



**TMU**  
TAIPEI  
MEDICAL  
UNIVERSITY

臺北醫學大學醫學院  
COLLEGE OF MEDICINE  
TAIPEI MEDICAL UNIVERSITY, TAIWAN  
SCIENTIFIC REPORT 2018

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**Han-Pin Kuo, M.D., Ph.D.**

**Professor and Dean**

**Department of Internal Medicine**

**College of Medicine**

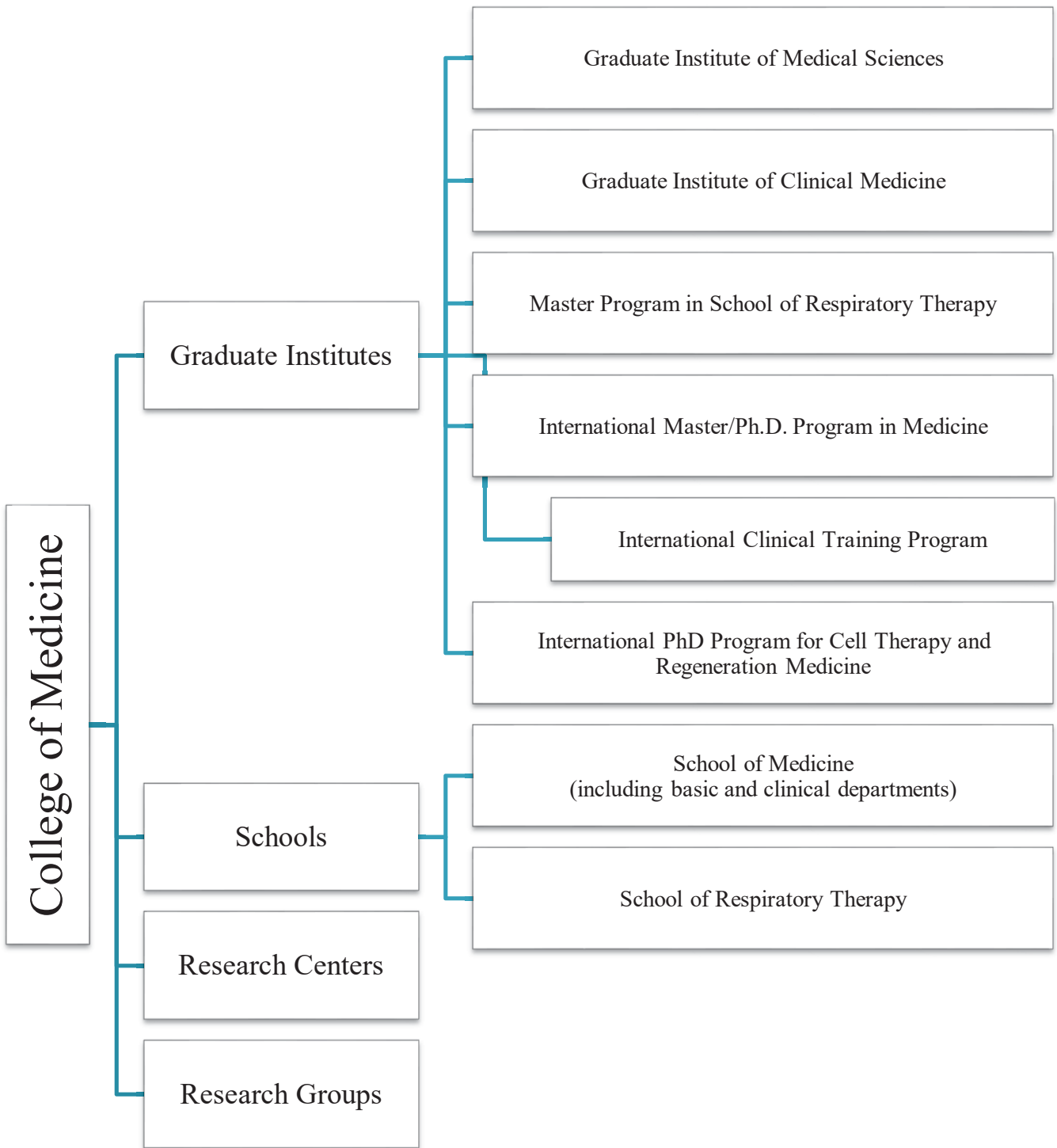
**Taipei Medical University**



Founded in 1960, the College of Medicine, Taipei Medical University is now composed of seven academic units. We currently have close to 600 faculty members, including full-time professors, adjunct professors, and clinical instructors, and a total of 1600 students comprised of undergraduate students, Master's degree and Ph.D. students. We integrate resources from not only 3 JCI-accredited affiliated hospitals, Taiwan Medical University Hospital, Taipei Medical University Wang-Fang Hospital and Taipei Medical University Shuang-Ho Hospital, but also Graduate Institutes, and Research Centers to nurture researchers and students in the field of Basic Medical Sciences, Clinical Medicine and Applied Medicine.

To achieve greater perfection in medical research and education, we have developed several translational research groups in different research fields. In addition, we hold “Mushan Biomedical Research Seminar” monthly inviting domestic and oversea distinguished experts to share their research journeys. Several international symposiums are also held annually to boost the collaboration between TMU and other renowned universities. Furthermore, we have signed MOUs to establish official relationship with universities all over the world, and also the Dual Degree/Joint Degree Agreements with America and Canada; we expect to provide the opportunity for international academic exchange and broaden students' global vision to cultivate advanced physician scientists.

We will continue on our missions to advance the discovery of disease treatment and improve human health via providing a high quality and interactive research environment. We believe our researchers and students will be the very pioneers in medical research fields. In the meanwhile we are committed to maintaining an academic culture that respects diversity and fosters compassion to change our students into professionals who will be leaders in healthcare.



## Graduate Institutes

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**About**

The research teams in the Graduate Institute of Medical Sciences were established based on disease-oriented missions. We had four major fields of interest as follows:

1. The neuroscience translational medicine team works active research based on collaboration of basic neuroscientists and clinicians in neurology, neurosurgery, psychiatry and rehabilitation.
2. The inflammation research group provides several research platforms for lung fibrosis research, including molecular mechanics, clinical translational studies, anti-fibrotic drug design, and small molecule drug screening.
3. The breast cancer translational research team integrates basic research and clinical resources to develop novel tumor markers for targeted anti-cancer drug development.
4. The mission of the stem cell research group is to develop the closely cooperation with experts in basic research and clinical medicine, and to promote translational medicine of cell/stem cell in TMU.

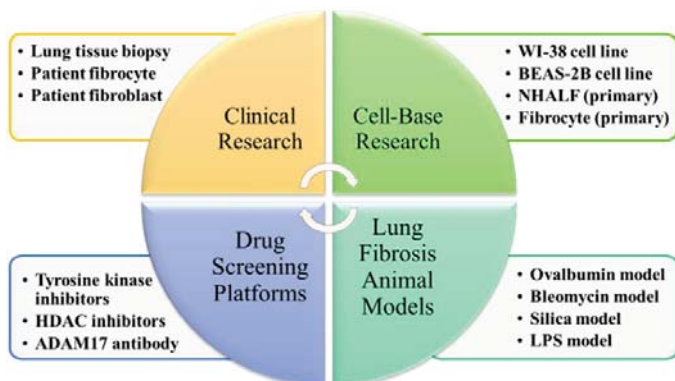


Rucui-Ming Chen  
Ph.D.  
Distinguished Professor  
and Director

**Major achievements**

**The lung inflammatory team**

Demonstrated that a disintegrin and metalloproteinases 17(ADAM17) and  $\alpha$ -SMA are overexpressed in fibroblasts from patients with COA compared to normal subjects. They also demonstrated that C/EBP $\beta$ -mediated hypoxia induced expression of ADAM17 and  $\alpha$ -SMA as well as fibroblast differentiation. The main focus of this team is on why ADAM17 is the key mediator in the progression of fibroblast differentiation and pulmonary fibrosis. Delineation of the ADAM17 signaling processes in the lung fibroblast cell types will not only help elucidate the mechanisms underlying the development of pulmonary fibrosis, but facilitate the development of novel therapeutic strategies for curing or alleviating pulmonary fibrosis.



Lung inflammatory research group: The integrative research team.

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**The neuroscience research team**

TMU has established a University-grade “Center for Neurotrauma and Regeneration Medicine” and a Sleep Center for patients. There are 4 main teams : New diagnosis and treatment for neurological or psychiatric sequelae following traumatic brain injury (TBI); Impact of Sleep Disorders on Metabolic Functions; Impact of BBB / Neurovascular unit / Hypoxia in neurological or psychiatric diseases; New drug development for glioma.

1. The TBI team has established a translational research framework for early detection, therapeutic design from cellular or animal studies, and extended to health care for TBI patients. This team also established International Collaboration with NIH in USA with an ongoing integrated program project led by Dr. Wen-Chang Chang.
2. The team in sleep medicine has established a reliable and valid animal model of maternal early-life sleep deprivation and found

trans-generational impact of sleep deprivation.

3. Neurovascular research team focuses on cerebrovascular studies in hypoxia, ischemia, white matter injury and neurodegenerative diseases.
4. The glioma team has established orthotopic xenograft and allograft animal models and identified new biomarkers for glioma and potential new therapeutic approaches.

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**Major publications**

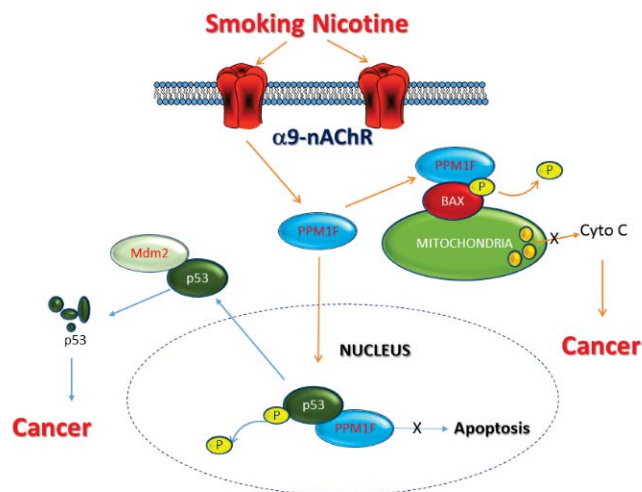
- [1] Lin JW, Chen JT, Hong CY, et al. Honokiol traverses the blood-brain barrier and induces apoptosis of neuroblastoma cells via an intrinsic Bax-mitochondrion-cytochrome c-caspase protease pathway. *Neuro-Oncology* 2012;14:302-314
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- [3] Yeh PS, Wang W, Chang YA, et al. Honokiol induces autophagy of neuroblastoma cells through activating the PI3K/Akt/mTOR and endoplasmic reticular stress/ERK1/2 signaling pathways and suppressing cell migration. *Cancer Letters* 2016;370(1):66-77
- [4] Kuo YC, Au HK, Hsu JL, et al. IGF-1R promotes symmetric self-renewal and migration of alkaline phosphatase<sup>+</sup> germ stem cells through hif-2 $\alpha$ -oct4/cxcr4 loop under hypoxia. *Stem Cell Rep* 2018; 10:524-37.
- [5] Chang TS, Wu YC, Ching CC, et al. Activation of IL6/IGF-1R confers poor prognosis of HBV-related hepatocellular carcinoma through induction of OCT4/NANOG expression. *Clin Cancer Res* 2015; 21:201-210.
- [6] Chang TS, Wu YC, Tung SY, et al. Alpha-fetoprotein measurement benefits hepatocellular carcinoma surveillance in patients with cirrhosis. *Am J Gastroenterol* 2015; 110:836-44.
- [7] Huang ZW, Lien GS, Chen BC, et al. p300 and C/EBP $\beta$ -regulated IKK $\beta$  expression are involved in thrombin-induced IL-8/CXCL8 expression in human lung epithelial cells. *Pharmacol Res.* 2017; 121:33-41.
- [8] Yang LY, Greig NH, Huang YN, et al. Post-traumatic administration of the p53 inactivator pifithrin- $\alpha$  oxygen analogue reduces hippocampal neuronal loss and improves cognitive deficits after experimental traumatic brain injury. *Neurobiol Dis.* 2016; 96: 216-26.



**The breast cancer team**

This research team has provide the molecular evidence for smoking-induced breast cancer formation. They focused on three major aims as follows:

1. Develop a therapeutic antibody for the  $\alpha 9$ -nAChR.
2. Validate the therapeutic efficacy of the  $\alpha 9$ -nAChR-specific antibody.
3. Evaluate the  $\alpha 9$ -nAChR molecule as an early-diagnostic marker for breast cancer patients.
4. Establish the down-stream signaling mechanisms of smoking-induced carcinogenesis.



After nicotine treatment, the protein phosphatase  $Mg^{2+}/Mn^{2+}$  dependent 1F (PPM1F), a Ser/Thr protein phosphatase, triggered the inactivation of both p-p53 and p-BAX by dephosphorylating them at specific sites. These results suggest that PPM1F could be downstream of  $\alpha 9$ -nAChR in nicotine-induced breast cancer formation, and could attenuate p-p53 (Ser-20)- and p-BAX (Ser-184)-induced pro-apoptotic pathways. Thus, PPM1F expression could be used for prognostic diagnosis or inhibited for cancer prevention and therapy.

**International Connection**

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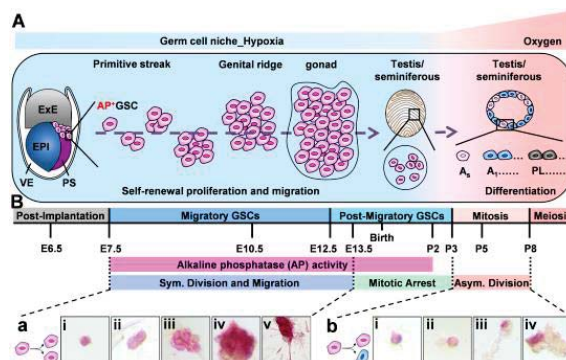
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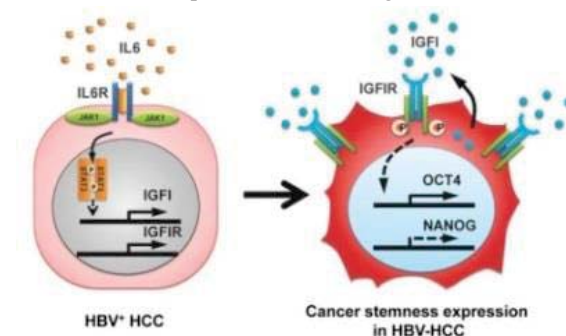
**The stem cell research team**

Our main efforts will focus on basic research, drug targeting on cancer stemness and disease-specific induced pluripotent stem cells (disease iPS), and disease-indication of preclinical animal studies. Future cooperation in medicine research, clinical treatment, and product innovation of cell/stem cell will be highlighted. The major aims of the stem cell research team as follows.

1. Pluripotent stem cells, embryonic germ cells and induced pluripotent stem cells (iPS cells).
2. Niche regulation of stemness expression in stem cell and cancer.
3. Homeostasis regulation of pluripotent transcription factor OCT4 in stem cell and cancer.
4. Preclinical animal studies of small blood cells and mesenchymal stem cells in bone repair and wound healing.
5. Drug screening of disease iPS cells and cancer stem cells.



Schematic of mouse postimplantation germ cell development in symmetric self-renewal proliferation and migration.



IL6 increases the expression of pluripotent gene OCT4 and NANOG through IGFIR activation in human HBV-HCC cells.

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## About

The Graduate Institute of Clinical Medicine was established to enhance the health of the public through prospective clinical and translational medical research, the exploration and solving of clinical problems, and the development of advanced diagnosis tools and treatments in order to earlier detecting and preventing diseases.

Both the master's and doctoral programs are designed to train students to the highest standards of this institute.

Our curriculum characteristics are three aspects, including Disease-Oriented Research, Research-Oriented Learning and Dual mentorship. We offer courses in clinical trials, translational medicine, clinical & translational epidemiology, clinical evidenced medicine, cell biology, molecular biology, lab rotation and research techniques, applied statistics, research design, advanced paper writing and genetic medicine. All students are given guidance and counseling by two supervisors who possess backgrounds in clinical medicine and research.

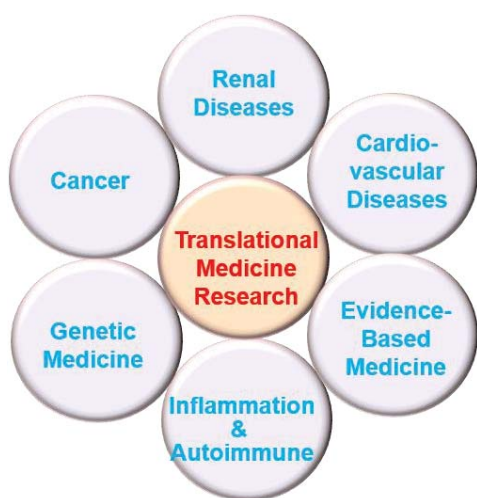


Kuan-Chou Chen  
M.D., Ph.D.

Professor and Director

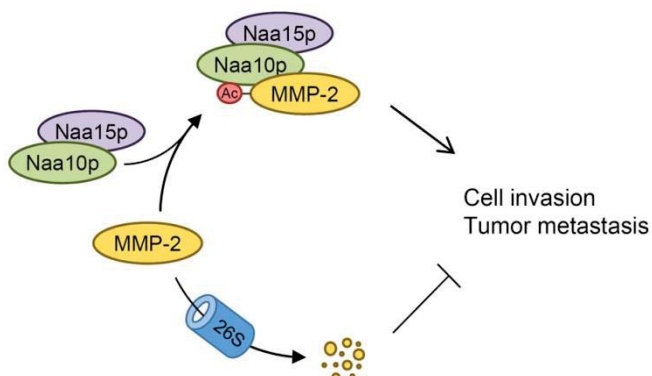
## Major achievements

### Research teams:



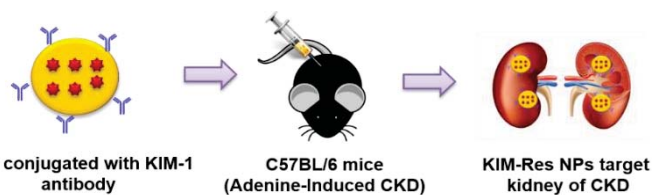
### Cancer

N- $\alpha$ -acetyltransferase 10 protein (Naa10p) is a poor prognostic factor the expression of which is correlated with metastasis and shorter survival in osteosarcomas. We propose that Naa10p can act as an oncogene by stabilizing MMP-2 protein expression in osteosarcomas. Our findings may provide a possible strategy for targeting Naa10p-MMP-2 regulation to prevent the highly metastatic property of osteosarcomas.



Effects of Naa10p on MMP-2 stabilization. In invasive osteosarcoma cells, Naa10p was highly expressed and formed a complex with Naa15p to acetylate and stabilize the MMP-2 protein thus contributing to cell invasion and metastasis.

### Renal Diseases

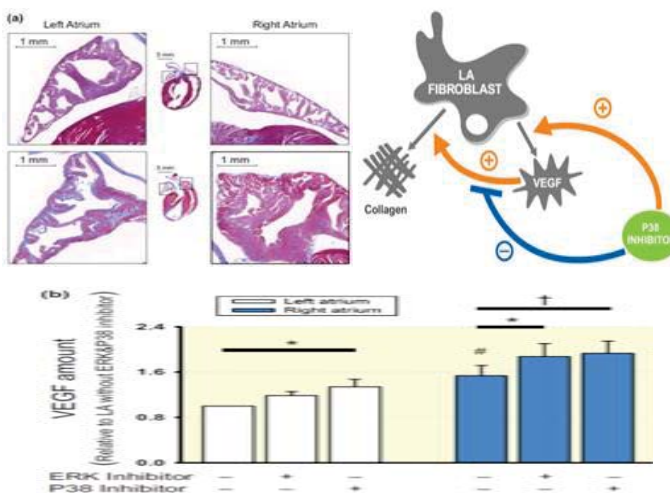


We used resveratrol-loaded nanoparticles (Res NPs) as a novel method for improving the pharmacokinetic properties of Res and analyzed the effect of Res NPs in chronic kidney disease (CKD)

Res NPs had low toxicity and induced autophagy. Res NPs inhibited the NLRP3 inflammasome and IL-1 $\beta$  secretion. Higher NLRP3 expression levels were observed in peripheral blood monocytic cells of CKD patients than healthy individuals. Treatment with KIM-1-Res NPs significantly reduced creatinine and protected against tubulointerstitial injury in murine model of CKD. Res NPs through NLRP3 inflammasome attenuation and autophagy induction may be as a strategy to prevent CKD.

### Cardiovascular Diseases

Atrial fibrosis plays a pivotal role in the pathophysiology of heart failure (HF). The left atrium (LA) experiences greater fibrosis than the right atrium (RA) during HF. Study elucidated differences in profibrotic activity between LA and RA fibroblasts may be caused by different responses to mitogen-activated protein kinase signaling.



a. Interstitial fibrosis of left atrium (LA) and right atrium (LA) tissues in healthy and heart failure rats.

b. Illustration of vascular endothelial growth factor (VEGF) on collagen production and interaction between VEGF and MAPK signaling in LA and RA.

### Genetic Medicine

Interleukin-6 (IL-6) is an inflammatory cytokines that plays a role in the

**Inflammation & Autoimmune**

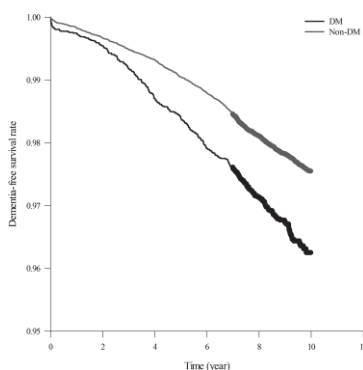
Possible associations of single-nucleotide polymorphisms (SNPs) of melatonin receptor type 1A (MTNR1A) and 1B (MTNR1B), with autoimmune thyroid disease in an ethnic Chinese (i.e., Taiwanese) population were examined.

	Genetic variant	Smoking	FH
	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
rs6553010			
AA	1	1.84 (1.20-2.81)*	5.74 (3.50-9.42)*
AG+GG	0.70 (0.50-0.97)*		
rs13140012			
AA	1	1.81 (1.19-2.77)*	5.66 (3.45-9.29)*
AT+TT	0.70 (0.49-0.96)*		
rs2119882			
TT	1	1.79 (1.17-2.75)*	5.62 (3.43-9.22)*
TC+CC	0.67 (0.48-0.93)*		
rs13140012/rs2119882			
AATT	1	1.81 (1.18-2.76)*	5.76 (3.51-9.47)*
Non AATT	0.61 (0.43-0.85)*		

\* p < 0.05; AOR, adjusted odds ratio; CI, confidence interval; FH, family history of thyroid disease.

Genetic variants of melatonin receptor type 1A and the AT haplotype of the combination of rs2119882 and rs13140012 were associated with GD susceptibility in an ethnic Chinese population.

**Evidence-Based Medicine**



**Background:** This study investigated whether incident hypertension, incident hyperlipidemia, or both, increased the dementia risk in patients with and without prior diabetes mellitus (DM).

**Major findings:** The dementia risk was higher in the DM cohort than in the non-DM cohort (adjusted hazard ratio (HR) = 1.47). In the non-DM cohort, patients with both hypertension and hyperlipidemia had a higher dementia risk (adjusted HR = 1.33).

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development of cancer. The relationships between IL-6 -174G>C polymorphism and bladder cancer risk are still inconclusive. A comprehensive literature search was performed to identify eligible studies regarding IL-6 -174G>C polymorphism and bladder cancer. Finally, five studies were included. In the fixed-effect analysis, significantly higher bladder cancer risks of 1.20 and 1.30 were found for dominant model (C/C+G/C vs. G/G) and recessive model (C/C vs. G/C+G/G), respectively. Especially for the Asian population, significantly greater bladder cancer risks of 1.63 and 1.54 were observed for dominant model and recessive model, respectively. In conclusion, our findings suggest that IL-6 -174G>C polymorphism is significantly associated with bladder cancer in the Asian population. Further studies with a larger sample size are needed to validate the effects of IL-6 polymorphisms on bladder cancer.

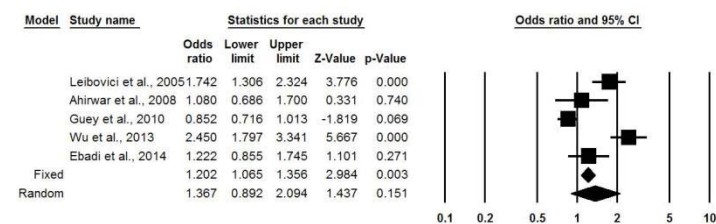


Fig. 2 Forest plot for the dominant model (C/C+G/C vs. G/G genotypes).

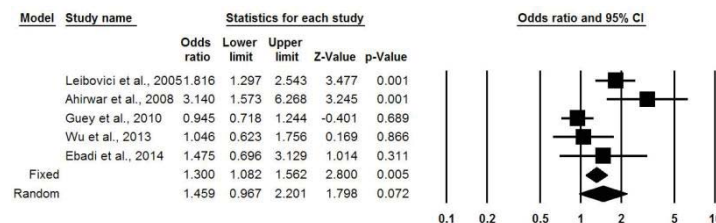


Fig. 3 Forest plot for the recessive model (C/C vs. G/C+G/G genotypes).

**Table 3** The pooled ORs and 95% CIs for IL-6 rs1800795 (-174G/C) polymorphism and bladder cancer risk stratified by ethnicity

No.	Model	C/C+G/C versus G/G (Dominant model)		C/C versus G/C+G/G (Recessive model)	
		OR (95%CI)	P-value	OR (95%CI)	P-value
Total	Fixed	1.20 (1.07-1.36)	0.003	1.30 (1.08-1.56)	0.005
	Random	1.37 (0.89-2.09)	0.151	1.46 (0.97-2.20)	0.072
Ethnicity					
Asian	Fixed	1.63 (1.32-2.00)	0.001	1.54 (1.07-2.21)	0.021
	Random	1.50 (0.89-2.55)	0.132	1.65 (0.85-3.19)	0.138
Caucasian	Fixed	1.03 (0.89-1.19)	0.700	1.23 (0.99-1.52)	0.059
	Random	1.21 (0.59-2.43)	0.600	1.30 (0.69-2.47)	0.421

**Major publications**

- Chien MH, Lee WJ, Yang YC, et al. N-α-acetyltransferase 10 protein promotes metastasis by stabilizing matrix metalloproteinase-2 protein in human osteosarcomas. *Cancer Lett.* 2018; 433:86-98.
- Y-F Lin, Y-H Lee, Y-H Hsu, Y-J Chen, Y-F Lin, F-Y Cheng and H-W Chiu. Resveratrol-loaded nanoparticles conjugated with kidney injury molecule-1 as a drug delivery system for potential use in chronic kidney disease. *Nanomedicine* 2017; 12:2741-2756.
- Chung CC, Kao YH, Yao CJ, et al. A comparison of left and right atrial fibroblasts reveals different collagen production activity and stress-induced mitogen-activated protein kinase signalling in rats. *Acta Physiol (Oxf)*. 2017 Aug;220(4):432-445. doi: 10.1111/apha.12835. Epub 2017 Jan 16.
- Zheng JQ, Lai HJ, Wang YH. et al. Association of stroke subtypes with risk of hip fracture: a population-based study in Taiwan. *Archives of Osteoporosis*. 2017 Nov 22;12(1):104.
- Lin JD, Yang SF, Wang YH, et al. Associations of melatonin receptor gene polymorphisms with Graves' disease. *PLoS One*. 2017; 12(9): e0185529.
- Fan YC, Hsu JL, Bai CH, et al. Increased dementia risk predominantly in diabetes mellitus rather than in hypertension or hyperlipidemia: a population-based cohort study. *Fan et al. Alzheimer's Research & Therapy* (2017) 9:7 DOI 10.1186/s13195-017-0236-z

## About

The School of Respiratory Therapy offers a Master of Science (M.S.) degree, with a specialization in respiratory therapy, to prepare future experts in the profession as well as advanced clinical practitioners.

Faculties in our programs integrate critical thinking and simulation into teaching and research in order to provide students opportunities to excel their profession. The healthcare systems in Taipei Medical University also provide students more chances to perform translational research.

We also offer a dual M.S. degree with the integrated master program of Respiratory Therapy in Georgia State University (GSU), USA.



Bing-Chang Chen  
Ph.D.

Professor and Director.

## This Program is for highly motivated and academically accomplished baccalaureate graduate who wants to:

1. To enhance the ability to perform respiratory care in the clinical site at an advanced level as a respiratory therapy specialist.
2. To develop the ability to examine the scientific basis of respiratory care procedures and evaluate technology used in respiratory care.
3. To develop professions in respiratory sciences for faculty in academic institutes.

## We have seven core research groups in the Master Program

1. Respiratory pharmacology and lung fibrosis
2. Diagnostics and therapy in critical respiratory care
3. Verification and development of respiratory therapy equipment
4. Long-term respiratory care and rehabilitation
5. Infectious pulmonary disease and tuberculosis
6. Environmental pulmonary disease
7. Inflammation-induced airway hyperreactivity

## Program highlights

1. 30 credits program
2. Web-enhanced program designed for the working professionals
3. Interdisciplinary research

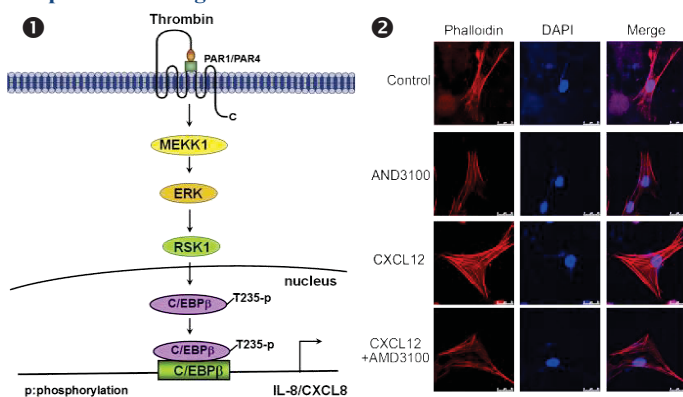
## Program information

1. Program of study (30 credits)
2. Respiratory therapy Core: 16 credits
3. Specialized Curriculum: 8 credits
4. Thesis: 6 credits

## Prospects after graduation

1. Advanced respiratory therapists
2. R&D in respiratory therapy and critical care medicine

## Representative figures



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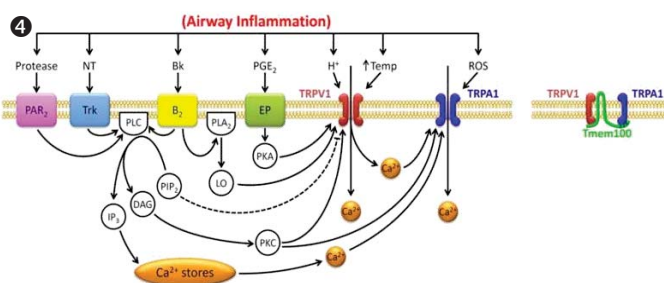
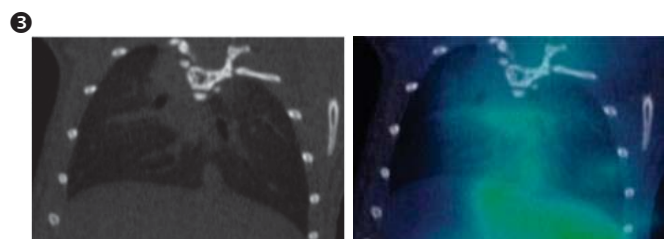
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- ① MEKK1/ERK/RSK1 mediates thrombin-induced C/EBPβ activation and IL-8/CXCL8 expression in lung epithelial cells.
- ② CXCR4 mediates CXCL12-stimulated stress fiber formation in lung fibroblasts
- ③ Determination of inflammopathology in mouse using CT(Left) and SPECT(Right)
- ④ Hypothesized mechanisms involved in the TRPA1-TRPV1 interaction in pulmonary sensory neurons

## Major publications

- [1] Hsu CC, Lee LY. Role of calcium ions in the positive interaction between TRPA1 and TRPV1 channels in bronchopulmonary sensory neurons. *J Appl Physiol* 2015; 118:1533-43.
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- [3] Huang ZW, Lien GS, Lin CH, et al. p300 and C/EBPβ-regulated IKKβ expression are involved in thrombin-induced IL-8/CXCL8 expression in human lung epithelial cells. *Pharmacol Res* 2017; 121:33-41.
- [4] Lai CY, Lai CH, Chuang HC, et al. Physicochemistry and cardiovascular toxicity of metal fume PM2.5: a study of human coronary artery endothelial cells and welding workers. *Sci Rep* 2016; 6:33515.
- [5] Hsu CC, Lin YS, Lin RL, Lee LY. Immediate and delayed potentiating effects of tumor necrosis factor-α on TRPV1 sensitivity of rat vagal pulmonary sensory neurons. *Am J Physiol Lung Cell Mol Physiol* 2017; (Accepted)
- [6] Weng CM, Chen BC, Wang CH, et al. The endothelin A receptor mediates fibrocyte differentiation in chronic obstructive asthma. The involvement of connective tissue growth factor. *Am J Respir Crit Care Med* 2013; 188:298-308.

## About

The International Master/Ph.D. Program in Medicine (IGPM) started recruiting students in the fall of 2016. This program offers both degree of Master/Ph.D. degree in medical sciences. IGPM provides its students with interdisciplinary research and clinical training opportunities in the world-class laboratories of doctoral faculty located both at campuses of Taipei Medical University (TMU) and at the affiliated hospitals in TMU healthcare system, which include TMU hospital, TMU Wanfang Hospital and TMU Shuang-Ho Hospital. Students will receive a fundamental orientation and training in the current field of biomedical sciences as well as mastery of the knowledge and investigative approaches in his or her chosen areas of specialization. In addition, International Clinical Training Program (ICTP) is also provided for resident and fellow training. Residents or fellows will receive certifications after finishing this program.



Yen-Chou Chen  
Ph.D.  
Professor and Director

## Eligibility

1. Non-citizen of Taiwan
2. Hold a bachelor degree in science related to biomedical fields (for applicants in Master program)
3. Hold a master degree in science or art related to biomedical fields (for applicants in Doctoral program)
4. An MD degree and at least two years of documented clinical training with publication(s) equivalent to a master's thesis (for applicants in Doctoral program)

## Missions

1. To prepare master candidates to have broad range of knowledge in the fields of medical sciences, leading to bolster their preparation for further study or entry into the biomedical workforce
2. To prepare doctoral candidates to become research professionals equipped to teach in university programs and for leadership positions in biotechnology and research

## Requirements for Master degree

1. 12 credits in Required Courses (including 6 credits in Thesis)
2. 18 credits in Elective Courses
3. Research Ethics (No credit)
4. Thesis
5. Pass oral thesis defense

## Requirements for Ph.D. degree

1. 18 credits in Required Courses (including 12 credits in Dissertation)
2. 12 credits in Elective Courses
3. Research Ethics (No credit)
4. Pass Qualification Examination (QE) to advance doctoral candidate
5. At least one article published in a SCI/SSCI/A&HCI/EI/THCI Core journal (ranked in top 50%) as the first author
6. Dissertation
7. Pass oral dissertation defense

## Staff and contact information

**Shing-Chuan Shen, Ph.D., Professor and Counselor**

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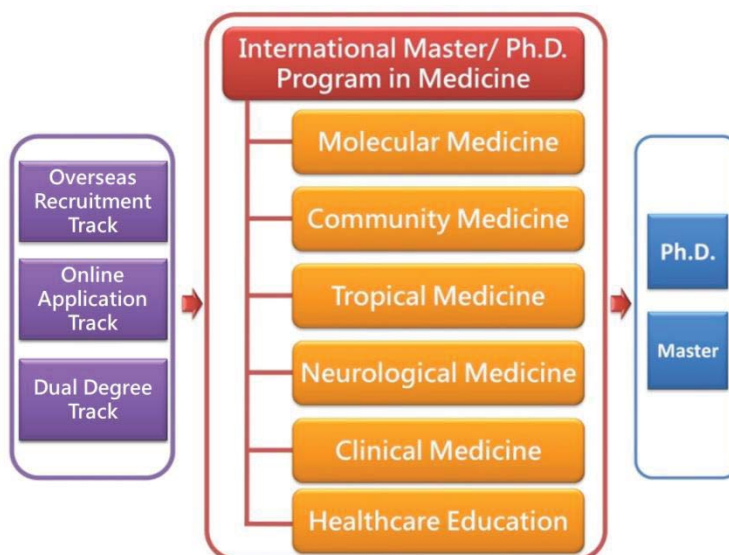
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URL: <http://igpm.tmu.edu.tw>;

<https://www.facebook.com/TMUIGPM/>



## Major publications

- [1] Cheng TC, Tu SH, Chen LC, et al. Down-regulation of L- fucosidase 1 expression confers inferior survival for triple- negative breast cancer patients by modulating the glycosylation status of the tumor cell surface. *Oncotarget* 2015; 6:21283-21300.
- [2] Chang TS, Wu YC, Ching CC, et al. Activation of IL6/IGF-IR confers poor prognosis of HBV-related hepatocellular carcinoma through induction of OCT4/NANOG expression. *Clinical Cancer Res* 2015; 21:201-10.
- [3] Yang SF, Lee WJ, Tan P, et al. Upregulation of miR-328 and inhibition of CREB-DNA-binding activity are critical for resveratrol-mediated suppression of matrix metalloproteinase-2 and subsequent metastatic ability in human osteosarcomas. *Oncotarget* 2015; 6:2736-53.
- [4] Guan SS, Chang J, Cheng CC, et al. Afatinib and its encapsulated polymeric micelles inhibits HER2-overexpressed colorectal tumor cell growth in vitro and in vivo. *Oncotarget* 2014; 5:4868-80.

## About

Under the umbrella of International Master/Ph.D. Program in Medicine which provides a wide range of master and doctoral degrees, the International Clinical Training Program (ICTP) provides opportunities for foreign clinicians to join the clinical training in three affiliated hospitals of TMU. The trainee includes residents, fellows and visiting scholars. The period may range from 1 month to 2 years depending on the training level and specialty. The trainees of ICTP programs may join the courses of International Master/Ph.D. Program in Medicine at school and participate in the patient care at hospitals. We encourage trainees to apply for International Master/Ph.D. Program in Medicine after finishing ICTP. Courses taken during the ICTP will be credited in the International Master/Ph.D. Program in Medicine. We value the diversity that visiting residents/fellows bring to our program, and they have every opportunity to experience what we have to offer.

## Eligibility

1. Non-citizen of Taiwan.
2. Hold either the M.D. degree certificate or the diploma given by College of Medicine.
3. Hold medical doctor license and clinical training experience for at least 1 year.
4. Be able to communicate in English.

## Notice

1. ICTP trainee is permitted making clinical decisions, diagnosis or giving advices on any medical issues during the program span under the supervision of mentors.
2. ICTP trainee has to choose from departments for apprenticeship.
3. Training contents, durations and further prerequisites vary from department to department.
4. Housing may be arranged upon request but is subject to availability; fees may apply and are subject to different dormitories.
5. ICTP trainee will receive a clinical training certificate issued by the university after finishing all training courses.

## Materials Required for Application

1. Application form.
2. Curriculum Vitae.
3. Copy of M.D. degree certificate or the diploma given by College of Medicine.
4. Copy of medical doctor license.
5. Certificate of clinical training experience.
6. At least one recommendation letter from the head of the department which the applicant belongs to at the hospital or the Dean of the Medical School.
7. Copy of valid passport.
8. Health record, immunization record within the last three months (prior the arrival).
9. Proof of personal health/accident insurance with overseas coverage or proof of national health insurance (prior the arrival).

## Training Fees

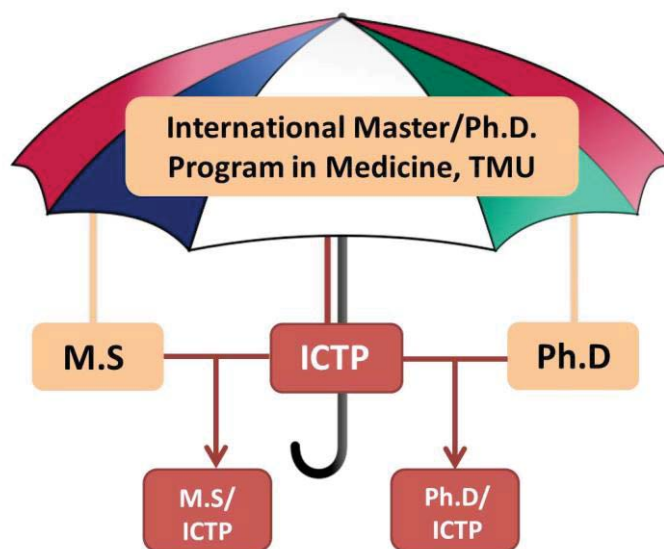
1. The fees vary according to the policy of the applied affiliation.
2. Students studied in TMU International Master/Ph.D. Program in Medicine are exempt from the fees.
3. The fees are non-refundable after registration.

## Staff and contact information

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## Rotation Clinical Departments

1. Breast Cancer Training Program
2. Cardiovascular Medicine
3. Gastroenterology and Hepatology
4. Laparoscopic Surgical Training Program
5. Minimal Invasive Surgery and Epigenetics of Gynecological Oncology
6. Minimally Invasive Thoracic Surgery
7. Minimally Invasive Urologic Surgery
8. Neurology
9. Orthopaedics Surgery and Sports Medicine
10. Physical Medicine and Rehabilitation
11. Plastic and Reconstructive Surgery
12. Pulmonary Medicine
13. Radiology
14. Renal Medicine

**Major research aims**

Research in medical education aims at examining teaching and learning processes and the human attributes, interactions, organizations, and institutions that shape outcomes of medical education. Educational research encompasses a broad range of methodologies, and the development of new methods is sometimes used. For instance, we conducted qualitative studies on students' reflective journals to ensure the reasonableness of our curricular innovations in medical humanities. These innovations included early clinical exposure courses and teaching medical ethics. To find convenient and effective models for teaching, learning and assessing clinical skills, our empirical studies focus on simulation education, technology-enhanced learning and competency-based education.



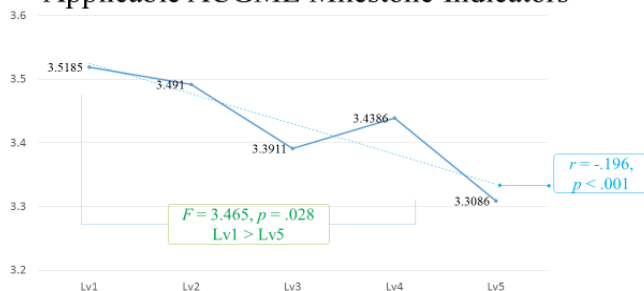
Wu, Chien-Chih  
M.D., Ph.D.

**Major achievements**

1. The International Conference of Clinical Competence and Simulation Education in Healthcare (Since 2013).
2. Authenticated training program for IMPROVING SIMULATION INSTRUCTIONAL METHODS (ISIM).
3. The Establishment of ACGME Milestone Project in Acta Anaesthesiologica Taiwanica.
4. The Development of a Situational Judgement Checklist for Collaborative Ethics Teaching.

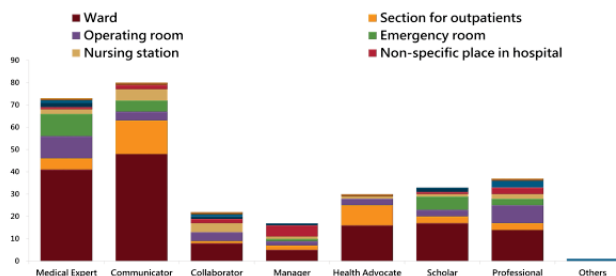
**Representative figures**

**1 Results of Delphi Method to Identify the Applicable ACGME Milestone Indicators**



This table shows that all ACGME competency indicators declined significantly in Level 5 according to the consensus of 38 local experts.

**2 CanMEDS Roles as Framework for Analyzing Taiwanese Medical Students' Reflective Journals: an Exploratory Research for Cross-cultural Compatibility**



149 reflective journals of Year-6 medical students (M/F = 45/12); The local scenarios embodied all CanMEDS key competencies. Only one (0.7%) scenario cannot fit in with the CanMEDS framework. The role expectation for a good Communicator was mostly emphasized. In most scenarios, more than one role was involved.

**Staff and contact information**

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**3 An Exploratory Study on Simulated Clinical Skill Learning Satisfaction in the Flipped Approach**



Seventy eight fifth grade medical students took flipped nasogastric insertion course and filled learning satisfaction questionnaire. The questionnaire was consisted of three domains satisfaction in learning nasogastric insertion knowledge, nasogastric insertion skill, and affective learning. The result showed that:

1. students have high learning satisfaction in flipped classroom.
2. There was no statistical difference among three domains and overall average of students' learning satisfaction in flipped classroom.

Table 1 Satisfaction on Bloom's taxonomy of learning domains

Domain	M	SD	t-value	p-value
Cognitive	4.03	0.72	6.45	< .001
Psychomotor	4.12	0.64	8.44	< .001
Affective	4.10	0.71	7.46	< .001

One-sample t-test, test value: 3.5.

**Major publications**

- [1] Lin CW, Clinciu DL, Swartz MH, et al. An integrative OSCE methodology for enhancing the traditional OSCE program at Taipei medical university hospital-a feasibility study. BMC Med Educ 2013; 13:102.
- [2] Tang KP, Kang. YN, Ho JJ, et al. CanMEDS roles as framework for analyzing Taiwanese medical students' reflective journals: an exploratory research for cross-cultural compatibility. Bulletin of Medical Education - Taichung Veterans General Hospital 2015; 18:21-8.
- [3] Tang KP, Kang YN, Wu CC, et al. The Educational Implementation of Duo-Case Method in Teaching Medical Ethics on Ventilator-Dependent Patient Care. Bulletin of Medical Education - Taichung Veterans General Hospital 2017; 20:3-12.
- [4] Kang YN, Lin CW, Chen CY, et al. An Exploratory Study on Simulated Clinical Skill Learning Satisfaction in the Flipped Approach. Journal of Taiwan Society for Simulation in Healthcare 2016; 3:23-31.

## About

The International Ph.D. Program for Cell Therapy and Regeneration Medicine (IPCTRM) has begun to recruit students for the inaugural Fall semester 2017. The mission of this program is to promote translational medicine and clinical trials of cell/stem cell based therapy. Along with TMU's university-grade Center for Cell Therapy and Regeneration Medicine (TMU-CTRM), IPCTRM aims to cultivate talented young researchers in diverse fields, including immune cell applications in cancer treatment; blood and mesenchymal stem cell therapies for regenerative processes, wound healing, graft-versus-host disease, and multiple sclerosis; and drug screening platform with cancer stem cells and disease-specific induced pluripotent stem cells. IPCTRM brings experts and scientists together to not only facilitate outstanding research in basic studies but also place major emphasis on clinical translational medicine and industrial cell/stem cell product development.



Rita Yen-Hua Huang  
Ph.D.  
Distinguished Professor  
and Director

## Major Achievements

1. Establishment of university-grade "TMU Center for Cell Therapy and Regeneration Medicine" for integration of cell/stem cell researches between TMU and TMU-affiliated hospitals. ❶
2. Founding of "TMU Distinguished Stem Cell Translational Medicine Research Group".
3. Investigation of safety and efficacy of small blood cells and mesenchymal stem cells in preclinical animal studies. ❷
4. Investigation of niche hypoxia synergistically cooperates with the symmetric division and cell migration of Germ Stem Cells. ❸
5. Inauguration of Good Tissue Practice (GTP) Laboratory for preparation of clinical grade cells/stem cells for clinical use. ❹
6. Reinforcement of collaboration and transition between laboratory and patent/industry development.

## Program Highlights

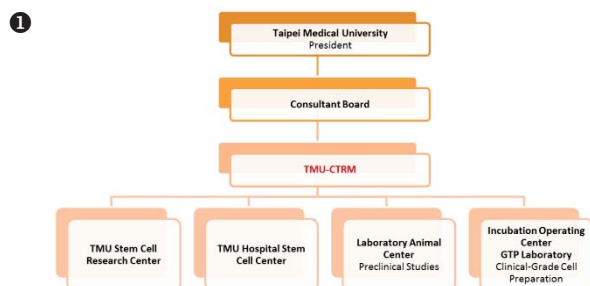
1. Cancer immunotherapy
2. Pluripotent stem cells: embryonic germ cells and iPS cells
3. Pluripotent small blood stem cells in clinical trials
4. Mesenchymal stem cells in clinical trials
5. Drug screening platform with disease iPS cells
6. FDA/TFDA regulations on cell therapy
7. CMC/ Pharm-Tox/ clinical trial/ IRB training

## Career Opportunities

Our graduates will become leaders in the following areas:

1. Clinical research coordination
2. Regulation development and review
3. Research and development
4. Clinical trial drafting and review
5. Academic research
6. Cell manufacturing process

## Representative Figures



Organization of TMU Center for Cell Therapy and Regeneration Medicine.

## Staff and contact information

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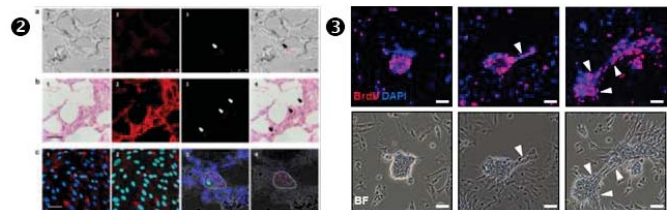
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<http://cctrm.tmu.edu.tw/main.php>



- ❷ HSA coated-fluorescent nanodiamond (FND)-labeled placenta chorion mesenchymal stem cells (pcMSCs) in pig lung tissues.
- ❸ Proliferation and metastasis of embryonic germline stem cell in a hypoxic micro-environment during the early embryonic stage.



The GTP Laboratory has two class 1,000 cleanrooms with clinical-grade flow cytometry, biological safety cabinet, centrifuge, and incubators.

## Major Publications

- [1] A phase I study of autologous adult peripheral small blood stem cells for human guided bone regeneration in dental implantation. 2018 (Under Revision)
- [2] Lin YH, Chen YH, Chang HY, et al. Chronic niche inflammation in endometriosis-associated infertility: current understanding and future therapeutic strategies. *Int J Mol Sci* 2018; 19:2385.
- [3] Kuo YC, Au HK, Hsu JL, et al. IGF-1R promotes symmetric self-renewal and migration of alkaline phosphatase<sup>+</sup> germ stem cells through hif-2 $\alpha$ -oct4/cxcr4 loop under hypoxia. *Stem Cell Rep* 2018; 10:524-37.
- [4] Su LJ, Wu MS, Hui YY, et al. Fluorescent nanodiamonds enable quantitative tracking of human mesenchymal stem cells in miniature pigs. *Sci Rep* 2017; 7:45607.
- [5] Chang TS, Wu YC, Ching CC, et al. Activation of IL6/IGF-1R confers poor prognosis of HBV-related hepatocellular carcinoma through induction of OCT4/NANOG expression. *Clin Cancer Res* 2015; 21:201-10.
- [6] Chang TS, Wu YC, Tung SY, et al. Alpha-fetoprotein measurement benefits hepatocellular carcinoma surveillance in patients with cirrhosis. *Am J Gastroenterol* 2015; 110:836-44.
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- [8] Huang YH, Chin CC, Ho HN, et al. Pluripotency of mouse spermatogonial stem cells maintained by IGF-1 dependent signaling pathway. *FASEB J* 2009; 23:2076-87.



## Research Centers

Cochrane Taiwan 17

Biostatistics Center 18

## Major research aims

Cochrane Taiwan is one of the official Cochrane societies supporting the global work of Cochrane and maximizing the use and the impact of Cochrane Reviews for Taiwan and East Asian region. Funded and based at Taipei Medical University, we support the education and the production of Cochrane Systematic Reviews. It is our goal to maximize the impact of Cochrane Reviews by disseminating and implementing the findings to health professionals, researchers, decision makers and the public. Research fields:

1. Evidence-Based Medicine (EBM): education, research and promotion
2. Systematic review and meta-analysis research
3. Knowledge translation (KT) and shared-decision making (SDM)
4. EBM application: health technology assessment (HTA), comparative effectiveness analysis (CEA), clinical practice guideline (CPG), etc.



Chieh-feng Chen  
M.D., M.P.H., Ph.D.  
Director

## Major achievements

### Activities:

1. We form the East Asian Cochrane Alliance (EACA) by inviting representatives from Hong Kong, Japan, Korea, Singapore, and Taiwan with the aim to promote the activities of Cochrane systematic reviews since 2007.
2. Recognized by Cochrane Translation Group, Cochrane Taiwan is the leading position of translating Cochrane Systematic Review abstracts into Mandarin.
3. In 2016, we held 11 workshops and 7 lectures related to EBM. We also co-organized activities with Taiwan Joint Commission of Hospital Accreditation on 16th Healthcare Quality Improvement Circle and EBM competition among Ministry Hospitals. For training EBM related website search, we carried out the onsite teaching 7 times at Ministry Hospitals.

### Academics:

1. During the study period, Directors of nursing (DON)s' EBP knowledge and skills increased, but their beliefs and attitudes did not significantly change. Furthermore, the use of Internet-based resources, including web portals, electronic textbooks, electronic journals, and evidence-based online databases, increased. Most barriers significantly declined after the intervention.
2. Five eligible studies were retrieved and analyzed. We divided sentinel lymph node (SLN) metastasis into two categories: SLN micrometastasis and SLN macrometastasis. In patients with 1 or 2 SLN micrometastasis, no significant difference was observed in overall survival (OS), disease-free survival (DFS), or recurrence rate between the axillary lymph node dissection (ALND) and non-ALND group. For patients with 1 or 2 SLN macrometastasis, only one trial with a moderate risk of bias was included, and non-ALND was the preferred management overall. However, ALND might be appropriate for patients who placed a greater emphasis on longer-term survival at any cost.

## In-service Master Program for Applied Evidence-Based Medicine (Graduate Institute of Clinical Medicine)

Total 30 credits (20 required credits including thesis and 10 elective credits) with multidisciplinary research team.

## Staff and contact information

**Chieh-feng (Cliff) Chen, M.D., M.P.H., Ph.D., Associate Professor and Director**

**Ken N. Kuo, M.D., EBM Consultant**

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## Representative figure

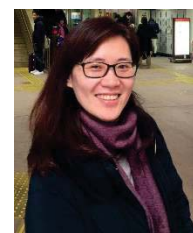


## Major publications

- [1] Chen C, Tam KW, Kuo KN. Choosing wisely in health care. *J Formos Med Assoc.* 2018 Jul 3.
- [2] Hou WH, Wang JD, Hsieh CL, et al. Rasch Analysis of the 9-Item Shared Decision Making Questionnaire in Women With Breast Cancer. *Cancer Nurs.* 2018 Apr
- [3] Shen WC, Loh EW, Tam KW, et al. Efficacy and Safety of Rituximab for the Treatment of Graves' Orbitopathy : A Meta-analysis of Randomized Controlled Trials. *Pharmacotherapy.* 2018 May
- [4] Chou YY, Loh EW, Tam KW, et al. The gap between currently available evidence and awareness in clinical practice of wound care: It is the time to shower earlier. *Surgery.* 2018 Mar
- [5] Loh EW, Chou YY, Tam KW, et al. Fluid Resuscitation in Patients With Severe Burns: A Meta-analysis of Randomized Controlled Trials. *Acad Emerg Med.* 2018 Mar
- [6] Loh EW, Yen Y, Tam KW, et al. Tyrosine kinase inhibitors for advanced or metastatic thyroid cancer: a meta-analysis of randomized controlled trials. *Curr Med Res Opin.* 2018 May
- [7] Tam KW, Chen C, Hou WH, et al. Validation of the European Health Literacy Survey Questionnaire in Women With Breast Cancer. *Cancer Nurs.* 2018 Mar/Apr

## Major research aims

The Research Center of Biostatistics is a research service facility under the College of Management in Taipei Medical University. Jin-Hua Chen, the center director, collaborates with senior professor Kuang-Fu Cheng in research on statistical methodology of associations between genetics and diseases, and in research on meta-analysis statistical methods. The Center provides consulting on study design, data management, biostatistical issues and data analysis problems. Research fellows and biostatisticians in the Center collaborate closely with investigators and medical doctors within the University, and analyze the database of National Health Insurance program of Taiwan to investigate risk factors, diagnoses, treatments and prognosis for human diseases. The Center developed “Data Analysis & Guiding System-Cloud, DAGS-C” and “I-Clinical”, which are web-based user-friendly statistical analyzing systems.



Jin-Hua Chen  
Ph.D.  
Director

## Major achievements

1. I-Clinical: helping investigators to choose the appropriate sample size, generate randomization plan from aspects of clinical studies and perform basic statistical analysis without the burden of downloading software.
2. Data Analysis & Guiding System-Cloud, DAGS-C: a user-friendly statistical analyzing system. (<http://www.r-web.com.tw/>)
3. The purpose of our study was to find Bayesian estimates for the Hurst dimension of a Fractional Brownian motion with a Beta prior when the process is observed at discrete times. Overestimation is observed though the overestimation is less severe as real  $H$  goes up. In addition, the estimated  $H$  decreases as Beta parameters go up given an Alpha value. In contrast, the estimated  $H$  increases as Alpha parameters go up given a Beta value. For the real-world data, the 2011 daily Taiwan stock index was used and the estimated Hurst index was 0.21.
4. A potential association between antidepressant and occurrence of dementia after controlling for the status of depression was observed. The hazard ratio (HR) of dementia among antidepressant users with depression was 2.42 (95% confidence interval (CI): 1.15-5.10), for those without depression was 4.05 (95% CI: 3.19-5.15), compared to antidepressant non-users respectively.
5. We found a prospective link between Chronic rhinosinusitis (CRS) and the subsequent development of cholesteatoma within a follow-up period of 8 years [representative figure]. After adjusting for potential confounders, patients with CRS had a 69% increased risk of cholesteatoma within 8 years, compared with those without CRS (HR, 1.69; 95% CI, 1.23-2.32).
6. We found that the risk of Parkinson disease (PD) was significantly higher in the autoimmune rheumatic diseases (ARDs) patients. The risk of PD was 1.37 times greater in ARD patients than in controls after adjustment for age, sex, and comorbidities.
7. Thoracic RT might be associated with overall survival in patients with unresectable stage IIIB-IV EGFR-mutant lungadenocarcinomas who received and responded to EGFR TKI treatment. The adjusted hazard ratio derived for thoracic RT for lung tumor after EGFR TKI use and tumor response compared with EGFR TKI treatment alone was 0.72 (95% CI: 0.60-0.85).

## Staff and contact information

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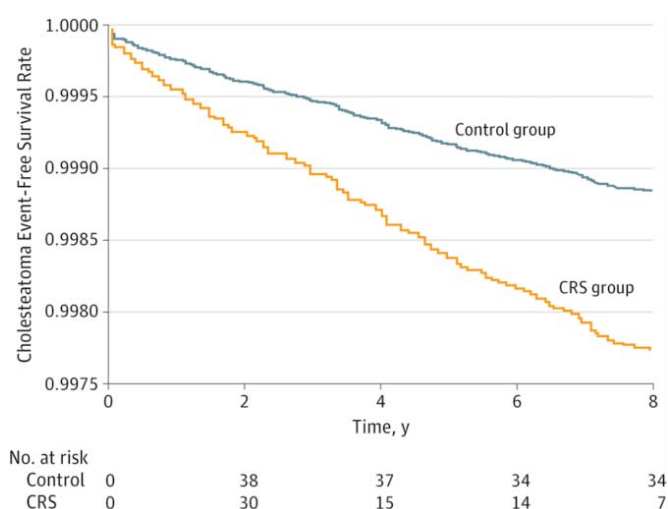
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URL: <http://biostat.tmu.edu.tw/>

<http://www.r-web.com.tw>



## Representative figures



(publications [3]) Cholesteatoma-Free Survival Rates Among Patients With Chronic Rhinosinusitis (CRS) and Those Serving as Controls. Significance at  $P < .001$  was determined with a log-rank test.

## Major publications

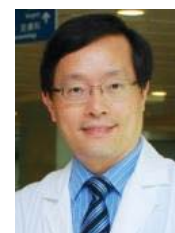
- [1] Chen CY, Shafie K., Lin YK. Bayesian estimation of the Hurst parameter of fractional Brownian motion. *Communications in Statistics-Simulation and Computation* 2017; 46:4760-66.
- [2] Then CK, Chi NF, Chung KH, et al. Risk analysis of use of different classes of antidepressants on subsequent dementia: A nationwide cohort study in Taiwan. *PLoS ONE* 2017;12: e0175187.
- [3] Kuo CL, Yen YC, Chang WP, et al. Association between middle ear cholesteatoma and chronic rhinosinusitis. *JAMA Otolaryngol Head Neck Surg* 2017; 143:757-63.
- [4] Chang CC, Lin TM, Chang YS, et al. Autoimmune rheumatic diseases and the risk of Parkinson disease: a nationwide population-based cohort study in Taiwan. *Ann Med*. 2018;50:83-90.
- [5] Yen YC, Hsu HL, Chang JH, et al. Efficacy of thoracic radiotherapy in patients with stage IIIB-IV epidermal growth factor receptor-mutant lung adenocarcinomas who received and responded to tyrosine kinase inhibitor treatment. *Radiother Oncol* 2018; [Epub ahead of print].

## Research Groups

Anesthesiology	20
Cardiovascular Medicine	21
Emergency Medicine	23
Gastroenterology	25
Microbiology & Immunology Research	26
Neuroscience	28
Obesity Medicine	34
Oncology	35
Orthopedic	40
Pediatrics	43
Pulmonary Research	47
Radiology	50
Rehabilitation Medicine	53
Renal Medicine	55
Sleep Medicine	57
Tropical Medicine Research	59
Woman Health	60

**Major research aims**

Perioperative medicine was consisted of preoperative assessment for various comorbidities, intraoperative management and adverse outcomes, such as postoperative complications and mortality. Using big sample size from Taiwan National Health Insurance Research Database (NHIRD, Taiwan), avoiding of selection and participation bias. We have studied the incidence, prevalence, managements, correlations and associations of various diseases and surgeries, and important information of healthcare utilization. Our team has published over 60 pieces of SCI papers with high impact factor (IF), 4 papers IF>10, and 16 papers IF>5 since 2012. Besides the perioperative issue, other important territories were also involved, such as traumatic brain injury, diabetes, stroke, mental disorders, and traditional Chinese medicine. In addition to the retrospective cohort studies, the evidence-based systematic review with meta-analysis was also further integrated to expect another new era of research in perioperative medicine.



Ta-Liang Chen  
M.D., Ph.D.

**Major achievements**

1. Perioperative outcomes for patients with psychiatric diseases.
2. Risk factors and outcomes of diabetes, stroke, traumatic brain injury, SLE, fractures, and epilepsy.
3. Prevalence, characteristics, associated factors, and outcomes of the usage of traditional Chinese medicine (TCM)

**Representative data**

①

**Table** —Risk of postoperative complications associated with diabetes in the multiple logistic regression models\*

	No diabetes (%)	Diabetes (%)	OR (95% CI)†
<b>Postoperative complications</b>			
Septicemia	4.2	10.0	2.76 (2.50–3.04)
Pneumonia	2.7	4.6	1.88 (1.65–2.14)
Stroke	2.8	4.4	1.70 (1.49–1.94)
Acute renal failure	0.7	2.4	3.59 (2.88–4.48)
Deep wound infection	0.8	1.0	1.33 (1.04–1.70)
Acute myocardial infarction	0.2	0.7	3.65 (2.43–5.49)
Any of the above	9.6	19.2	2.42 (2.26–2.60)
Any noninfectious complications	6.9	14.0	2.37 (2.18–2.56)
Any infectious complications	3.6	7.2	2.23 (2.00–2.49)
30-day postoperative mortality	0.8	1.3	1.84 (1.46–2.32)
Prolonged length of hospital stay	13.2	25.2	2.30 (2.16–2.44)
ICU stay	29.0	38.8	1.67 (1.59–1.76)
Increased medical expenditure	18.0	22.0	1.32 (1.25–1.40)

- ① The propensity score-matched study demonstrated that diabetes increases postoperative mortality, consumption of medical resources, and complications, particularly for acute myocardial infarction and renal failure, in patients with diabetes undergoing noncardiac surgeries.
- ② The follow-up results showed that patients with epilepsy were 4.6 times more likely than the non-epilepsy group to experience gastrointestinal hemorrhage (13.4 vs 2.9 per 1000 person-years), with an adjusted HR of 2.97 (95% CI, 2.49–3.53) after controlling for demographic factors and comorbidities.
- ③ Compared with controls had no mental disorders, the risk of mortality was significantly higher in schizophrenic patients with frequent psychiatric visits, previous psychiatric hospitalizations, and use of emergency services before surgery.

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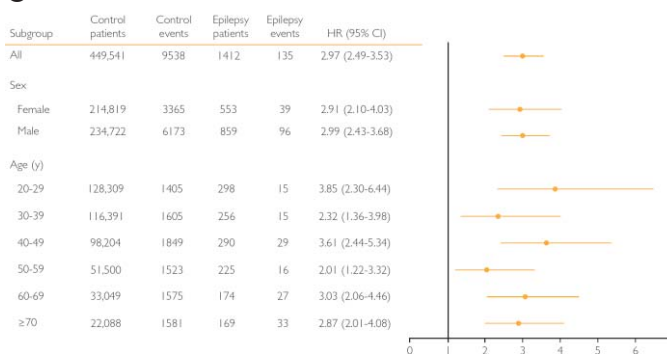
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②



**FIGURE.** Sex and age stratification of hazard ratios (HRs) and 95% CIs for gastrointestinal hemorrhage in association with epilepsy. Data are presented as No. of patients or events unless indicated otherwise. \*Graph at right depicts HRs.

③

**TABLE.** Risks of Postoperative Mortality After Complications for Surgical Patients With Severity of Schizophrenia Preoperatively

	Patient Number	Mortality OR (95% CI)
<b>Preoperative schizophrenia-related outpatient visits</b>		
Without mental disorders (no visit)	35,868	1.00 (reference)
Schizophrenic patients with 1–2 visit	2599	1.95 (1.25–3.02)
Schizophrenic patients with 3–18 visits	1955	2.62 (1.67–4.12)
Schizophrenic patients with 19–48 visits	2174	2.70 (1.72–4.23)
Schizophrenic patients with ≥49 visits	2239	3.97 (2.66–5.92)
<i>P</i> value for trend	<0.0001	
<b>Severity of schizophrenia</b>		
Controls	35,868	1.00 (reference)
General schizophrenia	7433	2.54 (1.93–3.34)
Severe schizophrenia	1534	3.69 (2.25–6.03)

**Major publications**

- [1] Yeh CC, Liao CC, Chang YC, et al. Adverse outcomes after noncardiac surgery in patients with diabetes: a nationwide population-based retrospective cohort study. *Diabetes Care* 2013; 36:3216–21.
- [2] Yeh CC, Wang HH, Chou YC, et al. High risk of gastrointestinal hemorrhage in patients with epilepsy: a nationwide cohort study. *Mayo Clin Proc* 2013; 88:1091–8.
- [3] Liao CC, Shen WW, Chang CC, et al. Surgical adverse outcomes in patients with schizophrenia: a population-based study. *Ann Surg* 2013; 257:433–8.
- [4] Lin JA, Liao CC, Lee YJ, et al. Adverse outcomes after major surgery in patients with systemic lupus erythematosus: a nationwide population-based study. *Ann Rheum Dis* 2014; 73:1646–51.
- [5] Liao CC, Lin CS, Shih CC, et al. Increased risk of fracture and postfracture adverse events in patients with diabetes: two nationwide population-based retrospective cohort studies. *Diabetes Care* 2014; 37:2246–52.

### Major research aims

Cardiovascular disease remains one of the leading causes of death in the world. My lab has devoted to deal with the cardiovascular disease especially in the field of cardiac arrhythmia, investigate the probable mechanisms and treatment either in basic research or in clinical applications. We had established a series of platform and animal models for research of the mechanism and potential treatment of cardiac disease. The research scope involves both atrial and ventricular arrhythmia and their potential etiologies such as renal failure, electrolytes imbalance, gender, dyslipidemia, chronic obstructive pulmonary disease, degenerated heart diseases (ex. Sinus node dysfunction), and the use of medication (ex. Non-Steroidal Anti-Inflammatory Drug (NSAID), novel oral anticoagulant (NOAC), etc), or their potential therapeutic agents such as Histone deacetylase (HDAC) inhibitor or antioxidant.

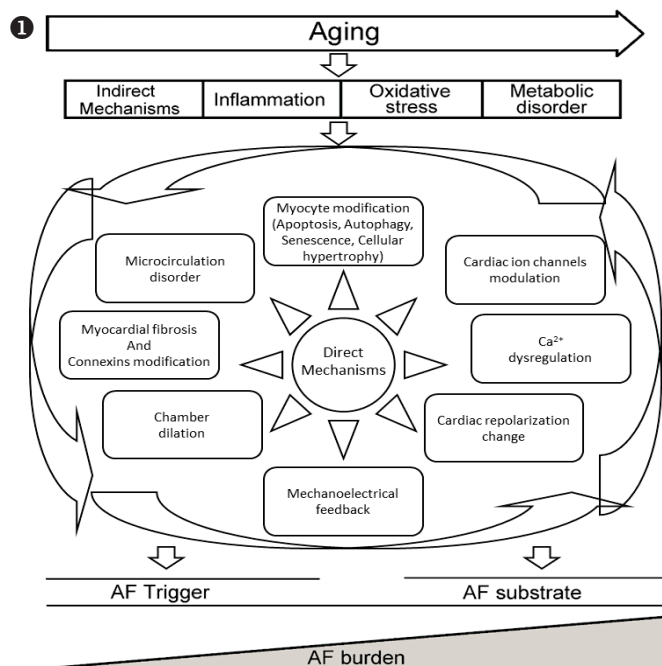


Yi-Jen Chen  
M.D., Ph.D.

### Major achievements

1. Discovery the therapeutic potential of HDAC inhibitor and antioxidant on treatment of atrial fibrillation, which may reduce atrial arrhythmogenesis through multiple target modifications.
2. Explore the role of renal failure, electrolytes imbalance, gender, dyslipidemia, degenerated heart (ex. Sinus node dysfunction), and the use of medication (ex. NSAID) in the pathogenesis of atrial tachyarrhythmia. These studies point out the electrical interactions of sinus node and pulmonary vein cardiomyocytes and dysregulated calcium homeostasis in the pathogenesis of atrial fibrillation (Figure 2).
3. Investigation of the mechanism how epicardial fat, adipocytokines, and fatty acids modulating Ionic currents and electrophysiologic characteristics of atria, which may potentiate the atrial fibrillation occurrence (Figure 3).
4. Research the regional difference of electrophysiological properties and the impact of absence of androgen receptor in RVOT - the potential ventricular tachycardia origin, which may provide better understanding or inspire novel therapy for RVOT associated VT.
5. Study of aging effect on atrial arrhythmia including aging associated cardiovascular comorbidities, oxidative stress, calcium dysregulation, atrial myopathy with apoptosis, and fibrosis, which all contribute to the genesis of AF (Figure 1).

### Representative figures



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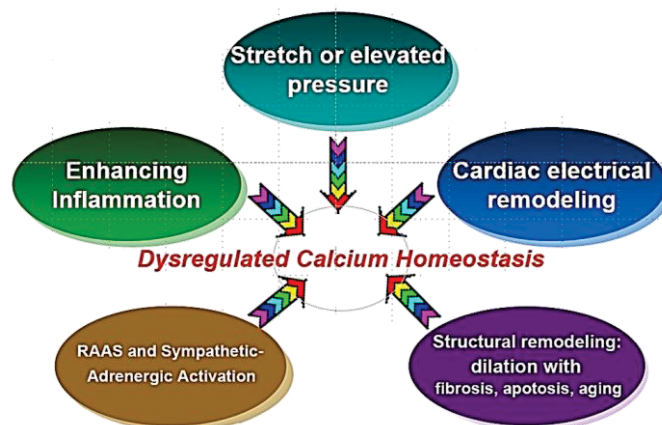
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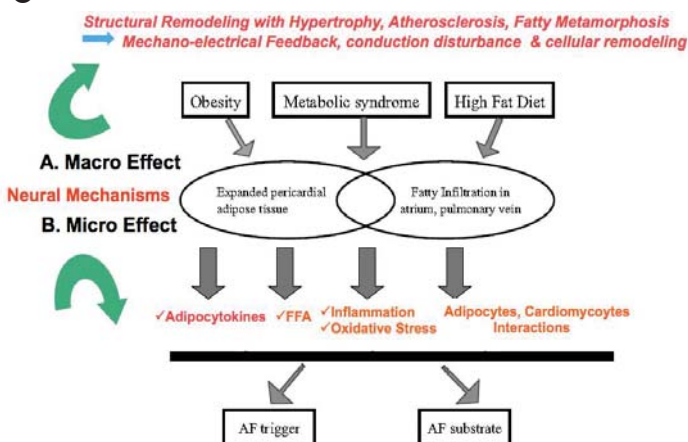
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3



### Major publications

- [1] Tsai WC, Lu YY, Chen YC, et al. Ablation of androgen receptor gene triggers right ventricular outflow tract ventricular tachycardia. *Int J Cardiol* 2015; 189:172-81.
- [2] Huang SY, Chen YC, Kao YH, et al. Renal failure induces atrial arrhythmogenesis from discrepant electrophysiological remodeling and calcium regulation in pulmonary veins, sinoatrial node, and atria. *Int J Cardiol* 2016; 202:846-57
- [3] Hu YF, Chen YJ, Lin YJ, et al. Inflammation and the pathogenesis of atrial fibrillation. *Nat Rev Cardiol* 2015; 12:230-43.
- [4] Lkhagva B, Kao YH, Chen YC, et al. Targeting histone deacetylases: A novel therapeutic strategy for atrial fibrillation. *Eur J Pharmacol* 2016; 781:250-7.
- [5] Chang CJ, Cheng CC, Chen YC, et al. Gap junction modifiers regulate electrical activities of the sinoatrial node and pulmonary vein: Therapeutic implications in atrial arrhythmogenesis. *Int J Cardiol* 2016; 221:529-36.

### Major research aims

Base on the theory of inflammation and dyslipidemia we establish a series platform focusing on research to investigate the pathophysiology, mechanisms and treatments on cardiovascular disease, especially for metabolic disorder-induced and infection-induced atherosclerosis. Incorporating the concept of translational medicine, we find clinical problems, investigate the probable mechanisms and treatment at laboratory, and return our findings to clinical applications finally. To increase the clinical care quality of patients is our ultimate goal.

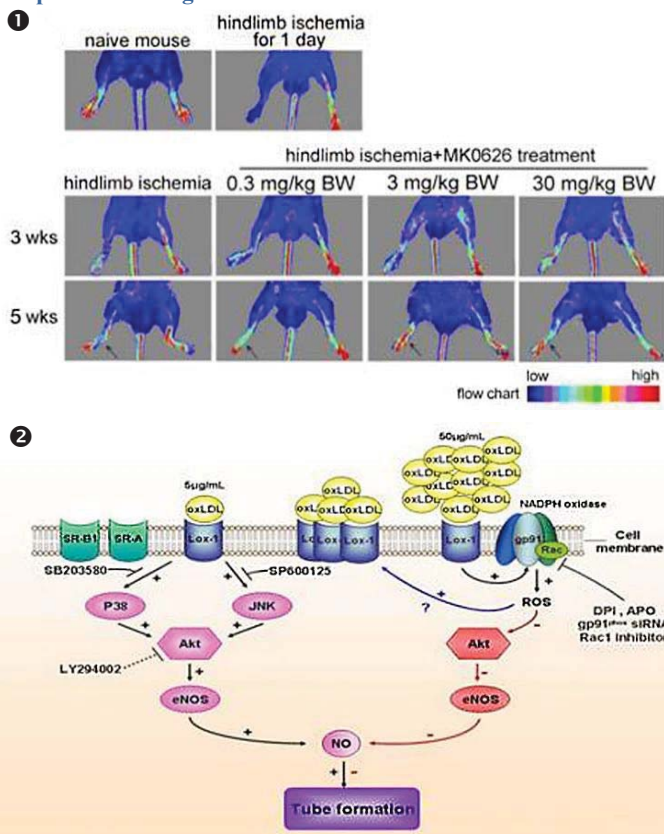


Chun-Yao Huang  
M.D., Ph.D.

### Major achievements

1. We highlight the therapeutic vasculogenesis potential of the Dipeptidyl peptidase 4 (DPP-4) inhibitor, statin, and lycopene by promoting endothelial progenitor cell (EPC) functions (figure 1).
2. Previous studies on dyslipidemia focus on the transportation function of each lipoproteins, We investigate the direct effects of oxidized low density lipoprotein (ox-LDL) and high density lipoprotein (HDL) on endothelial cell and EPCs. We explore oxLDL has concentration-dependent bi-phasic effects on EPCs function, and moderate to high concentrations of HDL paradoxically impaired EPCs tube formation in the absence of oxLDL. Under high ox-LDL condition, High HDL would reverse the adverse effect driven by ox-LDL (figure 2).
3. Bacterial infection, such as *C. pneumonia* and *P. gingivalis* may act as a potent virulence factor, contributing to the tumorigenesis and atherogenesis (figure 3).
4. We explore several useful clinical biomarkers which can detect subclinical atherosclerosis for early intervention to prevent from the full brown cardiovascular disease.

### Representative figures



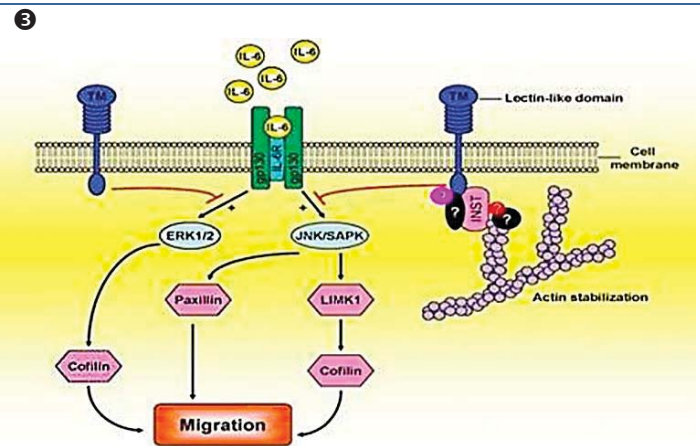
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### Major publications

- [1] Huang CY, Tsai CS, Chen CH, et al. Eotaxin-2 increased toll-like receptor 4 expression in endothelial cells in vitro and exacerbates high-cholesterol diet-induced atherogenesis in vivo. *Am J Transl Res* 2016; 8:5338-53.
- [2] Tsai CS, Lin YW, Huang CY, et al. Thrombomodulin regulates monocyte differentiation via PKC $\delta$  and ERK1/2 pathway in vitro and in atherosclerotic lesion. *Sci Rep* 2016; 6:38421.
- [3] Huang CY, Shih CM, Tsao NW, et al. The GroEL protein of *Porphyromonas gingivalis* regulates atherogenic phenomena in endothelial cells mediated by toll-like receptor 4 expression. *Am J Transl Res* 2016; 8:384-404.
- [4] Chiang KH, Cheng WL, Shih CM, et al. Statins, HMG-CoA Reductase Inhibitors, Improve Neovascularization by Increasing the Expression Density of CXCR4 in Endothelial Progenitor Cells. *PLoS One* 2015; 10:e0136405.
- [5] Lin FY, Tsao NW, Shih CM, et al. The biphasic effects of oxidized-low density lipoprotein on the vasculogenic function of endothelial progenitor cells. *PLoS One* 2015; 10:e0123971.
- [6] Lu HY, Huang CY, Shih CM, et al. Dipeptidyl peptidase-4 inhibitor decreases abdominal aortic aneurysm formation through GLP-1- dependent monocytic activity in mice. *PLoS One* 2015; 10:e0121077.
- [7] Lin FY, Huang CY, Lu HY, et al. The GroEL protein of *Porphyromonas gingivalis* accelerates tumor growth by enhancing endothelial progenitor cell function and neovascularization. *Mol Oral Microbiol* 2015; 30:198-216.
- [8] Sung LC, Chao HH, Chen CH, et al. Lycopene inhibits cyclic strain-induced endothelin-1 expression through the suppression of reactive oxygen species generation and induction of heme oxygenase -1 in human umbilical vein endothelial cells. *Clin Exp Pharmacol Physiol* 2015; 42:632-9.

### Major research aims

Emergency Air Medical transport (EAMT) has rescued patients from remote islands for decades because of the geographical limits in Taiwan. Debates persist regarding the cost-effectiveness, safety of helicopter transport, mortality, and benefit. Proper criteria are needed to determine when EAMT is warranted and most likely to benefit patients. Transport of critical patients by air has become an integral part of regionalized systems of healthcare. Allocation of manpower, software/hardware upgrading and incorporation of video-telemedicine system are keys to improve local healthcare capabilities. This has won the 2018 SNQ – Symbol of National Quality.



Shin-Han Tsai  
M.D., Ph.D.



Hon-Ping Ma  
M.D., Ms.

### Major achievements

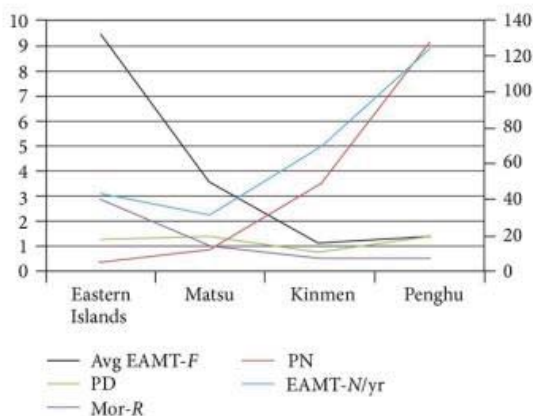
1. The preflight screening by National Aeromedical Approval Center (NAAC) has no patient safety or flight safety issue after 2002. (figure 1)
2. Emergency air medical transport (EAMT) became a major part of the modern trauma care system and most of remote-island patients were transferred via EAMT. (figure 2)
3. The overall mortality rate was 7.56% in 1684 airlifted patients. Among them, 26.3% were acute myocardial infarction and 25.8% were traumatic brain injury. (figure 3)
4. Male predominates in the head injury patients (M:F = 2.6:1) (figure 4)
5. Increasing utilization of EAMT in current National Health Care Scheme is necessary according to the NAAC database.

### Representative figures

1



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### Staff and contact information

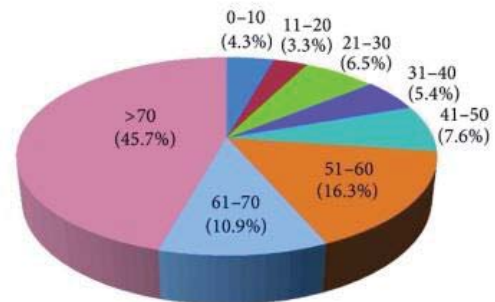
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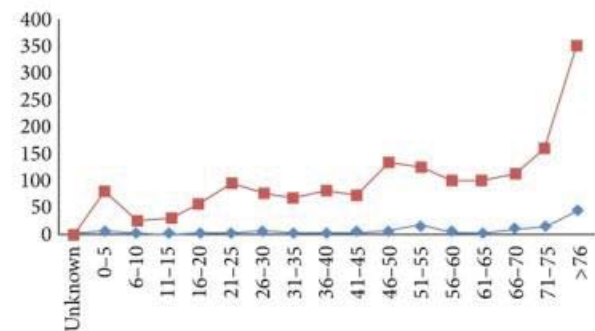
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4



### Major publications

- [1] Tsai SH, Chen WL, Chiu WT, et al. Principles and direction of air medical transport in Taiwan. Ira J. Blumen, Daniel L. Lemkin. Principles and Direction of Air Medical Transport (2ed) 2015; Ch89: 940-944.
- [2] Chen KC, Lu R, Iqbal U, et al. Interactions between Traditional Chinese Medicine and Western Drugs in Taiwan: A Population-based Study. Computer Methods and Programs in Biomedicine 2015; 122:462-470.
- [3] Chen WL, Chiu WT, Wu MS, et al. Translational research of telecare for the treatment of hepatitis C. Biomed Res Int. 2014; Epub.
- [4] Liao KH, Sung CW, Chu SF, et al. Reduced power spectra of heart rate variability are correlated with anxiety in patients with mild traumatic brain injury. Psychiatry Res. 2016; 243:349-56.
- [5] Sung CW, Lee HC, Chiang YH, et al. Early dysautonomia detected by heart rate variability predicts late depression in female patients following mild traumatic brain injury. Psychophysiology. 2016; 53: 455-64.
- [6] Chang CH, Lee CY, Feng SW, et al. Effects of salivary oxidative markers on edentulous patients' satisfaction with prosthetic denture treatments: a pilot study. PLoS One 2016; 11:e0151605.



### Major research aims

Emergency department (ED) hyperglycemia has been observed to be a strong predictor of the prognosis of critical illness and in-hospital outcomes.

1. Stress-induced hyperglycemia (SIH) is common in patients with critical illness, including sepsis, multiple trauma, major surgery, and acute myocardial infarction (AMI). In patients with critical illness, SIH have a high of risk for adverse outcome and occurrence of diabetes mellitus in non diabetes patients.
2. The American Diabetes Association (ADA) indicated that patients with HbA1c of 5.7% to 6.4% might have a prediabetic status and an increased risk of diabetes and cardiovascular mortality. HbA1c may be considered an effective indicator that facilitates the early detection of patients with potential adverse prognosis after nonfatal MI. HbA1c may strengthen the accuracy of clinical care in early intervention and secondary prevention.

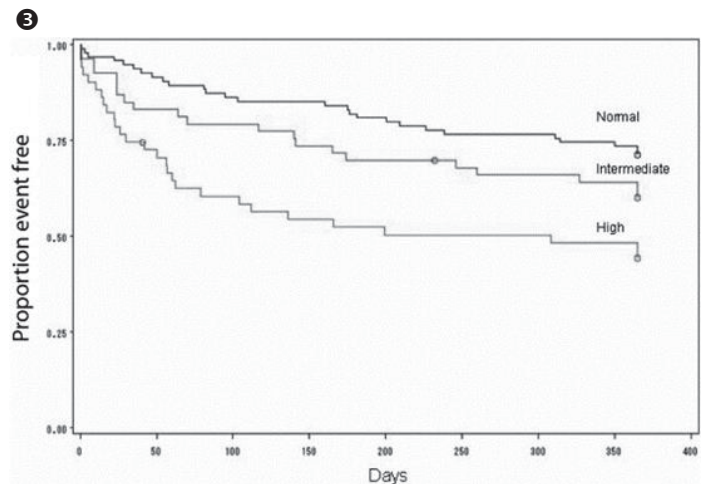
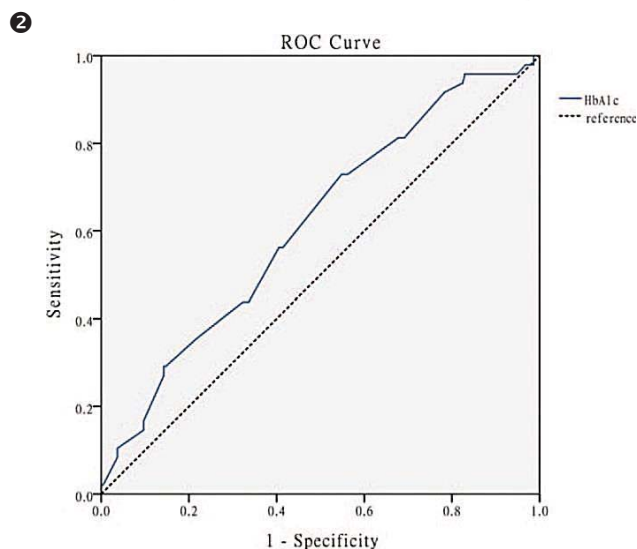
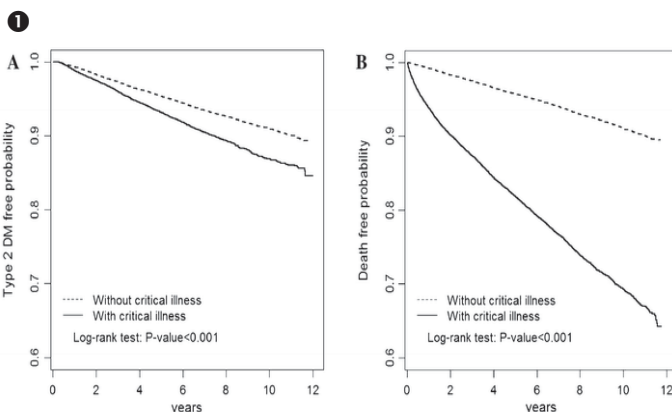


Chin-Wang Hsu  
M.D.

### Major achievements

1. Additional observation studies to establish whether critically ill patients have undiagnosed Type 2 DM (T2DM) prior to the onset of critical illness and to better control for established risk factors are necessary.
2. Our study showed that HbA1c is a significant predictor of MACEs after AMI in nondiabetic patients. This biomarker may strengthen the accuracy of clinical care in early intervention and secondary prevention.
3. A high initial glucose level in the ED is an important and independent predictor of short-and long-term adverse prognoses in patients with first acute myocardial infarction.

### Representative figures



- 1 T2DM-free probability (a) and death (b) with and without certain critical illnesses.
- 2 Receiver operating characteristic curve with the cutoff value of glycated hemoglobin for detecting major adverse cardiac events. Area under curve: 0.616, 95% confidence interval: 0.529 to 0.701; cutoff value: 5.78; P=.013 (sensitivity: 0.729 and specificity: 0.452).
- 3 The Kaplan-Meier cumulative survival curves for patients during the follow-up period of 1 year, stratified by the 3 initial glucose levels (log-rank test, P=.0002).

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### Major publications

- [1] Hsu CW, Lin CS, Chen SJ, et al. Risk of type 2 diabetes mellitus in patients with acute critical illness: a population-based cohort study. *Intensive Care Med* 2016; 42:38-45.
- [2] Chen CL, Yen DH, Lin CS, et al. Glycated hemoglobin level is an independent predictor of major adverse cardiac events after nonfatal acute myocardial infarction in nondiabetic patients: A retrospective observational study. *Medicine (Baltimore)* 2017; 96:e6743.
- [3] Hsu CW, Chen HH, Sheu WH, et al. Initial serum glucose level as a prognostic factor in the first acute myocardial infarction. *Ann Emerg Med* 2007; 49:618-26.

**Major research aims**

The aim of this study was to evaluate the safety and feasibility of magnetic-assisted capsule endoscope (MACE) in the upper gastrointestinal (GI) tract, including the esophagus, stomach and duodenum.

Capsule endoscopy have widely used as a noninvasive endoscopic examination of the gastrointestinal disorders. However, capsule endoscope does not allow the operator to control its navigation. The movement of the capsule is passive, as it proceeds by means of visceral peristalsis and gravity. We propose a handheld external magnetic field navigator (MFN) and an operational prototype magnetic field-guided capsule endoscope.

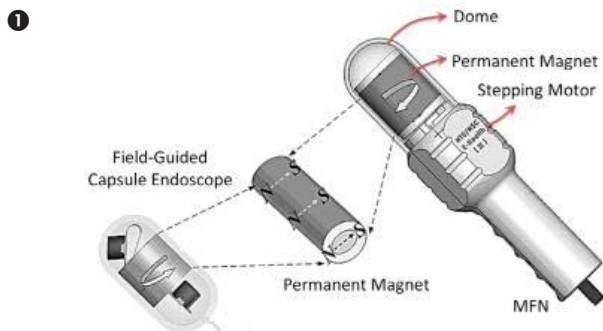
We evaluate the safety and feasibility of magnetic maneuvering of a capsule endoscope in the GI tract.



Gi-Shih Lien  
M.D., Ph.D.

**Major achievements**

1. A new type of the capsule endoscopy system is designed for examination of the GI tract.
2. Prototype capsule endoscope is equipped with two optical image modules to provide two simultaneous video feeds that the image modules' vertical axes are inclined at two angles ( $45^\circ$  and  $90^\circ$ ) with the view angle of  $112^\circ$ .
3. The maneuvering of the endoscopic capsule could be achieved by the external MFN with effectiveness, low-cost, and operation safety. The clinical trial of magnetic navigated capsule endoscopy in examination of the upper GI tract is ongoing.
4. Colonoscopy is considered the most effective method for diagnosing colorectal diseases. Magnetic control system can also apply on the colonoscopic examination. In a colon simulator mode, we have demonstrated that colonoscopy with assistance of magnetic control system can shorten the examination time and improve the problem of loop formation during the procedure.
5. The current capsule endoscopy is ineffective for the examination of the upper GI tract since the operator cannot navigate the capsule. External controllability of capsule endoscope with an applied magnetic field is a possible solution to solve the problem. We develop a novel MACE system, to attempt to view the whole upper GI tract.
6. We conducted an open clinical study enrolled 10 healthy volunteers. The average examination time was 27.1 min. Maneuverability of the capsule was assessed as good in 55.6%, and fair in 44.4%. The overall completeness of the examination was 100% in the esophagus, 85.2% in the stomach, and 86.1% in the duodenum. No severe adverse event happened in this study. All participants tolerated well for the MACE examination.
7. MACE system has good maneuverability and completeness of visualization. The acceptance and tolerance are excellent.

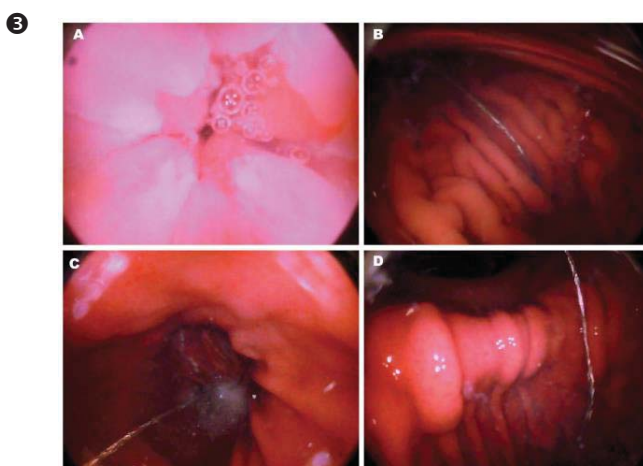
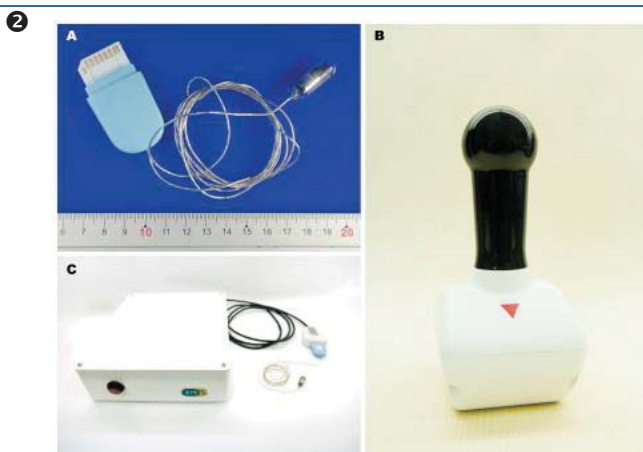
**Representative figures****Staff and contact information**

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- 1 Illustration of the method of operation of the magnetic field navigator.
- 2 The magnetic-assisted capsule endoscope system.
- 3 The capsule endoscopic images of the landmarks of upper GI tract.

**Major publications**

- [1] Lien GS, Wu MS, Chen CN, et al. Feasibility and safety of a novel magnetic-assisted capsule endoscope system in a preliminary examination for upper gastrointestinal tract. *Surg Endosc.* 2018 Apr;32(4):1937-1944
- [2] Yang CS, Suk FM, Chen CN, et al. Colonoscopy with magnetic control system to navigate the forepart of colonoscope shortens the cecal intubation time. *Surg Endosc* 2014; 28: 2480-3.
- [3] Lien GS, Liu CW, Jiang JA, et al. Magnetic control system targeted for capsule endoscopic operations in the stomach-design, fabrication, and in vitro and ex vivo evaluations. *IEEE Trans Biomed Eng* 2012; 59: 2068-79.
- [4] Lien GS, Liu CW, Teng MT, et al. Integration of two optical image modules and locomotion functions in capsule endoscope applications. *IEEE 13th Consumer Electronics International Symposium 2009*; 828-29.

Major research aims

Infectious diseases and inflammatory illnesses represent some of the most important human health issues. Major concerns include the development of antibiotic-resistant bacteria, viral inflammatory response, infective endocarditis, and airway inflammation. The infectious diseases and inflammation research team aims at addressing the above issues by investigating the mechanisms involved and revealing strategies for treatment intervention.



Chiou-Feng Lin  
Ph.D.

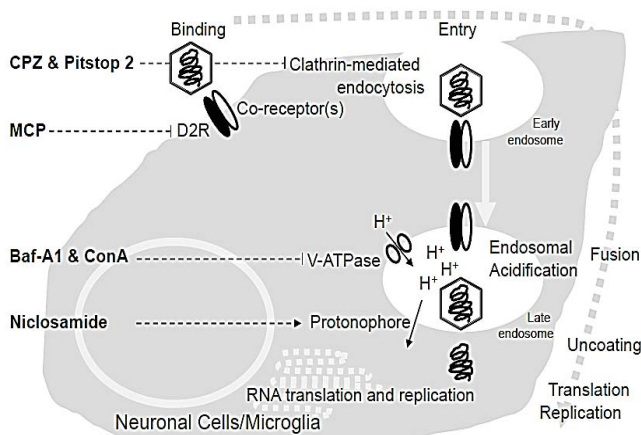
Major achievements

1. Investigation of antiviral drugs against dengue virus infection
2. Discovery of zerumbone which induces Th1 responses and ameliorates Th2-mediated airway allergic inflammation
3. Investigation of the roles of neutrophil extracellular traps in the pathogenesis of infective endocarditis
4. Transfer of antimicrobial-resistance gene NDM-1 among Klebsiella and Acinetobacter species

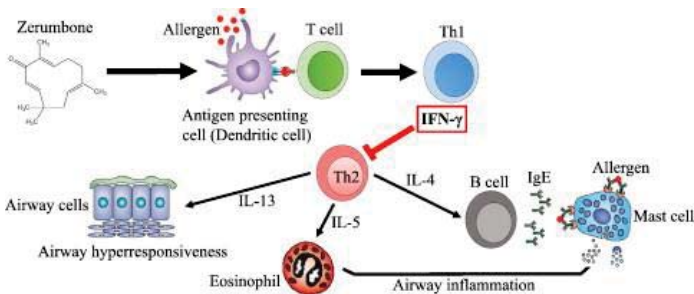
Representative figures

1

Targeting Endocytic Pathways as Anti-Dengue



2



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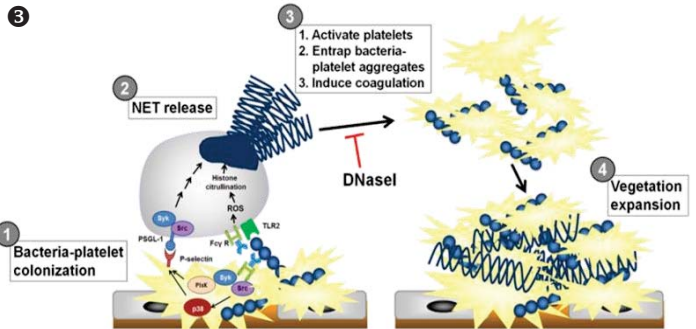
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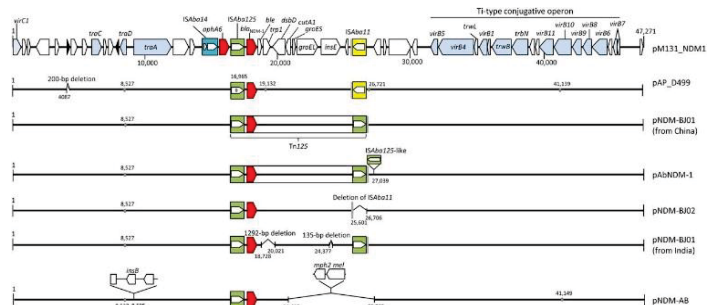
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3



4



- 1 Targeting endocytic pathways as antiviral strategy against dengue virus infection in neuronal cells and microglia *in vitro* and *in vivo*. [1]
- 2 Pathway of zerumbone ameliorating Th2 responses and airway inflammation by enhancing Th1 response. [2]
- 3 A hypothetical model for NET-induced vegetation expansion on injured heart valves. [3]
- 4 Schematic of sequence comparison of NDM-1-positive plasmids from several Acinetobacter isolates. [4]

Major publications

[1] Kao JC, et al. PLoS Negl Trop Dis. 2018 (In press)  
 Jhan MK, et al. J Leukoc Biol. 2018 (In press)  
 Tsai TT, et al. Antiviral Res. 2017 145:44-53.  
 Ho MR, et al. Sci Rep. 2017 7(1):6910.  
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[2] Shieh YH, et al. Zerumbone enhances the Th1 response and ameliorates ovalbumin-induced Th2 responses and airway inflammation in mice. Int Immunopharmacol 2015; 24:383-91.

[3] Jung CJ, et al. Endocarditis pathogen promotes vegetation formation by inducing intravascular neutrophil extracellular traps through activated platelets. Circulation 2015; 131:571-81.

[4] Huang TW, et al. Effective transfer of a 47-kb NDM-1 positive plasmid among Acinetobacter species. J Antimicrob Chemother 2015; 70:2734-8.

### Major research aims

Currently many emerging and re-emerging viruses lack effective vaccines and/or drug treatments. At the same time, viruses can be explored as a type of nanomedicine for the treatment of cancers. The Molecular Virology and Oncolytics Laboratory focuses on Emerging Viral Infectious Diseases & Oncolytic Viro-Immunotherapy (EVID & OVI) research themes:

- (1) **Viral Modeling:** building viral platforms to model and study the different stages of the viral life cycle.
  - (2) **Virus-Host Interactions:** deciphering host factors engaged by viruses in driving the viral pathogenesis.
  - (3) **Antivirals Development:** identifying drug candidates for therapeutic control of viral infections.
  - (4) **Oncolytic Viro-Immunotherapy:** engineering and reprogramming viruses for highly targeted cancer treatment.
- These research topics aim to promote the understanding host-pathogen interactions, develop antiviral strategies, and design virus-based precision cancer medicine.

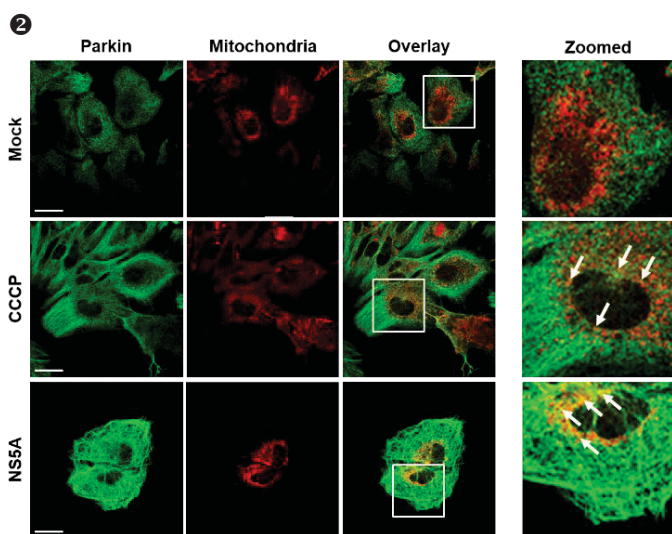
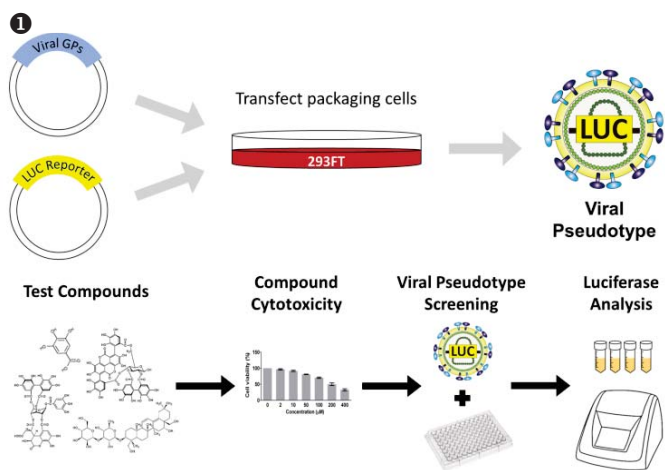


Liang-Tzung Lin  
Ph.D.

### Major achievements

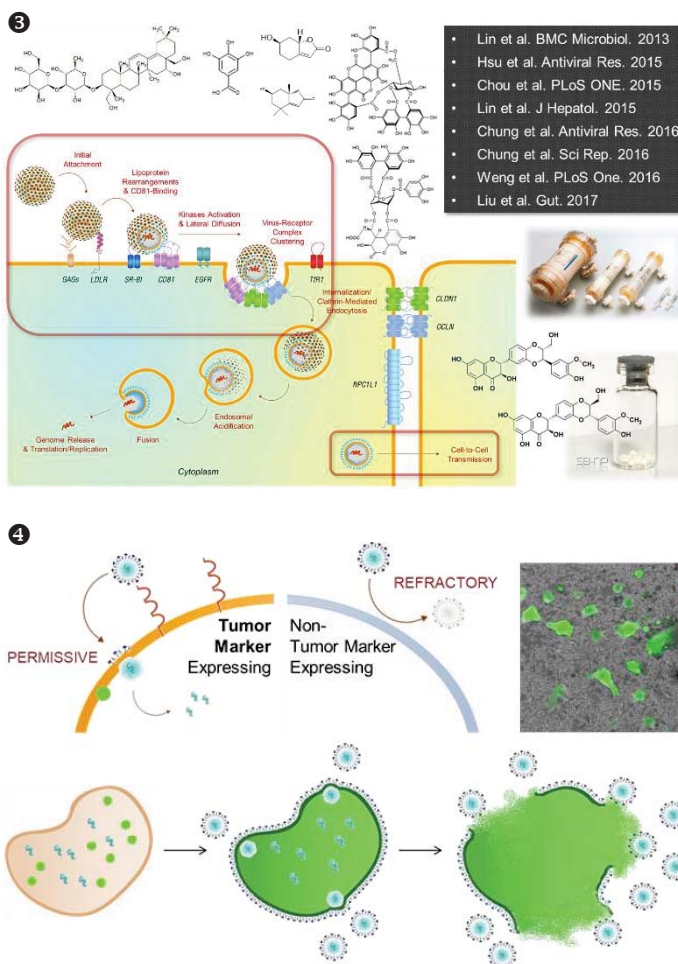
1. Establishment of viral pseudotype and virus-like particle (VLP) systems to study emerging viruses and develop antivirals and vaccines
2. Viral regulation of host mitophagy for promoting viral pathogenesis
3. Identification of antiviral natural products and strategies to preclude viral entry and cell-to-cell spread
4. Generation of programmable measles-based oncolytic viral vectors for tumor marker-targeted cancer treatment

### Representative figures



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### Major publications

- [1] Liu CH, Lin CC, Hsu WC, et al. Highly Bioavailable Silibinin Nanoparticles Inhibit HCV Infection. Gut. 2017 Oct;66(10):1853-1861.
- [2] Burnouf T, Liu CH, Lin LT. Strategies to Preclude Hepatitis C Virus Entry, in "Advances in Treatment of Hepatitis C and B". Allam N (Ed). InTech. 2017 Mar; ISBN: 978-953-51-2994-3.
- [3] Lin LT, Richardson CD. The Host Cell Receptors for Measles Virus and Their Interaction with the Viral Hemagglutinin (H) Protein. Viruses. 2016 Sep 20;8(9). Review.
- [4] Chung CY, Liu CH, Wang GH, et al. (4R,6S)-2-Dihydromenisdaurilide is a Butenolide that Efficiently Inhibits Hepatitis C Virus Entry. Sci Rep. 2016 Jul 18;6:29969.
- [5] Chung CY, Liu CH, Burnouf T, et al. Activity-based and fraction-guided analysis of Phyllanthus urinaria identifies loliolide as a potent inhibitor of hepatitis C virus entry. Antiviral Res. 2016 Jun;130:58-68.
- [6] Lin LT, Chung CY, Hsu WC, et al. Saikosaponin b2 is a naturally occurring terpenoid that efficiently inhibits hepatitis C virus entry. J Hepatol. 2015 Mar;62(3):541-8.

Major research aims

Dementia center accompanied by an unique dementia ward was established in Shunag Ho Hospital, Taipei Medical University in 2015. We are building up a platform for integration of clinical service and research. Dementia center provides a genetic panel for dementia genetic screening, Amyloid-PET and high quality MRI for diagnosis of dementia. There is a biobank of dementia in dementia center, including over 1500 detailed patient information and 300 biospecimens. Many clinical and preclinical researches, including a few global clinical trials and application of wearable devices in dementia patients are being conducted here. In the future, the goal of dementia center is to figure out a model of precision medicine for dementia. In our laboratory, we have transgenic mouse model of Alzheimer disease (AD), bilateral carotid artery occlusion (BCCAO) mouse model for vascular cognitive impairment. We are testing novel strategy for treatment of dementia and their molecular mechanisms.



Chaur-Jong Hu  
M.D.

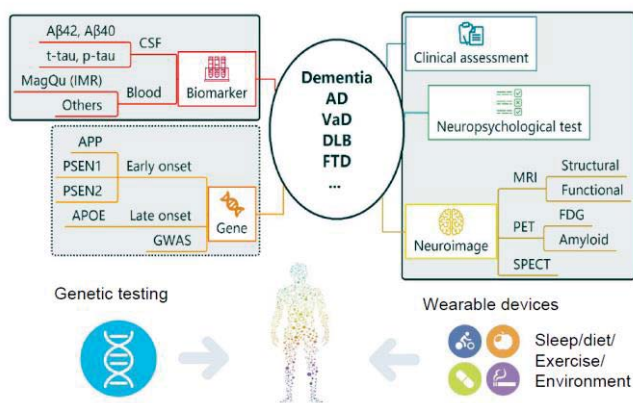
Major achievements

1. The precision medicine of dementia integrates clinical presentations, neuropsychological tests, neuro-imaging, novel blood-based biomarkers, genetic screening and information from wearable devices.
2. We are conducting a study about plasmon-activated water utilized in therapy of neuro-related diseases, including Alzheimer disease, Parkinson's disease and sleep deprivation (insomnia). PAW reduces booth amyloid accumulation and cognitive decline in AD mice.
3. The functional MRI (fMRI) assessment under working memory tasks showed more blood flow recruited in APOE4 carriers with comparison of the non-carriers. The fMRI patterns under working memory tasks also are different between the individuals with different BDNF polymorphisms.
4. Mild traumatic injury might affect the amyloid accumulation and cognitive function in few years later.

Representative figures

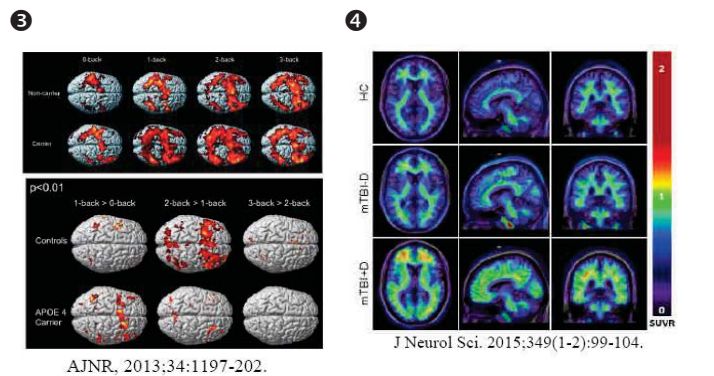
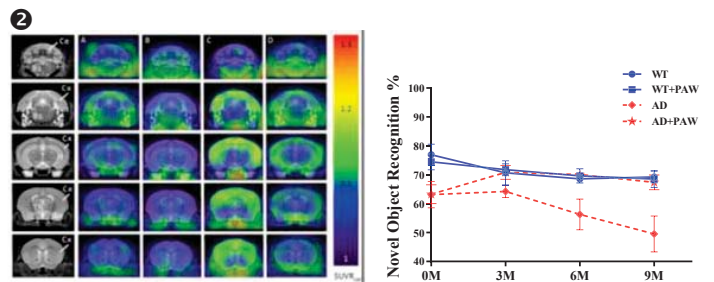
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Precision medicine of dementia



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- 1 the precision medicine of dementia
- 2 plasmon-activated water (PAW) treatment for 5 month old AD transgenic mice. (right) Novel objects recognition (NOR) tests showed AD animals with PAW but not without PAW stopped to decline in 9months and (left) decrease of amyloid accumulation by amyloid PET.
- 3 different fMRI patterns between APOE4 carriers and non-carriers
- 4 Amyloid PET study for traumatic brain injury patients with dementia

Major publications

- [1] Wu D, Tseng IJ, Yuan RY, et al. Memory consolidation and iNOS expression during different sleep stages in Parkinson's disease. *Sleep Med* 2014;15:116-20.
- [2] Yang ST, Hsiao IT, Hsieh CJ, et al. Accumulation of amyloid in cognitive impairment after mild traumatic brain injury. *J Neurol Sci* 2015; 349:99-104.
- [3] Chen CC, Chen CJ, Wu D, et al. BDNF Val66Met polymorphism on functional MRI during n-back working memory tasks. *Medicine (Baltimore)* 2015; 94:e1586.
- [4] Sung YF, Lu CC, Lee JT, et al. Homozygous ALDH2\*2 Is an Independent Risk Factor for Ischemic Stroke in Taiwanese Men. *Stroke*. 2016; 47(9):2174-9
- [5] Lien LM, Chiou HY, Yeh HL, et al. Significant Association Between Low Mitochondrial DNA Content in Peripheral Blood Leukocytes and Ischemic Stroke. *J Am Heart Assoc*. 2017 Nov 18; 6(11).

## Major research aims

Glucose-dependent insulintropic polypeptide (GIP) is a second incretin that, like GLP-1, stimulates glucose-dependent insulin secretion, increases insulin biosynthesis, and improves cell proliferation and survival via its cognate receptor. Importantly, GIP, similar to GLP-1 and its agonists, promotes synaptic plasticity via its reversal of hippocampal long-term potentiation (LTP) impairments and has neuroprotective and neurotrophic properties, suggesting a potential for halting or reversing neurodegenerative disorders. The GIP-R is also highly expressed across a number of CNS neurons, and GIP readily enters the brain. GIP, however, has been much less studied in animal models of neurodegeneration. We have previously shown the neuroprotective activity of GIP in an animal model of traumatic brain injury. We now report the efficacy of GIP in a rat model of PD induced by intracranial unilateral injection of the neurotoxin 6-OHDA, using behavioral tests.



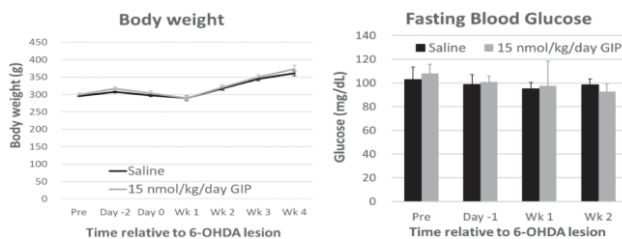
Yung-Hsiao Chiang  
M.D., Ph.D.

## Major achievements

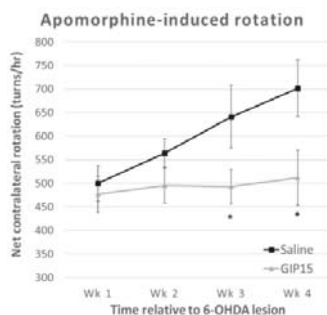
1. Direct infusion of GIP into healthy humans does not affect appetite, energy intake, or energy expenditure.
2. GIP treatment stabilized apomorphine-induced rotational behavior and showed positive changes in open field locomotor tests, as well as some anxiety-like behaviors.
3. GIP mitigates 6-OHDA-induced dysfunction, loss of dopaminergic phenotypic features, and cell death.

## Representative figures

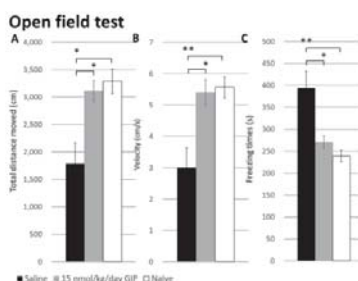
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## Staff and contact information

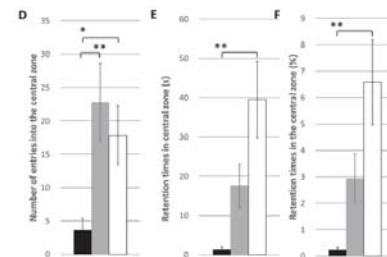
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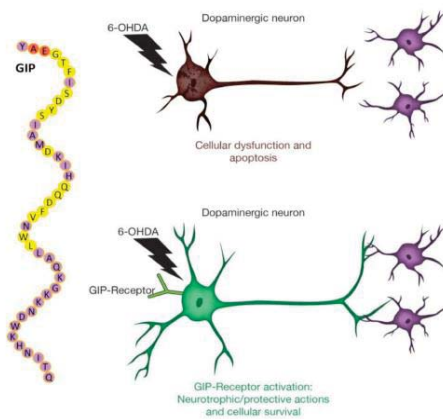
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4



- 1 The average body weight of both groups were similar. And after an overnight (12 h) fast, blood glucose was measured by glucometer in tail vein blood and showed no change during GIP treatment.
- 2 Apomorphine-induced rotation. The results obtained from apomorphine-induced rotational behavior tests after GIP vs. saline administration.
- 3 The effects of GIP in the open-field test. (A) Total distance moved; (B) velocity; and (C) freezing times in 10 min; (D) The number of entries and (E, F) retention times into the central zone was significantly higher in GIP treatment group compared to the saline group.
- 4 Target engagement and activation of the GIP receptor on dopaminergic neurons provides neuroprotective and neurotrophic actions.

## Major publications

- [1] Hsueh SC, Chen KY, Lai JH, et al. Voluntary Physical Exercise Improves Subsequent Motor and Cognitive Impairments in a Rat Model of Parkinson's Disease. *Int J Mol Sci.* 2018 Feb 8;19(2).
- [2] Yu YW, Hsueh SC, Lai JH, et al. Glucose-Dependent Insulintropic Polypeptide Mitigates 6-OHDA-Induced Behavioral Impairments in Parkinsonian Rats. *Int J Mol Sci.* 2018 Apr 11;19(4).

**Major research aims**

Traditionally, cerebrovascular disease is the consequence of atherosclerosis in both intracranial and extracranial artery. About one decade ago, we began the study of cerebrovenous system, a new trend of cerebrovascular treatment and research. The cerebrovenous system is the drainage system of cerebral circulation. The compression, stenosis, hypoplasia or flow insufficiency in extra- or intra-cranial cerebrovenous system will lead to the disruption of cerebrovascular regulatory system and cerebro-autonomic equilibrium. We demonstrated the relationship between cerebrovenous system and the neurodegenerative diseases, dementia, stroke, headache, transient global amnesia and transient monocular blindness etc. Another research interest is the development of new methods for the evaluation of cerebral blood flow regulation. We now have a software for real-time evaluation of cerebral autoregulation, by which we can monitor the cerebral hemodynamics during varieties of daily activity.

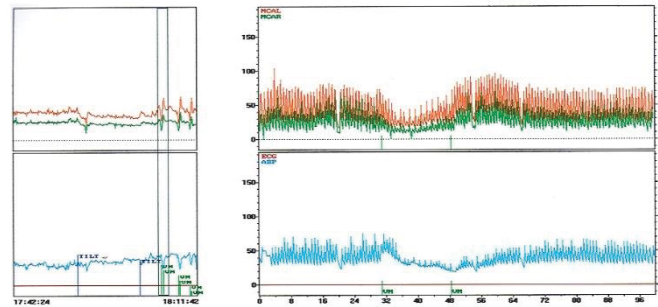


Han-Hwa Hu  
M.D.

**Major achievements**

1. The main purpose of the Cerebrovascular Treatment and Research Center(CTRC) is to train our members to become top professionalism in cerebrovascular treatment and research in Taiwan and lead Asia to be competitive on an International Level. (figure 1)
2. A sophisticated sonography technique for cerebral arterial and venous examinations, and rea-time monitor of cerebral blood flow regulation. (figure 2)
3. 7T high-resolution animal MRI and a well-equipped animal center can provide high quality pre-clinical animal modal.
4. Integrate three-affiliation hospital's stroke registry and researches, to expand our clinical research population and conduct phase I to III new drug development clinical study and technique development.

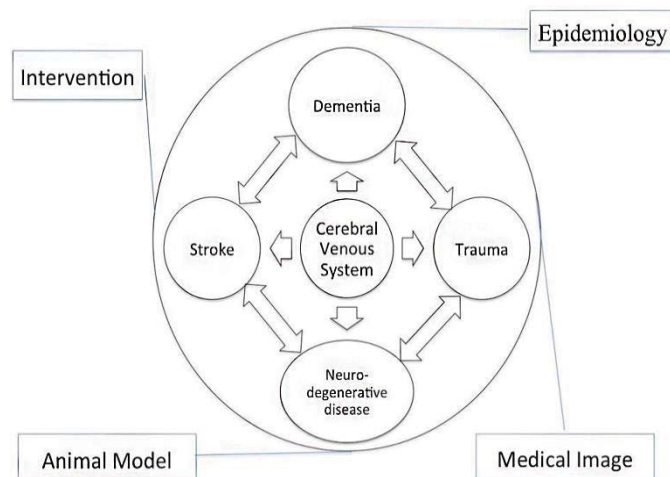
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② Head-up tilt test and Valsalva maneuver test for the blood flow regulation

**Representative figures**

①



① CTRC focuses on the cerebrovascular study in four different fields, stroke, dementia, trauma and other neurodegenerative diseases

**Major publications**

- [1] Chi NF, Ku HL, Wang CY, et al. Dynamic Cerebral Autoregulation Assessment Using Extracranial Internal Carotid Artery Doppler Ultrasonography. *Ultrasound Med Biol* 2017; 43:1307-13.
- [2] Liu IW, Ho BL, Chen CF, et al. Vertebral artery terminating in posterior inferior cerebellar artery: A normal variation with clinical significance. *PLoS One* 2017; 12:e0175264.
- [3] Hsieh CY, Lin RT, Hu HH, et al. Recent advances of stroke thrombolysis in Taiwan: A successful interaction between physicians, regulators, and National Health Insurance Administration. *J Formos Med Assoc* 2017; 116:411-412.
- [4] Han K, Chao AC, Chang FC, et al. Diagnosis of Transverse Sinus Hypoplasia in Magnetic Resonance Venography: New Insights Based on Magnetic Resonance Imaging in Combined Dataset of Venous Outflow Impairment Case-Control Studies: Post Hoc Case-Control Study. *Medicine (Baltimore)* 2016; 95:e2862.
- [5] Sung JY, Chen CI, Hsieh YC, et al. Comparison of admission random glucose, fasting glucose, and glycated hemoglobin in predicting the neurological outcome of acute ischemic stroke: a retrospective study. *Peer J* 2017; 5:e2948.

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Major research aims

Many neurological diseases have a genetic cause or are influenced by genetic factors. Dementia and Parkinson's disease (PD) are two most common neurodegenerative diseases affecting 2-4% and 1% of elderly aged older than 60 years. Albeit most of the patients (~90%) are sporadic cases, recent identification of genes linked to familiar form of dementia or parkinsonism led to a better understanding of novel proteins and molecular pathways that may cause the neurodegeneration. Ongoing studies include patients with Parkinson disease, dystonia, ataxia, hereditary causes of dementia to investigate contributing or causative genetic factors in these neurological disorders. The aim of our research is to identify new gene mutations that cause these diseases and to understand how gene mutations affect the pathogenesis. Elucidating the molecular disease mechanism would lead to the development of novel therapies. We also aim to improve strategies for clinical genetic testing for clinician and patients.

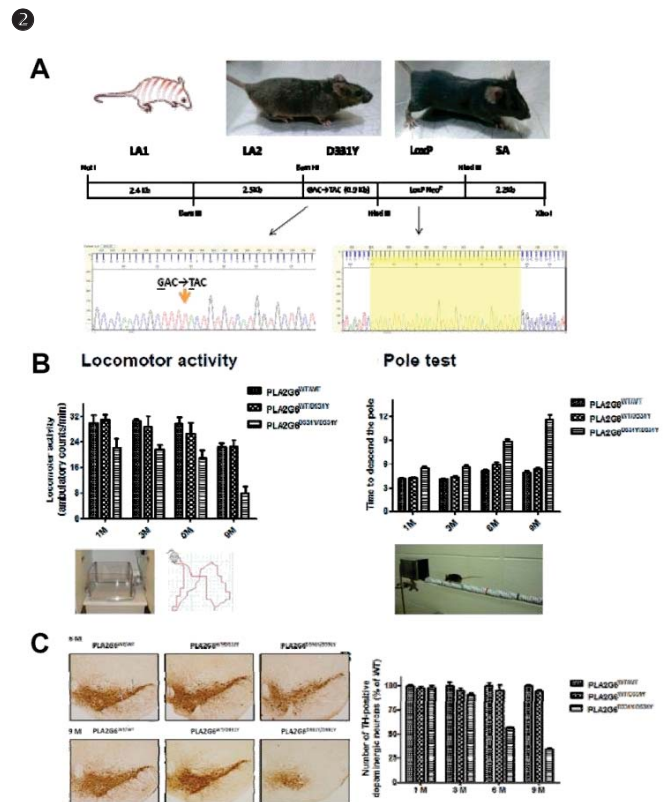
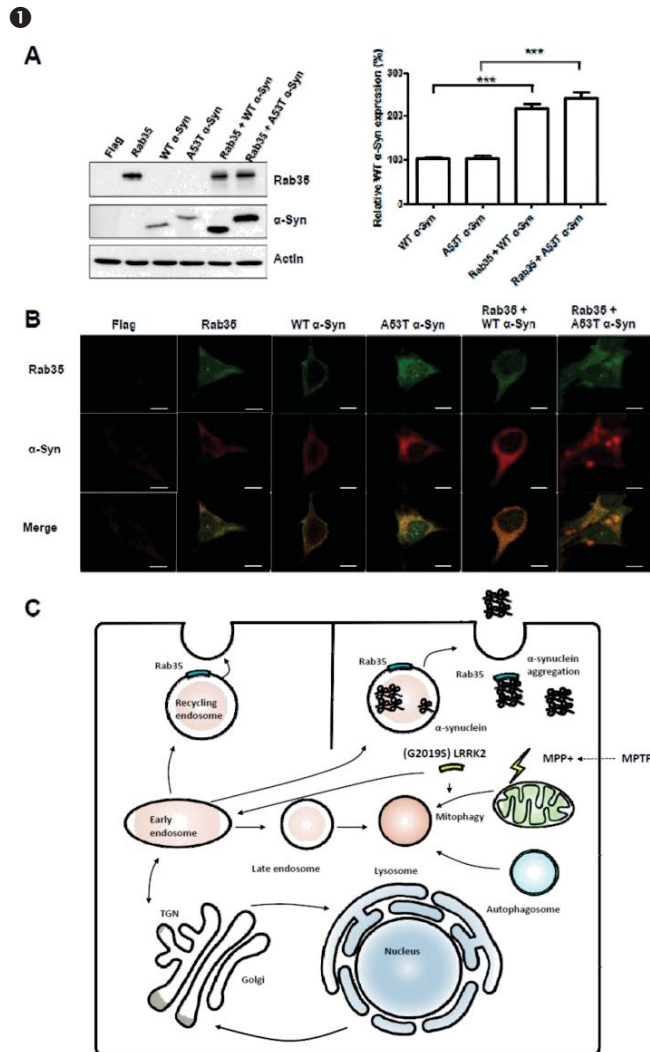


Tu-Hsueh Yeh  
M.D., Ph.D.

Major achievements

1. Serum biomarker study of Parkinson's disease. Rab35 expression is increased in PD patients and deteriorates neurodegeneration. (figure 1)
2. Establish a PARK14 mouse model with a PLA2G6 D331Y mutation. Reduced locomotor activity and dopaminergic neuron degeneration in midbrain was observed in 9-month-old mice. (figure 2)

Representative figures



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Major publications

- [1] Chiu CC, Yeh TH, Lai SC, et al. Increased Rab35 expression is a potential biomarker and implicated in the pathogenesis of Parkinson's disease. *Oncotarget* 2016; 7:54215-27.
- [2] Chiu CC, Yeh TH, Lai SC, et al. Neuroprotective effects of aldehyde dehydrogenase 2 activation in rotenone-induced cellular and animal models of parkinsonism. *Exp Neurol* 2015; 263:244-53.
- [3] Huang YC, Wei KC, Yeh TH. Transglutaminase 2 expression is increased as a function of malignancy grade and negatively regulates cell growth in meningioma. *PLoS One* 2014; 9: e108228.
- [4] Yeh TH, Lai SC, Weng YH, et al. Screening for C9orf72 repeat expansions in parkinsonian syndromes. *Neurobiol Aging* 2013; 34:1311.e3-4.



Major research aims

Spinal pain is a developing scientific field in recent years, and it involves the clinical diagnosis and symptomatology of spine diseases, the underlying pain mechanisms, and the connections between the pain mechanism and the spinal pathology. Knowledge of the underlying pain mechanism and its connections to the clinical symptoms and related spinal pathology is critical to the clinical management and the development of new treatments for spinal pain, so it is mandatory to integrate different scientific techniques to approach the problem from different scales. The clinical study and the national registry database help to find the important issue and the association between the pathology and the clinical symptoms. The computer-engineering techniques quantifies and classify the imaging findings. The animal models and its gene-modified animals explore the underlying pain mechanisms and the pathogenesis in molecular and cellular scales. Scientific techniques of various scales help us to probe the spinal pain and the consequent results could be translated to clinical medicine.

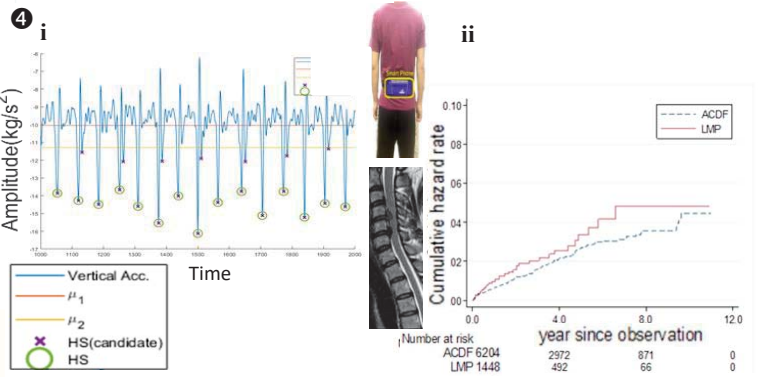
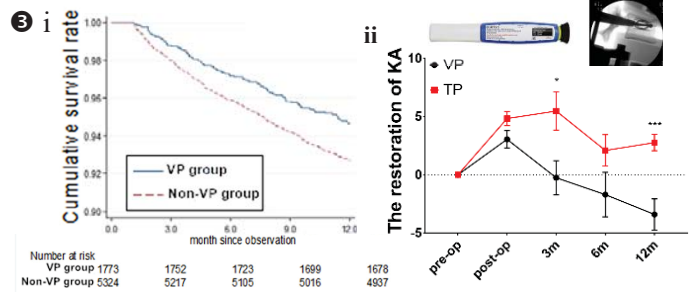
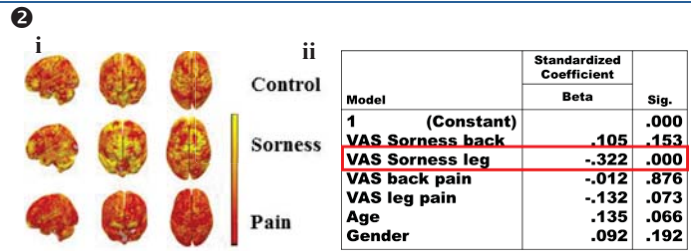
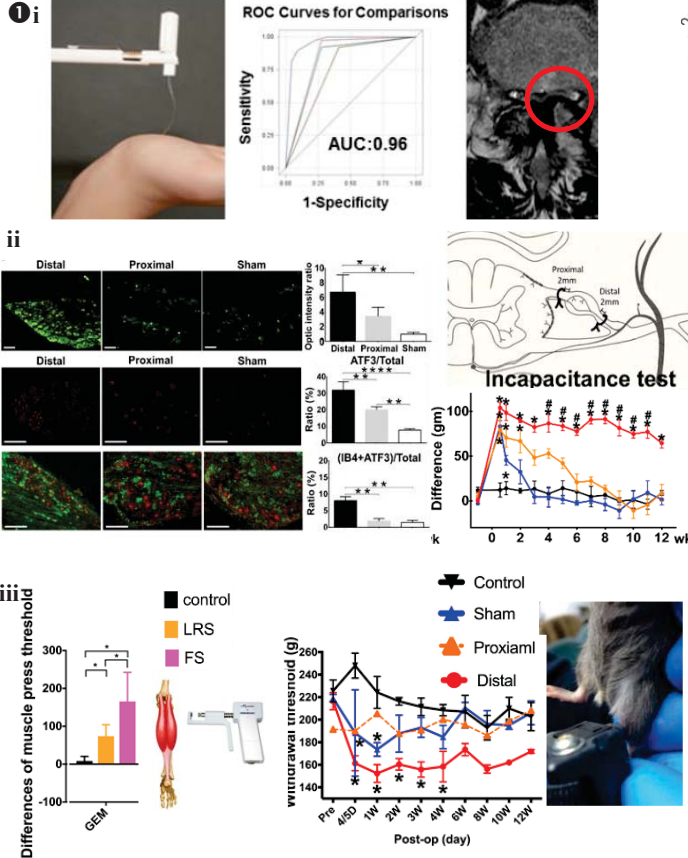


Jiann-Her Lin  
M.D., Ph.D.

Major achievements

1. Lumbar radiculopathy:
  - i. Standardized qualitative sensory test for the diagnosis of lateral stenosis.
  - ii. Hypoxia and DRG neurons injury associated with persistent pain in animal lumbar radiculopathy model.
  - iii. Evoked muscle pain associated with foraminal stenosis.
2. Sngception(soreness):
  - i. Sng (Soreness) is a distinct sensation from pain proved by fMRI.
  - ii. Sng (Soreness) is associated with mental health:
3. Vertebroplasty for osteoporotic vertebral compression fracture:
  - i. Early vertebroplasty associated with better survival rate.
  - ii. Intravertebral reduction device and teriparatide prevent refracture
4. Cervical spondylotic myelopathy (CSM):
  - i. Artificial-intelligence-assisted gait analysis for the diagnosis of CSM.
  - ii. Similar long-term reoperation rates between anterior and posterior cervical spine surgery for CSM

Representative figures



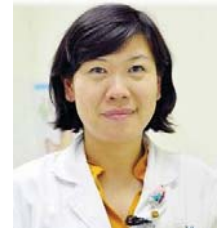
Major publications

- [1] Huang, G. S., Wu, C. C., Lin, J. Gait analysis by using tri-axial accelerometer of smart phones. In Computerized Healthcare (ICCH), 2012 International Conference on. IEEE, 2012; p. 29-34
- [2] Lin, J. H., Wang, S. H., Lin, E. Y., et al. Better height restoration, greater kyphosis correction, and fewer refractures of cemented vertebrae by using an intravertebral reduction device: a 1-year follow-up study. World neurosurgery 2016; 90: 391-396
- [3] Lin, J. H., Chien, L. N., Tsai, W. L., et al. Reoperation rates of anterior cervical discectomy and fusion versus posterior laminoplasty for multilevel cervical degenerative diseases: a population-based cohort study in Taiwan. The Spine Journal 2015; 16.12: 1428-1436.
- [4] Lin, J. H., Chien, L. N., Tsai, W. L., et al. Early vertebroplasty associated with a lower risk of mortality and respiratory failure in aged patients with painful vertebral compression fractures: a population-based cohort study in Taiwan. The Spine Journal 2017; 17.9: 1310-1318.
- [5] Lin, J. H., Hsieh, Y. C., Chen, Y. C., et al. Diagnostic accuracy of standardised qualitative sensory test in the detection of lumbar lateral stenosis involving the L5 nerve root. Scientific Reports 2017; 7.1: 10598.

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Jia-Ying Sung  
M.D., Ph.D.

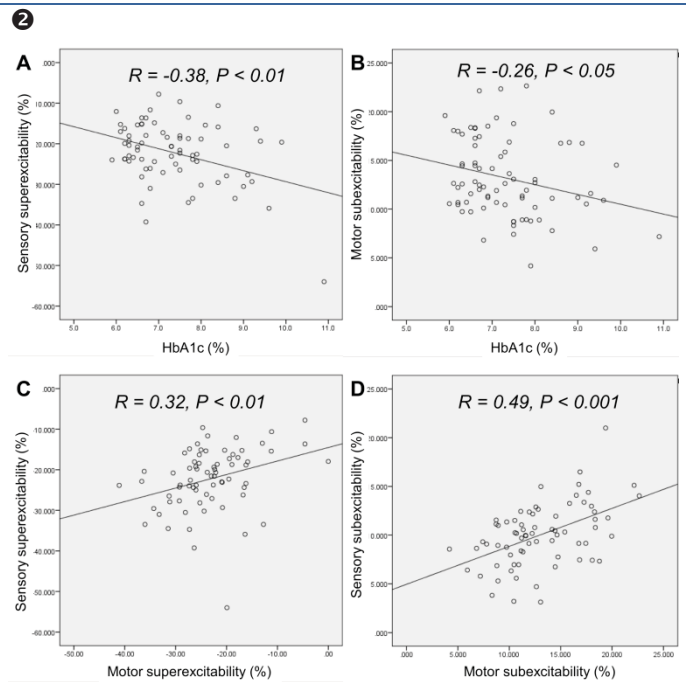
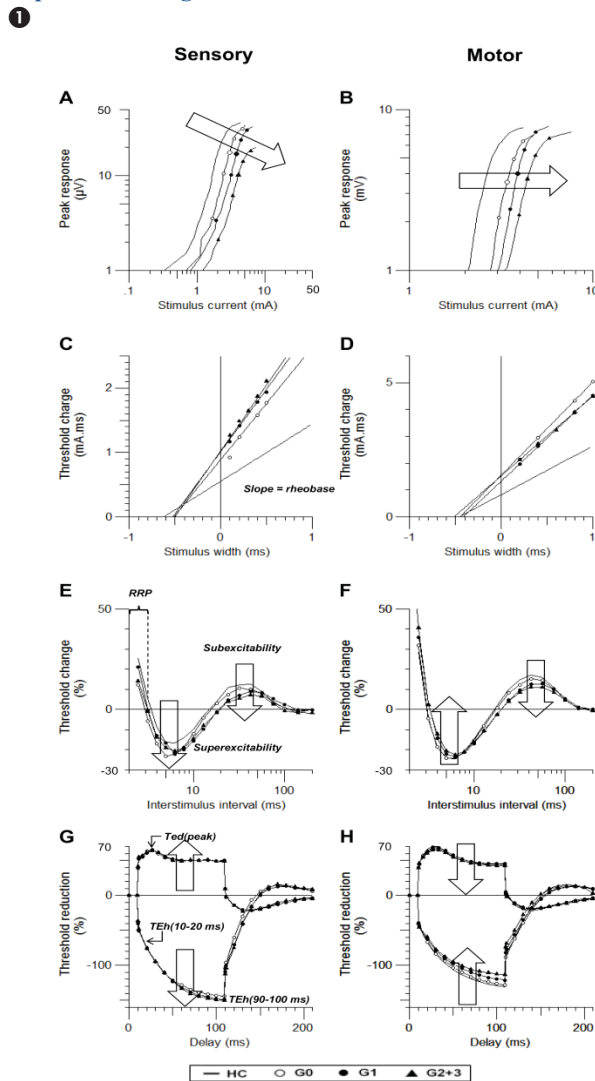
**Major research aims**

Diabetic neuropathy is a major cause of morbidity; it affected up to 50% of long standing diabetic patients, and impact greatly on patient’s life quality. Nerve excitability testing is a useful tool to provide further understanding regarding the pathogenesis of diabetic neuropathy. Previously, we demonstrated that the test can provide valuable electrophysiological data that added to our understanding of how diabetes causes dysfunction in motor nerves. It was also able to detect motor axonal dysfunction in diabetic patients even before the onset of diabetic neuropathy. Nevertheless, as sensory symptoms are typically more prominent than motor symptoms, an assessment of sensory nerve excitability could provide even more important insights into the pathogenesis of diabetic neuropathy from a nerve excitability viewpoint. It also has the potential to provide greater sensitivity in the detection of early axonal dysfunction.

**Major achievements**

1. Explore the progression of diabetic neuropathy in sensory axonal dysfunction, from asymptomatic patients to patients with severe diabetic neuropathy.
2. Sensory axons developed nerve dysfunction prior to and in a different fashion to that of motor axons.
3. The excitability changes in sensory axon correlate to the severity of diabetic neuropathy and positive/negative sensory symptoms.

**Representative figures**



- 1 (A and B) Comparison of the stimulus response curve, (C and D) strength-duration time constant, (E and F) recovery cycle, and (G and H) threshold electrotonus in diabetic patients (G0: empty circle, G1: filled circle, and G2: triangle) and healthy controls (line). Sensory profiles are shown in the left column, while motor profiles are shown in the right.
- 2 Correlation analysis in patients without clinically relevant neuropathy (n = 78). (A) Correlation between sensory superexcitability and HbA1c level. (B) Correlation between motor subexcitability and HbA1c level. (C) Correlation between sensory and motor superexcitability parameters. (D) Correlation between sensory and motor subexcitability parameters.

**Major publications**

- [1] Sung JY, Tani JW, Chang TS, et al. Uncovering sensory axonal dysfunction in asymptomatic type 2 diabetic neuropathy. PLoS One 2017; 12:e0171223.
- [2] Sung JY, Lin YC, Lin SY, et al. Sensory axonal dysfunction in asymptomatic diabetic patients. Clinical Neurophysiology 2014; 125:e5-6.
- [3] Tani JW, Chen CI, Sung JY. Nerve excitability changes in chronic inflammatory demyelinating polyneuropathy: a new clinical diagnostic biomarker. J Exp Clin Med 2014; 6:43-9.
- [4] Sung JY, Tani JW, Park SB, et al. Early identification of ‘acute-onset’ chronic inflammatory demyelinating polyneuropathy. Brain 2014; 137:2155-63.
- [5] Sung JY, Park SB, Liu YT, et al. Progressive axonal dysfunction precedes development of neuropathy in type 2 diabetes. Diabetes 2012; 61:1592-8.

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### Major research aims

The treatment of obesity includes lifestyle modification, diet control, exercise, medication and surgical intervention. The non-invasive treatment for the severely obese patients failed to reach a satisfactory long-term result. For treatment of morbidly obese and severely obese patients with related comorbidity, bariatric surgery has become the most effective and long-lasting treatment of choice. In recent decades, metabolic surgery for the remission of type II diabetes has become a suggestive option for obese patients, and high remission rate up to 80% has been presented. The comprehensive weight management center in our afflicted hospital is focus on the treatment of obesity for the past 8 years. Near 2,000 patients underwent bariatric and metabolic surgery. Complete data was documented from the surgical patients, and biobank including serum and resected stomach were well preserved.



Weu Wang  
M.D.

### Major achievements

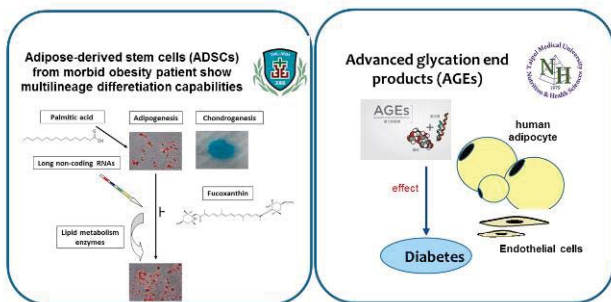
We not only focus on disease improvement and differences in body composition changes between genders, but also evaluate many human adipose cell models, including the adipose-derived stem cells (ADSCs). Adipose tissue will affect the change in hormones, cytokines and immune regulatory factors. Phytochemicals could change the adipogenesis and adipose angiogenesis pathway. We have constructed the ADSCs culture for obese subjects on gene expression. ADSCs have the potential to differentiate into myocardial cells, cartilage and osteogenic cells, and more intensive clinical application potential. Our research projects as following:

1. Highly advanced glycation end products on the ADSCs.
2. To investigate the association between insulin resistance and Parkinson's disease on the ADSCs.
3. Predictors of improvement of nonalcoholic fatty liver disease in morbidly obese patients undergoing bariatric surgery
4. Different kinds of antioxidants on adipose cells culture. For example, the effects of IBC on adipogenesis and adipose angiogenesis by using both animal and cultured cell models.
5. For the further study, we want to evaluate potential adjuvant therapy for metabolic diseases.

### Representative figures

#### 1 The relationship between predictability of gene expression on adipose-derived stem cells (ADSCs) of obese patients on cell culture in Taiwan

- Ping-Hsiao Shih Ph.D. Shuang Ho Hospital, TMU
- Chi-Hao Wu A.P. Nutrition & Health Science, TMU



- Yue-Hwa Chen Nutrition & Health Science, TMU



- Cell line: adipocyte
- Inflammation: TNF- $\alpha$  ↓
- microphage infiltration ↓
- Lipogenesis & lipolysis
- PPAR- $\gamma$  ↓ GPDH activity ↑
- Modify adipokines Adiponectin ↑
- Animal-model BW ↓ Fat tissue ↓
- Human cell

### Staff and contact information

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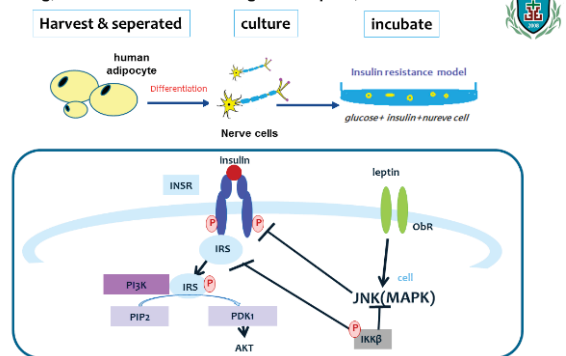
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#### 2 To investigate the association between insulin resistance and Parkinson's disease on (ADSCs)

- Hong, Chien-Tai M.D. Shuang Ho Hospital, TMU



#### 4 Global Quality accreditation and technology center



### Major publications

- [1] Lin WC, Shih PH, Wang W, et al. Inhibitory effects of high stability fucoxanthin on palmitic acid-induced lipid accumulation in human adipose-derived stem cells through modulation of long non-coding RNA. *Food Funct* 2015; 6:2215-23.
- [2] Yeh PS, Wang W, Chang YA, et al. Honokiol induces autophagy of neuroblastoma cells through activating the PI3K/Akt/mTOR and endoplasmic reticular stress/ERK1/2 signaling pathways and suppressing cell migration. *Cancer Lett* 2016; 370:66-77.
- [3] Wang W, Liou TH, Lee WJ, et al. ESR1 gene and insulin resistance remission are associated with serum uric acid decline for severely obese patients undergoing bariatric surgery. *Surg Obes Relat Dis* 2014; 10:14-22.
- [4] Yeh CL, Cheng IC, Hou YC, et al. MicroRNA-125a-3p expression in abdominal adipose tissues is associated with insulin signalling gene expressions in morbid obesity: observations in Taiwanese. *Asia Pac J Clin Nutr* 2014; 23:331-7.
- [5] Cheng IC, Wei SC, Yeh SL, et al. Comparison of weight loss and body composition changes in morbidly obese Taiwanese patients with different bariatric surgeries: a 1-year follow-up study. *Obes Surg* 2014; 24:572-7.



Tai-Tong Wong  
M.D.

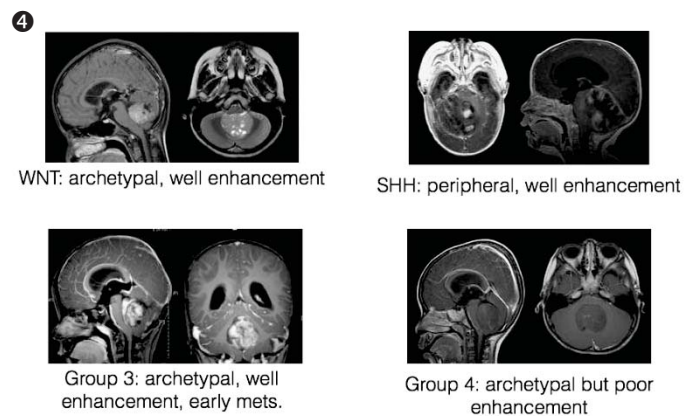
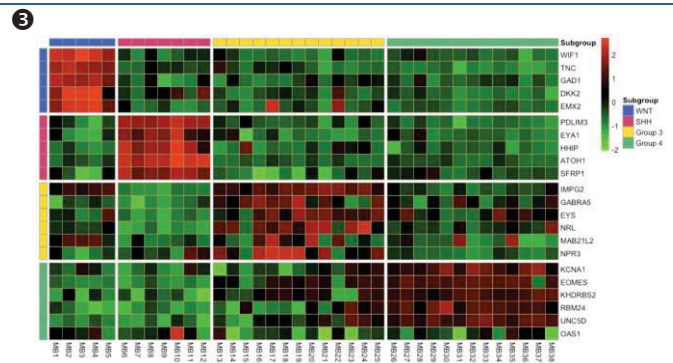
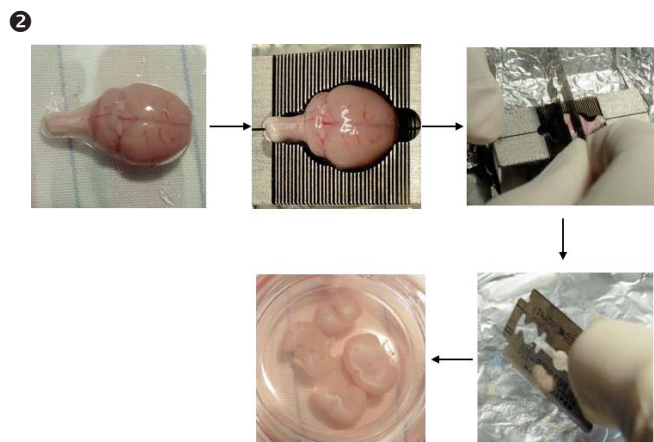
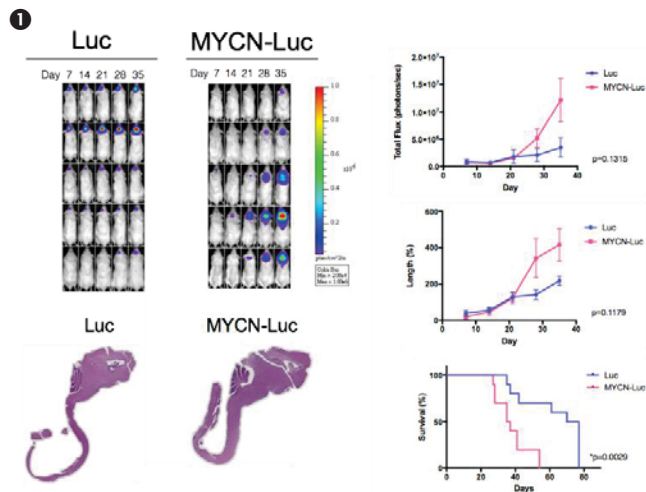
**Major research aims**

Astrocytic tumors, embryonal tumors, germ cell tumors, craniopharyngioma, and ependymal tumors are the five common entities of brain tumors in children. Over half of these tumors are highly malignant that requires post resection radiation therapy and/or chemotherapy treatment. The challenge for precise clinic practice is to provide optimal, effective, but protective treatment strategies for better survival along with good quality of life of patients. Therefore, we establish multidisciplinary team approach for total care of children with brain tumors. Furthermore, we build up pediatric brain tumor bank in biobank and inter-institute cooperative research team with other institutes for molecular profiling, histochemical, karyological, and MRI studies. By integrating clinical, and molecular factors, we look for more precise classification of brain tumors in children for the effective, protective, personalized treatment. In the meanwhile, we also focus on establishing patient-derived xenograft (PDX) mouse model to assess the mechanism of tumor progression. The purpose is to achieve more effective treatment in this group of high risk patients with metastatic brain tumors.

**Major achievements**

1. Development of a MYCN driven metastasis medulloblastoma mouse model.
2. Establishing AT/RT patient-derived xenograft (PDX) mouse model used as a platform for of the therapeutic effect study of targeted drug.
3. Developing organotypic brain slice culture technique to observe the migration/metastasis of tumor.
4. Gathering medulloblastomas to perform classification by molecular profiling and radiogenomics to improve the accuracy and efficiency in MB diagnosis and prognosis prediction.

**Representative figures**



- 1 A MYCN driven metastasis medulloblastoma mouse model.
- 2 The process of organotypic brain slice culture performed in mouse brain.
- 3 Subclassification of medulloblastomas by molecular profiling.
- 4 MRI characteristics of medulloblastoma molecular subgroups.

**Major publications**

- [1] Huang PI, Lin SC, Lee YY, et al. Large cell/ anaplastic medulloblastoma is associated with poor prognosis-a retrospective analysis at a single institute. *Childs Nerv Syst* 2017; 1-10..
- [2] Wong TT, Chen HH, Liang ML, et al. Clinical considerations and surgical approaches for low-grade gliomas in deep hemispheric locations: thalamic lesions. *Childs Nerv Syst* 2016; 32:1895-906.
- [3] Liang ML, Hsieh TH, Ng KH, et al. Downregulation of miR-137 and miR-6500-3p promotes cell proliferation in pediatric high-grade gliomas. *Oncotarget* 2016;7:19723-37.
- [4] Wong TT, Liu YL, Ho DMT, et al. Factors affecting survival of medulloblastoma in children: the changing concept of management. *Childs Nerv Syst* 2015; 31:1687-98.
- [5] Ho DMT, Shih CC, Wong TT, et al. Integrated genomics has identified a new AT/RT-like yet INI1-positive brain tumor subtype among primary pediatric embryonal tumors. *BMC Med Genomics* 2015;8:32.

**Staff and contact information**

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Major research aims

TMU Breast Cancer Translational Research Team integrates “basic research” and “clinical resources” to develop novel tumor markers for targeted anti-cancer drug development using translational medicine” research approaches and has formed a collaboration network between clinical and basic research teams. Our recent study demonstrated that the expression levels of the  $\alpha 9$ -nicotinic acetylcholine receptor ( $\alpha 9$ -nAChR), type 2 glucose transporter (GLUT2), and DNA primase polypeptide 1 (PRIM1) in breast cancer tissues were very high in Taiwanese patients, particularly in the tissues of late-stage patients (stages 3–4). This result indicated that these three markers can be used as a molecular target for cancer therapeutic purpose.



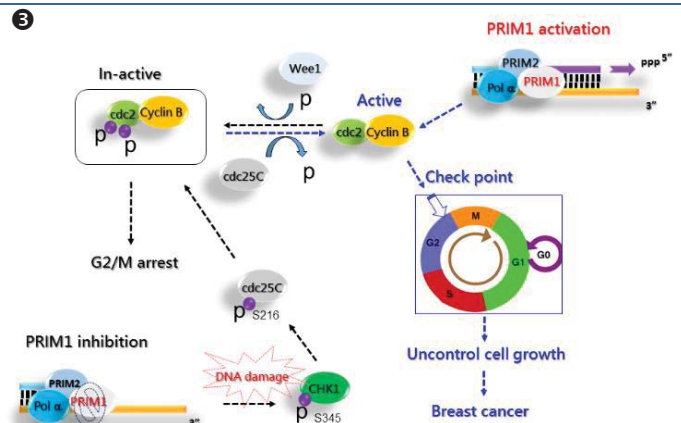
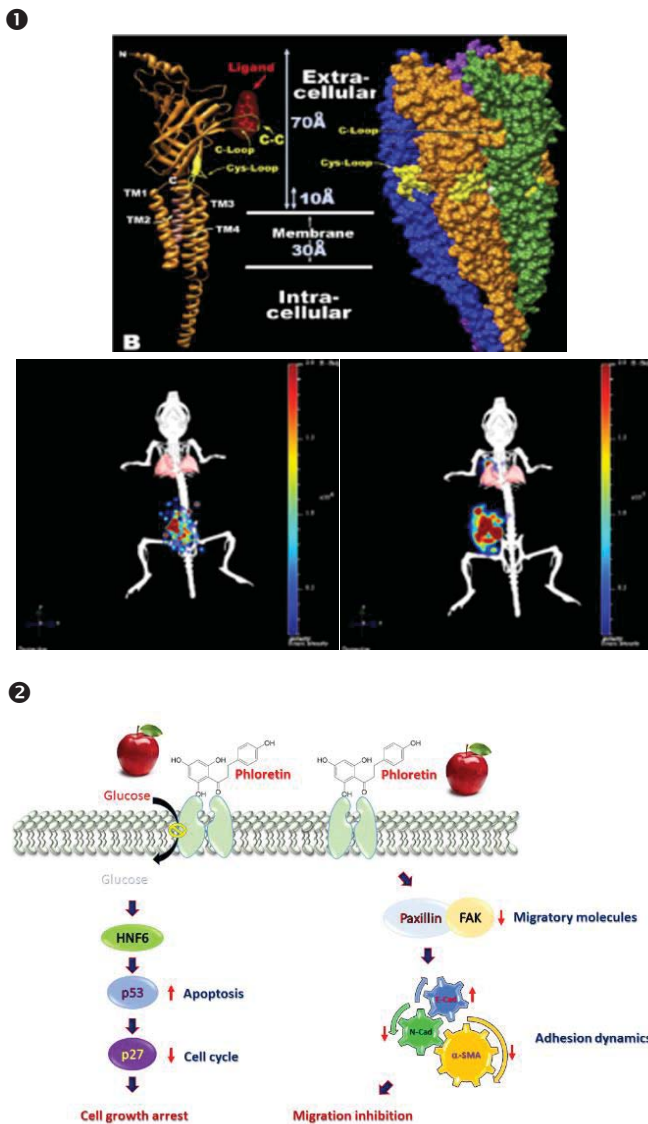
Yuan-Soon Ho  
Ph.D.

Major achievements

Three major aims were focus right now in our research team.

1. To develop therapeutic antibody for the  $\alpha 9$ -nAChR.
2. To validate the therapeutic efficacy of the GLUT2-specific antagonist which was isolated from apple (Phloretin).
3. To evaluate the PRIM1 molecule as an early-diagnosis marker for breast cancer patients.

Representative figures



- 1 A: The molecular model of the  $\alpha 9$ -nAChR (A) and (B) the suggested antibodies binding motif (yellow region). The  $\alpha 9$ -nAChR-specific antibodies have significant therapeutic efficacy (left) when compared to the non-specific antibody treatment group (right).
- 2 Our previous papers have demonstrated that apple polyphenol (phloretin) have significant antitumor effects on different kinds of tumors (such as liver and colon cancer). In response to Phloretin treatment, cell glucose uptake was suppressed through GLUT2 inhibition. Subsequently, low concentrations of intracellular glucose inhibit the breast cancer cell growth, migration and increased apoptotic cell death. Our results indicated that apple polyphenol Ph could be an important chemopreventive or therapeutic agent for TNBC breast cancer patients.
- 3 The DNA primase polypeptide 1 (PRIM1) is responsible for synthesizing small RNA primers for Okazaki fragments generated during discontinuous DNA replication. Our study provides evidences for PRIM1 involved in breast cancer formation and its importance for tumor therapeutic purpose. We also tested the anti-tumoral effects of a natural product; animals were administered inotilone (10 mg/kg, twice a week for 6 weeks), which resulted in significantly reduced BT-474 tumor growth volume compared with placebo control mice (n = 5 per group, \*p < 0.05).

Major publications

- [1] Wu CH, Lee CH, Ho YS. Nicotinic acetylcholine receptor-based blockade: applications of molecular targets for cancer therapy. Clin Cancer Res 2011; 17:3533-41.
- [2] Lee CH, Huang CS, Chen CS, et al. Overexpression and activation of the alpha9-nicotinic receptor during tumorigenesis in human breast epithelial cells. J Natl Cancer Inst 2010; 102:1322-35.
- [3] Jin G, Lee SW, Zhang X, et al. Skp2-Mediated RagA Ubiquitination Elicits a Negative Feedback to Prevent Amino-Acid-Dependent mTORC1 Hyperactivation by Recruiting GATOR1. Mol Cell 2015; 58:989 -1000.

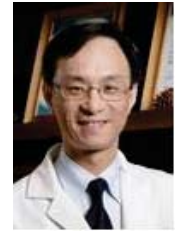
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Major research aims

The TMU Colorectal Cancer Group has broad interests including basic research in colorectal cancer cells and animal models on the cell-biological and molecular mechanisms underpinning the disease. The Group also conducts translational and clinical investigations on prognostic biomarkers, early detection and recurrence of disease, metastasis and cancer therapy. Samples from over 2,000 colorectal cancer patients are being used to create full pathological records and family histories to increase our understanding of the disease in TMU Biobanks. In addition, the bioinformatics methods were applied to predicate the novel targets and pathway involved in therapeutic-resistant in colon cancer.

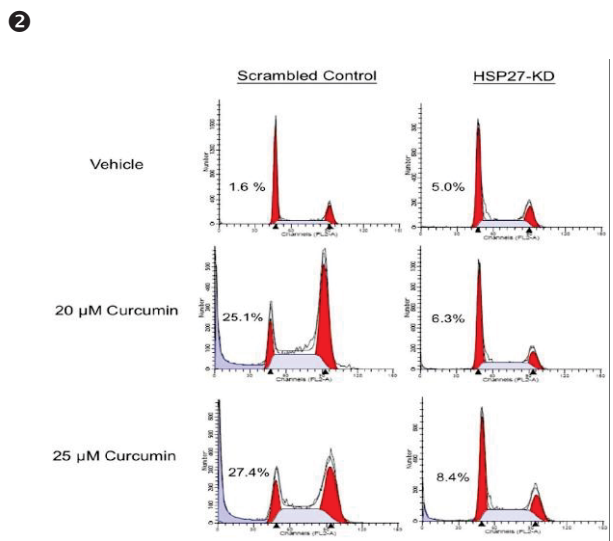
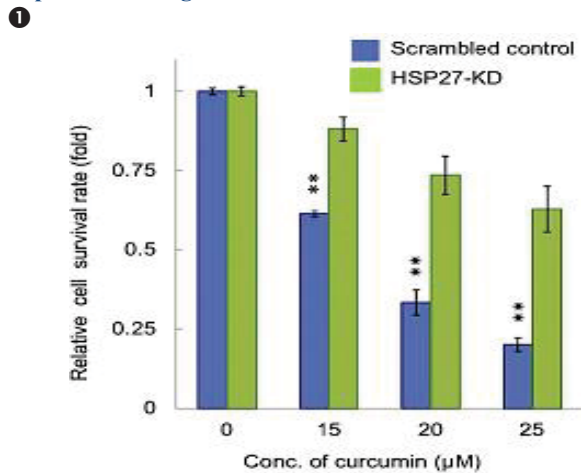


Po-Li Wei  
M.D., Ph.D.

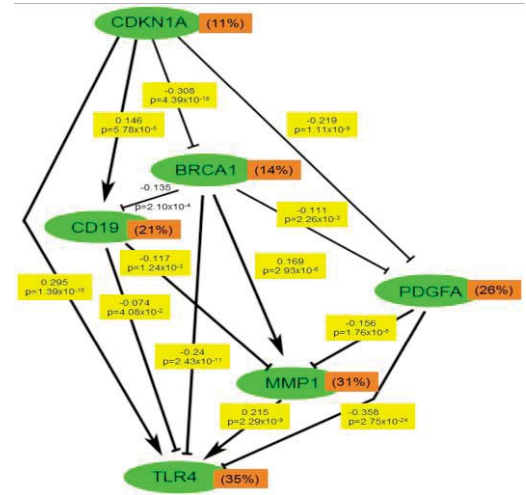
Major achievements

1. Silencing of HSP27 increases curcumin resistance by reducing apoptosis and reactive oxidative stress production, HSP27 is a potential selective target for curcumin treatment in CRC.
2. The clinical validation of the DEGs in mCRC (TNM clinical stages 3 and 4) revealed that high PDGFA expression levels were associated with poor overall survival, whereas high BRCA1 and MMP1 expression levels were associated with favorable progress free survival(PFS).
3. IMR (Immunomagnetic Reduction) shows higher clinical sensitivity and specificity than those of CLIA (chemiluminometric immunoassay).

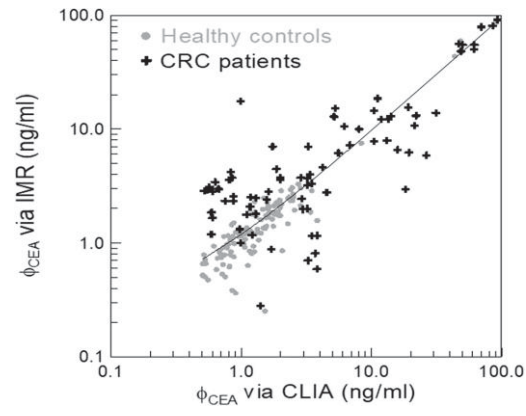
Representative figures



3



4



- 1 The cytotoxicity effects of curcumin were tested by the SRB method.
- 2 Flow cytometric cell cycle analysis was performed by staining DNA with PI.
- 3 Gene expression correlation of the DEGs involved in the pathways in the colorectal carcinoma tumor samples from TCGA data base
- 4 Detected CEA concentrations in human serum by using CLIA (x axis) and IMR (y axis).

Major publications

[1] Liang HH, Huang CY, Chou CW, et al. Heat shock protein 27 influences the anti-cancer effect of curcumin in colon cancer cells through ROS production and autophagy activation. *Life Sci.* 2018 Jul 26. pii: S0024-3205(18)30433-8.

[2] Makondi PT, Lee CH, Huang CY, et al. Prediction of novel target genes and pathways involved in bevacizumab-resistant colorectal cancer. *PLoS One* 2018 Jan 17;13(1):e0189582.

[3] Wei PL, Lee LT, Tseng LM, et al. Validation of Assaying Carcinoembryonic Antigen in Human Serum by Using Immunomagnetic Reduction. *Sci Rep.* 2018 Jul 3;8(1):10002.

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Major research aims

Prostate cancer is the 5th most common type of cancer in Taiwan with more than 1,200 patients died in cancer each year. However, prostate specific antigen (PSA) still the only biomarker with very low specificity and sensitivity. Therefore, it is urgent to develop better biomarkers for prostate cancer diagnosis. With our current efforts, our group identified factors for the cross-talk between prostate cancer and tumor microenvironment during prostate cancer progression. These factors could be value markers for the early diagnosis and prediction of distance organ metastasis. In addition, therapeutic co-targeting to prostate cancer epithelial cells and stromal cells could be a better therapeutic strategy than only targeting to cancer cells. Furthermore, biomarkers from liquid biopsy were also identified, included lncRNA, exosomes, and CTC were analyzed for the development of precision medicine in clinical studies.

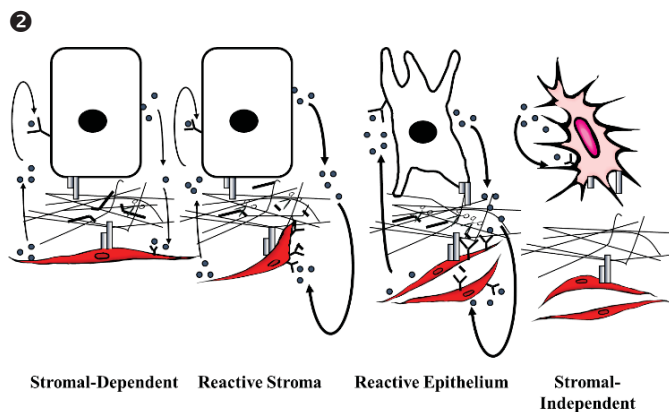
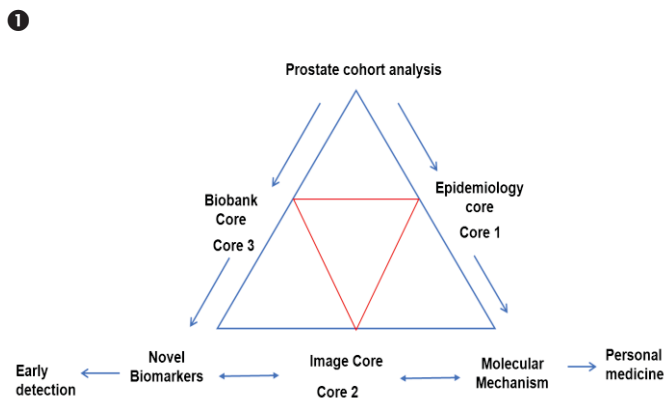


Kuan-Chou Chen  
M.D., Ph.D.

Major achievements

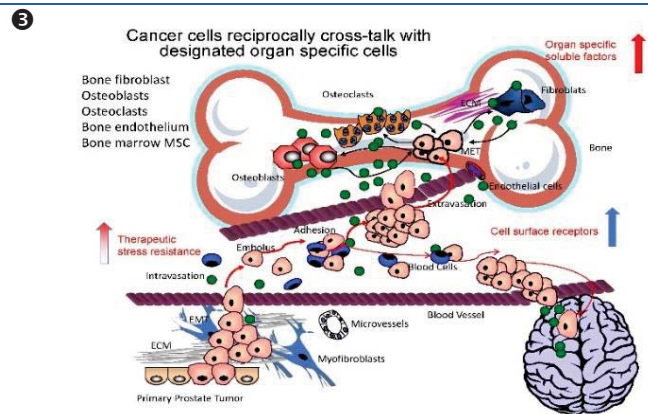
1. Novel prostate cancer therapeutic strategy by co-targeting prostate cancer epithelium and bone stroma
2. Nanobiosensor for diagnosis and surveillance of prostate cancer
3. Androgen receptor regulates stromal-epithelial direct cell contact interaction
4. Targeting tumor microenvironment as a therapeutic approach for prostate cancer

Representative figures



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1. Scheme illustrates the dynamic interaction of prostate cancer research team. These include the cores to assist collection and analysis of clinical samples.
2. Vicious cycle between prostate cancer epithelial cells and environmental cells induced prostate cancer malignant progression and metastasis. The cross-talk between cancer and stromal cells resulted in "education" the stromal cells to release factor for cancer progression.
3. Prostate cancer organ specific metastasis involved the initiation of cross-talk between indolent cancer that early metastasis to specific organ and organ specific stromal cells. This interaction induces chemotaxis factors released by tumor microenvironmental cells that further regulate malignant cancer metastasis.

Major publications

- [1] Hsieh CL, Liu CM, Chen HA, et al. Reactive oxygen species-mediated switching expression of MMP-3 in stromal fibroblasts and cancer cells during prostate cancer progression. *Sci. Rep* 2017 Under revision
- [2] Sung SY, Chang JL, Chen KC, et al. Co-targeting prostate cancer epithelium and bone stroma by human osteonectin -promoter-mediated suicide gene therapy effectively inhibits androgen-independent prostate cancer growth. *PLoS One* 2016; 11: e0153350.
- [3] Chen KC, Sung SY, Lin YT, et al. Benign prostatic hyperplasia complicated with T1DM can be alleviated by treadmill exercise-evidences revealed by the rat model. *BMC Urol* 2015; 15:113.
- [4] Sung SY, Wu IH, Chuang PH, et al. Targeting L1 cell adhesion molecule expression using liposome-encapsulated siRNA suppresses prostate cancer bone metastasis and growth. *Oncotarget* 2014; 5:9911-29.
- [5] Sung SY, Liao CH, Wu HP, et al. Loss of let-7 microRNA upregulates IL-6 in bone marrow-derived mesenchymal stem cells triggering a reactive stromal response to prostate cancer. *PLoS One* 2013; 8:e71637.
- [6] Liu CM, Hsieh CL, He YC, et al. In vivo targeting of ADAM9 gene expression using lentivirus-delivered shRNA suppresses prostate cancer growth by regulating REG4 dependent cell cycle progression. *PLoS One* 2013; 8:e53795.

**Major research aims**

Cancer metastasis is the main cause of patient mortality, whereas the underlying cellular and molecular mechanisms are still far from clear. Our research is aimed at identifying novel and critical regulators of cancer metastasis that may have important diagnostic and therapeutic implications. The Lab uses unique and integrative approaches combining genetics, proteomics, bioinformatics and tissue engineering principles to study the role of cancer cell heterogeneity in the metastatic process. Our work in these themes has led to the identification of a key mediator of cancer stemness and metastasis, which provides new insights into cancer aggressiveness. We have developed a ASPM-targeted nanocarrier gene therapy that holds promises to developing Wnt- and stemness-targeted anti-cancer therapy. Another line of our research is focused on the role of chemotherapy-treated stroma in tumor progression and therapeutic failure. We have uncovered a paradoxically oncogenic role of chemotherapy-treated stromal cells in cancer, and have delineated the underlying signaling pathways and molecular mechanisms. Targeting the therapy-induced stromal-epithelial signaling may be a new avenue for improving the therapeutic outcome of cancer patients.

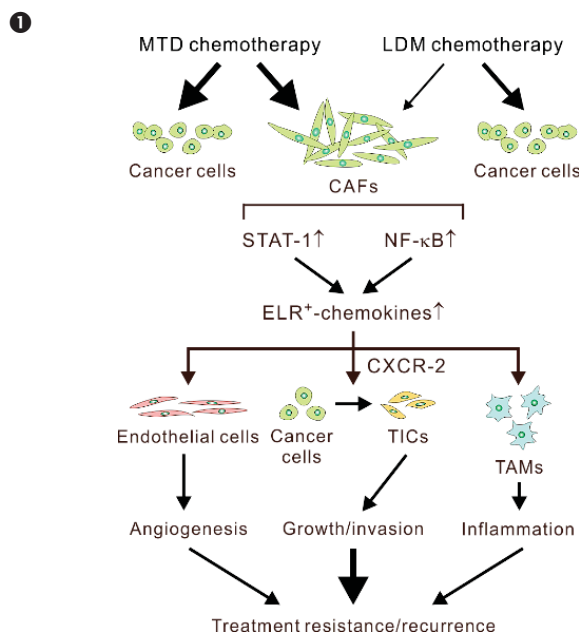


Kelvin K. Tsai  
M.D., Ph.D.

**Major achievements**

1. The identification of ASPM as a hub of Wnt signaling, cancer stemness and metastasis.
2. The characterization of stromal-epithelial signaling in cancers and its therapeutic implications.
3. The developments of tissue-architecture-specific prognostic markers in glandular cancers
4. The identification of cancer stem cells as novel targets of metronomic chemotherapy and the development of related clinical trials.

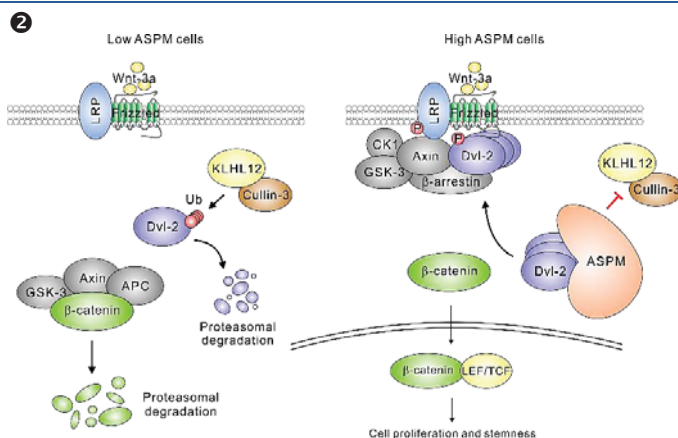
**Representative figures**



1 Schematic showing the proposed mechanisms underlying the pro-oncogenic functions of maximum tolerated dose chemotherapy-treated carcinoma associated fibroblasts that serve to antagonize the anti-tumor efficacy and leads to tumor recurrence and/or metastasis, whereas chemotherapy at low dose metronomic therapy regimens can exempt the stroma from these treatment-elicited stromal-epithelial signaling events.

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2 A working model of ASPM-mediated Wnt activation. In cells with high levels of ASPM expression (right panel), ASPM stabilizes Dvl and other upstream Wnt activators whereby Wnt proteins can signal through Frizzled and its coreceptors LRP to Dvl, leading to inhibition of the β-catenin destruction complex and β-catenin-dependent transcription in the nucleus. In contrast, in cells with low ASPM expression (left panel), Wnt activation signals cannot transmit to downstream Wnt effectors as Dvl protein is destabilized by proteasome-dependent degradation.

**Collaborators**

**Valerie M. Weaver, Ph.D., Professor and Director**  
 Department of Surgery & Anatomy & Bioengineering and Therapeutic Sciences, University of California, San Francisco, CA, USA  
**Robert S. Kerbel, Ph.D., Professor**  
 Sunnybrook Research Institute, Departments of Medical Biophysics & Lab. Medicine, University of Toronto

**Major publications**

- [1] Chan TS, Hsu CC, Pai VC, et al. Metronomic chemotherapy prevents therapy-induced stromal activation and induction of tumor-initiating cells. *J Exp Med* 2017; 213: 2967-88 (IF: 10.790).
- [2] Pai VC, Hsu CC, Chan TS, et al. ASPM promotes prostate cancer stemness and progression by augmenting Wnt-Dvl-3-β-catenin signaling. *Oncogene* 2018 (IF: 6.854; in press).
- [3] André N, Tsai KK, Carré M, Pasquier E. Metronomic chemotherapy: direct targeting of cancer cells after all? *Trends Cancer* 2017; 3:319-325.
- [4] Wang WY, Hsu CC, Wang TY, et al. A gene expression signature of epithelial tubulogenesis and a role for ASPM in pancreatic tumor progression. *Gastroenterology* 2013; 145:1110-20 (IF: 20.773).



### Major research aims

Platelet-rich plasma (PRP) is the plasma containing a high concentration of platelets which obtained from patient's serum and released of a multi-class growth factor such as platelet-derivative growth factor (PDGF), Transforming growth factor (TGF), vascular endothelial cell growth factor (VEGF), epidermal growth factor (EGF), insulin growth factor (IGF), fibroblast growth factor (FGF), connective tissue growth factor (CTGF), keratinocyte growth factor (KGF). These growth factors can promote cell proliferation, migration, differentiation, collagen synthesis, and angiogenesis. Our primarily focus on the basic research of PRP for functional recovery in osteoarthritic chondrocytes, regeneration of degenerative cartilage, attenuation proinflammatory chemokines for meniscocytes and articular chondrocytes healing, and regeneration of avascular necrosis of femoral head by inhibition of apoptosis.

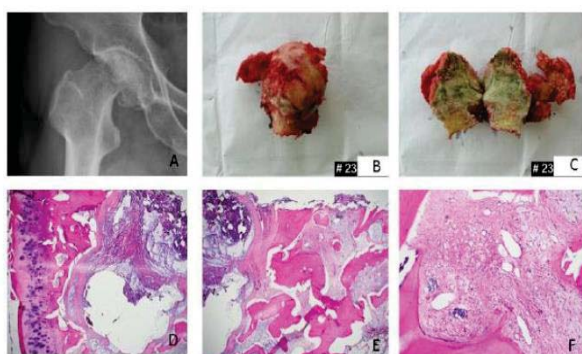
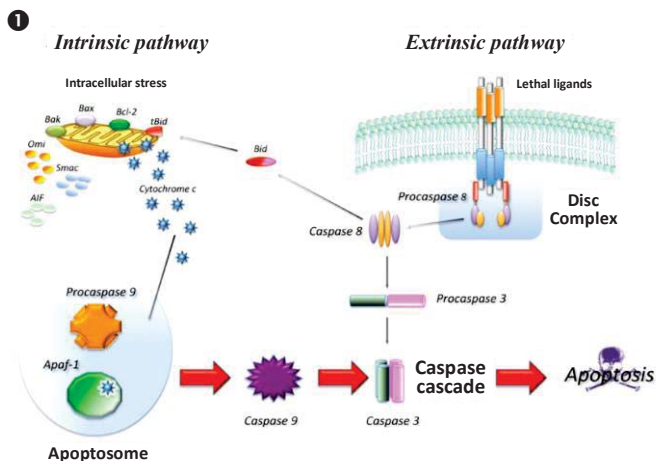


Chian-Her Lee  
M.D.

### Major achievements

1. Establish primary cultures of articular chondrocytes, meniscus fibrochondrocytes, and synovial fibroblasts.
2. Establish in vitro model for PRP treatment in primary cultures.
3. Establish the anti-inflammatory effect and/or modulation pattern of Toll-like receptor of PRP.
4. cDNA microarray analysis for above models to identify novel targets in the PRP system.
5. Mechanism analysis including protein phosphorylation array and cytokine array membrane to identify the specific signal transduction pathway and the cell biology function as well.
6. Establish an ex vivo model to identify the effects and mechanisms on the tissue level.

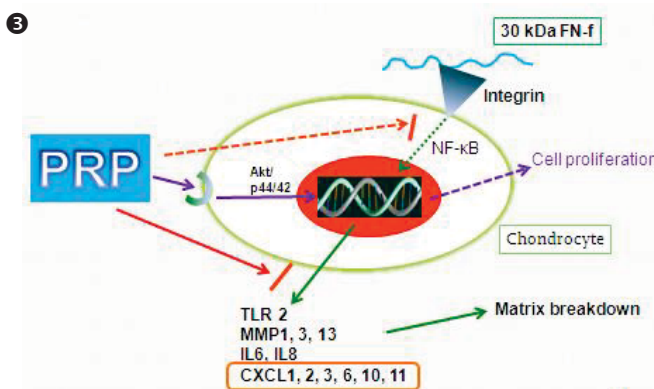
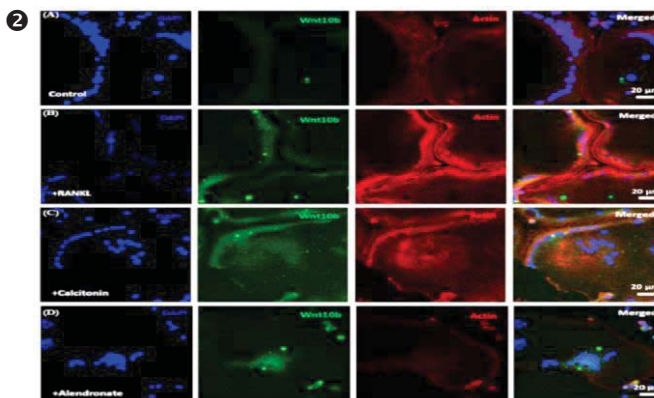
### Representative figures



① 30 kDa fibronectin fragment causes the worsen effects by upregulation of chemokines (CXCL1, CXCL2, CXCL3, CXCL6, CXCL10, CXCL11), IL6, IL8, MMPs (MMP1, MMP3, MMP13), TLR2 and NOS2 in both articular chondrocytes and fibrochondrocytes.

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- ② PRP could suppress those upregulated genes.
- ③ Regenerative potentials of PRP in avascular necrosis of femoral head

### Major publications

- [1] Chen WH, Lin CM, Huang CF, et al. Functional recovery in osteoarthritic chondrocytes through hyaluronic acid and platelet-rich plasma-Inhibited infrapatellar fat pad adipocytes. *Am J Sports Med* 2016; 44:2696-705.
- [2] Wang CC, Lee CH, Peng YJ, et al. Platelet-rich plasma attenuates 30-kDa fibronectin fragment-induced chemokine and matrix metalloproteinase expression by meniscocytes and articular chondrocytes. *Am J Sports Med* 2015; 43:2481-9.
- [3] Tsai PH, Lee HS, Siow TY, et al. Alternative effects of an oral alginate extract on experimental rabbit osteoarthritis. *J Biomed Sci* 2015; 22:64.
- [4] Chou CH, Lee MT, Song IW, et al. Insights into osteoarthritis progression revealed by analyses of both knee tibiofemoral compartments. *Osteoarthritis Cartilage* 2015; 23:571-80.
- [5] Chen WH, Lo WC, Hsu WC, et al. Synergistic anabolic actions of hyaluronic acid and platelet-rich plasma on cartilage regeneration in osteoarthritis therapy. *Biomaterials* 2014; 35: 9599-607.

### Major research aims

TMU bone and joint research team focus on tendon, bone, cartilage tissue regeneration using different biomaterials, cell types and technologies and invent novel strategy to enhance tendon to bone healing. Anterior cruciate ligament (ACL) repair with biological agents have been an option for future treatment of acute ACL injuries. Successful ACL reconstruction with tendon graft requires solid tendon to bone healing in the bone tunnels and progressive graft ligamentization for biological, structural, and functional recovery of ACL. Interface fibrocartilage formation as translational structure from tendon to bone is more physiological and functional after implantation of tendon graft into the bone tunnel. Biological enhancement techniques for tendon graft healing in the bone tunnel have been proposed by means of various biomaterials. Our strategy is to use periosteum, periosteal progenitor cell, hydrogel, cell sheet, and functionalized PHB sleeves to enhance tendon to bone healing.



Chih-Hwa Chen  
M.D., MBA.

### Major achievements

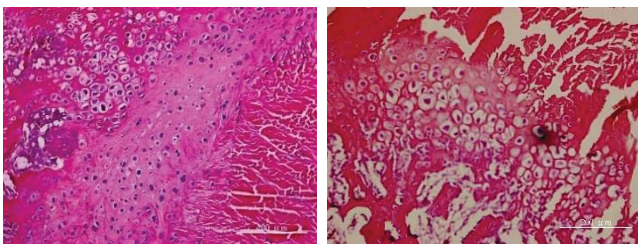
1. Periosteum enhances bone and fibrocartilage ingrowth into interface zone of tendon and bone.
2. PPC-BMP-2 hydrogel provides a powerful inductive ability to enhance tendon-bone healing through fibrocartilage.
3. Bioengineered PPC sheets offer a novel approach to enhance tendon-bone junction healing.
4. The use of functionalized PHB sleeves can enhance tendon to bone healing and the tendon sleeves might provide a novel method for ACL reconstruction.

### Representative figures

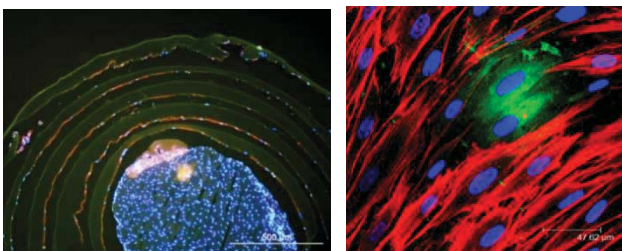
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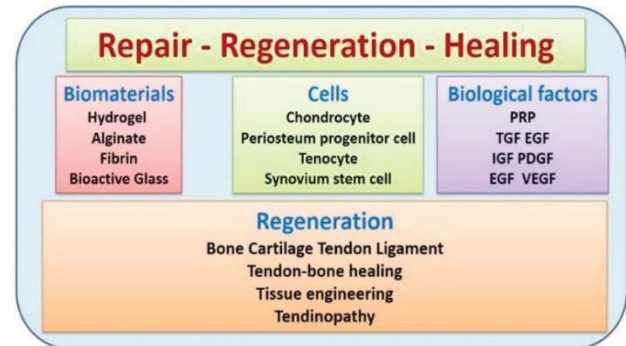
②



③



④



- ① Arthroscopic ACL reconstruction with hamstring tendon-periosteum autograft as a clinical application from the result of periosteum-tendon to bone healing in animal model.
- ② Fibrocartilage formation in the interface between tendon and bone with strong anchorage strength to improve the tendon to bone healing
- ③ Periosteum progenitor cell sheets wrapped around tendon to enhance tendon-bone tunnel healing.
- ④ The research focuses are biomaterials in orthopedics, tissue engineering in bone and cartilage, healing of tendon and healing after sports injury, tendinopathy, and development of novel biomedical device.

### Major publications

- [1] Liu HW, Chen CH, Tsai CL, et al. Heterobifunctional PEG-tethered growth factor stimulated bone marrow mesenchymal stem cells differentiation and osteogenesis. *Tissue Eng* 2007; 13:1113-24.
- [2] Chen CH, Liu HW, Tsai CL, et al. Photoencapsulation of bone morphogenetic protein-2 and periosteal progenitor cells improve tendon graft healing in a bone tunnel. *Am J Sports Med* 2008; 36: 461-73.
- [3] Lin BN, Whu SW, Chen CH, et al. Bone marrow mesenchymal stem cells, platelet rich plasma and nanohydroxyapatite-type I collagen beads were integral parts of biomimetic bone substitutes for bone regeneration. *J Tissue Eng Regen Med* 2013; 7:841-54.
- [4] Chen CH, Chang CH, Su GI, et al. Arthroscopic single-bundle anterior cruciate ligament reconstruction with periosteum-enveloping hamstring tendon graft, clinical outcome in 2 to 7 years. *Arthroscopy* 2010; 26:907-17.
- [5] Chen WC, CHEN CH, Tseng HW, et al. Surface functionalized electrospun fibrous poly(3-hydroxybutyrate) tendon sleeves: a novel approach for fixation in anterior cruciate ligament reconstruction. *J Mater Chem B* 2017; 5: 553-64.

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Major research aims

Low back pain and sciatica are the most common symptoms caused by spinal diseases. It is one of the many reasons why patients seek clinical evaluation from doctors. In order to surgically treat these diseases, the operator may perform a nerve decompression and spinal fusion procedure. Most of the surgical instruments and implants used in these procedures are imported from other countries. However, due to the variation in anatomical structures of Eastern and Western people, these instruments and implants are not necessarily suitable for all Taiwanese people to use. Furthermore, the development of minimally invasive surgical techniques is becoming the mainstay treatment. Spinal surgeons must understand the most suitable surgical instruments and implants for themselves, the patient and the Taiwanese people to use. While taking advantage of the advanced production technology in Taiwan, it is important to combine clinical aspects into the production of these instruments and implants in order to create the best minimally invasive system for surgeons to use in Taiwan.



Yang-Hwei Tsuang  
M.D., Ph.D.

Major achievements

1. Marketing of lumbar intervertebral fusion cage for use in minimally invasive spinal surgery. (figure 1)
2. Marketing of lumbar bone screws for use in minimally invasive spinal surgery. (figure 2)
3. Marketing of surgical instruments for use in minimally invasive spinal surgery. (figure 3)

Representative figures

1



United States Patent Tsuang et al.

Patent No.: US 8,784,493 B2  
Date of Patent: Jul. 22, 2014

INTEVERTEBRAL CAGE AND IMPLANTING APPARATUS AND OPERATING METHOD THEREOF

Inventors: Yang-Hwei Tsuang, Taipei (TW); Huang-Ren Liang, Hsinchu (TW); Chang-Jung Chiang, Taipei (TW); Chih-Hsien Chen, Nsoi (Taipei) (TW); Fong-Mu Hwang, Taipei (TW); Yang-Fang Tsai, Taichung (TW)

Assignee: Willtron Co., Ltd., Hsinchu County (TW)

Foreign Application Priority Data

Int. Cl. Class. H10B 1/24

Field of Classification Search

References Cited

16 Claims, 12 Drawing Sheets

2



3



United States Patent Application Publication

Pub. No.: US 2015/0127064 A1  
Pub. Date: May 7, 2015

INTEVERTEBRAL CAGE AND IMPLANTING APPARATUS AND OPERATING METHOD THEREOF

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Assignee: Willtron Co., Ltd., Hsinchu County (TW)

Foreign Application Priority Data

Int. Cl. Class. H10B 1/24

Field of Classification Search

References Cited

16 Claims, 12 Drawing Sheets

United States Patent Application Publication

Pub. No.: US 2012/032242 A1  
Pub. Date: Dec. 20, 2012

MINIMALLY INVASIVE SPINAL STABILIZATION SYSTEM

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Assignee: Willtron Co., Ltd., Hsinchu County (TW)

Foreign Application Priority Data

Int. Cl. Class. A61B 1/24

Field of Classification Search

References Cited

16 Claims, 12 Drawing Sheets

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Major publications

- [1] Minimally Invasive Spinal Stabilization System. United States Patent No. US8,784,424 B2. 2014/07/22~
- [2] Intervertebral Cage and Implanting Apparatus and Operating Method Thereof. United States Patent No. US8,784,493 B2. 2014/07/22~
- [3] Spinal Cage and Implanting Method Thereof. United States Patent No. US8,840,648 B2. 2014/09/23~
- [4] Minimally Invasive Spinal Stabilization Method. United States Patent No. US8,870,879 B2. 2014/10/28~
- [5] Spinal Disc Anulus Repair Method and Apparatus. United States Patent No. US8,876,841 B2. 2014/11/04~
- [6] Insertion Apparatus for Aligning Cage of Intervertebral Fusion. United States Patent No. US8,177,844 B2. 2012/05/15~

Major research aims

The gastrointestinal (GI) tract is important in children for nutritional requirement but also for its key role in immunity and gut-brain axis. Gut flora is involved in a variety of diseases and a reservoir of antibiotic resistance. Dr. Fang's studies focus on (1) rapid accurate detection of *Salmonella* and its antibiotic resistance, (2) effects of probiotics and health foods on human GI infections, (3) pathogen-host interactions using human intestinal *in vitro* organ cultures and *in vitro* M cell models, and (4) gut microbiota. Dr. Fang discovered six *Salmonella* virulence genes in UK, including *yqiC* that is required for bacterial colonization in human cells. He is characterizing YqiC for identifying its inhibitors as specific antibiotics, developing multigene diagnostic tools for detecting *Salmonella* and antibiotic resistance, validating probiotics for decolonizing vancomycin-resistant *enterococci* (VRE), and studying microbiota-related diseases, showing his great interest in translational medicine bridging basic and clinical sciences.

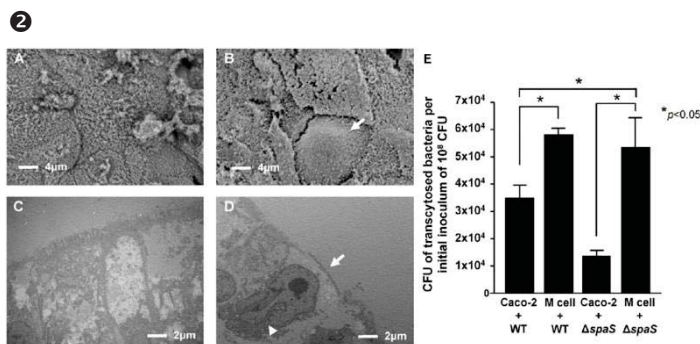
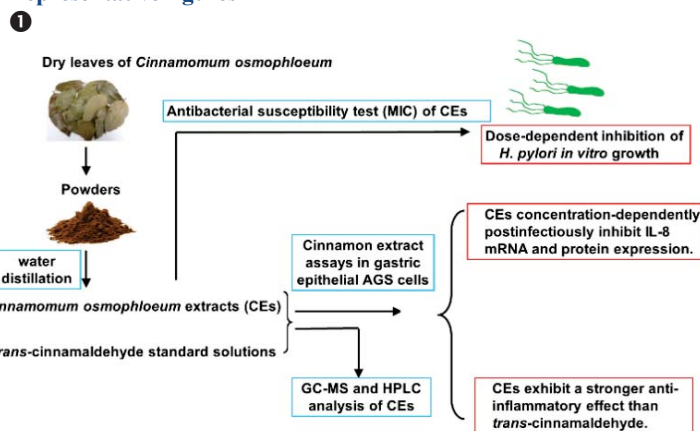


Shiuh-Bin Fang  
M.D., Ph.D.

Major achievements

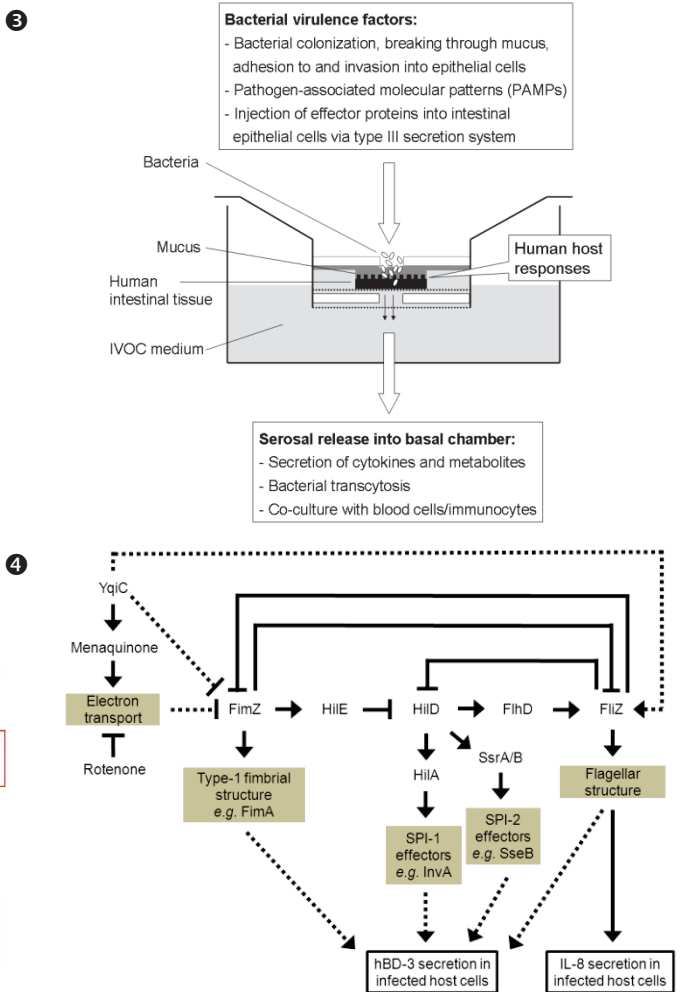
1. The first report of indigenous cinnamon to inhibit growth of *Helicobacter pylori* and postinfectious inflammation in the gastric epigastrium *in vitro* (Figure 1)
2. Establishment of the first *in vitro* M-cell model (morphology and transcytosis function) in Taiwan (Figure 2)
3. Establishment of the first human intestinal polarized *in vitro* organ culture (IVOC) in Taiwan (Figure 3)
4. Characterization of *Salmonella* virulence genes *yqiC* in its role in bacterial colonization, regulation of pathogenicity and host immunity (Figure 4)
5. Discovery of the multiple gene combination using next generation sequencing (NGS) that can be applied to the development of rapid accurate diagnostic tools for detecting ampicillin resistance in *Salmonella*

Representative figures



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Major publications

- [1] Fang SB, Huang CJ, Huang CH, et al. *speG* is required for intracellular replication of *Salmonella* in various human cells and affects its polyamine metabolism and global transcriptomes. *Front Microbiol* 2017;8:2245.
- [2] Wang KC, Huang CH, Ding SM, et al. Role of *yqiC* in the pathogenicity of *Salmonella* and innate immune responses of human intestinal epithelium. *Front Microbiol* 2016;7:1614.
- [3] Wang KC, Huang CH, Huang CJ, et al. Impacts of *Salmonella enterica* serovar Typhimurium and its *speG* gene on the transcriptomes of *in vitro* M cells and Caco-2 cells. *PLoS One* 2016;11: e0153444.
- [4] Fang SB, Ko HY, Huang ST, et al. *Cinnamomum osmophloeum* extracts inhibits growth of *Helicobacter pylori* and postinfectious interleukin-8 expression in human gastric epithelial cells. *RSC Adv* 2015;5:22097-105.
- [5] Fang SB, Schüller S, Phillips AD. Human intestinal *in vitro* organ culture as a model for investigation of bacteria-host interactions. *J Exp Clin Med* 2013;5:43-50.

Major research aims

Metabolic neuromuscular disorders (MNMD) encompass a broad-spectrum of disorders which involving dis-regulation of glycogenesis, muscle fat oxidation and mitochondrial-associated function. The clinical manifestations were included floppy, muscle weakness, exercise intolerance, muscle cramps, atrophy, and rhabdomyolysis. Understanding the pathophysiologic changes will aid clinical research and policies focused on treatment and prevention of diseases. Among our research team, we focus the skeletal muscle critical physiological function including energy expenditure, metabolism, and physical strength. Another leading role- mitochondria, transcriptionally control the down-stream express of nuclear and mitochondrial genes. For the translational medicine, we do the researches on patient-based study, from the clinical information, the laboratory examination, and muscle biopsy to the next generation sequencing genetic study. Furthermore, we manipulate the muscle cells, fibroblasts and peripheral lymphocytes to bench for the extra-vivo functional test or drug-treating screen.

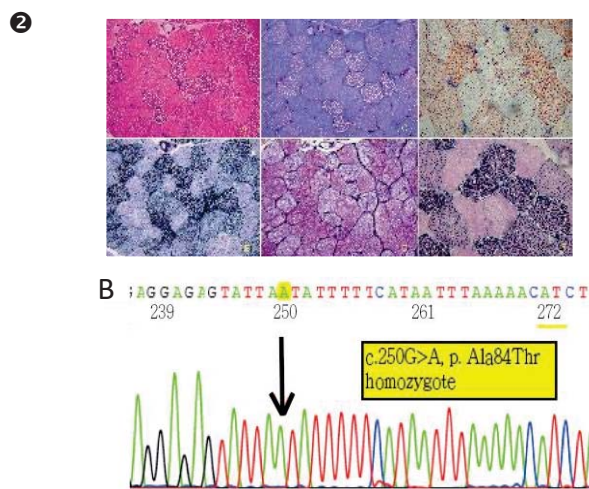
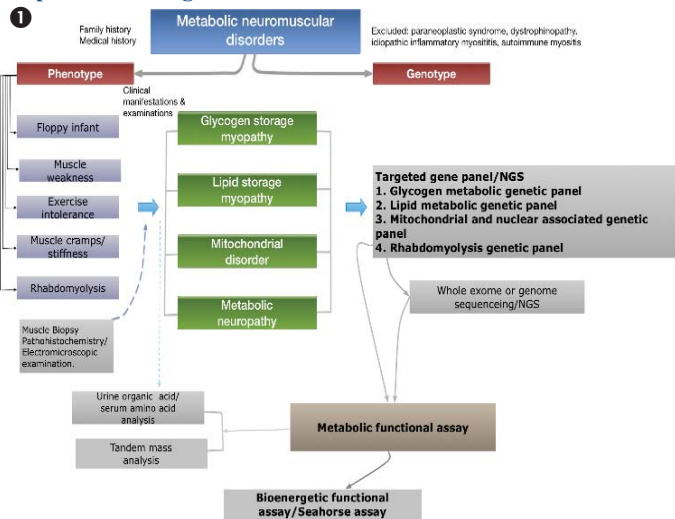


Yung-Ting Kuo  
M.D., Ph.D.

Major achievements

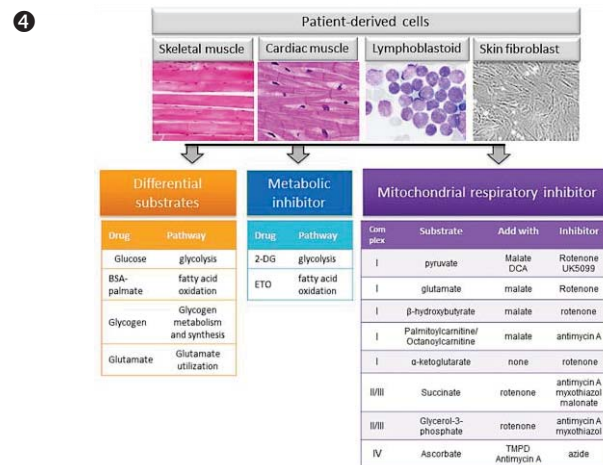
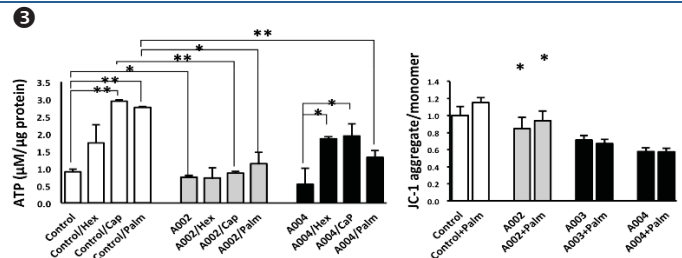
1. Transcriptional medical research in the late onset Pompe patients via the clinical features, muscle histopathology and the functional assay of genotype p.[W746C;G576S], p.V939LfsX78.
2. Elucidate the pivotal role FOXO1 in the metabolic switch from the utilization of carbohydrate to the oxidation of lipids.
3. Explore the role of CoQ10 in the treatment functional survey via the lymphoblasts from the patients diagnosed lipid storage myopathy with ETFDH mutant.
4. Elucidate the effects in activating the mitochondrial OXPHOS pathway via the PGC-1 $\alpha$  to prevent skeletal atrophy after denervation.

Representative figures



Staff and contact information

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1. The diagnosis process to clarify the relationships between phenotype and genotype of the MNMD.
2. (A) Lipid droplets were accumulated in the muscle sections in the patient with homozygous ETFDH mutation. (B) The c.250G>A transition mutation in ETFDH exon 3 results in p.Ala84Thr homozygous mutation is proved from patients with lipid storage myopathy.
3. The effects of ETFDH mutation on ATP synthesis and mitochondrial membrane potential.
4. Establishment of a screening platform for identifying abnormal cell metabolic pathways.

Major publications

- [1] Kuo YT, Shih PH, Kao SH, et al. Pyrroloquinoline quinone resists denervation-induced skeletal muscle atrophy by activating PGC-1 $\alpha$  and integrating mitochondrial electron transport chain complexes. PLoS One 2015; 10:e0143600.
- [2] Lin WC, Shih PH, Wang W, et al. Inhibitory effects of high satbility fucoxanthin on palmitic acid-induced lipid accumulation in human adipose-derived stem cells through modulation of long non-coding RNA. Food Funct 2015; 6:2215 -23.
- [3] Kuo YT, Lin TH, Chen WL, et al. Alpha-Lipoic acid induces adipose triglyceride lipase expression and decreases intracellular lipid accumulation in HepG2 cells. Eur J Pharmacol 2012; 692:10-8.
- [4] Yang CC, Chien YH, Lee NC, et al. Rapid progressive course of later-onset pompe disease in chinese patients. Mol Genet Metab 2011; 104:284-8.

Major research aims

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease that develops in preterm neonates treated with oxygen and positive-pressure ventilation. Despite recent improvements in treating respiratory distress syndrome in preterm infants, BPD remains a major cause of morbidity and mortality and many infants experience significant respiratory illnesses. No effective therapy is currently clinically available to prevent the development and long-term pulmonary sequelae of BPD. The lung development and injury research team established an experimental model of BPD induced by maternal inflammation and postnatal hyperoxia exposure in neonatal rats. The research aims are to explore the mechanisms of the development of BPD, discover the link between BPD and long-term respiratory morbidities, and find new therapeutic strategies for BPD.

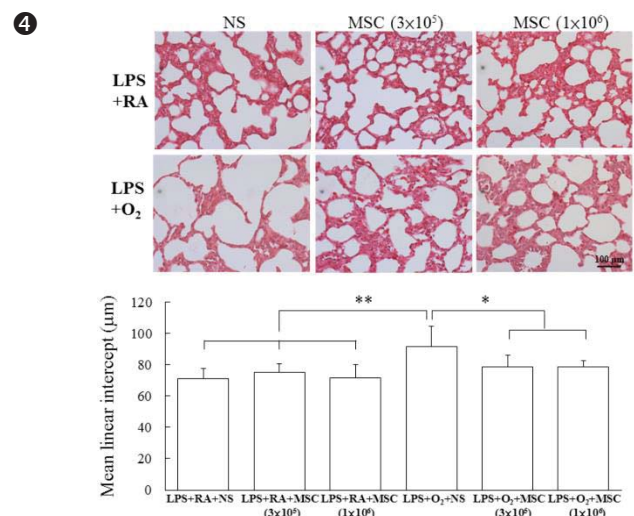
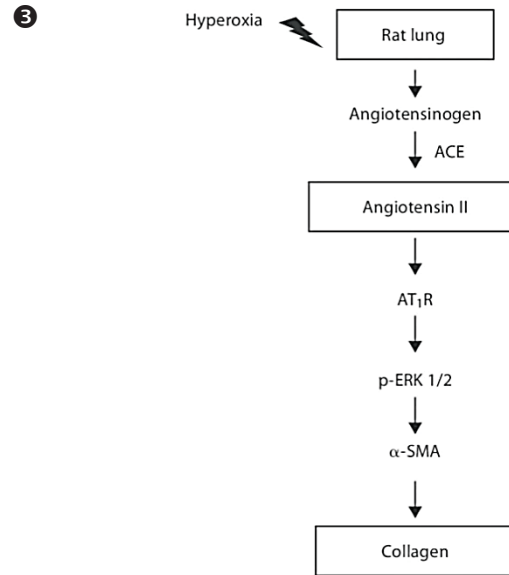
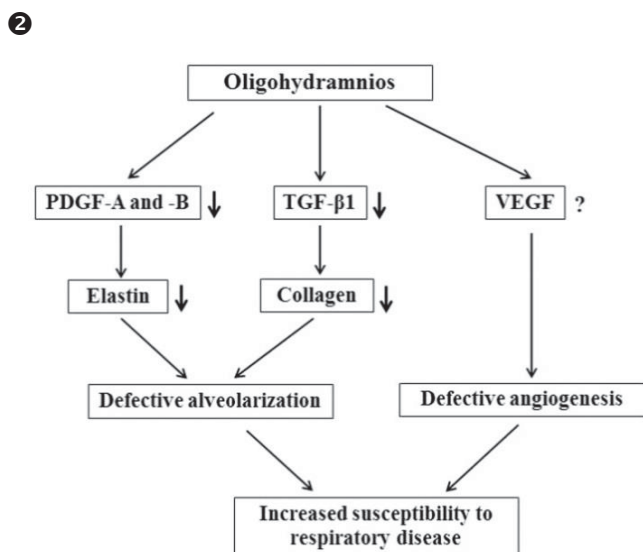
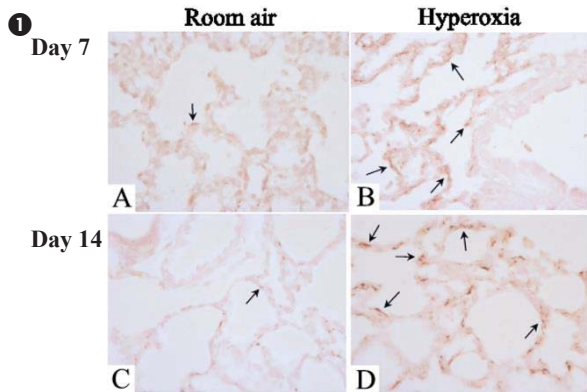


Chung-Ming Chen  
M.D., Ph.D.

Major achievements

1. Discovery of connective tissue growth factor (CTGF) up-regulation preceding the fibrotic phase of the hyperoxia-induced lung injury (Figure 1).
2. Exploration of the mechanisms of oligohydramnios-induced pulmonary hypoplasia and describe the long-term respiratory outcomes in childhood of oligohydramnios-exposed fetuses by a population-based study (Figure 2).
3. Clarification of the role of renin-angiotensin system in hyperoxia-induced lung injury (Figure 3).
4. Validation of the effectiveness of human mesenchymal stem cells on alleviating experimental bronchopulmonary dysplasia and pulmonary hypertension (Figure 4).

Representative figures



Major publications

- [1] Su CL, Chou HC, Huang LT, et al. Combined effects of maternal inflammation and neonatal hyperoxia on lung fibrosis and RAGE expression in newborn rats. *Pediatr Res* 2014; 75:273-80.
- [2] Huang LT, Chou HC, Lin CM, et al. Maternal nicotine exposure exacerbates neonatal hyperoxia-induced lung fibrosis in rats. *Neonatology* 2014; 106:94-101.
- [3] Chen CM, Chou HC, Huang LT. Maternal nicotine exposure induces epithelial-mesenchymal transition in rat offspring lungs. *Neonatology* 2015; 108:179-87.
- [4] Yeh TF, Chen CM, Wu SY, et al. Intra-tracheal administration of budesonide/surfactant to prevent bronchopulmonary dysplasia. *Am J Respir Crit Care Med* 2016; 193:86-95.
- [5] Chou HC, Li YT, Chen CM. Human mesenchymal stem cells attenuate experimental bronchopulmonary dysplasia induced by perinatal inflammation and hyperoxia. *Am J Transl Res* 2016; 8:342-53.

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Major research aims

Epilepsy surgery for children with refractory epilepsy is an important treatment option. Surgically remediable epilepsies should be identified early. The etiological diseases for localization-related epilepsy include malformation of cortical development, cerebral hemispheric tumor, cerebral ischemia/infarction, hippocampal sclerosis, Sturge-Weber syndrome, hypothalamic hamartoma (HH), Rasmussen encephalitis, and others. We can perform complete phase I and II presurgical evaluation such as long-term video electroencephalography (EEG) monitoring, electrocorticography, neuropsychological evaluation, 3T MRI/fMRI, FDG PET and MRI-PET. Epilepsy animal model and stem cell research were also conducted in different laboratories in TMU.

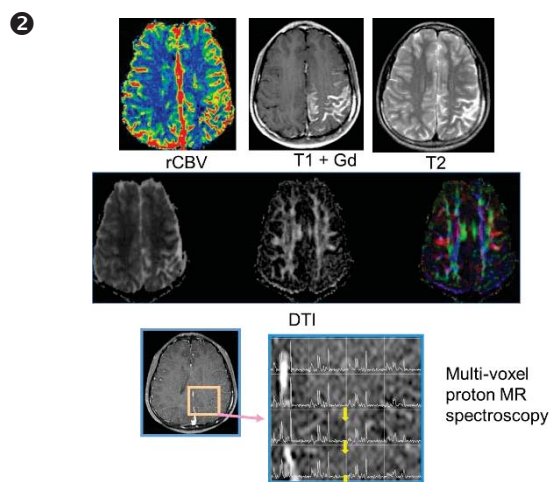
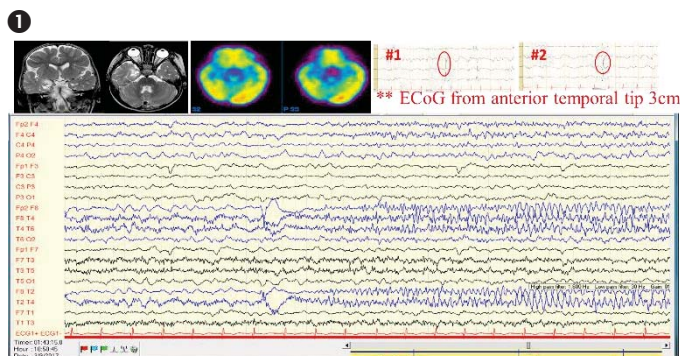


Tai-Tong Wong  
M.D.

Major achievements

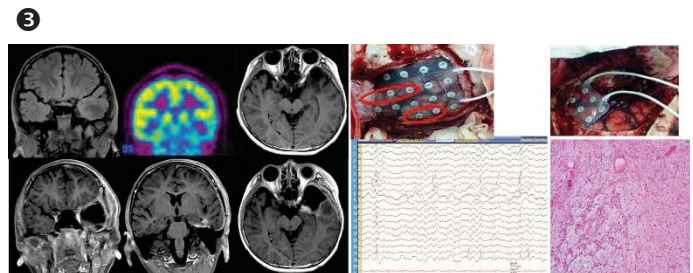
1. Established long-term video EEG monitoring system and intraoperative electrocorticography (ECoGs) for children with intractable epilepsy.
2. Complete presurgical evaluation including 3D-MRI, PET scan for determining the region of seizure onset in lesional and nonlesional epilepsy surgery in children
3. ECoGs are used for mapping the irritative and epileptogenic zone during epilepsy surgery and based on epileptiform activity and high-frequency oscillation EEG changes.
4. For eloquent cortex resections, the environment of pre-surgical functional MRI study integrating with neuronavigation, invasive subdural grid monitoring, and intraoperative neurophysiological monitoring has been established.

Representative figures



Staff and contact information

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- 1 This 2y7m-old girl with intractable seizures. VEEG showed ictal epileptogenicity from right anterior and mid-temporal area. Intraoperative ECoGs showed epileptiform discharges from inferior temporal regions. MRI and PET showed a lesion over right anterior medial temporal lobe. After surgery, this patient is seizure free. The pathology showed ganglioglioma.
- 2 14-years-old boy with Sturge Weber syndrome (SWS): Perfusion imaging: Increased CBV due to pial angiomas, part of pathogenicity of SWS. T1: leptomeningeal enhancement. T2 focal atrophy. DTI: Loss of white matter fractional anisotropy in the region of focal atrophy. Multivoxel proton MR spectroscopy: Decreased N-acetylaspartate at 2.0 ppm, indicating neuron loss (yellow arrows) in the region of focal brain atrophy.
- 3 9-year-old boy with intractable seizures. Upper panel of MRIs and PET showed a lesion over left temporal lobe and second panel of pictures showed after operation. Lower 2 panels showed intraoperative ECoG and pathology picture. The final pathology diagnosis is dysembryoplastic neuroepithelial tumor.

Major publications

- [1] Tsai ML, Liu YL, Chang H, et al. Epilepsy in children with brain tumor: a retrospective clinical analysis. *Brain & Development* 2017; 39:149.
- [2] Tsai ML, Chang H, Wong TT, et al. Quantitative study of intraoperative electrocorticography and seizure outcome in children with intractable epilepsy. *International Child Neurology Congress, Amsterdam 2016.*
- [3] Tsai ML, Hung KL, Jiang YY, et al. Long-term neurocognitive outcome and auditory event-related potentials after complex febrile seizures in children. *Epilepsy Behav* 2015; 47:55-60.
- [4] Chiang KL, Wong TT, Kwan SY, et al. Finding on brain MRI mimicking focal cortical dysplasia in early Rasmussen's encephalitis: a case report and review. *Childs Nerv Syst* 2009; 25:1501-6
- [5] Wong TT, Shih YS, Chang CN, et al. Epilepsy surgery programs in Taiwan. *Neurology Asia* 2007; 12:17-21
- [6] Wong TT, Kwan SY, Chang KP, et al. Corpus callosotomy in children. *Childs Nerv Syst* 2006; 22:999-1011.

### Major research aims

Pulmonary fibrosis diseases including chronic obstructive asthma (COA) involve a significant degree of airway remodeling and lung fibrosis. Knowledge and understanding of the possible mechanisms and pathways underlying the inflammatory responses is urgently required to the development of therapy and drug designs leading to better clinical care to patients with lung fibrosis. Therefore, it is important to collaborate pulmonary medicine (from the three affiliated hospitals in Taipei Medical University) with basic sciences. Based on the concept of translational medicine, the inflammation research group (IRG) provides several research platforms for lung fibrosis research, including molecular mechanics, clinical translational study, and anti-fibrotic drug design. International collaboration is also a major task to IRG for the leading role in lung fibrosis research. The consequent results/techniques will be transferred to patents for health and human welfare.

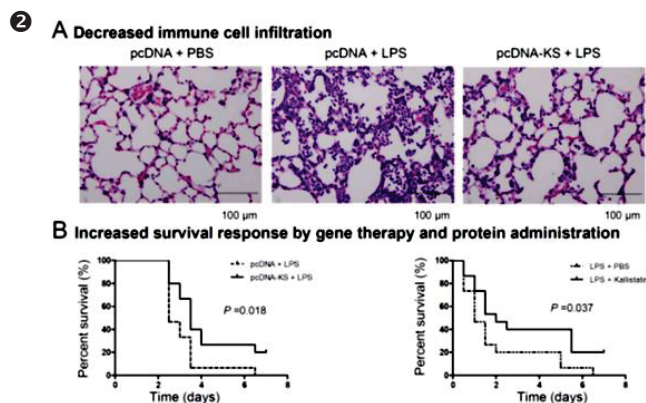
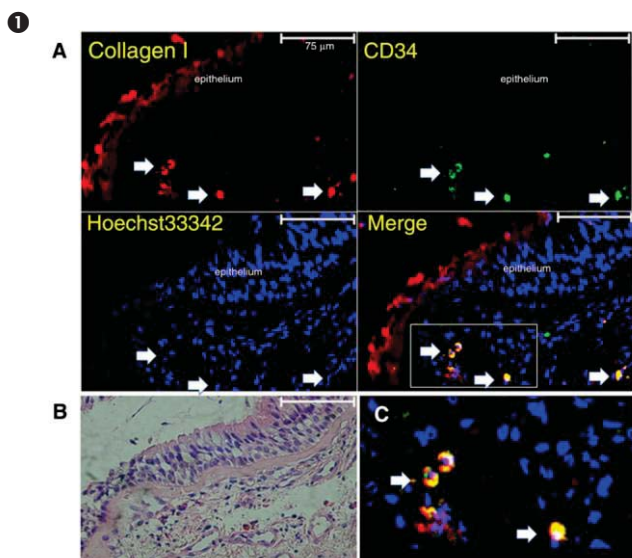


Chien-Huang Lin  
Ph.D.

### Major achievements

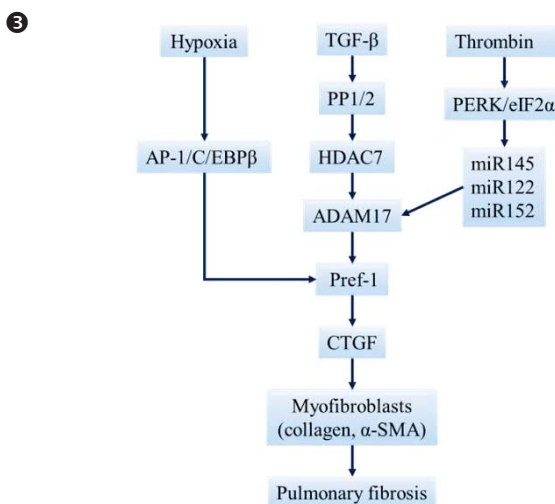
1. The endothelin A receptor mediates fibrocyte differentiation in chronic obstructive asthma (COA).
2. HDAC2 and HDAC7 regulate CTGF expression and pulmonary fibrosis in COA.
3. The protective role of kallistatin against oxidative stress-regulated NF- $\kappa$ B activation and Fas-mediated lung epithelial cell apoptosis in LPS-induced acute lung injury.
4. The role of ADAM 17 in hypoxia-induced CTGF expression and pulmonary fibrosis.
5. Pre-clinical study for lung fibrosis drug.

### Representative figures



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- 1 Identification of collagen I (Col-I)<sup>+</sup>/CD34<sup>+</sup> fibrocytes in the airway walls of patients with chronic obstructive asthma (COA). (A–C) The paraffin sections of airway tissue from patients with COA were stained for the CD34 surface marker (green), intracellular Col-I (red), and nuclei (blue) (A), and for hematoxylin and eosin staining (B). The arrows indicate the Col-I<sup>+</sup>/CD34<sup>+</sup> fibrocytes with significant yellow fluorescence in the merged image, and C shows a magnification of the merged image.
- 2 (A) Kallistatin gene delivery significantly attenuates LPS-induced lung inflammation. (B) Kallistatin gene or protein delivery improves survival in mice with LPS-induced acute lung injury.
- 3 HDAC, ADAM17 and miRNA regulate CTGF expression and pulmonary fibrosis.

### Major publications

- [1] Weng CM, Chen BC, Wang CH, et al. The endothelin A receptor mediates fibrocyte differentiation in chronic obstructive asthma. The involvement of connective tissue growth factor. *Am J Respir Crit Care Med* 2013; 188:298-308.
- [2] Weng CM, Yu CC, Kuo ML, et al. Endothelin-1 induces connective tissue growth factor expression in human lung fibroblasts by ETAR-dependent JNK/AP-1 pathway. *Biochem Pharmacol* 2014; 88:402-11.
- [3] Huang ZW, Lien GS, Chen BC, et al. p300 and C/EBP $\beta$ -regulated IKK $\beta$  expression are involved in thrombin-induced IL-8/CXCL8 expression in human lung epithelial cells. *Pharmacol Res* 2017; 121:33-41.
- [4] Ho SC, Wu SM, Lee KY, et al. Noncanonical NF- $\kappa$ B mediates the suppressive effect of neutrophil elastase on IL-8/CXCL8 by inducing NKRF in human airway smooth muscle. *Sci Rep* 2017; 7:44930.
- [5] Lin WC, Chen CW, Lin CF, et al. Kallistatin protects against sepsis-related acute lung injury via inhibiting inflammation and apoptosis. *Sci Rep* 2015; 5:12463.



### Major research aims

Chronic obstructive airway disease (COPD), a chronic inflammatory pulmonary disease characterized by a progressive airflow limitation, is a leading cause of morbidity and mortality worldwide. An abnormal inflammatory response of the lung to noxious particles or gases, mostly to smoking, appears to play a central role in the disease pathogenesis. COPD not only focuses on the lung, but also has systemic inflammation that might cause systemic manifestations of this disease. Recently, we reported that reduced expression of NKRF the NF- $\kappa$ B repressor and the repressive epigenetic writer SUV39H1 are critically implicated in the abnormal inflammation. Mechanistically, we found that NKRF can be induced by the non-canonical RelB/NF- $\kappa$ B pathway in human airway smooth muscle cells (hASM). This may provide new therapeutic potential for chronic inflammatory diseases. To explore the upstream factors leading the molecular changes, we currently focused on environmental factors. Specifically, we found an association of the novel protein ITIH4 protein with particulate matter (PM) in patients with COPD. The role of ITIH4 in COPD is currently under investigation.

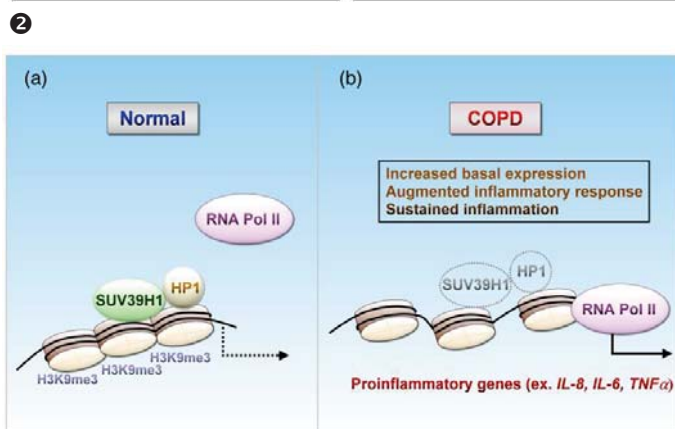
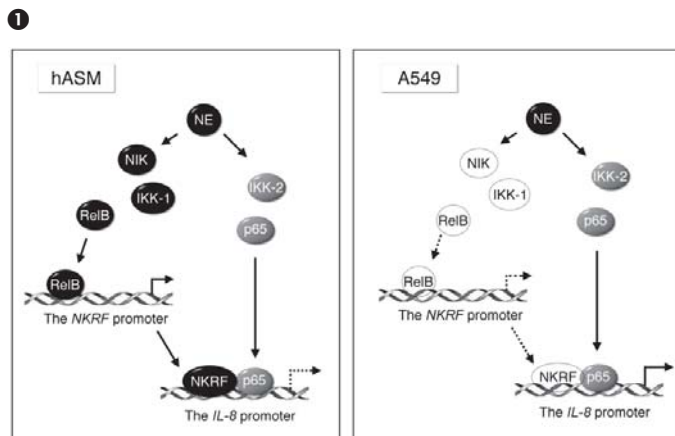


Kang-Yun Lee  
M.D., Ph.D.

### Major achievements

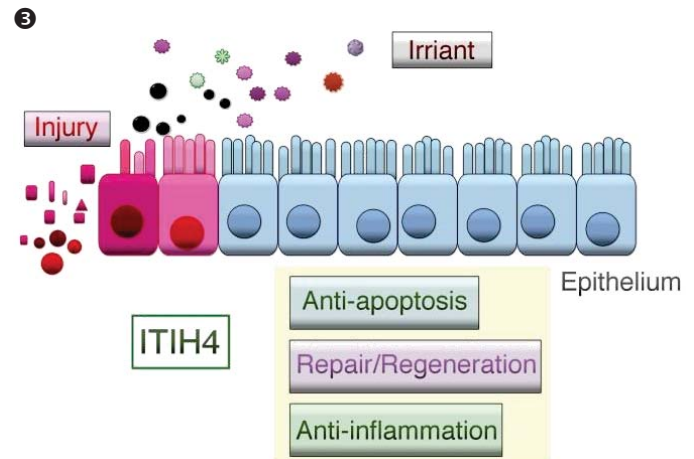
1. Neutrophil elastase (NE) suppresses IL-8 in hASM cells while stimulating its production in respiratory epithelial cells. This differential effect is mediated by the selective induction of NF- $\kappa$ B-repressing factor (NKRF) and dysregulation in chronic inflammatory diseases.
2. SUV39H1, a histone methyltransferase, epigenetically controls a distinct panel of pro-inflammatory cytokines in COPD. Its reduction leads to a loss of the repressive chromatin mark H3K9me3 and confers an abnormal inflammatory response to stimulators.
3. Analysis of serum from human revealed that inter-alpha-trypsin inhibitor heavy chain 4 (ITIH4) is reduced in COPD patients, which was strongly correlated to PM.

### Representative figures



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- 1 In hASM, NE activates rapidly the non-canonical NIK/IKK1/RelB axis. Nuclear translocated RelB binds to the  $\kappa$ B site in the NKRF promoter, transactivates and produces NKRF. Although NE stimulates the canonical IKK2/p65 pathway, the inducible NKRF bound at the IL-8 promoter abolishes the transcriptional activity of p65 NF- $\kappa$ B, leading to the suppression of IL-8.
- 2 Reduction of SUV39H1 modulation releases repressive chromatin and enhances cytokine secretion to the inflammatory environment in COPD, which potentially amplifies the inflammation response and disease progression.
- 3 ITIH4 might protect from the extracellular matrix destruction or lung epithelial cell injury and mediate anti-inflammatory or anti-apoptosis effect.

### Major publications

- [1] Ho SC, Wu SM, Feng PH, et al. Noncanonical NF- $\kappa$ B mediates the suppressive effect of neutrophil elastase on IL-8/CXCL8 by inducing NKRF in human airway smooth muscle. *Sci Rep* 2017 ;7:44930.
- [2] Chen TT, Wu SM, Ho SC, et al. SUV39H1 reduction is implicated in abnormal inflammation in COPD. *Sci Rep* 2017 ; 7:46667.
- [3] Lee KY, Chiang LL, Ho SC, et al. Associations of autophagy with lung diffusion capacity and oxygen saturation in severe COPD: effects of particulate air pollution. *Int J Chron Obstruct Pulmon Dis* 2016; 11:1569-78.
- [4] Lee KY, Feng PH, Ho SC, et al. Inter-alpha-trypsin inhibitor heavy chain 4: A novel biomarker for environmental exposure to particulate air pollution in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2015; 10:831-41.
- [5] Lee KY, Ho SC, Chan YF, et al. Reduced NF- $\kappa$ B repressing factor: a link toward systemic inflammation in COPD. *Eur Respir J* 2012; 40(4): 863-73.

Major research aims

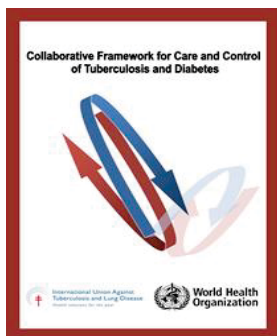
Tuberculosis (TB) is one of the most important health problems in Taiwan. The incidence of TB has been decreasing in Taiwan; however, there is a trend of an increasing proportion (53% in 2016) of TB among the elderly. The ‘Mobilization Plan to Reduce Tuberculosis by Half in Ten Years’ strategy was implemented by the Taiwan Centers for Disease Control in 2006, which includes high-quality directly observed treatment, short-course (DOTS) enhancement. We focus to study the influence of smoking, end-stage renal disease with dialysis, diabetes mellitus and long-term glycemic control on the pulmonary TB. Moreover, we also explore the impact of pulmonary TB on the clinical outcomes among long-term dialysis patients before and after DOTS implementation in Taiwan.



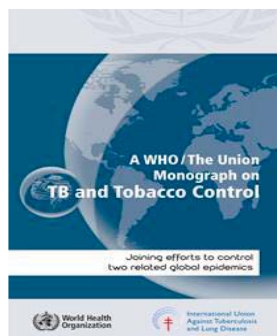
Kuan-Jen Bai  
M.D.

Major achievements

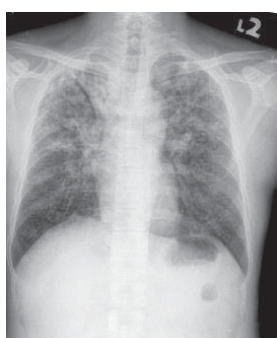
1. Smoking and diabetes have joint effects on a pretreatment positive smear. Diabetic smokers had more than a 5-fold increased risk of a pretreatment positive smear than did non-diabetic non-smokers, indicating remarkable joint effects of diabetes and smoking on the risk of TB transmission.
2. The Bureau of National Health Insurance (NHI) has implemented a pay-for-performance (p4p) program for diabetes mellitus (DM) in Taiwan. We found that enhanced case management of DM reduced risk and improved outcomes of TB among patients with DM.
3. Pulmonary TB increases the risk of morbidity and mortality in dialysis patients; DOTS implementation reduces some morbidities and TB relapse. We suggested that continuing DOTS implementation should be encouraged to improve clinical outcomes in dialysis patients.



TB and DM



TB and Smoke

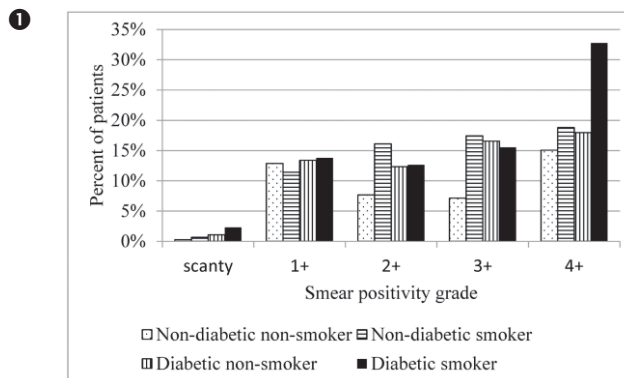


MDR-TB



TB in dialysis patients

Representative figures



②

	DM-p4p			DM-non-p4p			Non-DM		
	Number at risk	Cumulative number	Cumulative incidence	Number at risk	Cumulative number	Cumulative incidence	Number at risk	Cumulative number	Cumulative incidence
Total	79471			100000			100000		
2008 cohort	46226			85810			48334		
1-year		63	136		239	279		33	68
2-year		130	281		429	500		61	126
3-year		204	441		603	703		95	197
2009 cohort	33245			14190			51666		
1-year		34	102		63	444		49	95
2-year		85	256		81	571		85	165

③

	Total n	Success n (%)	Died n (%)	Other n (%)
Number(row %)	766	544 (71.0)	141 (18.4)	81 (10.6)
DM status				
DM-p4p	164	124 (75.6)	21 (12.8)	19 (11.6)
DM-non-p4p	492	339 (68.9)	99 (20.1)	51 (11.0)
Non-DM	110	81 (73.6)	21 (19.1)	8 (7.3)

- ① Pre-treatment smear positivity grades by smoking and diabetes
- ② Cumulative incidence rates of TB of DM- p4p, DM non-p4p and non-DM patients
- ③ Factors associated with the outcome of TB.

Major publications

- [1] Bai KJ, Lee JJ, Chien ST, et al. The influence of smoking on pulmonary tuberculosis in diabetic and non-diabetic patients. PLoS ONE 2016; 11:e0156677.
- [2] Lo HY, Yang SL, Lin HH, et al. Does enhanced diabetic management reduce the risk and improve the outcome of tuberculosis? Int J Tuberc Lung Dis 2016; 20:376-82.
- [3] Chiang CY, Van Deun A, Rieder HL. Gatifloxacin for short, effective treatment of multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2016; 20:1143-7.
- [4] Bai KJ, Huang KC, Lee CH, et al. Effect of pulmonary tuberculosis on clinical outcomes of long-term dialysis patients: Pre- and post-DOTS implementation in Taiwan. Respirology 2017; 22:991-99
- [5] Chen KY, Chuang KJ, Liu HC, et al. Particulate matter is associated with sputum culture conversion in patients with culture-positive tuberculosis. Ther Clin Risk Manag 2016; 12:41-6.

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Major research aims

Glioblastoma (GBM; WHO grade IV astrocytoma) is the most common malignant primary brain tumor. Although the treatments have been improved in the last 10 years, the prognosis remains elusive due to tumor heterogeneity and inherent chemoresistance. Numerous studies have reported the associations between MR phenotypes and specific gene mutations. To study the tumor heterogeneity, site-specific tissue samples for enhancing, infiltrative, and necrotic tumor portions were extracted by MR-guided stereotaxic surgery from patients with primary glioblastoma. Our purpose was to develop the MRI-based radiogenomics of glioblastoma and to determine the relations between image features and the underlying genotypes. We hypothesized that the tumor MR phenotypes can reflect the genotypes pattern and resistance related epigenomic modification status at a certain level, and therefore can be used to differentiate subtypes, predict the patient survivals, and thus guide therapy.

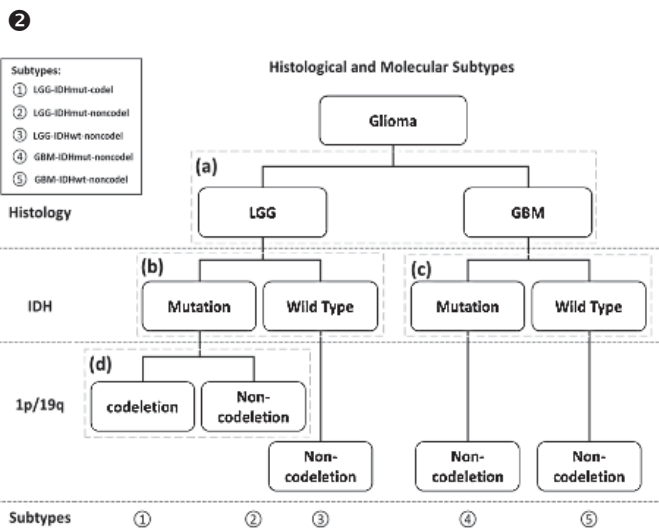
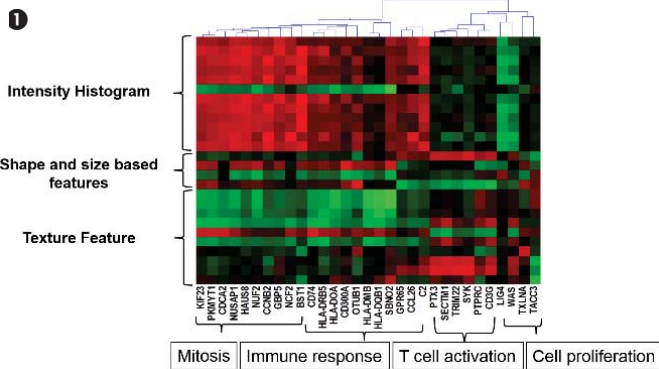


Cheng-Yu Chen  
M.D.

Major achievements

1. Novel imaging platform combining multi-modality MR techniques and multi-feature analyses, such as histogram, geometry, and texture analyses, were constructed to decode the tumor phenotypes into quantifiable features.
2. We provided insights into the connections between the genetic profiles and MR imaging phenotypes of gliomas.
3. We established imaging predicted model for predicting treatment response, tumor recurrence, and patient survivals.
4. MR epigenomic biomarker was also developed for treatment response evaluation and tumor recurrent prediction.

Representative figures



Staff and contact information

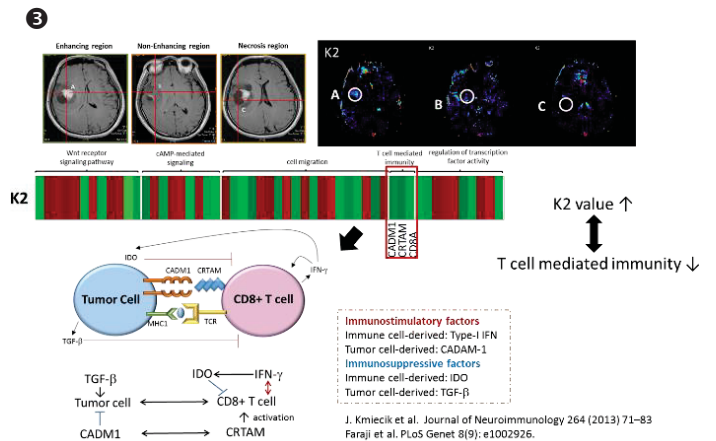
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1. Group-based correlation map between image features and Gene Ontology biological profile based on the TCGA/TCIA glioblastoma database. The hierarchical clustering of three categories of image features can well differentiate gene expressions of five biological processes.
2. The three-level machine learning classification of five glioma molecular subtypes based on MR radiomic features. Based on the MRI data of 117 subjects with glioblastoma (GBM, grade IV) and 113 subjects with lower-grade glioma (LGG, grades II and III) in TCGA/TCIA database, the machine learning classifications can achieve over 80% accuracy for differentiating molecular profiles.
3. Demonstration of vascular permeability (K2 index) in revealing the underlying T cell mediated immunity in glioblastoma. The K2 maps derived from the MR perfusion imaging from enhancing (A), infiltrative (B), and necrotic tumor (C) portions of gliomas shown a higher value in the enhancing portion and negatively correlated to the T cell mediated immunity.

Major publications

- [1] Hsieh KL, Chen CY, Lo CM. Radiomic model for predicting mutations in the isocitrate dehydrogenase gene in glioblastomas. *Oncotarget* 2017; 8:45888-45897.
- [2] Hsieh KL, Chen CY, Lo CM. Quantitative glioma grading using transformed gray-scale invariant textures of MRI. *Comput Biol Med* 2017; 83:102-108.
- [3] Hsieh KL, Hsiao CJ, Lo CM. Computer-aided grading of gliomas based on local and global MRI features. *Comput Methods Programs Biomed* 2017;139: 31-38.
- [4] Kao HW, Chiang SW, Chung CW, et al. Advanced MR imaging of gliomas: an update. *Biomed Res Int* 2013; Epub.

### Major research aims

Our team aims at the comprehensive clinical research on the atherosclerotic stenosis disease of the cerebral arteries, from the aspect of plaque pathophysiology, blood flow mechanics, cerebral hemodynamics, and brain function. Furthermore, we utilize these knowledge to provide better disease diagnosis, evaluation, and endovascular treatment to our patients. The current research focus are:

Plaque pathophysiology and stroke risk with high resolution vascular wall imaging by the 3T Magnetic Resonance Imaging (MRI). Cerebral perfusion/vascular reactivity and hyperperfusion syndrome with CT/MR perfusion and Blood oxygenation level dependent (BOLD) Functional magnetic resonance imaging (fMRI). Blood flow mechanics and endothelial injury with phase contrast Magnetic resonance angiogram (MRA) technique. Clinical outcome after endovascular treatment and stent follow-up with gemstone spectral CT.

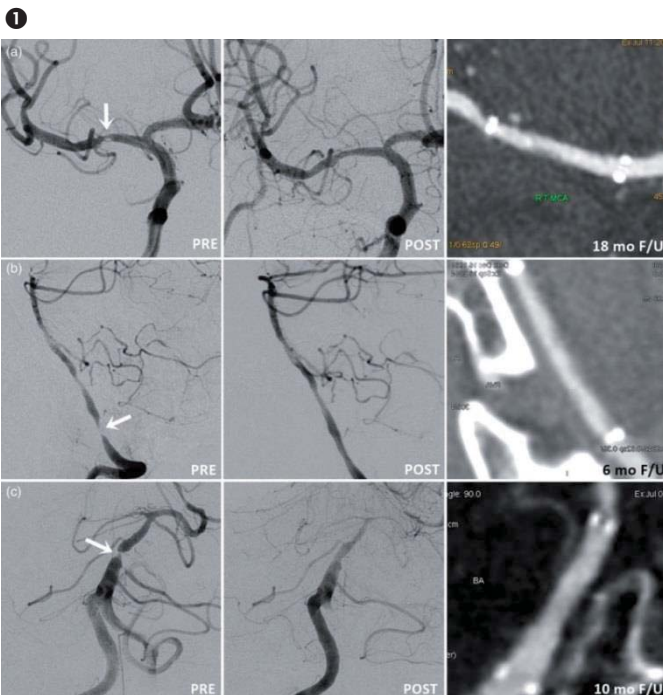


Chi-Jen Chen  
M.D.

### Major achievements

1. Multislice CT angiography had an excellent correlation with catheter angiography and may be considered as a substitute in diagnosing total versus near occlusion of the ICA.
2. Our research suggested that patients with a prolonged dMTT of more than 3 seconds should be closely monitored for evidence of hyperperfusion after undergoing carotid stenting.
3. Spectral CT may provide a noninvasive modality for following-up patients with in-stent stenosis and Iodine (water) images can help reduce stent-related artifacts of Enterprise and enhance contrast of in-stent lumen.
4. Case series from our hospital shows that using undersized angioplasty and Enterprise stenting may effectively treat high-degree symptomatic intracranial arterial stenosis with favorable clinical and angiographic outcome.

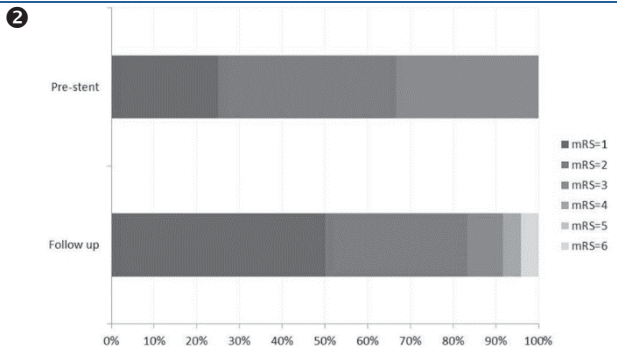
### Representative figures



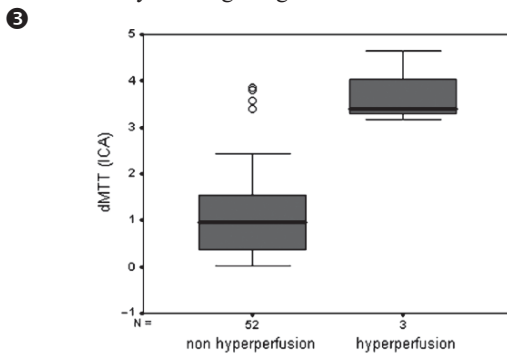
Representative angiographic images of pre-stenting, post-stenting and follow-up CTA image in cases of high-grade intracranial arterial stenosis. (a) MCA, (b) intracranial VA, and (c) BA treated with PTA and Enterprise stent deployment.

### Staff and contact information

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The favorable clinical outcome in our hospital suggests that using undersized angioplasty and Enterprise stenting may effectively treat high-degree intracranial arterial stenosis.



CT perfusion (dMTT) predict post-stent hyperperfusion

### Major publications

- [1] Lee KY, Chen DY, Hsu HL, et al. Undersized angioplasty and stenting of symptomatic intracranial tight stenosis with Enterprise: evaluation of clinical and vascular outcome. *Interv Neuroradiol* 2016; 22:187-95.
- [2] Chiang CH, Tseng YC, Chen AC, et al. In vitro comparison of intracranial stent visibility using various concentrations of gadolinium contrast agent under 1.5 T and 3 T MR angiography. *J NeuroIntervent Surg* 2017; 9:1-8.
- [3] Weng CL, Tseng YC, Chen DY, et al. Spectral imaging for intracranial stents and stent lumen. *PLoS One* 2016; 11:e0145999.
- [4] Tseng YC, Hsu HL, Lee TH, et al. Prediction of cerebral hyperperfusion syndrome after carotid stenting a cerebral perfusion CT study. *J Computer Assisted Tomography* 2009; 33: 540-45.
- [5] Chen CJ, Tseng YC, Lee TH, et al. Multisection CT Angiography compared with catheter angiography in diagnosing vertebral artery dissection. *AJNR Am J Neuroradiol* 2004; 25:769-74.
- [6] Chen CJ, Lee TH, Hsu HL, et al. Multi-slice CT angiography in diagnosing total versus near occlusions of the internal carotid artery: comparison with conventional angiography. *Stroke* 2004; 35: 83-85.

### Major research aims

We undertake osteoporosis and body composition to improve the precision and accuracy of diagnosing osteoporosis (and related fractures), sarcopenia (and falls), and obesity (and metabolic risk) in Taiwan and worldwide. Collaborates with multidisciplinary professionals to ensure osteoporosis and body composition research has real-world impact that is subsequently helpful to patients. We undertake research in osteoarthritis and platelet-rich fibrin (PRF) to make substantial contributions to knowledge of the structure and distribution of cytokines in PRF and early diagnosis of the osteoarthritic knee, and undertake research in osteonecrosis and bone marrow to make substantial contributions to knowledge of the mechanism of osteonecrosis of the femoral head (ONFH) and its clinical impact.

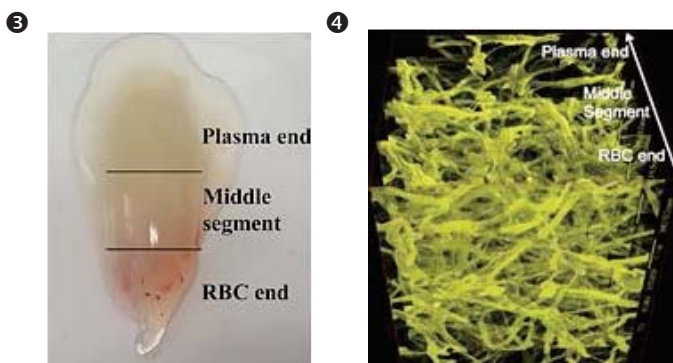
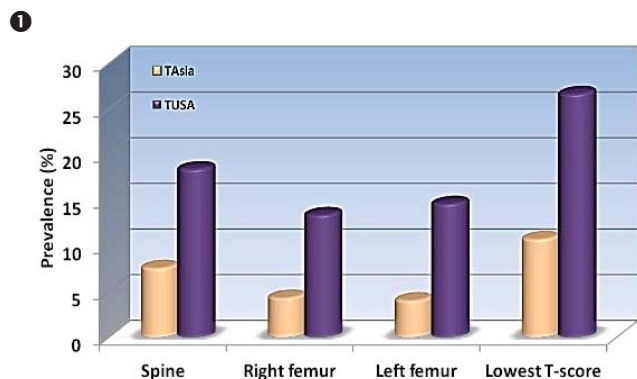


Wing P. Chan  
M.D.

### Major achievements

1. Provided the first evidence that a diagnosis of osteoporosis based on the lowest T-score from multiple-site BMD measurements using a Caucasian reference rather can improve detection of osteoporosis in a Chinese population aged 50 years or more. This change was made in clinical practice nationwide.
2. Found excellent reproducibility and repeatability via a computer tomography-based measurement of abdominal subcutaneous and visceral adipose tissues.
3. Discovered the RBC layer of a PRF gel richest in platelets and cytokines (essence PRF, or ePRF), and its properties are strongly related to its three-dimensional structure, another discovery of our team.
4. Investigated, for the first time, use of PRF and cartilage granules to facilitate the healing process of injured articular cartilage in rabbit knees in a one-step cartilage repair surgery.
5. Investigated, for the first time, delayed peak enhancement in the femoral head on DCE-MRI with negative findings on conventional MRI and intertrochanteric stasis in advanced ONFH.

### Representative figures



- ① Prevalence was found to be 26.64% using lowest T-score from 3 measuring sites by NHANES database as reference value (vs. 10.75%, Asian Reference data), which is close to the level found in post-menopausal Caucasian women (30%) as defined by WHO.
- ② Axial views of an abdominal CT scan. The SAT (red) and VAT (blue) area estimated by AZE Virtual Place software through the umbilical plane.
- ③ A PRF gel forms between the plasma layer (top) and the red blood cell (RBC) layer (bottom).
- ④ The cross-section of the PRF gel. An arrow indicates the direction of gradually decreasing compactness and increasing porosity of the PRF microstructure from the RBC end to the plasma end.

### Major publications

- [1] Chan WP, Liu YJ, Huang GS, et al. Relationship of idiopathic osteonecrosis of the femoral head to perfusion changes in the proximal femur by dynamic contrast-enhanced MRI. *AJR Am J Roentgenol* 2011; 196:637-43.
- [2] Kuo TF, Lin MF, Lin YH, et al. Implantation of platelet-rich fibrin and cartilage granules can facilitate cartilage repair in the injured rabbit knee: preliminary report. *Clinics* 2011; 66:1835-8.
- [3] Lu YC, Lin YC, Lin YK, et al. Prevalence of osteoporosis and low bone mass in older Chinese population based on bone mineral density at multiple skeletal sites. *Sci Rep* 2016; 6:25206.
- [4] Bai MY, Wang CW, Wang JY, et al. Three-dimensional structure and cytokine distribution of platelet-rich fibrin. *Clinics (Sao Paulo)* 2017; 72:116-24.
- [5] Lee YH, Hsiao HF, Yang HT, et al. Reproducibility and repeatability of computer tomography-based measurement of abdominal subcutaneous and visceral adipose tissues. *Sci Rep* 2017; 7:40389.

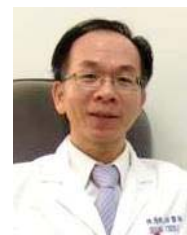
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### Major research aims

The main clinical characteristics after neurological disorders are weakness of specific muscle, loss function, and lack of mobility. Therefore, the major research goals of neurorehabilitation in our team are as follows:

1. Promote recovery from lost function and enhance independency of life in individuals with neurological disorders by using functional electrical stimulation, robot-assisted rehabilitation technology, virtual reality, neuromodulation, non-invasive brain stimulation, assistive technology and etc.
2. Incorporate clinical rehabilitation with translational medicine to facilitate outcome and efficacy of neuro-rehabilitation in individuals with neurological disorders.
3. Develop and innovate assistive technology and telemedicine to improve independency of life and early reintegration into domestic and social activity of daily living in individuals with neurological disorders



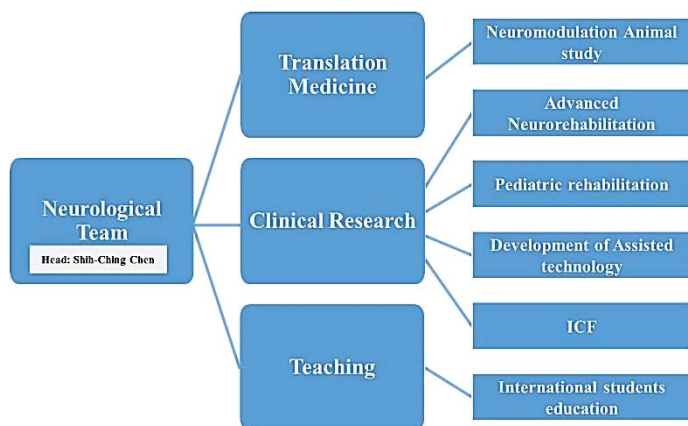
Shih-Ching Chen  
M.D., Ph.D.

### Major achievements

1. Eleven Grants regarding neurorehabilitation 2016.
2. Eighteen published journal papers about neurorehabilitation 2016.
3. Submitted three patents regarding neurorehabilitation.
4. Organizing 2017 International Conference on Biomechanics, Rehabilitation Engineering and Assistive Technology.
5. Organizing and hosting 2017 conference of Taiwan Rehabilitation Engineering and Assistive Technology Society (TREATS).
6. Organizing and hosting 2016 TREATS International Conference of Gerontechnology for Smart Life
7. Signing MoU with iHomeLab of Lucerne University of Applied Sciences and Arts in Switzerland.
8. Running the MOHW project: "The study of information and communication technology (ICT) life for the elderly and establish international cooperation".
9. Managing and operating the Assistive Devices Center entrusted by Taipei City Government

### Representative figures

①



Scheme of Neurorehabilitation Team

### Core team member:

Prof. Shih-Ching Chen, Prof. Tsan-Hon Liou,  
Assoc. Prof. Chien-Hung Lai, Assoc. Prof. Jiunn-Hong Kang, Assoc.  
Prof. Sung-Hui Tseng, Assoc. Prof. Chih-Wei Peng

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②



① Scheme of neurorehabilitation team.

② Pictures of specific neurorehabilitation including:

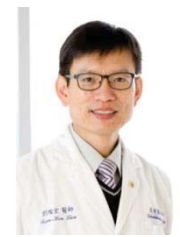
- (A) Translation medicine
- (B) Robot-assisted Rehabilitation
- (C) Virtual Reality Rehabilitation
- (D) Non-invasive Brain Stimulation
- (E) Assistive Technology

### Major publications

- [1] Wang TY, Chen SC, Lai CH et al. Relevance of nerve conduction velocity in the assessment of balance performance in older adults with diabetes mellitus. *disability rehabilitation* 2016; 3:1-9.
- [2] Lin YT, Hsieh TH, Chen SC et al. Effects of pudendal neuro-modulation on bladder functions in chronic spinal cord-injured rats. *J Formosan Med Assoc* 2016; 115:703-13.
- [3] Hsieh TH, Lin YT, Chen SC, et al. Chronic pudendal neuro-modulation by using an implantable microstimulator improves voiding function in diabetic rats. *J Neural Eng* 2016; 13:046001-12.
- [4] Chen SC, Hsieh TH, Fan WJ, et al. Design and evaluation of potentiometric principles for bladder volume monitoring: a preliminary study. *Sensors* 2015; 15:12802-15.
- [5] Lin YN, Hu CJ, Chi JY et al. Effects of repetitive transcranial magnetic stimulation of the unaffected hemisphere leg motor area in patients with subacute stroke and substantial leg impairment: A pilot study. *J Rehabil Med* 2015; 47: 305-10

### Major research aims

People with disability account for 15% of the global population, with an estimated population of 1 billion in the world. Disability is one of the most crucial concerns among non-communicable diseases identified by the World Health Organization (WHO) post-2015 agenda. The World Health Organization (WHO) developed the International Classification of Functioning, Disability, and Health (ICF) framework in 2001 to describe health and disability at both individual and societal levels. Moreover, from the concept of ICF WHO Disability Assessment Schedule 2.0 (WHODAS 2.0) was developed as an objective and quantitative assessment tool for disability status evaluation. The ICF framework provides a scientific approach for collecting reliable statistics on disabled populations.



Tsan-Hon Liou  
M.D., Ph.D.

### Major achievements

1. In 2007, Taiwan legislated a constitutional amendment known as the People with Disabilities Rights Protection Act. Since July 2012, the act has mandated that assessing individual eligibility for disability benefits should be based on the ICF framework.
2. From July 2012 to December 2015, more than 500,000 people applied for disability benefits and received mandated social welfare services to enhance their social participation.
3. We used the WHODAS 2.0 to measure these people's disabilities and observed that age, educational level, socioeconomic status, work status, aboriginal status, and degree of impairment were independent variables of disability after adjustment.
4. Taiwan is the first country to propose a social welfare system based on the WHO's ICF. Through this disability system, we can understand more clearly the prevalence, daily difficulties, and needs of people with various types of disability.
5. This can assist the government in providing appropriate and adequate social welfare services including environmental modifications, assistive devices, vocational rehabilitation, and special education.
6. Based on the framework of WHODAS 2.0, we continued to investigate the disability status caused by different kinds of diseases from Taiwan.

### Representative figures



### Staff and contact information

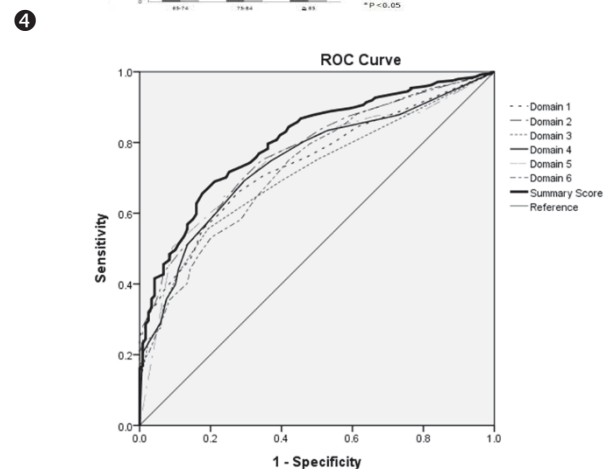
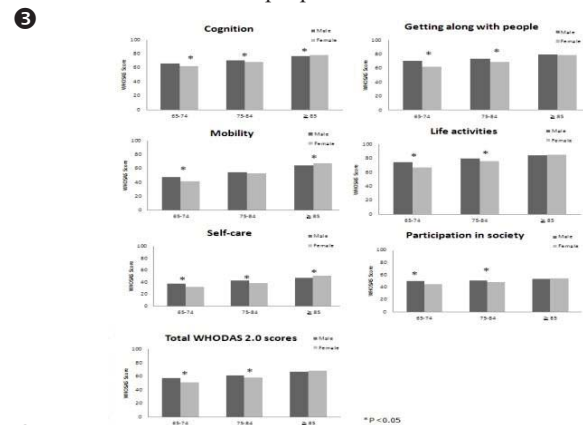
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The proposed system provides critical information to assist policy-makers in determining the optimal allocation of social welfare and medical resources for people with disabilities.



- 1 The principle investigator, Prof. Liou, was awarded research for disability and ICF
- 2 Team members of the ICF group
- 3 Comparison the scores of WHODAS 2.0 in different domains between male and female dementia patients when aged from 65 to 74, 75 to 84 and 85 years old.
- 4 Receiver operating characteristic (ROC) curve analyses of the opportunity to RTW in stroke patients, according to WHODAS 2.0 summary scores and domains.

### Major publications

- [1] Huang SW, Chang KH, Escorpizo Reuben, et al. Functioning and disability analysis by using WHO disability assessment schedule 2.0 in older adults Taiwanese patients with dementia. *Disabil Rehabil* 2016; 38:1652-63.
- [2] Huang SW, Chi WC, Yen CF, et al. Does more education mean less disability in people with dementia? A large cross-sectional study in Taiwan. *BMJ Open* 2017; 7:e013841.

### Major research aims

The TMU Renal Medicine, consisting of 21 nephrologists, extends our attention from clinical care to translational study. Multidisciplinary research in chronic kidney disease (CKD) includes big data analysis (national-wide project and data bank), clinical trial of periodontal disease in hemodialysis patients, animal model of renal fibrosis, new compound development for renal fibrosis, and artificial kidney (hollowfiber). The TMU Renal Medicine also initiated the integrated and cooperative project on the study of AKI to CKD. The clinical biomarkers and pathologic change of the transition were investigated. We delineate the inherited / acquired role of mitochondria dysfunction on the progression of renal disease. In addition, we participated in several international clinical trials, including (PI-initiated) the impact of periodontitis on outcomes in dialysis patients, and the trials of new medications for diabetic nephropathy.

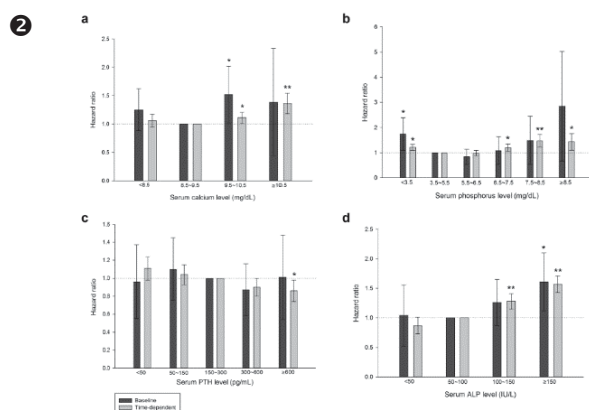
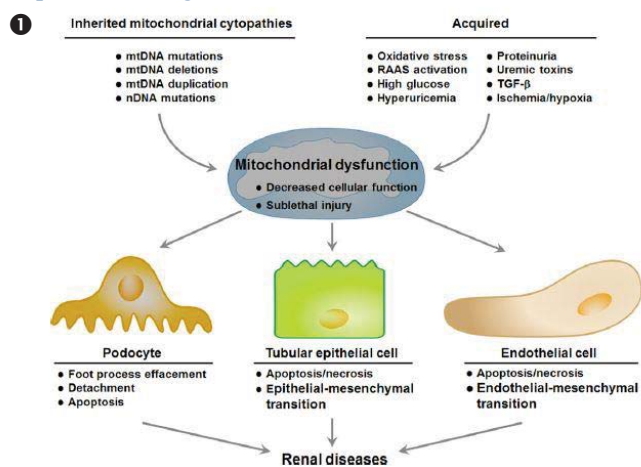


Mai-Szu Wu  
M.D.

### Major achievements

1. CKD-MBD biomarker: the detrimental effect of Alk-P on survival in chronic peritoneal dialysis patients
2. Anti-fibrosis in CKD: the effect of oligo-fucoidan from interfering with the interaction between CD44 and its extracellular ligands
3. Mitochondria dysfunction: inherited and acquired effects on the progression of renal disease (AKI to CKD)
4. Dialyzer membrane: Novel Microtube Array Membrane (MTAM) and its potential applications
5. Klotho on fibrosis: Klotho and TRPC6 inhibition act to protect against obstruction-induced renal fibrosis
6. PI-initiated clinical study: Periodontitis and its impact on outcomes in renal failure patients
7. Phase 3 international clinical trials: Finerenone for progression of diabetic nephropathy (Bayer®); Atrasentan in diabetic nephropathy (AbbVie®); Phase 2 of OMS721 in thrombotic microangiopathies (OMEROS®)

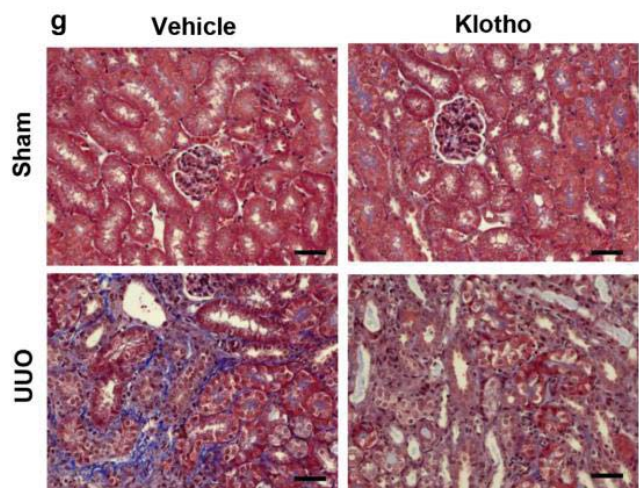
### Representative figures



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**3**



- 2016 Annual Report on Kidney Disease in Taiwan
- Detrimental effect of Alk-P on survival was more consistent in chronic peritoneal dialysis patients
- Oligo-fucoidan prevents renal tubulointerstitial fibrosis in a CKD model
- Klotho and TRPC6 inhibition act in the same pathway to protect against obstruction-induced renal fibrosis
- APD patients had similar outcomes to those of CAPD patients

### Major publications

- [1] 2016 Annual report on kidney disease in Taiwan.
- [2] Liu CT, Lin YC, Lin YC, et al. Roles of serum calcium, phosphorus, PTH and ALP on mortality in peritoneal dialysis patients: A nationwide, population-based longitudinal study using TWRDS 2005-2012. *Sci Rep* 2017; 7:33.
- [3] Chen CH, Sue YM, Cheng CY, et al. Oligo-fucoidan prevents renal tubulointerstitial fibrosis by inhibiting the CD44 signal pathway. *Sci Rep* 2017; 7:40183.
- [4] Wu YL, Xie J, An SW, et al. Inhibition of TRPC6 channels ameliorates renal fibrosis and contributes to renal protection by soluble klotho. *Kidney Int* 2017; 91:830-41.
- [5] Tang CH, Chen TH, Fang TC, et al. Do automated peritoneal dialysis and continuous ambulatory peritoneal dialysis have the same clinical outcomes? A Ten-year Cohort Study in Taiwan. *Sci Rep* 2016; 6:29276.



Major research aims

As the lack of effective prevention and treatment of acute kidney injury (AKI), the TMU-AKI research team tries to disclose major mechanisms of the disease and develop corresponding biomarkers and useful remedies. We found prostacyclin protects renal tubular cells from gentamicin-induced apoptosis via a PPAR $\alpha$ -dependent pathway. Including urotensin II, Rosuvastatin, L-carnitine and leptin, all revealed similar beneficial effects in the successive studies and provided potential treatments for AKI. We also found microRNA-494 reduces ATF3 expression and promotes AKI. MicroRNA-494 may be a specific and noninvasive biomarker for AKI. We disclosed the nephrotoxicity of Zinc oxide nanoparticles (ZnO NPs) and a protective role of hypoxia-inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) in adaptation to the toxicity of ZnO NPs. By the use of Taiwan National Health Insurance Research Database, we described the presentation and prognosis of AKI in critical ill patients. Currently, we are stepping in the intervention of AKI-CKD continuum.

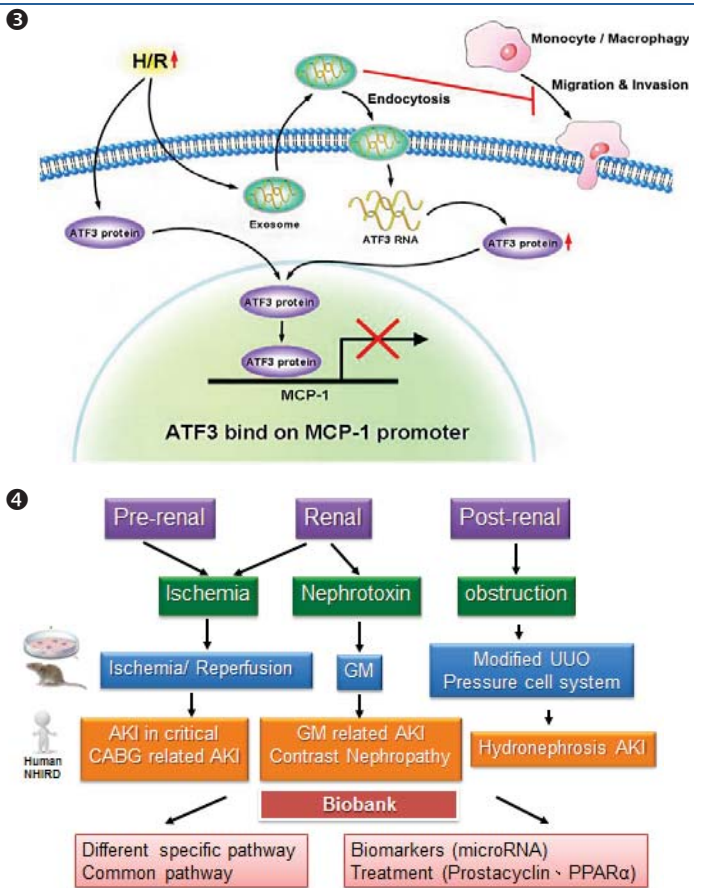
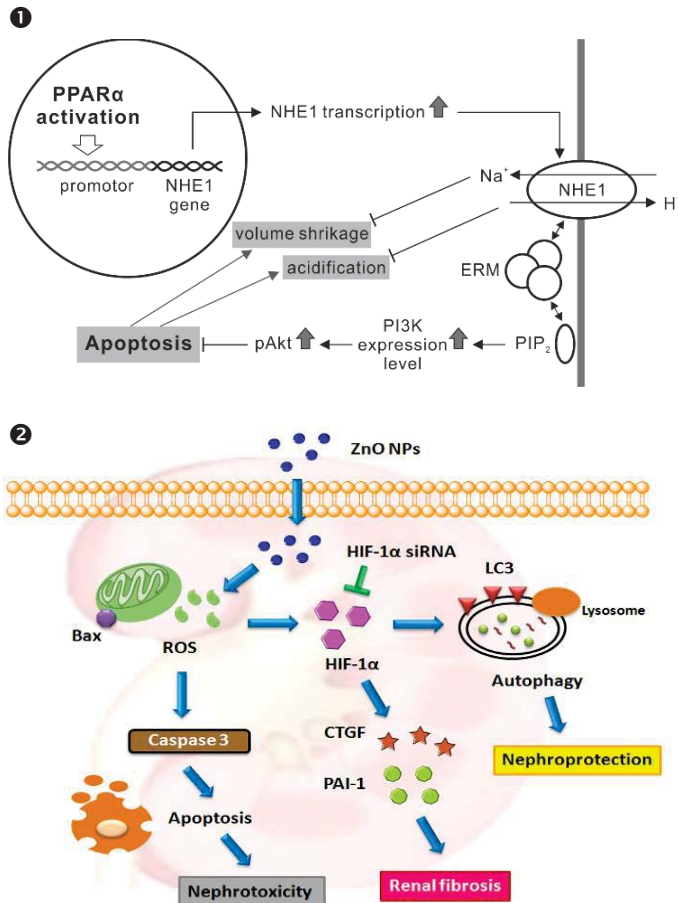


Yung-Ho Hsu  
M.D.

Major achievements

1. PPAR $\alpha$  upregulates Na<sup>+</sup>/H<sup>+</sup> exchanger NHE1 expression to inhibit renal tubular cell apoptosis through recruiting the ezrin/radixin/moesin signaling pathway.
2. Exosomal ATF3 RNA attenuates pro-inflammatory gene MCP-1 transcription in renal ischemia-reperfusion.
3. AKI in critical ill patients: a population-based cohort study in Taiwan.

Representative figures



1. A working model addressing the NHE1 role in the PPAR $\alpha$  antiapoptotic effect in renal tubular cells.
2. The role of hypoxia-inducible factor-1 $\alpha$  in zinc oxide nanoparticle-induced nephrotoxicity.
3. ATF3 regulates kidney epithelium cell inflammation and macrophage migration via MCP-1 pathway.
4. Acute Kidney Injury research in TMU.

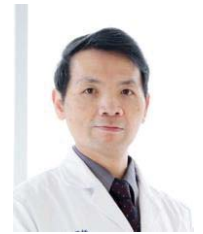
Major publications

- [1] Hsu YH, Chen CH, Hou CC, et al. Prostacyclin protects renal tubular cells from gentamicin-induced apoptosis via a PPAR $\alpha$ -dependent pathway. *Kidney Int* 2008; 73:578-87.
- [2] Lan YF, Chen HH, Lai PF, et al. MicroRNA-494 reduces ATF3 expression and promotes AKI. *J Am Soc Nephrol* 2012; 23: 2012-23.
- [3] Chen CH, Chen TH, Hsu YH, et al. Peroxisome proliferator-activated receptor alpha protects renal tubular cells from gentamicin-induced apoptosis via upregulating Na<sup>+</sup>/H<sup>+</sup> exchanger NHE1. *Mol Med* 2015; 23.
- [4] Lin YF, Chiu IJ, Cheng FY, et al. The role of hypoxia-inducible factor-1 $\alpha$  in zinc oxide nanoparticle-induced nephrotoxicity in vitro and in vivo. *particle and fibre Toxicology* 2016; 13:52.

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Wen-Te Liu  
M.D.

**Major research aims**

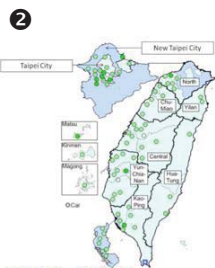
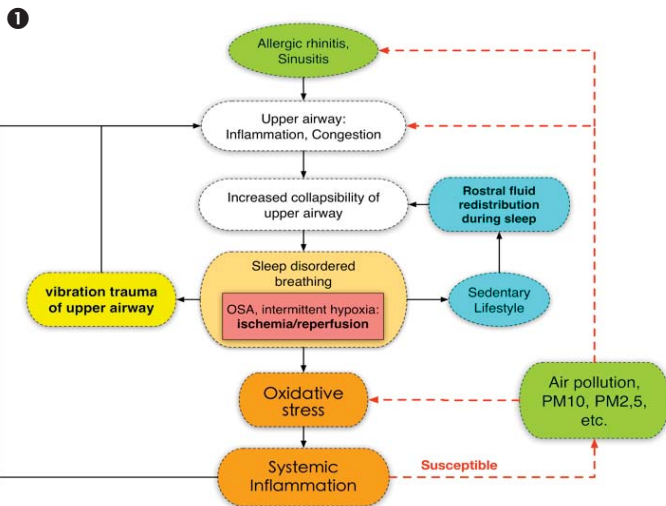
This research team provides multidisciplinary approaches to answer the critical questions about obstructive sleep apnea (OSA) from basic research to clinical management, including environmental factors of upper airway inflammation, gastroesophageal reflux associated airway collapsibility, oxidative stress induced by the intermittent hypoxemia during sleep and neurodegenerative complication by sleep deprivation, etc. The early detection of OSA is also the major part of our work, including the development of mathematical model for predicting the severity of OSA, novel technology with wearable device assisted home monitoring of sleep quality and physical activity for personalized evaluation. The major research aims:

1. To analyze the inflammatory profile and find out the new biomarkers in patients with sleep apnea syndrome.
2. To develop a telecare system for home-based, longitudinal observation of patients with sleep apnea.
3. To create an automatically scoring system for clinical assessment by big-data analysis technology.

**Major achievements**

1. OSA pathophysiology: environmental factors, associated lifestyle, and complications.
2. Exposure to air pollution was associated with change of blood pressure among patients with sleep-related breathing disorders, that could be modified by OSA severity and BMI.
3. Home-based monitoring system for longitudinal assessment of daily activity, sleep status and geographical information by wearable devices and new IT technology.
4. Mathematical models (Neuro-fuzzy inference, Support Vector Machine) for prediction of OSA severity by anthropometric features.

**Representative figures**



**Table 4**  
Beta coefficients (95% confidence interval) for effect modification of the association between diastolic blood pressure and 1-year mean air pollution exposure.

	PM <sub>2.5</sub>	NO <sub>2</sub>
Apnea-hypopnea index ≥30		
Yes	0.49 (0.01, 0.97)	0.58 (0.03, 1.14)
No	-0.35 (-0.94, 0.24)	-0.27 (-0.88, 0.34)
P-value for interaction	0.03	0.02
Body mass index >25		
Yes	0.57 (0.12, 1.02)	0.73 (0.24, 1.22)
No	0.04 (-0.36, 0.40)	-0.10 (-0.46, 0.26)
P-value for interaction	0.04	0.03

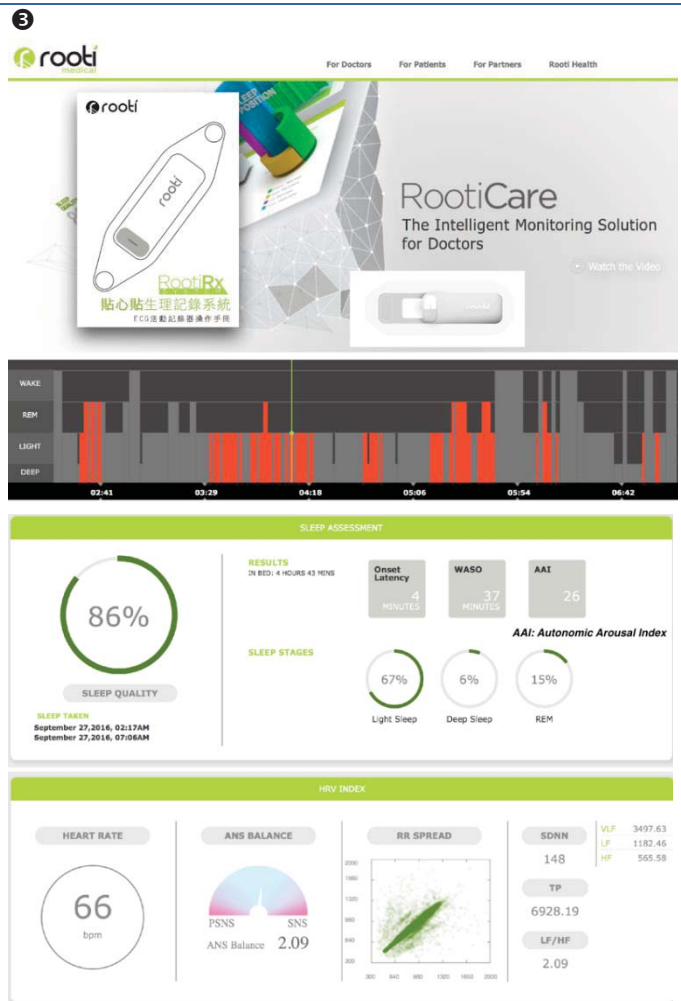
NO<sub>2</sub>, nitrogen dioxide; PM<sub>2.5</sub>, particles with aerodynamic diameters less than 2.5 μm. All models were adjusted for sex, age, body mass index, temperature, relative humidity.

2005~2012

- 1 OSA: pathophysiology and associated factors
- 2 Increases in air pollution leading to increased diastolic blood pressure (BP); Stronger BP response associated higher apnea-hypopnea index and higher BM

**Staff and contact information**

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- 3 Wearable devices and Cloud database for home-based, longitudinal monitoring and big-data analysis

**Major publications**

- [1] Liu WT, Wu HT, Juang JN, et al. Prediction of the severity of obstructive sleep apnea by anthropometric features via support vector machine. PLoS One 2017; 12(5):e0176991.
- [2] Liu WT, Lee KY, Lee HC, et al. The association of annual air pollution exposure with blood pressure among patients with sleep-disordered breathing. Sci Total Environ 2016; 543:61-6.
- [3] Wang TY, Lo YL, Liu WT, et al. Chronic cough and obstructive sleep apnoea in a sleep laboratory-based pulmonary practice. Cough 2013; 9:24.
- [4] Liu WT, Huang CD, Wang CH, et al. A mobile telephone-based interactive self-care system improves asthma control. Eur Respir J 2011; 37:310-7.



Hsin-Chien Lee  
M.D.

### Major research aims

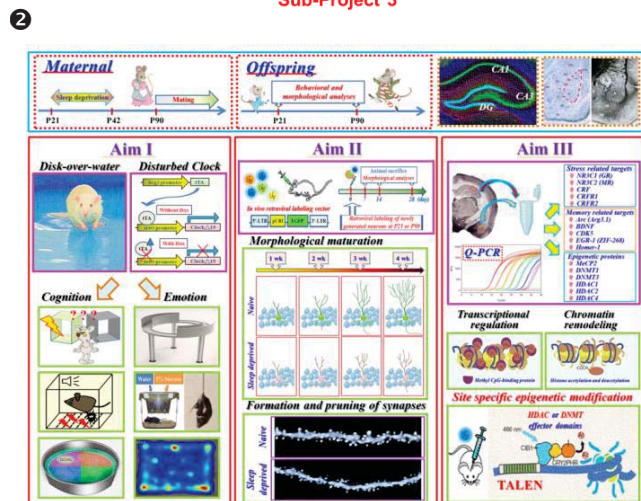
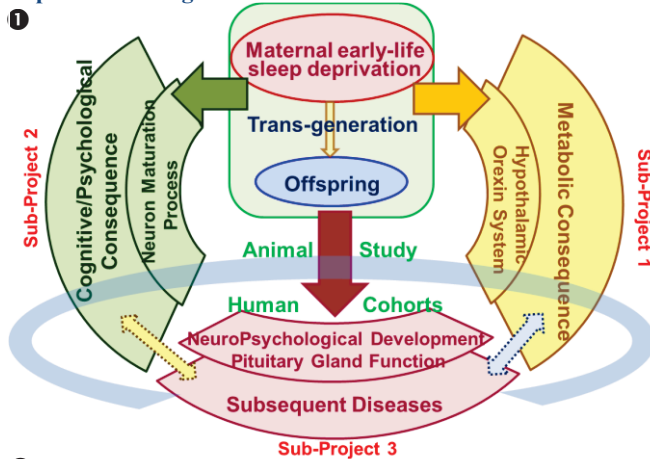
The multidisciplinary research team was organized to devote research efforts in the trans-generational effects of sleep deprivation. There are Four Major Research Aims:

1. To investigate the metabolic dysfunction and the role of Orexin system among offspring mice of maternal early-life sleep deprivation
2. To investigate the cognitive and psychological impairments among offspring mice of maternal early-life sleep deprivation
3. To explore the role of epigenetic reprogramming of germ cells as the mechanisms for above changes among offspring mice of maternal early-life sleep deprivation
4. To verify above findings by using human cohorts in the proximate situation of maternal early-life sleep deprivation

### Major achievements

1. Organize and consolidate a multidisciplinary research team devoting research efforts in the trans-generational effects of sleep deprivation.
2. Establish a reliable and valid animal model of maternal early-life sleep deprivation.
3. Preliminary data indicate the trans-generational impact of sleep deprivation.

### Representative figures



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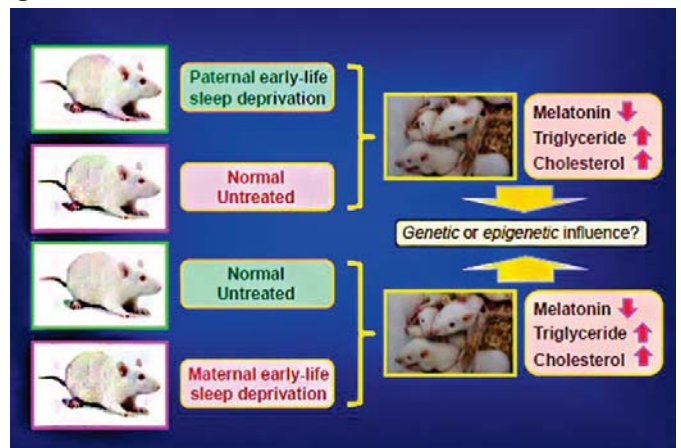
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**Hsin-Chien Lee, M.D., Associate Professor**

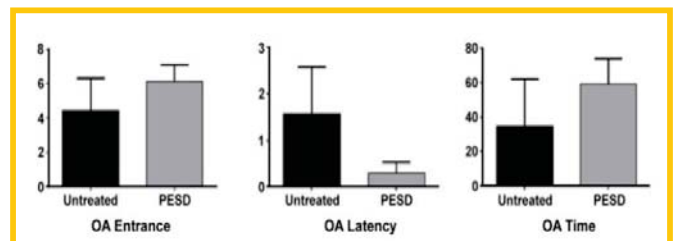
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3



Our preliminary data indicate trans-generational impact on the metabolic function of offspring mice of maternal, even paternal, early-life sleep deprivation.



Our preliminary data also indicate trans-generational impact on the cognitive function of offspring mice of maternal early-life sleep deprivation.

### Major publications

- [1] Chen LY, Tiong C, Tsai CH, et al. Early-life sleep deprivation persistently depresses melatonin production and bio-energetics of the pineal gland: potential implications for the development of metabolic deficiency. *Brain Struct Funct* 2015; 220:663-76.
- [2] Chang HM, Liao WC, Sheu JN, et al. Sleep deprivation impairs Ca<sup>2+</sup> expression in the hippocampus: ionic imaging analysis for cognitive deficiency with TOF-SIMS. *Microsc Microanal* 2012; 18:425-35.
- [3] Chang HM, Wu UI, Lan CT. Melatonin preserves longevity protein (sirtuin 1) expression in the hippocampus of total sleep-deprived rats. *J Pineal Res* 2009; 47:211-20.
- [4] Chang HM, Mai FD, Chen BJ, et al. Sleep deprivation predisposes liver to oxidative stress and phospholipid damage: a quantitative molecular imaging study. *J Anat* 2008; 212:295-305.

Major research aims

Our primary mission is devoted to the improvement of public health in developing countries affected by Neglected Tropical Diseases (NTDs). NTDs are a diverse group of communicable diseases that prevail in tropical and subtropical conditions in 149 countries and affect more than one billion people, costing developing economies billions of dollars every year. They mainly affect populations living in poverty, without adequate sanitation and in close contact with infectious vectors, domestic animals and livestock. Implementation of appropriate measures with high coverage will lead to achieving the Sustainable Development Goals 3 & 17 of United Nation as resulting in the elimination of NTDs and the eradication of at least two by 2020. Our major research fields cover molecular and immunopathogenesis of NTDs, particularly of zoonotic parasitosis, epidemiology, and construction of tropical disease prediction mode.

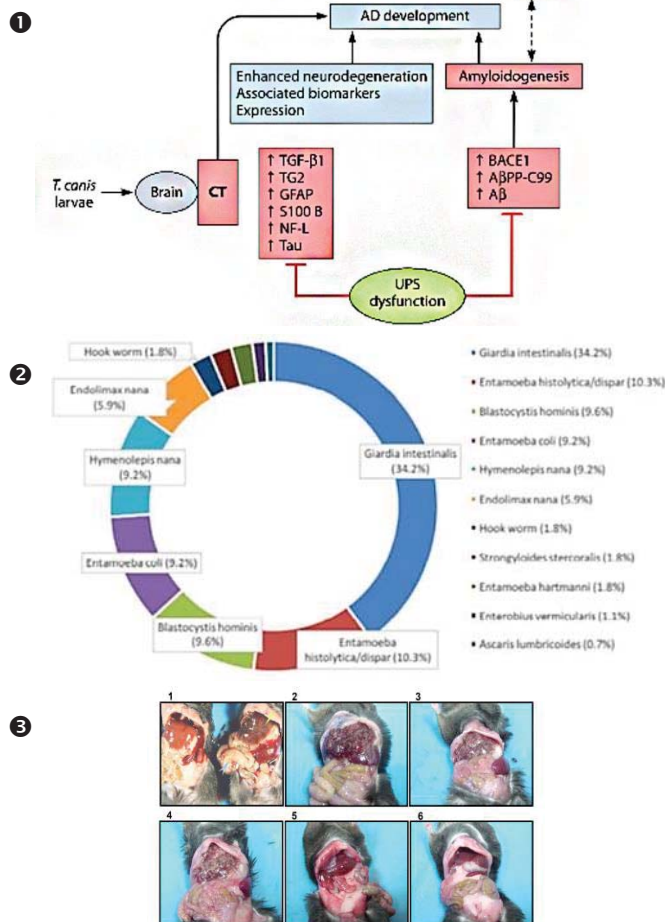


Chia-Kwung Fan  
LL.M., Ph.D.  
Professor and Director

Major achievements

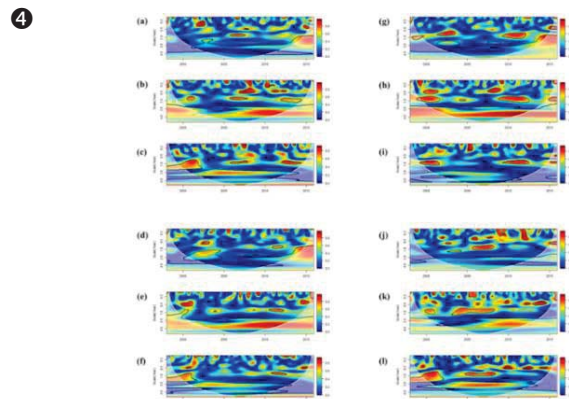
1. Our hypothesis indicate cerebral toxocariasis may develop into neurodegenerative diseases e.g., Alzheimer's diseases ①.
2. Combining GST DNA vaccine and recombinant GST protein with IL-12 plasmid as adjuvants for development of multi-functional complex vaccines against *Schistosoma japonicum* ②, ③.
3. International collaborative projects on NTDs have been accomplished in Asian Cambodia, African Eswatini, Sao Tomes e Principe and Nigeria as well as Micronesian Marshall Islands from 2009 to present.
4. A climate-based model for dengue early warning systems which is able to predict dengue transmission risk in Taiwan has been developed, revealing dengue transmission can be affected by regional climatic fluctuations, like ENSO or IOD ④.

Representative figures



Staff and contact information

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- ① Our hypothesis: cerebral toxocariasis may progress to Alzheimer's disease.
- ② Genotype studies on intestinal parasites and head lice from Cambodia.
- ③ Our pcDNA/SjGST vaccination by boosting with recombinant SjGST proteins not only enhanced the anti-parasite efficacy against schistosomiasis but also significantly increased the anti-pathological effects, as evident in the reduction in the quantity and size of liver granulomas observed in the rSjGST-boosted groups.
- ④ Cross-wavelet coherence analysis of monthly dengue incidence rates and local climate variables with different ENSO indices. (a-c) Multivariate ENSO Index (MEI) vs. dengue, minimum temperature, and precipitation. (d-f) NINO 1+2 Index vs. dengue, minimum temperature, and precipitation. (g-i) NINO 3 Index vs. dengue, minimum temperature, and precipitation. (j-l) NINO 4 Index vs. dengue, minimum temperature, and precipitation. The cross-wavelet coherence scale is from 0 (blue) to 1 (red). The cone of influence (results are not influenced by the data edges) and the significantly coherent time-frequency regions ( $p < 0.05$ ) are indicated by solid black lines.

Major publications

- [1] Fan CK, Liao CW, Cheng YC. Factors affecting disease manifestation of toxocarosis in humans: genetics and environment. *Vet Parasitol* 2003; 193:342-52.
- [2] Fan CK, Holland CV, Loxton K, et al. Cerebral Toxocarosis: Silent Progression to Neurodegenerative Disorders? *Clin Microbiol Rev* 2015; 28: 663-86.
- [3] Cheng PC, Lin CN, Peng SY, et al. Combined IL-12 Plasmid and Recombinant SjGST Enhance the Protective and Anti-pathology Effect of SjGST DNA Vaccine Against *Schistosoma japonicum*. *PLoS Negl Trop Dis* 2016; 10:4459-78.
- [4] Stanaway JD, Shepard DS, Undurraga EA, et al. The global burden of dengue: an analysis from the Global Burden of Disease Study 2013. *Lancet Infect Dis* 2016; 16:712-23.
- [5] Liao CW, Chiu KC, Chiang IC, et al. Prevalence and risk factors for intestinal parasitic infection in schoolchildren in Battambang, Cambodia. *Am J Trop Med Hyg* 2017; 96:583-88.

Major research aims

The Center for Reproductive Medicine was established in 1991. We are pursuing researches focusing on the development of embryos, preimplantation diagnosis, stem cell, mitochondria and ovarian aging, environmental hormone, disease biomarker and biochip, fertility preservation and reproductive ethics. By using advanced reproductive technologies, we have helped more than 20,000 infertile couples in the last two decades. The center's innovative research consistently has also set the landmarks for fertility treatment in Taiwan and pioneered autologous mitochondrial transfer to bring into the world a healthy baby, giving great hope in the problem of ovarian aging.

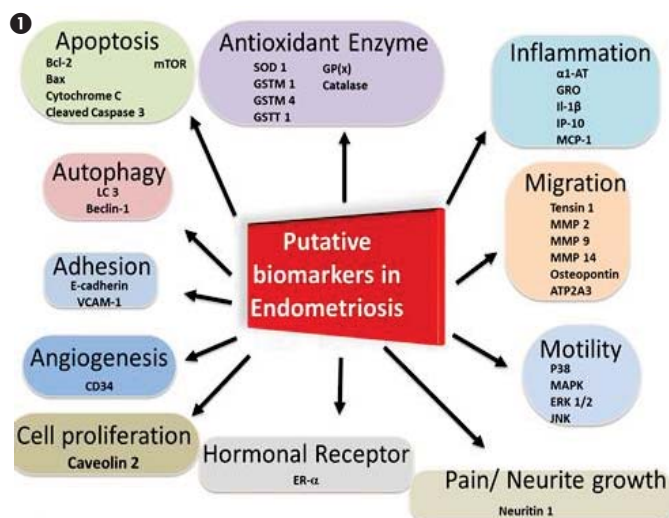


Chii-Ruey Tzeng  
M.D., M.P.H.

Major achievements

1. "Biosignatures for Endometriosis." Academia Sinica research grant project 2013-2017.
2. Prize Poster, "Downregulation of E-cadherin, CD34, and superoxide dismutase 1 expression and upregulation of GSTM4 expression by gonadotropin-releasing hormone agonist (GnRHa) in women with endometriosis." Asia Pacific Initiative on Reproduction (ASPIRE), Kuala Lumpur, Malaysia. Mar. 30- Apr. 2, 2017.
3. Travel Award, "Down regulation of Neuritin 1 following GnRH agonist Treatment in Women with Endometriosis." Asia Pacific Initiative on Reproduction (ASPIRE), Kuala Lumpur, Malaysia. Mar. 30- Apr. 2, 2017.
4. Prize Poster, " Investigation of four potential biomarkers for detecting endometriosis by proteomic approaches: E-cadherin, CD34, SOD1 and GSTM4", Asia Pacific Initiative on Reproduction (ASPIRE), Kuala Lumpur, Malaysia. Mar. 30- Apr. 2, 2017.
5. Travel Award, "Ultralong Protocol Improves Pregnancy Outcomes of in Vitro Fertilization in Infertile Women with Peritoneal Fluid." Asia Pacific Initiative on Reproduction (ASPIRE), Kuala Lumpur, Malaysia. Mar. 30- Apr. 2, 2017.

Representative figures

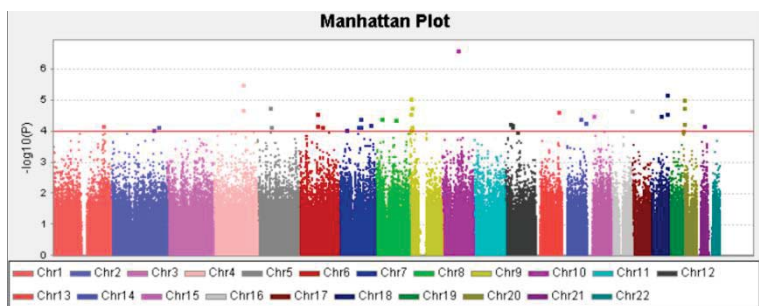


Staff and contact information

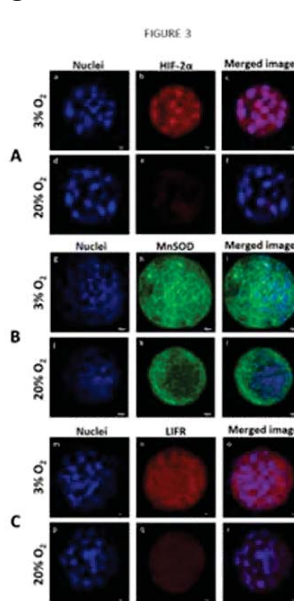
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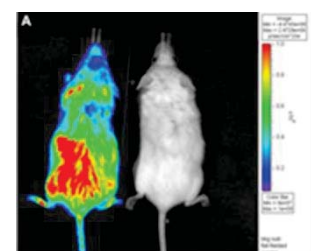
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- 1 Putative biomarkers in endometriosis.
- 2 Genome-wide association study of endometriosis
- 3 Immunofluorescence in mouse blastocysts with higher HIF-2α MnSOD and LIF culture under 3% O2 than 20% O2.
- 4 The transgenic mouse model for fertility preservation.

Major publications

- [1] Tzeng CR, Chang YC, Chang YC, et al. Cluster analysis of cardiovascular and metabolic risk factors in women of reproductive age. *Fertil Steril* 2014; 101:1404-10.
- [2] Tan SJ, Lee LJ, Tzeng CR, et al. Targeted anti-apoptosis activity for ovarian protection against chemotherapy-induced ovarian gonadotoxicity. *Reprod Biomed Online* 2014; 29:612-20.
- [3] Shen SH, Shen SY, Liou TH, et al. Obesity and inflammatory biomarkers in women with polycystic ovary syndrome. *Eur J Obstet Gynecol Reprod Biol* 2015; 192:66-71.
- [4] Li CJ, Yeh CY, Chen RY, et al. Biomonitoring of blood heavy metals and reproductive hormone level related to low semen quality. *J Hazard Mater* 2015; 300:815-22.
- [5] Lai GL, Yeh CC, Yeh CY, et al. Decreased zinc and increased lead blood levels are associated with endometriosis in Asian Women. *Reproductive Toxicology*. Volume 74, 2017;74:77-84.

Major research aims

Women cancer team at Shuang Ho Hospital pioneers in minimal invasive surgeries and translational cancer epigenetics. For early cancer detection, we discovered DNA methylation biomarker for cervical cancer, which has been approved as an in vitro diagnostics in Taiwan and is burgeoning in China and Europe. The discovery and translation of endometrial and ovarian cancer methylation biomarker is ongoing. For novel therapeutic development, we discovered a proteasome inhibitor for mucinous epithelial ovarian cancers (MuOC) and identified a sulfation modification that may interfere the efficiency of target therapy in ovarian cancer. Mechanistic investigations revealed PAX1 as a tumor suppressor by activating multiple phosphatases and TET1 an oncogenic role in ovarian cancer by reprogramming epigenome. Clinically, our team is the pioneer in robotic gynecological surgery, addressing much on training and education in minimal invasive surgery.

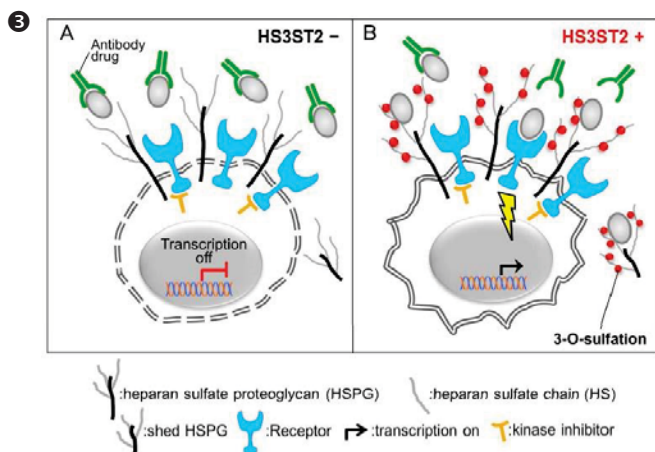
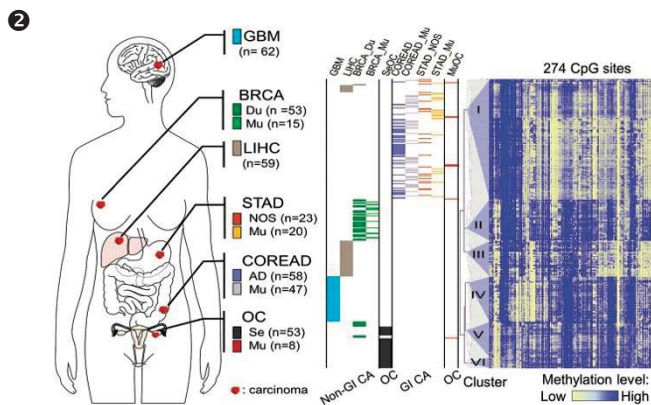


Hung-Cheng Lai  
M.D., Ph.D.

Major achievements

1. Discover DNA methylation biomarkers for cervical and endometrial cancer screening.
2. Translate PAX1 methylation testing as Cervi-M® (for cervical cancer screening, approved by TFDA).
3. Discover GATA3 as a prognostic marker in the ovarian cancer and maybe a predictive marker for epigenetic therapy.
4. Discover the proteasome inhibitor for MuOC treatment.
5. Discover the effect of sulfation of HS3ST2 in target therapy
6. Reveal TET1 reprogramming epigenome and TET1/CK2α as a therapeutic target in ovarian cancer.

Representative figures

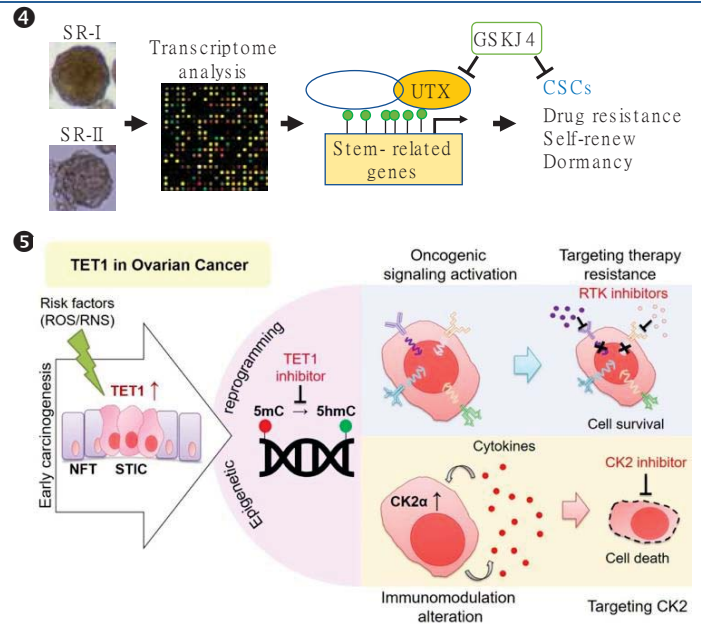


Staff and contact information

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- 1 Future perspective: one test for triple cancer screening.
- 2 Hierarchical clustering analysis of the methylation profiles on the distinction of different carcinoma.
- 3 Therapeutic antibodies might be highly antagonistic to oncogenic signaling in cancer cells with epigenetic loss of heparan sulfate 3-O-sulfation.
- 4 GATA3 is a master regulator in ovarian HGSC stemness and GATA3/UTX complex is a therapeutic target against ovarian HGSC.
- 5 TET1 reprograms the epigenetic landscape and activates oncogenic pathways in ovarian cancer.

Major publications

- [1] Chen HJ, Huang RL, Liew PL, et al. GATA3 as a master regulator and therapeutic target in ovarian high-grade serous carcinoma stem cells. *Int J Cancer*. 2018 Jul. Epub ahead of print.
- [2] Huang RL, Chen HJ, Chen LY, et al. Epigenetic loss of heparan sulfate 3-O-sulfation sensitizes ovarian carcinoma to oncogenic signals and predicts prognosis. *Int J Cancer*. 2018 May. Epub ahead of print.
- [3] Liew PL, Huang RL, Weng YC, et al. Distinct methylation profile of mucinous ovarian carcinoma reveals susceptibility to proteasome inhibitors. *Int J Cancer*. 2018 Jul 15;143(2):355-367.
- [4] Huang RL, Su PH, Liao YP, et al. Integrated epigenomics analysis reveals a DNA methylation panel for endometrial cancer detection using cervical scrapings. *Clin Cancer Res* 2017; 23:263-72.
- [5] Chen LY, Huang RL, Chan WY, et al. TET1 reprograms ovarian cancer epigenome and reveals casein kinase 2α as a therapeutic target. *EMBO Mol Med*. Submitted.
- [6] Patent pending: Taiwan: 106125367. PCT: PCT/CN2017/094917.

With a total of 4,123 beds in capacity, TMU Healthcare System will be one of the largest healthcare systems in Metropolitan Taipei. It comprises one medical university and four affiliated hospitals and integrates primary and specialty care with research and education. With the line-up of Taipei Medical University Hospital, Wan Fang Hospital, Shuang Ho Hospital and Ningbo Medical Center Lihuli Eastern Hospital, TMU Healthcare System becomes a heavy weight healthcare provider, which emphasizes the quality of medical service, teaching and clinical researches. TMU Healthcare System continuously strives to improve the quality of medical care and research with the goal of becoming the global healthcare destination.

### 3 JCI and AAHRRP-Accredited Affiliated Hospitals



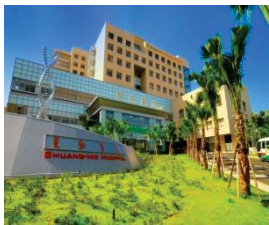
#### Taipei Medical University Hospital

Est. in 1976  
800 beds  
No. of staff: 1,946  
Cancer Excellent Research Center  
2011 National Quality Award



#### Wan-Fang Hospital

Est. in 1997  
743 beds  
No. of staff: 1,808  
National Drug Evaluation Center  
Emergency Operation Center



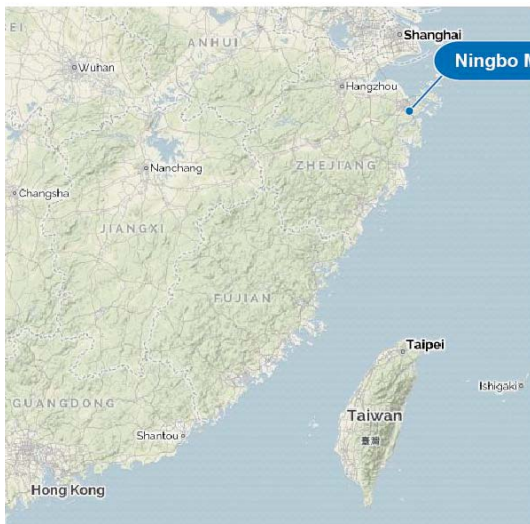
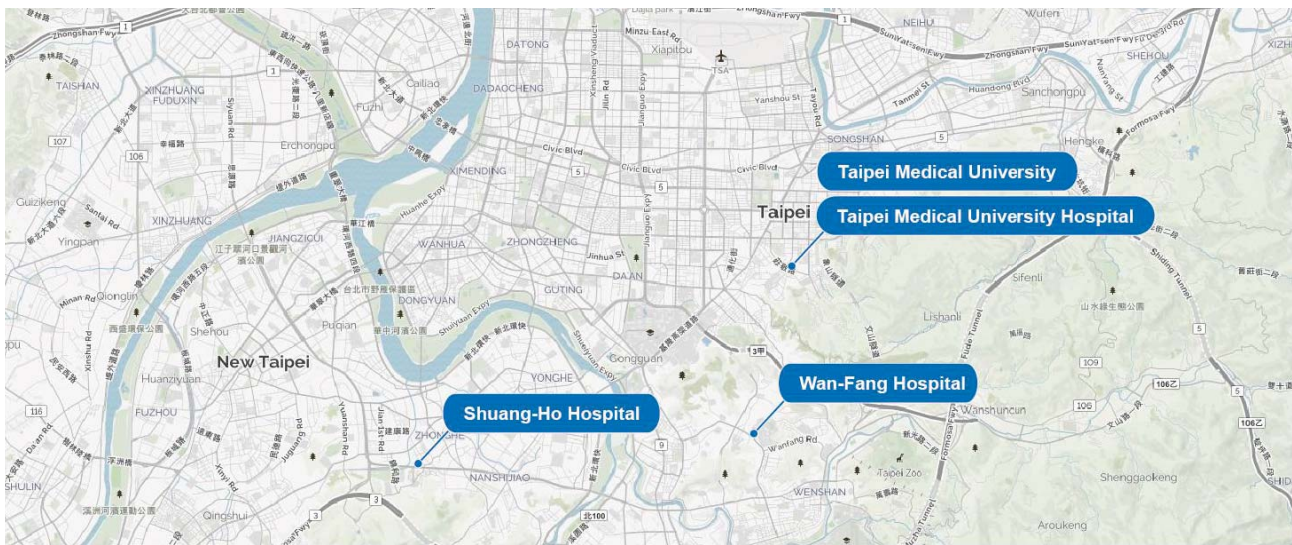
#### Shuang-Ho Hospital

Est. in 2008  
1,580 beds  
No. of staff: 2,109  
Emergency Air Medical Transport (EAMT) Hospital  
2012 National Quality Award



#### Ningbo Medical Center Lihuli Eastern Hospital

Est. in 2015  
1000 beds



#### Ningbo Medical Center Lihuli Eastern Hospital



## About

Taipei Medical University Hospital is a nationally recognized health center that serves the community needs as well as those of global guests from every corner of the world. We are a proud member of the JCI family and are dedicated to delivering the most advanced medical treatments available. We are highly committed to our global development and research collaborations on all continents. Our patient first focus is what makes us different and we invite you to experience it.

### TMUH in Numbers:

800 beds	2300 employees	410 medical professionals
25 departments	405 physicians	435 Administrators
40 specialties	855 nurses	212 outsourcing staff



## Medical Care

TMUH has many specialized centers, such as the Reproductive Medicine Center, Weight Management Center, Kidney Center, Bone and Joint Research Center, minimally invasive surgery center and many other diversified international pioneering medical services.

Enhancing the quality and patients' safety has led TMUH to be accredited as the International Safe Hospital by WHO Collaborating Centre on Community Safety Promotion, which is also the first hospital to pass the accreditation in the world. TMUH keeps fulfilling its core value of "high medical service quality" and "patient-centered" approach.



## Education

Our goal as Taipei Medical University's main university-affiliated teaching hospital is to strengthen the qualifications of our entire medical faculty, provide adequate teaching resources, and encourage all our medical staff to be enthusiastic in educating our students. This educational structure will be accomplished by recruiting and providing training to resident doctors, intern doctors, nurses, and other medical staff members under the standards established by the "New Teaching Hospital Accreditation."

## Research

In research, we encourage all our medical staff to continue and further their education with either a Master or PhD degree, continue to promote combined research in the field of clinical and basic science, and provide rewards for journal publications and successful research grants.

## Vision

**To become an internationally renowned university hospital.**

We hope that all staff members of Taipei Medical University Hospital understand that they are doing an extraordinary job, and continue to provide excellent patient service as well as making great achievements in teaching and research. This will allow Taipei Medical University Hospital to become the sole preference in hospital selection for the patients, and thus naturally it would be an honor to all university staff, students and alumni.





## About

Co-constructed with the Wanfang Hospital Station of the Taipei mass rapid transit system (MRT) Wenhua line (line1), the Hospital has 743 beds and over 300 medical specialists offering comprehensive professional services. Ever since its founding, the hospital has worked for highest attainable quality service to assure that patients receive care of the top standard. It is one of the first Taiwan hospitals to set up an international medical office for providing individualized medical services for patients from the abroad which is more than 38 countries up to now.



## Special Medical Care

In order to offer integrated care to patients, other than the dialysis center, cancer center, health management center, nursing home, reproductive medicine center, cosmetic medical service, sport rehabilitation center, laser excimer eye care center, weight control center, we also established different centers with advanced technology on special disease treatment, and to deal with catastrophic/emergency incidents as well as personalized cancer care management to reach the goal of becoming internationally recognized top-class university hospital.

## Education and Research

WanFang Hospital Teaching Department adopts the learner-centered approach which aims at nurturing professional knowledge, attitude, and skills for the trainees to provide comprehensive and continuous care to patients. We set up the center for excellent teaching, within which there are units for problem-based learning, evidence-based medicine, clinical skill training. We offer diversified activities such as simulation and clinical skills training, team care training to foster holistic care competence for medical staff.

Other than teaching, we are devoted to comprehensive research areas and integrate basic medicine, biotechnology, medical information technology, quality management with medical and teaching services. Thereby, medical care quality can be improved continuously. We have signed cooperative education agreements with dozens of domestic and overseas medical institutions for conducting academic exchange or medical training. We also cooperate with the top academic research institutions such as the Taiwan National Health Research Institute and the Academia Sinica to strengthen cross-institutional research.

## Vision

Taipei Municipal WanFang Hospital is the first public facility managed by private sector in Taipei City Government. Owing to support from all stakeholders and the efforts from all staff, we have proceeded from a local community hospital to medical center in a short time. Teaching, research, service and quality assurance are equally important as the mission of the Hospital. In addition, “Value the Community, Honor the Patients” as well as “Quality of Service Is Our Pride” are our fundamental philosophy and core values. Altogether, these solidify our strong and sustained commitment to carry out the social responsibility to citizens.



## About

Shuang Ho Hospital officially opened on July 1st, 2008, Taipei Medical University Shuang-Ho Hospital is the first Build-Operate-Transfer (BOT) project (construction / operation / management) commissioned by the Department of Health, Executive Yuan. It has 1,580 beds and is the largest hospital in Taipei County. Now, Shuang-Ho Hospital, Taipei Medical University Hospital, and Taipei Medical University Wan-Fang Hospital form a medical healthcare golden triangle in the Taipei area with a total capacity of 3,000 beds and can support each other whenever needed.

Since our establishment, Shuang Ho Hospital has been moving toward becoming a medical center. But we have not forgotten our mission as a community hospital.

Shuang

Ho Hospital upholds our belief in "Quality". Since our opening, our quality has been well-recognized. Our medical evaluation performances have been consistently excellent, and have passed the ISO9001, ISO14001, ISO27001 and HIMSS Stage6.0 international certifications. We are also the nation's first hospital to be awarded the Corporate Social Responsibility dual international certification, the JCI accreditation, and awarded "Excellent" in the New Teaching Hospital Accreditation. In 2013, less than 4 years since our opening, we were the proud winner of the National Quality Award.

## The Distinguishing Features of Shuang-Ho Hospital

Shuang-Ho Hospital not only has built up a perfect "Acute Severe Care" system with the unique "Medical Use hospital helipad" which offers 24-hour standby Air-EMS to patients and allocates scarce medical resources for off-shore islands, but also has a passionate ER medical team to provide 24 hours a day, 365 days a year, health care service. With fully and well equipped operation rooms plus strong and professional physical and surgical teams from famous medical centers, Shuang-Ho Hospital has extraordinary capability and good reputation on Neural Medical Center, Minimally Invasive Surgery Center, Ophthalmology and Visual Science Center, Cardiovascular Center, Rehabilitation Center, Multipolar Radiofrequency Ablation Center and Trauma Center. Moreover, Shuang-Ho Hospital has outstanding achievements on the following aspects.

- The Dialysis Center has a national-leading control measure to isolate the beds, equipment, and areas in order to prevent from hepatitis C infection.
- The first "Dental Care Center for Persons with Special Needs" in the country to provide dental care service to about 130,000 physically and mentally handicapped people in New Taipei City.
- The Cancer Center led by the world well-known Dr. Jacqueline Whang-Peng (member of Academia Sinica) offer the best radiation therapies and comprehensive cares with the most advanced facilities in the world in order to provide the best and most comfortable medical care environment.
- The Health Management Center in the 12F has professional service team and comfortable environment in order to provide comprehensive personal health management.



In addition to providing quality health care services, our hospital is also committed to research and teaching. We founded the Translational Medicine research lab for innovative research and the Brain and Consciousness research Center for Integrate cognitive neuroscience. We also built the Clinical Skill Center to help our medical staff cultivate professional competence, attitude and skills in their clinical practice, and provide our patients with complete care.

## Perspectives of Shuang-Ho Hospital

The visions of Shuang-Ho Hospital are to provide the best health service and medical care to the community, and to be the top center for medical education, research, and service. Moreover, to expand the medical service in Taiwan, we devote to cooperate with medical institutions all over the world. Finally, with the full supports from Taipei Medical University, the commitment of top management, and all employees' engagement, the long-term mission to become one of the top university hospitals in the world with the best medical quality and performance will come true in future.



## About

LiHuiLi Eastern Hospital provides 1,000 beds with a comprehensive, exceptional, and safe healthcare environment. The hospital commenced operation in Dec. 2015.

Introducing advanced hospital management concepts from Taipei Medical University and its affiliated hospitals, East hospital entrusts TMU to operate and manage for the first 10 years.

LiHuiLi Eastern Hospital pioneered hospital cooperation management model in China: the hospital is established by the government operated by the private sector.

The medical center specializes in tumor treatment, organ transplantation, urinary kidney disease, gynecology surgery and pediatrics, health examinations and international medical care.



## Taiwan Hospital Thoughtful Service

TMU management team in Ningbo create a new hospital experience for local people. Simplify the hospital process and combine with high tech resources, utilize information and communication platform to provide convenience clinic experience. One person, one medical consulting room and one nurse who helps doctor to diagnose and treat, which ensures the patient privacy.

User-friendly open counter, free wheelchair, and automatic cashier/registration machine. Cozy waiting area with multiple function information desk, convenient stores, book corner and light music by piano volunteers distress patients and families.

## Medical Quality

With the level of first-class comprehensive hospital, LiHuiLi Eastern Hospital will gear to international JCI standard in the early future to build a high quality public hospital which integrates medical treatment, teaching and scientific research. Also the hospital seeks to practice the "medical ethics" and "humanity and art" within its whole medical service system while integrating Taiwan's high medical standards.

## Vision

Patient-centered, the hospital will accomplish the mission of service, teaching and research based on the concept of caring, outstanding and innovation.



## Campus Life

The university facilities include a library which contains 150,000 volumes, a swimming pool, a food court with an Italian restaurant, a convenient store, a dormitory (four students in one air-conditioned room with beds and desks for each student, restrooms, balconies, etc.), a computer lab, meeting rooms, and offices for nearly 80 student club. TMU is within walking distance to the biggest shopping area in Taipei. In ten minutes, one could arrive at Taipei 101, Cinema with six department stores and one 24hour book store.

### Sports facilities

TMU Gymnasium provides a complete range of facilities for indoor sports, such as standard-size swimming pool, whirlpool, sauna, aerobics room, cycling room, weight training room, table tennis and badminton areas. Outdoor sports courts for baseball, softball, basketball, tennis and golf are also available on campus.



### Student clubs

Student clubs are abundant at Taipei Medical University! Eighty-five clubs offer opportunities in service, entertainment, academics, performance and management. TMU leads Taiwan's universities in student activities, which are important part of the TMU experience, especially medical service activities. Normally nine groups serve in remote villages or foreign countries each winter vacation, while in summer a dozen groups offer help in underserved areas. Students participating in these groups are not only offered free medical services and health care education, but also perform live shows to entertain their host communities. South India and Malawi were the destinations of recent trips.



### Food court and restaurants

Inexpensive and nutritious meals are easy to find on campus. The food court in the lower level of the United Medical Building offers sandwiches, hamburgers, Chinese lunch boxes, fresh fruit drinks, noodles, and vegetarian food. The upper level is Mr. J, an Italian-French restaurant sponsored by popular singer and composer Jay Chou and friends. A convenience store next door offers other meal options.

### Library

Taipei Medical University's main library was established in 1962. The collections include printed and electronic books, journals and databases in Chinese, English, Japanese and other languages. The library receives more than 10 newspapers and 230 magazines every day and all the databases can be accessed online. In addition to circulation services, the library provides other services such as library orientation and instruction, reference service, inter-library loan and selective dissemination of information.





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