SCHOOL OF BIOMEDICAL SCIENCES

SBS RESEARCH DAY 2023

SYMPOSIUM ON

CANCER BIOLOGY & EXPERIMENTAL THERAPEUTICS

ENGAGE | LEARN | NETWORK

14 JUNE 2023 | HYBRID

G/F, Lo Kwee-Seong Integrated
Biomedical Sciences Building, Area 39,
The Chinese University of Hong Kong

ZOOMING IN ON CANCER

revealing the hidden intricacies of cellular biology
to develop novel experimental therapeutics

CU Medicine HONG KONG
香港中文大學醫學院
Faculty of Medicine
The Chinese University of Hong Kong

40th Anniversary
四十週年

香港中文大學 生物醫學學院
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School of Biomedical Sciences Research Day 2023

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Welcome Message from the Pro-Vice-Chancellor / Vice-President (Strategic Developments), CUHK

It is my great pleasure to welcome all of you to the 14th School of Biomedical Sciences (SBS) Research Day.

The first SBS Research Day took place in 2010 and it has been held annually ever since. This annual event serves as a significant platform to engage faculty and researchers in the School with distinguished researchers from the University and other institutions, to showcase accomplishments and share the important discoveries.

This year we are much honoured to have three outstanding keynote speakers joining this event, including Prof. Andreas MÖLLER from the Department of Otorhinolaryngology, Head and Neck Surgery, The Chinese University of Hong Kong (CUHK); Prof. Rihe LIU from Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy; and Prof. Mei-Po KWAN, from the Institute of Space and Earth Information Science, CUHK.

Together with seven more experts and three trainees from CUHK, The University of Hong Kong, Phase Scientific and Cell Press, delivering talks on the area of “Liquid Biopsies for Cancer”, “Innovative Cancer Therapeutics” and “Exposomes, Epigenetics and Emerging Cancer Trends”, I am sure there will be many exciting discussions and collaborations emerge from this meeting.

The Research Day is not only for the presentation of research progress in advancing biomedical sciences, but also for unique networking and learning opportunities. I trust that you will enjoy this one-day program and find it to be rewarding and a valuable experience!

Wai-Yee Chan, Ph.D.
Li Ka Shing Professor of Biomedical Sciences
Pro-Vice-Chancellor/Vice-President
The Chinese University of Hong Kong

Welcome Message from the Director of School of Biomedical Sciences

I am pleased to welcome you to the School of Biomedical Sciences Research Day 2023.

The Research Day is one of the most significant events in our School. It provides an excellent opportunity for our School members, clinical colleagues, and friends from other higher education institutions to come together, participate in exchanging their latest findings, and expand their academic connections.

This year's theme is "Cancer Biology & Experimental Therapeutics" and we are thrilled to have six speakers from CUHK and four external speakers from The University of Hong Kong, UNC Eshelman School of Pharmacy, Phase Scientific, and Cell Press. Graduate students, postdoctoral fellows, or other early-stage scientists and senior staff are encouraged to learn and discuss with these established leaders through close interaction.

To further connect the researchers with young investigators, three trainee talks are also included in the program. Your active involvement during the seminars and Q&A sessions will aid in the development of fresh viewpoints and boost the scientific value of our work. We hope that this collaborative exchange of ideas will inspire you to forge new connections and explore opportunities for future research collaborations.

I would like to express my gratitude to the members of the Organizing Committee for their unwavering dedication and tireless efforts in coordinating this event, as well as to the sponsoring companies for their abundant support. Thank you sincerely for your participation and wish you great enjoyment of this event!

Andrew M. Chan
Professor and Director
School of Biomedical Sciences
Faculty of Medicine
The Chinese University of Hong Kong

SBS Research Day 2023 Programme
Symposium on "Cancer Biology and Experimental Therapeutics"
14 June 2023 (Wednesday)

09:00-09:20	**Opening Ceremony:** Prof. CHAN Wai Yee (Pro-Vice-Chancellor / Vice-President, CUHK) & Prof. CHAN Man Lok Andrew (Director of School of Biomedical Sciences) Presentation of the prize for Programme Book Cover / Banner Design Competition Presentation of the Dr. Clement Chan Service Awards Photo Taking

Time	*Title of Presentation*	*Speaker*	*Abstract No.*
Session 1: Liquid Biopsies for Cancer			
09:20-10:00	Roles of extracellular vesicles in cancer progression and diagnostics	Andreas MÖLLER (ENT, CUHK)	O1 (Keynote)
10:00-10:20	Identification of novel diagnostic and gemcitabine response prediction biomarkers for pancreatic cancer	Yangchao CHEN (SBS, CUHK)	O2
10:20-10:40	A novel method for liquid-phase extraction of cell-free DNA for detection of circulating tumour DNA	Ricky CHIU (Phase Scientific)	O3
10:40-10:55	Panel discussion and Q&A Moderator: Prof. Carol TONG (SBS, CUHK)		
10:55-11:30	***Tea Break***		
11:30-11:50	Trainee Talk and Q&A Study of TCR Knockout CAR-T cells for cancer treatment	Chenzi ZHANG (SBS, CUHK)	O4
Special seminar			
11:50-12:20	Special seminar: Publishing at Cell and Cell Press	Jiaying TAN (Cell Press)	O5
12:20-12:30	Discussion and Q&A Moderator: Prof. Andrew CHAN, SBS, CUHK		
12:30-14:00	***Lunch***		
Session 2: Innovative Cancer Therapeutics			
14:00-14:40	Translational studies of mRNA therapeutics for treating solid tumours	Rihe LIU (UNC Eshelman School of Pharmacy)	O6 (Keynote)
14:40-15:00	Drug treatment for HCC: Where are we now?	Stephen CHAN (CLO, CUHK)	O7
15:00-15:20	Isoformic PD-1 regulates host immunity in infection and hepatocellular carcinoma	Zhiwei CHEN (MIC, HKU)	O8
15:20-15:35	Panel discussion and Q&A Moderator: Prof. Jingying ZHOU (SBS, CUHK)		
15:35-15:55	Trainee Talk and Q&A Targeting PPAR-gamma counteracts tumour adaptation to immune-checkpoint blockade in hepatocellular carcinoma	Zhewen XIONG (SBS, CUHK)	O9
15:55-16:15	***Tea Break***		

SBS Research Day 2023 Programme
Symposium on "Cancer Biology and Experimental Therapeutics"
14 June 2023 (Wednesday)

Time	*Title of Presentation*	*Speaker*	*Abstract No.*
Session 3: Exposomes, Epigenetics and Emerging Cancer Trends			
16:15-16:55	How advanced geospatial methods can help address the challenge of environmental exposure assessment in environmental health and epigenetic research	Mei-Po KWAN (ISEIS, CUHK)	O10 (Keynote)
16:55-17:15	Obesity, diabetes and cancers: what are the links?	Alice KONG (M&T, CUHK)	O11
17:15-17:35	An epigenetic link between obesity and liver cancer	Alfred CHENG (SBS, CUHK)	O12
17:35-17:50	Panel discussion and Q&A Moderator: Prof. Vincent CHEUNG (SBS, CUHK)		
17:50-18:10	Trainee Talk and Q&A Revealing the neural basis of muscle synergies through motor cortical stimulations in glioma patients undergoing awake craniotomy	Jodie XIE (SBS, CUHK)	O13

18:10-18:15 Closing Remarks

18:30-21:00 ***Conference Banquet (by invitation)***

Abbreviations:
CLO = Department of Clinical Oncology
CUHK = The Chinese University of Hong Kong
ENT = Department of Otorhinolaryngology, Head and Neck Surgery
ISEIS = Institute of Space and Earth Information Science
HKU = The University of Hong Kong
M&T = Department of Medicine and Therapeutics
MIC = Department of Microbiology
SBS = School of Biomedical Sciences
UNC = University of North Carolina at Chapel Hill

Session 1: Liquid Biopsies for Cancer

Speaker Biography

Prof. MÖLLER Andreas is the newly appointed Global STEM Professor in the Faculty of Medicine at The Chinese University of Hong Kong (CUHK) and Director of the JC STEM Lab of Personalised Cancer Medicine. He is also adjunct Professor the School of Biomedical Science at the Queensland University of Technology. Before joining CUHK, Prof. Möller was Group Leader of the Tumour Microenvironment Laboratory at the QIMR Berghofer Medical Research Institute, Brisbane, Australia. He received his doctoral training at the German Cancer Research Centre (DKFZ) in Heidelberg, Germany, followed by postdoctoral training at the University of Berne, Switzerland, and the Peter MacCallum Cancer Center, Melbourne, Australia. Prof. Möller is an expert in cancer metastasis and cancer immunology, and international leader in the field of Extracellular Vesicles (EVs), with over 15 years of experience. He is elected Board member of the International Society of Extracellular Vesicles, Executive Board Member of the Asian Pacific Societies for Extracellular Vesicles and has Field-weighted citation Index (FWCI) of over 19. His work incorporates clinical and commercial collaborations, a number of EV-related patents and is focused on gaining a better understanding of the role of EVs in cancer progression, and their use as cancer biomarkers.

Five recent representative publications

1. Richard J Lobb, …, **Andreas Möller**. "An epithelial-to-mesenchymal transition induced extracellular vesicle prognostic signature in non-small cell lung cancer." ***Communications Biology***, 2023; 6(1):68. doi: 10.1038/s42003-022-04350-4.
2. Kekoolani S Visan, …, **Andreas Möller**. "Comparative analysis of tangential flow filtration and ultracentrifugation, both combined with subsequent size exclusion chromatography, for the isolation of small extracellular vesicles." ***Journal of Extracellular Vesicles***, 2022; 11(9):e12266 doi: 10.1002/jev2.12266.
3. Luize G Lima, …, **Andreas Möller**. "Tumour microenvironmental cytokines bound to cancer-derived exosomes determine specific uptake by cytokine receptor-expressing cells and alter biodistribution." ***Nature Communications***, 2021; 12(1):3543. doi: 10.1038/s41467-021-23946-8.
4. **Andreas Möller**, Richard Lobb. "The evolving translational potential of small extracellular vesicles in cancer." ***Nature Reviews Cancer***, 2020; 20(12):697-709. doi: 10.1038/s41568-020-00299-w.
5. Richard J Lobb, …, **Andreas Möller**. "Optimized exosome isolation protocol for cell culture supernatant and human plasma." ***Journal of Extracellular Vesicles***, 2015; 4:27031. doi: 10.3402/jev.v4.27031.

Research interests / Technical expertise

- ✧ Cancer biomarkers
- ✧ Cancer progression and metastasis
- ✧ Extracellular vesicles

Abstract

Roles of extracellular vesicles in cancer progression and diagnostics

MÖLLER Andreas

Department of Otorhinolaryngology, Head and Neck Surgery, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
JC STEM Lab of Personalised Cancer Medicine

Cancer diagnosis and subsequent therapy decisions commonly rely on invasive tissue biopsies and imaging technologies. Small extracellular vesicles (sEVs, also called exosomes) in body fluids (liquid biopsy) could potentially serve as a non-invasive method for identifying cancer. However, specific markers that accurately identify cancer-derived sEVs, or prognosticate cancer patient outcomes at baseline, are currently lacking.

My team developed a sensitive liquid biopsy capability for cancer screening based on the complex proteomic cargo of cancer-derived sEVs. Furthermore, we developed an additional blood-based sEV protein biomarker panel capable of accurately prognosticating outcomes of Non-Small Cell Lung Cancer patients at baseline.

Supplementing these clinical research areas, we generated intriguing data on how cancer-derived EVs can specifically distribute to certain organs in the body, and increase metastatic spread.

Session 1: Liquid Biopsies for Cancer

Speaker Biography

Prof. CHEN Yangchao（陳揚超）is currently a Professor at School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). He obtained his Ph.D. from Sun Yat-sen University in 2003 and later on was trained as a postdoctoral fellow at University of Washington, Seattle. He has been faculty member as Research Assistant Professor, Assistant Professor and Associate Professor at Faculty of Medicine CUHK since 2007. His research interests include epigenetics in cancer, histone modification particularly methylation, long and short non-coding RNAs, development of novel therapeutics for liver and pancreatic cancer. The ultimate goal of his lab is aimed at the identification of novel diagnostic markers and therapeutic targets for pancreatic and liver cancer.

Five recent representative publications

1. Wong CH, Li CH, Man Tong JHM, Zheng D, He Q, Luo Z, Lou UK, Wang J, To KF, **Chen Y**. "The establishment of CDK9/RNA PolII/H3K4me3/DNA methylation feedback promotes HOTAIR expression by RNA elongation enhancement in cancer." ***Molecular Therapy***, 2022; 30(4):1597-1609. doi: 10.1016/j.ymthe.2022.01.038.
2. Wong CH, Lou UK, Fung FK, Tong JHM, Zhang CH, To KF, Chan SL, **Chen Y**. "CircRTN4 promotes pancreatic cancer progression through a novel CircRNA-miRNA-lncRNA pathway and stabilizing epithelial-mesenchymal transition protein." ***Molecular Cancer***, 2022; 21(1):10. doi: 10.1186/s12943-021-01481-w.
3. Zhu YX, Li CH, Li G, Feng H, Xia T, Wong CH, Fung FKC, Tong JHM, To KF, Chen R, **Chen Y**. "LLGL1 regulates gemcitabine resistance by modulating the ERK-SP1-OSMR pathway in pancreatic ductal adenocarcinoma." ***Cellular and Molecular Gastroenterology and Hepatology***, 2020; 10(4):811-828. doi: 10.1016/j.jcmgh.2020.06.009.
4. Wong CH, Lou UK, Li Y, Chan SL, Tong JHM, To KF, **Chen Y**. "CircFOXK2 promotes growth and metastasis of pancreatic ductal adenocarcinoma by complexing with RNA-binding proteins and sponging MiR-942." ***Cancer Research***, 2020; 80(11):2138-2149. doi: 10.1158/0008-5472.CAN-19-3268.
5. Xu, F, Li CH, Wong CH, Chen GG, Lai PBS, Shao S, Chan SL, **Chen Y***. "Genome-wide screening and functional analysis identifies tumor suppressor long non-coding RNAs epigenetically silenced in hepatocellular carcinoma." ***Cancer Research***, 2019; 79:1305-1317. doi: 10.1158/0008-5472.CAN-18-1659.

Research interests / Technical expertise

- ✧ RNA biomarker
- ✧ RNA therapeutics
- ✧ Cancer

Abstract

Identification of novel diagnostic and gemcitabine response prediction biomarkers for pancreatic cancer

CHEN Yangchao

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Currently the five year survival rate of pancreatic cancer is less than 12%. One of the main reasons leading to the poor prognosis of pancreatic cancer is due to the lack of effective diagnostic biomarker. In the past years, we performed genome-wide identification of lncRNAs and circRNAs highly associated with pancreatic cancer. We identified lncRNAs and circRNAs with diagnostic potential in pancreatic cancer. Another major reason leading to the poor diagnosis of pancreatic cancer is chemoresistance. Gemcitabine is the first line chemotherapeutic drug for pancreatic cancer patients. However, gemcitabine resistance is rapidly acquired by pancreatic cancer patients. Novel approaches that predict the gemcitabine response of patients and enhance gemcitabine chemosensitivity are important to improve patients' survival. We identified lethal giant larvae homolog 1 (LLGL1) gene as a novel biomarker to predict gemcitabine response in pancreatic cancer patients.

Session 1: Liquid Biopsies for Cancer

Speaker Biography

Dr. CHIU Yin To Ricky（招彥燾）is the Chairman and CEO of PHASE Scientific International Limited, as well as the lead inventor of the company's core technology. He has been selected as one of the recipients of the Ten Outstanding Young Persons of the World, the Ten Outstanding of Young Persons in Hong Kong, the InnoStars Awards, the Young Industrialist of Hong Kong Awards and the HKSAR Chief Executive's Commendation for Community Service for his outstanding research achievements in biotechnology innovations and his notable contributions to the fight against COVID-19 pandemic.

As a leading innovator in the field of biotechnology, Ricky has made significant breakthroughs and developments in the fields of liquid biopsy and rapid point-of-care testing using the proprietary sample preparation technology he developed. With 36 patents granted, the technology provides an innovative solution to the problem of low-concentration target molecule detection. By concentrating target molecules, such as DNA, RNA, proteins, bacteria, and viruses, the technology improves the performance of diagnostic testing, making it faster, more accurate and more cost-effective.

Ricky is among the few who have received recognition in both the West and the East. From receiving research funding from world-renowned entities and FDA approval to his high-efficiency COVID-19 RNA extraction technology being designated as a "Major Technology" by the Ministry of Science and Technology of China, Ricky's inventions have positioned him as a changemaker who can uniquely straddle both worlds. Ricky and the PHASE Scientific team are currently engaged in research and product development for the detection of cancer and infectious diseases.

Five recent representative publications

1. **Chiu RYT**, Kojima N, Mosley GL, Cheng K, Pereira DY, Brobeck M, Chan T, Zee J, Kittur H, Chung T, Tsang E, Maran K, Yung R, Leung A, Siu R, Ng J, Choi T, Fung M, Chan W, Lam H, Lee K, Parkin S, Chao F, Ho S, Marshak DR, Ma E, Klausner JD. "Evaluation of the INDICAID COVID-19 Rapid Antigen Test in symptomatic populations and asymptomatic community testing." ***Microbiology Spectrum***, 2021; 9(1):e0034221. doi: 10.1128/Spectrum.00342-21.
2. Chu A, Yip C, Chan W, Ng A, Chan D, Siu R, Chung T, Ng J, Kittur H, Mosley GL, Poon RW, **Chiu RYT**, To KK. "Evaluation of an automated high-throughput liquid-based RNA extraction platform on pooled nasopharyngeal or saliva specimens for SARS-CoV-2 RT-PCR." ***Viruses***, 2021; 13(4):615. doi: 10.3390/v13040615.
3. Janku F, Huang HJ, Pereira DY, Kobayashi M, Chiu CH, Call SG, Woodbury KT, Chao F, Marshak DR, **Chiu RYT**. "A novel method for liquid-phase extraction of cell-free DNA for detection of circulating tumour DNA." ***Scientific Reports***, 2021; 11(1):19653. doi: 10.1038/s41598-021-98815-x.
4. **Chiu RYT**, Thach AV, Wu CM, Wu BM, Kamei DT. "An aqueous two-phase system for the concentration and extraction of proteins from the Interface for detection using the lateral-flow immunoassay." ***PloS One***, 2015; 10(11):e0142654. doi: 10.1371/journal.pone.0142654.
5. **Chiu RYT**, Jue E, Yip AT, Berg AR, Wang SJ, Kivnick AR, Nguyen PT, Kamei DT. "Simultaneous concentration and detection of biomarkers on paper." ***Lab Chip***, 2014 ;14(16):3021-3028. doi: 10.1039/c4lc00532e.

Research interests / Technical expertise

- ✧ COVID-19
- ✧ Liquid biopsy
- ✧ Entrepreneurship

Abstract

A novel method for liquid-phase extraction of cell-free DNA for detection of circulating tumour DNA

JANKU Filip[1], HUANG Helen J[2], PEREIRA David Y[3], KOBAYASHI Masae[3], CHIU CH[4], CHAN TL[4], ADVAIT V[4], CHUNG CY[4], BRADBURY B[4], CALL SG[2], WOODBURY Kristen T[2], CHAO Felix[3,4], MARSHAK Daniel R[3,4], CHIU Ricky YT[3,4]

[1] Department of Investigational Cancer Therapeutics (Phase 1 Clinical Trials Program)-Unit 455, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX, 77030, USA. fjanku@me.com.

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[3] Phase Scientific International Ltd, Garden Grove, CA, USA.

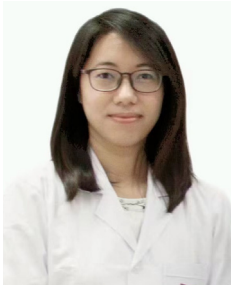
[4] Phase Scientific International Ltd, Shatin, Hong Kong SAR, P.R. China.

Low yields of extracted cell-free DNA (cfDNA) from plasma and urine limit continued development of liquid biopsy in cancer, especially in early-stage cancer diagnostics and cancer screening applications. We investigate a novel liquid-phase-based DNA isolation method that utilizes aqueous two-phase systems to purify and concentrate circulating cfDNA. The PHASIFY MAX and PHASIFY ENRICH kits were compared to a commonly employed solid-phase extraction method on their ability to extract cfDNA at MD Anderson Oncology Center. Our results indicate that this novel extraction technique offers higher cfDNA recovery resulting in better sensitivity for detection of cfDNA mutations compared to a commonly used solid-phase extraction method.

Recently in Hong Kong, we have demonstrated significant success in using liquid biopsy for biomarker detection in prostate cancer, compared to the classical formalin-fixed paraffin-embedded (FFPE) approach. The turnaround time and positive rate are both improved, allowing for a more accurate molecular profile of a patient's tumour and more personalized treatment plans, which can improve outcomes. Furthermore, we have developed PHASIFY URINE for large-volume urine cfDNA extraction, which is expected to increase the sensitivity of urine specimens by more than 10-fold. This advance could significantly broaden the application of cfDNA detection for patients with variety of cancers.

Trainee Talk

Speaker Biography



Dr. ZHANG Chenzi（張辰子）received her bachelor's degree in Preventive Medicine from Fujian Medical University and her master's degree in Preventive Medicine with a specialization in Toxicology from Sun Yat-sen University. In 2020, she obtained her Ph.D. in Biomedical Sciences under the guidance of Prof. Feng Bo at the School of Biomedical Sciences in The Chinese University of Hong Kong (CUHK), where she is currently pursuing her postdoctoral training. During the same year of her graduation, Dr. Zhang was honored with the CUHK Young Scholar Thesis Award for her exceptional work. Dr. Zhang's interests are focused on the application of CRISPR-based genome-editing technologies to develop innovative cell / gene-based therapy strategies for treating human diseases, including cancer. Currently, she is engaged in using CRISPR / Cas9 in combination with AAV virus to generate T cell receptor (TCR) gene knock-out universal Chimeric Antigen Receptor (CAR)-T cells for the treatment of hematological malignancies.

Five recent representative publications

1. He X, Zhang Z, Xue JY, Wang YF, Zhang SQ, Wei JK, **Zhang CZ**, Wang J, Urip BA, Ngan CC, Sun JJ, Li YF, Lu ZQ, Zhao H, Pei DQ, Li CK, Feng B. "Low-dose AAV-CRISPR-mediated liver-specific knock-in restored hemostasis in neonatal hemophilia B mice with subtle antibody response." ***Nature Communications***, 2022; 13(1):7275. doi: 10.1038/s41467-022-34898-y.
2. Wang J*, **Zhang CZ***, Feng B. "The rapidly advancing class 2 CRISPR-Cas technologies: A customizable toolbox for molecular manipulations." ***Journal of Cellular and Molecular Medicine***, 2020; 24(6):3256-3270. doi: 10.1111/jcmm.15039.
3. **Zhang C***, He X*, Kwok YK, Wang F, Xue J, Zhao H, Suen KW, Wang CC, Ren J, Chen GG, Lai PBS, Li J, Xia Y, Chan AM, Chan WY*, Feng B*. "Homology-independent multiallelic disruption via CRISPR/Cas9-based knock-in yields distinct functional outcomes in human cells." ***BMC Biology***, 2018; 16(1):151. doi: 10.1186/s12915-018-0616-2.
4. Geng L, Kong CW, Wong AOT, Shum AMY, Chow MZY, Che H, **Zhang C**, Yau KL, Chan CW, Keung W, Li RA. "Probing flecainide block of I_{Na} using human pluripotent stem cell-derived ventricular cardiomyocytes adapted to automated patch-clamping and 2D monolayers." ***Toxicology Letters***, 2018; 294:61-72. doi: 10.1016/j.toxlet.2018.05.006.
5. Shum AMY, Che H, Wong AOT, **Zhang C**, Wu H, Chan CWY, Costa K, Khine M, Kong CW, Li RA. "A micro-patterned human pluripotent stem cell-based ventricular cardiac anisotropic sheet for visualizing drug-induced arrhythmogenicity." ***Advanced Materials***, 2017; 29(1):201602448. doi: 10.1002/adma.201602448.

Research interests / Technical expertise

- ✧ Gene editing technologies using CRISPR/Cas9 and AAV
- ✧ T cells engineering for cancer treatment
- ✧ CAR-related immunotherapy

Study of TCR-Knockout CAR-T cells for cancer treatment

ZHANG Chenzi[1,2,6], NGAN Chun Christopher[1,6], ZHANG Zhenjie[1,2,5], WANG Jingyi[1], WANG Yaofeng[2,3], TSANG Kin Ching Anson[1], XUE Junyi[1], LI Chi-Kong[4], FENG Bo[1,2,5]

[1] School of Biomedical Sciences, MOE Key Lab, Faculty of Medicine; Institute for Tissue Engineering and Regenerative Medicine (iTERM), The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Centre for Regenerative Medicine and Health, Hong Kong Institute of Science & Innovation, Chinese Academy of Sciences, Hong Kong SAR, P.R. China.
[3] Guangzhou Institute of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou 510530, P.R. China.
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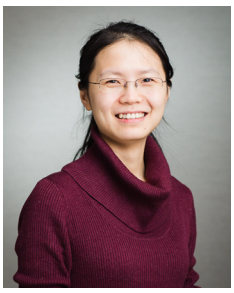
[5] The Chinese University of Hong Kong, Shenzhen Research Institute, Shenzhen 518000, P.R. China.
[6] These authors contributed equally.

Chimeric antigen receptor T-cell (CAR-T) therapy is a revolutionary immunotherapy that engineers patients' T cells to express a tumour-specific CAR, which enables them to eliminate cancer cells. While CAR-T cell therapy has shown impressive success in treating B cell hematological malignancies, its commercial availability is limited by significant obstacles such as lengthy manufacturing times, high costs, and uncontrollable quality and quantity of obtainable T-lymphocytes through apheresis. To overcome these drawbacks, the development of an allogenic universal CAR-T therapy presents an attractive breakthrough point. This approach involves genetically disrupting immune response-related genes, such as T cell receptor (TCR) genes in T cells, to effectively inhibit graft-versus-host disease (GVHD). In our study, we successfully used CRISPR-based knock-in technology combined with Adeno-associated virus (AAV) to generate TCR-negative universal CAR-T cells (AAV CAR-T) through a "one-step genome-editing" strategy. *In vitro* cytotoxicity assays and *in vivo* analysis using leukemia xenograft mouse models demonstrated the excellent efficacy of the AAV CAR-T cells. Thorough profiling assays revealed that AAV CAR-T cells maintain a more naive state and exhibit more robust cancer-killing activity than CAR T cells generated by conventional lentiviral methods. These findings suggest that AAV CAR-T therapy holds great promise as a universal approach to future cancer treatments.

Special seminar: Publishing at Cell and Cell Press

Speaker Biography



Dr. TAN Jiaying
Head of Strategy and Partnership in Greater China, Cell Press
Senior Scientific Editor, Cell

Dr. Tan is the Head of Strategy and Partnership in Greater China at Cell Press, and a Senior Scientific Editor at *Cell*. She earned her PhD in Molecular and Cellular Pathology in the University of Michigan-Ann Arbor in 2012, before moving to the Novartis Institutes for BioMedical Research in Shanghai to conduct postdoctoral research in cancer biology.

She joined the *Cell* editorial team in 2013. During the past few years, she has also served as a consulting editor at *Cell Reports*, the acting Editor-in-Chief of *The Lancet Haematology* from July 2018 to January 2019, and the co-acting Editor-in-Chief of *Cancer Cell* from October 2019 to February 2020.

Email: jtan@cell.com

Special seminar: Publishing at Cell and Cell Press

Session 2: Innovative Cancer Therapeutics

Speaker Biography

Prof. LIU Rihe received his bachelor's degree in Polymer Physics from the University of Science and Technology of China in 1988. He did his graduate work from 1992 to 1996 as a NASA NSCORT predoctoral fellow with Professor Leslie E. Orgel at the Salk Institute for Biological Studies and received his Ph.D. in Biochemistry from the University of California at San Diego. He then carried out his postdoctoral work from 1997 to 2001 as a Damon Runyon postdoctoral fellow with Professor Jack W. Szostak at the Department of Molecular Biology at Massachusetts General Hospital and the Department of Genetics at Harvard Medical School. He joined the faculty at the School of Pharmacy and Center for Genome Sciences at the University of North Carolina at Chapel Hill in 2002. He is currently a professor at the Division of Chemical Biology and Medicinal Chemistry at the UNC Eshelman School of Pharmacy. Prof. Liu pioneered the application of mRNA-display technology for *in vitro* selection of proteins with desired biological and therapeutic functions from various natural proteome libraries and synthetic protein domain/polypeptide libraries. His lab invented a panel of target-trapping biologics that bind to drug targets of interest, including CXCL12, CCL2, CCL5, IL-6, PD-L1/L2, Wnt family members, and LPS, and applied them for cancer immunotherapeutic studies. His lab also systemically explored the self-assembly approach to generate multivalent affinity molecules, including trimeric, tetrameric, pentameric, hexamer, and heptameric platforms, that mimic nature and allow to target viral or immunotherapeutic targets with high avidity and potency. Prof. Liu has extensive expertise in developing multifunctional biologics using integrative modalities, including the protein, the mRNA as well as the engineered immune cells.

Five recent representative publications

1. Wang Y, Tiruthani K, Li S, Hu M, Zhong G, Tang Y, Roy S, Zhang L, Liao C, Tan J, **Liu R***. "mRNA delivery of a bispecific single domain antibody to polarize tumour-associated macrophages and synergize the immunotherapy against liver malignancies." ***Advanced Materials***, 2021; 33(23):e2007603. doi: 10.1002/adma.202007603.
2. Song W, Shen L, Goodwin T, Liu Q, Li J, Dorosheva O, Liu T, Wang Y, Das M, **Liu R***, Huang L*. "Synergistic and low adverse effect cancer immunotherapy by immunogenic chemotherapy and locally expressed PD-L1 trap." ***Nature Communications***, 2018; 9(1):2237. doi: 10.1038/s41467-018-04605-x.
3. Wang H, Vilela M, Winkler A, Tarnawski M, Hartmann E, Schlichting I, Yumerefendi H, Kuhlman B, **Liu R***, Danuser G*, Hahn K*. "LOVTRAP: an optogenetic system for photoinduced protein dissociation." ***Nature Methods***, 2016; 13(9):755-8. doi: 10.1038/nmeth.3926.
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5. Cotten SW, Zou J, Valencia CA, **Liu R***. "Selection of proteins with desired properties from natural proteome libraries using mRNA display." ***Nature Protocols***, 2011; 6, 1163-1182. doi: 10.1038/nprot.2011.354.

Research interest

Prof. Liu's major research interests focus on the development and translational applications of novel drug target-binding affinity molecules by integrating directed molecular selection, design and engineering of multifunctional biologics, and mechanistic and theranostic studies in disease models that mirror human diseases.

Abstract

Translational studies of mRNA therapeutics for treating solid tumours

LIU Rihe

Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA.

Translational biomedical research, which bridges the gap between basic research and clinical practice and pharmaceutical products, has become a critical area of focus for researchers around the world. Despite significant progress in the fields, translational biomedical research is still in its early stage. This talk will use the novel mRNA therapeutics we developed with unique mechanisms of action as examples to shed light on the opportunities and challenges in the translational fields.

Session 2: Innovative Cancer Therapeutics

Speaker Biography

Prof. CHAN L. Stephen（陳林）is the Clinical Professor at the Department of Clinical Oncology of The Chinese University of Hong Kong. His main interest of research is clinical and translational studies on hepatobiliary-pancreatic and neuroendocrine cancers. Prof. Chan has published over 160 papers in peer reviewer journals and delivered over 100 international lectures.

Internationally, Prof. Chan is serving as the chairman of Education Committee of the International Liver Cancer Association (ILCA). He has also served in Scientific Steering Committee of the European Society for Medical Oncology Congress as a track chair in 2021 and committee member from 2022-2023. Besides, He has been invited to be Associate Editors in several journals including *Journal of Hepatology*, *Liver Cancer*, and *Therapeutic Advances in Medical Oncology*.

Locally, Prof. Chan is the Panel Member of Biology and Medicine Panel for the General Research Fund in Hong Kong. He has also established a charity, Hand in Hand Cancer Foundation, to serve patients in need.

Five recent representative publications

1. Abou-Alfa GK*, Lau G, Kudo M, **Chan SL***, Kelley RK, Furuse J, Sukeepaisarnjaroen W, Kang YK, Van Dao T, De Toni EN, et al. "Tremelimumab plus durvalumab in unresectable hepatocellular carcinoma." (*equal contribution). ***NEJM Évidence***, 2022; 1(8). doi: 10.1056/EVIDoa2100070.
2. **Chan SL**, Schuler M, Kang YK, Yen CJ, Edeline J, Choo SP, Lin CC, Okusaka T, Weiss KH, Macarulla T, Cattan S, Blanc JF, Lee KH, Maur M, Pant S, Kudo M, Assenat E, Zhu AX, Yau T, Lim HY, Bruix J, Geier A, Guillén-Ponce C, Fasolo A, Finn RS, Fan J, Vogel A, Qin S, Riester M, Katsanou V, Chaudhari M, Kakizume T, Gu Y, Porta DG, Myers A, Delord JP. "A first-in-human phase 1/2 study of FGF401 and combination of FGF401 with spartalizumab in patients with hepatocellular carcinoma or biomarker-selected solid tumours." ***Journal of Experimental & Clinical Cancer Research***, 2022; 41(1):189. doi: 10.1186/s13046-022-02383-5.
3. Qin S, **Chan SL**, Gu S, Bai Y, Ren Z, Lin X, Chen Z, Jia W, Jin Y, Guo Y, Sultanbaev AV, Pazgan-Simon M, Pisetska M, Liang X, Chen C, Nie Z, Wang L, Cheng AL, Kaseb A, Vogel A. "LBA35 Camrelizumab (C) plus rivoceranib (R) vs. sorafenib (S) as first-line therapy for unresectable hepatocellular carcinoma (uHCC): A randomized, phase III trial." ***Annals of Oncology***, 2022, 33:S1401 - S1402. doi: 10.1016/j.annonc.2022.08.032.
4. **Chan SL**, Cheng PNM, Liu AM, Chan LL, Li L, Chu CM, Chong CCN, Lau YM, Yeo W, Ng KKC, Yu SCH, Mok TSK, Chan AWH. "A phase II clinical study on the efficacy and predictive biomarker of pegylated recombinant arginase on hepatocellular carcinoma." ***Investigational New Drugs***, 2021; 39(5):1375-1382. doi: 10.1007/s10637-021-01111-8.
5. Kwong TT, Wong CH, Zhou JY, Cheng ASL, Sung JJY, Chan AWH, **Chan SL**. "Chemotherapy-induced recruitment of myeloid-derived suppressor cells abrogates efficacy of immune checkpoint blockade." ***JHEP Reports***, 2020; 3(2):100224. doi: 10.1016/j.jhepr.2020.100224.

Research interests / Technical expertise

- ✧ Clinical and translational researches on hepato-pancreatobiliary cancers and neuroendocrine tumours

Drug treatment for HCC: Where are we now?

CHAN L. Stephen, MD FRCP

Department of Clinical Oncology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Hepatocellular carcinoma is known to be a chemo-refractory tumour. Biomarker driven targeted agents have been tested but found to have limited success due to a lack of well-defined actionable mutations in the tumour. Recent advances on the immune checkpoint inhibitors have improved the response rate and long-term survivors. However, primary and secondary subsequent resistance to immunotherapy remains frequent. Our group has aimed to understand and develop strategies to enhance the efficacy of immunotherapy in HCC in the clinics. Related data and experiences will be shared in the lecture.

Session 2: Innovative Cancer Therapeutics

Speaker Biography

Prof. CHEN Zhiwei（陳志偉）is the founding director of the AIDS Institute of the University of Hong Kong (HKU), which was established at HKU Li Ka Shing Faculty of Medicine in 2007. He is now a tenured full professor in Department of Microbiology.

In 1996, he finished his postgraduate studies with Prof. Preston A. Marx at the Aaron Diamond AIDS Research Center (ADARC) of the Rockefeller University and obtained his Ph.D. degree from New York University School of Medicine in the USA. From 1996 to 2007, he was trained with Prof. David D. Ho and progressed from a post-doc to a research scientist, and then to a staff investigator/assistant professor all at ADARC. In 2007, he joined HKU as an associate professor in Microbiology.

Since 1991, he has been engaged in studies of HIV origin, molecular mechanisms of HIV/SIV entry, and AIDS/SARS/COVID vaccines. In recent years, he has been focusing on functional cure of HIV/AIDS (TRS project), COVID-19 vaccine and immunopathogenesis as well as cancer immunotherapy. He has published over 180 peer-reviewed SCI papers. He serves as an editorial board member for *AIDS*, *JAIDS*, *JMP* and *JNIP*, etc.

https://www.med.hku.hk/aidsinst/Chenzhiwei.html

Five recent representative publications

1. Tan Z, …, **Chen Z***. “Isoformic PD-1-mediated immunosuppression underlies resistance to PD-1 blockade in hepatocellular carcinoma patients.” ***Gut***, 2022; gutjnl-2022-327133. doi: gutjnl-2022-327133.
2. Zhou B, …, **Chen Z***. “A broadly neutralizing antibody protects Syrian hamsters against SARS-CoV-2 Omicron challenge.” ***Nature Communications***, 2022; 13(1):3589. doi: 10.1038/s41467-022-31259-7.
3. Zhou D, …, **Chen Z***. “Robust SARS-CoV-2 infection in nasal turbinates after treatment with systemic neutralizing antibodies.” ***Cell Host & Microbe***, 2021; 29(4):551-563.e5. doi: 10.1016/j.chom.2021.02.019.
4. Zhou R, …, **Chen Z***. “Acute SARS-CoV-2 infection impairs dendritic cell and T cell responses.” ***Immunity***, 2020; 53(4):864-877.e5. doi: 10.1016/j.immuni.2020.07.026.
5. Cheung AK, …, **Chen Z***. “Gut-homing Δ42PD1+Vδ2 T cells promote innate mucosal damage via TLR4 during acute HIV type 1 infection.” ***Nature Microbiology***, 2017; 2(10):1389-1402. doi: 10.1038/s41564-017-0006-5.

Research interests / Technical expertise

- ✧ Functional cure of HIV/AIDS
- ✧ SARS-CoV-2 pathogenesis, vaccine and immunotherapy
- ✧ Cancer immunotherapy

Isoformic PD-1 regulates host immunity in infection and hepatocellular carcinoma

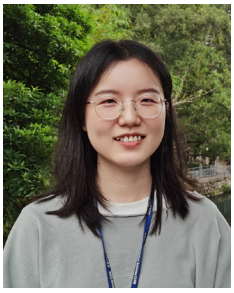
CHEN Zhiwei

AIDS Institute and Department of Microbiology, School of Clinical Medicine, Li Ka Shing Faculty of Medicine, State Key Laboratory of Emerging Infectious Diseases, The University of Hong Kong, Hong Kong SAR, P.R. China.

Checkpoint inhibitor immunotherapy has significantly improved existing treatments against cancer and infection, yet the role of PD-1 isoforms in patients remains elusive. Here, we report our discovery of a human isoformic PD-1, namely Δ42PD-1. Generating Δ42PD-1-specific monoclonal antibodies, we further revealed the functionality of Δ42PD-1 during HIV-1 infection and hepatocellular carcinoma (HCC). For the recent HCC study, we analyzed a cohort of 38 HCC patients using freshly isolated peripheral blood mononuclear cell (PBMC), 25 samples of paired HCC and adjacent non-tumour tissues, as well as 6 HCC patients treated with Nivolumab. By multicolour flow analysis identified a population of αβ T cells in patients' PBMC that only express Δ42PD-1, on up to 71% of cytotoxic T lymphocytes. Δ42PD-1$^+$ T cells were preferentially tumour-infiltrating and functionally more exhausted than PD-1$^+$ T cells. Tumour-infiltrated Δ42PD-1$^+$ T cells associated with HCC development partially by triggering TLR4-signaling for producing tumorigenic inflammatory cytokines. Anti-Δ42PD-1 antibody CH101, but not Nivolumab, inhibited tumour growth significantly in three subcutaneous and orthotopic HCC models of humanized mice. HCC patients treated with Nivolumab showed effective PD-1 blockade but increased frequencies of Δ42PD-1$^+$ T cells over time. Our findings demonstrated that HCC-induced Δ42PD-1 as a underlying mechanism conferring resistance to PD-1 blockade and warranted the development of humanized anti-Δ42PD-1 antibody for cancer immunotherapy.

Trainee Talk

Speaker Biography



Dr. XIONG Zhewen（熊哲文）is a postdoctoral fellow in the School of Biomedical Sciences, The Chinese University of Hong Kong (CUHK). She received her Ph.D. in 2020 and continued her postdoctoral training in CUHK under the supervision of Prof. CHENG Sze-Lok Alfred. Her research mainly focuses on adaptive resistance to immune checkpoint blockade (ICB) in hepatocellular carcinoma (HCC). She has established novel ICB-resistant mouse models that recapitulate the immune landscape of human 'cold' HCC. Integrative single-cell and functional analysis uncovered an adaptive transcriptional program to evade therapeutic pressure by immunosuppressive tumour microenvironment remodeling, thus providing a strategy for counteracting ICB resistance in HCC. She also works on single-cell dissection of heterogeneity and dynamics of tumour ecosystem upon ICB therapy in human HCC. The goal of her research is to identify personalized therapeutic approaches that expand the long-term clinical benefit of cancer immunotherapy.

Five recent representative publications

1. **Xiong Z**[#], Chan SL[#], Zhou J[#], Vong JSL, Kwong TT, Zeng X, Wu H, Cao J, Tu Y, Feng Y, Yang W, Wong PPC, Si-Tou WWY, Liu X, Wang J, Tang W, Liang Z, Lu J, Li KM, Low JT, Chan MWY, Leung HHW, Chan AWH, To KF, Yip KYL, Lo YMD, Sung JJY, Cheng ASL. "Targeting PPAR-gamma counteracts tumour adaptation to immune-checkpoint blockade in hepatocellular carcinoma." ***Gut***, 2023; doi: 10.1136/gutjnl-2022-328364.
2. Tang W, Zhou J, Yang W, Feng Y, Wu H, Mok MTS, Zhang L, Liang Z, Liu X, **Xiong Z**, Zeng X, Wang J, Lu J, Li J, Sun H, Tian X, Yeung PC, Hou Y, Lee HM, Lam CCH, Leung HHW, Chan AWH, To KF, Wong J, Lai PBS, Ng KKC, Wong SKH, Wong VWS, Kong APS, Sung JJY, Cheng ASL. "Aberrant cholesterol metabolic signaling impairs antitumor immunosurveillance through natural killer T cell dysfunction in obese liver." ***Cellular & Molecular Immunology***, 2022; 19(7):834-847. doi: 10.1038/s41423-022-00872-3.
3. Zeng X, Zhou J, **Xiong Z**, Sun H, Yang W, Mok MTS, Wang J, Li J, Liu M, Tang W, Feng Y, Wang HKS, Tsang SW, Chou KL, Yeung PC, Wong J, Lai PBS, Chan AWH, To KF, Chan SL, Xia Q, Xue J, Chen X, Yu J, Peng S, Sung JJY, Kuang M, Cheng ASL*. "Cell cycle-related kinase reprograms the liver immune microenvironment to promote cancer metastasis." ***Cellular & Molecular Immunology***, 2021; 18(4):1005-1015. doi: 10.1038/s41423-020-00534-2.
4. Shen F[#], **Xiong Z**[#], Kong J, Wang L, Cheng Y, Jin J, Huang Z. "Triptolide impairs thioredoxin system by suppressing Notch1-mediated PTEN/Akt/Txnip signaling in hepatocytes." ***Toxicology Letters***, 2019; 300: 105-115. doi: 10.1016/j.toxlet.2018.10.024.
5. Wang W, Yang Y, **Xiong Z**, Kong J, Fu X, Shen F, Huang Z. "Inhibition of glycogen synthase kinase 3beta ameliorates triptolide-induced acute cardiac injury by desensitizing mitochondrial permeability transition." ***Toxicology and Applied Pharmacology***, 2016; 313:195-203. doi: 10.1016/j.taap.2016.10.007.

Research interests / Technical expertise

- ✧ Single-cell RNA sequencing
- ✧ Orthotopic and spontaneous pre-clinical models of HCC
- ✧ High-dimensional flow cytometry and immune cell functional assays

Targeting PPAR-gamma counteracts tumour adaptation to immune-checkpoint blockade in hepatocellular carcinoma

XIONG Zhewen[1], CHAN Lam Stephen[2,3], ZHOU Jingying[1], SUNG Jao-Yiu Joseph[4,5], CHENG Sze-Lok Alfred[1]*

[1] School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[2] Department of Clinical Oncology, Sir YK Pao Centre for Cancer, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[3] State Key Laboratory of Translational Oncology, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.
[4] Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore.
[5] State Key Laboratory of Digestive Disease, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Therapy-induced tumour microenvironment (TME) remodeling poses a major hurdle for cancer cure. As the majority of patients with hepatocellular carcinoma (HCC) exhibits primary or acquired resistance to anti-programmed cell death (ligand)-1(anti-PD-[L]1) therapies, we aimed to investigate the mechanisms underlying tumour adaptation to immune-checkpoint blockade (ICB). By serial orthotopic implantation of HCC cells in anti-PD-L1-treated immunocompetent mice, we established two mouse models of adaptive ICB resistance that recapitulate the immune landscape of human 'cold' HCC. Integrative single-cell and functional analysis revealed that tumour cell-intrinsic up-regulation of peroxisome proliferator-activated receptor-gamma (PPARγ) transcriptionally activated vascular endothelial growth factor-A (VEGF-A) production to drive myeloid-derived suppressor cell expansion and $CD8^+$ T cell dysfunction. A selective PPARγ antagonist triggered an immune suppressive-to-stimulatory TME conversion and re-sensitized tumours to anti-PD-L1 therapy in orthotopic and spontaneous HCC models. Importantly, 40% (6/15) of HCC patients resistant to pembrolizumab exhibited tumoural PPARγ induction. Moreover, higher baseline PPARγ expression was associated with poorer survival of anti-PD-(L)1-treated patients in multiple cancer types. In summary, we uncover an adaptive transcriptional program by which tumour cells evade immune-checkpoint targeting via PPARγ/VEGF-A-mediated TME immunosuppression, thus providing a strategy for counteracting immunotherapeutic resistance in HCC.

Acknowledgements: This project is supported by the Collaborative Research Fund (C4045-18W to AS-LC), the General Research Fund (14115820 and 14120621 to AS-LC), the Li Ka Shing Foundation (grant number not applicable to AS-LC), the Health and Medical Research Fund (07180556 to JZ), the Terry Fox Foundation—Terry Fox Run, Hong Kong (I1008 to SLC, AS-LC), the CUHK Strategic Seed Funding for Collaborative Research Scheme (grant number not applicable to AS-LC) and the Charlie Lee Charitable Foundation (grant number not applicable). We also acknowledge support (funding and study medications) by Merck Sharp and Dohme (MSD-IIS 55253 to SLC) for the clinical trial (NCT03419481).

Session 3: Exposomes, Epigenetics and Emerging Cancer Trends

Speaker Biography

Prof. KWAN Mei-Po（關美寶）is Choh-Ming Li Professor of Geography and Resource Management and Director of the Institute of Space and Earth Information Science at The Chinese University of Hong Kong. She has made ground-breaking contributions to research on environmental health, human mobility, transport/health issues in cities, and geographic information science. She discovered the uncertain geographic context problem and the neighborhood effect averaging problem. She is a leading researcher in deploying real-time GPS tracking and mobile sensing to collect individual-level data in environmental health research. Prof. Kwan has received many prestigious honours and awards, including the James R. Anderson Medal of Honor in Applied Geography, the Distinguished Scholarship Honors, the Wilbanks Prize for Transformational Research in Geography, and the Stanley Brunn Award for Creativity in Geography from the American Association of Geographers.

Her recent projects examine the health impacts of individual environmental exposure (e.g., noise, air pollution, green space), the space-time dynamics of the COVID-19 pandemic, and the protection of geoprivacy via the development of a Geospatial Virtual Data Enclave (GVDE).

Five recent representative publications

1. **Kwan MP**. "The stationarity bias in research on the environmental determinants of health." ***Health & Place***, 2021; 70: 102609. doi: 10.1016/j.healthplace.2021.102609.
2. **Kwan MP**. "The limits of the neighborhood effect: Contextual uncertainties in geographic, environmental health, and social science research." ***Annals of the American Association of Geographers***, 2018; 108(6): 1482-1490. doi: 10.1080/24694452.2018.1453777.
3. **Kwan MP**. "The neighborhood effect averaging problem (NEAP): An elusive confounder of the neighborhood effect." ***International Journal of Environmental Research and Public Health***, 2018; 15(9):1841. doi: 10.3390/ijerph15091841.
4. **Kwan MP**. "How GIS can help address the uncertain geographic context problem in social science research." ***Annals of GIS***, 2012; 18(4):245-255. doi: 10.1080/19475683.2012.727867.
5. **Kwan MP**. "The uncertain geographic context problem." ***Annals of the Association of American Geographers***, 2012; 102(5):958-968. doi: 10.1080/00045608.2012.687349.

Research interests / Technical expertise

- ✧ Geographies of health and wellbeing
- ✧ Human mobility, urban travel, and sustainable transportation
- ✧ Urban, environmental, health, and transport issues in U.S. and Chinese cities

Abstract

How advanced geospatial methods can help address the challenge of environmental exposure assessment in environmental health and epigenetic research

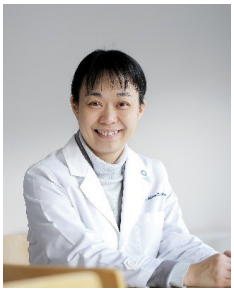
KWAN Mei Po

Department of Geography and Resource Management and Institute of Space and Earth Information Science, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Development in environmental epigenetics in the past few decades has greatly advanced our knowledge of the specific microbiological pathways between environmental exposures and human diseases (e.g., exposures to toxic chemicals like air pollutants may induce DNA methylation or histone acetylation that affects gene expression and disease risk). Environmental epigenetics seeks to examine how environmentally induced epigenetic changes (i.e., changes in gene activity and expression that can be transmitted over cell divisions or over generations without changing or damaging DNA sequence) lead to human diseases. However, due to various uncertainties arising from the space-time dynamics of environmental factors and human mobility (e.g., the uncertain geographic context problem), the assessment of individual exposures to environmental influences in epigenetic research can be inaccurate. Using advanced geospatial technologies such as real-time GPS tracking and mobile sensing (e.g., mobile pollutant sensors), researchers can now collect enormous amounts of high-resolution space-time data of individual exposure that greatly enhance the reliability and accuracy of environmental exposure assessment. In this presentation, I will discuss how advanced geospatial methods can help address the challenge of environmental exposure assessment in environmental health and epigenetic research. Drawing upon my recent projects on individual exposures to green/blue spaces, light-at-night, and air and noise pollution, I explore how the collection and analysis of high-resolution space-time data enabled by advanced geospatial and mobile technologies can help measure individual environmental exposure more accurately. Because more accurate and reliable environmental exposure assessments will enable researchers to more accurately ascertain the extent to which specific environmental factors (e.g., air pollutants) may induce certain epigenetic changes and human diseases, deploying advanced geospatial methods and integrating them into environmental health and epigenetic research will be a promising direction for advancing these fields in the future.

Session 3: Exposomes, Epigenetics and Emerging Cancer Trends

Speaker Biography



Prof. KONG Pik Shan Alice（江碧珊）is the Professor in the Department of Medicine and Therapeutics at The Chinese University of Hong Kong (CUHK), and Honorary Consultant at the Prince of Wales Hospital, Hong Kong. Prof. Kong graduated from CUHK and completed her training in General Medicine and Endocrinology at the Queen Elizabeth Hospital, Hong Kong. She had her overseas training as postdoctoral fellow under the mentorship of Prof. Robert Henry at the Division of Endocrinology, Department of Medicine at University of California, San Diego, United States between 1998 and 1999. She became a Fellow of the Hong Kong Academy of Medicine in 2000, with accreditation in Advanced Internal Medicine, Endocrinology, Diabetes and Metabolism. She is also a Fellow of the Royal College of Physicians, Glasgow, Edinburgh and London. She is the chairperson of Specialty Board in Advanced Internal Medicine, Hong Kong College of Physicians between 2017 and 2021.

Prof. Kong's research interests are obesity and diabetes with focus on epidemiological studies and clinical trials related to sleep and diet in adults and adolescents. Prof. Kong is the member of Nominating Committee for President, World Obesity Federation. She is the Steering Committee Member of Joint Asia Diabetes Evaluation (JADE) program, Council Member of Diabetes Hong Kong and The Hong Kong Society of Endocrinology, Metabolism and Reproduction, and the former Vice President of Hong Kong Association for the Study of Obesity. She is the Editor in Chief of *Primary Care Diabetes*, International Associate Editor of *Diabetes Technology and Therapeutics* and an editorial board member of *Diabetes Care* and *Current Diabetes Reports*. Prof. Kong is dedicated to teaching and won the Faculty Education Award in 2022. She has presented at numerous local, regional and international meetings and has published over 300 articles in international peer-reviewed journals.

Five recent representative publications

1. Cao H, Chung ACK, Ming X, Mao D, Lee HM, Cao X, Rutter GA, Chan JCN, Tian XY, **Kong APS**. "Autotaxin signaling facilitates β cell dedifferentiation and dysfunction induced by Sirtuin 3 deficiency." ***Molecular Metabolism***, 2022; 60:101493. doi: 10.1016/j.molmet.2022.101493.
2. **Kong AP**, Lew T, Lau ESH, Lim LL, Kesavadev J, Jia W, Sheu WH, Sobrepena L, Tan ATB, Nguyen TK, Yoon KH, Wang K, Kodiappan K, Treuer T, Chan JCN; JADE Collaborative Study Group. "Real-world data reveal unmet clinical needs in insulin treatment in Asian people with type 2 diabetes: the Joint Asia Diabetes Evaluation (JADE) Register." ***Diabetes, Obesity and Metabolism***, 2020; 22(4):669-679. doi: 10.1111/dom.13950.
3. **Kong AP**, Yang X, So WY, Luk A, Ma RC, Ozaki R, Cheung KK, Lee HM, Yu L, Xu G, Chow CC, Chan JC. "Additive effects of blood glucose lowering drugs, statins and renin-angiotensin system blockers on all-site cancer risk in patients with type 2 diabetes." ***BMC Medicine***, 2014; 12:76. doi: 10.1186/1741-7015-12-76.
4. **Kong AP**, Yang X, Luk A, Ma RC, So WY, Ozaki R, Ting R, Cheung K, Ho CS, Chan MH, Chow CC, Chan JC. "Severe hypoglycemia identifies vulnerable patients with type 2 diabetes at risk for premature death and all-site cancer: the Hong Kong diabetes registry." ***Diabetes Care***, 2014; 37(4):1024-1031. doi: 10.2337/dc13-2507.
5. **Kong AP**, Xu G, Brown N, So WY, Ma RC, Chan JC. "Diabetes and its comorbidities-where East meets West." ***Nature Reviews Endocrinology***, 2013; 9(9):537-547. doi: 10.1038/nrendo.2013.102.

Research interests / Technical expertise

- ✧ Obesity
- ✧ Diabetes
- ✧ Non-alcoholic fatty liver disease

Obesity, diabetes and cancers: what are the links?

KONG Pik Shan Alice, MD

Division of Endocrinology, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

Modernization has led to rapid increases in chronic diseases, notably obesity and diabetes, which explain 60-70% of global morbidity and mortality. As intensive control of cardiovascular risk factors prolong their lifespan, patients with type 2 diabetes are consequently more likely to die prematurely due to cancers. From data in the Hong Kong diabetes register, one fifth of patients with diabetes died from cancers, comparable to the death toll of cardiovascular disease. For each 1% HbA_{1c} increment above 6.5%, there was an 18% increased risk of all-site cancers in people with diabetes. Controlling blood lipids, blood pressure and blood glucose as well as inhibiting the 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCR) and renin angiotensin system (RAS) using statins, angiotensin converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB) are shown to substantially reduce the risk of cardiovascular-renal events as well as cancers in diabetes.

Diabetes is multifaceted with obesity being a key driver. Yet, the exact mechanisms linking obesity, diabetes and cancer remain unknown. The frequent but not invariable clustering of these diseases suggests common aetiologies. This talk aims to have an overview of the current literature investigating the links between obesity, diabetes and cancers.

Session 3: Exposomes, Epigenetics and Emerging Cancer Trends

Speaker Biography

Prof. CHENG Sze Lok Alfred（鄭詩樂）is a Professor and Assistant Dean in Research of the Faculty of Medicine at The Chinese University of Hong Kong (CUHK). He completed his Ph.D. under the mentorship of Prof. Joseph Sung at CUHK and his postdoctoral training in the laboratory of Prof. Tim Huang at The Ohio State University. His research aims at advancing the basic understanding and precision immunotherapy of hepatocellular carcinoma. His multi-disciplinary collaborative team has employed the cutting-edge single-cell multi-omics and AI innovation to understand tumour adaptation to immune-checkpoint blockade and identify the cellular and molecular mechanisms of immunotherapeutic resistance. His recent works on the development of effective and durable combination immunotherapies have been published and highlighted in top journals of the field such as *Gut*, *Journal of Hepatology*, and *Science Translational Medicine*. He is the recipient of the Most Promising Young Investigator Award by the HK Government (2014) and CUHK (2015, 2019), and the 10th HMRF Anniversary Award in Breakthrough Research by the Food and Health Bureau of HK Government (2021).

Five recent representative publications

1. Xiong Z, Chan SL, Zhou J, Vong JS, Kwong TT, Zeng X, Wu H, Cao J, Tu Y, Feng Y, Yang W, Wong PC, Si-Tou WW, Liu X, Wang J, Tang W, Liang Z, Lu J, Li KM, Low JT, Chan MWY, Leung HH, Chan AW, To KF, Yip KY, Lo DY, Sung JJ*, **Cheng AS***. "Targeting PPAR-gamma counteracts tumour adaptation to immune-checkpoint blockade in hepatocellular carcinoma." ***Gut***, 2023. doi: 10.1136/gutjnl-2022-328364.
2. Yang W, Feng Y, Zhou J, Cheung OK, Cao JQ, Wang J, Tang WS, Tu YL, Xu LL, Wu F, Tan Z, Sun H, Tian Y, Wong J, Lai PB, Chan SL, Chan AW, Tan P, Chen Z, Sung JJ, Yip KY, To KF, **Cheng AS***. "A selective HDAC8 inhibitor potentiates antitumor immunity and efficacy of immune checkpoint blockade in hepatocellular carcinoma." ***Science Translational Medicine***, 2021; 13(588):eaaz6804. doi: 10.1126/scitranslmed.aaz6804.
3. Liu M, Zhou J, Liu X, Feng Y, Yang W, Wu F, Cheung OK, Sun H, Zeng X, Tang W, Mok MT, Wong J, Yeung PC, Lai PB, Chen Z, Jin H, Chen J, Chan SL, Chan AW, To KF, Sung JJ, Chen M, **Cheng AS***. "Targeting monocyte-intrinsic enhancer reprogramming improves immunotherapy efficacy in hepatocellular carcinoma." ***Gut***, 2020; 69(2):365-379. doi: 10.1136/gutjnl-2018-317257.
4. Zhou J, Liu M, Sun H, Feng Y, Xu L, Chan AWH, Tong JH, Wong J, Chong CCN, Lai PBS, Wang HK, Tsang SW, Goodwin T, Liu R, Huang L, Chen Z, Sung JJ, Chow KL, To KF, **Cheng AS***. "Hepatoma-intrinsic CCRK inhibition diminishes myeloid-derived suppressor cell immunosuppression and enhances immune-checkpoint blockade efficacy." ***Gut***, 2018; 67(5):931-944. doi: 10.1136/gutjnl-2017-314032.
5. Sun H, Yang W, Tian Y, Zeng X, Zhou J, Mok MTS, Tang W, Feng Y, Xu L, Chan AWH, Tong JH, Cheung YS, Lai PBS, Wang HKS, Tsang SW, Chow KL, Hu M, Liu R, Huang L, Yang B, Yang P, To KF, Sung JJY, Wong GLH*, Wong VWS*, **Cheng AS***. "An inflammatory-CCRK circuitry drives mTORC1-dependent metabolic and immunosuppressive reprogramming in obesity-associated hepatocellular carcinoma." ***Nature Communications***, 2018; 9(1):5214. doi: 10.1038/s41467-018-07402-8.

Research interests / Technical expertise

- ✧ Cancer epigenetics
- ✧ Tumour immunology and immunotherapy
- ✧ Hepatocellular carcinoma

An epigenetic link between obesity and liver cancer

CHENG Sze-Lok Alfred

School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, P.R. China.

DNA and histones are targets of multiple chemical modifications that convey flexibility to the genome. However, these epigenetic events are often hijacked in carcinogenesis. While chronic hepatitis B remains the major etiology of hepatocellular carcinoma (HCC), the growing epidemic of obesity which leads to non-alcoholic fatty liver disease (NAFLD) has emerged as an important risk factor. The rapidly accumulating evidence that epigenetics converts inflammatory and over-nutrient microenvironment into aberrant transcriptional activity thus underscores the fundamental roles of epigenetic regulation in HCC pathogenesis. Through integrated omics, single-cell and high-dimensional flow analysis in preclinical models and clinical specimens, our multi-disciplinary team creates synergistic interactions in the pursuit of cellular and molecular vulnerabilities in NAFLD-associated HCC, with an aim to revert the transcriptional abnormalities in the tumour microenvironment. The long-term goal of our efforts is to develop the next generation of effective and durable epigenetic therapeutics in immuno-oncology for clinical translation.

Trainee Talk

Speaker Biography

Dr. XIE Jinpging Jodie（謝靖萍）finished her residency training and worked as a physician at the Department of Neural Rehabilitation in Guangzhou, performing clinical duties for stroke and spinal cord injury patients. While working at the department, she developed her interest in the field of motor neuroscience, and then she became a full-time PhD student at The Chinese University of Hong Kong (CUHK) and started her own research in 2019. After getting her PhD by the end of 2022, she continues her research work as a postdoctoral fellow at CUHK. She has demonstrated the motor control strategy with the muscle-synergy model by applying both invasive and non-invasive brain stimulation techniques over the human motor cortex. Now she is trying to reconstruct the functional distributions of these control strategies using different brain mapping techniques over the human motor cortex. Supported by the physiological evidence from human studies, the application of muscle synergies can be further extended, from improved training for expertise, and therapeutic and diagnostic biomarkers for motor rehabilitation, to the development of brain-computer interfaces soon.

Five recent representative publications since 2020

1. **Xie J**, Huang S, Lau K, Chan R, Kong A, Woo P, Cheung V*. “Revealing the neural basis of muscle synergies through motor cortical stimulations in glioma patients undergoing awake craniotomy”. (In preparation).
2. **Xie J**, Chou I, Lau K, Leung O, Cheung R, Mak A, Cheung V*. “Revealing the neural basis of muscle synergies in humans through transcranial magnetic stimulation on the motor cortex and motor imagery-based fMRI.” (In preparation).
3. Huang S, **Xie J**, Mak A, Cheung V, Chan R*. “Expertise-related alteration of synergetic control of upper-limb muscles in a complex motor task”. (In preparation).
4. Guo X, He B, Lau KYS, Chan PPK, Liu R, **Xie J**, Ha SCW, Chen C, Cheing GLY, Cheung RTH, Chan RHM*, Cheung VCK*. “Age-related modifications of the muscle synergies and their temporal activations for overground walking.” ***IEEE Transactions on Neural Systems and Rehabilitation Engineering***, 2022; 30:2700-2709. doi: 10.1109/TNSRE.2022.3206887.
5. **Xie J**, Pan R, Zhan J, Chen H*. “Research progress on the pharmacological effects and clinical applications of Qingpeng ointment.” ***Guiding Journal of Traditional Chinese Medicine and Pharmacy***, 2020; 26(9).

Research interests / Technical expertise

- ✧ Motor neuroscience, motor control strategy
- ✧ Neural rehabilitation strategy and related clinical application
- ✧ Human brain mapping techniques (invasive/non-invasive stimulations, fMRI, ECoG)

Revealing the neural basis of muscle synergies through motor cortical stimulations in glioma patients undergoing awake craniotomy

XIE J Jodie[1], HUANG Subing [2], LAU Kelvin [1], CHAN HM Rosa[2], KONG HS Amy[3], WOO YM Peter[4], CHEUNG CK Vincent[1]

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[2] Department of Electrical Engineering, City University of Hong Kong, Hong Kong SAR, P.R. China.

[3] Department of Anaesthesiology and Operating Theatre Services, Kwong Wah Hospital, Hong Kong SAR, P.R. China.

[4] Department of Neurosurgery, Kwong Wah Hospital, Hong Kong SAR, P.R. China.

The diversity of voluntary movement is achieved by complex motor commands generated in the central nervous system (CNS). A tremendous number of animal studies has suggested that these motor commands can be represented and coordinated through muscle synergies, discrete motor-activation units that recruit specific groups of muscles. However, direct neurophysiological evidence for the existence of muscle synergies in humans is still lacking. We seek to demonstrate the neural basis of upper limb muscle synergies in humans by independently retrieving the behavioral synergies through direct electrical stimulation (DES) delivered to focal motor cortical loci during awake craniotomy in human patients undergoing tumour-removal surgery. Patients diagnosed with gliomas while still having normal motor functions (N=13) participated in three experimental sessions — the pre-, intra- and post-operative sessions. In the pre- and post-operative sessions, surface electromyographic signals (EMGs; 12-14 muscles) were recorded during 8-10 tasks related to activities of daily living. In the intra-operative session, EMGs were collected as different motor cortical loci were stimulated with bipolar DES (2-5mA, 60 Hz, 1-3s) while the subject was at rest but awake, or performing specific motor tasks (grasping, gripping etc.). Behavioral muscle synergies and DES-derived muscle synergies were decomposed from the recorded EMGs by the Non-Negative Matrix Factorization algorithm. The characteristics of the DES- derived and behavioral muscle synergies were compared and evaluated by statistical methods. We found that the DES-derived muscle synergies showed higher dimensionality and sparseness as compared with their corresponding behavioral muscle synergies. Across subjects, 50% of the pre/post-operative behavioral synergies could be directly matched to the subjects' own DES-derived muscle synergies with high similarity. Another 15% of the behavioral synergies could be explained by merging or fractionating the DES-derived synergies. The remaining 35% of the behavioral synergies could not be accounted for by the DES synergies. Overall, our results support that many muscle synergies extracted from the EMGs of daily motor tasks (~60%) are encoded in the motor system of humans. We demonstrate that it is possible to access the muscle synergies and map out their representations in the primary motor cortex of humans by applying DES in a neurosurgical setting.

Acknowledgements: All procedures in this work were approved by institutional IRB (Hong Kong Hospital Authority Research Ethics Committee for Kowloon Central/Kowloon East Clusters, KC/KE-21-0012/ER-2). This work is supported by The Hong Kong Research Grants Council (14114721, 14119022, N_CUHK456/21, R4022-18F), CUHK RSFS (3133184), CUHK Faculty of Medicine Direct Grants (4054652, 4054710), and GD-TCM Translational Research Fund (7105730).

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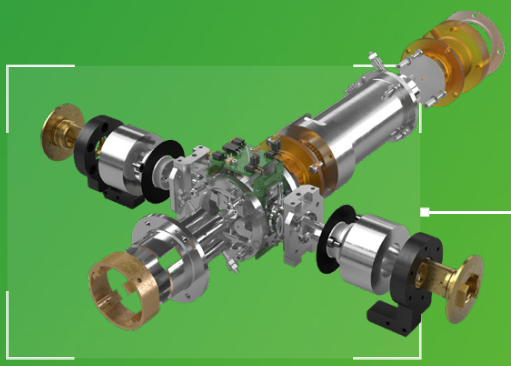

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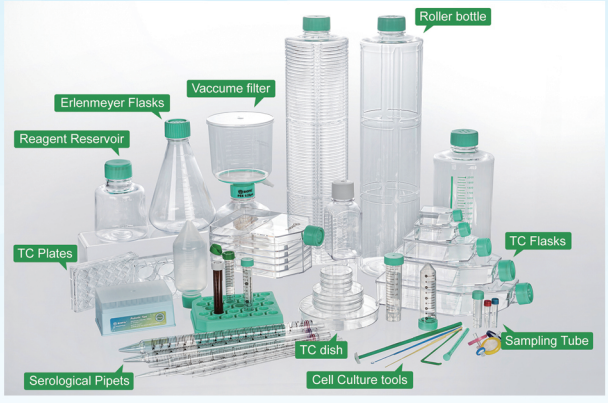

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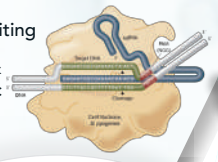

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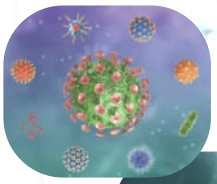

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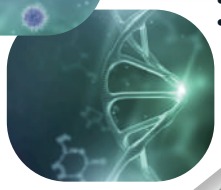

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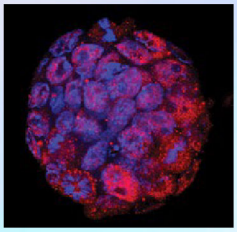

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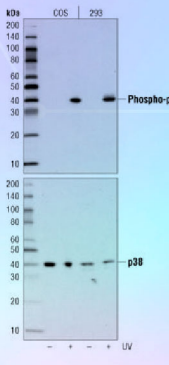

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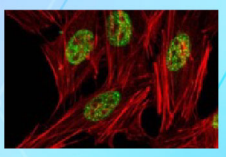

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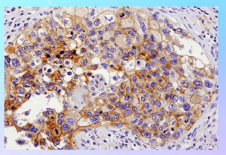

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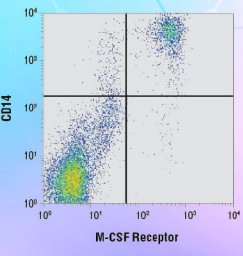

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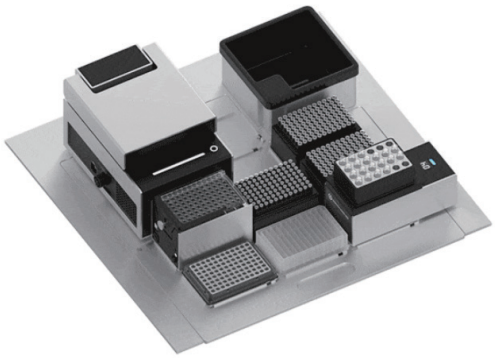

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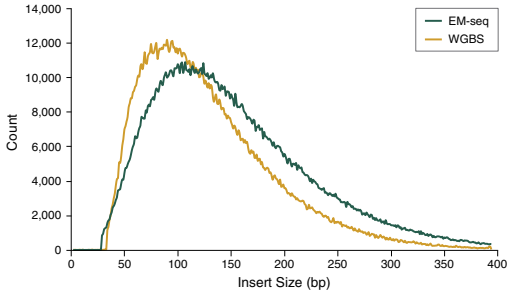

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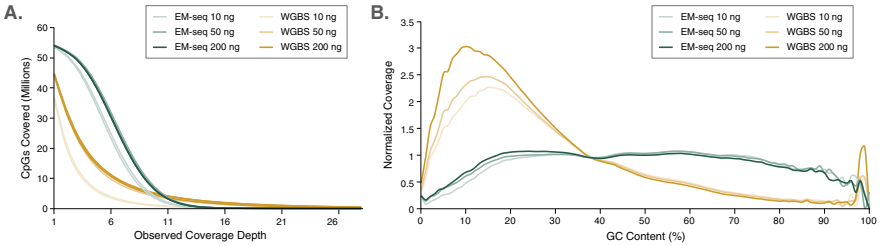

采用 Covaris S2 仪器将 10 ng、50 ng 和 200 ng 不同起始量的人 NA12878 基因组 DNA 打断至 300 bp，同时作为 EM-Seq 和 WGBS 建库的起始样本。对于 WGBS 方法，使用 NEBNext Ultra II DNA 进行建库，随后采用 Zymo Research EZ DNA Methylation-Gold™ 试剂盒进行重亚硫酸盐转化。两个文库均使用 Illumina NovaSeq® 6000（2 X 100 bases）测序，使用 bwa-meth 0.2.2 将测序数据与 hg38 进行比对。

A: CpG 位点检测：通过分析 3.24 亿双端数据得到 EM-Seq 和 WGBS 文库的 CpG 位点覆盖度，其中每条链都独立计数，最终得到最多 5600 万个可能的 CpG 位点。结果显示：EM-Seq 在更低测序深度能检测到更多的 CpG 位点。

B: GC 覆盖度：使用 Picard 2.17.2 计算 GC 覆盖度，图中显示不同 GC 含量时（0-100%），标准化后覆盖度的分布情况。结果显示：EM-Seq 文库显著提高 GC 覆盖度的均一性，无 AT 过度测序，也无 GC 测序不足，后两项都是 WGBS 文库的典型缺陷。

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Novogene is committed to pioneering applications of cutting-edge molecular biology technology and high-performance, computing in the fields of life science research and human health. Our vision is to become the global leader in providing genomic services and solutions.

Core Services

- Genome Sequencing
- Transcriptome Sequencing
- Metagenomics
- Epigenomics
- Pre-made Library Sequencing

NEW TECHNOLOGIES
NEW PROMOTION

NovaSeq™ X Plus **Pacbio Revio**

Areas where Novogene provides service

7 laboratories **18** subsidiaries Our business covers around **70** countries across **6** continents

For more information, please contact:

website: www.novogene.com/amea-en/
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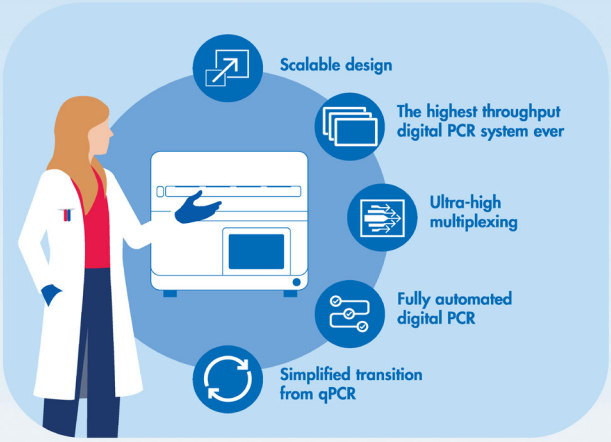
- Flexible and scalable instruments for various throughput need

QIAcuity™ Fully integrated nanoplate based digital PCR
QIAcuity One/Four/Eight, 2/5plex

Features and benefits



Applications

Rare mutation detection
dPCR LNA Mutation Assays

Pathogen detection
dPCR Microbial DNA Detection Assays
QIAcuity UCP Probe PCR Kit

Copy number variation
dPCR Copy Number Assays

Gene expression
QuantiNova LNA PCR Assays

miRNA detection
miRCURY LNA miRNA PCR Assays

Cell and gene therapy
QIAcuity Cell and Gene Therapy (CGT) dPCR Assays
QIAcuity Residual DNA Quantification Kits

Wastewater testing
QIAcuity OneStep Advanced Probe Kit

Liquid biopsy
dPCR LNA Mutation Assays
dPCR CNV Probe Assays

GMO detection
dPCR Copy Number Assays

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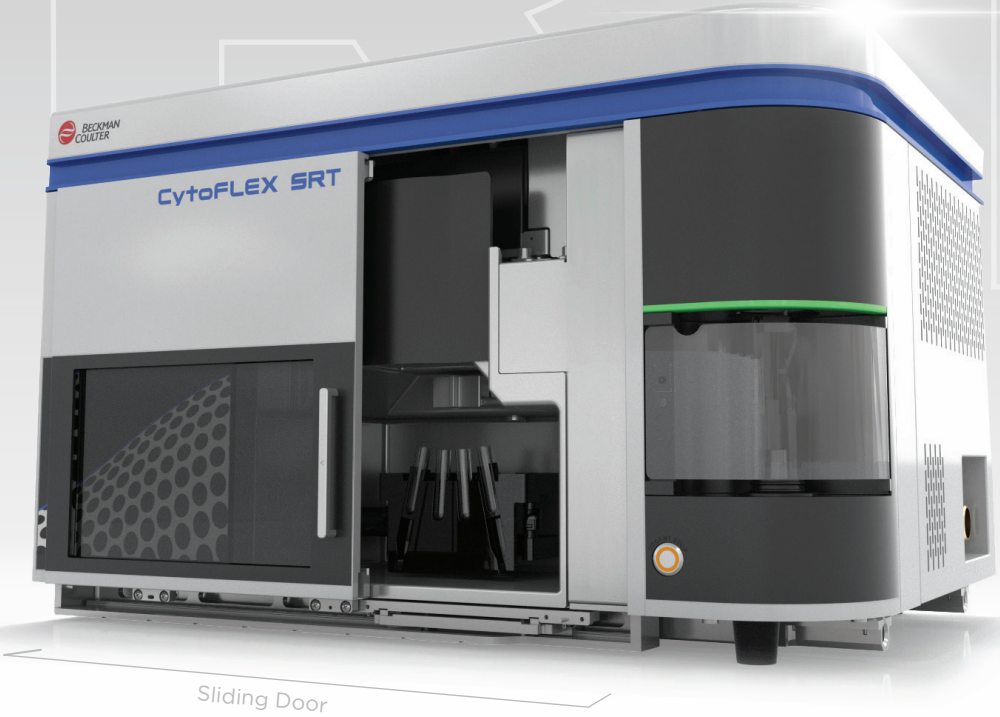

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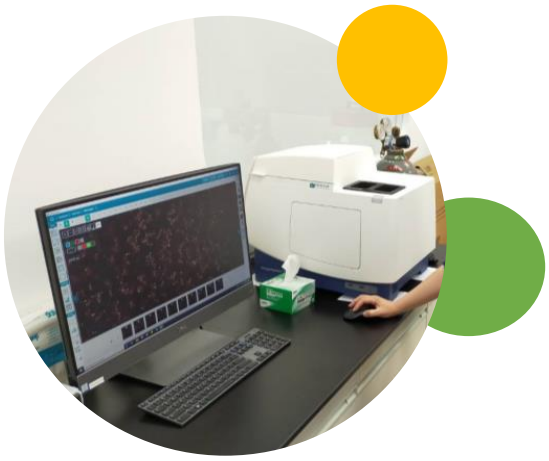

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Notes:

Map of Meeting Venue

G/F, Lo Kwee-Seong Integrated Biomedical Sciences Building