

第九屆胰臟癌國際研討會暨林炳文教授紀念演講會
The 9th International Conference and Commemorative Lecture of
Pin-Wen Lin of Pancreatic Cancer

時 間：105 年 7 月 1 日 (星期五) 13:50~17:40

105 年 7 月 2 日 (星期六) 08:20~16:00

地 點：國衛院南部臨床研究中心-統一健康研究大樓何曼德講堂
 (地址：台南市勝利路 367 號 B1F)

主辦單位：國衛院癌研所 成功大學醫學院附設醫院 台灣胰臟醫學會 中華民國癌症醫學
 會 費用:不收費

The 9 th International Conference and Commemorative Lecture of Pin-Wen Lin of Pancreatic Cancer (Jul1- 2, 2016)			
Time	Topic	Speaker	Moderator
July 01, PM 13:50-14:00	Opening:1. Mayor of Tainan: Lai Ching-Te (賴清德) 2. President of National Cheng Kung University: Huey-Jen Su (蘇慧貞) 3. Superintendent: Chyun-Yu Yang (楊俊佑) 4. Dean of College of Medicine, NCKU::Jang-Yang Chang (張俊彥), 4. Chief of Taiwan Pancreas Society: Lee CL (李嘉龍)		
Memory Lecture of Pin-Wen Lin: International cooperation			
14:00-14:30	Precision Medicine for Cancer Therapy	Pan-Chyr Yang (楊泮池)	Jang-Yang Chang (張俊彥), Min-Liang Kuo (郭明良)
14:30~15:00	Experience of Global Collaboration in Australia GI Trial Group	David Goldstein	
15:00~15:30	Pancreatic Cancer Treatment in Japan	Junji Furuse (古瀨純司)	
15:30-16:00	Pancreatic Cancer Trials in Taiwan Cooperative Oncology Group	Li-Tzong Chen (陳立宗)	
Coffee break			
16:15~16:45	An introduction of Taiwan Biobank and Biosignature	Hu-Tong Liu (劉扶東)	Tsang-Wu Liu (劉滄梧) Jaw-Town Lin (林肇堂)
16:45~17:15	Asian and Taiwan Neuroendocrine Tumor Registration Program	Tsann-Long Hwang (黃燦龍)	
17:15~17:40	Investigating the risk factors of pancreatic cancer	Jeffrey Shu-Ming Chang (張書銘)	
18:30 PM Welcome Dinner			
July 2nd : Translational researches and novel therapeutic strategies development in pancreatic cancer			
08:20-09:00	Keynote: Novel therapeutic agents development in pancreatic cancer	Ching-Shih Chen (陳慶士)	Wen-Chun Hung (洪文俊), Kelvin K.C. Tsai (蔡坤志)
09:00-09:30	Prognostic and predictive factors in metastatic pancreas cancer	David Goldstein	
09:30-09:50	Targeting lymphangiogenesis and lymphatic metastasis: recent mechanistic insight and drug development	Mei-Jen Pan (潘美仁)	
09:50~10:10	Inactivation of APC Cooperates with Kras and P53 Loss to Accelerate PDAC metastasis in Mice.	Kung-Hung Cheng (鄭光宏)	
10:10~10:20	Coffee Break		
Treatment for Lymph Node Metastases in Pancreatic Cancer			
10:20~10:50	Keynote: Extensive LN dissection in pancreatic cancer, including CP-CAR	Hiroki Yamaue (山上裕機)	Cheng-Hsi Su (蘇正熙) King-Teh Lee (李金德)
10:50~11:20	Experience and role of Robotic Surgery in Pancreatic Cancer: The pitfalls for success	Peng Chenghong (彭承宏)	
11:20~11:40	Most pancreatic surgeries for pancreatic cancer are R1 resection?	Ta-Sen Yeh (葉大森)	
11:40~12:00	Role of CCRT in adjuvant therapy of post-resection pancreatic cancer – TCOG trial	Yan-Shen Shan (沈延盛)	
12:00PM – 13:30PM: Lunch			
Translational study in pancreatic cancer			

13:30~13:50	Loss of Kruppel Like Factor 10 Enhanced Epithelial Mesenchymal Transition of Pancreatic Cancer by Modulating Glucose Metabolism via Sirt 6 and PKM2	Hui-Ju Ch'ang (常慧如)	Wu-Chou Su (蘇五洲) Yi-Yin Jan (詹益銀)
13:50~14:10	PAI-1 Activates Pancreatic Stellate Cells to Increase the Stiffness of Tumor and Determines Early Relapse of Pancreatic Cancer	Hao-Chen Wang (王昊宸)	
14:10~14:30	IL-8 and cancer cachexia in pancreatic cancer	Ya-Chin Hou (侯雅琴)	
14:30~14:40	Coffee break		
Epidemiology and diagnosis for pancreatic cancer in Taiwan			
14:40~15:00	The application of EUS for diagnosis of pancreatic cancer	Hsiu-Po Wang (王秀伯)	JY Wu (吳俊穎), Lein-Ray Mo (牟聯瑞)
15:00~15:20	PET/MRI as a Hybrid Biomarker of Pancreatic Cancer -- Clinical Diagnosis and Outcome Prediction	Tiffany Ting-Fang Shih (施庭芳)	
15:20~15:40	CT-guided coaxial core biopsy of the pancreas via a fat traversing route	Yi-Sheng Liu (劉益勝)	
15:40~16:00	Type 2 Diabetes and the Risk of Pancreatic Cancer	Wei-Chih Liao (廖偉智)	
Closing Remark			

教育積分：

台灣外科醫學會	(申請中)	台灣內科醫學會	(申請中)
台灣消化系外科醫學會	(申請中)	台灣消化系內視鏡醫學會	(申請中)
台灣消化系醫學會	(申請中)	中華民國醫用超音波醫學會	(申請中)
中華民國放射線醫學會	3分	中華民國癌症醫學會	(申請中)

交通資訊：

一、**搭乘客運：**搭乘國光、統聯或和欣等客運，至台南前站下車，經過車站地下道到達後站出口，沿大學路至勝利路左轉步行約 10 分鐘即可抵達國衛院。

二、**搭乘台鐵：**抵達台南車站，由後站出口，沿大學路至勝利路左轉步行約 10 分鐘即可抵達國衛院。

三、**搭乘高鐵：**抵達台南高鐵站，轉乘興南客運於成功大學小東路光復校區下車，沿小東路至勝利路左轉步行約 3 分鐘即可抵達國衛院(興南客運票價：40 元)。

四、**自行開車：**南下：走中山高速公路南下->於永康交流道下高速公路->走中正南路(西向)往台南市區->轉中華路->達小東路口右轉(西向)直走->遇勝利路右轉即可抵國衛院統一健康研究大樓。

北上：走中山高速公路北上->於仁德交流道下高速公路->走東門路(西向)往台南市區->東門路過長榮路遇勝利路右轉即可抵國衛院統一健康研究大樓。

Pan-Chyr Yang, MD, PhD
President
National Taiwan University

Dr. Yang currently is the President of National Taiwan University and Professor in the Department of Internal Medicine, National Taiwan University College of Medicine. His major research interests are pulmonary and critical care medicine, molecular and cellular biology, lung cancer genomics and personalized cancer therapy. He was elected member of Academia Sinica in 2006 because of his contributions in leading the translational research and implementation of precision therapy for lung cancer in Taiwan, which have significantly improved the survival in lung cancer patients. His research group identified novel genes and pathways that associated with lung cancer progression. They established new platform for development of lung cancer stem cell directed therapy and discovered the autocrine-paracrine interaction between the lung cancer stem cell with cancer microenvironment. They also identified specific gene expression and microRNA biomarkers that might be beneficial for precision therapy of lung cancer patients.

Email: pcyang@ntu.edu.tw

Date of Birth: February 8, 1951

Education:

1990 Ph.D., Graduate Institute of Clinical Medicine, National Taiwan University

1979 M.D., College of Medicine, National Taiwan University,

Professional Interests and Specialties:

1. Internal Medicine
2. Pulmonary and Critical Care Medicine
3. Cancer Biology and Molecular Biology
4. Lung Cancer Genomics and Molecular Carcinogenesis
5. Medical Ultrasound

Selected Publications:

1. Chen HY, Yu SL, Chen CH, Chang GC, Chen CY, Yuan A; Cheng CL, Wang CH, Terng HJ, Kao SF, Chan WK, Li HN, Liu CC, Singh S, Chen WJ, Chen JJW, Yang PC: A five-gene signature and clinical outcome in non-small cell lung cancer. *N Engl J Med* 2007;356:11-20.
2. Yu SL, Chen HY, Chang GC, Chen CY, Chen HW, Singh S, Cheng CL, Yu CJ, Lee YC, Chen HS, Su TJ, Chiang CC, Li HN, Hong QS, Su HY, Chen CC, Chen WJ, Liu CC, Chan WK, Chen WJ, Li KC, Chen JJW, Yang PC: MicroRNA signature predicts survival and relapse in lung cancer. *Cancer Cell* 2008;13:1-10.
3. Yang CH, Yu CJ, Shih JY, Chang YC, Hu FC, Tsai MC, Chen KY, Lin ZZ, Huang CH, Shun CT, Huang CL, Bean J, Cheng AL, Pao W, Yang PC: Specific EGFR mutations predict treatment outcome of stage III/IV chemo-naïve NSCLC patients receiving first-line gefitinib monotherapy. *J Clin Oncol* 2008;26:2745-53.
4. Wu JY, Yu CJ, Yang CH, Wu SG, Chiu YH, Gow CH, Chang YC, Hsu YC, Wei PF, Shih JY, Yang PC: First- or second-line therapy with gefitinib produces equal survival in non-small cell lung cancer. *Am J Respir Crit Care Med* 2008 ;178:847-53.
5. Wang SP, Wang WL, Chang YL, Wu CT, Chao YC, Kao SH, Yuan A, Lin CW, Yang SC, Chan WK, Li KC, Hong TM, Yang PC: p53 controls cancer cell invasion by inducing the MDM2-mediated degradation of Slug. *Nat Cell Biol* 2009;11:694-704.
6. Yuan S, Yu SL, Chen HY, Hsu YC, Su KY, Chen HW, Chen CY, Yu CJ, Shih JY, Chang YL, Cheng CL, Hsu CP, Hsia JY, Lin CY, Wu G, Liu CH, Wang CD, Yang KC, Chen YW, Lai YL, Hsu CC, Lin TC, Yang TY, Chen KC, Hsu KH, Chen JJ, Chang GC, Li KC, Yang PC: Clustered genomic alterations in chromosome 7p dictate outcomes and targeted treatment responses of lung

adenocarcinoma with EGFR-activating mutations. *J Clin Oncol* 2011;29(25):3435-42

7. Pan SH, Chao YC, Hung PH, Chen HY, Yang SC, Chang YL, Wu CT, Chang CC, Wang WL, Chan WK, Wu YY, Che TF, Wang LK, Lin CY, Lee YC, Kuo ML, Lee CH, Chen JJW, Hong TM, Yang PC: The ability of LCRMP-1 to promote cancer invasion by enhancing filopodia formation is antagonized by CRMP-1. *J Clin Invest* 2011;121(8):3189-205.
8. Su KY, Chen HY, Li KC, Kuo ML, Yang JC, Chan WK, Ho BC, Chang GC, Shih JY, Yu SL, Yang PC: Pretreatment epidermal growth factor receptor (EGFR) T790M mutation predicts shorter EGFR tyrosine kinase inhibitor response duration in patients with non-small-cell lung cancer. *J Clin Oncol*. 2012 Feb 1;30(4):433-40.
9. Lin CW, Chang YL, Chang YC, Lin JC, Chen CC, Pan SH, Wu CT, Chen HY, Yang SC, Hong TM, Yang PC. MicroRNA-135b promotes lung cancer metastasis by regulating multiple targets in the Hippo pathway and LZTS1. *Nat Commun* 2013;4:1877.
10. Chen WJ, Ho CC, Chang YL, Chen HY, Lin CA, Ling TY, Yu SL, Yuan SS, Chen YJ, Lin CY, Pan SH, Chou HY, Chen YJ, Chang GC, Chu WC, Lee YM, Lee JY, Lee PJ, Li KC, Chen HW, Yang PC. Cancer-associated fibroblasts regulate the plasticity of lung cancer stemness via paracrine signalling. *Nat Commun* 2014 Mar 25;5:3472.

Precision Medicine for Cancer Therapy

**Pan-Chyr Yang MD, PhD.
National Taiwan University**

Precision medicine is a concept to take individual variability into account in disease prevention and treatment. It has become possible because of the recent development of human genome sequencing and pan-omics technologies as well as the application of large-scale biologic databases to characterize patients and guide clinical practice. It has significantly improved treatment outcome of human diseases including cancers. Here I use lung cancer as an example to show how precision medicine has improved the patients' treatment outcome. Lung cancer is the leading cause of cancer mortality worldwide. Since the identification of EGFR activating mutations in 2004 and the discovery of specific targeting agents, the treatment of lung cancer has entering a new era of precision therapy. The mutated EGFR may function as an oncogenic driver in more than 50% of Asian and 10-15% of Caucasian lung adenocarcinomas. Patients harboring activating EGFR mutants, most commonly L858R or Ex19Del, usually present good initial responses to EGFR-TKIs and survival improvement, but eventually develop disease progression after a median of 12 months. T790M mutation accounts for 60% of these resistant cases. Other resistant mechanisms include the activation of alternative oncogenic pathways or small cell transformation. There are several strategies to overcome EGFR-TKIs resistance including a switch to chemotherapy; turn off the compensatory oncogenic pathways; dual inhibition with anti-EGFR antibodies and TKIs; development of new generation EGFR TKIs (AZD9291, CO-1686); and knockdown of EGFR by siRNA or specific T790M DNzyme. Promising new approaches include immunotherapy with checkpoint inhibition by anti-PD-1/PD-L1 antibodies, adoptive T cell and cancer stem cell (CSC)/microenvironment directed therapy. We have developed aptamer based immune checkpoint inhibitors against PD-1, PD-L1 and CTLA4, which showed potential for development of cancer immunotherapy. We established CSC culture and screening platform to identify new drug against CSC and cancer microenvironment. The recent study by Lung Cancer Mutation Consortium confirmed that multiplexed gene testing is feasible for precision lung cancer therapy. Taiwan established national reference laboratory to provide standardized gene-testing platform for all lung cancer patients. Taiwan National Health Insurance reimbursed Gefitinib and Erlotinib for first line therapy of EGFR mutant lung cancer patients since 2011. With the implementation of nation-wide gene testing and personalized therapy, the overall 5-year survival for NSCLC has improved from 16% to 32%. The precision medicine has significantly improved the treatment outcome for NSCLC.

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DATE AND PLACE OF BIRTH: August 6, 1955; Wing-Ling County, Taiwan

EDUCATION:

1992.08 – 2001.07 Ph.D. Post-graduate School, Kaohsiung Medical University

1975.08 – 1982.07 M.D. Kaohsiung Medical College, Kaohsiung, Taiwan

BRIEF CHRONOLOGY OF EMPLOYMENT:

2014.08 – *present* Director, National Institute of Cancer Research, National Health Research Institutes

2014.08 – *present* Distinguished Investigator, National Institute of Cancer Research, National Health Research Institutes

2013.08 – 2014.07 Acting Director, National Institute of Cancer Research, National Health Research Institutes

2013.08 – *present* Joint-Appointment Professor, Kaohsiung Medical University

2012.09 – *present* Adjunct Professor, Taipei Medical University

2012.09 – *present* Adjunct Attending Physician, Division of Gastroenterology, Department of Medicine, Kaohsiung Medical University Hospital, Kaohsiung

2012.09 – 2013.07 Vice Superintendent, Kaohsiung Medical University Hospital

2012.09 – 2013.07 Director of Cancer Center, Kaohsiung Medical University Hospital

2012.09 – 2013.07 Director of Division of Cancer Research, Department of Medical Research, Kaohsiung Medical University Hospital

2008.03 – 2013.07 Deputy Director, National Institute of Cancer Research, National Health Research Institutes

2007.07 – *present* Joint-Appointment Attending Physician, Department of Internal Medicine, National Cheng-Kung University Hospital, Tainan

2006.08 – 2007.07 Adjunct Attending Physician, Department of Internal Medicine, Tri-Service General Hospital, Taipei

2006.01 – *present* Investigator and Attending Physician, National Institute of Cancer Research, National Health Research Institutes

2005.07 – 2012.07 Associate Professor, College of Medicine, Kaohsiung Medical University

2002.08 – 2005.12 Associate Investigator, National Health Research Institutes

1995.08 – 2009.09 Adjunct Attending Physician, Department of Oncology, National Taiwan University Hospital, Taipei

1995.08 – 2006.07 Adjunct Attending Physician, Department of Internal Medicine, Veteran General Hospital, Taipei

1988.08 – 2012.08 Attending Physician, Division of Gastroenterology, Department of Medicine, Kaohsiung Medical University Hospital, Kaohsiung

1988.04 – 1990.03 Fellowship of Medical Oncology Training Program Institute of Biomedical Science, Academia Sinica, Taipei

1987.08 – 1988.07 Chief Resident, Department of Medicine, Kaohsiung Medical College Hospital

- 1984.08 – 1987.07 Residency training, Department of Medicine, Kaohsiung Medical University Hospital
- 1982.09 – 1984.08 Military service
- 1981.08 – 1982.07 Internship, Kaohsiung Medical College Hospital

HONORS:

- 2013.08 – *present* Chair, Council Internal Medicine (II) Program, Minister of Science and Technology (MOST)
- 2012.08 – 2013.07 Co-chair, Council Internal Medicine (II) Program, Minister of Science and Technology (MOST)
- 2011.05 – 2013.05 Member of Council, The Chinese Oncology Society
- 2010.07 – *present* Chair, Institution Review Board, National Health Research Institutes
- 2009.10 – *present* Member of Council, Taiwan Pancreas Society
- 2009.05 – 2011.05 Member of Council, The Chinese Oncology Society
- 2009.03 – 2012.03 Board of Supervisor (監事), The Gastroenterological Society of Taiwan
- 2008.11 – *present* Chair, Protocol Review Committee, Taiwan Cooperative Oncology Group, National Health Research Institutes
- 2008.08 – 2010.07 Consultant, Institution Review Board, National Cheng Kung University Hospital
- 2005.05 – 2007.05 Member of Council, The Chinese Oncology Society
- 2003.08 – 2005.05 Secretary General, The Chinese Oncology Society
- 2001.04 – 2003.08 Member of Council (理事), The Chinese Oncology Society
- 1996.08 – 2008.07 Secretary General, Data and Safety Monitoring Committee, Taiwan Cooperative Oncology Group, National Health Research Institutes

AWARDS:

- 2014 The 3rd Kobayashi Foundation Award, the Asian Clinical Oncology Society (ACOS)
- 2010 Outstanding Research Achievement Award, National Health Research Institutes (NHRI)
- 2006 Outstanding Research Award, Kaohsiung Medical University
- 2005 Outstanding Research Award, Kaohsiung Medical University
- 2003 Chien-Tien Hsu (徐千田) Outstanding Cancer Clinical Research Award, the Chinese Oncology Society
- 2001 Excellence Award of Poster Presentation, 6th Annual Joint Meeting of Taiwan Oncology Societies
- 2000 Excellence Award of Poster Presentation, 5th Annual Joint Meeting of Taiwan Oncology Societies
- 1999 Excellence Award of Poster Presentation, 4th Annual Joint Meeting of Taiwan Oncology Societies

LICENSURE AND CERTIFICATION:

- 2012 Professor, Ministry of Education(No. 019832)
- 1990 Certificate of Gastroenterology, R.O.C.(No. 0293)
- 1990 Certificate of Medical Oncology, R.O.C.(No. 79042)
- 1989 Certificate of Internal Medicine, R.O.C.(No. 001808)
- 1982 Certificate of National Medical Board of Republic of China(No. 010816)

SOCIETY MEMBERSHIPS:

- 2008 European Society of Medical Oncology, ESMO
- 2007 American Society of Clinical Oncology, ASCO
- 1992 Digestive Endoscopy Society of Taiwan

1990 Society of Gastroenterology Society of Taiwan
1990 The Chinese Oncology Society, R.O.C.
1988 Society of Internal Medicine, Taiwan, R.O.C.
1988 Society of Ultrasound in Medicine, Taiwan
1984 Formosan Medical Association

MAJOR RESEARCH INTERESTS:

1. Diagnosis, Treatment and Prognosis in Cancers of Digestive System
2. Clinical Trial in Cancer Therapy

PATENT:

1. 治療肝細胞癌之醫藥組合：中華民國專利發明第I257865號(2006.7.11)

PUBLICATIONS: 183

黃燦龍簡歷

(Tsann-Long Hwang)

2016, April

一、學歷

國立台灣大學醫學院醫學系醫學士 1970~1977

二、經歷

國立台灣大學附設醫院外科 1978~1982
美國哈佛大學外科營養研究 1985~1986
美國外科學院院士 1993~迄今
國際外科學院院士 1990~迄今
長庚紀念醫院台北院區副院長 2000~2008
長庚大學醫學院醫學系主任 2000~2008
台灣胰臟醫學會理事長 2006~2009
台灣靜脈暨腸道營養醫學會理事長 1996~2000
台灣消化外科醫學會理事長 2012~2014
國際外科學院中華民國總會理事長 2013~2015

三、現職

長庚紀念醫院一般外科主治醫師 1983~迄今
長庚大學醫學院外科教授 1994~迄今
長庚紀念醫院靜脈暨腸道營養委員會召集人 2009~迄今
長庚紀念醫院幹細胞暨組織工程研究團隊召集人 2009~迄今

四、學會代表

亞洲大學外科學會理事暨國家代表 1999~迄今
亞洲外科醫學會理事暨國家代表 2006~迄今
亞太地區醫學問題導向學習學會理事暨國家代表 2002~迄今
亞洲靜脈暨腸道營養醫學會理事及 Advisor 1997~迄今
國家衛生院胰臟癌研究小組(TCOG)召集人 2002~迄今
台灣外科醫學會理事 2016~迄今
台灣生命倫理學會理事 2006~迄今
財團法人林天祐肝癌研究基金會董事 2001~迄今

五、研究領域或專長

1. 消化道外科
2. 醫療營養
3. 外科重症
4. 醫學教育

六、國際雜誌編輯

Journal of Hepato-Biliary Pancreatic Sciences: Editor

Asian J. Surgery: Editor

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EDUCATION:

2006 **PhD** **Epidemiology**, School of Public Health, University of California, Berkeley
2001 **MPH** **Infectious Diseases**, School of Public Health, University of California, Berkeley
1998 **MD** **Medicine**, College of Medicine, University of Illinois at Chicago
1994 **BA** **Molecular and Cell Biology**, University of California, Berkeley

MAJOR RESEARCH INTERESTS:

Cancer epidemiology
Genetic and molecular epidemiology
Gene-environment interaction

PROFESSIONAL EXPERIENCE:

Jan 2015-present **Associate Investigator**, National Institute of Cancer Research, National Health Research Institutes, Taiwan
Feb 2010-Dec 2014 **Assistant Investigator**, National Institute of Cancer Research, National Health Research Institutes, Taiwan
Jul 2006-Jun 2009 **Postdoctoral Research Fellow in Genetic/Molecular Epidemiology of Cancer**, Department of Epidemiology and Biostatistics, University of California, San Francisco
Jul 2003-Jun 2006 **Graduate Student Researcher**, School of Public Health, University of California, Berkeley
Jul 2001-Jun 2003 **Research Associate III/Supervisor**, Division of Cancer Epidemiology Department of Epidemiology and Biostatistics, University of California, San Francisco
Feb 2000-Dec 2000 **Post-Graduate Researcher**, Office of AIDS, California Department of Health Services
June 1998-Jan 1999 **Resident Doctor**, Department of Pathology, University of California at San Francisco Medical Center

AWARDS AND HONORS:

2015 **Research Achievement Award for Junior Research Investigators**, National Health Research Institutes
2014 **1st Prize in Poster Competition**, Society for Epidemiologic Research Annual Meeting, Seattle, Washington, June 24-27, 2014.
2007 **Aflac Scholar-in-Training Travel Award**, American Association for Cancer Research Special Conference, "Approaches to Complex Pathways in Molecular Epidemiology", Santa Ana Pueblo, New Mexico, May 30-June 2, 2007.
2006 **Postdoctoral fellowship in genetic/molecular epidemiology**, awarded through the National Institute of Health R25 training grant (R25 CA112355, PI: John Witte, PhD),
2005 **Presenter, Student Dissertation Workshop**, Society for Epidemiologic Research-Canadian Society for Epidemiology and Biostatistics joint meeting, Toronto, June 27-30, 2005.

OTHER PROFESSIONAL ACTIVITIES:

American Association for Cancer Research (AACR)-Active member; AACR-Molecular Epidemiology Group (MEG)-Member
American College of Epidemiology (ACE)-Member
International Genetic Epidemiology Society (IGES)-Member

Investigating the risk factors of pancreatic cancer

Jeffrey Shu-Ming Chang

Approximately 338,000 cases (incidence = 4.2 per 100,000) of pancreatic cancer are diagnosed worldwide annually, making it the 15th most common cancer in the world. While the survivals of many cancers, such as breast cancer and prostate cancer, have improved substantially, the survival of pancreatic cancer has remained dismal with an extremely low 5-year survival rate of 3-5%. The increasing incidence and the continued poor survival of pancreatic cancer indicate that it is critical to identify the risk factors of pancreatic cancer in order to establish preventive strategies to reduce the occurrence of pancreatic cancer. The majority of pancreatic cancer have unknown etiologies. Cigarette smoking is a major risk factor of pancreatic cancer and accounts for 20-25% of pancreatic cancer cases. Long-term diabetes is also a strong risk factor of pancreatic cancer. Other possible environmental factors of pancreatic cancer that require further confirmation include alcohol drinking, sedentary lifestyle, obesity, chronic pancreatitis, allergies, periodontal disease, and infections. Genetic factors may also play a role in the development of pancreatic cancer. Five to ten percent of pancreatic cancer patients are familial and are due to rare genetic mutations. Although the majority (>90%) of pancreatic cancer cases are sporadic, genetic polymorphisms may be important in modulating the individuals' responses to environmental carcinogens for the development of pancreatic cancer. This presentation will discuss the preliminary results of an original hospital-based case-control study from Taiwan for investigating the risk factors of pancreatic cancer.

CURRICULUM VITAE
Ching-Shih Chen, Ph.D.陳慶士

I. General Information

Distinguished Research Fellow & Director
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Lucius A. Wing Chair of Cancer Research and
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II. Education

<u>Institution</u>	<u>Degree</u>	<u>Years</u>	<u>Area of Study</u>
National Taiwan University	B.S.	9/74 – 6/78	Agricultural Chemistry
National Taiwan University	M.S.	9/78 – 6/80	Biochemistry
University of Wisconsin - Madison	Ph.D.	9/80 – 1/85	Pharmaceutical Biochemistry
University of Wisconsin – Madison	Postdoc.	1/85 – 12/86	Medicinal Chemistry

III. Academic Appointments

The Ohio State University

April 2001 - Professor of Medicinal Chemistry
April 2001 - Member, The Comprehensive Cancer Center and Chemistry-Biology
Interface Training Program
June 2002 - Professor of Internal Medicine and Urology

University of Kentucky

July 1998 – March 2001 Professor of Pharmaceutical Sciences
July 1995 – June 1998 Associate Professor of Pharmaceutical Sciences
July 1995 – March 2001 Member, Markey Cancer Center

University of Rhode Island

July 1991 – June 1995 Associate Professor of Medicinal Chemistry & Pharmacognosy
January 1987 – June 1991 Assistant Professor of Medicinal Chemistry & Pharmacognosy

III. Honors

United States

2009 - 2010 Clinical trials of two drugs developed in my lab, OSU-03012 (AR12) and OSU-HDAC42 (AR42), in solid and hematological malignancies at OSUCCC and in the United Kingdom
2010 - 2012 Programmatic Review Committee, CDMRP Prostate Cancer Research Program
2007, 2008 Prostate Cancer Foundation (formerly CapCure) Research Awards for two consecutive years
2008 Hearst Foundation Research Award
2004 - Elected Fellow, American Association for the Advancement of Science (AAAS)
2004 Winner of the V Foundation-AACR Grants in Translational Cancer Research
1994 Shannon Award, NIH

The Ohio State University

2005 - Present The Lucius A. Wing Chair of Cancer Research and Therapy, OSU Medical Center
2010 The Inaugural Innovator of the Year Award, OSU
2010 Distinguished University Scholar Award, OSU

2008 Innovation in Drug Discovery Award, College of Pharmacy, OSU

2003 - 2006 Kimberly Chair Professorship, OSU College of Pharmacy

Taiwan

2005 - 2014 Scientific Advisory Committee, Institute of Biological Chemistry, Academia Sinica, Taiwan

2005 - 2011 Scientific Advisory Committee, National Science and Technology Program in Biotechnology and Pharmaceuticals, Taiwan

2009- Present Honorary Chair Professor, Institute of Molecular and Cell Biology, National Chung-Hsin University, Taiwan

2013- Present Honorary Chair Professor, College of Medicine, National Cheng Kung University

2007- Present Adjunct Professor, College of Pharmacy, National Taiwan University

2006 - 2010 Honorary Chair Professor, Department of Biological Science and Technology, China Medical University

2004 - 2006 Honorary Chair Professor, College of Pharmacy, Kaohsiung Medical University, Taiwan

University of Kentucky and University of Rhode Island

2000 Outstanding Faculty Award, College of Pharmacy, University of Kentucky

1999 Outstanding Professor Award, College of Pharmacy, University of Kentucky

1992 Teacher of the Year Award, College of Pharmacy, University of Rhode Island

IV. Grant Review Panel

2010 - 2012 CDMRP Prostate Cancer Research Program, Programmatic Review Committee

2009 NCI Drug Discovery and Development P01 Special Emphasis Panel, ZCA1 RPPB-P

2009 Canadian Cancer Society Research Institute, Program project Site Visit at University of Montreal

2004 - 2009 Chartered member, Basic Mechanism for Cancer Therapeutics (BMCT) Study Section, NCI

2008 NCI Drug Discovery and Development P01 Special Emphasis Panel, ZCA1 RPPB-M

2006 California Breast Cancer Research Program, Pathogenesis committee

2005 California Breast Cancer Research Program, Innovative Treatments/Earlier Detection committee

2004 CDMRP Prostate Cancer Research Program CET-3 grant reviews

2004 NICDC Special Emphasis Panel to evaluate clinical center grant (P50) application

2003 CDMRP, Prostate Cancer Research Program, Clinical & Experimental Therapeutics #3, CET-3

2003 Co-chair, NIDDK O'Brien Urology Center Grants Review

2003 NCI Special Emphasis Panel Member. FLAIR applications

2002 NCI Program Project Site Visit (P01 CA100336-01)

2002 NCI Initial Review Group, Subcommittee C

2001 NIH, NIDDK Special Emphasis Panel, RFA: Role of Hormones and Growth Factors in Prostate Cancer

1999 -2001 California Breast Cancer Research Program, Pathogenesis Review Committee

V. Teaching Activity

Professional Pharmacy Courses

Biopharmacy II (The Ohio State University)

Physiological Chemistry and Molecular Biology II (University of Kentucky) Basic Principles
of Pharmaceutical Science: Drug Form Design (Univ. of Kentucky)
Pharmacognosy I: Basic Immunology & Biologics (University of Rhode Island)
Pharmacognosy II: Antibiotics (University of Rhode Island)
Graduate-Level Courses
Graduate Seminars (The Ohio State University)
Drug Discovery and Design (two lectures; The Ohio State University)
Biocatalysis (The Ohio State University)
Natural Products Chemistry (University of Kentucky)
Graduate Seminars (University of Kentucky; Fall 1997 – Spring 1999)
Biocatalysis - Principle and Application (University of Rhode Island)

VI. Advising Activity

A. Students

University of Rhode Island (1987 – 1995)

	Student/degree	Date completed	Current position
1	Shawn Harriman/M.S.	5/1990	-
2	Pei-Heng Lu/M.S.	5/1990	-
3	Yeuk-Chuen Liu/Ph.D.	5/1992	Assoc. Professor, National Taiwan Ocean University
4	Joyce Li/Ph.D.	5/1995	Pharmaceutical industry, Taiwan

CURRICULUM VITAE

個人簡歷

Name: Kuang-hung Cheng (鄭光宏)

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E-mail: khcheng@faculty.nsysu.edu.tw

Tel: 07-5252000 ext 5817

EDUCATION:

Ph.D. in Pathology and Laboratory Medicine, Boston University School of Medicine, Boston, MA USA (2004)

M.S. in Molecular Biology, National Chung Hsing University, Taichung, Taiwan (1995)

B.S. in Technology for Medical Sciences, Kaohsiung Medical College, Kaohsiung, Taiwan (1992)

APPOINTMENTS:

- 8/2014-Present** Associate Professor, Graduate Institute of Biomedical Science
National Sun Yat-Sen University
Kaohsiung, Taiwan
- 8/2008-7/2014** Assistant Professor, Graduate Institute of Biomedical Science
National Sun Yat-Sen University
Kaohsiung, Taiwan
- 1/2007-7/2008** Research fellow, Department of Pathology,
Brigham and Women's Hospital/Harvard Medical School,
Boston, MA USA
- 1/2005-1/2007** Research fellow, Cancer Center, Department of Medicine,
Massachusetts General Hospital/ Harvard Medical School,
Boston, MA USA

SELECTED PUBLICATIONS:

1. Kuo TZ, Kuo KK, Weng CC, Wu DC, Hung WC, **Cheng KH.** (2016) Non-invasive detection of candidate biomarkers in the feces of human pancreatic cancer based on fecal proteome analysis of an engineered mouse model. (*submitted to J Proteome Res.*) (SCI)
2. Kuo TZ, Weng CC, Kuo KK, Chen CY, Wu DC, Hung WC, **Cheng KH.** (2016) APC haploinsufficiency coupled with p53 loss sufficiently induces mucinous cystic neoplasms and invasive pancreatic carcinoma in mice. *Oncogene* 2016 March. doi: 10.1038/onc.2015.284. (SCI)
3. Weng CC, Kuo KK, Kuo TL, Wu DC, Hung WC, **Cheng KH.** (2016) Pancreatic tumor progression associated with CD133 overexpression: involvement of increased TERT expression and EGFR-dependent Akt Activation. *Pancreas (In print)*. (SCI)
4. Kuo KK, Kuo CJ, Chiu CY, Liang SS, Huang CH, Chi SW, Tsai KB, Chen CY, Hsi E, **Cheng KH,** Chiou SH. (2015) Quantitative proteomic analysis of differentially expressed protein profiles involved in pancreatic ductal adenocarcinoma. *Pancreas*. 2015 Aug 10. [Epub ahead of print] (SCI)

5. Huang CC, Kuo KK, Cheng TC, Chuang CH, Kao CH, Hsieh YC, **Cheng KH**, Wang JY, Cheng CM, Chen CS, Cheng TL. (2015) Development of Membrane-Bound GM-CSF and IL-18 as an Effective Tumor Vaccine. *PLoS One*. 2015 Jul 17;10(7):e0133470. (SCI)
6. Kuo KK, Jian SF, Li YJ, Wan SW, Weng CC, Fang KT, Wu DC and **Cheng KH**. (2015). Epigenetic Inactivation of TGF β 1 Target Gene HEYL, a Novel Tumor Suppressor, Involved in the P53 Induced Apoptotic Pathway in Hepatocellular Carcinoma. *Hepatology Research* 2015 Jul;45(7):782-93. (SCI)
7. Liu CJ, Kuo FC, Hu HM, Chen CY, Huang YB, **Cheng KH**, Yokoyama KK, Wu DC, Hsieh S, Kuo CH (2014). 17 β -Estradiol inhibition of IL-6-Src/Cas/paxillin pathway suppresses human mesenchymal stem cells-mediated gastric cancer cell motility. *Transl Res*. 2014 Sep;164(3):232-43. (SCI)
8. Wang, P.-C., Kuo T.L., C.-C Weng, Strong Wu, M.-F. Hou and **K.H. Cheng** (2014) Overexpression of VCAM-1 promotes tumor progression and drug resistance in breast cancer. *Int.J. Mol. Sci*. 2014 Mar 22;15(3). 3560-3579.(SCI)
9. Chu TH, Chan HH, Kuo HM, Liu LF, Hu TH, Sun CK, Kung ML, Lin SW, Wang EM, Ma YL, **Cheng KH**, Lai KH, Wen ZH, Hsu PI, Tai MH (2014). Celecoxib suppresses hepatoma stemness and progression by up-regulating *PTEN*. *Oncotarget*. 2014 Mar 30;5(6):1475-90. (SCI)
10. Tsai JH, Kuo CH, Yang PC, **Cheng KH**, Wang PW, Chen CC, Hung SH (2014). Effects of antidepressants on type 1 T helper cell-related chemokines in human monocytes. *Int. J. Mol. Sci*. 2014 Jul 28;15(8):13223-35. (SCI)
11. Chen YW, Hsiao PJ, Weng CC, Kuo KK, Kuo TL, Wu DC, Hung WC, **Cheng KH** (2014) SMAD4 loss triggers the phenotypic changes of pancreatic ductal adenocarcinoma cells. *BMC Cancer* 2014 March 14; 14(1) 181. (SCI)
12. Kailasa SK*, **Cheng KH***, Wu HF, (2013) Semiconductor nanomaterials-based fluorescence spectrometric and MALDI mass spectrometric approaches to proteome analyses, *Material* 2013, 6(12), 5763-5795. (co-first author) (SCI)
13. Jian SF, Hsiao CC, Chen SY, Weng CC, Kuo TL, Wu DC, Hung WC and **Cheng KH** (2014). Utilization of liquid chromatography mass spectrometry analyses to identify LKB1-APC interaction in modulating Wnt/ β -Catenin pathway of lung cancer cells. *Molecular Cancer Research*. 2014 Apr;12(4):622-35. (SCI)

Inactivation of APC Cooperates with Kras and P53 Loss to Accelerate PDAC metastasis in Mice.

Kuang-hung Cheng Ph.D.

Institute of Biomedical Science, National Sun Yat-sen University, Kaohsiung Taiwan

ABSTRACT

Adenomatosis polyposis coli (APC), a key tumor suppressor gene which causes most cases of familial adenomatous polyposis FAP, have been considered a “gatekeeper” because alterations in this gene occur as an early event in the neoplastic transformation. The APC tumor suppressor is an essential inhibitor in the evolutionarily conserved Wnt/Wingless (Wg) signaling pathway. During normal development, Wnt signaling is required not only to induce cell proliferation and cell fate specification, but also to maintain somatic stem cell activity. Aberrant Wnt signaling by mutated APC has been implicated in a wide variety of human cancers, including pancreatic adenocarcinoma (PDAC). According to our preliminary result, we have identified APC mutation in ~10% of patients with pancreatic cancer and 20% β -catenin mutation in PDAC patients. Herein, we examined the overexpression and knockdown of APC gene or β -catenin in human PDAC cells to investigate the alteration of PDAC cell morphologies, proliferation kinetics and the tumor suppression of based on growth in soft agar and tumor formation in nude mice. Secondly, we established engineered mouse models representing the inactivation of APC synergizes with Kras activation or/and P53 loss in PDAC development, and mouse model itself has been well characterized with respect to the kinetics of progression which will provide a valuable tool to dissect the APC/ β -catenin signaling network during PDAC carcinogenesis, and assess the impact of APC/ β -catenin inhibitors on the pancreatic carcinogenesis in vivo. In addition, our preliminary results also indicated that inhibition of Wnt/ β -catenin signaling blocked proliferation and induced apoptosis of culture PDAC cells to support a new therapeutically strategies of Wnt/ β -catenin pathway in as a therapeutic and preventive target for human pancreatic cancer with APC mutation in the near future.

CURRICULUM VITAE

Name: Ta-Sen Yeh, MD, Ph D
Professor

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Chief, Division of General Surgery, Chang Gung Memorial Hospital
at Linkou

Selected bibliography (* corresponding author)

1. **Yeh TS**, Jan YY, Chen MF. Roux loop obstruction after pancreatico- duodenectomy. *Br J Surg* 1997;84:323-4.
2. **Yeh TS**, Jan YY, Jeng LB, et al. Pancreaticojejunal anastomotic leak following pancreaticoduodenectomy. Multivariate analysis of perioperative risk factors. *J Surg Res* 1997; 67:119-25.
3. **Yeh TS**, Jan YY, Jeng LB, et al. Pyogenic liver abscess in patients with malignancy. A report of 52 cases treated at a single institute. *Arch Surg* 1998; 133:242-5.
4. Jan YY, **Yeh TS**,* Chen MF. Cholangiocarcinoma presenting as pyogenic liver abscess. Is its outcome influenced by concomitant hepatolithiasis. *Am J Gastroenterol* 1998;93:253-5.
5. **Yeh TS**, Jan YY, Tseng JH, et al. Value of magnetic resonance cholangio- pancreatography in demonstrating major bile duct injury following laparoscopic cholecystectomy. *Br J Surg* 1999;86:181-4
6. **Yeh TS**, Jan YY, Tseng JH, et al. Malignant perihilar biliary obstruction: MRCP findings. *Am J Gastroenterol* 2000;95: 432-40
7. **Yeh TS**, Jan YY, Chiu CT, et al. Characterisation of oestrogen receptor, progesterone receptor, trefoil factor 1, and epidermal growth factor and its receptor in pancreatic cystic neoplasms and pancreatic ductal adenocarcinoma. *Gut*, 2002;51:712-6.
8. Jan YY, **Yeh TS**,* Yeh CN, et al. Expression of epidermal growth factor receptor, apomucins, matrix metalloproteinases, and p53 in rat and human cholangiocarcinoma. Appraisal of animal model for cholangiocarcinoma. *Ann Surg* 2004;240:89-94
9. **Yeh TS**, Ho YP, Huang SF, et al. Thalidomide salvages lethal hepatic necroinflammation and accelerates recovery from cirrhosis in rats. *J Hepatol* 2004;41:606-12.
10. **Yeh TS**, HoYP, CT Chiu, et al. Aberrant expression of *cdx2* homeobox gene in intraductal papillary-mucinous neoplasm of the pancreas but not in pancreatic ductal adenocarcinoma. *Pancreas* 2005;30:233-8.
11. **Yeh TS**, Tseng JH, Liu NJ, et al. Significance of cellular distribution of ezrin in pancreatic cystic neoplasms and ductal adenocarcinoma. *Arch Surg* 2005; 140: 1184 -90.
12. **Yeh TS**, Tseng JH, MD, Chen TC, et al. Characterization of intraductal growth type intrahepatic cholangiocarcinoma and its precursor. *Hepatology* 2005; 42: 657-64.
13. **Yeh TS**, Tseng JH, Chiu CT, et al. Cholangiographic spectrum of intraductal papillary mucinous neoplasm of the bile ducts. *Ann Surg* 2006;244:248-53.
14. Liu MS, Yang PY, **Yeh TS***. Sonic hedgehog signaling pathway in pancreatic cystic neoplasms and ductal adenocarcinoma. *Pancreas* 2007;34:340-6.

15. Lieu KH, Liao LM, **Yeh TS***, et al. Thalidomide attenuates tumor growth and preserves fast-twitch skeletal muscle fibers of cholangiocarcinoma rats. *Surgery* 2008;143:375-83.
16. Lin KJ, Liao CH, Hsiao IT, Yen TC, Chen TC, **Yeh TS***. Improved hepatocyte function of future liver remnant of cirrhotic rats after portal vein ligation: a bonus other than volume shifting. *Surgery* 2009;145:202-11.
17. Hsiao IT, Lin KJ, Chang SI, Yen TC, Chen TC, **Yeh TS.*** Impaired liver regeneration of steatotic rats after portal vein ligation: particular emphasis on ^{99m}Tc-DISIDA scintigraphy and adiponectin signaling. *J Hepatol* 2010;52:540-9
18. Cheng CT, Tsai CY, Hsu JT, Vinayak R, Liu KH, Yeh CN, **Yeh TS***, et al. Aggressive Surgical Approach for Patients with T4 Gastric Carcinoma: Promise or Myth? *Ann Surg Oncol*. 2011;18:1606-14
19. Hsu JT, Chen TC, Tseng JH, Chiu CT, Liu KH, Yeh CN, Hwang TL, Jan YY, **Yeh TS.*** Impact of HER-2 overexpression/amplification on the prognosis of gastric cancer patients undergoing resection: A single-center study of 1,036 patients. *Oncologist* 2011;16:1706-13.
20. Chen TC, Jan YY, **Yeh TS.*** K-ras mutation is strongly associated with perineural invasion and represents an independent prognostic factor of intrahepatic cholangiocarcinoma after hepatectomy. *Ann Surg Oncol* 2012, S3:S675-81
21. Bang YJ, Kim YW, Yang HK, Chung HC, Park YK, Lee KH, Lee KW, Kim YH, Noh SI, Cho JY, Mok YJ, Ji Jiafu, **Yeh TS** , et al. Adjuvant capecitabine and oxaliplatin for gastric cancer after D2 gastrectomy (CLASSIC): a phase 3 open-label, randomised controlled trial. *The Lancet*, 2012;379: 315-21.
22. **Yeh TS,*** Wang F, Chen TC, et al. Expression profile of microRNA-200 family in hepatocellular carcinoma with bile duct tumor thrombus. *Ann Surg* 2014;259: 346-54.
23. Chu CH, Chou W, Wang F, Yeh CN, Chen TC, **Yeh TS.*** Expression profile of microRNA-200 family in cholangiocarcinoma arising from choledochal cyst. *J Gastroenterol Hepatol* 2016;31:1052-9.
24. Tsai CY, Liu YY, Liu KH, Hsu JT, Chen TC, Chiu CT, **Yeh TS.*** Comprehensive profiling of virus microRNAs of Epstein-Barr virus-associated gastric carcinoma --- highlighting the interactions of ebv-Bart9 and host tumor cells. *J Gastroenterol Hepatol* 2016 (e publication)

Most pancreatic surgeries for pancreatic cancer are R1 resection?

Ta-Sen Yeh, MD, PhD

Department of Surgery, Chang Gung Memorial Hospital at Linko, Taiwan

Pancreatic cancer is the fourth leading cause of cancer-related death in Western societies and is projected to be second leading cause within a decade. Surgical resection is the only hope for cure. Because of the late presentation of the disease, particularly for those with pancreatic body or tail lesion lacking of overt and specific symptoms, <15% of patients are eligible for pancreatic resection. More than this, the prognosis of pancreatic cancer remains dismal in those with potentially resectable disease. The five-year survival following pancreaticoduodenectomy is about 25-30% for node-negative, and 10% for node-positive tumors. The prognosis of pancreatic body/tail cancer after pancreatectomy is even worse. Many investigators assume that the dismal prognosis after surgical resection might be due to unclear surgical margins, either microscopically (R1) or R2 (macroscopically), particularly at the facets of retroperitoneal plane and portal vein groove in addition to the traditional one. Many pathologists have even claimed that most of the pancreatic surgery are R1 resection. To elucidate this puzzling issue, we conducted an in-depth pathological examination by inking different colored dyes upon the surgical specimen to carefully evaluate the radicality, which was then correlated with the findings of the computed tomography. By doing so, we might shade a light on this annoying surgical issue worldwide.

Curriculum Vitae

Name: 沈延盛 Yan-Shen Shan MD, PhD

Gender: Male, Birth Date: Mar 17, 1963

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Tel: 886-6-2353535 ext 5181 or 3116

E-mail: ysshan@mail.ncku.edu.tw

Education:

2006.11-2007.9 Visiting Scholar of University of Pennsylvania and Thomas Jefferson Hospital, USA

1998.9-2004.6 PhD of Clinical Medicine, National Cheng Kung University

1988.9-1993.6 MD, School of Medicine, National Cheng Kung University

Clinical Training:

1981.9-1985.6 Rehabilitation Medicine, School of Medicine, National Taiwan University

1993.7-1998.7 Residency of Surgery, National Cheng Kung University Hospital

Clinical and Academic Appointments:

1998.8 Department of Surgery, NCKUH

2002.8~2008.7 Assistant professor

2008.8~2012.7 Associate professor of Surgery

2009.10~ Convener of UGI Cancer in NCKUH

2010.8~2012.7 Associate professor of Institute of Clinical Medicine

2010.9~ Chief of Division of Trauma

2012.8~ Professor of Institute of Clinical Medicine and Surgery

Professional Membership

Formosan Association of Surgery

Taiwan Surgical Society of Gastroenterology (member of a council)

Taiwan Pancreas Society(member of a council)

Taiwan Society of Endoscopic Surgery (member of a supervisor)

Taiwan Surgical Society of Trauma

中華民國癌症醫學會(腫瘤外科專科醫師 and 指導醫師)

台灣代謝及減重外科醫學會(member of a council)

International Hepato-Pancreato-Biliary Association (M2527)

International Association of Surgeon and Gastrpenterologists

The Society for Surgeon of the Alimentary Tract, USA

Curriculum Vitae

May, 2016

Name: 常慧如 Hui-Ju Mandy Ch'ang, M.D.

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Phone: 886-37-246-166 ext 35105 **Fax:** 886-37-586-463

E-mail: hjmc@nhri.org.tw

Education/Position:

- 1979-1983 Medical College, Department of Medical Technology, National Taiwan University, Taipei, Taiwan
- 1983-1984 Assistant Teacher, Medical College, Dept. of Biochemistry, NTUH
- 1984-1989 Medical College, Dept. of Medicine, NTU
- 1989-1992 Resident, Internal Medicine, National Taiwan University Hospital
- 1992-1993 Chief Resident and Clinical Fellow, Medical Oncology, NTUH
- 1993-1995 Resident, Radiation Oncology, NTUH
- 1995-1998 Resident, Radiation Oncology, Sun Yat-Sen Cancer Center, Taipei
- 1998-2000 Research Fellow, Division of Cancer Research, National Health Research Institutes, Taipei
- 2000-2001 Research Fellow, Laboratory of Radiation Research, Memorial Sloan-Kettering Cancer Center, New York
- 2000- Visiting Staff, Division of Cancer Research, National Health Research Institutes, Taipei
- 2002-2007 Visiting Staff, Division of Oncology, National Taiwan University Hospital
- 2005-2012 Assistant Investigator, National Institute of Cancer Research, National Health Research Institutes, Tainan
- 2008-2014 Visiting Staff, Division of Radiation Oncology, National Cheng Kung University Hospital
- 2008- Executive Secretary, Data Monitoring and Safety Committee, Taiwan Cooperative Oncology Group.
- 2012- Associate Investigator, National Institute of Cancer Research, National Health Research Institutes, Tainan
- 2015- Visiting Staff and Assistant Professor, Division of Radiation Oncology, Taipei Medical University Hospital and Taipei Cancer Center

Board Certification:

- 1983~ Diploma, Board of Medical Technology
- 1989~ Diploma, Board of Medicine
- 1992~ Board of Specialist of Internal Medicine
- 1995~ Medical Oncology Board
- 1998~ Radiation Oncology Board

Society:

- Member of the Taiwan Oncology Society
- Member of Taiwan Society of Internal Medicine
- Member of Formosan Medical Society
- Member of the Taiwan Radiation Oncology Society

Professional Activities:

1. Principle Investigator, National Health Research Institutes
 - (1) De Novo Ceramide Synthesis Pathway in the Evolution of Radiation-Induced GI Syndrome (NHRI 2002)
 - (2) Influence of Bone Marrow on Radiation Induced Gastrointestinal Damage (NHRI 2003)
 - (3) A Phase II Study of Postoperative Local Irradiation plus Oral Thalidomide in

Glioblastoma Multiforme (NHRI 2003-2005)

- (4) The role of Mesenchymal-Epithelial Interaction in Radiation Induced Intestinal Mucosa Damage Repair (NHRI 2004~2006)
- (5) A Phase II Study of Induction Chemotherapy followed by Concurrent Chemotherapy with Radiotherapy in Locally Advanced Pancreatic Cancer (NHRI 2004~2009)
- (6) A Pilot Clinical and Mechanistic Study of Radiotherapy plus Thalidomide for Locally Advanced Hepatocellular Carcinoma (HCC) (NHRI 2004~2009)
- (7) Mobilization of Bone Marrow Stem Cells and Cancer Cells by Granulocyte Colony-Stimulating Factor in Cancer Therapy (NHRI 2007~2010)
- (8) Bone Marrow Enhances Intestinal Stromal Cell Proliferation and Protects Intestine from Radiation Damage Through Paracrine Mechanism (NSC2008-2010)
- (9) A randomized phase III study of adjuvant gemcitabine versus gemcitabine plus concurrent chemoradiation in pancreatic cancer underwent curative intent (R0/R1) (2008~)
- (10) The Clinical Significance of VEGF and SDF-1/CXCR4 Signaling Pathway Biomarkers in Patients with Pancreatic Cancer (DOH2008~2009)
- (11) A Phase II Randomized Study of Induction Chemotherapy followed by Concurrent Chemo-radiotherapy in Locally Advanced Pancreatic Cancer (NHRI 2010~)
- (12) Molecular Mechanisms of Shear Stress in Regulating Cellular Radiation Sensitivity (NHRI 2010~2011)
- (13) Molecular Mechanisms of Shear Stress in Regulating Cellular Radiation Sensitivity of Pancreatic Carcinoma (NHRI 2011~2014)
- (14) Fusion between Bone Marrow and Intestine Stromal Cells Contributes to Intestine Fibrosis after Radiation (NSC 2011/8-2012/7)
- (15) Strategies Targeting Fusion Machinery of Bone Marrow Derived Macrophage May Ameliorate Intestinal Fibrosis after Radiation (NSC 2012/8-2015/7)
- (16) Study the Klf10 alters metabolic pathways in genetic-deficient mice and human pancreatic ductal carcinoma. (NSC 2012/8-2014/7)
- (17) Molecular Mechanisms of Krüppel like factor 10 in Regulating Pancreatic Cancer Progression and Radiation Sensitivity (NSC 2015/8-2018/7)
- (18) The role of cell fusion between macrophage and cancer cells in pancreatic cancer progression after radiation (NHRI 2015~2018)

2. Research Fellow, Memorial Sloan-Kettering Cancer Center, Laboratory of Radiation Research in 2000

- (1) De Novo Synthesis of Ceramide in Mitochondria after Radiation of HeLa Cells
- (2) Role of Ceramide Synthase in Radiation Hyperensitivity of ATM Knock Out Mice.

2. Research Fellow, NHRI (National Health Research Institutes), TCOG (Taiwan Cooperative Oncology Group) Laboratory, Urine Therapy Study in 1998:

- (1) Reversal of Drug Resistance in Breast Cancer Cells by Human Urine Extract

3. Study Coordinator, SYSCC Cancer Study Protocol in 1995:

- (1) Preoperative concurrent chemotherapy and radiotherapy in rectal cancer patients.
- (2) Postoperative concurrent chemotherapy and radiotherapy for resectable locally advanced gastric cancer patients.

Loss of Kruppel Like Factor 10 Enhanced Epithelial Mesenchymal Transition of Pancreatic Cancer by Modulating Glucose Metabolism via Sirt 6 and PKM2 **Hui-Ju Ch'ang^{1,3*}, Yi-Chih Tsai¹, Su-Liang Chen¹, Vincent HS Chang²**

¹ National Institute of Cancer Research, National Health Research Institutes, Zhunan, Miaoli County, Taiwan

² Program for Translation Medicine, College of Medical Science and Technology, Taipei Medical University, Taipei, Taiwan.

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Introduction:

Pancreatic Cancer is well known for its deregulated TGF β signaling. We have reported that the expression level of Kruppel like factor 10 (Klf10), a TGF β early response transcription factor, is associated with clinical outcomes of pancreatic cancer patients. In this study, we would like to evaluate the mechanisms of Klf10 in promoting distant metastasis of pancreatic cancer.

Materials and Methods:

Klf10 over-expressing- or depleting-human pancreatic cancer cell lines were established. Epithelial-mesenchymal transition (EMT) markers and glycolysis related molecules were evaluated by immunoblots. Cancer cell migration was measured by trans-well assay. Luciferase-labeled Panc-1 cells with or without Klf10 mRNA silencing were injected via tail veins of NOD/SCID mice to evaluate their metastatic ability. The glucose consumption, lactate production and mitochondrial respiration of pancreatic cancer cells were measured by assay kit or XF^e Extracellular Flux Analyzers.

Results:

Down-regulating Klf10 in Panc-1 cells was associated with enhanced migration and invasion ability by in vitro and in vivo studies. Immunoblots of cell lysates revealed decreased expression level of E-cadherin and increased Twist, MMP9. Glycolysis activity was elevated while mitochondrial respiration decreased after silencing Klf10 mRNA in Panc-1 cells. The phenomenon was in parallel with decreased Sirt 6 and increased HIF-1 α as well as PKM2 expression. We demonstrated that Klf10 bind to the promoter and transcriptionally regulated Sirt 6. Modulating Sirt 6 and PKM2 reversed the EMT and metastatic phenotype of Panc-1 cells with Klf10mRNA silencing.

Discussion:

Loss of Klf10 enhanced the migratory ability of pancreatic cancer cells. Klf10 transcriptionally regulated Sirt 6 which modulated glycolytic enzymes including PKM2 via HIF-1 α . Elevated PKM2 promoted EMT phenotype and distant metastasis of pancreatic cancer. Klf10 is a potential prognostic and therapeutic biomarker for pancreatic cancer.

Curriculum Vitae

Personal information

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Education

2004-2012 Ph.D., Institute of Basic Medical Science, College of Medicine, National Cheng Kung University, Tainan, Taiwan

1995-1997 M.S., Department of Physiology, College of Medicine, National Cheng Kung University, Tainan, Taiwan

Working experience

1999-2004 Associate Researcher, Product and Process Research Center, Food Industry Research and Development Institute, Hsinchu, Taiwan

Research interests

✧ Molecular biology

✧ Tumor biology

Publications (recent 5 years)

1. **Wang HC**, Yeh HH, Huang WL, Lin CC, Su WP, Chen HH, Lai WW, Su WC*. Activation of the signal transducer and activator of transcription 3 pathway up-regulates estrogen receptor-beta expression in lung adenocarcinoma cells. *Mol Endocrinol.* 2011 Jul;25(7):1145-58.
2. Tsai TL, Hou CC, **Wang HC**, Yang ZS, Yeh CS, Shieh DB, Su WC*. Nucleocytoplasmic transport blockage by SV40 peptide-modified gold nanoparticles induces cellular autophagy. *Int J Nanomedicine.* 2012;7:5215-34.
3. Su WP, Lo YC, Yan JJ, Liao IC, Tsai PJ, **Wang HC**, Yeh HH, Lin CC, Chen HH, Lai WW, Su WC*. Mitochondrial uncoupling protein 2 regulates the effects of paclitaxel on Stat3 activation and cellular survival in lung cancer cells. *Carcinogenesis.* 2012 Nov;33(11):2065-75.

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Education

2010-present Ph.D. program, Institute of Basic Medical Science, College of Medicine, National Cheng Kung University, Tainan, Taiwan

2006-2008 M.S. Graduate Institute of Biotechnology, National Chung Hsing University, Taichung, Taiwan

Doctoral research

Thesis title: Tumor associated macrophage and stemness in pancreatic cancer stem-like cells

Working experience

2009-2010 Research Assistant Department of Biochemistry and Molecular Biology, College of Medicine, National Cheng Kung University, Tainan, Taiwan

2004-2006 Research Assistant HS Biotechnology company, Taichung, Taiwan

Research interests

- ✧ Tumor biology
- ✧ Tumor microenvironment
- ✧ Cancer stem cell

Publications (recent 5 years)

1. Hsu YH, Li HH, Sung JM, Chen WT, **Hou YC**, and Chang MS. Interleukin-19 Mediates Tissue Damage in Murine Ischemic Acute Kidney Injury. PLoS ONE. 2013; 8 (2): 1-10.

Curriculum Vitae

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Training & Working Experience:

- 1983-1984 Rotating Intern in National Taiwan University Hospital.
- 1984-1985 Resident, Department of Internal Medicine,
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- 1987-1988 Chief Resident, Department of Radiology, National Taiwan University Hospital.
- 1989-1990 Clinical Instructor, Department of Radiological Science, UCLA Medical Center.
- 1989-1996 Assistant Professor, National Taiwan University College of Medicine.
- 1996-2004 Associate Professor, National Taiwan University College of Medicine.
- 1995-2008 Head, section of Musculoskeletal Radiology, National Taiwan University Hospital.
- 2002-2008 Vice Chairman, Department of Medical Imaging and Radiology, National Taiwan University Hospital and College of Medicine.
- 2008-2014 Chairman, Department of Medical Imaging and Radiology, National Taiwan University Hospital and College of Medicine.
- 1988-present Visiting Staff, Department of Medical Imaging, National Taiwan University Hospital.
- 2004-present Professor, Department of Radiology, National Taiwan University College of Medicine.
- 2016-present Deputy Chief Strategy Officer, Taipei City Hospital.
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PET/MRI as a Hybrid Biomarker of Pancreatic Cancer

— Clinical Diagnosis and Outcome Prediction

To correlate the clinical stage and prognosis of pancreatic or periampullary cancer with the imaging biomarkers on diffusion-weighted imaging, magnetic resonance spectroscopy and glucose metabolic activity derived from integrated PET/MRI. This prospective study was approved by the institutional review board and informed consent was obtained. The study group comprised 60 consecutive patients with pancreatic or periampullary cancer who underwent PET/MRI before treatment. The imaging biomarkers were the minimal apparent diffusion coefficient (ADC_{min}), choline levels, standardized uptake values, metabolic tumour volume (MTV), and total lesion glycolysis (TLG) of the tumours. The relationships between these biomarkers and clinical TNM stage were evaluated using the Pearson test and the Mann-Whitney U test. The area under the receiver operating characteristic curve (AUROC) was used to evaluate accuracy. The correlation between the imaging biomarker and progression-free survival (PFS) was investigated using the Cox proportional hazards model. ADC_{min} was significantly lower in N1 and TNM stage 3+ tumours. Choline levels significantly higher in T4 tumours. TLG was significantly higher in T4, N1 and TNM stage 3+ tumours. MTV was significantly higher in T4, N1, M1, and TNM stage 3+ tumours (all $P < 0.05$). The MTV/ADC_{min} ratio exhibited the highest AUROC for predicting T4, N1, M1, and advanced TNM stages tumours, and was an independent predictor of PFS ($P = 0.018$) after adjustment for age, sex, tumour size and stage. The imaging biomarkers from integrated PET/MRI may predict clinical stage and PFS in patients with pancreatic or periampullary cancer.

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Medical Education

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Memorial Hospital

Professional Experience

2007 Radiologist Certified by the Radiological Society of Republic of China
2006~ Staff Radiologist in Department of Diagnostic Radiology, National Cheng Kung
University Hospital
2010~ Staff in Division of Traumatic Surgery, Department of Surgery, National Cheng Kung
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2012~ Staff in Innovation Center of Medical Devices and Technology, National Cheng Kung
University Hospital
2013~ Assistant professor, Department of Medicine, National Cheng Kung University
2014~ Chief in Division of Interventional Radiology, Department of Diagnostic Radiology,
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Publications

1. Liu YS, Wu DK, Lu CY, Hsu JS. Interruption of Left Pulmonary Artery with Atrial Septal Defect and Right Side Aortic Arch: a Case Report Diagnosed with MRA. Chinese Journal of Radiology 2006; 31(3):133-137
2. CM Chou, CC Hsieh, CL Tsai, CY Chen, HM Tsai, YS Liu. Post-evacuation film on double contrast barium enema increased the diagnostic rate of the diverticulosis. Chinese Journal of Radiological Technology 2009; 33(1):51-54
3. LC Hung, YS Liu, YS Tsai, MT Chuang. Familial paraganglioma syndrome. Acta Neurologica Belgica 2011; 111(3):255-256 (SCI)

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5. CW Chen, YS Liu, CY Chen, HM Tsai, SC Chen, MT Chuang. Use of carbon dioxide as negative contrast agent for magnetic resonance cholangiopancreatography. *World Journal of Radiology* 2011; 3(2):47-50
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Patent:

1. 林錫璋, 蔡宏名, 劉益勝, 王覺寬, 呂宗行, 陳必恆, 王儷蓁, 曾柏勳, 李昱翰, 陳炯瑜. 栓塞用微粒. 中華民國專利證書, 發明第I503132號, 2015-2032

International Oral Presentation:

1. Drug-eluting Beads Provide Better Treatment Results than Conventional Transcatheter Arterial Chemoembolization for Hepatoma. The Asian Pacific Association for the Study of the Liver (APASL) 2012. Taipei, Taiwan.
2. Clinical Experience of DEB-TACE for HCC patients. GEST in China 2013. Tianjin, China.
3. Getting Out of Trouble: Transarterial Embolization with Drug-eluting Microsphere (HepaSphere). Kuala Lumpur Interventional Conference (KLIC) 2014. Kuala Lumpur, Malaysia.
4. Optimizing TACE Treatment in Patients with HCC. Canton Intervention Forum 2015. Guangzhou, China.
5. Comparison of Microspheres for TACE in an Animal Experiment. Singapore Congress of Radiology (SGCR) 2016. Singapore.
6. New Trend for HCC Patient Treatment. Asian-Pacific Congress of Cardiovascular & Interventional Radiology (APCCVIR) 2016. Suzhou, China.
7. Drug-eluting Bead for HCC Patients. Asian-Pacific Congress of Cardiovascular & Interventional Radiology (APCCVIR) 2016. Suzhou, China.

CT-Guided Coaxial Core Biopsy of the Pancreas via a Fat Traversing Route

Yi -Sheng Liu

Purpose: To evaluate the safety and efficacy of computed tomography (CT)-guided coaxial core biopsy of pancreatic lesions.

Patients and Methods: Of the 180 patients (75 females, 105 males of comparable age) who underwent CT-guided pancreatic biopsy with and without the use of a coaxial needle, 122 underwent coaxial needle biopsy of their pancreas (coaxial group) compared with 58 patients who underwent biopsy without coaxial needle use (non-coaxial group). A detour route traversing fat was used, where feasible, to avoid non-target organ puncture. Multivariable regression analysis evaluated group differences.

Results: More lesions in the coaxial group were located within pancreatic head (44.3%) compared with the non-coaxial group (25.9%). Significantly more patients in the coaxial group underwent biopsy via the detour route compared with the non-coaxial group (93.4% vs. 1.7%, respectively; $p < 0.001$). No patient in the coaxial group had biopsy via trans-organ route compared with five (8.6%) patients in the non-coaxial group ($p = 0.003$); the coaxial group had significantly less complications than the non-coaxial group (4.1% vs. 15.5%, respectively; $p = 0.014$). The coaxial group had significantly more successful diagnoses compared with the non-coaxial group (96.7% vs. 79.3%, $p < 0.001$). Multivariable logistic regression analyses showed that, compared with the non-coaxial group, patients in the coaxial group were less likely to have negative tissue from the biopsy (OR = 0.07, $p < 0.001$), after adjusting for age, gender, and pancreatic lesion size.

Conclusion: Compared with biopsy performed without a coaxial needle, CT-guided coaxial core biopsy appeared to be a safer and more effective method for pancreatic lesion biopsy possibly due to the use of a detour route through fat afforded by coaxial needle use.

Biographical Sketch

<u>Name</u> Wei-Chih Liao	<u>Position Title</u> Attending physician. Department of internal medicine, National Taiwan University Hospital (2005 – present) Clinical associate professor. National Taiwan University College of Medicine (2015 – present)
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<u>Education/Training</u>			
Institution	Degree	Year(s)	Field of Study
National Taiwan University College of Medicine	MD	2005	Medicine
Institute of Epidemiology, National Taiwan University	MSc	2009	Epidemiology
Institute of Epidemiology and Preventive Medicine, National Taiwan University	PhD	2014	Epidemiology

<u>Professional and Research Experience</u>	
1995 - 1996	Internship. National Taiwan University Hospital
1998 - 2001	Residency. National Taiwan University Hospital
2001 - 2003	Fellowship. National Taiwan University Hospital
2005 – present	Attending physician. Department of internal medicine, National Taiwan University Hospital
2015 – present	Clinical associate professor. National Taiwan University College of Medicine

<u>Research Interest</u>
Clinical and epidemiological research on pancreatic cancer and pancreatitis
Biliary and pancreatic endoscopy
Endoscopic training

<u>Honors</u>	
2012	American Society for Gastrointestinal Endoscopy (ASGE) Ambassador
2012-2014	Outstanding Reviewer for GIE: Gastrointestinal Endoscopy
2014	Outstanding Research Award for Junior Faculty, National Taiwan University Hospital

<u>Selected Publication</u>	
1.	Lee YC, Chiang TH, Chou CK, Tu YK, <u>Liao WC</u> (corresponding author), Wu MS, Graham DY. Association between Helicobacter pylori eradication and gastric cancer incidence: a systematic review and meta-analysis. Gastroenterology 2016 May;150(5):1113-1124.
2.	<u>Liao WC</u> , Tu YK, Wu MS, Lin JT, Wang HP, Chien KL. Blood glucose concentration and risk of pancreatic cancer: systematic review and dose-response meta-analysis. The BMJ 2015 Jan;349:g7371.
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11. Liao WC, Wu MS, Wang HP, Tien YW, Lin JT. Serum heat shock protein 27 is increased in chronic pancreatitis and pancreatic carcinoma. *Pancreas* 2009 May;38(4):422-6.
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15. Han ML, Lin HF, Liu KL, Lee TH, Liao WC (corresponding author). Anaerobic bacteremia in a patient with necrotizing pancreatitis. *GUT* 2008 Nov;57(11):1530, 1553.
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20. Kamisawa T, Kim MH, Liao WC, Liu Q, Balakrishnan V, Okazaki K, Shimosegawa T, Chung JB, Lee KT, Wang HP, Lee TC, Choudhuri G. Clinical characteristics of 327 Asian patients with autoimmune pancreatitis based on Asian diagnostic criteria. *Pancreas* 2011 Mar;40(2):200-5.

Type 2 Diabetes and the Risk of Pancreatic Cancer

Wei-Chih Liao

Pancreatic adenocarcinoma (PAC) is the most lethal cancer, with a 5-year survival rate of less than 5%. The incidence and mortality rates of PAC are increasing, underscoring the urgent need for better understanding and control of its risk factors.

Epidemiologic evidence supports that type 2 diabetes and its precursor, prediabetes, are risk factors for PAC. Meta-analyses of observational studies have demonstrated a positive association between chronic diabetes and PAC risk, and that there is a strong linear dose-response association between fasting blood glucose and the rate of PAC. On the other hand, diabetes may also be a presentation of PAC. A population-based cohort study from Taiwan found that diabetes of less than 2 years is associated with a marked increase in PAC risk.

The link between prediabetes/type 2 diabetes and PAC are not completely understood. Chronic hyperinsulinemia and hyperglycemia associated with prediabetes/diabetes have been proposed as the underlying mechanisms. Insulin may promote proliferation and reduces apoptosis in pancreatic cancer cells, both directly and indirectly through increased bioavailability of insulin-like growth factor-1. Hyperglycemia may also enhance proliferation and invasion ability in pancreatic cancer.

Type 2 diabetes is increasing rapidly worldwide; this alarming trend could result in further increase in PAC incidence. Efforts toward early detection of diabetes in conjunction with lifestyle modifications and pharmacologic treatments may represent a viable strategy to curb the increasing incidence of pancreatic cancer.