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### Research Interests

#### ● 老藥新用藥物篩選平台

- **老藥新用藥物篩選平台**：是以基因表現圖譜為基礎，首先針對疾病或藥物以基因微陣列晶片做分析，以得到疾病或藥物作用的基因表現圖譜，再透過與生物資訊的結合，利用 Connectivity map—簡稱 CMap，一個儲存了大量 FDA 核准之老藥的基因表現圖譜的資料庫—將疾病、基因表現及藥物三者做一個連結，快速的找出治療癌症的藥物；使用 CMap 除了加速藥物篩選外，從過去的藥物或已上市之藥物切入，能夠大幅降低後續臨床試驗的失敗率，更是一項關鍵的優勢。癌症治療的瓶頸在於抗藥性及高復發率，欲突破這個瓶頸我們從對抗癌症幹細胞著手，以癌症幹細胞的基因表現圖譜來比對 CMap 中的資料，透過上述的篩選平台我們找到兩個小分子用藥(T2 及 CY001)可以有效殺死癌症幹細胞，並能克服抗藥性的問題，且其效果已在動物實驗模式上得到證實。
- **CY001**:此藥在仿單核准適應症外的使用 (off-label use)上發現可使數個病人的腫瘤縮小或趨於穩定的現象，目前獲得 Si2C 及科技部的支持進入臨床試驗，並授權給業界。

#### ● 中草藥物的藥物研發

- **石蓮花**：近年來以中草藥作為疾病(例如慢性肝臟疾病)替代療法的例子大幅增加，我們以本土植物為開發重點，我們證實部分純化過的石蓮花對治療肝硬化及肝癌有顯著的效果，並與生技中心合作進行製程放大與管控(CMC)後，此項專利目前已授權業界，陽明分得 33%。
- **YQ1**：現今認為化療產生的抗藥性和助於腫瘤生長的癌症幹細胞，這都是癌症病人治療失敗和腫瘤復發的主要因素。透過基因微陣列技術、CMap 和 LINCS 的分析，發現以黃耆為底的複方(以 YQ1 表示)可能與癌症幹細胞、EGFR 的訊息傳遞和免疫反應有關。細胞實驗的結果指出 YQ1 能夠抑制肺癌細胞株的各種能力，並能克服抗藥性的問題。在老鼠實驗中，cisplatin 搭配 YQ1 可以明顯的抑制腫瘤的生長。此外，在 YQ1 搭配化療藥物相較於單獨化療的治療會有較顯著的延長肺癌病人存活時間。本團隊的未來目標是將 YQ1 建立為癌症幹細胞的抑制劑，並與業界準備向美國提出新藥臨床試驗申請。目前陽明大學與長庚醫院共同與業界洽談技轉中。

### Professional Experience

- Chairman in Institute of Biopharmaceutical Sciences, National Yang Ming Chiao Tung University (陽明交通大學生物藥學研究所) (2020-present)
- Distinguished Professor in Institute of Biopharmaceutical Sciences, National Yang Ming Chiao Tung University (陽明交通大學生物藥學研究所) (2019-present)
- Board of Director at PharmaEngine Inc. (Legal Representative Of The National Development Fund, Executive Yuan) (智擎生技製藥股份有限公司) (2019- present)
- Deputy Director in Biomedical Engineering Research and Development Center, National Yang Ming Chiao Tung University (陽明交通大學醫學工程研發中心) (2018-present)
- Professor in Institute of Biopharmaceutical Sciences, National Yang-Ming University (陽明大學生物藥學研究所) (2017- 2019)
- Professor and chairman in Institute of Biopharmaceutical Sciences, National Yang-Ming University (陽明大學生物藥學研究所) (2011-2017)
- Join appointments: Institute of Clinical Medicine, Institute of Biomedical Informatics and Department of Biotechnology and Laboratory Science in Medicine, National Yang-Ming University (陽明大學醫學生物技術暨檢驗學系暨研究所、生物醫學資訊研究所、臨床醫學研究所合聘) (2007-present)
- Associate Investigator in Institute of Cancer Research, National Health Research Institutes (國家衛生研究院癌症

研究所) (2005-2007)

- Associate Investigator in Division of Molecular and Genomic Medicine, NHRI (國家衛生研究院分子與基因醫學組) (2003-2005)
- Adjunct Associate Professor in Department of Computer Science and Information Engineer, National Taiwan University (台灣大學資訊工程研究所) (2003-2009)
- Adjunct Associate Professor in Institute of Biotechnology in Medicine and Institute of Bio-Pharmaceutical Sciences, National Yang-Ming University (陽明大學生物醫學技術研究所(2003-2007)及生物藥學研究所(2006-2007))
- Adjunct Associate Professor in Graduate Institute of Life Sciences, National Defense Medical Center (國防大學生命科學研究所) (1999-2007)
- Assistant Investigator in Division of Molecular and Genomic Medicine (National Health Research Institutes) (1998-2003)
- Postdoctoral Fellow (Stanford University) (1994-1998) (Laboratory of James E. Ferrell, Jr.)
- Ph.D. in Biochemistry and Biophysics (Iowa State University) (1988-1994) (Laboratory of Donald J. Graves)
- Research Assistant in Institute of Botany (Academia Sinica) (1987-1988) (Laboratory of Li-Chun Huang)
- Military Service (Taiwan) (1985-1987)
- B.S. in Chemistry (Tunghai University) (1981-1985)

### Honors

- Leukemia Society of America Career Development Award (1998-1999)
- Leukemia Society of America Fellowship (1996-1998)
- Keystone Symposium Travel Award (1997)
- Stanford Dean's Postdoctoral Fellowship (1994-1995)
- Graduate Research Excellence Award (Iowa State University) (1994)
- The Honor Society of Agriculture (Gamma Sigma Delta) (1989)
- 第十四屆國家新創獎—學研新創獎 (2017)

### Publications

1. **Chi-Ying F. Huang**, Chiun-Jye Yuan, Nataliya B. Livanova, and Donald J. Graves. Expression, purification, characterization, and deletion mutations of phosphorylase kinase  $\gamma$  subunit: identification of an inhibitory domain in the  $\gamma$  subunit. *Molecular and Cellular Biochemistry* 127-128:7-18 (1993).
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6. Siquan Luo, **Chi-Ying F. Huang**, John F. McClelland, and Donald J. Graves. A study of protein secondary structures by photoacoustic infrared spectroscopy. *Analytical Biochemistry* 216(1):67-76 (1994).
7. **Chi-Ying F. Huang**, Chiun-Jye Yuan, Donald K. Blumenthal, and Donald J. Graves. Identification of the substrate and pseudosubstrate binding sites of phosphorylase kinase  $\gamma$  subunit. *The Journal of Biological Chemistry* 270:7183-7188 (1995).
8. **Chi-Ying F. Huang** and James E. Ferrell, Jr. Ultrasensitivity in the mitogen-activated protein kinase cascade. *Proceedings of the National Academy of Sciences of the United States of America* 93(19):10078-10083 (1996).
9. **Chi-Ying F. Huang** and James E. Ferrell, Jr. Dependence of Mos-induced Cdc2 activation on MAP kinase function in a cell-free system. *The EMBO Journal* 15(9): 2169-2173 (1996).
10. **Chi-Ying F. Huang**, Chao-Pei Betty Chang, Chia-Lin Huang, and James E. Ferrell, Jr. M-phase phosphorylation of cytoplasmic dynein intermediate chain and p150<sup>Glued</sup>. *The Journal of Biological Chemistry* 274:14262-14269 (1999).
11. See-Chang Huang, **Chi-Ying F. Huang**, and Te-Chang Lee. Induction of mitosis-mediated apoptosis by sodium arsenite in HeLa S3 cells. *Biochemical Pharmacology* 60(6):771-780 (2000).
12. Wey-Jinq Lin, Yaun-Fu Chang, Wei-Li Wang, and **Chi-Ying F. Huang\***. The mitogen-stimulated TIS21 protein interacts with a protein kinase C $\alpha$  binding protein rPICK1. *Biochemical Journal* 354:635-643 (2001).

13. Yi-Mi Wu, Chia-Lin Huang, Hsing-Jien Kung, and **Chi-Ying F. Huang\***. Proteolytic activation of Etk/Bmx tyrosine kinase by caspases. *The Journal of Biological Chemistry* 276:17672-17678 (2001).
14. **Chi-Ying F. Huang**, Yi-Mi Wu, Chiung-Yueh Hsu, Wan-Shu Lee, Ming-Derg Lai, Te-Jung Lu, Chia-Lin Huang, Tzeng-Horng Leu, Hsiu-Ming Shih, Hsin-I Fang, Dan R. Robinson, Hsing-Jien Kung, and Chiun-Jye Yuan. Caspase activation of mammalian sterile 20-like kinase 3 (Mst3): nuclear translocation and induction of apoptosis. *The Journal of Biological Chemistry* 277:34367-34374 (2002).
15. Chiu-Ya Wang, Huey-Jing Lei, **Chi-Ying F. Huang**, Zhongjian Zhang, Anil B. Mukherjee, and Chiun-Jye Yuan. Induction of cyclooxygenase-2 by staurosporine through the activation of nuclear factor for IL-6 (NF-IL6) and activator protein 2 (AP2) in an osteoblast-like cell line. *Biochemical Pharmacology* 64:177-184 (2002).
16. Ann-Ping Tsou<sup>#</sup>, Chu-Wen Yang<sup>#</sup>, **Chi-Ying F. Huang<sup>#</sup>**, Chang-Tze R. Yu, Yuan-Chii G. Lee, Cha-Wei Chang, Bo-Rue Chen, Yu-Fang Chung, Ming-Ji Fann, Chin-Wen Chi, Jen-Hwey Chiu, and Chen-Kung Chou. Identification of a novel cell cycle regulated gene, HURP, overexpressed in human hepatocellular carcinoma. *Oncogene* 22:298-307 (2003) (<sup>#</sup>contributed equally).
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18. Chang-Han Chen, Shen-Long Howng, Tai-Shan Cheng, Meng-Hui Chou, **Chi-Ying F. Huang**, and Yi-Ren Hong. Molecular characterization of human ninein protein: Two distinct subdomains required for centrosomal targeting and regulating signals in cell cycle. *Biochemical and Biophysical Research Communications* 308:975-983 (2003).
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  45. Li-Jen Su, Ching-Wei Chang, Yu-Chung Wu, Kuang-Chi Chen, Chien-Ju Lin, Shu-Ching Liang, Chi-Hung Lin, Jacqueline Whang-Peng, Shih-Lan Hsu, Chen-Hsin Chen and **Chi-Ying F. Huang\***. Selection of DDX5 as a Novel Internal Control for Q-RT-PCR from microarray data: Using a Block Bootstrap Re-sampling scheme. *BMC Genomics* 8(1):140 (2007).
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  47. Wei-Li Wang, Sheau-Farn Yeh, Eagle Yi-Kung Huang, Yu-Ling Lu, Chun-Fa Wang, **Chi-Ying F. Huang** and Wey-Jinq Lin. Mitochondrial anchoring of PKCa by PICK1 confers resistance to etoposide-induced apoptosis. *Apoptosis* 12(10):1857-71 (2007).
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### **Book Chapter**

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### **Patents**

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21. 黃奇英(Chi-Ying Huang)、許照惠(Jane Hsiao)、楊泮池(Pan-Chyr Yang)、李孟樺(Meng-Hua Lee) "Pharmaceutical Composition for Treatment of Cancer Using Phenothiazine" (美國發明專利證書第 10,888,568) (獲證日：12 January, 2021) 2021/01/12-
22. 黃奇英(Chi-Ying Huang)、張牧新(Peter Mu-Hsin Chang)、陳冠宇(Kuan-Yu Chen)、吳駿翹(Alexander Jun-Hong Wu)、鄭大山(Tai-Shan Cheng)、余晟豪(Cheng-Hao Yu)，“抗藥性癌症之治療方法/Method for Treating Drug Resistant Cancer” (台灣發明專利領證中)。

### **技術轉移**

1. 解析肝癌化過程中相關之磷酸化蛋白質體學：自 1001 個磷酸激酶/去磷酸酶/磷酸化蛋白質抗體之製備以鑑定肝癌治療標的 (2009)
2. 利用電腦模擬藥物篩選平台解析中草藥之表現特徵來發展其生物仿製藥物計畫之技術授權金 (2011)
3. 石蓮花藥物開發 (2012)
4. 利用電腦模擬藥物篩選平台解析中草藥之表現特徵來發展其生物仿製藥物計畫 (2012)
5. 對抗癌症幹細胞及克服癌症抗藥性之藥物開發 (2015)
6. 對抗癌症幹細胞及克服癌症抗藥性之藥物開發 (2015)
7. 治療非小細胞肺癌之醫藥組合物及其方法 (2018)
8. 用於癌症治療之 CY001 化合物 (2018)

### **其他協助產業技術發展之具體績效**

1. 許多蛋白激酶(protein kinase)為癌症藥物標靶，蛋白激酶磷酸化狀態的改變可反應出細胞內訊息路徑的活化與否，為了分析癌化過程蛋白激酶磷酸化的程度，我們與生技公司合作生產蛋白激酶及磷酸化的蛋白質抗體，為了增加磷酸化抗體的靈敏度與專一性，我們利用 PLA 分析的方式(即利用蛋白激酶及其磷酸化的配對抗體來偵測細胞內蛋白激酶磷酸化及蛋白質交互作用的情形)，以偵測蛋白激酶參與的訊息網絡或細胞癌化的過程，我們的成果如下：
  - a. 製造並上市 268 個以 PLA 形式配對的磷酸化蛋白質的抗體。
  - b. 製造並上市 612 個以 PLA 形式配對的蛋白質交互作用抗體。
2. 執行經濟部計畫「利用電腦模擬藥物篩選平台解析中草藥之表現特徵來發展其生物仿製藥物三年計畫」，已與兩家生物科技股份有限公司簽訂先期技術授權。