American society of biochemistry and molecular biology, Experimental Biology meeting. 2018/04/24
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Patents:

17. **Pai-Sheng Chen**, Jie-Ning Li, Yao-Lung Kuo, Ming-Yang Wang. Method of Evaluating Drug Resistance and Treatment Effect. European Patent No. 3 539 541 歐盟(德、英、法) 2020/11(公告核准日)~2038/10
18. Using TRBP as a biomarker for hormone therapy resistance. **Pai-Sheng Chen**, Jie-Ning Li, Ming-Yang Wang, Yao-Lung Kuo. US provisional patent, Application number 62/641,387.
19. Detecting snoRNAs expression for breast cancer diagnosis and prediction of prognosis. **Pai-Sheng Chen**, Jie-Ning Li, Yao-Lung Kuo US provisional patent, Application number 62/641,385.

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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.
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4. Statt S, Ruan JW, Hung LY, Chang CY, Huang CT, Lim JH, Li JD, Wu R, Kao CY. Statin-conferred enhanced cellular resistance against bacterial pore-forming toxins in airway epithelial cells. Am J Respir Cell Mol Biol. 2015 Nov;53(5):689-702. doi: 10.1165/rcmb.2014-0391OC.

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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：

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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.
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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.
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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：

1. Chen C. H., Wang Y. J., Huang J. M., Huang F. C., Lin W. C. (2021, Mar). Inhibitory effect of host ocular microenvironmental factors on chlorhexidine digluconate activity.. Antimicrobial Agents and Chemotherapy. MOST 109-2628- B-006-022. 本人為通訊作者.
2. Wang, Y. J., Li S. C., Lin, W. C.* and Huang, F. C.* (2021, Feb). Intracellular microbiome profiling of the Acanthamoeba clinical isolates from lens-associated keratitis.. Pathogens, 10, 266. MOST 109-2628-B-006-022. 本人為通訊作者.
3. Mani, K., Lin, W. C., Wang, C. F., Panigrahi, B., Wu, Y. J., Wu, C. L. & Chen, C. Y. (2020, Dec). A Multi-Inlet Microfluidic Nozzle Head with Shape Memory Alloy-Based Switching for Biomaterial Printing with Precise Flow Control. Biochip Journal, 14, 4, p. 340-348.
4. Chih Ming Tsai, Jenn Wei Chen, Wei Chen Lin (2020, Nov). Effects of Acanthamoeba castellanii on the dissolved oxygen and the microbial community under the experimental aquatic model. Experimental Parasitology, 218:107985. MOST 109-2628-B-006-022. 本人為通訊作者.
5. Hsin-Yu Huang, Cheng-Lin Wu, Sheng-Hsiang Lin, Wei-Chen Lin, Fu-Chin Huang, Jia-Horung Hung, Sung-Huei Tseng (2020, Nov). Microsporidial stromal keratitis: Clinical characteristics, histopathologic and ultrastructural studies, and treatment outcomes.. British Journal of Ophthalmology, 2020/11. 104, 11, p. 1613-1620.
6. Yu-Hao Ke, Jen-Wei Huang, Wei-Chen Lin, and Bijay Prasad Jaysawal (2020, Mar). Finding Possible Promoter Binding Sites in DNA Sequences by Sequential Patterns Mining with Specific Numbers of Gaps. IEEE/ACM Transactions on Computational Biology and Bioinformatics.
7. Chun-Hsien Chen, Chao-Li Huang, Ming-Shan He, Fu-Chin Huang, Wei-Chen Lin (2020, Feb). Characterization of the beta-lactam-resistant enzyme in Acanthamoeba castellanii. International Journal of Antimicrobial Agents, 55, 2, 105823.. MOST 106-2320-B-006-070-MY3. 本人為通訊作者.
8. Jian-Ming Huang, Yao-Tsung Chang, and Wei-Chen Lin (2019, Dec). The Biochemical and Functional Characterization of M28 Aminopeptidase Protein Secreted by Acanthamoeba spp. on Host Cell Interaction. molecules, 24, 4573. MOST 106-2320-B-006-070-MY3. 本人為通訊作者.
9. Yu-Jen Wang, Wei-Chen Lin*, Ming-Shan He* (2019, Nov). The Acanthamoeba SBDS, a cytoskeleton-associated gene, is highly expressed during phagocytosis and encystation.. Journal of Microbiology, Immunology and Infection. MOST 106-2320-B-006-070-MY3. 本人為通訊作者.
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11. Jian-Ming Huang, Yao-Tsung Chang, Min-Hsiu Shih, Wei-Chen Lin, Fu-Chin Huang (2019, May). Identification and characterization of a secreted M28 aminopeptidase protein in Acanthamoeba. Parasitology Research, 118(6) 1865–1874. MOST 106-2320-B-006-070-MY3. 本人為通訊作者.
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13. Pei-Yu Chen, Cho-Chiang Shih, Wei-Chen Lin, Teng Ma, Qifa Zhou, K. Kirk Shung and Chih-Chung Huang (2018, Dec). High-Resolution Shear Wave Imaging of the Human Cornea Using a Dual-Element Transducer. Sensors, 18(12), 4244.
14. Pei Lin, Wen-Chien Ko, Wei-Chen Lin and Ming-Chi Li (2018, Jun). Liver abscess caused by coexisting Salmonella enteritidis and Entamoeba histolytica in a HIV-infected patient.. Journal of Microbiology, Immunology and Infection, pii: S1684-1182(18)30162-2.
15. Jian-Ming Huang, Chen-Chieh Liao, Chung-Ching Kuo, Lih-Ren Chen, Lynn L. H. Huang, Jyh-Wei Shin, and Wei-Chen Lin (2017, Dec). Pathogenic Acanthamoeba castellanii Secretes the Extracellular Aminopeptidase M20/M25/M40 Family Protein to Target Cells for Phagocytosis by Disruption. Molecules, pii: E2263. MOST 106-2320-B-006-070-MY3. 本人為通訊作者.
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18. Chen-Chieh Liao, Eing-Ju Song, Tsuey-Yu Chang, Wei-Chen Lin, Hsiao-Sheng Liu, Lih-Ren Chen, Lynn L. H. Huang, Jyh-wei Shin. (2016, May). Evaluation of cellular retinoic acid binding protein 2 gene expression through the retinoic acid pathway by coincubation of Blastocystis ST1 with HT29 cells in vitro. Parasitology Research, 115(5)1965–1975.

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專長說明：

寄生蟲學、細胞生物學

研究興趣:

1. 一氧化氮（nitric oxide，NO）在陰道鞭毛蟲體內的調控角色
2. 人體腔道寄生性原蟲之分子演化

近五年代表作:

1. Lee C-C, Huang P-J, Yeh Y-M, Li P-H, Chiu C-H, **Cheng W-H**, Tang P: Helminth Egg Analysis Platform (HEAP): An opened platform for microscopic helminth egg identification and quantification based on the integration of deep learning architectures. J Microbiol Immunol Infect, 2022, 395-404 (IF: 10.273; rank in Microbiology: 12.5%) **(co-corresponding author)**

2. Huang P-J, Huang C-Y, Li Y-X, Liu Y-C, Chu L J, Yeh Y-M, **Cheng W-H**, Chen R-M, Lee C-C, Chen L- C, Lin H-C, Chiu S-F, Lin W-N, Lyu P-C, Tang P, Huang K-Y: Dissecting the transcriptomes of multiple metronidazole-resistant and sensitive *Trichomonas vaginalis* strains identified distinct genes and pathways associated with drug resistance and cell death. Biomedicines, 2021, 9(12), 1817 (IF:4.757; rank in Pharmacology & Pharmacy : 30.8%)

3. Chiu S-F, Huang P-J, **Cheng W-H**, Huang C-Y, Chu L-J, Lee C-C, Lin H-C, Chen L-C, Lin W-N, Tsao C- H, Tang P, Yeh Y-M, and Huang K-Y: Vaginal microbiota of the sexually transmitted infections caused by *Chlamydia trachoma2s* and *Trichomonas vaginalis* in women with vaginitis in Taiwan. Microorganisms, 2021, 9, 1864 (IF:4.926; rank in Microbiology: 39.7%)

4. **Cheng W-H**, Huang K-Y, Huang P-J, Lee C-C, Omg S-C, Yeh Y-M, Ku F-M, Lin R, Chiu C-H, Tang P: Protein cysteine S-nitrosylation provides the reducing power via enhancing lactate dehydrogenase activity in *Trichomonas vaginalis* upon iron deficiency. Parasites Vectors, 2020, 12:477 (IF: 4.053; rank in tropical medicine: 12.5**%**) **(first author)**

5. Huang P-J, Chang J-H, Lin H-H, Li Y-X, Lee C-C, Su C-T, Li Y-L, Chang M-T, **Cheng W-H**, Chiu C-H, Tang P: Deep Variant-on-Spark: Small-scale genome analysis using cloud-based computing framework. COMPUT MATH METHOD M, 2020, Article ID 7231205 (IF: 2.809; rank in Mathematical & Computational Biology: 45.6%)

6. Lin H-C, Chu L-J, Huang P-J, **Cheng W-H**, Zheng Y-H, Huang C-Y, Hong S-W, Chen L-C, Lin H-A, Wang J-Y, Chen R-M, Lin W-N, Tang P, Huang K-Y: Proteomic signatures of metronidazole-resistant *Trichomonas vaginalis* reveal novel proteins associated with drug resistance. Parasites Vectors 2020, 13:274 (IF: 4.053; rank in tropical medicine: 12.5**%**)

7. Lee C-C, Huang P-J, Yeh Y-M, Chen S-Y, Chou C-H, **Cheng W-H**, Tang P: Pathogenic Protist Transmembranome database (PPTdb): A web-based platform for searching and analysis of protist transmembrane proteins. BMC Bioinformatics 2019, 20 (Suppl 13): 382 (IF: 3.328; rang in mathematical & computational biology: 35.1%) **(co-corresponding author)**

8. Huang K-Y, Chen R-M, Lin H-C, **Cheng W-H**, Lin H-A, Lin W-N, Huang P-J, Chiu C-H, Tang P: Potential role of autophagy in proteolysis in *Trichomonas vaginalis*. J Microbiol Immunol Infect 2019, 52(2): 336-344. (IF: 10.273; rank in Microbiology: 12.5%)

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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。

近五年代表作:

1. Hsu CC, Chiang CW, Cheng HC, Chang WT, Chou CY, Tsai HW, Lee CT, Wu ZH, Lee TY, Chao A, Chow NH, ***Ho CL (corresponding).** Identifying LRRC16B as an oncofetal gene with transforming enhancing capability using a combined bioinformatics and experimental approach. Oncogene. 2011 Feb 10;30(6):654-67.
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專長與研究興趣:

1. **建立膀胱癌致癌的基因模式:**
   臺灣南部地區，膀胱癌不論在發生率、死亡率方面均明顯地高於平均值。我們針對一些常見致癌基因及抑癌基因進行一系列的臨床研究，已建立了國人膀胱癌致癌的基因模式(圖一)。利用微小衛星體 (microsatellite) 定位的分子遺傳研究裏，我們也建立了一個參與膀胱癌惡化 (progression) 的染色體變化模式(圖二)。 在人類基因計劃的基因序列資料公佈之後，未來希望能嘗試找尋新的重要基因，也幫助癌症的早期診斷，有效的治療以及準確的預後指標找尋。
2. **發展新穎的標靶治療:**
   經過多年的基因表現藍圖篩選、生物資訊分析和分子腫瘤學的研究，我們已找到一些膀胱癌新穎致癌基因、重要受體型酪胺酸激酶 (receptor tyrosine kinase, RTK）如表皮生長因子受體 (EGFR)、c-Met 、RON、 Axl 和 PDGFR-α等相關標靶、以及血管新生相關標靶有關的標靶。同時也發現了這些基因參與致癌的分子機轉: 如細胞基質的互動、生長因子受體的交叉對話 (cross-talk)、對抗壓力或缺氧的能力等(圖三)。為了進一步改善現今組合性化療的癌症治療成效，減少毒性和抗藥性的問題，我們將朝向發展高特異性、低毒性的標靶治療，最終目的是希望提高癌症的治療成效。目前的標靶治療研究，也延伸到乳癌、大腸癌和腎臟癌方面的應用。

近年代表作:

1. Wang YW, Tuan YL, Kuo YL, et al. (in press): The potential of epithelial membrane protein 3 as a novel therapeutic target for human breast cancer. Int J Med Sci.
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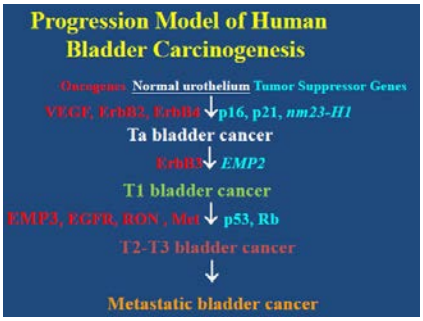
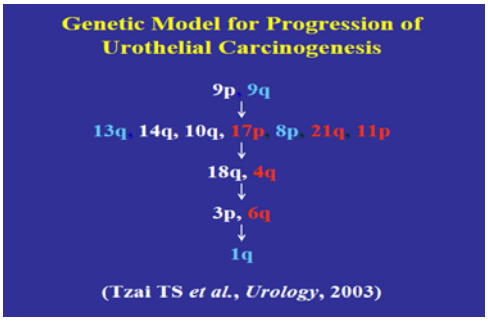
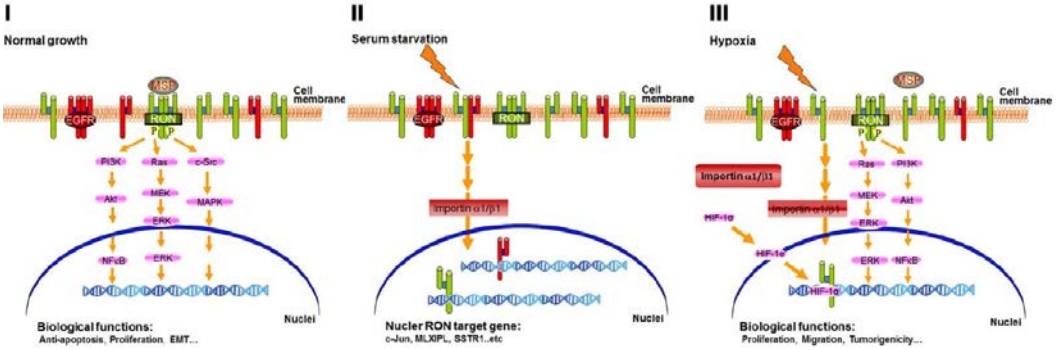
圖一



圖二



圖三



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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

近五年代表作：

1. Chen YR, Yu SC, Wang RC, Lee CL, Song HL, Medeiros LJ, Yue CT, **Chang KC*(corresponding author).** *Am J Surg Pathol.* 2023 Mar 1;47(3):387-396. Lymph Nodes with Increased IgG4-positive Plasma Cells and Patterns Suspicious for IgG4-related Disease: Can Lymph Nodes Be the Only Site of Disease?
2. Lu YS, Chiang PM, Huang YC, Yang SJ, Hung LY, Medeiros L.J, Chen YP, Chen TY, Chang MS, **Chang KC*(corresponding author).** Overexpression of interleukin-20 correlates with favorable prognosis in diffuse large B-cell lymphoma. *Pathology.* 2022 Sep 6;S0031-3025(22)00249-5.
3. Chen HC, Wang RC, Tsai HP, Medeiros LJ, **Chang KC*(corresponding author).** Morphologic Spectrum of Lymphadenopathy in Drug Reaction With Eosinophilia and Systemic Symptoms Syndrome. *Arch Pathol Lab Med.* 2022 Sep 1;146(9):1084-1093.
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6. Thingujam B, Syue LS, Wang RC, Chen CJ, Yu SC, Chen CC, Medeiros LJ, Liao IC, Tsai JW, **Chang KC*(Corresponding author).** Morphologic Spectrum of Lymphadenopathy in Adult-onset Immunodeficiency (Anti-interferon-γ Autoantibodies). *Am J Surg Pathol*. 2021 Nov 1;45(11):1561-1572.
7. Lin HC, Chang Y, Chen RY, Hung LY, Chen PC, Chen YP, Medeiros LJ, Chiang PM*****, **Chang KC*(Co-corresponding author).** Epstein-Barr virus latent membrane protein-1 upregulates autophagy and promotes viability in Hodgkin lymphoma: Implications for targeted therapy. *Cancer Sci.* 2021 Apr;112(4):1589-1602.
8. **Chang KC*(corresponding author)**, Chen RY, Wang YC, Hung LY, Medeiros LJ, Chen YP, Chen TY, Yang JC, Chiang PM. Stem cell characteristics promote aggressiveness of diffuse large B-cell lymphoma. *Sci Rep.* 2020 Dec 7;10(1):21342.
9. Hsu YT, Wang YC, Chen RY, Hung LY, Li SS, Yen CC, Chen TY, Medeiros LJ, **Chang KC*(corresponding author).** Angioimmunoblastic T-cell lymphoma in Taiwan reveals worse progression-free survival for RHOA G17V mutated subtype. *Leuk Lymphoma.* 2020 May;61(5):1108-18.
10. Piris MA, Medeiros LJ, **Chang KC*(corresponding author).** Hodgkin lymphoma: a review of pathological features and recent advances in pathogenesis. *Pathology*. 2020 Jan;52(1):154-165.

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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：

1. Chih-Chieh Yen, Chia-Jui Yen, Yan-Shen Shan, Yih-Jyh Lin, I-Ting Liu, Hsuan-Yi Huang, Matthew M Yeh, Shin-Huang Chan, **Hung-Wen Tsai** (corresponding author). (2021) Comparing the Clinicopathological Characteristics of Combined Hepatocellular-Cholangiocarcinoma with Other Primary Liver Cancers Using the Updated WHO Classification. Histopathology. 2021 Oct;79(4):556-572. doi: 10.1111/his.14384.

2. **Hung-Wen Tsai** (corresponding author), Chung-Liang Ho, Shu-Wen Cheng, Yih-Jyh Lin, Chou-Cheng Chen, Pin-Nan Cheng, Chia-Jui Yen, Ting-Tsung Chang, Po-Min Chiang, Shih-Huang Chan, Cheng-Hsun Ho, Shu-Hui Chen, Yi-Wen Wang, Nan-Haw Chow, Jou-Chun Lin. (2018, Mar). Progesterone receptor membrane component 1 as a potential prognostic biomarker for hepatocellular carcinoma. World Journal of Gastroenterology , 24(10): 1152-1166.

3. **Hung-Wen Tsai,** Yih-Jyh Lin, Han-Chieh Wu, Ting-Tsung Chang, I-Chin Wu, Pin-Nan Cheng, Chia-Jui Yen, Shih-Huang Chan, Wenya Huang, Ih-Jen Su. (2016, Mar). Resistance of ground glass hepatocytes to oral antivirals in chronic hepatitis B patients and implication for the development of hepatocellular carcinoma. . Oncotarget , 7,(19)27724-27734.
4. Han-Chieh Wu, **Hung-Wen Tsai** (Co-first author), Chiao-Fang Teng, Wen-Chuan Hsieh, Yi-Chi Lin, Lily Hui-Ching Wang, Quan Yuan, Ih-Jen Su. 2014. Ground Glass Hepatocytes Co-expressing Hepatitis B Virus X Protein and Surface Antigens Exhibit Enhanced Oncogenic Effects and Tumorigenesis. Human pathology 2014 Jun;45(6):1294-301..

5. Shu-Wen Cheng, **Hung-Wen Tsai (Co-first author)**, Yih-Jyh Lin, Pin-Nan Cheng,Yu-Chung Chang, Chia-Jui Yen, Hsuan-Pang Huang, Yun-Pei Chung, Ting-Tsung Chang, Chung-Ta Lee, Anning Chao, Cheng-Yang Chou, Shih-Huang Chan, Nan-Haw Chow, Chung-Liang Ho. 2013. Lin28B is an oncofetal circulating cancer stem cell-like marker associated with recurrence of hepatocellular carcinoma. PLoS One 2013 Nov 14;8(11):e80053.

6. **Hung-Wen Tsai**, Yih-Jyh Lin,Pin-Wen Lin,Han-Chieh Wu, Kai-Hsi Hsu, Chia-Jui Yen, Shih-Huang Chan, Wenya Huang and Ih-Jen Su (2011) A Clustered Ground-Glass Hepatocyte Pattern Represents a New Prognostic Marker for the Recurrence of Hepatocellular Carcinoma After Surgery. ***CANCER*** 117(13): 2951-2960 **DOI:** 10.1002/cncr.25837.

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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：

1. Chien-An Chu, Yi-Wen Wang, Yi-Lin Chen, Hui-Wen Chen, Jing-Jing Chuang, Hong-Yi Chang, Chung-Liang Ho, Chen Chang, Nan-Haw Chow, **Chung-Ta Lee (李忠達)**. The role of phosphatidylinositol 3-kinase catalytic subunit type 3 in the pathogenesis of human cancer. Int J Mol Sci. 2021 Oct 11;22(20):10964.
2. **Chung-Ta Lee (李忠達)**, Nan-Haw Chow, Yi-Lin Chen, Chung-Liang Ho, Yu-Min Yeh, Shao-Chieh Lin, Peng-Chan Lin, Bo-Wen Lin, Chien-An Chu, Hung-Wen Tsai, Jenq-Chang Lee. Clinicopathological features of mismatch repair protein expression patterns in colorectal cancer. Pathol Res Pract. 2021 Jan;217:153288.
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5. Yu-Min Yeh, Peng-Chan Lin, **Chung-Ta Lee (李忠達)**, Shang-Hung Chen, Bo-Wen Lin, Shao-Chieh Lin, Po-Chuan Chen, Ren-Hao Chan, Meng-Ru Shen. Treatment monitoring of colorectal cancer by integrated analysis of plasma concentration and sequencing of circulating tumor DNA. Mol Cancer. 2020 Oct 26;19(1):150.
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