

長庚大學臨床醫學研究所教師個人資料表

一、 個人基本資料

教師姓名	職級	教學年資	到職日
蔡七女	副教授	16 年	93, 10, 18
學歷	博士	陽明大學微生物暨免疫研究所	
	學士	中興大學植物系	
專長	病毒學，基因體，表觀遺傳，基因調控，腫瘤致癌機制		
榮譽	Member of Phi-Tau Phi Scholastic Honor Society (June, 1990) 國科會助理研究學者獎助(2004)		
教師專長與類組發展方向與特色之關連性	臨研所之設立便是希望能結合臨床與基礎之研究，由於學生來源主要來自長庚醫院之醫師或是臨床工作人員，因此希望學生藉由醫院豐富的臨床資料庫，提出臨床上觀察到有趣的問題或是現象，老師的角色則是借由基礎研究的經驗來思考如何來解釋或是研究這些臨床問題，並提出解決的方法。本人之研究專長為病毒學、基因體、表觀遺傳、基因調控、及腫瘤致癌機制。因此未來希望能與學生教學相長共同來研究腫瘤細胞之基因體學或是表觀遺傳上之變化，進一步探討基因體上的變化對於轉錄體的影響及其調控機制。而另一方面我們也希望這些基因的變化(gene profile)能運用在臨床上，篩選一些預後不好的肝癌病人，結合基礎與臨床的知識並運用於臨床上是研究最終的目標。		

二、 經歷

(一) 學術經歷 (請填曾任職服務之學術機構，其中起訖年月請以民國.月份表示)

服務機構	服務部門	職稱	起訖年月
長庚大學	臨床醫學研究所	副教授	2019/08~ present
長庚大學	臨床醫學研究所	助理教授	2004/10~2019/07
長庚大學	基研所	助理研究學者	2004/8~ 2004/10
長庚大學	基研所	博士後研究員	1997/8~ 2004/7

三、 研究

<p>研究</p> <p>目前實驗室研究的方向主要聚焦在肝癌的治病機轉、及腫瘤與微環境之交互作用。</p> <p>1. 關於早期肝癌的研究，從 2000 年我們開始追蹤一小群 B 型肝炎(n=25)，以 Affymetrix U133A chip 來分析早期 B 肝腫瘤檢體中的基因標記(gene signature)，在這研究中找到了 GPC3、SPP1 為獨立危險因子。再以比較多肝癌檢體(n=100)驗證：早期肝癌腫瘤組織中高度表達 GPC3 及 SPP1，病人癒後極差 (Yu <i>et al.</i>, 2012)。接續這個研究，我們也發現有些基因在比較 advance stage 肝癌檢體中表現較高，例於: SOX4。研究後發現腫瘤組織中 SOX4 過度表現之肝癌病人為容易血管侵犯，遠端轉移，及癒後差。繼續探討其分子機制，發現在肝癌細胞中 SOX4 表現會活化 CXCL12 promoter 促進其分泌，分泌之 CXCL12 進而影響 endothelial cells migration、tube formation、angiogenesis 同時也影響</p>
--

到腫瘤微環境中 extracellular matrix deposition (Tsai *et al.*, 2020)。這部份除了繼續探討 SOX4 與腫瘤微環境交互作用及致病機轉。

2. 同時這肝癌病人我們也以 Affymetrix OncoScan 平台來分析病人染色體拷貝數的變化，我們除了找出一般論文中常提到在早期肝癌中會有變化的區域(chr1q, 4q, 8p, 8q, 17p, 17q)外，由於 OncoScan 平台比傳統的 CGH 解析度高很多，因此我們發現早期肝癌中腫瘤細胞有六基因染色體拷貝數異常與病人存活有關，分別是染色體拷貝數增多 MYC, ELAC2, SYK 及染色體拷貝數減少 GAK, MECOM, WRN 為獨立危險因子。在第一期 (stage I) 肝炎病人中只要有此六個基因的染色體拷貝數異常癒後即不好，同時早期肝癌病人若是在此 6 個基因中有 3 個以上的基因染色體拷貝數異常癒後十分差 (開刀後三年內死亡率 100%)，在 TCGA 亞洲族群 stage I HCC 同時看到相同的結果，因此這些結果似乎指出早期肝癌病人其檢體中這六個基因 (MYC, ELAC2, SYK, GAK, MECOM, WRN) 染色體拷貝數異常，可以預測亞洲早期肝癌病人之癒後 (Yu *et al.*, 2017)。同時這些病人中約 30 位病人後來發展為 advanced stage HCC，使用 sorafenib。發現在 chromosome 7 amplification 時(包含了 ABCB1 gene amplification)，與病人使用 sorafenib 反應有關 (目前投稿修改中)。目前我們以 Nanostring CNAs customer chip 來分析染色體拷貝數與病人癒後相關，這部份朝向臨床運用為主。
3. Vault RNA 2-1 (VTRNA2-1，也稱為 nc886) 是一種 108 個核苷酸的非編碼轉錄因子，可通過其啟動子的 18 CpG 二核苷酸修飾進行表觀遺傳控制，我們萃取了提取 HCC 正常組織相比腫瘤的基因組 DNA，並對亞硫酸氫鹽進行了修飾。VTRNA2-1 啟動子區域進行 PCR 擴增並進行焦磷酸測序。我們發現肝癌中 VTRNA2-1 啟動子的差異性高甲基化狀態，即肝內肝組織和正常組織的差異，與 the American Joint Committee on Cancer 肝細胞癌分期系統(AJCC staging system) I 和 II 期腫瘤相比，III 期 HCC 腫瘤中 VTRNA-2-1 啟動子的甲基化增加 (64.7%對 36.0%， $p = 0.030$)，同時差異性高甲基化狀態與大腫瘤 ($p = 0.001$)，病理性血管浸潤 ($p = 0.036$)，腫瘤復發($p = 0.007$)和晚期腫瘤分期 (III AJCC) 的存在密切相關。使用多變量 Cox 回歸分析，VTRNA2-1 啟動子的差異性高甲基化狀態是部分肝切除術後患者預後的獨立因素 ($p = 0.011$ ， $HR = 2.305$) (Yu *et al.*, 2020)。因此這部份除了繼續探討其致病機轉外，一樣將朝向臨床運用為主。

實驗室成員

A. 目前在學臨研所博士班:

1.賴正洲 (林口長庚大腸直腸外科)

Topic: The role of estrogen receptors in predict prognosis in stage III colorectal cancer smoker patients

2. 蔡之佑 (林口長庚新陳代謝科)

Topic: Microbiota analysis in Type II diabetes patients and drug response

畢業生:

博士班

1. 陳世彥 (林口長庚兒童醫院胃腸科，與邱政洵醫師共同指導)

published paper:

1. **Chen SY**, Chang YC, Lee YS, Chao HC, Tsao KC, Lin TY, Ko TY, **Tsai CN*** and Chiu CH. Molecular Epidemiology and Clinical Manifestations of Viral Gastroenteritis in Hospitalized Pediatric Patients in Northern Taiwan. Journal of clinical microbiology, June 2007, p. 2054–2057.

2. **Chen SY#**, **Tsai CN#**, Chao HC, Lai MW, Lin TY, Ko TY, and Chiu CH*. Acute Gastroenteritis

Caused by Multiple Enteric Pathogens in Children in Northern Taiwan, Epidemiology and Infection, 2009 Jul;137(7):932-5. (# contribute equally)

3. **Chen SY**#, **Tsai CN**#, Lai MW, Chen TY, Lin TY and Chiu CH*. Norovirus is as a causative agent for Benign infantile convulsions, Clinical Infectious Diseases, 2009 Apr 1;48(7):849-55, (# contribute equally)

參與會議論文：

1. **Chen SY**, Chang YC, Lee YS, Chao HC, Lin TY, Chiu CH and Tsai CN. Etiology and Clinical Features of Acute Viral Gastroenteritis of Children in Taiwan. 1st Asian pediatric meeting (Japan, 2004), oral presentation, Traveling award.
2. **Chen SY**, Chao HC, Lin TY, Chiu CH and Tsai CN. Asian society of pediatric research 4th (Hawaii, 2008) poster section, Traveling award.

2. **林志隆 (林口長庚腦神經外科)**

Topic: Mediated plasticity and regeneration of nociceptive axons within the spinal cord by dorsal root ganglion NGF injection after dorsal root crush injury

Published paper: **C-L Lin**, Heron Paula, Hamann SR, Smith GM: Functional distinction between NGF-mediated plasticity and regeneration of nociceptive axons within the spinal cord. Neuroscience. 272(2014): 76–87.

3. **林嘉鴻 (林口長庚新陳代謝科)**

Topic: The genetic signature of diabetes mellitus-from treatment to diagnosis

Published paper: **Lin CH**, Lee YS, Hung YY, Hsieh SH, Chen ZS, and Tsai CN*.

Polymorphisms of Glucagon-Like Peptide-1 (GLP-1) Receptor Gene and Response to GLP-1 Analogue in Patients with Poorly Controlled Type 2 Diabetes, Journal of Diabetes research, 2015, <http://dx.doi.org/10.1155/2015/176949>

4. **廖家志 (林口長庚麻醉科, 指導教授柳復兆, 共同指導: 蔡七女)**

5. **郭玟伶 (林口長庚一般外科)**

Topic: Establishment of breast mammalian cells and cancer cell lines from Asian women

Published paper:

1. **Kuo WL**, Yu MC, Lee JF, **Tsai CN**, Chen TC, Chen MF* Imatinib Mesylate Improves Liver Regeneration and Attenuates Liver Fibrogenesis in CCL4-treated Mice, **Journal of Gastrointestinal Surgery**, 2012, 16(2):361-9
1. **Kuo WL**, Ueng SH, Wu CH, Lee LY, Lee YS, Yu MC, Chen SC, Yu CC, and **Tsai CN***. Establishment and characterization of two basal-like breast cancer cell lines with low tumorigenicity derived from Taiwanese women. 2018, **Human Cell**, DOI: 10.1007/s13577-017-0197-3

6. **李兆偉 (林口長庚一般外科)**

Topic: Study CK19-mediated pathogenesis mechanism in metastasis of hepatocellular carcinoma.

Published paper:

1. **Lee CW**, Kuo WL, Yu MC, Chen TC, **Tsai CN**, Lee WC and Chen MF. The Expression of Cytokeratin 19 in Lymph Nodes was a Poor Prognostic Factor for Hepatocellular Carcinoma after Hepatic Resection, **World Journal of Surgical Oncology**, 2013 Jun 12;11(1):136. [Epub ahead of print]
2. **Lee CW**, Lin SE, Tsai HI, Su PJ, Hsieh CH, Kuo YC, Sung CM, Lin CY, **Tsai CN** and Yu MC*. Cadherin 17 is related to recurrence and poor prognosis of cytokeratin 19-positive hepatocellular carcinoma, 2017 **Oncology Letters**, DOI: 10.3892/ol.2017.7320
3. Yu MC, **Lee CW**, Lee YS, Lian JH, Tsai CL, Liu YP, Wu CH, and **Tsai CN***. Prediction of

early-stage hepatocellular carcinoma using OncoScan chromosomal copy number aberration data. **World Journal of Gastroenterology**, 2017 November 28; 23(44): 7818-7829

碩士班

1. 楊世維 (基隆長庚耳鼻喉科)

Topic: Molecular Epidemiological Analysis of Human Papillomavirus in Malignant and Premalignant Lesions of Head and Neck

Published paper:

1. **Yang SW**, Lee YS, Chen TA, Wu CJ, and **Tsai CN***. Human papillomavirus in oral leukoplakia is no prognostic indicator of malignant transformation. *Cancer Epidemiology*, (2009), 33:118-122.
2. **Yang SW***, Wu CJ, Lee YS, Chen TA and **Tsai CN**. Postoperative Recurrence as an Associated Factor of Malignant Transformation of Oral Dysplastic Leukoplakia, *ORL J Otorhinolaryngol Relat Spec*. 2010 Aug 25;72(5):280- 290.

2. 詹維軒 (雙和醫院耳鼻喉科)

Topic: Study regulation of DLEC1 in head and neck squamous cell carcinoma

Published paper:

Jan WS, Chang KP, Yang SW, Yao TC, Ko TY, Tsai CL and **Tsai CN***.

Promoter methylation of DLEC1 is an early event for tumor progression and its down-regulation level is associated with the depth of tumor invasion in oral squamous cell carcinoma, *oral oncology*, 2010, 46:874-9

3. 周怡君 (署立桃園醫院小兒科)

Topic: Association of single nucleotide polymorphism in beta2-adrenergic and beta3-adrenergic receptor gene with adolescent obesity in Taiwanese.

Published paper:

Chou YC, Tsai CN, Lee YS, and Pei JS* The association of β -2 and β -3 adrenergic receptor genes polymorphisms with adolescent obesity in Taiwan, *pediatric international journal*, 2012 Feb;54(1):111-6. .

4. 張伯宏 (林口長庚耳鼻喉科)

Topic: Study regulation of DLEC1 in sinonasal inverted papilloma and squamous cell carcinomas

Published paper:

1. Huang CC, Lee TJ*, **Chang PH**, Lee YS, Chuang CC, Jhang YJ, Chen YW, Chen CW, **Tsai CN***. Desmoglein 3 is overexpressed in inverted papilloma and squamous cell carcinoma of sinonasal cavity, *Laryngoscope*, 2010, 120(1):26-29.
2. Huang CC, Lee TJ, **Chang PH**, Lee YS, Chuang CC, Jhang YJ, Chen YW, Chen CW, Fu CH and **Tsai CN*** Expression of cathepsin S and its inhibitor stefin A in sinonasal inverted papilloma, *Rhinology International Journal*, 2010, 48(3): 352-357
3. Wu CC, Lee TJ, **Chang PH**, **Tsai CN**, Lee YS, Fu CH and Huang CC. Similar cellular proliferation activities in nasal polyps and adjacent inferior turbinate, *American Journal of Otolaryngology*, 2012 Jan;33(1):14-9.
4. **Chang PH**, Huang CC, Lee TJ, Jhang YJ, Lai YC, Lee YS, and **Tsai CN***. Down-regulation of a functional tumor suppression gene, DLEC1, in sinonasal inverted papilloma and squamous cell carcinoma, *Journal of Otolaryngology-Head & Neck Surgery*, 2012, 41(2):94-101.

四、 教授課程

(一) 任教課程 (請填所有可教授之課程)

開設於本 所之課程	基礎基因體學, 腫瘤生物學, 生物醫學技術, 現代生物技術, 微生物致病 機制, 博碩士班專題討論, 基因調控
可支援其他 系所之課程	Molecular biology, Cell biology, 生物醫學技術(護理組), 儀器分析法及實 驗, 專題討論, Tumor biology, Genomics, Virology, 大學部-醫學遺傳(表觀 遺傳)
教師專長與教學科 目配合度	1. 我的研究主要是: 癌症研究, 基因體學, 及表觀遺傳, 生化及分生 等, 因此在臨研所及他所教授課程也以此方面為主。 2. 在臨研所部份, 本所學生都是在職的臨床醫師, 對於掌握基礎醫學 的知識與技術較為陌生, 因而缺乏設計基礎實驗、嘗試解決問題 的能力。而本人負責基因調控特論, 及基礎基因體醫學, 課程內容以現 行期刊為主, 同時在課堂中加入現行新的技術的應用, 引導學生如 何從現象去思考如何解決問題, 讓這些臨床醫師了解到, 國外的研究 學者如何結合臨床的發現及深入探討基礎醫學研究的方式! 藉此訓 練培養其從事基礎研究的能力。而本人所教授之其他課程也與本人 專長相符, 例如分子生物學部份: 本人共有四堂課: Human genome, useful website in molecular biology, Tumor biology and Tumor virus, 幾乎都是我本人專長。
學術經驗與教學研 究配合度	在本人在過去幾年中不只積極參與研究工作, 同時也學會如何引導學生 思考, 因此過去的教學中學生反應良好, 本人將秉持著與學生互動的方 式繼續教學。同時將積極參與研究工作。

研究

(二) 近五年論文、專書、專文、專利發表明細 (請務必註明 SCI, EI 等)

論文: (請依期刊/會議分列, 並註明屬 SCI/EI/等等, 受引用次數)	
期刊論文: (*corresponding author, #equal contribution)	
1.	Yu MC, Lee CW, Lin CH, Lee YS, Tsai CL, Wu CH and Tsai CN * Differential hypermethylation status of VTRNA2-1 promoter was an independent factor for patients with hepatocellular carcinoma: Tumor Marker Prognostic Study. International Journal of Surgery , 2020 May 14. pii: S1743-9191(20)30399-X. doi: 10.1016/j.ijssu.2020.05.016. [Epub ahead of print]
2.	Tsai CN , Yu SC, Lee CW, Pang Su JH, Wu CH, Lin SE, Chuang YH, Tsai CL, Hsieh SY and Yu MC* SOX4 activates CXCL12 in hepatocellular carcinoma cells to modulate endothelial cells migration and angiogenesis <i>in vivo</i> , Oncogene 2020, DOI:10.1038/s41388-020-1319-z [Epub ahead of print]
3.	Tsai CL, Tsai CN , Lee YS, Wang SH, Lee LY, Lin CY, Yang SW, Chao A* Genetic analysis of a Taiwanese family identifies a DMRT3-OAS3 interaction that is involved in human sexual differentiation through the regulation of ESR1 expression. Fertility and Sterility, 2020 https://doi.org/10.1016/j.fertnstert.2020.03.008
4.	Chen YE, Lee CC, Chiu CH, Chang YC, Tsai CN , Chao HC, Kong SS, Chen SY. Divergence of group A rotavirus with genetic variations before and after introduction of

- rotavirus vaccines in northern Taiwan. **Medicine (Baltimore)**. 2020 Feb;**99(9):e19253**. doi: **10.1097/MD.00000000000019253**.
5. Chen YF, Lai MW, **Tsai CN**, Lai JY, Yang YC, Chen SY* Gut Microbiota Composition and Copy Number Variation in Biliary Atresia Infants with Different Outcomes after Kasai Operation, **Pediatrics & Neonatology**, 2020 Jan 7. pii: S1875-9572(19)30561-3. doi: **10.1016/j.pedneo.2019.12.011**.
 6. Huang CC, Wu PW, Lee TJ, Chen CL, Wang CH, **Tsai CN** and Chiu CH* Differential IL-17A response to S. pneumoniae in adenoid tissue of children with sleep disordered breathing and otitis media with effusion. **Scientific Reports**, 2019 Dec 27;**9(1):19839**. doi: **10.1038/s41598-019-56415-w**.
 7. **Tsai CN**, Tsai CL, Yi JS, Kao HK, Huang YL, Lee YS, and Chang KP*. Activin A activates the epidermal growth factor receptor promoter by activating the AKT/SP1 pathway in oral squamous cell carcinoma cells. **Scientific Reports**, 2019 Mar 26;**9(1):5197**. doi: 10.1038/s41598-019-41396-7.
 8. Huang CC, Wu PW, Chen CL, Wang CH, Lee TJ, **Tsai CN**, Chiu CH. IL-17A expression in the adenoid tissue from children with sleep disordered breathing and its association with pneumococcal carriage. **Scientific Reports**, 2018 Nov 13;**8(1):16770**. doi: 10.1038/s41598-018-35169
 9. Kuo WL, Ueng SH, Wu CH, Lee LY, Lee YS, Yu MC, Chen SC, Yu CC, and **Tsai CN***. Establishment of two basal-like breast cancer cell lines with extremely low tumorigenicity from taiwanese premenopausal women, 2018, **Human Cell**, DOI: **10.1007/s13577-017-0197-3**
 10. Lee CC, Chen SY, **Tsai CN***, Chiu CH*. Genome Sequence analysis of a G2P[4] Group A Rotavirus Strain with an unusual canine origin nonstructural proteins 1 (NSP1), A15 genotype. 2017, **Genome Announcements**, DOI:**10.1128/genomeA.01315-17**.
 11. Yu MC, Lee CW, Lee YS, Lian JH, Tsai CL, Liu YP, Wu CH, and **Tsai CN***. Prediction of early-stage hepatocellular carcinoma using OncoScan chromosomal copy number aberration data. **World Journal of Gastroenterology**, 2017 November 28; **23(44): 7818-7829**.
 12. Yu WJ, Chen SY*, **Tsai CN**, Chao HC, Kong MS, Chang YJ, and Chiu CH. Long-term Impact of Suboptimal Rotavirus Vaccines on Acute Gastroenteritis in Hospitalized Children in Northern Taiwan, 2017 **Journal of the Formosan Medical Association**; DOI: **10.1016/j.jfma.2017.09.009**.
 13. Lee CW, Lin SE, Tsai HI, Su PJ, Hsieh CH, Kuo YC, Sung CM, Lin CY, **Tsai CN** and Yu MC*. Cadherin 17 is related to recurrence and poor prognosis of cytokeratin 19-positive hepatocellular carcinoma, 2017 **Oncology Letters**, DOI: **10.3892/ol.2017.7320**
 14. Chang KP[#], Wang CI[#], Pickering CR, Huang YL, **Tsai CN**, Tseng NM, Kao HK, Cheng MH and Myers JN. Promoter mutations in the TERT gene occur frequently in oral cavity squamous cell carcinoma. **Head Neck**. 2017 Feb 23. doi: **10.1002/hed.24728**. [Epub ahead of print]
 15. Chen SY, **Tsai CN**, Lee YS, Lin CY, Huang KY, Chao HC, Lai MW, Chiu CH*. Intestinal

- microbiome in children with severe and complicated acute viral gastroenteritis **Sci Rep. 2017 Apr 11;7:46130. doi: 10.1038/srep46130.**
16. Shiue HS, Lee YS, **Tsai CN**, Chang HH. Treatment of allergic rhinitis with acupoint herbal plaster: an oligonucleotide chip analysis. **BMC Complement Altern Med. 2016 Nov 4;16(1):436.**
17. Wang PL[#], Chen SY[#], **Tsai CN**, Chao HC, Lai MW, Chang YJ, Chen CL, Chiu CH. Complicated norovirus infection and assessment of severity by a modified Vesikari disease score system in hospitalized children. **BMC Pediatrics. 2016 Oct 5;16(1):162.**
18. Tsai CL, Chao A, Jung SM, **Tsai CN**, Lin CY, Chen SH, Sue SC, Wang TH, Wang HS and Lai CH. Stress-induced phosphoprotein-1 maintains the stability of JAK2 in cancer cells. **Oncotarget, 2016 Jul 8. doi: 10.18632/oncotarget.10500. [Epub ahead of print]**
19. Hsu HC, Thiam TK, Lu YJ, Yeh CY, Tsai WS, You JF, Hung HY, **Tsai CN**, Hsu A, Chen HC, Chen SJ*, Yang TS. Mutations of KRAS/NRAS/BRAF predict cetuximab resistance in metastatic colorectal cancer patients. **Oncotarget. 2016 Mar 14. doi: 10.18632/oncotarget.8076. [Epub ahead of print]**
20. Lee CC[#], Feng Y[#], Chen SY, **Tsai CN**, Lai MW, Chiu CH. Emerging Norovirus GII.17 in Taiwan, **Clin Infect Dis. 2015 Aug 25. pii: civ647. [Epub ahead of print].**
21. Huang YH, Ming YC, Wang TM, **Tsai CN**, Pang JH "IFI27, a novel EGF-stabilized protein, regulates the proliferation and cell cycling of human skin keratinocytes". **Cell Proliferation, 2015 Apr;48(2):187-197. doi: 10.1111/cpr.12168. Epub 2015 Feb 9.**
22. Lin CH, Lee YS, Hung YY, Hsieh SH, Chen ZS, and **Tsai CN***. Polymorphisms of Glucagon-Like Peptide-1 (GLP-1) Receptor Gene and Response to GLP-1 Analogue in Patients with Poorly Controlled Type 2 Diabetes, **Journal of Diabetes research, 2015, <http://dx.doi.org/10.1155/2015/176949>**
23. Chen SY, Feng Y, Chao HC, Lai MW, Huang WL, Lin CY, **Tsai CN**, Chen CL, Chiu CH*. Emergence in Taiwan of Novel Norovirus GII.4 Variants Causing Acute Gastroenteritis and Intestinal Hemorrhage in Children. **Journal of Medical Microbiology, 2014 Feb;86(2):335-46**
24. **Tsai CN**, Lin CY, Lin CW, Shih KC, Chiu CH and Chen SY*. Clinical relevance and genotypes of circulating noroviruses in northern Taiwan, 2006–2011, **Journal of Medical Virology, 2014 Feb;86(2):335-46**
25. Lin SW, **Tsai CN**, Lee YS, Chu SF, Chen NH. Gene expression profiles in peripheral blood mononuclear cells of asian obstructive sleep apnea patients. **Biomed J. 2014 Mar-Apr;37(2):60-70.**
26. Shih KC, Lee CC, **Tsai CN**, Lin YS, Tang CY. Develop Human Dihydroorotate Dehydrogenase (hDHODH) Pharma-Similarity Index Approach with Scaffold Hopping Strategy for Design Novel Potential Inhibitors. **PLoS One, 2014, Feb 4;9(2):e87960.**
27. Lee CW, Kuo WL, Yu MC, Chen TC, **Tsai CN**, Lee WC and Chen MF. The Expression of Cytokeratin 19 in Lymph Nodes was a Poor Prognostic Factor for Hepatocellular Carcinoma after Hepatic Resection, **2013, World Journal of Surgical Oncology, 2013 Jun 12;11(1):136.**
28. Chen SY, **Tsai CN**, Chen CL, Chao SC, Lee YS, Lai MW, Chen CC, Huang WL, Chiu CH. Severe Viral Gastroenteritis in Children after Sub-optimal Rotavirus Immunization in Taiwan. **Pediatric Infect Dis J. 2013, 32(12): 1335-1339**
29. Wu CC, Lee TJ, Chang PH, **Tsai CN**, Lee YS, Fu CH and Huang CC. Similar cellular proliferation activities in nasal polyps and adjacent inferior turbinate, **American Journal of Otolaryngology, 2012 Jan;33(1):14-9.**
30. Chou YC, **Tsai CN**, Lee YS, and Pei JS* The association of β -2 and β -3 adrenergic receptor genes polymorphisms with adolescent obesity in Taiwan, **Pediatric International, 2012 Feb;54(1):111-6.**

31. Chao A, Lin CY, Lee YS, Tsai CL, Wei PC, Hsueh S, Wu TI, **Tsai CN**, Wang CJ, Chao AS, Wang TH, Lai CH. Regulation of ovarian cancer progression by microRNA-187 through targeting Disabled homolog-2. **Oncogene**. 2012, Feb 9;31(6):764-75
32. Yu MC, Kuo WL, Lee JF, **Tsai CN**, Chen TC, Chen MF* Imatinib Mesylate Improves Liver Regeneration and Attenuates Liver Fibrogenesis in CCL4-treated Mice, **J Gastrointest Surg**. 2012 Feb;16(2):361-9. Epub 2011 Nov 9.
33. Tsai HC, Wei KC, **Tsai CN**, Huang YC, Chen PY, Chen SM, Lu YJ, Lee ST. Effect of valproic acid on the outcome of glioblastoma multiforme. **British Journal of Neurosurgery**, 2012 Jun;26(3):347-54. Epub 2011 Dec 15
34. Lu YC, Wang HM, Tsai CY, Chen WH, Huang YC, Fan HK, **Tsai CN**, Huang SF, Kang CJ, Chang J and Cheng AJ*. Oncogenic function and early detection potential of miRNA-10b in oral cancer as identified by microRNA profiling, **Cancer Prev Res**. 2012, 5(4):665-74
35. Chang PH, Huang CC, Lee TJ, Lee YS and **Tsai CN***. Down-regulation of DLEC1 in sinonasal inverted papilloma and squamous cell carcinoma. **Journal of Otolaryngology -Head & Neck Surgery**, 2012 Jan;33(1):14-9.
36. Chan CK, Wu KH, Lee YS, Hwang SM, Laio SK, Cheng EH, See LC, **Tsai CN**, Kuo ML, and Huang JL. The Comparison of Interleukin-6 Associated Immunosuppressive Effects of Human ESCs, Fetal-Type MSCs, and Adult-Type MSCs. **Transplantation**, 2012, 94(2): 132-8.
37. Yu TH, **Tsai CN**, Lai MW, Chen CC, Chao HC, Chiu CH and Chen SY* Antigenemia and Cytokine Expression in Rotavirus Gastroenteritis in Children, **Journal of Microbiology, Immunology and Infectious**, 2012 Aug;45(4):265-70. Epub 2011 Dec 12.
38. Chang CT#, **Tsai CN#**, Tang CY, Chen CH, Lian JH, Hu CY, Tsai CL, Chao A, Lai CH, Wang TH* and Lee YS*. Mixed Sequence Reader (MSR) for Analyzing DNA sequences with heterozygous base calling chromatography to detect genomic variations with a reference database. **The Scientific World Journal**, 2012;2012:365104. Epub 2012 Jun 18
39. Shei WL, Lin YK, **Tsai CN**, Wang TM, Chen TY, Pang JH. Indirubin, the acting component of indigo naturalis, inhibits EGFR activation and EGF-induced CDC25B gene expression in epidermal keratinocytes. **Journal of Dermatological Science**. 2012 Aug;67(2):140-6. Epub 2012 Jun 2.
40. Tsai CL, **Tsai CN**, Lin CY, Chen HW, Lee YS, Chao A, Wang TH*, Wang HS, Lai CH. Secreted stress-induced phosphoprotein 1 activates the ALK2-SMAD signaling pathways and promotes cell proliferation of ovarian cancer cells. **Cell Repots**, 2012, Aug 30;2(2):283-93.
41. Yu MC, Lee YS, Lin SE, Wu HY, Chen TC, Lee WC, Chen MF*, and **Tsai CN*** Recurrence and Poor Prognosis following Resection of Small Hepatitis B-Related Hepatocellular Carcinoma Lesions are Associated with Aberrant Tumor Expression Profiles of Glypican 3 and Osteopontin. **Annals of surgical oncology**, 2012 Jul;19 Suppl 3:455-63.
42. Yang SW*, **Tsai CN**, Lee YS, Chen TA. Treatment outcome of dysplastic oral leukoplakia with carbon dioxide laser - Emphasis on the factors affecting recurrence. **Journal of Oral and Maxillofacial Surgery**, 2011 Jun;69(6):e78-87
43. Chan WH, Chang KP, Yang SW, Yao TC, Ko TY, Lee YS, Tsai CL and **Tsai CN***. Transcriptional repression of DLEC1 associates with the depth of tumor invasion in oral squamous cell carcinoma. **Oral oncology**, 2010, 46:874-9
44. Yang SW*, Wu CJ, Lee YS, Chen TA and **Tsai CN**. Postoperative Recurrence as an Associated Factor of Malignant Transformation of Oral Dysplastic Leukoplakia, **ORL J Otorhinolaryngol Relat Spec**. 2010 Aug 25;72(5):280- 290.
45. Chang KP; Kao HK; Liang Y; Cheng MC; Liu SC; Lin YC; Lee YS; Tsai CL; Hao SP; **Tsai CN*** Overexpression of activin A is associated with poor prognosis in patients with oral squamous cell carcinoma and promotes the proliferation, motility and invasion of oral cancer cells, **Annals of Surgical Oncology**, 2010 Jul;17(7):1945-56
46. Huang CC, Lee TJ, Chang PH, Lee YS, Chuang CC, Jhang YJ, Chen YW, Chen CW, Fu CH

- p>and
- Tsai CN***
- Expression of cathepsin S and its inhibitor stefin A in sinonasal inverted papilloma,
- 2010, Rhinology International Journal, 48(3): 352-357**
47. Huang CC, Lee TJ*, Chang PH, Lee YS, Chuang CC, Jhang YJ, Chen YW, Chen CW, **Tsai CN*** Desmoglein 3 is overexpressed in inverted papilloma and squamous cell carcinoma of sinonasal cavity, **Laryngoscope, 2010 Jan;120(1):26-9.**
 48. Shiue, HS, Lee YS, **Tsai CN**, Hsueh YM, Sheu JR, Chang HH* Gene expression profile of Phadiatop positive and negative Allergic Rhinitis Patients treated with Acupuncture, **Journal of Alternative and Complementary Medicine 2010, Volume 16(2): 1–10.**
 49. Chao A#, Tsai CL#, Wei PC, Hsueh S, Chao AS, Wang CJ, **Tsai CN**, Lee YS, Wang TH, Lai CH. Decreased expression of microRNA-199b increases protein levels of SET (phosphatase 2A inhibitor) in human choriocarcinoma. **Cancer letter, 2010, 291:99-107.**
 50. Chen SY#, **Tsai CN#**, Chao HC, Lai MW, Lin TY, Ko TY, and Chiu CH*. Acute Gastroenteritis Caused by Multiple Enteric Pathogens in Children in Northern Taiwan, **Epidemiology and Infection, 2009 Jul;137(7):932-5.**
 51. Yang SW, Lee YS, Chen TA, Wu CJ, and **Tsai CN***. Human papillomavirus in oral leukoplakia is no prognostic indicator of malignant transformation. **Cancer Epidemiology 2009, 33:118-122.**
 52. Chao A #, **Tsai CN** #, Hsueh S, Chen TC, Huang SL, Lee LY, Chao FY and CH Lai*. Does Epstein-Barr virus play a role in lymphoepithelioma-like carcinoma of the uterine cervix? **International Journal of Gynecological Pathology, 2009, 28(3):279-85** (# contributes equally)
 53. Lee YS, Chen CH, **Tsai CN**, Tsai CL, Chao A*, and Wang TH*. Microarray Labeling Extension Values: Laboratory Signatures for Affymetrix GeneChips. **Nucleic Acid Research, 2009 May;37(8):e61.**
 54. Chen SY#, **Tsai CN#**, Lai MW, Chen TY, Lin TY and Chiu CH*. Norovirus is as a causative agent for Benign infantile convulsions, **Clinical Infectious Diseases, 2009 Apr 1;48(7):849-55, (# contribute equally)**
 55. Shiue HS, Lee YS, **Tsai CN**, Hsueh YM, Sheu JR and Chang HH*. DNA Microarray Analysis of Inflammation Effect in Patients of Allergic Rhinitis Treated with Acupuncture, **Journal of Alternative and Complementary Medicine, 2008, 14(6): 689-698.**
 56. Lee YS, **Tsai CN**, Tsai CL, ChangSD, Hsueh DW, Liu JT, Ma CT, Lin SH, Wang TH* and Wang HS. Comparison of whole genome amplification methods for further quantitative analysis with microarray-based comparative genomic hybridization. **Taiwanese Journal of Obstetrics & Gynecology, 2008, 47(1):32-41.**
 57. Chou A, Wang TH, Lee YS, Hong JH, **Tsai CN**, Chen CK, Chao AS, and Lai CH* Changes of gene expression profiles in the peripheral blood of patients with cervical cancer undergoing concurrent chemoradiation: A pilot study. **Radiation Research, 2008, 169(1):76-86.**
 58. Chang KP, Ho SP, Tsang NM, Chang YL, Cheng MH, Liu CT, Lee YS, Tsai CL, Lee TJ, Wang TH, and **Tsai CN*** Gene Expression and Promoter Polymorphisms of DNMT3B in Nasopharyngeal Carcinomas in Taiwanese people: A Case-Control Study. **Oncology reports 2008, 19: 217-222.**
 59. Chen SY, Chang YC, Lee YS, Chao HC, Lin TY, Ko TY, **Tsai CN*** and Chiu CH* Etiology and Clinical Features of Acute Viral Gastroenteritis of Children in Taiwan, 2004~ 2006. **Journal of Clinical Microbiology 2007, 45: 2504-7**
 60. Chang KP, Ho SP, Liu CT, Cheng MH, Chang YL, Lee YS, Wang TH, and **Tsai CN*** DNMT3B polymorphisms in risk of Head and Neck Squamous Cell Carcinoma (HNSCC) in Taiwan: a case-control study. **Oral Oncology 2007, 43(4):345-351**
 61. Wu CC, **Tsai CN**, Kuo TT, Wong WR, Hong HS and Chuang YH. Early congenital syphilis presenting as erythema multiforme-like targetoid lesions in a one-day-old male newborn and detection of Treponema pallidum genomic DNA using nested polymerase chain reaction.

- Journal of the American Academy of Dermatology 2006 Aug; 55 (2 Suppl):S11-5.9.**
62. **Tsai CN**, Tsai CL, Tse KP, Chang HY, and Chang YS. The Epstein-Barr virus oncogene product, Latent Membrane Protein 1, induces the down-regulation of E-cadherin gene expression via activation of DNA methyltransferases. **2002 Proc Natl Acad Sci, USA 99:10084-89**
63. Liang CL, **Tsai CN**, Chung PJ, Chen JL, Sun CM, Chen RH, Hong JH, Chang YS. Transcription of Epstein-Barr virus-encoded nuclear antigen 1 promoter Qp is repressed by transforming growth factor-beta via Smad4 binding element in human BL cells. **Virology 2000, 277(1):184-92.**
64. **Tsai CN**, Lee CM, Chien CK, Kuo SC, Chang YS. Additive effect of Sp1 and Sp3 in regulation of the ED-L1E promoter of the EBV LMP 1 gene in human epithelial cells. **Virology 1999, 261(2):288-94**
65. **Tsai CN**, Liu ST, Chang YS. Identification of a novel promoter located within the Bam HI Q region of the Epstein-Barr virus genome for the EBNA 1 gene. **DNA Cell Biol 1995, 14(9):767-76**
66. Chang YS, Lin YJ, **Tsai CN**, Shu CH, Tsai MS, Choo KB, Liu ST. Detection of mutations in the p53 gene in human head and neck carcinomas by single strand conformation polymorphism analysis. **Cancer Lett 1992 24;67(2-3):167-74.**
67. Chen ML, **Tsai CN**, Liang CL, Shu CH, Huang CR, Sulitzeanu D, Liu ST, Chang YS. Cloning and characterization of the latent membrane protein (LMP) of a specific Epstein-Barr virus variant derived from the nasopharyngeal carcinoma in the Taiwanese population. **Oncogene 1992 7(11):2131-40.**