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Education

Kaohsiung Medical University School of Dentistry PhD 2008/09-2013/06

Kaohsiung Medical University of Department of Oral Hygiene MS 2006/09-2008/06

Current position and relevant experience

Assistant Professor (2017/08~), Kaohsiung Medical University School of Dentistry

Postdoctoral Research Fellow (2014/08-2017/07), Department of Medical Research,
Kaohsiung Medical University Hospital

Assistant Researcher(2013/07-2014/07), Taiwan Instrument Research Institute,
National Applied Research Laboratories

Specialty

Molecular Biology of Oral Cancer

Oral Hygiene

Oral Epidemiology

Translational Research

Publications & Grants

期刊論文

1. YEN-YUN WANG^{1*}, PEN-TZU FANG*, CHANG-WEI SU, YUK-KWAN CHEN, JOH-JONG HUANG⁹, MING-YII HUANG and SHYNG-SHIOU F. YUAN (2021, Mar). Excision repair cross-complementing group 2 upregulation is a potential predictive biomarker for oral squamous cell carcinoma recurrence. *Oncology letters*. 本人為第一作者.
2. Yen-Yun Wang[#], Wen-Chen Wang[#], Chiang-Wei Su, Ching-Wei Hsu, Shyng-Shiou Yuan, Yuk-Kwan Chen* (2021, Jan). Overexpression of sprouty 1 protein in human oral squamous cell carcinogenesis.. *Journal of dental sciences*, 2021 Jan;16(1):21-28. 本人為第一作者.
3. Yen-Yun Wang, Huan-Da Chen, Steven Lo, Yuk-Kwan Chen, Yu-Ci Huang, Stephen Chu-Sung Hu, Ya-Ching Hsieh, Amos C. Hung, Ming-Feng Hou, Shyng-Shiou F. Yuan * (2020, Dec). Visfatin enhances breast cancer progression through CXCL1

induction in tumor-associated macrophages. *Cancers*. (Accepted). 本人為第一作者.

4. Yen-Yun Wang, Yuk-Kwan Chen, Steven Lo, Tsung-Chen Chi, Yi-Hua Chen, Stephen Chu-Sung Hu, Ya-Wen Chen, Shih Sheng Jiang, Fang-Yu Tsai, Wangta Liu, Ruei-Nian Li, Ya-Ching Hsieh, Chih-Jen Huang, and Shyng-Shiou F. Yuan (2020, Dec). MRE11 promotes oral cancer progression through RUNX2/CXCR4/AKT/FOXA2 signaling in a nuclease-independent manner. *Oncogene*. (Accepted). 本人為第一作者.
5. Ling-Yu Huang #, Yi-Ping Hsieh #, Yen-Yun Wang #, Daw-Yang Hwang #, Shih Sheng Jiang #, Wen-Tsung Huang #, Wei-Fan Chiang, Ko-Jiunn Liu, Tze-Ta Huang* (2020, Nov). Single-Cell Analysis of Different Stages of Oral Cancer Carcinogenesis in a Mouse Model. *International Journal of Molecular Sciences*, Int. J. Mol. Sci. 2020, 21(21), 8171; <https://doi.org/10.3390/ijms21218171>. (Accepted). 本人為第一作者.
6. Ping-Ho Chen, Chia-Min Chung, Yen-Yun Wang, Hurng-Wern Huang, Bin Huang, Ka-Wo Lee, Shyng-Shiou Yuan, Che-Wei Wu, Lee-Shuan Lin, Leong-Perng Chan* (2020, Nov). CYP26A1 Is a Novel Biomarker for Betel Quid-Related Oral and Pharyngeal Cancers. *Diagnostics*, Diagnostics 2020, 10(11), 982.
7. Sheng-Yao Peng, Yen-Yun Wang, Ting-Hsun Lan, Li-Ching Lin, Shyng-Shiou F. Yuan, Jen-Yang Tang*, Hsueh-Wei Chang* (2020, Nov). Low Dose Combined Treatment with Ultraviolet-C and Withaferin a Enhances Selective Killing of Oral Cancer Cells. *Antioxidants (Basel)*, 2020 Nov 13;9(11):1120.
8. Yen-Yun Wang, Amos C. Hung, Steven Lo*, Shyng-Shiou F. Yuan* (2020, Nov). Adipocytokines visfatin and resistin in breast cancer: Clinical relevance, biological mechanisms, and therapeutic potential. *Cancer Letters*, Available online 3 November 2020 In Press. 本人為第一作者.
9. Sheng-Chieh Wang, Yen-Yun Wang, Li-Ching Lin, Meng-Yang Chang, Shyng-Shiou F. Yuan, Jen-Yang Tang* and Hsueh-Wei Chang* (2020, Sep). Combined Treatment of Sulfonyl Chromen-4-Ones (CHW09) and Ultraviolet-C (UVC) Enhances Proliferation Inhibition, Apoptosis, Oxidative Stress, and DNA Damage against Oral Cancer Cells. *INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES*, Volume 21 Issue 17 10.3390/ijms21176443 .
10. Jen-Yang Tang, Kuang-Han Wu, Yen-Yun Wang, Ammad Ahmad Farooqi, Hurng-Wern Huang, Shyng-Shiou F. Yuan, Ru-In Jian, Li-Yi Tsao, Po-An Chen, Fang-Rong Chang, Yuan-Bin Cheng, Hao-Chun Hu *, Hsueh-Wei Chang * (2020, Jul). Methanol Extract of *Usnea barbata* Inhibits Proliferation and Induces Apoptosis and DNA Damage against Oral Cancer Cells through Oxidative. *Antioxidants*. (Accepted).

11. Tzu-Jung Yu, Jen-Yang Tang, Fu Ou-Yang, Yen-Yun Wang, Shyng-Shiou F Yuan, Kevin Tseng, Li-Ching Lin, Hsueh-Wei Chang* (2020, May). Low Concentration of Withaferin a Inhibits Oxidative Stress-Mediated Migration and Invasion in Oral Cancer Cells. *Biomolecules*, 10(5), E777. (SCI, 58/299, BIOCHEMISTRY & MOLECULAR BIOLOGY).
12. Yi-Fang Yang, Yen-Yun Wang, Michael Hsiao, Steven Lo, Yu-Chan Chang, Yi-Hua Jan, Tsung-Ching Lai, Yi-Chen Lee, Ya-Ching Hsieh, Shyng-Shiou F Yuan* (2020, May). IMPAD1 Functions as Mitochondrial Electron Transport Inhibitor That Prevents ROS Production and Promotes Lung Cancer Metastasis Through the AMPK-Notch1-HEY1 Pathway. *CANCER LETTERS*, In Press. (SCI, 29/230, ONCOLOGY).
13. Anupama Vadhan, Yen-Yun Wang, Shyng-Shiou F. Yuan, Yi-Chen Lee, Stephen Chu-Sung Hu, Jyuan-Yuan Huang, Takashi Ishikawa, Ming-Feng Hou* (2020, Apr). EMI2 expression as a poor prognostic factor in patients with breast cancer. *KAOHSIUNG JOURNAL OF MEDICAL SCIENCES*, Epub. (SCI, 114/136, medicine, research & experimental).
14. Yen-Yun Wang, Ling-Yi Xiao, Yuk-Kwan Chen, Pao-Chu Wu, Yi-Hua Chen, Stephen Chu-Sung Hu, and Shyng-Shiou F. Yuan* (2020, Mar). Orabase-Formulated Benzalkonium Chloride Effectively Suppressed Oral Potentially Malignant Disorder In Vitro and In Vivo. *ACS Omega*, 5(12), 7018–7024. (SCI, 76/172, chemistry, multidisciplinary). 本人為第一作者.
15. Yu-Fen Tsai, Yen-Yun Wang, Shyng-Shiou F. Yuan* (2020, Mar). Comet tail, an indicator for DNA damage or repair?: Refers to Liu et al. Oral Oncology 2020 Jan;100:104469. *Oral Oncology*. (SCI, 6/91, dentistry, oral surgery & medicine).
16. Yen-Yun Wang, Ling-Yi Xiao, Pao-Chu Wu, Yuk-Kwan Chen, Steven Lo, Stephen-Chu -Sung Hu, Yi-Hua Chen, Charles-Chien-Chih Chiu, Shyng-Shiou F. Yuan* (2020, Jan). Orabase-formulated gentian violet effectively improved oral potentially malignant disorder in vitro and in vivo. *Biochemical pharmacology*, 171, 113713. (SCI, 25/267, pharmacology & pharmacy). 高醫附院 : MOHW108-TDU-B-212-124016. 本人為第一作者.
17. Yung-ding Bow#, Yen-yun Wang#, Yuk-kwan Chen, Chang-wei Su, Ching-wei Hsu, Ling-yi Xiao, Shyng-shiou Yuan*, and Ruei-nian Li* (2020, Jan). Silencing of FOXA2 decreases E-cadherin expression and is associated with lymph node metastasis in oral cancer. *Oral Diseases*, Epub . (Accepted). (SCI, 17/91, dentistry, oral surgery & medicine). 本人為第一作者.
18. Jyun-Yuan Huang, Yen-Yun Wang, Steven Lo, Ling-Ming Tseng, Dar-Ren Chen, Yi-Chia Wu, Ming-Feng Hou, Shyng-Shiou F. Yuan * (2019, Dec). Visfatin mediates malignant behaviors through adipose-derived stem cells intermediary

in breast cancer. *Cancers*, 12(1), 29. (SCI, 31/229, oncology).

19. Wen-Chin Chiu, Pen-Tzu Fang, Yi-Chen Lee, Yen-Yun Wang, Yu-Han Su, Stephen Chu-Sung Hu, Yuk-Kwan Chen, Yu-Tong Tsui, Ying-Hsien Kao, Ming-Yii Huang*, Shyng-Shiou F. Yuan* (2019, Nov). DNA Repair Protein Rad51 Induces Tumor Growth and Metastasis in Esophageal Squamous Cell Carcinoma via a p38/Akt-Dependent Pathway. *Annals of surgical oncology* . (SCI, 81/230, oncology). 高醫大: KMU-TC108A04.
20. Hui-Ru Wang, Jen-Yang Tang, Yen-Yun Wang, Ammad Ahmad Farooqi, Ching-Yu Yen, Shyng-Shiou F. Yuan, Hurng-Wern Huang*, Hsueh-Wei Chang* (2019, Sep). Manolidide Preferentially Provides Antiproliferation of Oral Cancer Cells by Oxidative Stress-Mediated Apoptosis and DNA Damage. *Cancers*, 11(9), 1303. (SCI, 31/230, oncology). MOST 108-2320-B-037-015-MY3.
21. Yi-Chen Lee, Chun-Yu Lin, Yen-Hsu Chen, Wen-Chin Chiu, Yen-Yun Wang, Chin Hsu, Stephen Chu-Sung Hu, Yu-Han Su and Shyng-Shiou F. Yuan* (2019, Apr). Essential Role of Visfatin in Lipopolysaccharide and Colon Ascendens Stent Peritonitis-Induced Acute Lung Injury. *International Journal of Molecular Sciences*, 20(7), 1678. (SCI, 78/299, biochemistry & molecular biology).
22. Yi-Fang Yang, Yi-Chen Lee, Yen-Yun Wang, Chie-Hong Wang, Ming-Feng Hou, Shyng-Shiou F. Yuan* (2019, Apr). YWHAE promotes proliferation, metastasis, and hemoresistance in breast cancer cells . *The Kaohsiung journal of medical sciences*, 35(7), 408-416.
23. Yao-Kuang Wang, Wei-Chung Chen, Ying-Ho Lai, Yi-Hsun Chen ,Ming-Tsang Wu,Chie-Tong Kuo, Yen-Yun Wang, Shyng-Shiou F. Yuan, Yu-Peng Liu,* and I-Chen Wu* (2019, Mar). Influence of Tea Consumption on the Development of Second Esophageal Neoplasm in Patients with Head and Neck Cancer. *Cancers*, 11(3), 387. (SCI, 31/230, oncology).
24. Yen-Yun Wang, Yuk-Kwan Chen, Chu-Sung Hu, Ling-Yi Xiao, Wan-Ling Huang, Tsung-Chen Chi, Kuang-Hung Cheng, Yun-Ming Wang*, Shyng-Shiou F. Yuan* (2019, Jan). MAL-PDT inhibits oral precancerous cells and lesions via autophagic cell death. *Oral Diseases*, 25(3), 758-771. (SCI, 17/91, dentistry, oral surgery & medicine). 本人為第一作者.
25. Chih-Jen Huang, Ming-Yii Huang, Pen-Tzu Fang, Frank Chen, Yu-Tsang Wang, Chung-Ho Chen, Shyng-Shiou Yuan, Chun-Ming Huang, Kuei-Hau Luo, Hung-Yi Chuang, Yen-Yun Wang, Hsin-Hua Lee* (2018, Nov). Randomized Double-Blind, Placebo-Controlled Phase III trial Evaluating the Effect of Oral Glutamine on Radiation-Induced Oral Mucositis and Neck Dermatitis in Head and Neck Cancer Patients. *American Journal of Clinical Nutrition*, 102(3), 298. (SCI, 4/83, nutrition & dietetics).

26. Hsueh-Wei Chang, Ching-Yu Yen, Chung-Ho Chen, Jun-Hsu Tsai, Jen-Yang Tang, Yung-Ting Chang, Yu-Hsun Kao, Yen-Yun Wang, Shyng-Shiou F. Yuan, Sheng-Yang Lee* (2018, Jan). Evaluation of the mRNA expressions of integrins $\alpha 3$, $\alpha 5$, $\beta 1$ and $\beta 6$ as tumor biomarkers of oral squamous cell carcinoma. *Oncology Letters*, 16(4), 4773–4781. (SCI, 194/223, oncology).
27. Pei-Hsien Liao, Yen-Yun Wang#, Wen-Chen Wang, Yue-Chuan Kao, Jing-Wei Hsu, Ching-Yi Chen, Shyng-Shiou Yuan*, Yuk-Kwan Chen* (2017, Dec). Overexpression of sprouty2 in human oral squamous cell carcinogenesis. *Archives of Oral Biology*, 87, 131-142. (SCI, 33/90, dentistry, oral surgery & medicine). 本人為第一作者.
28. Yen-Yun Wang, Pei-Wen Hsieh, Yuk-Kwan Chen, Stephen Chu-Sung Hu, Ya-Ling Hsu, Chun-Hao Tsai, Shyng-Shiou F. Yuan* (2017, Sep). CYT-Rx20 inhibits cervical cancer cell growth and migration through oxidative stress-induced DNA damage, cell apoptosis and EMT inhibition. *International Journal of Gynecological Cancer*, 27, 1306-1317. (SCI, 141/217, oncology). 本人為第一作者.
29. Chih-Chang Hung, Chen-Yu Chien, Pei-Yu hu, Yu-Jen Wu; Chang-Shen Lin, Chih-Jen Huang, Leong-Perng Chan, Yen Yun Wang, Shyng-Shiou F. Yuan, Tzyh-Chyuan Hour*, Jeff Yi-Fu Chen* (2017, Aug). Differential resistance to platinum-based drugs and 5-fluorouracil in p22phox-overexpressing oral squamous cell carcinoma: implications of alternative treatment strategies. *Journal for The Sciences & Specialties of The Head and Neck*, 39(8), 1621-1630. (SCI, 1/42, otorhinolaryngology).
30. Yen-Yun Wang, Yuk-Kwan Chen, Stephen Chu-Sung Hu, Ya-Ling Hsu, Chun-Hao Tsai, Tsung-Chen Chi, Pei-Wen Hsieh, Shyng-Shiou F. Yuan* (2017, Jun). CYT-Rx20 inhibits ovarian cancer cells in vitro and in vivo through oxidative stress-induced DNA damage and cell apoptosis. *Cancer Chemotherapy and Pharmacology*, 79(6), 1129-1140. (SCI, 122/217, oncology). 本人為第一作者.
31. Chun-Hao Tsai, Pei-Wen Hsieh, Yi-Chen Lee, Chie-Hong Wang, Wen-Chin Chiu, Chun-Wun Lu, Yen-Yun Wang, Stephen Chu-Sung Hu, Tain-Lu Cheng, Shyng-Shiou F. Yuan* (2017, Mar). 3'-hydroxy-4'-methoxy- β -methyl- β -nitrostyrene inhibits tumor growth through ROS generation and GSH depletion in lung cancer cells. *Life Sciences*, 172, 19-26. (SCI, 94/257, pharmacology & pharmacy).
32. Tze-Ta Huang, Jehn-Shyun Huang, Yen-Yun Wang, Ken-Chung Chen, Tung-Yiu Wong, Yi-Chun Chen, Che-Wei Wu, Leong-Perng Chan, Yi-Chu Lin, Yu-Hsun Kao, Shoko Nioka, Shyng-Shiou F. Yuan*, Pau-Choo Chung* (2017, Mar). Novel Quantitative Analysis of the Autofluorescence Images for Oral Cancer Screen. *Oral Oncology*, 68, 20-26. (SCI, 53/217, oncology).

33. Yen-Yun Wang, Yuk-Kwan Chen, Ya-Ling Hsu, MS, Wen-Chin Chiu, Chun-Hao Tsai, Stephen Chu-Sung Hu, Pei-Wen Hsieh, Shyng-Shiou F. Yuan* (2017, Jan). The synthetic β -nitrostyrene derivative CYT-Rx20 inhibits oral cancer cell proliferation and tumor growth through GSH suppression and ROS induction. *Journal for The Sciences & Specialties of The Head and Neck*, 39(6):1055-1064. (SCI, 1/42, otorhinolaryngology). 本人為第一作者.
34. Wen-Chin Chiu, Yi-Chen Lee, Yu-Han Su, Yen-Yun Wang, Chun-Hao Tsai, Yi-An Hou, Chie-Hong Wang, Ying-Fong Huang, Chih-Jen Huang, Shah-Hwa Chou, Pei-Wen Hsieh, Shyng-Shiou F. Yuan* (2016, Nov). The Synthetic β -Nitrostyrene Derivative CYT-Rx20 Inhibits Esophageal Tumor Growth and Metastasis via PI3K/AKT and STAT3 Pathways. *PLOS ONE*, 11(11), e0166453. (SCI, 11/63, multidisciplinary sciences).
35. Wu TL, Tsai CC, Yen-Yun Wang, Ho KY, Wu YM, Hung HC, Lin YC* (2015, Dec). The association between the RAGE G82S polymorphism, sRAGE and chronic periodontitis in Taiwanese individuals with and without diabetes. *journal of periodontal research*, 50(6):881-9. (SCI, 16/88, dentistry, oral surgery & medicine).
36. Tze-Kiong Er, Yen-Yun Wang, Chih-Chieh Chen, Marta Herreros-Villanueva, Ta-Chih Liu, Shyng-Shiou F. Yuan* (2015, Oct). Molecular characterization of oral squamous cell carcinoma using targeted next-generation sequencing. *ORAL DISEASES*, 21(7), 872-8.. (SCI, 17/88, dentistry, oral surgery & medicine). 本人為第一作者.
37. Sheng-Hung Wang, Hsin-Chia Hung, Chi-Cheng Tsai, Meng-Chuan Huang, Kun-Yen Ho, Yi-Min Wu, Yen-Yun Wang, Ying-Chu Lin, (2014, Aug). Plasma polyunsaturated fatty acids and periodontal recovery in Taiwanese with periodontitis: A significant relationship. *Archives of Oral Biology*, 59(8), 800-7. (SCI, 23/83, dentistry, oral surgery & medicine).
38. Yen-Yun Wang, Yen-Hsuan Tail, Wen-Chen Wang, Ching-Yi Chen, Yu-Hsun Kao, Yuk-Kwan Chen*, and Chung-Ho Chen* (2014, Aug). Malignant transformation in 5071 southern Taiwanese patients with potentially malignant oral mucosal disorders. *BMC Oral Health*, 14(99). (SCI, 48/83, dentistry, oral surgery & medicine). 本人為第一作者.
39. Shyh-Jong Wu, Yun-Ju Chen, Tien-Yu Shieh, Chun-Ming Chen, Yen-Yun Wang, Kun-Tsung Lee, Yueh-Ming Lin, Pei-Hsuan Chien, and Ping-Ho Chen (2014, Jun). Association Study between Novel CYP26 Polymorphisms and the Risk of Betel Quid-Related Malignant Oral Disorders. *The Scientific World Journal*, 2015(160185).
40. Yen-Yun Wang , Ying-Chu Lin , Hsin-Chia Hung , Wan-Yu Tien , Tien-Yu Shieh

(2013, Nov). Polymorphisms in Kallikrein7 and 10 genes and oral cancer risks in Taiwan betel quid chewers and smokers. *ORAL DISEASES*, 19(8), 824-32. 本人為第一作者。

41. Wang LH, Ting SC, Chen CH, Tsai CC, Lung O, Liu TC, Lee CW, Wang YY, Tsai CL, Lin YC. (2010, Feb). Polymorphisms in the apoptosis-associated genes FAS and FASL and risk of oral cancer and malignant potential of oral premalignant lesions in a Taiwanese population.. *Journal of Oral Pathology & Medicine* , 39(2):155-61.

近三年研究計劃

中文計畫名稱	計畫內擔任的工	起訖年月	補助或委託機構	執行情形	經費總額
TRPM2與TRPM6表現與人類口腔鱗狀細胞癌預後之相關性探討(109-2314-B-037-015-MY2)	共同主持人	2020/08/01~2022/07/31	科技部	執行中	2,700,000
抵抗素與脂肪幹細胞的交互作用如何藉由NDUFS1粒線體電子傳遞鏈酵素來影響乳癌的發展(1/3)(109-2314-B-037-122-)	共同主持人	2020/08/01~2021/07/31	科技部	執行中	1,650,000
β化功能性色酮(CHW09)對口腔癌細胞的X-ray增敏作用(108-2314-B-037-020-)	共同主持人	2019/08/01~2019/08/01	科技部	已結案	880,000
DSB修復核酸分解酵素MRE11在口腔癌中的探討(108-2314-B-037-014-)	主持人	2019/08/01~2019/08/01	科技部	已結案	735,000
STIM表現與人類口腔鱗狀細胞癌預後之相關性探討(108-2314-B-037-017-)	共同主持人	2019/08/01~2019/08/01	科技部	已結案	1,070,000
牙科?復物光澤度量測系統開發(107-2622-E-492-016-CC3)	共同主持人	2018/11/01~2018/11/01	科技部	已結案	610,000
Oral與STIM表現與人類口腔鱗狀細胞癌預後之相關性探討(107-2314-B-037-045-)	共同主持人	2018/08/01~2018/08/01	科技部	已結案	1,000,000
探討高低ITGA3表現對PARPi與X-ray的單獨與結合處理口腔癌細胞的生長抑制作用與機制(107-2314-B-037-048-)	共同主持人	2018/08/01~2019/07/31	科技部	已結案	700,000
探討DNA修復蛋白MRE11在口腔癌轉移過程中扮演的角色(107-2314-B-037-007-)	主持人	2018/01/01~2018/01/01	科技部	已結案	650,000
提升口腔癌前病變及口腔癌診斷率之整合性研究	總計畫共同主持人分項計畫主持人	2018/01/01~2021/12/31	衛生福利部	執行中	49,200,000
細胞質內的RAD51對乳癌進展的功能性研究	共同主持人	2018/08/01~2018/08/01	高雄醫學大學	已結案	1,030,000
針對口腔潛在惡性病變開發口內膏劑型臨床用藥	計畫主持人	2018/12/01~2018/12/01	高雄醫學大學	已結案	200,000
MAL光動力治療誘導口腔癌細胞走向凋亡	計畫主持人	2019/01/01~2019/01/01	高雄醫學大學	已結案	200,000
探討MRE11透過下游CD44在口腔癌轉移過程中扮演的角色	計畫主持人	2019/01/01~2019/12/31	高雄醫學大學、國立中山大學	已結案	260,000
代謝相關酵素在癌症轉移中 所扮演的角色	計畫主持人	2019/03/21~2019/03/21	高雄醫學大學	執行中	1,000,000
聚焦口腔癌惡化的微環境因子: 機轉探究及治療策略開發	總計畫主持人、子計畫三主持人	2020/01/01~2020/12/31	高醫-中山合作計畫	已結案	1,600,000
探討陽極處理的Ti-7.5Mo對小鼠骨髓間質細胞骨分化影響	計畫主持人	2020/01/01~2020/12/31	高雄醫學大學/屏東科技大學	已結案	600,000
探討陽極處理的Ti-7.5Mo合金對小鼠骨髓間質細胞骨分化影響	計畫主持人	2020/01/01~2020/12/31	高雄醫學大學、屏東科技大學	已結案	600,000
IL-1RA如何藉由調控癌細胞幹性與腫瘤微環境來影響口腔癌的治療抗性	主持人	2021/01/01~2021/01/01	高雄醫學大學	執行中	200,000