

腫瘤分子生物學研究室

➤ **主持人：謝宗樺 博士**

➤ **聯絡方式**

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➤ **學歷**

學 校	系(所)	學 位
高雄醫學大學	醫學研究所	博士
義守大學	生物醫學工程學系	碩士
中原大學	生物醫學工程學系	學士

➤ **經歷**

服務機關	職 稱	期 間
義大醫院/醫學研究部	副研究員	2019/07~迄今
高雄醫學大學/婦產部	副研究員	2016/08~2019/06
高雄醫學大學/婦產部	助理研究員	2013/03~2016/07
高雄醫學大學/婦產部	博士後研究人員	2012/11~2013/02

➤ **學術專長 (選)**

1. 癌症分子醫學
2. 分子模擬

3. 細胞免疫療法

4. 環境醫學

➤ **研究室簡介**

本研究室主要是藉由癌症分子醫學，分子模擬，細胞免疫療法和環境醫學來進行癌症的研究。我們利用體學的方法研究疾病和癌症之血液、組織和尿液檢體並利用次世代定序鑑定其基因序列。之後搭配生物資訊在數據分析、結構預測和分子動態模擬技術，開發有療效之小分子藥物以及找尋早期診斷癌症之非侵入式生物標記，藉由開發小分子胜肽或海洋萃取物針對癌症或疾病探討其治療的效果。最後再結合細胞免疫療法來進行預防、診斷及臨床需求之研究，透過跨領域、跨校等方式來符合系所和學校之發展方向與重點。研究方向主要有下列三領域主題：

1. 探討細胞免疫療法相關蛋白在癌症中所扮演的角色
2. 探討 KRAS 突變基因調控腫瘤的分子生物功能和訊息傳遞機制
3. 利用分子模擬開發和篩選有抑癌效果之小分子藥物

➤ **研究室成員：吳佳薇(研究助理)**

➤ **實驗室設備與研究技術**

1. 實驗設備：二氧化碳培養箱、倒立式相位差顯微鏡、蛋白質垂直電泳設備、冷凍離心機、4°C、-20°C、-80°C冰箱、液態氮細胞貯存桶、IHC 全自動染片機。
2. 研究技術：細胞培養、組織病理切片、免疫組織化學染色、免疫螢光染色、西方點墨法、基

因表現檢測。

3. 基因轉殖鼠: LSL-KRAS^{G12D}、LSL-K19-KRAS^{G12D}、LSL-P53^{flxed}、LSL-PTEN^{flxed}、AhR^{flxed}

➤ 近五年研究計畫

計畫名稱		計畫主持人	補助單位	執行期間
1	探討內膜異位症 ARID1A 保守性突變經由 HDAC6/IL-10 影響巨噬細胞極化的能力 (MOST 110-2314-B-650-004)	謝宗樺	科技部	202108~2022/07
2	探討 ARID1A-HDAC6-KRAS 軸在卵巢腫瘤癌化所扮演的角色 (MOST-108-2314-B-650-011)	謝宗樺	科技部	2019/08~2020/07
3	修飾胞外泌體攜帶 miRNA 作為內膜異位症的新療法 (MOST-108-2314-B-037-069-MY3)	謝宗樺(共同主持人)	科技部	2019/08~2022/07
4	探討塑化劑暴露之乳癌易感受基因與臨床特徵值相互關係性 (MOST-108-2314-B-037-068)	謝宗樺 (共同主持人)	科技部	2019/08~2020/07
5	以分子模擬方法研究 ALK 突變使肺癌細胞對標靶藥物產生抗藥性之機制並以 ALK 為標的篩選具潛力之抑制劑 (MOST-107-2311-B-110 -001)	謝宗樺 (共同主持人)	科技部	2018/08~2019/07
6	miRNA 對內膜異位症癌化之研究 (MOST-105-2314-B-037-052-MY3)	謝宗樺 (共同主持人)	科技部	2016/08~2019/07
7	探討 mir-18a-3p/4286 在幽門螺旋桿菌誘導胃癌中所扮演的角色並利用分子模擬輔助乙醯化藥物開發 (MOST-106-2320-B-037-019)	謝宗樺	科技部	2017/08~2018/07
8	開發鄰苯二甲酸酯抑制劑拮抗乳癌之標靶藥物(MOST-104-2314-B-037-091)	謝宗樺	科技部	2015/12~2016/10

➤ 研究成果【#共同第一作者(equal contribution); *通訊作者(Corresponding author)】

2022

1. Chen CC, Zhuang ZJ, Wu CW, Tan YL, Huang CH, Hsu CY, Tsai EM and **Hsieh TH**. Venetoclax decrease the expression of spike-protein through amino acids Q493 and S494 in SARS-CoV-2. *Cells*. 2022 Jun 14;11(12):1924 (IF=7.666, Ranking: CELL BIOLOGY:51/194).
2. Tseng CC , Huang SY ,Tsai HP , Wu CW and **Hsieh TH**. HDAC6 is a prognostic biomarker that mediates IL-13 expression to regulate macrophage polarization through AP-1 in oral squamous cell carcinoma. *Scientific Reports*. 2022 Jun 22;12(1):10513 (IF=4.996, Ranking: MULTIDISCIPLINARY SCIENCES:19/73).
3. Wang SH, Wu CH, Tsai CC, Chen TY, Tsai KJ, Hung CM, Hsu CY, Wu CC and **Hsieh TH** Effects of Luteolin on Human Breast Cancer Using Gene Expression Array: Inferring Novel Genes. *Current Issues in Molecular Biology*. 2022 May 9;44(5):2107-2121. (IF=2.976, Ranking: BIOCHEMISTRY & MOLECULAR BIOLOGY:216/296)
4. Tseng CC, Tsou CH, Huang SY, Wu CW and **Hsieh TH**. Using Next-Generation Sequencing and Bioinformatic Methods to Predict New Genes That May Be Regulated by CD47 in Oral Squamous Cell Carcinoma. *Current Issues in Molecular Biology*. 2022 May 17;44(5):2243-2256. (IF=2.976, Ranking: BIOCHEMISTRY & MOLECULAR BIOLOGY:216/296)
5. Yang PJ, Hou MF, Ou-Yang F, **Hsieh TH**, Lee YJ, Tsai EM, Wang TN. Association between recurrent breast cancer and phthalate exposure modified by hormone receptors and body mass index. *Scientific Reports*. 2022 Feb 21;12(1):2858. (IF=4.996, Ranking: MULTIDISCIPLINARY SCIENCES:19/73).
6. **Hsieh TH**, Hsu CY, Yang PJ, Chiu CC, Liang SS, Ou-Yang F, Kan JY, Hou MF, Wang TN* and Tsai EM*. DEHP Mediates Drug Resistance by Directly Targeting AhR in Human Breast Cancer. *Biomedicine & Pharmacotherapy*. 2022 Jan;145:112400. (IF=7.419, Ranking: PHARMACOLOGY & PHARMACY:26/279)

2021

7. Tsai KJ, Tsai HY, Tsai CC, Chen TY, **Hsieh TH**, Chen CL, Mbuyisa L, Huang YB, Lin MW. Luteolin Inhibits Breast Cancer Stemness and Enhances Chemosensitivity through the Nrf2-Mediated Pathway. *Molecules*. 2021 Oct 26;26(21):6452. doi: 10.3390/molecules26216452.(IF=4.927, Ranking: CHEMISTRY, MULTIDISCIPLINARY:65/179)

8. Hsu CY, **Hsieh TH**, Lin HY, Lu CY, Lo HW, Tsai CC, Tsai EM. Characterization and Proteomic Analysis of Endometrial Stromal Cell-Derived Small Extracellular Vesicles. *Journal of Clinical Endocrinology and Metabolism*. 2021 Apr 23;106(5):1516-1529 (IF=5.799, Ranking: ENDOCRINOLOGY & METABOLISM:9/93)

2020

9. Tsai CC, Chen TY, Tsai KJ, Lin MW, Hsu CY, Wu DC, Tsai EM, **Hsieh TH**. NF- κ B/miR-18a-3p and miR-4286/BZRAP1 axis may mediate carcinogenesis in Helicobacter pylori-Associated gastric cancer. *Biomedicine & Pharmacotherapy*. 2020 Dec;132:110869 (IF=7.419, Ranking: PHARMACOLOGY & PHARMACY:26/279)
10. Chen CC, Hsu CY, Lin HY, Zeng HQ, Cheng KH, Wu CW, Tsai EM, **Hsieh TH**. KRAS K104 modification affects the KRASG12D-GEF interaction and mediates cell growth and motility. *Scientific Reports*. 2020 Oct 15;10(1):17447. (IF=4.996, Ranking: MULTIDISCIPLINARY SCIENCES:19/73).
11. Wang TN, Yang PJ, Tseng YT, Tsai YS, Kuo PL, Chiu CC, Liang SS, **Hsieh TH**, Hou MF, Tsai EM. Visceral obesity and cell cycle pathways serve as links in the association between bisphenol A exposure and breast cancer. *Oncology Letters*. 2020 Jul;20(1):33-42(IF=3.111, Ranking:ONCOLOGY:176/245)

2019

12. Wang CL, Lin MJ, Hsu CY, Lin HY, Tsai HP, Long CY, Tsai EM, **Hsieh TH**, Wu CH. CD47 promotes cell growth and motility in epithelial ovarian cancer. *Biomedicine & Pharmacotherapy*. 2019 Nov;119:109105 (IF=7.419, Ranking: PHARMACOLOGY & PHARMACY:26/279)

2018

13. Hsu CY, **Hsieh TH**, Er TK, Chen HS, Tsai CC, Tsai EM*. miR-381 regulates cell motility, growth and colony formation through PIK3CA in endometriosis-associated clear cell and endometrioid ovarian cancer. *Oncology reports*. 2018 Dec;40(6):3734-3742 (IF=4.136, Ranking: Oncology:128/245)
14. Wu CH, Chuang YH, Hsu CY, Long CY, **Hsieh TH**, Wang CL, Tsai EM. Estradiol induces cell proliferation through HER2/COX-2 in MCF-7 mammospheres. *Molecular Medicine Reports*. 2019 Mar;19(3):2341-2349 (IF=3.423, Ranking: MEDICINE, RESEARCH & EXPERIMENTAL:87/139)

2017

15. Chen HS, Hsu CY, Chang YC, Chuang HY, Long CY, **Hsieh TH***, Tsai EM*. (*Correspondence author) Benzyl butyl phthalate decreases myogenic differentiation of endometrial mesenchymal stem/stromal cells through miR-137-mediated regulation of PITX2. *Scientific Reports*. 2017 Mar 15;7(1):186 (IF=4.996, Ranking: MULTIDISCIPLINARY SCIENCES:19/73).
16. Tang FH*, **Hsieh TH***, Hsu CY, Lin HY, Long CY, Cheng KH and Tsai EM. (* contributed equally) KRAS mutation coupled with p53 loss is sufficient to induce ovarian carcinosarcomas in mice.

2016

17. Er TK, Su YF, Wu CC, Chen CC, Wang J, **Hsieh TH**, Herreros-Villanueva M, Chen WT, Chen YT, Liu TC, Chen HS, Tsai EM. Targeted next-generation sequencing for molecular diagnosis of endometriosis-associated ovarian cancer. *Journal of Molecular Medicine*. 2016 Jul;94(7):835-47 (IF=5.606, Ranking: MEDICINE, RESEARCH & EXPERIMENTAL:47/139)
18. Hsu CY, **Hsieh TH**, Tsai CF, Chen HS, Liang PI, Hsu YL, Tsai EM. Synthetic Steroid Hormones Regulated Cell Proliferation Through MicroRNA-34a-5p in Human Ovarian Endometrioma. *Biology of Reproduction*. 2016 Mar;94(3):60 (IF=4.161, Ranking: REPRODUCTIVE BIOLOGY:10/31)
19. **Hsieh TH**, Hsu CY, Tsai CF, Chiu CC, Liang SS, Wang TN, Kuo PL, Long CY, Tsai EM. A novel cell-penetrating peptide suppresses breast tumorigenesis by inhibiting β -catenin/LEF-1 signaling. *Scientific Reports*. 2016 Jan 11; 6 :19156. (IF=4.996, Ranking: MULTIDISCIPLINARY SCIENCES:19/73).

2015

20. Tsai CF, **Hsieh TH**, Lee JN, Hsu CY, Wang YC, Kuo KK, Wu HL, Chiu CC, Tsai EM, Kuo PL. Curcumin Suppresses Phthalate-Induced Metastasis and the Proportion of Cancer Stem Cell (CSC)-like Cells via the Inhibition of AhR/ERK/SK1 Signaling in Hepatocellular Carcinoma. *Journal of Agricultural and Food Chemistry*. 2015 Dec 9;63(48):10388-98. (IF=5.895, Ranking: AGRICULTURE, MULTIDISCIPLINARY:6/59)
21. **Hsieh TH**, Hsu CY, Tsai CF, Long CY, Wu CH, Wu DC, Lee JN, Chang WC, Tsai EM. HDAC Inhibitors Target HDAC5, Upregulate MicroRNA-125a-5p, and Induce Apoptosis in Breast Cancer Cells. *Molecular Therapy*. 2015 Apr;23(4):656-66. (IF=12.910, Ranking: GENETICS & HEREDITY:7/175)
22. **Hsieh TH**, Hsu CY, Tsai CF, Long CY, Chai CY, Hou MF, Lee JN, Wu DC, Wang SC, Tsai EM. miR-125a-5p is a prognostic biomarker that targets HDAC4 to suppress breast tumorigenesis. *Oncotarget*. 2015 Jan 1;6(1):494-509. (IF=5.168, Ranking: ONCOLOG:44/217)

2014

23. Tsai CF, **Hsieh TH**, Lee JN, Hsu CY, Wang YC, Lai FJ, Kuo KK, Wu HL, Tsai EM, Kuo PL. Benzyl butyl phthalate induces migration, invasion, and angiogenesis of Huh7 hepatocellular carcinoma cells through nongenomic AhR/G-protein signaling. *BMC Cancer*. 2014 Aug 1;14:556. (IF=4.638, Ranking: ONCOLOGY:109/245)

2013

24. Hsu CY, **Hsieh TH**, Tsai CF, Tsai HP, Chen HS, Chang Y, Chuang HY, Lee JN, Hsu YL, Tsai EM. miRNA-199a-5p regulates VEGFA in endometrial mesenchymal stem cells and contributes to the pathogenesis of endometriosis. *Journal of Pathology*. 2013 Oct 23. (IF=9.883, Ranking: PATHOLOGY:4/77)
25. Suen JL, Chang Y, Chiu PR, **Hsieh TH**, Hsi E, Chen YC, Chen YF, Tsai EM. Serum Level of IL-10 Is Increased in Patients with Endometriosis, and IL-10 Promotes the Growth of Lesions in a Murine Model. *American Journal of Pathology*. 2013 Dec 8 (IF=5.770, Ranking: PATHOLOGY:12/77)

2012

26. **Hsieh TH**, Tsai CF, Hsu CY, Kuo PL, Lee JN, Chai CY, Wang SC, Tsai EM. Phthalates induce proliferation and invasiveness of estrogen receptor-negative breast cancer through the

AhR/HDAC6/c-Myc signaling pathway. *FASEB Journal*. 2012 Feb;26(2):778-87 (IF=5.834, Ranking: BIOLOGY:16/94)

27. **Hsieh TH**, Tsai CF, Hsu CY, Kuo PL, Lee JN, Chai CY, Hou MF, Chang CC, Long CY, Ko YC, Tsai EM. Phthalates stimulate the epithelial to mesenchymal transition through an HDAC6-dependent mechanism in human breast epithelial stem cells. *Toxicological Sciences*. 2012 Aug;128 (2):365-76. (IF=4.109, Ranking: TOXICOLOGY:30/94)
28. **Hsieh TH**, Tsai CF, Hsu CY, Kuo PL, Hsi E, Suen JL, Hung CH, Lee JN, Chai CY, Wang SC, Tsai EM. n-Butyl benzyl phthalate promotes breast cancer progression by inducing expression of lymphoid enhancer factor 1. *PLoS One*. 2012;7(8):e42750. (IF=3.752, Ranking: MULTIDISCIPLINARY SCIENCES:29/73)
29. Wang YC, Chen HS, Long CY, Tsai CF, **Hsieh TH**, Hsu CY, Tsai EM. Possible mechanism of phthalates-induced tumorigenesis. *Kaohsiung Journal of Medical Sciences*. 2012 Jul;28(7 Suppl):S22-7 (IF=2.996, Ranking: MEDICINE, RESEARCH & EXPERIMENTAL:97/139)
30. Chen HS, Chiang PH, Wang YC, Kao MC, **Hsieh TH**, Tsai CF, Tsai EM. Benzyl butyl phthalate induces necrosis by AhR mediation of CYP1B1 expression in human granulosa cells. *Reproductive Toxicology*. 2012 Jan;33(1):67-75 105 (IF=3.421, Ranking: REPRODUCTIVE BIOLOGY:15/31)

2011

31. Kao AP, Wang KH, Chang CC, Lee JN, Long CY, Chen HS, Tsai CF, **Hsieh TH**, Tsai EM. Comparative study of human eutopic and ectopic endometrial mesenchymal stem cells and the development of an in vivo endometriotic invasion model. *Fertility and Sterility*. 2011 Mar 15;95(4):1308-15. (IF=7.490, Ranking: REPRODUCTIVE BIOLOGY:2/31)
32. Kao AP, Wang KH, Long CY, Chai CY, Tsai CF, **Hsieh TH**, Hsu CY, Chang CC, Lee JN, Tsai EM. Interleukin-1 β induces cyclooxygenase-2 expression and promotes the invasive ability of human mesenchymal stem cells derived from ovarian endometrioma. *Fertility and Sterility*. 2011 Sep;96(3):678-684 (IF=7.490, Ranking: REPRODUCTIVE BIOLOGY:2/31)