Hsin-Pai Li (黎欣白)

Title: Professor **教授**	**Lab: Tumor Virus and Cancer Research Lab** **病毒與癌症研究實驗室**	
Highest Degree: Ph.D. **博士**	**School: University of Southern California/ USA** **(Department of Microbiology) 美國南加州大學(微生物)**	
Ext: #3593	**e-mail: paili@mail.cgu.edu.tw**	
Location: Rm 0757		
MS students (at present): 2 **Undergraduate students (at present): 1**	**Research Assistant: 1**	**Ph D students graduated: 2** **MS students graduated: 21** **Undergraduate students graduated: 26**

2012 Teaching Awards (Medical School-Basic Sciences) 優良教師/教學獎

2014 Counseling Awards (Medical School) 優良教師/輔導獎

<u>Research Focus:</u>

(1) Epstein Barr Virus (Tumor virus)

(2) Cancer Research

(3) DNA Methylation & Gene Expression Regulation in Nasopharyngeal Carcinoma (NPC)

(4) NPC patient derived xenograft (PDX) and drug screening

研究方向:

EBV 潛伏膜蛋白 1（latent membrane protein 1, LMP1）是病毒致癌蛋白，可活化細胞“DNA 甲基轉移酶”(DNA methyltransferase 1, DNMT1) 基因的轉錄，導致許多基因過度甲基化和使基因默化(gene silencing)。我們之前的實驗結果證明 LMP1 透過其蛋白質 C-端激活區域 2 (C-terminal activation domain 2, CTAR2)最後 3 個胺基酸 YYD 區域直接誘導 *DNMT1* 啟動子活化(圖 1A, B)。LMP1 誘發 DNMT1 的活化涉及上游 JNK 激酶的活化，卻不涉及 NF-κB 和 p38 /有絲分裂原激活的蛋白激酶(MAPK)訊號傳導。此外 LMP1 誘導由 DNMT1 和 histone deacetylase (HDAC)組成的轉錄抑制複合物(transcriptional repression complex, DNMT-HDAC)的形成，該複合物位於 *E-cadherin* 基因啟動子上(圖 1B)。利用 JNK 抑制劑 SP600125 處理 NPC 細胞可防止這種轉錄抑制複合物的形成。總括而言，我們的結果釐清 JNK-AP-1 訊號傳導與 EBV 致癌蛋白 LMP1 誘導的 DNA 甲基化之間的機制關聯。(Can Res 2006; 66(24): 11668-76) IF= 12.701

圖1A

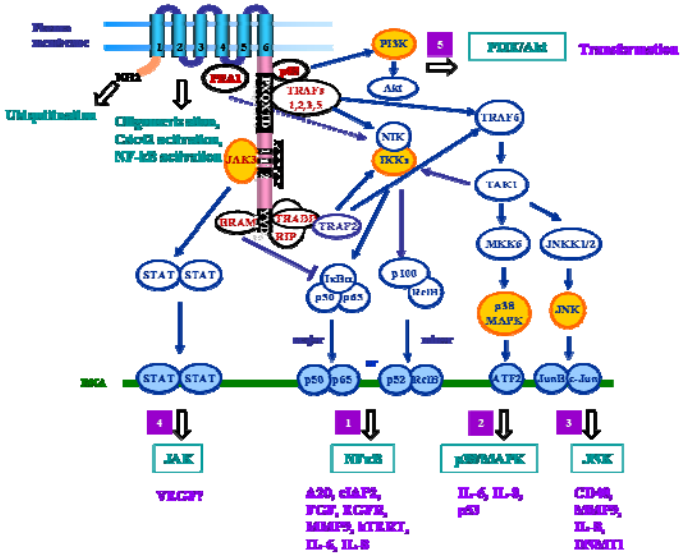


圖1B

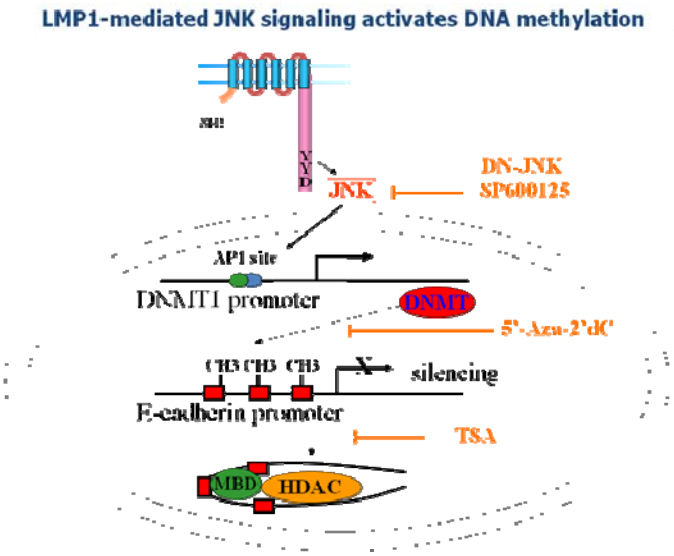


Fig.1 (A). EBV oncoprotein latent membrane protein (LMP1) activates at least 5 different oncogenic cellular signaling pathways and promotes NPC tumor progression [adapted from 2010 Human Oncogenic Viruses: Ch5 EBV and its Oncogenesis (World Scientific)]. 1 (B) A model for LMP1-mediated DNMT1 activation via JNK/AP-1 signaling. Activated DNMT1 hypermethylates E-cadherin promoter and recruits a transcriptional repression complex leading to gene silencing. The YYD domain of LMP1 activates the JNK signaling pathway and activated JNK, in turn,phosphorylat es transcription factor c-Jun. Phosphorylated c-Jun of AP-1 complex binds and transactivates the dnmt1 promoter. Elevated DNMT1 expression leads to hypermethylation of E-cadherin gene and formation of a transcriptional repression complex including DNMTs,meth yl-binding proteins (MBD),and HDAC. This LMP1-mediated DNMT1 activation can be blocked by JNK inhibitor SP600125, dominant negative mutant (DN-JNK), and siRNAs (si-JNK, si-c-Jun, si-TRADD and si-LMP1).

(1) Aberrantly hypermethylated transcription repressor homeobox A2 derepresses metalloproteinase-9 activity through TBP and promotes invasion in nasopharyngeal carcinoma. (Oncotarget 2013; 4:2154-2165)

在NPC腫瘤中鑑定出一個差異化的高甲基化轉錄抑制因子Homeobox A2（HOXA2），導致這個基因的缺失，使NPC細胞具有侵襲性和轉移性。 *HOXA2*的異常甲基化導致NPC腫瘤和細胞中RNA的低表達，加入甲基化抑製劑5'aza可恢復NPC細胞中HOXA2 RNA的表達。高度甲基化的*HOXA2*啟動子，會不利於轉錄活化因子p300與DNA的結合，從而使*HOXA2*的轉錄受到抑制。在NPC細胞中重新大量表達*HOXA2*會降低NPC細胞的侵襲能力，金屬蛋白酶(Metalloprotease 9, MMP-9) mRNA和蛋白質表達降低有關。啟動子活性測試、ChIP 染色質沈澱和DNA pull down試驗證明HOXA2與轉錄激活因子TATA-box結合蛋白（TBP）互相競爭靠近MMP-9轉錄起始位點的辨識序列，因此當HOXA2作為抑制因子與TBP拮抗共同調控MMP-9的表達。而NPC中甲基化的*HOXA2*則失去抑制MMP-9的能力，導致MMP-9產生並增加NPC細胞的侵襲。在NPC血漿樣品中，血漿EBV拷貝數增加與血液中游離的甲基化*HOXA2*水平升高和MMP-9蛋白酶水平升高相關。

圖2

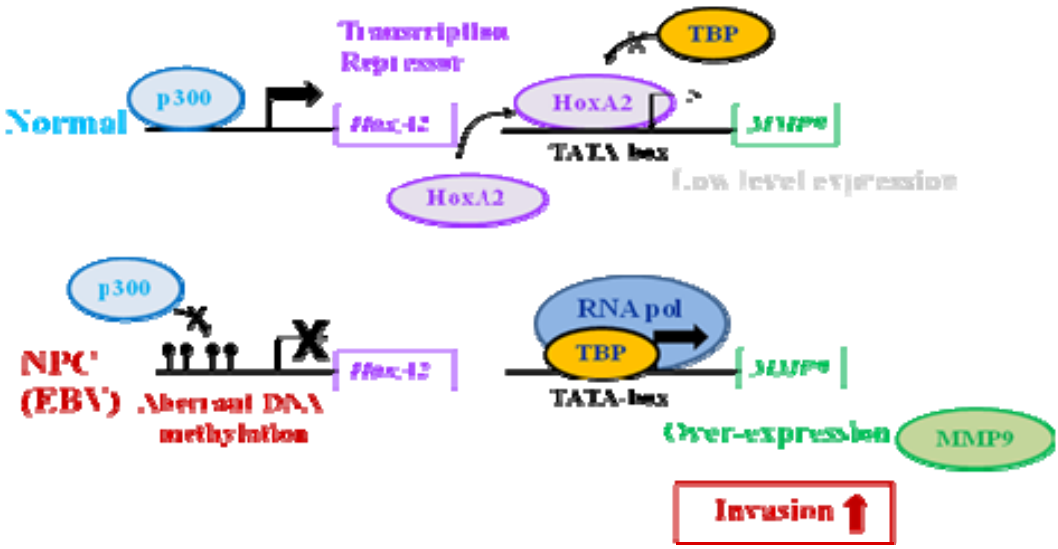


Fig. 2. In normal cells, transcription of *HOXA2* is activated by p300 binding. Subsequently, HOXA2 binds to the *MMP-9* TATA-box and interferes the binding of TBP resulting in suppression of *MMP-9* expression. In NPC cells, methylation of the *HOXA2* impairs the p300 binding thereby inactivates the *HOXA2* gene. In the absence of transcription repressor HOXA2, TBP and RNA polII can bind to the TATA-box of *MMP-9* and activate *MMP-9* expression. Elevated MMP-9 level, in turn, promotes the invasiveness of NPC cells.

(2) Silencing of miRNA-148a by hypermethylation activates the integrin-mediated signaling pathway in nasopharyngeal carcinoma.

(Oncotarget 2014; (5)17:7610-24)

與鄰近的正常細胞和NP細胞相比，NPC檢體組織和NPC細胞中*miRNA-148a*基因由於高度甲基化導致其基因的轉讓下降。啟動子分析顯示，上游活化因子1（upstream stimulating factor 1, USF1）是激活*miR-148a*啟動子活性的關鍵轉錄因子。EMSA分析證實，帶有CG序列甲基化的USF1探針與沒有甲基化的探針相比，以重組純化的USF1與無甲基化的探針結合較好，代表DNA甲基化會扯擾蛋白質與DNA的結合。若在NPC細胞中大量表達*miR-148a*，使*miR-148a*負調控下游目標基因(target gene)，包括讓參與細胞表面的粘附分子integrin signaling(負責和細胞外基質ECM作用)相關的系列VAV2、WASL和ROCK1其蛋白質表達量下降，進而抑制了integrin的訊息傳導，最終抑制了NPC細胞的遷移，表示miR-148a有抑癌功能。此外免疫組織化學染色和Western blotting分析顯示，在NPC檢體中miR-148a的上述3個致癌目標VAV2、WASL和ROCK1都有過量蛋白質表達，這表示由異常DNA甲基化導致*miR-148a*基因失活，促進了NPC細胞的遷移及癌化過程。總體而言，我們的發現miR-148a的功能可作為NPC的抑癌的miRNA。

圖3

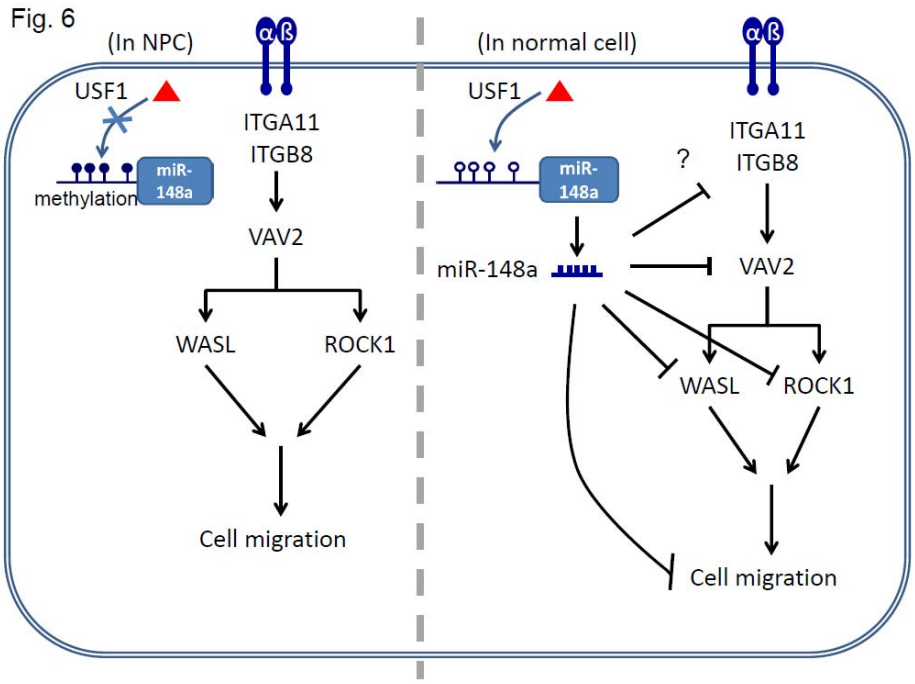


Fig. 3. In normal cells, hypomethylated miR-148a promoter allows the binding of transcription activator USF1, resulting in the activation of miR-148a expression. Mature miR-148a represses the protein expression of the integrin pathway downstream targets such as ITGB8, VAV2, ROCK1 and WASL, and thereby inhibits cell migration. Conversely, in NPC cells, hypermethylated miR-148a promoter prevents the binding of USF1 and causes silencing of miR-148a. In the absence of miR-148a, NPC cells overexpress oncogenic integrin pathway targets and, in turn, trigger cell migration.

(3) Inactivation of the tight junction gene CLDN11 by aberrant hypermethylation modulates tubulins polymerization and promotes cell migration in nasopharyngeal carcinoma (Journal of Experimental & Clinical Cancer Research 2018 37:102; IF=11.161)

我們在 NPC 細胞中鑑定出一個差別高度甲基化和表達量下降的緊密連接基因 *CLDN11*，在 7 對的 NPC 臨床檢體中，*CLDN11* 啟動子其亞硫酸定序和 *CLDN11* mRNA 的 qRT-PCR 表明，啟動子的甲基化程度與 mRNA 表達量成反比。用另外的 NPC 臨床樣本的免疫染色結果顯示，在 9 對的 NPC 腫瘤樣本中，有 7 個樣本的 CLDN11 蛋白表達量與週邊正常組織呈現下降狀況。用 DNA 甲基抑制劑 5'aza 處理可恢復 NPC 細胞中 CLDN11 RNA 的表達。*CLDN11* 啟動子的不同片段和定點突變實驗顯示，上游序列含有轉錄因子 GATA1 結合位點(-62 至-53) 是主要活化的區域。重新大量表達 *CLDN11* 可抑制 NPC 細胞的細胞遷移和侵襲能力。透過免疫共沉澱和 LC-MS / MS，接下來確定微管蛋白(tubulin) TUBA1B 和 TUBB3 是最新被報導與 CLDN11 相互作用蛋白。 CLDN11 透過其蛋白質細胞內環(intracellular domain)和 C-端片段與上述兩個微管蛋白相互作用。更重要的是，這些蛋白片段是 CLDN11 主要執行抑制細胞遷移的必需區域。用微管蛋白聚合抑製劑 nocadazole，可抑制 NPC 細胞的遷移。總括來說，我們的數據提供了有力證據， CLDN11 可作為抑癌基因，而 DNA 高度甲基化使 *CLDN11* 基因失活會促進 NPC 的進展。

圖 4

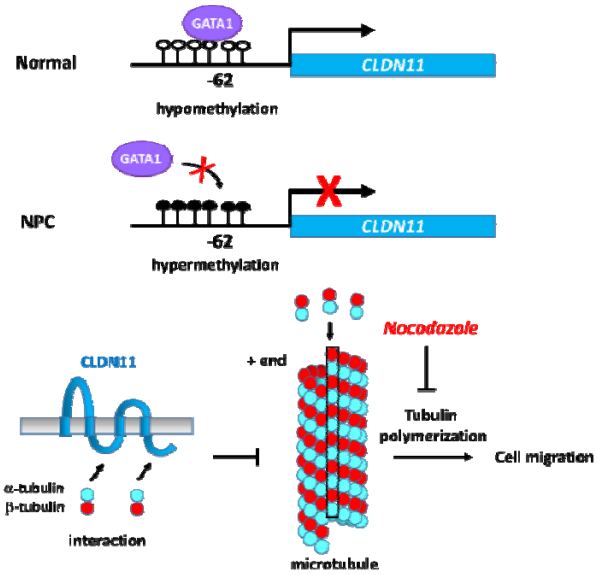


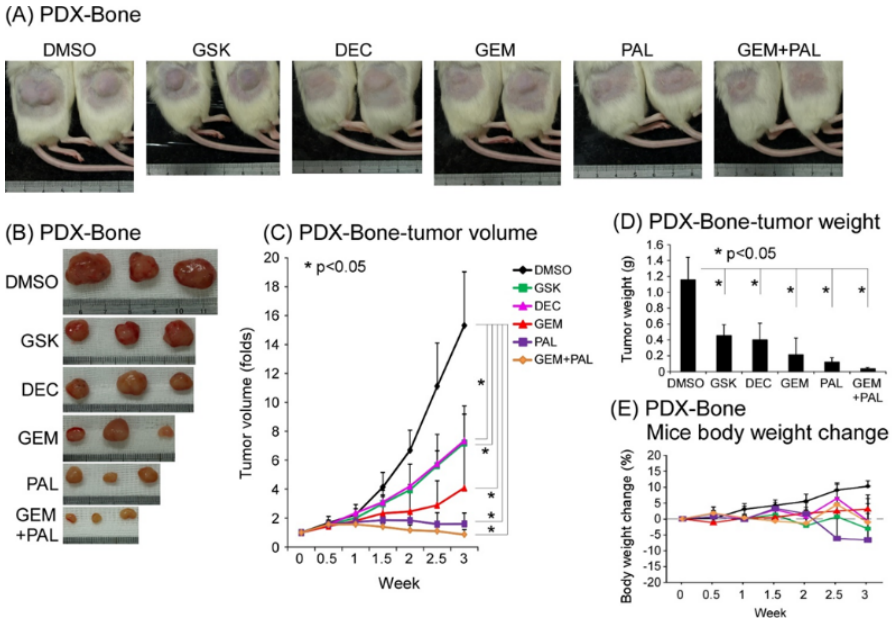
Fig. 4. In a normal nasopharynx, CLDN11 is transcriptionally activated by transcription activators, GATA1 and GATA2. The integral membrane tight junction protein CLDN11, expressed on the apical surface of the epithelial cells, maintains tight junction integrity and epithelial cell polarity and morphology. In addition, CLDN11 serves as the scaffold to recruit tubulins through its intracellular loop and C-terminal domains. The interaction between CLDN11 and the tubulins TUBA1B and TUBB3 may sequester the availability of α- and β-tubulin subunits in the cytoplasm. Thus, the presence of CLDN11 may prevent cell migration and invasion by interfering with the microtubule polymerization dynamics. By contrast, in NPC cells, aberrant promoter hypermethylation impairs GATA binding and causes transcriptional silencing of CLDN11. In the absence of CLDN11, microtubules undergo rapid polymerization, in turn promoting basement membrane breakdown, motility, invasiveness, plasticity, and cell cycle, thus contributing to a more cancerous phenotype of NPC cells. The tubulin polymerization inhibitor nocodazole can serve as a therapeutic drug to block migration in NPC.

(4) Integrated genomic analyses in PDX model reveal a cyclin-dependent kinase inhibitor Palbociclib as a novel candidate drug for nasopharyngeal carcinoma

(Journal of Experimental & Clinical Cancer Research 2018 37:233; IF=11.161)

腫瘤異種移植(patient-derived xenograft, PDX）小鼠動物模型已成為一種新方法，用來篩選、測試和評估有藥物可治療的腫瘤突變，基於突變的靶標篩选和評估個性化的癌症藥物。我們建立了五個鼻咽癌 NPC-PDX 小鼠模型。隨後，進行了全外顯子測序（whole exome sequence, WES）和基因組突變分析，以尋找癌組織中的突變基因，作為抗癌藥品的基因標的。將潛在的藥物處理 2 種上述 NPC PDX 小鼠模型中，並評估藥物抑制腫瘤的能力。其中一組 NPC PDX 小鼠中進行 RNA 測序和轉錄組分析，證明抗癌藥有效抑制腫瘤中與生長相關基因的表達，鼻咽癌腫瘤中常發現細胞週期(cell cycle)相關基因的拷貝數有變異（copy number variation, CNV）。在 5 個 NPC-PDX 中就有 3 個發生 *cyclin D1*（*CCND1*）基因的擴增，而 4 個則有 *cell cycle dependent kinase 2A* (*CDKN2A*) 基因的缺失。此外在>90%FFPE 臨床轉移的 NPC 腫瘤中觀察到常有 CCND1 過量表達(87/91)，並與鼻咽癌不良預後相關。CNV 分析顯示，血漿中 *CCND1 / CDKN2A* 測到的 cell free DNA (cfDNA)比率與 NPC 患者血漿中 EBV DNA 量有關，可作為篩檢試驗，並選擇用 CDK4 / 6 抑製劑作為治療候選藥物，根據我們的 NPC PDX 模型和 RNA 測序，CDKN2A 激酶抑製劑 Palbociclib 透過誘導 cell cycle 進入 G1 arrest 證實具有抗癌作用。一名患有肝轉移的 NPC 患者接受了 Palbociclib 治療，病情穩定，血液中 EBV DNA 的濃度也隨著下降。

圖 5



Candidate drugs (GSK, DEC, GEM, PAL and GEM+PAL, DMSO as control) were tested in 2 cyclin D1 overexpression PDX lines, NPC02 and NPC13. In NPC13 PDX studies, both gross tumor on mice (Fig. 5. A1) and after excision (Fig. 5. A2) showed these drugs could suppress xenograft growth comparing to DMSO with statistical significance (Fig. 5. A3, A4) and tolerable body weight change (Fig. 5. A5). Combination of PAL and GEM had the tendency of addictive effect comparing to either GEM or PAL. Staining of cyclin D1 after treatment showed more homogenized overexpression of cyclin D1 in PAL treatment group (Fig. 5. A6), implying this drug may arrest cancer cells in cell cycle.

Publication List 2022：

(1) Chiao-Yun Lin†, Ren-Chin Wu†, Chen-Yang Huang†, Chyong-Huey Lai, An-Shine Chao, **Hsin-Pai Li**, Chia-Lung Tsai, Elizabeth Joo-Wen Kuek, Cheng-Lung Hsu,* and Angel Chao*
A Patient-Derived Xenograft Model of Dedifferentiated Endometrial Carcinoma: A Proof-Of-Concept Study for the Identification of New Molecularly Informed Treatment Approaches
Cancers 2021 13(23), 5962-5979
https://doi.org/10.3390/cancers13235962
(IF=6.639; R/C=51/242=21%; ONCOLOGY)

(2) Hsin-Pai Li, Chen-Yang Huang, Kar-Wai Lui, Yin-Kai Chao, Chun-Nan Yeh, Li-Yu Lee, Yenlin Huang, Tung-Liang Lin, Yung-Chia Kuo, Mei-Yuan Huang, Yi-Ru Lai, Yuan-Ming Yeh, Hsien-Chi Fan, An-Chi Lin, Jason Chia-Hsun Hsieh, Kai-Ping Chang, Chien-Yu Lin, Hung-Ming Wang, Yu-Sun Chang and Cheng-Lung Hsu
Combination of Epithelial Growth Factor Receptor Blockers and CDK4/6 Inhibitor for Nasopharyngeal Carcinoma Treatment
Cancers 2021 volume 13, issue 12, 2954-2971
2021/6/12
https://doi.org/10.3390/cancers13122954
(IF=6.639; R/C=51/242=21%; ONCOLOGY)

(3) Chi-Sheng Wu, Ian Yi-Feng Chang, Jui-lung Hung, Wei-Chao Liao, Yi-Ru Lai, Kai-Ping Chang, **Hsin-Pai Li** & Yu-Sun Chang
ASC modulates HIF-1α stability and induces cell mobility in OSCC
Cell Death & Disease 2020 volume 11, Article number: 721
https://www.nature.com/articles/s41419-020-02927-7
(IF= 8.469; R/C=37/195 = 18.9%, CELL BIOLOGY)

(4) Chao-Wei Hsu, Horng-Heng Juang, Chien-Yi Kuo, **Hsin-Pai Li**, Shan-Bei Iang, Siao-Han Lin, Chau-Ting Yeh and Mei Chao*
Structural Pattern Differences in Unbranched Rod-Like RNA of Hepatitis Delta Virus Affect RNA Editing
Viruses 2019, 11, 934; doi:10.3390/v11100934 www.mdpi.com/journal/viruses
(IF=5.048; R/C=10/36= 27.77%, VIROLOGY)

(5) An-Ko Chung, Chun-Nan OuYang, Hsuan Liu, Mei Chao, Ji-Dung Luo, Cheng-Yang Lee, Yen-Jung Lu, I-Che Chung, Lih-Chyang Chen, Shao-Min Wu, Ngan-Ming Tsang, Kai-Ping Chang, Cheng-Lung Hsu, **Hsin-Pai Li***, Yu-Sun Chang* (*Co-corresponding)
Targeted sequencing of cancer-related genes in nasopharyngeal carcinoma identifies mutations in the TGF-β pathway
Cancer Medicine 2019 8:5116-5127 (IF= 4.452; R/C=107/242=44.21%; ONCOLOGY)
2019 July 22
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6718742/pdf/CAM4-8-5116.pdf

(6) Cheng-Lung Hsu, Kar-Wai Lui, Lang-Ming Chi, Yung-Chia Kuo, Yin-Kai Chao, Chun-Nan Yeh, Li-Yu Lee, Yenlin Huang, Tung-Liang Lin, Mei-Yuan Huang, Yi-Ru Lai, Yuan-Ming Yeh, Hsien-Chi Fan, An-Chi Lin, Yen-Jung Lu, Chia-Hsun Hsieh, Kai-Ping Chang, Ngan-Ming Tsang , Hung-Ming Wang, Alex Y Chang, Yu-Sun Chang, **Hsin-Pai Li** * (*Corresponding)
Integrated genomic analyses in PDX model reveal a cyclin-dependent kinase inhibitor Palbociclib as a novel candidate drug for nasopharyngeal carcinoma
Journal of Experimental & Clinical Cancer Research 2018 37:233 (IF=11.161; R/C=25/242=10.33%; ONCOLOGY) 2018 Sept. 20
https://jeccr.biomedcentral.com/articles/10.1186/s13046-018-0873-5

(7) **Hsin-Pai Li***†, Chen-Ching Peng†, Chih-Ching Wu, Chien-Hsun Chen, Meng-Jhe Shih, Mei-Yuan Huang, Yi-Ru Lai, Yung-Li Chen, Ting-Wen Chen, Petrus Tang, Yu-Sun Chang, Kai-Ping Chang and Cheng-Lung Hsu (†Co-first author; *Corresponding)
Inactivation of the tight junction gene CLDN11 by aberrant hypermethylation modulates tubulins polymerization and promotes cell migration in nasopharyngeal carcinoma
Journal of Experimental & Clinical Cancer Research 2018 37:102 (IF=11.161; R/C=25/242=10.33%; ONCOLOGY) 2018 May 10
https://jeccr.biomedcentral.com/articles/10.1186/s13046-018-0754-y

(8) Ting-Wen Chen, Chi-Ching Lee, Hsuan Liu, Chi-Sheng Wu, Curtis R. Pickering , Po-Jung Huang, Jing Wang, Ian Yi-Feng Chang, Yuan-Ming Yeh, Chih-De Chen, **Hsin-Pai Li**, Ji-Dung Luo, Bertrand Chin-Ming Tan, Timothy En Haw Chan, Chuen Hsueh, Lichieh Julie Chu, Yi-Ting Chen, Bing Zhang, Chia-Yu Yang, Chih-Ching Wu, Chia-Wei Hsu , Lai-Chu See, Petrus Tang, Jau-Song Yu, Wei-Chao Liao, Wei-Fan Chiang, Henry Rodriguez, Jeffrey N. Myers, Kai-Ping Chang & Yu-Sun Chang

(9) APOBEC3A is an oral cancer prognostic biomarker in Taiwanese carriers of an APOBEC deletion polymorphism
Nature Communication 2017; 6;8(1):465 (IF=14.919; R/C=4/73=5.48%; MULTIDISCIPLINARY SCIENCES)

(10) I-Che Chung, Chun-Nan OuYang, Sheng-Ning Yuan, **Hsin-Pai Li**, Jeng-Ting Chen, Hui-Ru Shieh, Yu-Jen Chen, David M. Ojcius, Ching-Liang Chu, Jau-Song Yu, Yu-Sun Chang & Lih-Chyang Chen
Pyk2 activates the NLRP3 inflammasome by directly phosphorylating ASC and contributes to inflammasome-dependent peritonitis
Scientific Reports 2016; 6:36214 (IF=4.379; R/C=17/73=23.29%; MULTIDISCIPLINARY SCIENCES)

(11) Hung-Ming Wang*, Tung-Liang Lin*, Yung-Chia Kuo, **Hsin-Pai Li**, Kai-Ping Chang, Chien-Yu Lin, Hsien-Chi Fan, An-Chi Lin, Chia-Hsun Hsieh, Ngan-Ming Tsang, Li-Yu Lee, Sheng-Chieh Chan, Kar-Wai Lui, Yu-Sun Chang, Cheng-Lung Hsu

Correlation between overall survival and differential plasma and tissue tumor marker expression in nasopharyngeal carcinoma patients with different sites of organ metastasis

Oncotarget 2016; (7)33:53217-53229 (IF=5.168; R/C= 44/217=20.27%; ONCOLOGY) 2016-JCR

(12) Mei Chao, Chia-Chi Lin, Feng-Ming Lin, **Hsin-Pai Li** and Shan-Bei Iang
Whole-genome analysis of genetic recombination of hepatitis delta virus: molecular domain in delta antigen determining trans-activating efficiency
Journal of General Virology 2015, 96:3460–3469 (IF=3.891; R/C= 61/159=38.36%; BIOTECHNOLOGY & APPLIED MICROBIOLOGY)

(13) Chia-Chi Lin, Chi-Ching Lee, Siao-Han Lin, Po-Jung Huang, **Hsin-Pai Li**, Yu-Sun Chang, Petrus Tang*, Mei Chao*
RNA recombination in Hepatitis delta virus: Identification of a novel naturally occurring recombinant
Journal of Microbiology Immunology and Infection (2015) doi: 10.1016/j.jmii.2015.10.013 **(IF= 4.399; R/C= 46/137=33.58%; MICROBIOLOGY)**

(14) Cheng-Lung Hsu, Yung-Chia Kuo, Yenlin Huang, Yin-Cheng Huang, Kar-Wai Lui, Kai-Ping Chang, Tung-Liang Lin, Hsien-Chi Fan, An-Chi Lin, Chia-Hsun Hsieh, Li-Yu Lee, Hung-Ming Wang, **Hsin-Pai Li**, Yu-Sun Chang
Application of a patient-derived xenograft model in cytolytic viral activation therapy for nasopharyngeal carcinoma
Oncotarget 2015; (6)31: 31323-31334 (IF=5.168; R/C= 44/217=20.27%; ONCOLOGY) 2016-JCR

(15) **Hsin-Pai Li**†*, Hsin-Yi Huang†, Yi-Ru Lai, Jing-Xuan Huang, Kai-Ping Chang, Chuen Hsueh and Yu-Sun Chang (†Co-first author; *Corresponding)
Silencing of miRNA-148a by hypermethylation activates the integrin-mediated signaling pathway in nasopharyngeal carcinoma
Oncotarget 2014; (5)17:7610-24 (IF=5.168; R/C= 44/217=20.27%; ONCOLOGY) 2017-JCR

(16) Ting-Wen Chen†, **Hsin-Pai Li**†, Chi-Ching Lee, Ruei-Chi Gan, Po-Jung Huang, Timothy H Wu, Cheng-Yang Lee, Yi-Feng Chang and Petrus Tang* (†Co-first author)
ChIPseek, a web-based analysis tool for ChIP data
BMC Genomics 2014, 15:539 (IF=3.969; R/C= 57/159 =35.85%; BIOTECHNOLOGY & APPLIED MICROBIOLOGY)

(17) I-Che Chung†, Lih-Chyang Chen†, An-Ko Chung, Mei Chao, Hsin-Yi Huang, Chuen Hsueh, Ngan-Ming Tsang, Kai-Ping Chang, Ying Liang, **Hsin-Pai Li*** and Yu-Sun Chang* (*Co-corresponding)
Matrix metalloproteinase 12 is induced by heterogeneous nuclear ribonucleoprotein K and promotes migration and invasion in nasopharyngeal carcinoma
BMC Cancer 2014, 14:348-361 (IF= 4.430; R/C= 109/242=45.04%; ONCOLOGY)

(18) **Hsin-Pai Li***†, Chen-Ching Peng+, I-Che Chung, Mei-Yuan Huang, Shao-Tung Huang, Chia-Chun Chen, Kai-Ping Chang, Cheng-Lung Hsu, Yu-Sun Chang (†Co-first author; *Corresponding)
Aberrantly Hypermethylated Homeobox A2 Derepresses Metalloproteinase-9 Through TBP and Promotes Invasion in Nasopharyngeal Carcinoma
Oncotarget 2013; 4: 2154-2165 (IF=5.168; R/C= 44/217=20.27%; ONCOLOGY) 2017-JCR

(19) Wen-I Lee*, Jainn-Jim Lin, Meng-Ying Hsieh, Syh-Jae Lin, Tang-Her Jaing, Shih-Hsiang Chen, Iou-Jih Hung, Chao-Ping Yang, Chin-Jung Chen, Yhu-Chering Huang, **Hsin-Pai Li**, Jing-Long Huang*
Immunologic Difference between Hypersensitivity to Mosquito Bite and Hemophagocytic Lymphohistiocytosis Associated with Epstein-Barr Virus Infection
PLoS ONE 2013; Volume 8 | Issue 10 | e76711 (IF= 3.240; R/C= 26/73=35.61%, MULTIDISCIPLINARY SCIENCES)

(20) Cheng-Lung Hsu, Kai-Ping Chang, Chien-Yu Lin, Hsien-Kun Chang, Cheng-Hsu Wang, Tung-Liang Lin, Chun-Ta Liao, Ngan-Ming Tsang, Li-Yu Lee, Sheng-Chieh Chan, Shu-Hang Ng, **Hsin-Pai Li**, Yu-Sun Chang and Hung-Ming Wang
Plasma EBV DNA Concentration and Clearance Rate as Novel Prognostic Factors for Metastatic Nasopharyngeal Carcinoma
Head & Neck 2012; 1-8 DOI: 10.1002/hed.21890 (IF=3.135; R/C= 9/42= 21.43%, OTORHINOLARYNGOLOGY)

(21) Chia-Chen Hsu†, **Hsin-Pai Li**†, Yu-Hung Hung , Yu-Wei Leu , Wu-Hsiung Wu, Feng-Sheng Wang , Kuan-Der Lee , Pey-Jium Chang , Chi-Sheng Wu, Yen-Jung Lu , Tim H.-M. Huang, Yu-Sun Chang, Shu-Huei Hsiao (†Co-first author)
Targeted Methylation of CMV and E1A viral promoters
Biochemical and Biophysical Research Communications 2010; 402: 228–234 (IF=3.575; R/C=30/72 =41.67%, BIOPHYSICS)
https://www.sciencedirect.com/science/article/pii/S0006291X1001853X?via%3Dihub

(22) Yen-Jung Lu, Chi-Sheng Wu, **Hsin-Pai Li***, Hao-Ping Liu, Chang-Yi Lu, Yu-Wei Leu, Chia-Siu Wang, Lih-Chyang Chen, Kwang-Huei Lin, and Yu-Sun Chang* (*Co-corresponding)
Aberrant Methylation Impairs Low Density Lipoprotein Receptor-Related Protein 1B (LRP1B) Tumor Suppressor Function in Gastric Cancer.
GENES CHROMOSOMES & CANCER 2010; 49(5):412-24. (IF= 5.006; R/C= 39/175 =22.29%; GENETICS & HEREDITY)

(23) Chi-Sheng Wu†, Yen-Jung Lu†, **Hsin-Pai Li**, Chuen Hsueh, Chang-Yi Lu, Yu-Wei Leu, Hao-Ping Liu, Kwang-Huei Lin, Tim Hui-Ming Huang and Yu-Sun Chang (†Co-first author)
Glutamate receptor, ionotropic, kainate 2 silencing by DNA hypermethylation possesses tumor suppressor function in gastric cancer.
International Journal of Cancer 2010; 126(11):2542-52. (IF=7.396; R/C= 42/242 =17.36%; ONCOLOGY)

(24) **Hsin-Pai Li**, Mei Chao, Su-Jen Chen, Yu-Sun Chang
Human Oncogenic Viruses: **Epstein-Barr Virus and Its Oncogenesis** (Invited Chapter)
p. 209-267
ISBN: 978-981-283-346-4
World Scientific 2010, Editors: Jing-Hsiung James Ou and T. S. Benedict Yen

(25) Lih-Chyang Chen, Hao-Ping Liu, **Hsin-Pai Li**, Chuen Hsueh, Jau-Song Yu, Ying Liang, Yu-Sun Chang
Thymidine phosphorylase mRNA stability and protein levels are increased through ERK-mediated cytoplasmic accumulation of hnRNP K in nasopharyngeal carcinoma cells.
Oncogene 2009; 28(17):1904-15**. (IF= 9.867; R/C= 29/298 =9.73%; BIOCHEMISTRY & MOLECULAR BIOLOGY)**

(26) Wei-Chun Tai, **Hsin-Pai Li**,Tze-Yi. Chen-Yuan. Lin, and Meng-Tse Wu
Response of extranodal NK/T-cell lymphoma, nasal type, to interferon-a, corticosteroid, and narrowband ultraviolet B phototherapy.
Clinical and Experimental Dermatology 2009 Dec;34(8):e927-30. (IF= 3.470; R/C= 25/68 =36.76%; DERMATOLOGY)

(27) Wen-I Lee, MD, Shih-Hsiang Chen, Iou-Jih Hung, Chao-Ping Yang, Tang-Her Jaing, Chih-Jung Chen, **Hsin-Pai Li**, and Jing-Long Huang
Clinical Aspects, Immunologic Assessment, and Genetic Analysis in Taiwanese Children With Hemophagocytic Lymphohistiocytosis
Pediatric Infectious Disease Journal 2009 January; 28 (1):30-34 (IF=2.129; R/C= 69/129=53.49%; PEDIATRICS) ISSN 0891-3668

(28) Ka-Po Tse, Nang-Ming Tsang, Kung-Den Chen, **Hsin-Pai Li***, Ying Liang, Chuen Hsueh, Kai-Ping Chang, Jau-Song Yu, Sheng-Po Hao, Ling-Ling Hsieh, and Yu-Sun Chang
MCP-1 Promoter Polymorphism at -2518 is Associated with Metastasis of Nasopharyngeal Carcinoma after Treatment.
Clinical Cancer Research 2007; 13:6320-6326. (IF= 12.531; R/C= 18/242 =7.44%; ONCOLOGY)

(29) Chia-Lung Tsai†, **Hsin-Pai Li**†, Chuen Hsueh, Ying Liang, Chi-Long Chen, Sai Wah Tsao, Ka-Po Tse, Yen-Jung Lu, Jau-Song Yu and Yu-Sun Chang († Co-first author)
Activation of DNA methyltransferase 1 by Epstein-Barr Virus LMP1 involves JNK signaling.
Cancer Research 2006; 66:11668-11674. (IF= 12.701; R/C= 17/242 =7.02%; ONCOLOGY)
2006 Dec

(30) Lee YN, Chen LK, Ma HC, Yang HH, **Li HP***, Lo SY
Thermal aggregation of SARS-CoV membrane protein
J Virological Methods 2005 Jul; 129:152-161 (IF= 2.014; R/C= 59/77 =76.62%; BIOCHEMICAL RESEARCH METHODS)

(31) **Li HP**, Leu YW, Chang YS.
Epigenetic changes in virus-associated human cancers
Cell Research 2005 Apr; 15(4):262-271 (IF= 25.617; R/C= 8/195 =4.1%; CELL BIOLOGY)

https://www.nature.com/articles/7290295

(32) **Li HP**, Chang YS.
Epstein-Barr virus latent membrane protein 1: structure and functions.
J Biomed Sci 2003 Sep-Oct; 10:490–504 (IF= 8.410; R/C=15/140 =10.71%; MEDICINE, RESEARCH & EXPERIMENTAL)

(33) Yu JS, Tsai HC, Wu CC, Weng LP, **Li HP**, Chung PJ, Chang YS.
Induction of inducible nitric oxide synthase by Epstein-Barr virus B95-8-derived LMP1 in Balb/3T3 cells promotes stress-induced cell death and impairs LMP1-mediated transformation.
Oncogene, 2002 Nov 14;21(52):8047-61 (IF= 9.867; R/C= 12/175 =6.86%; GENETICS & HEREDITY)
https://www.nature.com/articles/1205990

(34) Shi ST, Huang P, **Li HP**, Lai MM.
Heterogeneous nuclear ribonucleoprotein A1 regulates RNA synthesis of a cytoplasmic virus.
EMBO J 2000 Sep 1;19(17):4701-11 (IF= 11.598; R/C= 22/298 =7.38%; BIOCHEMISTRY & MOLECULAR BIOLOGY)
http://emboj.embopress.org/content/19/17/4701.long

(35) Zhang X, **Li HP**, Xue W, Lai MM.
Formation of a ribonucleoprotein complex of mouse hepatitis virus involving heterogeneous nuclear ribonucleoprotein A1 and transcription-regulatory elements of viral RNA.
Virology 1999 Nov 10;264(1):115-24 (IF= 3.616; R/C= 19/36 =52.78%; VIROLOGY)
https://www.sciencedirect.com/science/article/pii/S0042682299999701?via%3Dihub

(36) **Li HP**, Huang P, Park S, Lai MM.
Polypyrimidine tract-binding protein binds to the leader RNA of mouse hepatitis virus and serves as a regulator of viral transcription.
J Virol 1999 Jan;73(1):772-7 (IF= 5.103; R/C= 9/36 =25%; VIROLOGY)
https://jvi.asm.org/content/73/1/772.long

(37) Zhang X, **Li HP**, Xue W, Lai MM.
Cellular protein hnRNP-A1 interacts with the 3'-end and the intergenic sequence of mouse hepatitis virus negative-strand RNA to form a ribonucleoprotein complex.
Adv Exp Med Biol 1998;440:227-34 (IF= 0.663; R/C= 41/93 =44.09% ; BIOLOGY)
https://link.springer.com/chapter/10.1007/978-1-4615-5331-1_28

(38) Kraeft SK, Chen DS, **Li HP**, Chen LB, Lai MM.
Mouse hepatitis virus infection induces an early, transient calcium influx in mouse astrocytoma cells.
Exp Cell Res 1997 Nov 25;237(1):55-62 (IF= 3.905; R/C= 116/244 =55.37%; ONCOLOGY)
https://www.sciencedirect.com/science/article/pii/S001448279793768X?via%3Dihub

(39) **Li HP**, Zhang X, Duncan R, Comai L, Lai MM.
Heterogeneous nuclear ribonucleoprotein A1 binds to the transcription-regulatory region of mouse hepatitis virus RNA.

(40) **Proc Natl Acad Sci U S A 1997 Sep 2;94(18):9544-9 (IF=11.205; R/C= 8/73 =10.96%; MULTIDISCIPLINARY SCIENCES)**
http://www.pnas.org/content/94/18/9544.long

(41) Chen DS, Asanaka M, Yokomori K, Wang F, Hwang SB, **Li HP**, Lai MM.
A pregnancy-specific glycoprotein is expressed in the brain and serves as a receptor for mouse hepatitis virus.
Proc Natl Acad Sci U S A 1995 Dec 19;92(26):12095-9 (IF=11.205; R/C= 8/73 =10.96%; MULTIDISCIPLINARY SCIENCES)
http://www.pnas.org/content/92/26/12095.long

(42) Lai MY, Chang HC, **Li HP**, Ku CK, Chen P J, Sheu J C, Huang G T, Lee PH, Chen DC.
Splicing mutations of the p53 gene in human hepatocellular carcinoma.
Can Res 1993 Apr 1;53(7): 1653-6 (IF= 12.701; R/C= 17/242 =7.02%; ONCOLOGY)
http://cancerres.aacrjournals.org/content/53/7/1653.long

Patent

中華民國專利證書

發明第　I680297　號

發 明 名 稱：評估罹癌個體是否適用抗癌藥物的方法

專 利 權 人：長庚大學、長庚醫療財團法人林口長庚紀念醫院

發　明　人：黎欣白、徐正龍

專利權期間：自2019年12月21日至2038年7月3日止

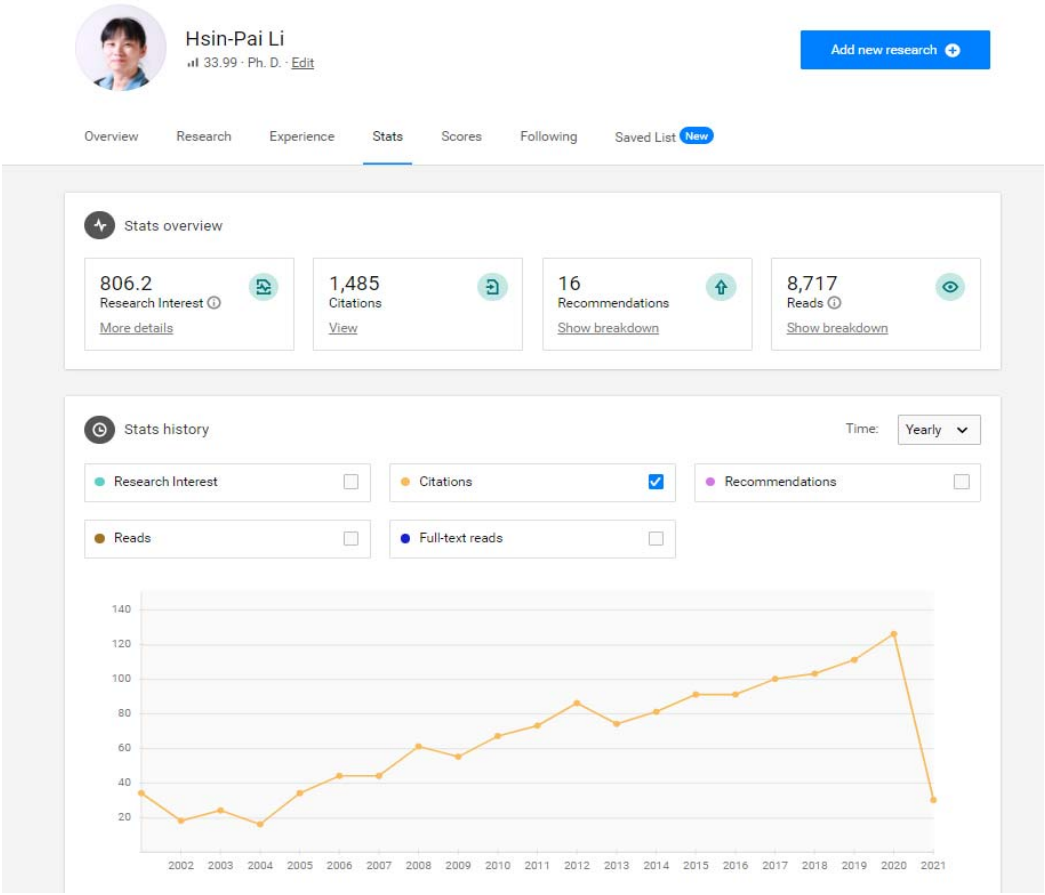
上開發明業經專利權人依專利法之規定取得專利權

經濟部智慧財產局 局長　洪淑敏

中華民國　108　年　12　月　21　日

注意：專利權人未依法繳納年費者，其專利權自原繳費期限屆滿後消滅。

ResearchGate (statistics)



RG Score: 33.99, 引用 Citations: 1485, Reads: 8717 (2021 March)

HPL Lab Photos