

# CGMH Conference: Precision Immune Cell Therapies for Cancers

癌症精準免疫細胞治療國際研討會



# **Welcome Message**



From the Superintendent of Chang Gung Memorial Hospital, Linkou

It is our great pleasure to welcome you all to attend the CGMH Conference: Precision Immune Cell Therapies for Cancers on December 7th, 2019 at Chang Gung Memorial Hospital, Linkou branch, Taoyuan, Taiwan.

On behalf of Linkou Chang Gung Memorial Hospital, I would like to express my greetings to everyone attending the meeting, especially for our distinguished guests from United States, Japan, China, Taiwan and all colleagues from Chang Gung Memorial Hospital, Chang Gung University, and other hospitals or biotech pharma.

The conference will focus on precision immunotherapies for cancers. The experts are going to share their outstanding research achievements in the fields of personalized neoantigen cancer vaccines, adoptive T cell therapy, manufacturing automation, and CAR-T, DC, NK cell therapies, etc. I hope all of you enjoy the meeting and wish you a very pleasant stay in Taiwan.

Wen-Jin Cherng, MD

Professor and Superintendent,

Chang Gung Memorial Hospital, Linkou, Taiwan

# 長庚醫院癌症精準免疫細胞治療國際研討會 CGMH Conference: Precision Immune Cell Therapies for Cancers

Date: Saturday, December 7th, 2019

Place: 1C, Research Building, Chang Gung Memorial Hospital (CGMH), Linkou, Taiwan

Time	Торіс	Speaker	Moderator		
08:30-09:00	Registration				
09:00-09:10	Opening & Introduction 程文俊主委/院長 Wen-Jin Cherng, MD. President Chang Gung Memorial Hospital Linkou Branch				
09:10-09:30	Cell Therapy Regulations in Taiwan	Chung-Liang Shih, MD (石崇良司長) Director-General, Department of Medical Affairs, The Ministry of Health and Welfare, ( 衛生福利部)	<i>Wen-Jin Cherng, MD</i> <i>(</i> 程文俊主委/院長) President, CGMH		
09:30-10:20	Personalized Neoantigen Cancer Vaccines	Patrick A. Ott, MD, Ph.D.  Clinical Director, Melanoma Center, Dana- Farber Cancer Institute Clinical Director, Center for Immuno- Oncology, Dana-Farber Cancer Institute Associate Professor of Medicine, Harvard Medical School, USA	Alice Lin-Tsing Yu, MD, Ph.D. (陳鈴津院士) Co-Director, Inst. Stem Cell & Translational Cancer Research, CGMH Academician, Academia Sinica		
10:20-10:40		Coffee Break			
10:40-11:30	Adoptive T Cell Therapy: Challenges and Opportunities in Solid Tumor Malignancies	Cassian Yee, MD  Professor, Department of Melanoma Medical Oncology, Department of Immunology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center Director, Department of Solid Tumor Cell Therapy, Division of Center for Cancer Immunology Research, The University of Texas MD Anderson Cancer Center, USA	John Yu, MD, Ph.D. (游正博所長) Director, Cell Therapy Center, CGMH Director, Inst. Stem Cell & Translational Cancer Research, CGMH		
11:30-12:00	Trends for cell culture technology and automation in regenerative medicine: Experience from Hitachi, Ltd.	Shizu Takeda, Ph.D.  Corporate Officer, Corporate Chief Scientist, Research & Development Group and Laboratory Manager of the Hitachi Kobe Laboratory, Center for Exploratory Research, Hitachi, Ltd. Japan	Kuo-Chen Wei, MD (魏國珍主任) Director, Dept. of Neurosurgery, Industry-Academia Center, CGMH		
	Lunch speech: Automated Cell Culturing Equipment: Features and application examples.  Yusuke Tomozoe Assistant Manager, Clinical Laboratory Systems Sales Dept. Hitachi, Ltd. Japan				

Time	Торіс	Speaker	Moderator	
13:00-13:40	Anti-CDR3/EGFR-CAR-T Immunotherapy	Chi-Meng Tzeng, Ph.D. (曾子晏教授) Professor and Executive Director Key Laboratory for Cancer T-Cell Theranostics and Clinical Translation (CTCTCT) & Translational Medicine Research Center (TMRC) School of Pharmaceutical Sciences, Xiamen University, China	Tang-Her Jaing, MD (江東和部長) Chairman. Cord Blood Transplantation Center, Division of Hematology and Oncology, Department of Pediatrics, CGMH	
13:40-14:10	Dendritic Cell-Based Immunotherapy in Cancer Precision Medicine	Kuo-Chen Wei, MD (魏國珍主任) Director, Dept. of Neurosurgery, Industry- Academia Center, CGMH	<i>Chen-Nen Chang, MD., PhD.</i> (張承能副院長) Prof. Dept. of Neurosurgery,	
14:10-14:40	DC Therapy for HCC: Data of the Previous Trials in CGMH	Wei-Chen Lee, MD (李威震主任) Director, General Surgery, Division of Liver and Transplantation Surgery, Chang Gung Transplantation Institute, CGMH	CGMH Vice President ,Xiamen Chang Gung Hospital, China	
14:40-15:00		Coffee Break		
15:00-15:25	Targeting Neoantigens for Precision Immune Cell Therapy Against Cancers	Shuen-Iu Hung, Ph.D. (洪舜郁教授) Director, Cancer Vaccine and Immune Cell Therapy Core Lab, CGMH		
15:25-15:50	Neoantigen Identification	Shu-Jen Chen, Ph.D. (陳淑貞技術長) Chief Scientific Officer, Cofounder, ACT genomics, Inc. (行動基因生技公司)	John Wen-Cheng Chang, MD (張文震主任)	
15:50-16:15	Development Story of UWC19 (Welgenaleucel): From Bench to Clinical Bed	Jerry Kuo, Ph.D. (郭正宜副總經理) General Manager, Uwell Biopharma, Inc. (鑫品/宇越生技公司)	Director, Immune-Oncology Center of Excellence, CGMH Chairman, Taiwan Society for Immunotherapy of Cancer	
16:15-16:40	NK Cell Therapy	Alarng Chang, Ph.D. (張順浪總經理) General Manager, Medigen Biotechnology Corp. (基亞生技公司)		
16:40-16:50		Discussion		
16:50-17:00	Clo	osing Remarks	John Wen-Cheng Chang, MD (張文震主任) CGMH	



# 座長介紹 ABOUT MODERATOR



# 程文俊主委 / 院長 (Wen-Jin Cherng, MD)

FACC., FAHA, FESC
President
Chang Gung Memorial Hospital Linkou Branch

### **Education**

1974-1981 Kaohsiung Medical University, College of Medicine, Taiwan

## **Post-Graduate Education**

- July 1991-Sep 1991
   Cardiology Dep, National Cardiovascular Center, Japan
   (Scholarship of Japan Society of Ultrasonics in Medicine)
- Oct 1991-Nov 1992
   Cardiology Dep, Strong Memorial Hospital, University of Rochester, Rochester, New York, USA (Scholarship of Paul N. Yu Fellowship)

#### **Fulltime Employments**

- 1. May 1980 June 1981, Intern, rotating system, Kaohsiung Medical College Hospital, Kaohsiung,
- 2. July 1981 June 1984, Resident (R1, R2, R3), rotating system in Internal Medicine, Chang Gung Memorial Hospital, Linkou, Taoyuan.
- 3. July 1984 June 1986, Chief Resident (R4), Fellowship (R4, R5) in Cardiology, Chang Gung Memorial Hospital, Linkou, Taoyuan.
- 4. July 1986 present, Attending Physician in Cardiology.
- 5. July 1986 March 1994, Chief, Intensive Care Unit, Chang Gung Memorial Hospital, Keelung.
- 6. May 1994 Nov. 1998, Chairman, Department of Medicine, Chang Gung Memorial Hospital, Keelung.
- 7. May 1994– June 2003, Chief, Division of Cardiovascular Disease, Chang Gung Memorial Hospital, Keelung.
- 8. Nov 1997 Feb. 2003, Chairman, Department of Medicine, Chang Gung Memorial Hospital, Linkou, Taoyuan.
- 9. Feb. 2001 Oct. 2003, Vice-Superintendent, Chang Gung Memorial Hospital, Keelung.
- 10.Nov.2003 June. 2016. Superintendent, Chang Gung Memorial Hospital, Keelung.
- 11. Nov 21, 2016 present. Director of Board, Chang Gung Medical Foundation.
- 12. July, 2017~present. Chairman. Chang Gung Steering Committee.
- 13. July, 2017~present. Superintendent. Chang Gung Memorial Hospital, Linkou, Taoyuan.

## **Academic Appointments**

- July 1988 Feb 1993, Lecturer of Cardiology, Chang Gung Medical College, Chang Gung University.
- Jan 1990 June 1991, Lecturer of Medicine, Der-Yu Junior College of Nursing.
- July 1993 July 1994, Associated Professor of Medicine, China Medical College.
- July 1996 June 1997, Associated Professor of Cardiology, Yang-Ming University.
- Feb 1993 May 2004, Associated Professor of Cardiology, Chang Gung Medical College, Chang Gung University.
- Nov 1999 present, Professor of Medicine, Chang Gung Memorial Hospital.
- May 2004 present, Professor of Medicine, Chang Gung Medical College, Chang Gung University.

**Research Projects: (35)** 

Bibliography: (168)



# 講師介紹 ABOUT SPEAKER



# 石崇良司長 (Chung-Liang Shih, MD)

Director-General
Department of Medical Affairs
The Ministry of Health and Welfare
(行政院衛生福利部醫事司)

## 現職

行政院衛生福利部醫事司 司長	2016.8 迄今
台灣大學醫學院 兼任助理教授	2006.2 迄今
台灣大學公共衛生學院 兼任助理教授	2006.2 迄今
學歷	
考試院高階文官培訓美國聯邦文官學院 (FEI) 受訓結業	2013.9
行政院高階公務人員新加坡李光耀學院受訓結業	2010.6
行政院國家政務研習班第一期結業	2008

行政院國家政務研習班第一期結業 2008 教育部部定助理教授 2008.5 台灣大學公共衛生學院伊惠斯等與管理研究所博士 2008.6

台灣大學公共衛生學院健康政策與管理研究所博士 2000.9-2006.1 私立高雄醫學大學醫學士 1984.9-1991.6

## 經歷

行政院衛生福利部 主任秘書	2015.2-2016.7
行政院衛生福利部綜合規劃司 司長	2013.7-2015.1
行政院衛生署企劃處 處長	2012.8-2013.7
行政院衛生署醫事處 處長	2008.6-2012.7
行政院衛生署桃園醫院 主治醫師兼醫務秘書	2007.7-2008.5
財團法人醫院評鑑暨醫療品質策進會副執行長	2005.3-2008.3
台灣大學附設醫院急診醫學部主治醫師	1998.7-2007.6
教育部醫學教育委員會委員	2007.3
衛生署醫療品質暨病人安全委員會委員兼執行秘書	2006.1
衛生署病人安全委員會委員兼執行秘書	2003.2
台灣災難醫學會監事	2000.12-2003.1
台灣國際(印尼)救難隊隨隊醫師	2000.6
中華民國急診專科醫師	1998-
中華民國内科專科醫師	1996-

## 專長領域

急診醫學、模擬分析、病人安全與醫療品質管理、醫事法律、公共衛生政策

#### **榮譽事**場

2011年行政院衛生署模範公務人員

## **ABSTRACT 09:10-09:30 ≻**

# **Cell Therapy Regulations in Taiwan**

Chung-Liang Shih, MD

Department of Medical Affairs, The Ministry of Health and Welfare

Ministry of Health and Welfare Taiwan has announced the revision of The Regulation Governing the Application of Specific Medical Examination Technique and Medical Device with a new chapter for cell therapy medical technique on Sep 6th 2018, which includes 6 types of cell therapy that utilize autologous cells to cure specific clinical indications. The revised regulation stipulates the requirements for hospitals that offer cell therapy medical techniques to patients with specific indications, including standards of cell processing unit facility, and qualification of medical professional. A mandatory review mechanism is added into the newly revised regulation. All hospitals offering approved cell therapy will have to submit implementation report on an annual basis to the MoHW. The cell processing unit will be examined by TFDA with Good Tissue Practice (GTP) in accordance to the same level of safety control as medicinal product.



# 座長介紹 ABOUT MODERATOR



# 陳鈴津院士 (Alice Lin-Tsing Yu, MD, Ph.D.)

Distinguished Chair Professor & Co-director Institute of Stem Cell and Translational Cancer Research Gung Memorial Hospital Linkou Branch Email: aliceyu@cgmh.org.tw

Dr. Alice Yu is an Academician, a Distinguished Professor & Co-Director of the Institute of Stem Cell & Cancer Translational Research in Chang Gung Memorial Hospital at Linko, Taiwan, and a Professor Emeritus at the University of California in San Diego. Formerly, she was the Chief of Pediatric Hematology/Oncology at the University of California in San Diego, and the distinguished research fellow and deputy director of the Genomics Research Center of Academia Sinica in Taiwan.

Dr. Yu received her MD at the National Taiwan University Medical College, and a PhD in microbiology/ immunology at University of Chicago. Her research focuses on translational cancer research, especially in the area of glycan-targeted cancer immunotherapy. As a pioneer in cancer immunotherapy targeting GD2, Dr. Yu has taken an anti-GD2 monoclonal antibody from IND application through phase III clinical trial, culminating in FDA approval of this chimeric anti-GD2 (Dinutuximab) for the treatment if high-risk neuroblastoma in 2015. This marks the first immunotherapeutic agent to target carbohydrate, thereby widening the net of potential pharmaceutical targets. In addition, her group has uncovered the roles of another glycan, Globo H, in cancer as an immune checkpoint molecule and an angiogenic factor, providing rationales for the ongoing development of Globo H-targeted immunotherapeutics. Recently, Dr. Yu's group is investigating the use of NKT-stimulatoryglycolipids as anti-cancer therapeutics and vaccine adjuvants.

Previously, Dr. Yu's research focused on translational research of childhood leukaemia, especially T-cell acute lymphoblastic leukaemia (T-ALL). She was the first to obtain an IND for deoxycoformycin to target an enzyme crucial for T-cell functions, adenosine deaminase, for the treatment of T-ALL, based on her in vitro studies. The promising results of her phase I study sparked interests in its applications to adult haematological malignancies, leading to its FDA approval for the treatment of hairy cell leukaemia in 1991. Dr. Yu elucidated the role of p15/16

in the pathogenesis of T-ALL, and generated preclinical evidence for targeting deficiency of p15/p16 and methylthioadenosyl phosphorylase with CDK4/6 inhibitors and alanosine, respectively, for cancer therapy. Her notion has borne out by the recently approved CDK4/6 inhibitor, palbociclib, showing that the sensitivity indeed depends on p16-Cdk4-Rb axis. In recent years, her group has identified new biomarkers for breast cancer stem cells and the molecular mechanisms involved. Dr. Yu has received many other awards including Academic Award from the Ministry of Education, Wang Min-Ning Memorial Award for Outstanding Contribution to the Development Medical Science and Technology, National Health and Society, and "Key to Life" Award from the Leukemia & Lymphoma Society in USA, Excellence in Technology Transfer Award 2016 from Federal Laboratory Consortium, USA: "Discovery to Commercialization: New Immunotherapy for Rare Childhood Cancer, Neuroblastoma" etc..

Recently, Dr. John Yu and her group have developed a strategy to target cancer stem cells by peptides that bind to protein X on the surface of cancer cells, but not normal cells. They are developing novel cancer therapeutics using the optimized cancer targeting peptides as "guided missiles" for a broad spectrum of cancer types and preferentially targeting "cancer stem cell", for which they received the 16th National Innovation Award.



# 講師介紹 ABOUT SPEAKER



## Patrick A. Ott, MD, Ph.D.

Clinical Director, Melanoma Disease Center
Clinical Director, Center for Immuno-Oncology
Dana-Farber Cancer Institute, USA
Associate Professor
Medicine, Harvard Medical School, USA
Email: PATRICK OTT@dfci.harvard.edu

Dr. Patrick Ott is currently the Clinical Director of both the Melanoma Disease Center and the Center for Immuno-Oncology at DFCI, serves as attending physician in the Department of Medicine at Brigham and Women's Hospital, and has an appointment as Associate Professor at Harvard Medical School in Boston, MA. Dr. Ott received his MD and PhD from Ludwig Maximilians University of Munich, Germany. He completed post-doctoral training in Immunology and residency training in Medicine at Case Western Reserve University. After a fellowship in Hematology-Oncology and 4 years on the faculty at New York University, he moved to Dana Farber Cancer Institute (DFCI) in 2012.

He is a clinical investigator and an integral member of the clinical trials program at Dana Farber/Harvard Cancer Center, where he designs and conducts phase 1 immunotherapy trials for patients with melanoma and a wide range of other tumors. His primary research interests are in melanoma and immunotherapy, specifically the development of innovative tumor vaccine approaches. Dr. Ott has been the Principal Investigator of a first in man clinical trial testing a personalized neoantigen vaccine (NeoVax) in patients with melanoma. The results of the study, reported in in Nature in 2017, established the feasibility and safety of this novel cancer vaccine approach for the first time in a coordinated clinical trial setting. Strong and consistent immunogenicity was demonstrated in patients with high risk melanoma, providing the basis for further testing of this innovative new treatment concept in other cancers. He has been the Principal Investigator and co-investigator on over 30 treatment trials, including those that have been instrumental in the clinical development of the newly FDA approved drugs pembrolizumab and nivolumab for the treatment of advanced melanoma, small cell lung cancer, and many other cancers. This work has resulted in numerous high impact publications including the New England Journal of Medicine, the Lancet Oncology, and the Journal of Clinical Oncology.

## **ABSTRACT 09:30-10:20** >

## **Personalized Neoantigen Cancer Vaccines**

Patrick A. Ott, MD, Ph.D.

Melanoma Disease Center, Dana-Farber Cancer Institute, USA

Cancer vaccines have been envisioned as an effective tool to generate, amplify, and diversify T cell responses against tumors. Tumor neoantigens are key targets of effective antitumor immune responses. Recently, we have demonstrated that a neoantigen vaccine (NeoVax), consisting of up to 20 long peptides and poly-ICLC, induced strong polyfunctional neoantigenspecific T cells that recognized patient tumor in vitro. All 6 patients we initially reported on (Ott &Wu, Nature, 2017) and 2 new patients are alive. New data on persistence of immune responses over several years, epitope spreading, analyses of single cell transcriptomics and TCR clonotypes over time will be presented. We also performed a clinical trial testing NeoVax in patients with glioblastoma multiforme (GBM) as well as in patients with metastatic melanoma, non-small cell lung cancer, and urothelial cancer who received NeoVax in combination with anti-PD-1 therapy. In the GBM study we demonstrated trafficking of NeoVax specific T cells into the intracranial tumor and assessed single cell transcriptomics of intratumoral T cells after vaccination. In the combination study (NeoVax + nivolumab) we found encouraging prolonged median PFS compared to historical controls, evidence of vaccine specific T cells in post-vaccine metastatic tumors, evidence for epitope spreading which is associated with durable clinical benefit. An update on this trial will be presented.



# 座長介紹 ABOUT MODERATOR



# 游正博所長 (John Yu, M.D., Ph.D.)

Distinguished Chair Professor & Director

Institute of Stem Cell and Translational Cancer Research (ISCTCR), Director

Cell Therapy Center, Chang Gung Memorial Hospital, Linkou and Chang Gung University Distinguished Visiting Fellow

Institute of Cellular & Organismic Biology, Academia Sinica

Email: Johnyu@cgmh.org.tw

#### **Education**

M.D., National Taiwan University; Ph.D. in Biophysics, University of Chicago; Fellow in Biology, The Biological Laboratories, Harvard University

#### **Fields of Specialty**

Stem cell biology; Regulation of hematopoiesis; Tumorigenesis

#### **Academic Appointments**

2016 –Present	Director, Cell Therapy Center, Chang Gung Memorial Hospital at Linkou
2013 – Present	Distinguished Chair Professor and Director, Institute of Stem Cell and Translational
	Cancer Research, Chang Gung Memorial Hospital at Linkou
2013 – Present	Distinguished visiting fellow, Institute of Cellular & Organismic Biology, Academia
	Sinica; Distinguished Chair Professor, Chang Gung University
2002 – 2013	Chief, Stem Cell Program, The Genomics Research Center, Academia Sinica.
2005 – 2009	President, Taiwan Society for Stem Cell Research
2002 – 2009	Distinguished Research Fellow & Director, Institute of Cellular & Organismic Biology,
	AS
2009 – 2013	Distinguished Research Fellow, Institute of Cellular & Organismic Biology, Academia
	Sinica
2004 – 2013	Distinguished Research Fellow, The Genomics Research Center, Academia Sinica

#### **Academic Awards and Honors**

- Founding President, Taiwan Society for Stem Cell Research, Taiwan, 2005-2009
- Government Affairs Committee, International Society for Stem Cell Research, 2005-2010
- International hESC Guidelines Task Force, International Society for Stem Cell Research, 2006-2007
- 柳川研究講座 , China Medical Univ. 2006; 台大内科經典講座 , National Taiwan Univ Hospital, 2005; 姆山研究講座 , Taipei Medical University, 2005
- Established Investigatorship Award, American Heart Association, 1978-1983

### **Key Government Services**

- Advisory Board of Regenerative Medicine and Cell Therapy, Ministry of Health and Welfare
- Member, Advisory Committee for the Studies of Regenerative Medicine, Ministry of Science and Technology
- Member, Advisory Committee for the Evaluation of Medical Technologies, Ministry of Health and Welfare

- Board of Directors, National Applied Research Laboratories, Taiwan, 2003-2009
- Advisory Board, Ministry of Education, Taiwan, 2005-2007
- The Consolidated Plan of Stem Cell Research in Taiwan (台灣幹細胞研究資源整體規劃計畫) 2005-2008
- The Plan for Primate Research Center in Taiwan 2004-2008
- Advisory Board, Natl Exp Animal Center, 2004-08, 2009-13
- NIH Special Grants Review Committee DDK-D 1995-2000
- NIH Committee for Physician Scientists 1995-2000
- NIH Review Committee for Small Business Innovation Research 1997-1999
- NIH Review Committee for Center of Excellence in Molecular Hematology 1993
- NIH Cellular Biology and Physiology Study Section 1989

## Selected Recent Publications (Selected from publications after 2006)

- 1. Ling, T.Y., Yu, J.\* (2006) Identification of pulmonary Oct-4+ stem/progenitor cells and demonstration of their susceptibility to SARS-CoV infection in vitro. PNAS USA, 103: 9530-9535.
- 2. Daley, G.Q., Yu, J., et al. (2007) The ISSCR guidelines for human embryonic stem cell research. Science, 315:603-604 with 64 pages of supplementary online materials.
- 3. Chang, W.W., .. Yu, J., Wong, C.H., Yu, A.L.\* (2008) Expression of Globo H and SSEA3 in breast cancer stem cells and the involvement of fucosyl transferases 1 & 2 in Globo H synthesis. PNAS USA, 105: 11667.
- 4. Andrews, P. W., Yu, J., et al. (2009) Consensus guidance for banking and supply of human embryonic stem cell lines for research purposes- international cell banking initiative. Stem Cell Rev. 5:301-314.
- 5. Huang, C.J., ···, Yu, J.\*, Chang Y.C.\* (2010) The influence of collagen film nanostructure on pulmonary stem cells and collagen-stromal cell interactions. Biomaterials, 31:8271-8280.
- 6. Liang, Y. J., "Yu, J.\* (2010) Switching of the core structures of glycosphingolipids from globo- and lacto- to ganglio-series upon human embryonic stem cell differentiation. PNAS USA, 107: 22564-22569.
- 7. Liang, Y.J., Yu, J.\* (2011) Changes in glycosphingolipid composition during differentiation of human embryonic stem cells to ectodermal or endodermal lineages. Stem Cells, 29: 1995-2004.
- 8. Cho, H.C., Yu, J.\* (2011) Identification of tumorigenic cells in KrasG12D-induced lung adenocarcinoma. Cancer Research, 71:7250-7258.
- 9. Chen, Y.H., Yu, J.\* (2012) Ectopic expression of Fgf3 leads to aberrant lineage segregation in the mouse parthenote preimplantation embryos. Developmental Dynamics, 241: 1651-1664.
- 10. Wang, S.H., Yu, J.\* (2013) HotLig: a molecular surface-directed approach to scoring protein-ligand interactions. Journal of Chemical Information and Modeling, 53:2181–2195.
- 11. Wu T.J.,..., Yu J.\* (2013) Tracking the engraftment and regenerative capabilities of transplanted lung stem cells using fluorescent nanodiamonds. Nat Nanotechnol 8: 682-689.
- 12.Lin, J.J., Huang, C.S., Yu, J., ···· Yu, A.L.\* (2014) Malignant phyllodes tumors display mesenchymal stem cell features and ALDH/GD2 identify their tumor stem cells. Breast Cancer Research, 16:R29.
- 13.Fu, C.H., Lin, R.J., Yu, J., ··· Yu, A.L.\* (2014) Oncogenic role of SH2-containing-5'-inositol phosphatase-2 in breast cancer stem cells. Stem Cells, 32(8): 2048-60.
- 14.Cheng, J.Y., ··· Yu, J., ···, Yu, A.L.\* (2014) Globo-H ceramide shed from cancer cells triggers translinassociated factor X-dependent angiogenesis. Cancer Research, 74:6856-66.
- 15.Chen, E., Yu, J.\* (2015) Epigenetic disruptions of histone signatures for the trophectoderm and inner cell mass in mouse parthenogenetic embryos. Stem Cells and Development, 24:550-64.
- 16. Wang S.H., ···, Yu A.L.\*, Yu J.\*Structure-based optimization of GRP78-binding peptides that enhances efficacy in cancer imaging and therapy. Biomaterials 2016, 94:31-44.
- 17.Yu A.L., Hung J.T., Ho M.Y., Yu J.\*Alterations of glycosphingolipids in embryonic stem cell

# **(1)**

## 長庚醫院癌症精準免疫細能治療國際研討會

- differentiation and development of glycan-targeting cancer immunotherapy. Stem Cells Dev2016, 25(20): 1532-1548.
- 18.Tan K.P., ..., Yu J., Hung J.T., Yu A.L.\* Fucosylation of LAMP-1 and LAMP-2 by FUT1 correlates with lysosomal positioning and autophagic flux of breast cancer cells. Cell Death & Disease2016, 7(8): e2347.
- 19.Wu T.J., Chiu H.Y., Yu J.\*Fluorescent nanodiamonds for tracking the engraftment and repair of lung stem cells. In Nanotechnologies in Preventive and Regenerative Medicine, Chapter 14.Elsevier, Oxford, UK, 2016.
- 20.Ho M.Y., Yu A.L., Yu J.\*Glycosphingolipid dynamics in human embryonic stem cell and cancer: their characterization and biomedical implications. Glycoconjugate Journal 2017, 34(6):765-777.
- 21.Liang Y.J., Yu J.\*Interaction of glycosphingolipids GD3 and GD2 with growth factor receptors maintains breast cancer stem cell phenotype. Oncotarget 2017, 8(29):47454-73.
- 22.Kuo H.H.,,, Yu J.\*, Yu A.L.\* High expression FUT1 and B3GALT5 is an independent predictor of postoperative recurrence and survival in hepatocellular carcinoma. Scientific Reports2017, 7:10750.
- 23. Wang SH, Yu J\*Structure-based design for binding peptides in anti-cancer therapy. Biomaterials 2018, 156: 1.
- 24.Wu T.J., Chiu H.Y., Yu J.\*Fluorescent nanodiamonds for tracking the engraftment and repair of lung stem cells. In Nanotechnologies in Preventive and Regenerative Medicine. Elsevier, UK, 2018.
- 25.Liao C.H., ..., Yu J.\*Leucine-rich Repeat Neuronal Protein 1 Regulates Differentiation of Human Embryonic Stem Cells by Posttranslational Modifications of Pluripotency Factors. Stem Cells2018, 36: 1514-24.
- 26.Fan T.C., ···, Yu J., Yu A.L.\* Reciprocal feedback regulation of ST3GAL1 and GFRA1 signaling in breast cancer cells. Cancer Letters2018, 434: 184-195.
- 27.Yeo H.L., ..., Yu J.\*, Yu A.L.\* Sialylation of vasorin by ST3Gal1 facilitates TGF-b1 mediated tumor angiogenesis and progression. Int. J. Ca.2019, 144(8): 1996-2007.
- 28.Wu Y.C., ···Yu J.\*Differential response of non-cancerous and malignant breast cancer cells to conditioned medium of adipose tissue-derived stromal cells (ASCs). Int. J. Med. Sci.2019, 16(6): 893-901.
- 29. Cheng K.C., ..., Yu J., Yu A.L.\* FAM129B, an antioxidative protein, reduces chemosensitivity by competing with Nrf2 for Keap1 binding. EBioMedicine2019,45: 25-38.
- 30.Wu Y.C., ···, Yu J.\*Fluorescent nanodiamonds enable long-term detection of human adipose-derived stem/stromal cells in an in vivo chondrogenesis model using decellularized extracellular matrices and fibrin

# Memo

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# 講師介紹 ABOUT SPEAKER



# Cassian Yee, MD

Professor, Department of Melanoma Medical Oncology, Department of Immunology, The University of Texas MD Anderson Cancer Center

Director, Department of Solid Tumor Cell Therapy, Division of Center for Cancer Immunology Research, The University of Texas MD Anderson Cancer Center, USA Email: CYee@mdanderson.org

Dr. Yee is Professor in the Departments of Melanoma Medical Oncology and Immunology, Co-Director of the Adoptive Cellular Therapy Platform and Director of Solid Tumor Cell Therapy at UT MD Anderson Cancer Center. He received his medical training in Canada, residency at Stanford and fellowship at Fred Hutchinson Cancer Research Center. He is an elected member of the American Society of Clinical Investigators, recipient of Clinical Translational Scientist Award from Burroughs Wellcome Fund, CPRIT Clinical Investigator award, co-Leader of the Stand Up to Cancer- American Association for Cancer Research / Cancer Research Institute Immunotherapy Dream Team and Member of the Parker Institute for Cancer Immunotherapy.

Over the last 20+ years, Dr. Yee has pioneered a form of ACT, known as Endogenous T Cell (ETC) therapy, using peripheral blood to generate antigen-specific memory T cells for the treatment of patients with cancer. His lab has performed several seminal first-in-human studies using a well-defined, uniform population of ex vivo expanded antigen-specific T cells to delineate the requirements for effective immune-based therapies He is author of publications in top-tier journals including The New England Journal of Medicine, Nature, Science, Nature Medicine, Journal of Clinical Oncology and Journal of Experimental Medicine. He holds international patents and seeks to extend immunotherapy-based cancer treatments globally with collaborators. His work converges multidisciplinary approaches in bioengineering, metabolism, molecular immunology and cellular biology to develop effective immunotherapy strategies and adoptive cellular therapy, in particular, as a treatment modality for patients with malignant diseases.

## **ABSTRACT 10:40-11:30** >

# Adoptive T Cell Therapy: Challenges and Opportunities in Solid Tumor Malignancies

Cassian Yee, MD

Department of Melanoma Medical Oncology

The University of Texas MD Anderson Cancer Center, USA

Adoptive Cell Therapy (ACT) has enjoyed a revival in recent years for hematologic malignancies but advancing its use for the treatment of patients with solid tumors will require addressing effector cell intrinsic as well as tumor micro environmental hurdles and exploiting a broader ACT platform that includes not only engineered CAR-T cells, but also other forms of ACT including Endogenous T Cell (ETC) Therapy Endogenous T cell (ETC) therapy requires specialized methods to isolate and expand from peripheral blood, tumor-reactive T cells, often present at very low frequency, and, by sourcing effectors from the entire TCR repertoire, provide the greatest flexibility in delivering a T cell product of defined specificity and phenotype. Several first-in-human studies performed by our lab demonstrate the importance of antigen spreading in generating long-lasting clinical responses as well as identifying T cells with specialized memory properties. The ETC therapy approach allows for the greatest flexibility in targeting personalized and shared tumor-associated antigens and rapid implementation of adoptive cell therapy from epitope identification to T cell infusion. To broaden the pool of patients and extend the use of adoptive cell therapy to several solid tumor malignancies such as ovarian, lung, GI and breast cancers, we have validated several high value target tumor antigens that are expressed in significant fraction of these tumors.



# 座長介紹 ABOUT MODERATOR



# 魏國珍主任 (Kuo-Chen Wei, MD)

Director,

Department of Neurosurgery, Industry-Academia Center, Chang Gung Memorial Hospital, Linkou Branch, Taiwan Email: kuochenwei@cgmh.org.tw

## 學歷

• 中山醫學大學

## 現任

- 林口長庚醫院外科部 副部長
- 林口長庚醫院產學合作中心 主任
- 教育部 部定副教授
- 衛生署疾病管制局症候群重症通報系統 委員
- 健保局台北分局健保醫事審查委員會 委員
- 台灣神經腫瘤學學會 理事長
- 台灣立體定位功能性神經外科及放射手術學會 理事

#### 經歷

- 加洲大學舊金山校區 (U.C.S.F.) 腦瘤研究中心 博士後研究員
- 林口長庚醫院神經外科系 主任
- 林口長庚醫院腦腫瘤神經外科主任

## 專長

- 腦部膠質瘤之腫瘤標記
- 惡性腦瘤之蛋白質體及基因體學研究
- 腦部藥物傳輸及分子標的之奈米醫學研究
- 惡性腦瘤、腦部膠質細胞瘤

(C)

# Precision Immune Cell Therapies for Cancers

# Memo

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# 講師介紹 ABOUT SPEAKER



# Shizu Takeda 武田志津, Ph.D.

Corporate Officer, Corporate Chief Scientist, Research & Development Group and Laboratory Manager of the Hitachi Kobe Laboratory,

Center for Exploratory Research, Hitachi, Ltd. Japan

Email: shizu.takeda.me@hitachi.com

## **Education**

March 1988 Graduated from the University of Tokyo, Faculty of Pharmaceutical Sciences

March 1990 Graduated from the University of Tokyo, Graduate School of Pharmaceutical Sciences,

Master course

March 1993 Graduated from the University of Tokyo, Graduate School of Pharmaceutical Sciences,

Doctor course PhD degree (Pharmaceutical Sciences)

## **Carrier Experience**

April 1990 Research Fellow, Japan Society for the Promotion of Science

March 1993 Medical Research Fellow, Harvard Medical School

March 1995 PhD Researcher, Rockefeller University

March 1997 PhD Researcher, Graduate School of Pharmaceutical Sciences, The University of Tokyo

April 2001 Joined Hitachi, Ltd.

April 2013 Department Manager, Advanced Research Department, Life Science Research Center,

Central Research Laboratory

April 2015 Senior Chief Scientist and Project Leader, Center for Exploratory Research, Research and

Development Group

April 2017 Senior Chief Scientist and Laboratory Manager of Hitachi Kobe Laboratory, Research and

**Development Group** 

April 2018 Corporate Chief Scientist and Laboratory Manager of Hitachi Kobe Laboratory, Research

and Development Group

April 2019 Corporate Officer, Corporate Chief Scientist and Laboratory Manager of Hitachi Kobe

Laboratory, Research and Development Group

#### Officer of External Organization

April 2017 – Present Member of Nanotechnology and Materials Science and Technology

Committee, Ministry of Education, Culture, Sports, Science and Technology

September 2015 – Present Member of Specified Approval for Regenerative Medicine Committee,

Tokai University

December 2015 -December 2017 Member of Ethical Review Committee, Japan Biological

Informatics Consortium

June 2018-Present Board Member of Kobe Port Island Drug Development Forum

August 2018 – Present Member of Steering Committee, Kobe Biomedical Innovation Cluster

## **ABSTRACT 11:30-12:00** >

# Trends for cell culture technology and automation in regenerative medicine: Experience from Hitachi, Ltd.

Shizu Takeda, Ph.D.

Corporate Officer, Corporate Chief Scientist, Research & Development Group and L aboratory Manager of the Hitachi Kobe Laboratory, Center for Exploratory Research, Hitachi, Ltd. Japan

Regenerative medicine opens up the possibility of providing new treatments using cultured and processed cells for overcoming incurable diseases such as cancers. The production of cells for autologous cell therapy involves many steps from harvesting the source cells from a patient to finally transplanting the cells into the patient, including cell preparation, culturing, processing, testing, and transportation. Although the cell culturing for medical use is largely performed manually at present, the key to more widespread application to cell therapy lies in the use of techniques for automated cell culture for rationalization of cell production cost and the reliable supply of high-quality cells. To achieve wider adoption of cell therapy, Hitachi is developing the automated cell culture technology through engaging in government-academia-industry open innovation in Japan. The advantage is that our closed system enables the cell culturing with excellent sterility preventing the contamination of microorganism. In this seminar, I will introduce the trends for cell culture technology and automation in regenerative medicine.



# 座長介紹 ABOUT MODERATOR



# 江東和部長 (Tang-Her Jaing, MD)

Chairman,

Cord Blood Transplantation Center,

Division of Hematology and Oncology,

Department of Pediatrics,

Chang Gung Memorial Hospital Linkou Branch

Email: jaing001@cgmh.org.tw

### **Year of Medical Graduation**

1980-1987 Bachelor at Kaohsiung Medical College

### **Postdoctoral Experience**

1986-1987	Internship-Rotating, Chang Gung Memorial Hospital, Taipei, Taiwan
1989-1991	Resident, Pediatrics, Chang Gung Memorial Hospital, Taipei, Taiwan
1991-1992	Resident Fellow, Pediatric Hematology/Oncology,
	Chang-Gung Memorial Hospital, Taipei, Taiwan
1992-1993	Senior Fellow, Pediatric Hematology/Oncology,
	Chang Gung Memorial Hospital, Taipei, Taiwan
1997-1998	Fellow, Pediatric Bone Marrow Transplant,
	University of Minnesota, USA

#### **Appointments**

1993- now Attending Pediatrician, Chang Gung Memorial Hospital, Taipei, Taiwan

1994- now Attending Physician, Pediatric Hematology/Oncology,

Chang Gung Memorial Hospital, Linkou, Taiwan

#### Fields of Interest

Pediatric Hematology/Oncology; Hematologic stem cell transplan

## **Publications (2017-2019)**

- 1. Huang YJ, Coustan-Smith E, Kao HW, Liu HC, Chen SH, Hsiao CC, Yang CP, Tang-Her Jaing, Yeh TC, Kuo MC, Lai CL, Chang CH, Campana D, Liang DC, Shih LY. Concordance of two approaches in monitoring of minimal residual disease in B-precursor acute lymphoblastic leukemia: Fusion transcripts and leukemia-associated immunophenotypes. J Formos Med Assoc. 2017;116:774-81.
- 2. Li MJ, Liu HC, Yen HJ, Tang-Her Jaing, Lin DT, Yang CP, Lin KH, Hung IJ, Jou ST, Lu MY, Hsiao CC, Peng CT, Chang TT, Wang SC, Lin MT, Chen JS, Chang TK, Hung GY, Wu KH, Yang YL, Chang HH, Chen SH, Yeh TC, Cheng CN, Lin PC, Chiou SS, Sheen JM, Cheng SN, Chen SH, Chang YH, Ho WL, Chao YH, Chen RL, Chen BW, Wang JL, Hsieh YL, Liao YM, Yang SH, Chang WH, Chao YY, Liang DC. Treatment for childhood acute lymphoblastic leukemia in Taiwan: Taiwan Pediatric Oncology Group ALL-2002 study emphasizing optimal reinduction therapy and CNS preventive therapy without cranial radiation. Pediatr Blood Cancer 2017;64:234-41.
- 3. Chang TY, Lai JY, Wang CJ, Chen SY, Tang-Her Jaing, Hsueh C, Shih LY, Chen SH. Development of a

- gastric carcinoid tumor following allogeneic hematopoietic stem cell transplantation for early T-cell precursor acute lymphoblastic leukemia. Pediatr Transplant. 2017;21:12911.
- 4. Chang TY, Tang-Her Jaing, Chen SH. Treatment of Critical Hypercalcemia Using Pamidronate in Acute Megakaryoblastic Leukemia in an 18-month-old Girl. Pediatr Neonatol 2017;58:462-4.
- 5. Yen HJ, Chen SH, Chang TY, Yang CP, Lin DT, Hung IJ, Lin KH, Chen JS, Hsiao CC, Chang TT, Chang TK, Peng CT, Lin MT, Tang-Her Jaing, Liu HC, Jou ST, Lu MY, Cheng CN, Sheen JM, Chiou SS, Hung GY, Wu KH, Yeh TC, Wang SC, Chen RL, Chang HH, Yang YL, Chen SH, Cheng SN, Chang YH, Chen BW, Hsieh YL, Huang FL, Ho WL, Wang JL, Chang CY, Chao YH, Lin PC, Chen YC, Liao YM, Lin TH, Shih LY, Liang DC. Pediatric acute lymphoblastic leukemia with t(1;19)/TCF3-PBX1 in Taiwan. Pediatr Blood Cancer 2017 Oct;64(10).
- 6. Lee WI, Chen CC, Tang-Her Jaing, Ou LS, Hsueh C, Huang JL. A Nationwide Study of Severe and Protracted Diarrhoea in Patients with Primary Immunodeficiency Diseases. Sci Rep. 2017;7:3669
- 7. Tang-Her Jaing, Tsay PK, Chang TY, Wen YC, Yang YC, Chen SH, Tian YC. BK virus-associated hemorrhagic cystitis in children undergoing allogeneic hematopoietic stem cell transplantation a single institution experience. HK J Paediatr 2017;22:144-50.
- 8. Liang DC, Chen SH, Liu HC, Yang CP, Yeh TC, Tang-Her Jaing, Hung IJ, Hou JY, Lin TH, Lin CH, Shih LY. Mutational status of NRAS, KRAS, and PTPN11 genes is associated with genetic/cytogenetic features in children with B-precursor acute lymphoblastic leukemia. Pediatr Blood Cancer 2018;65:26786
- 9. Huang IA, Tang-Her Jaing, Wu CT, Chang CJ, Hsia SH, Huang N. A tale of two systems: practice patterns of a single group of emergency medical physicians in Taiwan and China. BMC Health Serv Res. 2017;17:642.
- 10.Lien R, Lin YF, Lai MW, Weng HY, Wu RC, Tang-Her Jaing, Huang JL, Tsai SF, Lee WI. Novel Mutations of the Tetratricopeptide Repeat Domain 7A Gene and Phenotype/Genotype Comparison. Front Immunol. 2017;8:1066.
- 11. Tang-Her Jaing, Chen SH, Wen YC, Chang TY, Tsai DY, Chung HT, Tsay PK. Factors Affecting Survival in Children with Pericardial Effusion after Hematopoietic Stem Cell Transplantation. Cell Transplant. 2017;26:1792-7.
- 12. Tang-Her Jaing. Is the Benefit–Risk Ratio for Patients with Transfusion-Dependent Thalassemia Treated by Unrelated Cord Blood Transplantation Favorable? Int J Mol Sci. 2017;18,2472
- 13.Lee CF, Chen CH, Wen YC, Chang TY, Lai MW, Tang-Her Jaing\*. Copper-associated hepatitis in a patient with chronic myeloid leukemia following hematopoietic stem cell transplantation: A case report. Medicine. 2017;96:e9041.
- 14. Tang-Her Jaing, Chen SH, Wen YC, Chang TY, Yang YC, Tsay PK. Effects of cryopreservation duration on the outcome of single-unit cord blood transplantation. Cell transplant. 2018;27:515-9.
- 15. Tang-Her Jaing, Chang TY, Chen SH, Wen YC, Chuang WY, Yang CP. Small cell variant of ALK-positive anaplastic large cell lymphoma with primary subcutaneous presentation: A case report. Medicine. 2018;97:e11222.
- 16.Chen DP\*, Chang SW\*, Tang-Her Jaing\*, Wang WT, Hus FP, Tseng CP. Single nucleotide polymorphisms within HLA region are associated with disease relapse for patients with unrelated cord blood transplantation. PeerJ. 2018;6:e5228.
- 17. Hsiao HJ, Chen SH, Tang-Her Jaing, Yang CP, Chang TY, Li MY, Chiu CH, Huang JL. Psychosocial interventions for reduction of distress in children with leukemia during bone marrow aspiration and lumbar puncture. Pediatr Neonatol. 2018
- 18.Chang CC, Lee MY, Wen YC, Yu TJ, Chen SH, Tang-Her Jaing\*. "Do-not-resuscitate" orders in children with cancer at the end of life: a retrospective review. J Palliat Care Med. 2018.8:4
- 19.Yeh TC, Liang DC, Hou JY, Tang-Her Jaing, Lin DT, Yang CP, Peng CT, Hung IJ, Lin KH, Hsiao CC, Jou ST, Chiou SS, Chen JS, Wang SC, Chang TK, Wu KH, Sheen JM, Yen HJ, Chen SH, Lu MY, Li MJ, Chang TT, Huang TH, Chang YH, Chen SH, Yang YL, Chang HH, Chen BW, Lin PC, Cheng CN, Chao YH, Yang SH,



## 長庚醫院癌症精準免疫細能治療國際研討會

- Chao YY, Liu HC. Treatment of childhood acute lymphoblastic leukemia with delayed first intrathecal therapy and omission of prophylactic cranial irradiation: Results of the TPOG-ALL-2002 study. Cancer. 2018;124:4538-47.
- 20. Yeh TC, Liang DC, Liu HC, Tang-Her Jaing, Chen SH, Hou JY, Yang CP, Huang YJ, Yao HW, Huang TY, Lin TH, Shih LY. Clinical and biological relevance of genetic alternations in pediatric T-cell lymphoblastic leukemia in Taiwan. Pediatr Blood Cancer. 2019;66:e27496.
- 21. Chen SH, Chen JS, Jou ST, Wu KH, Hung IJ, Sheen JM, Lu MY, Chen BW, Tang-Her Jaing, Wang SC, Lin MT, Chang TK, Liu HC, Yang CP. Outcome and prognosis of anaplastic large cell lymphoma in children: a report from the Taiwan Pediatric Oncology Group. Leuk Lymphoma. 2019 (in press)
- 22.Tang-Her Jaing, Chang TY, Chen SH, Wen YC, Yu TJ, Lee CF, Yang CP, Tsay PK. Factors associated with cytomegalovirus infection in children undergoing allogeneic hematopoietic stem-cell transplantation. Medicine. 2019;98:e14172

# Memo

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# 講師介紹 ABOUT SPEAKER



# 曾子晏教授 (Chi-Meng Tzeng, Ph.D.)

Professor and Executive Director,

Key Laboratory for Cancer T-Cell Theranostics and Clinical Translation (CTCTCT) & Translational Medicine Research Center (TMRC), School of Pharmaceutical Sciences, Xiamen University, China

Email: cmtzeng@xmu.edu.cn

Dr. Tzeng received comprehensively graduated training in National Tsing-Hua University (NTHU, School of Nuclear Sciences in Radiation Biology, advised by Dr. Rong-Long Pan, in 1989~1993) and Stanford University (SU, Medical School in Biochemistry, advised by Dr. Arthur Kornberg, Nobel Prize Laureate, in 1995~1999). Moreover, he also expansively practiced either in academic or in industrial executive position from Academic Sinica, National Taiwan University Hospital, U-Vision Biotech, VitaGenomics/ GeneCore/ ABI, SBC/MaxyBio, Beckman Coulter, BSI, Innova Cell Theranostics, Xiamen University and Nanjing Technology University to Nanjing Medical University since 2000 till now.

Dr. Tzeng possesses skills of protein chemistry/biochemistry, -omics, translation medicine and Clinical Theranostics holding more than 60 peer-reviewed SCI/IE scientific articles, 3 book chapters, 13 PCT/China patents and in excess of 13 commercialized diagnostic products and 2 healthcare management programs. He is interested in integrating biomedical research, marketing analysis, financial manipulation, manufacturing SOPs/QC/A, and big health data and entrepreneur atmosphere to cash out clinical/biomedical commercialization.

Dr. Tzeng currently is leading and puzzling clinical resources, academic force and biopharmaceutical-industrial energy to decipher the biomarkers, drug target and personalized medicine from projects of adenocarcinoma (T-/NK-cell Theranostics), regenerative medicine (MSC theranostics), neuro-degradation (Leukoaraiosis, PD/AD and aromatherapy) and e-Healthcare solution (Artificial Intelligent-chronic/tumor disease management, AI-Driven) for three National Hi-Tech Industrial Development Parks.

## **ABSTRACT 13:00-13:40** >

## **Anti-CDR3/EGFR-CAR-T Immunotherapy**

Chi-Meng Tzeng, Ph.D.

Key Laboratory for Cancer T-Cell Theranostics and Clinical Translation (CTCTCT)
& Translational Medicine Research Center (TMRC),
School of Pharmaceutical Sciences, Xiamen University, China

T cell malignances are a class of Hematologic cancers originating from single T lymphoid precursor cells, including T Lymphoblastic Leukemia/Lymphoma. They have unique histopathological and clinical features; these cancers are accounting for 25% of the lymphatic system malignances. Compared to B cell Leukemia /Lymphoma, they are more aggressive, the traditional chemotherapy in these patients is poor result. All these events prompt us to study the potential use of targeted therapies in T cell malignances through CAR-T technologies.

After used NGS and immune Repertoire (IR), we found that the T cell receptor's Complementary Determinant Region 3 (TCR-CDR3) peptide on the surface of malignant T cells is specificity individually. Therefore, we expected that TCR-CDR3 may be a target for precise treatment in these diseases as tumor associated/specific antigen (TAA/TSA), neoantigen for T Lymphoblastic Leukemia/Lymphoma. We collected the bone marrow and lymph gland from 74 patients with T cell malignance and also harvested the peripheral blood from 20 healthy for building Phage Display antibody library to display the CDR3 peptide as neoantigen.

We found that they have well targeted killing ability to the Primary cancer cell and T cell malignant cell lines Jurkat and Molt-4 in vivo and in vitro, respectively. In the T Lymphoblastic Leukemia/Lymphoma patients' clinical observation and trial, over 90% of anti-CDR3 Car-T immunotherapy were over stable development and further removing the malignancy. This research and clinical trial provide a translational medicine strategy for the clinical treatment of T cell malignances.



# 座長介紹 ABOUT MODERATOR



# 張承能副院長 (Chen-Nen Chang, MD)

Professor,
Department of Neurosurgery,
Chang Gung Memorial Hospital
Vice President,
Xiamen Chang Gung Hospital, China

#### **Present Appointment**

- 1. Clinic Professor, Department of Neurosurgery, Chang Gung Memorial Hospital, Taipei, Taiwan
- 2. Chairman, Committee of Admission Evaluation for Medical Student. School of Medicine, Chang Gung University (CGU)

## **Education and Training**

1969/9/1 - 1976/6/30 M.D., National Taiwan University Medical College, Taipei, Taiwan
 1978/7/1 - 1983/6/30 Resident training, Department of Surgery and Neurosurgery: CGMH
 1980/7/1 - 1981/9/30 Resident, Division of Neuropathology, Vancouver General Hospital, University of British Columbia, Vancouver, B.C., Canada
 1987/6/1 - 1988/5/31 Epilepsy Surgery:

- 1. Senior fellow, Epilepsy Center, Department of Neurological Surgery, University of Washington, Seattle, Washington, U.S.A.
- 2. Senior fellow, Division of Neurosurgery, University of British Columbia, Vancouver, B.C., Canada

2006/4/1 - 2011/3/31 Ph.D. Faculty of medical science, University of Fukui, Fukui, Japan

#### **Academic Appointment Record**

1983/07 – Present	Full-time attending staff, Department of Neurosurgery, CGMH
1989/08 - 1993/05	Chief, Department of Neurosurgery, CGMH
1993/02 - 2004/12	Chief, First Division of Neurosurgery, CGMH
1993/07	Associate Professor, CGU, Taipei, Taiwan
2001/02 - 2003/02	Chairman, Department of Surgery, CGMH
2004/07 - 2010/01	Director, Brain Tumor Team, Cancer Center, CGMH
2005/04 - 2008/06	Chief, Brain Tumor Division of Neurosurgery, CGMH
2005/11 - 2006/11	President, Taiwan Skull Base Surgery Society, Taiwan
2006/07 – Present	Clinical Professor, Department of Neurosurgery CGMH
2007/11 - 2009/11	President, Taiwan Neuro-Oncology Society
2008/07 – Present	Chairman, Medical Student Entrance Evaluation Committee, Medical School,
	CGU , Taipei, Taiwan,
2017/06 – Present	Pident, Taiwan Pituitary Society

## **Research Interest**

Epilepsy surgery, glioma, pituitary tumor, immunotherapy, cranio-facial surgery, c-spine.

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# Precision Immune Cell Therapies for Cancers

# Memo

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# 講師介紹 ABOUT SPEAKER

Email: kuochenwei@cgmh.org.tw



# 魏國珍主任 (Kuo-Chen Wei, MD)

Director,

Department of Neurosurgery, Industry-Academia Center, Chang Gung Memorial Hospital, Linkou Branch, Taiwan

## 學歷

中山醫學大學

## 現任

林口長庚醫院外科部 副部長 林口長庚醫院產學合作中心 主任 教育部 部定副教授 衛生署疾病管制局症候群重症通報系統 委員 健保局台北分局健保醫事審查委員會 委員 台灣神經腫瘤學學會 理事長 台灣立體定位功能性神經外科及放射手術學會 理事

#### 經縣

加洲大學舊金山校區 (U.C.S.F.) 腦瘤研究中心 博士後研究員 林口長庚醫院神經外科系 主任 林口長庚醫院腦腫瘤神經外科 主任

## 專長

腦部膠質瘤之腫瘤標記 惡性腦瘤之蛋白質體及基因體學研究 腦部藥物傳輸及分子標的之奈米醫學研究 惡性腦瘤、腦部膠質細胞瘤

## ABSTRACT 13:40-14:10 >

# Dendritic Cell-Based Immunotherapy in Cancer Precision Medicine

Kuo-Chen Wei, MD

Department of Neurosurgery, Chang Gung Memorial Hospital

Cell-based immunotherapy is a novel strategy for treating all cancer types. It includes immune cells in both innate and adaptive immunity such as NK cells, dendritic cells, and T cells. The first FDA-approved cell-based immunotherapy is Sipuleucel-T, a dendritic cell-based therapy for treating hormonal refractory asymptomatic or minimally symptomatic metastatic prostate cancer. Dendritic cells (DCs) are antigen presenting cells that bridge innate and adaptive immunity and function to induce antigen specific T cell response. There are several ways to stimulate the maturation of dendritic cells and the ex vivo stimulation is the most effective and efficient way so far. The ex vivo stimulation of DCs involves collection of DCs from patients by leukapheresis, inducing the activation and maturation of DCs, and stably presenting tumor-specific antigens to T cells. As the most crucial step for DC-based therapy is to stably and effectively present tumor-specific antigen to T cells, great effort has been made on developing efficacious approaches to generate tumor-specific DCs, such as stimulation of DCs by different tumor-derived proteins or RNAs and addition of cytokines as co-stimulators for DC maturation. Glioblastoma (GBM) is one of the representative cancers currently undergoing clinical trials of DC-based immunotherapy, which refers to DC vaccine. The DC vaccine is a safe treatment across many trials, but it did little effect on the overall survival of GBM patients without any filtration or grouping. However, recent studies demonstrated that DC vaccine treatment improved progression-free survival and quality of life of newly diagnosed GBM patients and researches did find different treatment response in different subgroups of GBM patients. As lots of efforts have been put on cell-based immunotherapy, the results will be references for following clinical trials and light the therapeutic future of DC-based immunotherapy for cancer treatment.



# 講師介紹 ABOUT SPEAKER



# 李威震主任 (Wei-Chen Lee, MD)

Director,

General Surgery, Division of Liver and Transplantation Surgery,

Chang Gung Transplantation Institute,

Chang Gung Memorial Hospital, Linkou Branch, Taiwan

Email: weichen@cgmh.org.tw

#### Education

1. Taipei Medical College 1980-1987

#### **Postgraduate Training**

1. Surgical resident, Department of Surgery, 1989 - 1994

Chang Gung Memorial Hospital

1994.7- until now 2. Attending doctor, Department of general surgery,

Chang Gung Memorial Hospital

3. Research fellow, Transplantation Department, 1996.6 - 1998.5

UPMC, University of Pittsburgh

#### **Academic Appointment**

- 1. Chief, Division of Liver and Transplantation Surgery
- 2. Chief, Chang-Gung Transplantation Institute, LinKou
- 3. Chief, Department of General Surgery, since July, 2016

#### **Employment Record**

1. Surgical resident, Department of general surgery, 1989.07-1993.06

Chang Gung Memorial Hospital.

Chang Gung Memorial Hospital.

2. Surgical chief resident, Department of general surgery, 1993.07-1994.06

3. Attending doctor, Department of general surgery, Chang Gung Memorial Hospital.

1994.07-till now

4. Assistant professor, Department of general surgery, Chang Gung Memorial Hospital.

1997.07-2001.06

5. Associate professor, Department of general surgery, Chang Gung Memorial Hospital.

2001.07-2008.06

6. Professor, Department of general surgery, Chang Gung Memorial Hospital.

2008.07-till now

#### **Licensure**

- 1. Republic of China License No.:015704
- 2. Board of Surgery, Republic of China No.:003027
- 3. Board of Gastroenterology Surgery No.:686

## **Professional Affiliations**

- 1. Surgical Association, Republic of China
- 2. Formosa Medical Association
- 3. Surgical Society of Gastroenterology, R.O.C.
- 4. Taiwan Transplantation Society
- 5. International Society of transplantation
- 6. Member of American Society of Transplantation
- 7. Member, internation society of liver transplantation
- 8. Member, IHPBA

## **Professional Activities**

Chair, Taiwan transplantation society, 2015-2017
The Council member of Taiwan Transplantation Society
The Council member of Taiwan Surgery Society
The Council member of Taiwan Liver Tumor Society

#### **Research Interest**

transplantation immunology, tumor immunology

#### **Publications (selected 2017-2019)**

- 1. Lee CF, Lu CY, Zidan A, Lee CS, Wu TH, Chan KM, Lee WC\*. Microscope-assisted hepatic artery reconstruction in adult living donor liver transplantation-a review of 325 consecutive cases in a single center. Clinical Transplantation. 2017; Feb;31(2), e12879.
- 2. Abdelhamid NM, Chen YC, Wang YC, Cheng CH, Wu TJ, Lee CF, Wu TH, Chou HS, Chan KM, Lee WC, Soong RS\*. Pre-Transplantation Immune Cell Distribution and Early Post-Transplant Fungal Infection Are the Main Risk Factors of Liver Transplantation Recipients in Lower Model of End-Stage Liver Disease. Transplantation Proceedings. 2017;49(1):92-97.
- Weng LC, Huang HL, Tsai HH, Lee WC. Predictors of decision ambivalence and the differences between actual living liver donors and potential living liver donors. PLOS ONE https://doi. org/10.1371/journal.pone.0175672 May 17, 2017.
- 4. Lee WC\*, Chou HS, Wu TJ, Lee CF, Hsu P-Y, Hsu H-Y, Wu TH, Chan KM. Down-regulation of metabolic proteins in hepatocellular carcinoma with portal vein thrombosis. Clinical Proteomics. 2017; 14:29.
- 5. Lee WC\*, Wu TH, Wang YC, Cheng CH, Lee CF, Wu TJ, Chou HS, Chan KM, Lee CS. Renal Function Improvement by Telbivudine in Liver Transplant Recipients with Chronic Kidney Disease. BioMed Research International. 2017; August. doi.org/ 10.1155/ 2017/ 9324310. Article ID 9324310, 8 pages.
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- 8. Lee WC. Cell-mediated immunotherapy for hepatocellular carcinoma. J Cancer Metastasis Treat. 2017;3: 244-249.
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- 13.Lee WC, Chou HS, Lee CS, Wu TH, Wang YC, Cheng CH, Lee CF, Wu TJ, Chan KM. Viral activity and outcome of hepatitis B surface antigen-positive grafts in deceased liver transplantation. J Viral Hepat. 2018;1-4. DOI: 10.1111/jvh.12880.
- 14. Chan KM, Wu TH, Wang YC, Lee CF, Wu TJ, Chou HS, Lee WC, Chiang JM, Chen JS. Clinical relevance of oncologic prognostic factors in the decision-making of pre-hepatectomy chemotherapy for colorectal cancer hepatic metastasis: the priority of hepatectomy. World J Surg Oncol. 2018 Feb;16(1):24.
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- 16.Chu YD, Lin KH, Huang YH, Lin CC, Hung CF, Yeh TS, Lee WC, Yeh CT. A novel thyroid function index associated with opposite therapeutic outcomes in advanced hepatocellular carcinoma patients receiving chemotherapy or sorafenib. Asia Pac J Clin Oncol. 2018 May 21.
- 17. Chan KM, Cheng CH, Wu TH, Lee CF, Wu TJ, Chou HS, Lee WC. De Novo Endotoxin-Induced Production of Antibodies against the Bile Salt Export Pump Associated with Bacterial Infection following Major Hepatectomy. Biomed Res Int. 2018 Apr 23;2018:6197152.
- 18. Cheng YL, Chang CH, Chen WT, Tsai MH, Lee WC, Tu KH, Tian YC, Chen YC, Hung CC, Fang JT, Yang CW, Chang MY. Prognostic factors and treatment effect of standard-volume plasma exchange for acute and acute-on-chronic liver failure: A single-center retrospective study. Transfus Apher Sci. 2018 Jun 2.
- 19. Huang SF, Chang IC, Hong CC, Yen TC, Chen CL, Wu CC, Tsai CC, Ho MC, Lee WC, Yu HC, Shen YY, Eng HL, Wang J, Tseng HH, Jeng YM, Yeh CT, Chen CL, Chen PJ, Liaw YF. Metabolic risk factors are associated with non-hepatitis B non-hepatitis C hepatocellular carcinoma in Taiwan, an endemic area of chronic hepatitis B. Hepatol Commun. 2018 Apr 18;2(6):747-759.
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- 21. Huang YH, Lin KH, Yu JS, Wu TJ, Lee WC, Chao CC, Pan TL, Yeh CT. Targeting HSP60 by subcutaneous injections of jetPEI/HSP60-shRNA destabilizes cytoplasmic survivin and inhibits hepatocellular carcinoma growth. Mol Carcinog. 2018 Sep;57(9):1087-1101.
- 22.Li-Chueh Weng, RN, PhDa,b, , Hsiu-Li Huang, RN, PhDc, Wei-Chen Lee, MDb, Yu-Hsia Tsai, RN, PhDa,d, Ching-Rong Lin, RN, PhDa,e,f, Woan-Shyuan Wang, RN, MSNa, Yi-Wen Wang, RN, PhDa, Tsui-Yun Yang, RN, PhDa, Li-Chuan Tseng, RN, MSNg. Psychological profiles of excluded living liver donor candidates: An observational study .Mol Carcinog. 2018 Sep;57(9):1087-1101. Medicine. 2018;97:52(e13898).
- 23. Kun-Ming Chan, Tsung-Han Wu, Chih-Hsien Cheng, Chen-Fang Lee, Ting-Jung Wu, Hong-Shiue Chou, Wei-Chen Lee. Inferior Outcomes Associated with the Coexistence of Hepatocellular Carcinoma Recurrence and Hepatic Virus Reinfection After Living Donor Liver Transplantation. Journal of Gastrointestinal Surgery. 2019; https://doi.org/10.1007/s11605-019-04116-0.
- 24.Li-Chueh Weng, Hsiu-Li Huang, Wei-Chen Lee, Yu-Hsia Tsai, Woan-Shyuan Wang, Kang-Hua Chen. Health-related quality of life of living liver donors 1 year after donation. HepatoBiliary Surg Nutr 2019;8(1):1-9.
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26.Lee WC, Wang YC, Cheng CH, Wu TH, Lee CF, Wu TJ, Chou HS, Chan KM. Myeloid-derived suppressor cells in the patients with liver resection for hepatitis B virus-related hepatocellular carcinoma. Scientific Reports. 2019;9:2269 https://doi.org/10.1038/s41598-019-38785-3



# 座長介紹 ABOUT MODERATOR



# 張文震主任 (John Wen-Cheng Chang, MD)

Attending Physician and Associate Professor,

Division of Hematology-Oncology,

Department of Internal Medicine,

Chang Gung Memorial Hospital at Linkou Branch, Taipei, Taiwan

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#### **Education**

1982-1989 Chung Shan Medical University, Tai-Chung, Taiwan

### **Positions and Employment**

1989-1992	Resident, Department of Internal Medicine, Chang Gung Memorial Hospital (CGMH),
1303 1332	
	Taipei, Taiwan
1992-1994	Clinical Fellow, Division of Medical Oncology, Department of Internal Medicine, CGMH
1994-1995	Clinical Fellow, Division of Hematology, Department of Internal Medicine, CGMH
1995-1997	Attending Physician, Division of Medical Oncology, CGMH
1997-1999	Research Fellow, Department of Surgery, Mount Zion Cancer Center, University of
	California, San Francisco
1999-present	Attending Physician, Division of Medical Oncology, CGMH
2009-present	Associate Professor, CGMH
2016-present	Chief, Division of Medical Oncology, CGMH
2016-present	Director, Immune-Oncology Center of Excellence, CGMH
2017-present	Chairman, Taiwan Society for Immunotherapy of Cancer (TSITC)

#### **Publication Lists (2017-2018)**

- 1. John Wen-Cheng Chang, Jun Guo, Chia-Yen Hung, Si Lu, Sang Joon Shin, Richard Quek, Anthony Ying, Gwo Fuang Ho, Huu Sau Nguyen, Boman Dhabhar, Virote Sriuranpong, Maria Luisa Tiambeng, Nugroho Prayogo, Naoya Yamazaki. Sunrise in melanoma management: Time to focus on melanoma burden in Asia. Asia Pac J Clin Oncol, 2017 Dec;13(6): 423-427. doi: 10.1111/ajco.12670.
- 2. Mei-Chia Wang, Chih-Liang Wang, Tai-Long Chen, John Wen-Cheng Chang, Jang-Jih Lu, Pi-Yueh Chang and Chiuan-Chian Chiou. Predicting outcomes of EGFR-targeted therapy in non-small cell lung cancer patients using pleural effusions samples and peptide nucleic acid probe assay. Clin Chem Lab Med, 2017; 55(12): 1979–1986. doi: 10.1515/cclm-2016-0809.
- 3. Dong-Yi Chen, Lai-Chu See, Jia-Rou Liu, Cheng-Keng Chuang, See-Tong Pang, I-Chang Hsieh, Ming-Shien Wen, Yung-Chang Lin, Chuang-Chi Liaw, Cheng-Lung Hsu, John Wen-Cheng Chang, Chang-Fu Kuo and Wen-Kuan Huang\*. Risk of Cardiovascular Ischemic Events After Surgical Castration and Gonadotropin-Releasing Hormone Agonist Therapy for Prostate Cancer: A Nationwide Cohort Study. J Clin Oncol. 2017 Oct 2; 35: 3697-3705. DOI: https://doi.org/10.1200/JCO.2016.71.4204
- 4. Chuang-Chi Liaw, Cheng-Keng Chuang, Ying-Hsu Chang, Tzu-Yao Liao, John Wen-Cheng Chang and Yu-Hsiang Juan. Bladder Urothelial Carcinoma with Peritoneal Involvement: Benefit of

Continuous Maintenance Chemotherapy. Anticancer Research 2017; 37: 6443-6451. doi:10.21873/anticanres.12099

- 5. Yi-Cheng Wu, Yung-Chi Shen, John Wen-Cheng Chang, Jia-Juan Hsieh, Yen Chu, Cheng-Hsu Wang. Autocrine CCL5 promotes tumor progression in esophageal squamous cell carcinoma in vitro. Cytokine 2018; 110: 94-103.
- 6. Chen-Yang Huang, Bo-Huan Chen, Wen-Chi Chou, Cheng-Ta Yang, John Wen-Cheng Chang. Factors associated with the prognosis and long-term survival of patients with metastatic lung adenocarcinoma: a retrospective analysis. Journal of Thoracic Disease 2018 Mar 18; doi: 10.21037/jtd.2018.03.143





# 洪舜郁教授 (Shuen-Iu Hung, Ph.D.)

Professor, Investigator
Cancer Vaccine and Immune Cell Therapy Core Lab,
Chang Gung Memorial Hospital, Linkou Branch, Taiwan
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### Education

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Institute of Microbiology and Immunology, National Yang-Ming	PhD	1994-2002	Immunology
University, Taipei, Taiwan Institute of Biomedical Sciences,	Post-doc	2002-2003	Genomics,
Academia Sinica, Taipei, Taiwan	1031 400	2002 2003	Pharmacogenomics
Experience/Position			
National Genotyping Center,	Assistant Director	2003-2006	Genomics,
Academia Sinica, Taipei, Taiwan			Pharmacogenomics
Institute of Pharmacology, National	Assistant Professor	2006-2010	Drug hypersensitivity,
Yang-Ming University, Taipei, Taiwan			Pharmacogenomics
Institute of Biomedical Sciences,	Adjunct Researcher	2009-2012	Genomics,
Academia Sinica, Taipei, Taiwan			Pharmacogenomics
Institute of Pharmacology, National	Associate Professor	2010-2017	Drug hypersensitivity,
Yang-Ming University, Taipei, Taiwan			Pharmacogenomics
Institute of Pharmacology, National	Professor	2017-2019	Drug hypersensitivity,
Yang-Ming University, Taipei, Taiwan			Pharmacogenomics,
			Precision Medicine
Cancer Vaccine & Immune cell therapy	Investigator/	2019-present	Precision Medicine
Core Lab, Chang Gung Memorial Hospital, Taoyuan, Taiwan	Professor		Neoantigen, Immune cell therapy
Institute of Pharmacology, National	Adjunct Professor	2019-present	Precision Medicine,
Yang-Ming University, Taipei, Taiwan			Neoantigen, Cell
			therapy

#### Honors, Prizes, Awards

- 2002: Excellent Ph.D. Dissertation, Award of 2002 Graduate Symposium, National Yang-Ming University, Taiwan
- 2004: Outstanding Post-Doctoral Research, Award of 2004 annual meeting of ACGA, Association of Chinese Geneticists in America (ACGA), USA.
- 2005: Distinguished Postdoctoral Scholar of Academia Sinica, Taiwan.
- 2005: HGM2005 Award for Young Scientist, 10th Annual Meeting of The Human Genome Organization

(HUGO)

- 2007: Award of Excellent Publication, National Yang-Ming University, Taiwan
- 2007~2008, 2012~2016: Award of Excellent Teacher, School of Medicine, National Yang-Ming University, Taiwan
- 2009: Award of Outstanding Technology Transfer, National Science Council, Taiwan (科技部 傑出技術移轉貢獻獎)
- 2010: Taiwan Outstanding Female Scientist-Junior Investigator 2010, Award of Wu Chien-Shiung Education Foundation (吳健雄學術基金會 台灣女科學家新秀獎 )
- 2011~2018: Award of Academic Success, National Yang-Ming University, Taiwan
- 2012: Dr. Wu, Da-You Research Award 2012, National Science Council, Taiwan (科技部 吳大猷先生紀念獎)
- 2013: 國家生技醫療品質 SNQ 銀獎
- 2015: Dr. Lee, Chen-Yuan Excellent Research Award, Taiwan Pharmacology Association, Taiwan (台灣藥理學會 李鎮源教授傑出研究獎)
- 2018 Aug: 台北生技獎 技轉合作獎銀獎
- 2018 Nov: 第 15 屆國家新創獎 臨床新創
- 2018 Dec: 科技部 2018 未來科技突破獎 (Future Tech Breakthrough Award)

#### **Research Interests**

Precision medicine, Neoantigen cancer vaccine, Precision immune cell therapy, Immunopharmacology, Immunogenomics, Pharmacogenomics

### **Selected Publications (\*Correspondence)**

- 1. Pan RY, Chu MT, Wang CW, Lee YS, Lemonnier F, Michels AW, Schutte R, Ostrov DA, Chen CB, Phillips EJ, Mallal SA, Mockenhaupt M, Bellón T, Tassaneeyakul W, White KD, Roujeau JC, Chung WH, Hung SI\*. Identification of drug-specific public TCR driving severe cutaneous adverse reactions. Nat Commun. 2019 Aug 8;10(1):3569. doi: 10.1038/s41467-019-11396-2. (SCI) (Impact factor: 11.88)
- 2. Yang CY, Chen CH, Deng ST, Huang CS, Lin YJ, Chen YJ, Wu CY, Hung SI\*, Chung WH\*. Allopurinol use and risk of fatal hypersensitivity reactions: A nationwide population-based study in Taiwan. JAMA Internal Med. 2015 Sep 1;175(9):1550-7. (IF: 19.989)
- 3. Chung WH, Chang WC, Stocker SL, Juo CG, Graham GG, Lee MH, Williams KM, Tian YC, Juan KC, Jan Wu YJ, Yang CH, Chang CJ, Lin YJ, Day RO\*, Hung SI\*. Insights into the poor prognosis of allopurinol-induced severe cutaneous adverse reactions: the impact of renal insufficiency, high plasma levels of oxypurinol and granulysin. Annals of the Rheumatic Diseases. 2015 Dec;74(12):2157-64. (IF: 12.350)
- 4. Lin CH, Chen JK, Ko TM, Wei CY, Wu JY, Chung WH, Chen SY, Liao YD, Hung SI\*, Chen YT\*. Immunologic basis for allopurinol-induced severe cutaneous adverse reactions: HLA-B\*58:01-restricted activation of drug-specific T cells and molecular interaction. J Allergy Clin Immunol. 2015 Apr;135(4):1063-5.e5. (IF: 13.258)
- 5. Chung WH\*, Chang WC, Lee YS, Wu YY, Yang CH, Ho HC, Chen MJ, Lin JY, Hui RC, Ho JC, Wu WM, Chen TJ, Wu T, Wu YR, Hsih MS, Tu PH, Chang CN, Hsu CN, Wu TL, Choon SE, Hsu CK, Chen DY, Liu CS, Lin CY, Kaniwa N, Saito Y, Takahashi Y, Nakamura R, Azukizawa H, Shi Y, Wang TH, Chuang SS, Tsai SF, Chang CJ, Chang YS, Hung SI\*. Taiwan Severe Cutaneous Adverse Reaction Consortium; Japan Pharmacogenomics Data Science Consortium. Genetic variants associated with phenytoin-related severe cutaneous adverse reactions. JAMA. 2014 Aug 6;312(5):525-34. (IF: 47.661)
- 6. Wang CW, Chung WH, Cheng YF, Ying NW, Peck K, Hung SI\*. A new nucleic acid-based agent inhibits cytotoxic T lymphocyte-mediated immune disorders. J Allergy Clin Immunol. 2013 Sep;132(3):713-722.e11. (IF: 13.258)
- 7. Wei CY, Chung WH, Huang HW, Chen YT\*, Hung SI\*. Direct interaction between HLA-B and carbamazepine activates T cells in Stevens-Johnson syndrome. J Allergy Clin Immunol.



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- 2012;129(6):1562-1569 (IF: 13.258)
- 8. Ko TM, Chung WH, Wei CY, Shih HY, Chen JK, Lin CH, Chen YT\*, Hung SI\*. Shared and restricted T-cell receptor use is crucial for carbamazepine-induced Stevens-Johnson syndrome. J Allergy Clin Immunol. 2011;128(6):1266-1276 (IF: 13.258)
- 9. Chung WH#, Hung SI#, Yang JY, Su SC, Huang SP, Wei CY, Chin SW, Chiou CC, Chu SC, Ho HC, Yang CH, Lu CF, Wu JY, Liao YD, Chen YT\*. Granulysin is a key mediator for disseminated keratinocyte death in Stevens-Johnson syndrome and toxic epidermal necrolysis. Nature Medicine 2008;14(12):1343-1350 (IF: 32.621) (#co-first author)
- 10.Yang CW, Hung SI\*, Juo CG, Lin YP, Fang WH, Lu IH, Chen ST, Chen YT\*. HLA-B \*1502-bound peptides: Implications for the pathogenesis of carbamazepine-induced Stevens-Johnson syndrome. J Allergy Clin Immunol. 2007;120(4):870-877 (IF: 13.258)
- 11. Hung SI, Chung WH, Liou LB, Chu CC, Lin M, Huang HP, Lin YL, Lan JL, Yang LC, Hong HS, Chen MJ, Lai PC, Wu MS, Chu CY, Wang KH, Chen CH, Fann CS, Wu JY, Chen YT\*. HLA-B\*5801 allele as a genetic marker for severe cutaneous adverse reactions caused by allopurinol. PNAS 2005;102(11):4134-4139. (IF: 9.661)
- 12. Chung WH, Hung SI, Hong HS, Hsih MS, Yang LC, Ho HC, Wu JY, Chen YT\*. Medical genetics: a marker for Stevens-Johnson syndrome. Nature 2004;428(6982):486.(IF: 42.351)

### **ABSTRACT 15:00-15:25** >

# Targeting neoantigens for precision immune cell therapy against cancers

Shuen-Iu Hung, PhD.

Professor, Cancer Vaccine and Immune Cell Therapy Core Lab, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan, Taiwan.

Personalized tumor-specific neoantigens have been considered as ideal targets for cancer immunotherapy. Neoantigens could be presented by the MHC molecules and then recognized by the T cell receptors (TCR) to induce the adaptive immunity, and trigger tumor-specific cytotoxic T cell killing. Targeting neoantigens for precision immunotherapy against cancers is becoming an emerging field for treating tumors. However, the efficacy of neoantigens presentation to the immune system may vary with the applied technologies as well as the patient populations due to the tumor heterogeneity, diversity of cancer somatic mutations, and MHC polymorphisms of individuals. Different approaches, including cancer vaccines and adoptive T cell therapy, are been developing to target neoantigens of cancers. We aim to develop personalized neoantigen-based T cell therapy for treating cancers in Asia populations, first focusing on Han Chinese. We apply a phase I clinical trial study to evaluate the dosage, safety, tolerability, and efficacy of neoantigen-expanded autologous immune cell therapy for advanced cancers. In the clinical setting, we will investigate the patient-specific tumor somatic mutations to generate "personalized cancer vaccine", then use the "neoantigen vaccine" to expand the autologous T cells, and re-infuse the immune cells into patients. Furthermore, we also apply the neoantigen-based immune cell therapy as clinical service for patients under the TFDA Regulations. With the rapid development of neoantigen-based personalized immunotherapy, we believe that tumors are becoming curable in the new era of precision medicine.





# 陳淑貞技術長 (Shu-Jen Chen, Ph.D.)

Chief Scientific Officer, Cofounder, ACT genomics, Inc. ( 行動基因生技公司 )

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Dr. Shu-Jen Chen received her Ph.D. degree in Biochemistry from Virginia Commonwealth University, did her Postdoctoral training at Baylor College of Medicine, and was a Research Assistant Professor at SUNY Buffalo. In 1998, she joined National Health Research Institute (NHRI) as an Assistant Investigator and established the high throughput screening program for the institute. As one of the founding scientists, Dr. Chen joined TaiGen Biotechnology in 2001 to lead the in vitro pharmacology group. In 2006, she moved to Chang Gung University as an Associate Professor of the Department of Biomedical Sciences. As a co-founder of ACT Genomics, Dr. Chen has served as the Chief Scientific Officer since 2014.

Dr. Chen has years of experience in biotechnology industry. She established the high throughput drug screening program for both NHRI and TaiGen Biotech, mainly focused on anticancer and anti-viral drug discovery. While working in academia, she built up the microarray and next-generation sequencing platforms for the Molecular Medicine Research Center at Chang Gung University. Her recent work centered on developing biomarkers for cancer diagnosis and for treatment prediction.

Dr. Chen specializes in automated drug screening system, genomics and transcriptomics technologies, omics data analysis and biological database integration. She is also familiar with cancer biology, system integration and database design. She currently leads the sequencing group and the bioinformatics group at ACT Genomics to implement cancer genome sequencing for research and clinical applications. With her experience in drug discovery and next generation sequencing, she is devoted to utilize the latest technology to turn the dream of "Precision Cancer Medicine" into a reality.

### **ABSTRACT 15:25-15:50** >

### **Neoantigen Identification**

Shu-Jen Chen, Ph.D.

Cofounder, ACT genomics, Inc.

Tumor is a group of genetic disorders. All tumor cells accumulate genetic alterations and mutated peptides during disease progression. Some of the mutated peptides may be deemed non-self and when presented by human leukocyte antigen (HLA) molecules could elicit T-cell responses. These neoantigens are tumor-specific and could be used to trigger immune response in the form of cancer vaccine or targeted by adoptive T-cell therapies. These strategies may be combined with immune checkpoint inhibitors to provide long-lasting therapeutic benefits for cancer patients. Recent genomic and bioinformatic technological advances have made it possible to predict the neoantigens encoded by tumor-specific mutations. However, timely and efficient identification of neoantigens remains a major obstacle to personalized neoantigen-based cancer immunotherapy. This presentation will review the existing strategies to identify candidate neoantigens and to evaluate their immunogenicity. In addition, factors that impact on neoantigen identification will be discussed.





# 郭正宜副總經理 (Jerry Kuo, Ph.D.)

General Manager, Uwell Biopharma, Inc. (鑫品/宇越生技公司)

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#### **Education**

Ph.D. Pharmaceutical Biology, Monash University, Melbourne, Australia. June 2007
M.Phil. Pharmacy and pharmacology, University of Bath, Bath, UK. September 2001
M.S., Agricultural Chemistry, National Taiwan University (NTU), Taipei, Taiwan. June 1996
B.S., Medical Technology, Chung-Shan Medical College, Taichung, Taiwan. June 1994

### **Expreiences**

- Vice president (Present) UWELL Biopharma Inc., Taiwan
- Adjunct Assistant Professor (Present) Graduate Institute of Biology and Anatomy, National Defense Medical Centre

#### **Experiences/Skills Summary**

- Pharmaceutical scientist with expertise in non-viral gene delivery for enteral administration and understanding and knowledge of gastrointestinal tract.
- Medical affairs professional with a comprehensive work experience, research and academic background across multiple therapeutic areas including neuroscience, cardiovascular diseases, microbiology, immunology, inflammatory diseases, metabolic disorders, infectious diseases, oncology, cell therapy & gene therapy.
- Skilled in clinical study design, data interpretation and delivering quality documents for publication.
- Skilled in developing relationships with key opinion leaders and collaborators.

### ABSTRACT 15:50-16:15 >

# Development Story of UWC19 (Welgenaleucel): From Bench to Clinical Bed

Jerry Kuo, Ph.D.

Uwell Biopharma, Inc

Genetically modifying autologous T cells to express an anti-CD19 chimeric antigen receptor (CAR) has emerged as a promising treatment for CD19+ B cell malignancies with impressive response rates. UWELL Biopharma developed CAR-T treatment, UWC19 (Welgenaleucel), a cellular therapy consisting of autologous T cells transduced with an anti-CD19 chimeric antigen receptor for the patients with relapsed or refractory CD19 positive Acute Lymphoblastic Leukemia (ALL) and Diffused Large B Cell Lymphoma (DLBCL). UWC19 has been evaluated for it pharmacological properties and toxicological effects. The results showed that UWC19 effectively eliminated CD19+ cancer cells in xenograft animals and that UWC19 had limited offtarget toxicity and tumorigenic potential. Taken favorable and acceptable, pre-clinical results, UWC19 had been investigated for its safety and efficacy in patients with B cell malignancy via a PI-initiated clinical trial conducted in China. Administration of UWC19 resulted in remission sustained in 60% of patients. ALL patients experienced cytokine-release syndrome and neurologic toxicity after infusion, whereas UWC19 was well tolerated in patients with DLBCL. Regarding clinical pharmacokinetics, the results showed that UWC19 persisted in DLBCL patients up to 200 days. Taken the exciting and promising results, UWC19 is on its clinical development path to NDA.





# 張順浪總經理 (Alarng Chang, Ph.D.)

General Manager,
Medigen Biotechnology Corp.
(基亞生技公司)
Email: Alarng@medigen.com.tw

#### **Education**

Post-doctor training: Tumor Immunology, Genentech USA. (1990~1993)

Ph.D.: Molecular Immunology, Michigan State Univ. (1984~1990) M.S.: Agricultural Chemistry, National Taiwan Univ. (1982~1984) B.S.: Agricultural Chemistry, National Taiwan Univ. (1976~1980)

### **Current Position**

President & CSO: Medigen Biotechnology Corp. Since 2016/3

#### **Prior Experiences**

- General Manager: Ivy Life Sciences Co. Ltd. (2004/4~2015/11)
- Vice President, R&D: Medigen Biotechnology Corp. (2000~2005)
- General Manager: MediGreen Biotechnology Corp. (2001~2005)
- Board member: Review Board of Technique Bureau, Administration of Economics (2004~2015)
- Consultant: Center of Radiation Application in Nuclear Research Institute (2005~2008)
- Acting director: Department of Immunology, Tzu-Chi University (1993~2000)
- Exchange Scholar: Sino-France Exchange Association (1993~1994)

### ABSTRACT 16:15-16:40 >

### **NK Cell Therapy**

Alarng Chang, Ph.D.

Medigen Biotechnology Corp.

Natural killer cell was discovered in the 1970's and is part of the innate immunity. It gains its name due to the fact that it can kill tumor cells without prior encounter. Ever since its discovery NK cell has become the center of immune cell therapies against malignancy. LAK (lymphokine-activated killer) cells and CIK (cytokine-induced killer) cells were the previous attempts trying to grow, ex vivo, large quantity of highly lytic NK cells for cancer therapy. However the clinical trials involving LAK cell or CIK cell were not successful. The amazingly inspiring success of CAR-T cell therapy against B cell-associated leukemia and lymphoma infused new hope and resources into CAR-T cell development around the world. As predicted by Dr. Rosenberg in 2016, soon CAR-T experts realize that, with a few exceptions, the present CAR-T products are difficult to treat solid tumors. Other disadvantages of current CAR-T cell treatment include that it is associated with fatal adverse effect such as cytokine release syndrome, requires a CAR recognizing tumor specific surface antigen and it is expensive. Based on the accumulated evidences, NK cell have the following characteristics. First, NK cell after being activated probably is the most cytotoxic immune cell against tumor comparing on the one to one basis. Second, NK cells can be manufactured as an off-the-shelf product and used in an allogeneic setting since they will not cause graft vs. host disease (GvHD). Third, NK cells recognize their target cells mainly through NKG2D receptor which binds with antigens that are commonly expressed on cancerous, virally transfected or stressed cells but not or seldomly on normal ones. With these seeming advantages of NK cells over T cells, NK cells have recently become one of the chosen cells to put CARs on in order to overcome the hurdles faced with the current CAR-T technology. In this presentation, the presenter will show the progress of CAR-NK and trends of cancer therapies involving NK and CAR-NK cells.



### 長庚醫院癌症精準免疫細能治療國際研討會

# Memo




CGMH Conference: Precision Immune Cell Therapies for Cancers 長庚醫院:癌症精準免疫細胞治療國際研討會