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The Chinese University of Hong Kong
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Li Ka Shing Institute of Health Sciences Progress Report
李嘉誠健康科學研究所進度報告
2023

PROGRESS REPORT



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

HEALTH
Li Ka Shing Institute of Health Sciences
李嘉誠健康科學研究所

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EXECUTIVE SUMMARY
報告摘要

In 2023, researchers at the Institute once again demonstrated their unwavering commitment to advancing the frontiers of scientific research. Their efforts, aligned with the Institute's mission to translate scientific discoveries into clinical applications, have significantly benefited patients and positively impacted society. This year, several of our Principal Investigators received prestigious awards, highlighting both their exceptional contributions and the Institute's ongoing dedication to excellence in medical research.

I am deeply honoured to have been elected a member of the Chinese Academy of Sciences (CAS) in recognition of my work in non-invasive prenatal testing and liquid biopsy for cancer detection. The CAS is the national academy for natural sciences as well as the highest advisory body for natural sciences and technology in China. Its members are elected based on their significant contributions to these fields.

Professor Siew Ng was named a New Cornerstone Investigator in Biology and Biomedical Sciences by the New Cornerstone Investigator Foundation, marking her as the first Hong Kong clinician-scientist to receive this prestigious recognition. This accolade, which includes a five-year grant, supports her groundbreaking research on diet-microbiome-immune interactions aimed at developing novel therapeutic targets for chronic inflammatory and immune-mediated diseases. Her pioneering work, including the introduction of faecal microbiota transplantation (FMT) to Hong Kong, has significantly advanced the understanding and treatment of Inflammatory Bowel Disease (IBD) in Asia.

I would also like to congratulate Professor Ling Qin and Professor Jun Yu, who were elected Foreign Members of the Academia Europaea, for outstanding achievements in their respective fields. Professor Qin's innovative work on biodegradable metals for orthopaedic applications and Professor Yu's research on digestive diseases, such as gastrointestinal cancers, gut microbiota, and fatty liver disease, were both widely recognised. Founded in 1988, the Academia Europaea is a pan-European academy dedicated to advancing and promoting excellence in scholarship across a wide range of disciplines, including medicine, natural sciences, and technology. The Academy's members comprise more than 80 Nobel laureates, reflecting its high standards of academic excellence.

Furthermore, Professor Jun Yu was elected a member of the Hong Kong Academy of Sciences (ASHK) for her contributions to gastrointestinal cancer research and therapy. Established in 2015 by leading local scientists, the Academy aims to advance science and technology in Hong Kong and elevate its status as a scientific hub. Membership in the Academy is the highest honour for scientists who have made significant advancements in science and technology in the city.

On the scientific front, Professor Allen Chan, Professor Peiyong Jiang, Dr. Jacky Lam and I used nasopharyngeal cancer (NPC) as a model to study the significance of positive cancer DNA tests in individuals without identifiable cancer. Through two rounds of screening approximately 20,000 volunteers over four years, we showed that plasma Epstein-Barr virus (EBV) DNA analysis could effectively detect early asymptomatic cancers and significantly reduce mortality. Importantly, individuals initially with positive results but no detectable cancer had a substantially higher risk of developing NPC later. This suggests that cancer-associated DNA changes can indicate both current asymptomatic cancers and future cancer risk. The findings have significant implications for developing plasma DNA-based tumour markers and were published in *NEJM Evidence* (July 2023).

In a recent study, Professor Jun Yu and her research team explored the preventive effects of dietary fibre on non-alcoholic steatohepatitis (NASH), a severe progression of non-alcoholic fatty liver disease (NAFLD). They discovered that soluble fibre is more effective than insoluble fibre in preventing NASH in mice, as soluble fibre is metabolised by gut microbes, leading to the production of beneficial metabolites. Using ^{13}C-labeled inulin as a tracer, the team identified specific gut bacteria and metabolites involved in the process. Notably, *Parabacteroides distasonis* was



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found to be the most effective in suppressing NASH by producing pentadecanoic acid, which restores gut barrier function and reduces liver inflammation. These findings, published in *Nature Microbiology* in August 2023, highlight the potential of a soluble fibre-microbe-metabolite axis in preventing NASH.

Professor Siew Ng and her research team conducted a large-scale, double-blind, randomised, placebo-controlled trial (RECOVERY) to evaluate the effectiveness of an oral synbiotic preparation (SIM01) in alleviating symptoms of post-acute COVID-19 syndrome (PACS). The trial results demonstrated that SIM01 significantly alleviated key PACS symptoms, including fatigue, cognitive difficulties, memory loss, gastrointestinal issues, and general unwellness. The treatment also enhanced gut microbiota diversity, promoted beneficial bacteria, and inhibited pathogenic bacteria, thereby maintaining microbial balance. These findings, published in *The Lancet Infectious Diseases* in December 2023, offer important insights for the treatment of PACS.

In diabetes research, Professor Juliana Chan and Professor Ronald Ma led a pioneering study aimed at developing a novel method to identify individuals at risk of diabetic kidney disease (DKD) and kidney failure using blood methylation markers. They found that these markers are strongly associated with kidney function and can predict the future decline in kidney function more accurately than traditional clinical risk factors. The study also highlighted key genes with differential methylation in DKD, reinforcing their functional relevance. A practical calculator based on these markers was created to aid in early intervention for high-risk patients, significantly enhancing preventive care. The findings were published in *Nature Communications* in May 2023.

Professor Ronald Wang and his research team addressed the challenge of treating nausea and vomiting in pregnancy, with severe cases leading to pregnancy terminations. Through a randomised controlled trial, the team demonstrated that both active acupuncture and doxylamine-pyridoxine were modestly effective in reducing symptoms and improving quality of life compared to sham acupuncture and placebo. Notably, the combination of both treatments provided the most significant benefit. Given the under-prescription of anti-nausea drugs due to concerns about birth defects, acupuncture presents a promising alternative for pregnant women reluctant to use pharmacologic treatments. These findings were published in *Annals of Internal Medicine* in June 2023.

We extend our heartfelt gratitude to the Li Ka Shing Foundation for its unwavering support in expanding and upgrading the research space and the new Experimental Animal Core Facility at the Li Ka Shing Medical Sciences Building. With renovations completed by the end of 2023, we believe these enhancements will significantly enhance the research and clinical translational efforts of our Principal Investigators.

李嘉誠健康科學研究所的研究人員在2023年再次展現了他們推動科學研究的堅定承諾。他們的努力與研究所將科學發現轉化為臨床應用的使命緊密相連，造福患者和社會。今年，我們的多位首席研究員榮獲多項權威獎項，不僅突顯了他們的卓越貢獻，更展現了研究所對醫學研究卓越追求的持續承諾。

本人非常榮幸因在無創產前檢測及癌症液體活檢領域的研究工作，當選為中國科學院院士。中國科學院是中國國家自然科學技術研究領域的最高權威諮詢機構，院士因其在各自科學領域的重大貢獻而被選出。

黃秀娟教授獲新基石科學基金會評選為「生物與醫學科學」領域的新基石研究員，成為香港首位獲此殊榮的醫生科學家。該研究項目獲得為期五年的資助，支持她在飲食、腸道菌群與宿主免疫機制相互作用方面的開創性研究，致力為慢性炎症和免疫功能障礙開發個性化活菌治療新方案。她的前瞻性工作，包括將腸道微生物群移植（FMT）引入香港，極大推動了亞洲對炎症性腸病（IBD）的理解與治療。

在此，我謹向秦嶺教授和于君教授表示祝賀，他們因各自領域的傑出成就而當選為歐洲科學院外籍院士。秦教授在生物降解金屬於骨科應用方面的創新研究，以及于教授在消化系統疾病，包括胃腸癌、腸道微生物群和脂肪肝病的研究，均獲得了高度認可。歐洲科學院成立於1988年，作為一個泛歐洲學術機構，致力於推動醫學、自然科學及技術等多領域的卓越研究。該學院的院士中有超過80位諾貝爾獎得主，這充分彰顯了其卓越的學術水準。

此外，于君教授因其在胃腸癌研究及治療領域的卓越貢獻，當選為香港科學院院士。香港科學院由本地頂尖科學家於2015年成立，致力於推動香港的科學技術發展，並提升香港作為科學中心的國際地位。成為香港科學院院士是對在本地科學技術進步方面作出重大貢獻的科學家所授予的最高榮譽。

在科研方面，陳君賜教授、江培勇教授、林偉棋醫生與本人利用鼻咽癌（NPC）作為模型，深入探討血漿中出現癌症DNA但未能即時檢測出癌症的長期臨床意義。研究團隊在四年內對大約兩萬名志願者進行了兩輪篩查，結果顯示，血漿EB病毒（EBV）DNA分析能有效檢測出早期無症狀癌症，並顯著降低死亡率。值得注意的是，那些最初檢測結果為陽性但未檢測出癌症的個體，後來患上鼻咽癌的風險顯著增加。這些發現表明，癌症相關的DNA變化不僅能提示無症狀性的癌症，還能預示未來的癌症風險。這一研究對基於血漿DNA的腫瘤標誌物的發展具有重大意義，並已於2023年7月在《新英格蘭醫學證據》期刊上發表。

在近期的研究中，于君教授及其團隊探討了膳食纖維對預防非酒精性脂肪性肝炎（NASH）的效果，這是非酒精性脂肪肝病（NAFLD）的一種嚴重病變。研究發現，與不溶性纖維相比，可溶性纖維在預防小鼠NASH方面效果更為顯著，因為可溶性纖維經腸道微生物代謝後會生成有益的代謝物。研究團隊使用碳-13標記的菊粉作為示踪劑，確定了參與該過程的特定腸道細菌和代謝物。尤其值得注意的是，研究發現狄氏副擬桿菌能夠通過產生十五烷酸來抑制NASH，該酸有助於恢復腸道屏障功能並減少肝臟炎症。這些發現突顯了可溶性纖維－微生物－代謝物軸在預防NASH中的潛在價值，並於2023年8月發表在《自然微生物學》期刊上。

黃秀娟教授及其研究團隊進行了一項大規模雙盲、隨機、安慰劑對照試驗（RECOVERY），評估口服合生製劑SIM01在緩解新冠後遺症（PACS）症狀方面的效果。試驗結果顯示，SIM01能顯著改善疲勞、認知障礙、記憶力減退、胃腸問題及全身不適等PACS的核心症狀。此外，該治療還增加了腸道微生物群的多樣性，促進有益菌群生長，同時抑制致病菌，從而有效維持腸道微生態的平衡。這些發現為PACS的治療提供了關鍵見解，並於2023年12月發表在《柳葉刀傳染病》期刊上。

在糖尿病研究領域，陳重娥教授和馬青雲教授領導一項開創性的研究，旨在利用血液中的甲基化標誌物來識別罹患糖尿病腎病（DKD）及腎衰竭風險的高危個體。他們發現，這些標誌物與腎功能密切相關，且比傳統臨床風險因素更準確地預測腎功能的未來下降。研究還揭示了在DKD患者中表現出差異甲基化的關鍵基因，強調了其功能的重要性。基於這些標誌物，研究團隊開發了一個實用的風險計算器，旨在幫助早期識別和干預高風險患者，從而顯著提升預防性護理的效果。該研究於2023年5月發表在《自然通訊》期刊上。

黃志超教授及其研究團隊針對妊娠期噁心和嘔吐的治療挑戰展開了研究，尤其嚴重情況可能導致終止妊娠。通過一項隨機對照試驗，團隊證實針灸與多西拉敏－吡哆醇相比假針灸和安慰劑組合均能有效減輕症狀並改善患者的生活質量，治療效果顯著。由於對出生缺陷的擔憂，抗噁心藥物的處方量往往不足，而針灸則為不願採用藥物治療的孕婦提供了一種具潛力的替代方案。這項研究成果已於2023年6月發表在《內科醫學年鑒》期刊上。

最後，我們衷心感謝李嘉誠基金會對研究空間擴展與升級，以及李嘉誠醫學大樓全新實驗動物核心設施建設的持續支持。隨著翻新工程於2023年底順利完成，我們深信這些改進將大幅加強首席研究員的科研發展及臨床轉化工作。



Steering Committee
督導委員會

GOVERNANCE AND ADMINISTRATION

管治與行政

The Steering Committee of the Li Ka Shing Institute of Health Sciences (LiHS) was formed in 2007. The seventeenth meeting of the Steering Committee was held on 29 December 2023 and was attended by the committee members who gave invaluable recommendations on the future development and direction of the Institute.

李嘉誠健康科學研究所督導委員會於2007年正式成立。本年度的督導委員會會議於2023年12月29日舉行，會上各成員就研究所的未來發展發表了寶貴的意見。

Francis Chan 陳家亮

Chairman 主席 (January 2013 - January 2024)

Dean of Medicine, CUHK
香港中文大學醫學院院長

Choh-Ming Li Professor of Medicine & Therapeutics, CUHK Director
香港中文大學卓敏內科及藥物治療學講座教授



Philip Chiu 趙偉仁

Chairman 主席 (From February 2024)

Dean of Medicine, CUHK
香港中文大學醫學院院長

Shun Hing Education and Charity Fund Professor of Robotic Surgery, CUHK
香港中文大學信興教育及慈善基金機械人外科教授

Director, Lui Che Woo Institute of Innovative Medicine, CUHK
香港中文大學呂志和創新醫學研究所所長

Director, Multi-Scale Medical Robotics Center, CUHK
香港中文大學醫療機械人創新技術中心主任

Director, Chow Yuk Ho Technology Centre for Innovative Medicine, CUHK
香港中文大學周毓浩創新醫學技術中心主任





Dennis Lo 盧煜明

Member 成員

Associate Dean (Research), Faculty of Medicine, CUHK
香港中文大學醫學院副院長（研究）

Li Ka Shing Professor of Medicine, CUHK
香港中文大學李嘉誠醫學講座教授

Chairman, Department of Chemical Pathology, Faculty of Medicine, CUHK
香港中文大學化學病理學系系主任

Director, Li Ka Shing Institute of Health Sciences, CUHK
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Professor of Chemical Pathology, CUHK
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Director, State Key Laboratory of Translational Oncology, CUHK
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Wai-yee Chan 陳偉儀

Member 成員

Pro-Vice-Chancellor/Vice-President (Strategic Developments), CUHK
香港中文大學副校長（策略發展）

Director, Institute for Tissue Engineering and Regenerative Medicine (iTERM), CUHK
香港中文大學組織工程與再生醫學研究所所長

Li Ka Shing Professor of Biomedical Sciences, School of Biomedical Sciences, CUHK
香港中文大學生物醫學學院李嘉誠生物醫學講座教授

Tony Mok 莫樹錦

Member 成員

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Li Shu Fan Medical Foundation Professor of Clinical Oncology, CUHK
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Ling Qin 秦嶺

Member 成員

Assistant Dean (Mainland Affairs), Faculty of Medicine, CUHK
香港中文大學醫學院助理院長（內地事務）

Director, Musculoskeletal Research Laboratory, CUHK
香港中文大學骨關節肌肉研究實驗室主任

Director, CUHK Hong Kong-Shenzhen Innovation and Technology Research Institute (Futian)
香港中文大學深圳創新研究院（福田）院長

Director, Innovative Orthopaedic Biomaterials and Drug Translational Research Laboratory of Li Ka Shing Institute of Health Sciences, CUHK
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Choh-Ming Li Professor of Department of Orthopaedics and Traumatology, Faculty of Medicine, CUHK
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Cecilia Leung

Secretary 秘書

Assistant Secretary of Li Ka Shing Institute of Health Sciences, CUHK
香港中文大學李嘉誠健康科學研究所助理秘書長



Executive Committee
執行委員會

The Executive Committee of the Li Ka Shing Institute of Health Sciences was established by the Steering Committee of the Institute. It is an executive and administrative body discharging its responsibilities of activities and affairs of the Institute. The Executive Committee acts and makes executive and administrative decisions on behalf of the Steering Committee and to report the decisions to the Steering Committee on regular basis.

The Executive Committee held its annual meeting on 7 May 2024 and was attended by the Committee members who gave invaluable recommendations with respect to the execution and administration of activities and affairs of the Institute.

李嘉誠健康科學研究所執行委員會由研究所督導委員會成立。執行委員會負責為研究所行政和決策作出方向性的指引，以履行研究所的活動和事務職責。執行委員會同時亦代表指導委員會向研究所作出管理和行政的決定，並定期向指導委員會匯報工作進度和決策記錄。

執行委員會於2024年5月7日舉行年度會議，各委員會成員就著研究所的未來執行和管理方向發表了寶貴的建議。

Dennis Lo 盧煜明

Chairman 主席

Associate Dean (Research), Faculty of Medicine, CUHK
香港中文大學醫學院副院長（研究）

Li Ka Shing Professor of Medicine, CUHK
香港中文大學李嘉誠醫學講座教授

Chairman, Department of Chemical Pathology, Faculty of Medicine, CUHK
香港中文大學化學病理學系系主任

Director of LiHS, CUHK
香港中文大學李嘉誠健康科學研究所所長

Professor of Chemical Pathology, CUHK
香港中文大學化學病理學講座教授

Director of State Key Laboratory of Translational Oncology
香港中文大學轉化腫瘤學國家重點實驗室主任



Jun Yu 于君

Member 成員

Assistant Dean (Mainland Affairs), Faculty of Medicine, CUHK
香港中文大學醫學院助理院長（內地事務）

Professor, Department of Medicine and Therapeutics, Faculty of Medicine, CUHK
香港中文大學內科及藥物治療學系教授

Director, Institute of Digestive Disease, CUHK
香港中文大學消化疾病研究所主任

Director, Research Laboratory of Institute of Digestive Disease, CUHK
香港中文大學消化疾病研究實驗室主任

Director, State Key Laboratory of Digestive Disease, CUHK
香港中文大學消化疾病研究國家重點實驗室主任



Siew Ng 黃秀娟

Member 成員



Assistant Dean (Development), Faculty of Medicine, CUHK
香港中文大學醫學院助理院長 (發展)

Croucher Professor of Medical Sciences, CUHK
香港中文大學裘槎醫學科學教授

Professor, Department of Medicine and Therapeutics, Faculty of Medicine, CUHK
香港中文大學內科及藥物治療學系教授

New Cornerstone Investigator
新基石研究員

Director, Microbiota I-Center (MagIC)
香港微生物菌群創新中心總監

Ronald Ma 馬青雲

Member 成員



Assistant Dean (External Affairs), Faculty of Medicine, CUHK
香港中文大學醫學院助理院長 (外務)

S.H. Ho Professor of Diabetes, CUHK
香港中文大學何善衡糖尿科教授

Professor, Department of Medicine and Therapeutics, Faculty of Medicine, CUHK
香港中文大學內科及藥物治療學系教授

Head (Academic Affairs), Division of Endocrinology and Diabetes, CUHK
香港中文大學內分泌及糖尿病科主任

Professor (by Courtesy), School of Biomedical Sciences, CUHK
香港中文大學生物醫學學院教授 (禮任)

Co-director, CUHK-SJTU Joint Research Centre in Diabetes Genomics and Precision Medicine, CUHK
香港中文大學–上海交通大學糖尿病基因組與精準醫療聯合研究中心主任

Steering Committee, Hong Kong Institute of Diabetes and Obesity, CUHK
香港中文大學香港糖尿病及肥胖症研究所督導委員

Cecilia Leung

Secretary 秘書

Assistant Secretary of Li Ka Shing Institute of Health Sciences, CUHK
香港中文大學李嘉誠健康科學研究所助理秘書長

LIHS OFFICE
研究所辦公室

As of December 2023, a total of 27 staff members in the LiHS Office were in post, including administrative, scientific, research and technical staff. During the reporting period, the LiHS office oversaw the general administration of the Institute, the Li Ka Shing Medical Sciences Building, and various core facilities, including the Biomedical Computing Centre, the Molecular Biology Core Facilities, and the Cell Biology Core Facilities.

截至2023年12月底，研究所辦公室共已聘任27名僱員，包括行政、科學、研究及技術人員，負責研究所的日常運作，並支援重點科研設施的運作，包括生物醫學計算機中心、分子生物學重點科研設施、和細胞生物學重點科研設施。



Director and Administration Team
研究所所長與行政團隊

In this photo, in the middle of the front row is Professor Dennis Lo, Cecilia Leung (fourth from the left), and other administration team members.

相片中前排中間為盧煜明教授、梁欣欣女士(左四)及其他行政團隊成員。

THE LI KA SHING MEDICAL SCIENCES BUILDING

李嘉誠醫學大樓



The Li Ka Shing Institute of Health Sciences was housed inside the 11-storey Li Ka Shing Medical Sciences Building. As of December 2023, there were approximately 583 research personnel working in the Building. Principal Investigators and their research groups were allocated research space inside the Building following assessment by the Faculty's Research Space Allocation Committee, based on their track records in research. In addition, several multi-disciplinary research laboratories were allocated on a departmental and/or strategic basis.

With the full support from the University and the Faculty, the Institute will recruit additional top-notched research scientists in order to enhance our competitiveness in research.

李嘉誠健康科學研究所建於樓高11層的李嘉誠醫學大樓內。截至2023年12月，約有583名科研人員於大樓內工作。醫學院研究空間分配委員會根據各項目負責人及其隊伍的研究成果分配各隊伍在研究所內可使用的研究空間。另外，委員會亦根據所屬部門及策略性原則分配各個多範疇的實驗室。

在大學和醫學院的全力支持下，研究所將招聘更多出類拔萃的科學家以提升我們的科研實力。

RESEARCH FACILITIES

研究設施

The Institute is committed to the provision of a good research environment for cutting-edge biomedical research projects and technological innovations. The diverse facilities at the Institute have enabled researchers from the University and the Faculty of Medicine to accomplish their dreams in research.

本研究所致力為走在時代尖端的研究項目及創新技術提供良好的科研環境。所內的多元化設施讓香港中文大學及其醫學院的研究員能夠專注實驗，開拓及實現他們的科研夢想。

LI KA SHING TRANSLATIONAL OMICS PLATFORM

李嘉誠轉化組學平台



The Li Ka Shing Translational Omics Platform (LKS TOP) aims to build a state-of-the-art, multi-omics platform specialising in cutting-edge genomics, proteomics, and metabolomics. The Platform consists of best-in-class research facilities that accelerate screening and biomarker discovery, in the fields of precision medicine, microbiota and nutrition sciences, drug development for emerging infectious diseases, cardiometabolic diseases, cancer, childhood diseases, and Traditional Chinese medicine.

李家誠轉化組學平台（LKS TOP）旨在建立一個專門利用尖端科技去研究基因組學、蛋白質組學和代謝組學的先進多組學平台。這平台包括一系列世界頂尖的科研設施 ，加速篩選和發現生物標誌物，特別適用於精準醫學、微生物群和營養科學、新興傳染病藥物開發、心血管代謝疾病、癌症、兒童疾病和中醫藥領域。

The Platform consists of two mass spectrometry systems: the Thermo Scientific TSQ Altis Triple Quadrupole and the Thermo Scientific Orbitrap Eclipse Tribrid. The TSQ Altis utilises the triple quadrupole technology to deliver reliable performance in targeted sample quantification and monitoring multi-reaction mixtures. It is also the recommended routine system for daily analyte quantification analysis.

平台包括Thermo Scientific TSQ Altis三重四極桿質譜儀和Thermo Scientific Orbitrap Eclipse四極桿-線性離子阱-電場軌道阱三合一質譜儀。TSQ Altis配備了三重四極桿技術，能可靠地靶向定量樣本和在多重反應監測中提供高性能，使其成為研究人員日常定量分析的有效系統。



Thermo Scientific TSQ Altis Triple Quadrupole Liquid Chromatography – Mass Spectrometer

Thermo Scientific TSQ Altis 三重四極桿液相色譜-質譜聯用儀



Thermo Scientific Orbitrap Eclipse Tribrid Liquid Chromatography – Mass Spectrometer

Thermo Scientific Orbitrap Eclipse 四極桿-線性離子阱-電場軌道阱三合一液相色譜-質譜聯用儀

The Orbitrap Eclipse is a three-in-one mass analyser that offers exceptional sensitivity and resolution. It allows the detection of low-abundance analytes and supports untargeted analysis by measuring numerous analytes simultaneously. The analyser can deliver robust performance for both qualitative and quantitative analyses for proteomics and metabolomics research.

Both mass spectrometers are coupled with an ultra-high performance liquid chromatography system (UHPLC), with an enhanced ability that can separate the target proteins or small molecules amongst complex mixtures.

Orbitrap Eclipse結合三種不同的質量分析器，提供卓越的靈敏度和分辨率，可以檢測稀有的分析物，並通過同時測量眾多分析物來作出非靶向分析。此質譜儀在蛋白質組學和代謝組學研究中提供了極優的定性和定量分析能力。

兩台質譜儀均與超高效能液相色譜系統(UHPLC)相結合，為它們提供了在複雜混合物中分離目標蛋白質或小分子的能力。

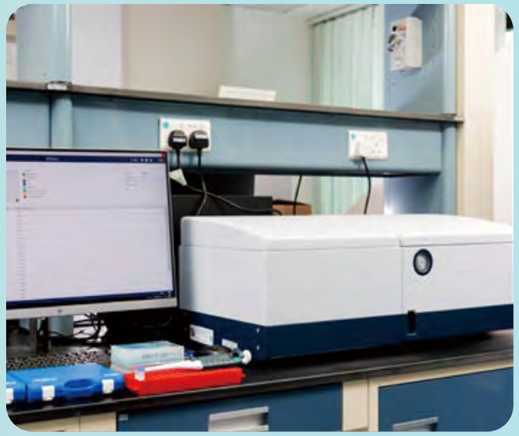
Two biotypers are also part of the Platform: the Bruker MALDI Biotyper Sirius and the IR Biotyper. Both biotypers offer robust, high-throughput and cost-effective taxonomical identification of micro-organisms. The MALDI Biotyper determines a micro-organism's species by analysing their unique proteomic fingerprint and matching it with the instrument's extensive reference library. Subsequently, the IR Biotyper can differentiate different micro-organisms to their sub-species levels by analysing their unique infrared absorption spectra, making it a powerful tool for investigating disease outbreaks.

平台還包括兩部微生物鑑定系統：Bruker基質輔助激光解吸電離質譜儀和Bruker傅立葉變換紅外光譜儀。兩部儀器均為快速、高通量和高效系統，常用於微生物的鑑定和分類。基質輔助激光解吸電離質譜儀通過分析微生物獨特的蛋白質體指紋，可以參考數據庫來確定未知微生物的物種。隨後，傅立葉變換紅外光譜儀通過分析微生物的紅外吸收光譜以確認其亞物種，使本儀器成為調查疾病爆發來源的強大工具。



Bruker MALDI Biotyper Sirius

Bruker 基質輔助激光解吸電離質譜儀

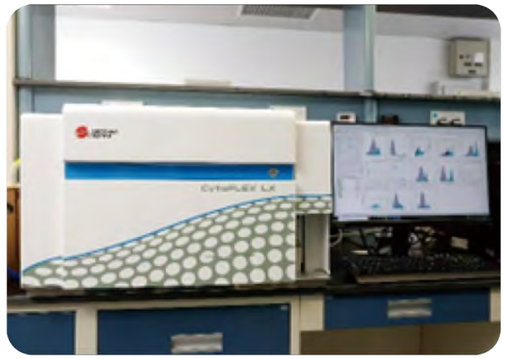


Bruker IR Biotyper

Bruker 傅立葉變換紅外光譜儀

Furthermore, our Platform is equipped with the Beckman Coulter CytoFlex LX flow cytometer. This cytometer measures cellular characteristics as cells pass through a laser beam in a fluidic stream. It is also capable of detecting up to 21 fluorescence parameters, the instrument allows the simultaneous analysis of multiple biomarkers within a single cell. In addition to cellular detection, this cytometer can also detect nanoparticles, such as extracellular vesicles, etc.

此外，我們平台配備了Beckman Coulter CytoFlex LX流式細胞儀。此細胞儀通過激光照射液體流中的細胞測量細胞特徵，並能夠同時檢測多達21個螢光參數及分析多個生物標記。除了檢測細胞外，此流式細胞儀還能夠檢測細胞外囊泡等納米粒子。



Beckman Coulter CytoFlex LX Flow Cytometer

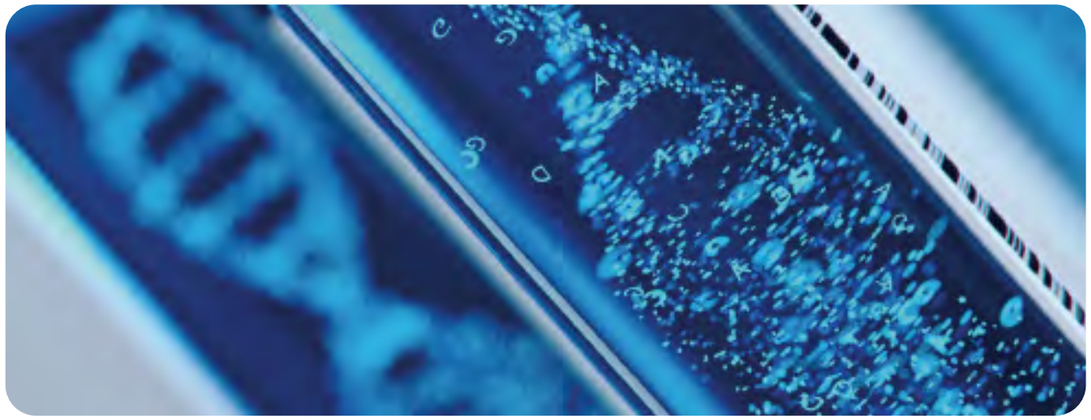
Beckman Coulter CytoFlex LX 流式細胞儀



Emulate Human Organ Emulation System
Emulate 仿真器官芯片和人體仿真系統

Additionally, our Platform is equipped with the Emulate Human Organ Emulation System, a powerful in *vitro* simulation system that can imitate the natural physiological environment and mechanical stretching on an organ-chip. Multiple types of organ-chips can be treated or co-cultured to mimic a range of diseases in different human organs such as gut barrier disruption, liver and kidney toxicity prediction, and drug-drug interactions predictions. This system provides higher specificity and sensitivity compared to traditional studies with animal models.

另外，我們的平台配備了Emulate人體仿真系統，是一個可以在器官芯片上模擬細胞自然生理環境及物理拉伸訊號的強大體外系統。本系統可運用多種器官芯片模仿和研究人體不同器官的一系列疾病，比如腸道屏障損壞，亦能對肝臟及腎臟的毒性預測、及判定藥物相互作用。比起傳統的動物實驗，本人體仿真系統能夠提供更高的特異性與敏感性。



Our Platform was officially opened to researchers of the Faculty of Medicine in 2021. Since then, a series of technical seminars and training workshops regarding our major instruments have been regularly held. Researchers can make online reservations for all of the instruments via the Li Ka Shing Institute of Health Sciences Registration and Booking System. In-house training on the basic operation of the equipment is provided by our institute staff members.

我們的平台於2021年起向香港中文大學醫學院的研究員正式開放，自此定期舉辦一系列介紹主要設備之技術研討會及訓練工作坊。研究人員可透過網上系統預約使用各種設備，平台亦會為研究人員提供儀器基本操作之培訓。

BIOMEDICAL COMPUTER CENTRE
生物醫學計算中心

The **Biomedical Computing Centre** (BCC) is one of the important facilities within the Institute and is an essential facility for supporting the next generation sequencing analysis (NGS), bioinformatics, data analysis, artificial intelligent (AI) based data analysis, bio-medical research and translational genomics are the focus of the Institute.

The Centre enhanced its data centre infrastructure (core network and structured cabling) and the overall computing servers, storage systems capacity, high-speed file systems and data management starting in 2021. All systems improvement and upgrade are based on the existing data centre infrastructural architecture, together with 12 IT equipment racks in the Research Data Centre (RDC) at Hong Kong Children's Hospital (HKCH).

The Centre continues the upgrade in 2023 and improve the equipment to provide better service and support to the researchers in performing their research jobs.

The major areas for this upgrade include:

- On top of the high performance computing servers for bio-informatics and AI acquired, a new cluster computing service was established and started servicing the researchers.
- The clustered computer nodes are now providing a total of 5,584 CPU Cores, 94TB of system memory and a total of 375.903 TFLOPS Processing Power. Our GPU systems have been integrated into a new GPU AI cluster computing architecture that can provide over 6 PetaFLOPS AI operations and 10 PetaOPS INT8 performance.
- At the same time, virtualization and other related cloud computing technologies were introduced. Services and resources can be released to users in a much flexible, highly efficient and secure manner.
- The Uninterrupted Power System (UPS) and its Li-Ion batteries were recently fine-tuned to support the operation of BCC and installed energy over 70kWh for long service years.

生物醫學計算中心是研究所內的重要設施之一，亦是支援次世代排序（NGS）、生物信息學、數據分析、人工智能數據分析，及研究生物醫學和轉譯基因組學的重要設施。

中心自2021年開始，就數據中心基礎設施（核心網絡和結構化佈線）以及對整體計算服務器、存儲系統容量、高速文件系統和數據管理等進行強化。所有系統優化、升級或整合均基於現有數據中心基礎設施架構以及使用香港兒童醫院內研究數據中心的12個IT設備機架完成。

在2023年, 中心將繼續完成有關的強化，並在強化的設施上，為研究人員提供更有效益的服務和支持。

是次中心設施及系統升級規劃的主要領域包括：

- 在中心的高性能計算服務器上，建立新的叢集計算服務，並開始為研究人員提供完整的服務。
- 中心計算架構內的服務器叢集現能提供整體5,584個CPU核心服務、94TB 內存和整體375.903 TFLOPS 的計算能力。我們的GPU系統已被集成到一個新的 GPU 人工智能叢集計算架構中，可以提供超過6 PetaFLOPS AI運作和 10 PetaOPS INT8的運算能力。
- 與此同時，我們也引入了虛擬化和其他相關的雲計算技術，讓新的服務和資源，可以以一個更精準，高效和安全的方式，提供給用戶。
- 不間斷電源系統（UPS）和其鋰離子電池亦已優化，以支持BCC的運行及裝機電量超過70kWh的長時間使用。

- With a simplistic and compact design for convenient maintenance, the advanced battery system has up to a 46% smaller footprint and is up to 20% lighter compared to the conventional lead-acid battery system.
- BCC will continuously explore the possibility to save more power in the future.
- A new data centre environmental monitoring system (EMS) was deployed in BCC.
- The system monitors data centre facilities and environments, critical conditions of their climate and equipment-sensitive commodities can be checked at any time.
- Besides monitoring, the EMS delivers alarms immediately via universal digital or analog exceptional inputs from the UPS, cooling modules and other systems at the data centre. Also, the EMS save all environmental data logs.

- 先進的電池系統採用簡單緊湊的設計，而且維護方便，與傳統鉛酸電池系統相比，佔地面積減少了46%，重量減輕了20%。
- BCC將繼續探索未來節省更多電量和能源的任何可能性。
- BCC亦部署了一個新的數據中心環境監控系統 (EMS)。
- 這個系統可以監測數據中心設備和環境，隨時檢查氣候條件和設備敏感的關鍵狀況。
- 除了監測之外，EMS 還可以從來自數據中心的UPS、冷卻模組和其他自動化裝置的通用數位或類比輸入的警報立即發送實時信號，亦會保存所有環境資料日誌。

32 + 12
local Remote

6 + 10
PetaFLOPS PetaOPS

>36
Petabytes Storage

94TB
RAM

5,584
CPU Cores &

157,696
CUDA Cores

100 GE & 200 GE
Backbone Network

25 GE to 100 GE
to Servers and Storage Systems

CORE FACILITIES
重點科研設施

The **Core Facilities** at the Institute include the following:
研究所內的**重點科研設施**包括：

Molecular Biology Core Facilities
分子生物學重點科研設施

Cell Biology Core Facilities
細胞生物學重點科研設施

MOLECULAR BIOLOGY CORE FACILITIES
分子生物學重點科研設施



The **Molecular Biology Core Facilities** provide a comprehensive molecular research platform for the researchers to perform a variety of fundamental yet crucial routine experimental procedures, including but not limited to, **Sample Quality Control, Transfection, Molecular Analysis**, and **Data Analysis**.

分子生物學重點科研設施致力為研究員提供全面的科研平台，進行**樣本的品質控制**、**基因轉染**、**分子分析**以及**數據分析**。

Sample Quality Control
樣本品質管制

Nucleic Acid Quantification and Quality Assessment
核酸定量分析和質量評估

Agilent 2100 Bioanalyzer
Agilent 2100 生物分析儀

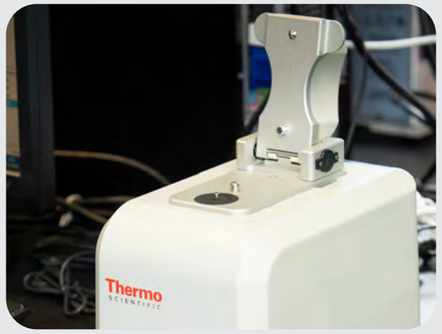


The Agilent 2100 Bioanalyzer is a microfluidic-based platform that provides simultaneous automated electrophoretic separation and detection of DNA/RNA/protein samples, and to provide data regarding their quantities and qualities in a swift and timely manner. Only with a tiny amount of samples, the system can provide qualification and quantification of the analytes. It is often used in a wide range of applications, including but not limited to gene expression analyses, RNA integrity evaluation, sizing of DNA fragments, and protein characterization. Thus, the system is highly favoured by researcher. It serves as a powerful analytical tool for quality control workflows across various life science research applications, from next-generation sequencing to biopharmaceutical development.

基於微流控技術， Agilent 2100 生物分析儀提供自動化的電泳分離和生物分子檢測，用以快速評估樣本的品質和濃度。這套系統只需少量的樣本，便能提供生物分子的定量和純度分析。它被廣泛應用於基因表達分析、RNA完整性評估、DNA片段大小測量和蛋白質表徵研究等多種領域。因此，它能成為一個廣受歡迎的分子分析工具，應用在各種生命科學領域的品質控制流程，包括新一代基因測序及生物製藥開發。

Thermo Fisher Scientific Nanodrop ND-1000 & ND-2000 Spectrophotometers

Nanodrop分光光度計



The NanoDrop Spectrophotometer is a compact instrument designed for the rapid and accurate quantification of nucleic acids, proteins, and other biomolecules. It utilises a patented sample retention system that comes with a minimal sample volume requirement (as low as 0.5 µL). The spectrophotometer covers a wide range of UV-Vis wavelengths, thus allowing the measurement of sample purity and concentration without even the need for cuvettes. It features intuitive software for data analysis and includes pre-configured methods for the most common assays.

NanoDrop分光光度計能夠快速且準確地測量核酸、蛋白質和其他生物分子的濃度。它的樣品測量系統擁有一項獲得專利的設計，每次量度只需要少至0.5微升的樣本。此分光光度計涵蓋了廣泛的紫外-可見光波長，因此可在無需使用分光液槽的情況下量度樣本的純度和濃度。 它簡單易用的軟件已經包含常見分析方法的配置，更可方便用家進行數據分析。

Invitrogen Qubit 2.0 Fluorometer

Qubit 2.0 螢光定量儀



The Qubit 2.0 Fluorometer is a versatile instrument that can quantify DNA, RNA, and protein samples using fluorescence-based assays. Specific dyes that can minimize impurities have been utilised by the instrument to make accurate sample measurements. The device features an intuitive interface, automatic standard curve plotting, a built-in dilution calculator and data storage in the .csv format which facilitate the quantification with as little as 1 µL of samples within 5 seconds.

Qubit 2.0螢光定量儀是一款利用螢光原理定量DNA、RNA和蛋白質的多功能儀器。它使用的特定染料把雜質對於量度的影響減到最低。該設備具有簡單易明的界面、會智能繪畫標準曲線、內置稀釋計算器以及 .csv的儲存格式等，方便用家能在少於5秒內準確測量少至1微升的樣本。

Transfection
基因轉染

Electroporation
電脈衝穿孔

Amaxa Nucleofector II
電穿孔轉殖儀



The Amaxa Nucleofector II is a transfection device that utilises electrical pulses to effectively transfect nucleic acids and small molecules into a wide range of cell types, like primary cells and difficult-to-transfect cell lines. Equipped with pre-optimised transfection buffers as well as tailor-made programs for more than 100 cell types, the Nucleofector II is also armed with a closed system design to minimise contamination to facilitate highly efficient transfections with a high cellular viability rate. Its scalable sample capacities are also favoured by scientists for transfections that are crucial for advanced cell biology research, gene expression studies, cell engineering and more.

Amaxa Nucleofector II 是一種能有效地利用電脈衝將小分子（如DNA和RNA）輸送至細胞核或細胞質的轉染裝置，原代細胞和一些難以轉染的細胞都同時被支持。它配備針對100多種細胞預先優化的轉染程式，亦同時配有可擴展樣品容量和防止污染的封閉系統設計。本儀器被廣泛應用於細胞生物學研究、基因表達研究、細胞工程等領域。

Molecular Analysis
分子分析

Gene Expression Profiling, Analysis and Genotyping
基因表達譜及基因型態分析

To analyse genotyping, copy number variation, DNA methylation and gene expression profiling.

分析基因型態、拷貝數變異、基因甲基化及基因表達特徵分析。

Bio-Rad QX200 Droplet Digital PCR System

微滴式數位聚合酶鏈式反應系統



The Bio-Rad QX200 Droplet Digital PCR (ddPCR) system offers precise, absolute nucleic acid quantification without the need for any standard curves. By partitioning the samples into thousands of nanoliter-sized oil droplets, this technology enables reliable detection of rare mutations, copy number variations, and precise quantification of nucleic acids with high sensitivity and reproducibility. Applications include cancer research for detecting low-frequency mutations, viral load quantification in infectious diseases, and accurate gene expression analyses.

透過使用Bio-Rad QX200 Droplet Digital PCR（ddPCR）系統，用家無需設定和參考核酸濃度標準曲線，便能精確、絕對的定量核酸。通過將樣本分割成數千個納升大小的小油滴，這項技術能可靠地檢測罕見基因突變、拷貝數變異，並支持精確且帶有極高靈敏度及實驗可重現性的核酸定量。它的常見應用包括檢測癌症研究基因低頻突變，感染性疾病研究中的病原定量，以及準確的基因表達分析。

Ilumina iScan Microarray System

芯片掃描系統



The iScan system provides accurate data with high resolution for genome-wide association studies (GWAS), gene expression profiling, and methylation analysis. Its automation and scalability make it the suitable device for a diverse range of research applications, including the understanding of complex genetic diseases, novel biomarker discovery, and pharmacogenomics research etc.

iScan系統能為全基因組聯合分析(GWAS)、基因表達分析和甲基化分析提供高解析度、準確的數據。其自動化和可擴展性適用於不同的研究範疇，常用於對複雜遺傳疾病的理解、生物標記物發現和藥物基因組學研究等等。

Life Technologies QuantStudio 12K Flex Real-Time PCR

定量實時聚合酶鏈鎖反應儀



The QuantStudio 12K Flex Real-Time PCR System supports high-throughput quantitative PCR applications, accommodating 96-well or 384-well plates per run with interchangeable block formats for flexibility. It features advanced optical components that enable precise and sensitive detection across multiple fluorescence channels, supporting gene expression, genotyping, and copy number variation analyses with TaqMan and SYBR Green. The system also offers automated data analysis and comprehensive software for experiment setup, data interpretation, and result reporting.

QuantStudio 12K Flex 實時 PCR 系統支持高通量螢光核酸定量，其發熱模組具有可互換的模塊設計，每次實驗最多可以同時支持 96 或 384 個樣本。它先進的光學組件可以在多個螢光通道上同時進行精確靈敏的訊號收集。它現時被廣泛使用於以 TaqMan 和 SYBR Green 等螢光試劑進行的基因分型和拷貝數變異分析。該系統的軟件還提供自動化數據分類，方便用家設計實驗、分析數據和實驗結果。



Multi-purpose Imaging System

多功能成像系統

Bio-Rad ChemiDoc MP Imaging System

多色螢光及化學發光成像系統

The ChemiDoc MP Imaging System combines advanced gel/blot imaging capabilities with versatile detection methods i.e. fluorescence, chemiluminescence, and colorimetric detections. It supports a variety of fluorescent reporters in a multiplexed manner, providing the users with a wide breadth of versatility. Its auto focusing, exposure fine tuning and simplified sample previewing, and the support of stain-free protein workflows are all beloved merits of this instrument. The stain-free approach saves time by eliminating lengthy staining and destaining steps. It provides more accurate and efficient protein quantitation and preserves proteins for further analysis like mass spectrometry or Western blotting. In addition, the automatic recognition feature of the Smart Trays ensures hassle-free automatic selection of the correct protocols based on the imaging tray being used. This system is mainly used in protein/nucleic acid gel documentation, western blotting, and protein-ligand interaction analysis etc.

ChemiDoc MP 影像系統具有先進的成像能力，它透過使用螢光、化學發光以及比色法等多種方法對樣本探針進行顯影及分析，為研究人員使用時提供靈活性。它具有自動對焦、曝光和預覽等功能去簡化用家的設定。系統可支援無染色技術，能免除耗時的染色和脫色步驟，提供快捷、準確的蛋白質分析及定量。這項技術有助於提高重覆性，能保留蛋白質作質譜分析或蛋白免疫印迹分析。此外，智能托盤的自動識別功能可確保自動選擇正確的協議，無需人工干預。本儀器能智能地選擇實驗程序，無須用家手動調整。該系統被廣泛應用於蛋白質/核酸凝膠分析、免疫印跡和蛋白質-配體相互作用等實驗。

Bead-based Suspension Analysis

磁珠懸浮偵測

Bio-Rad Bioplex-200 Bead-based Suspension Array System

磁珠懸浮液相芯片系統



The Bio-Plex 200 System is a multiplex immunoassay platform that supports the detection and quantification of up to 100 analytes in a single sample run. It is a magnetic bead-based flow cytometric platform to measure and characterise biomolecules. The integrated liquid handling system enables automated sample acquisition. Each bead is interrogated by lasers for identification and quantification of the bound analytes. It is now widely used in the field of immunology and oncology for drug discovery, enabling our researchers to delineate complex biological systems.

Bio-Plex 200 系統是一台多重免疫分析儀，可在單樣本中檢測和定量多達 100 種分析物。它結合了磁珠分離法與流式細胞技術來分析及測量樣本。它有一個集成的液體處理系統可以自動完成樣本採集、識別和定量其所結合的分析物。本系統現被廣泛應用於免疫學、腫瘤學和藥物發現，幫助研究人員了解複雜的生物系統。

CELL BIOLOGY CORE FACILITIES

分子生物學重點科研設施

The **Cell Biology Core Facilities** provide a series of comprehensive cellular research platforms for cell-biology related work.

細胞生物學重點科研設施為研究員提供全面的研究設備以進行**細胞篩選**及**細胞培育**。



Cell Selection
細胞篩擇

Micro-dissection
顯微切割

Leica LMD7000
Laser Micro-dissector
激光捕獲顯微切割器



The Leica LMD 7000 is a laser microdissection system designed for precise tissue dissection, that enables the isolation of specific cells or regions through high-resolution imaging with its highly customisable cutting parameters. Its user-friendly software facilitates the high purity sample collection with minimal risks of contamination. The system supports the purification of samples from complex tissue environments that are frequently encountered in genomic, transcriptomic, and proteomic studies in the field of cancer research, neuroscience, and developmental biology.

Leica LMD 7000 是一款雷射顯微切割系統，專為精確組織切割而設。它能夠透過設定高解析度成像和可自訂的切割參數來分離組織切片上特定的細胞或區域。此外，它具有簡單易用的軟件，方便用家準確地採集高純度樣本，減少對樣本的污染風險。此系統亦可以從複雜的組織環境中提取純淨、高品質的樣本，有助於對癌症、神經科學和發育生物學中的基因組、轉錄組和蛋白質組的研究。

Cellular Analysis & Collection
細胞分析與收集

BD FACSAria Fusion Flow Cytometry Cell Sorter
流式細胞分選儀



The BD FACSAria Fusion Flow Cytometry Cell Sorter provides a precise and efficient separation of complex cell populations. It enables the simultaneous detection and sorting of cells, up to 18 parameters, ensuring an in-depth phenotypic analysis. With gentle, targeted sorting that minimises impact on cell viability. The certified biosafety cabinet features a biocontainment design that ensures the safe handling of hazardous samples. This system is compatible with various sample types of collection devices, including single-cell deposition, benefiting researchers in field of immunology, stem cell biology, and cancer research in their downstream studies.

BD FACSAria Fusion流式細胞分選儀能對複雜細胞族群進行精確且高效的分離。它能夠同時偵測多達18個細胞參數，以進行深入的表型分析。透過溫和、針對性的分選，本儀器能以最大程度減少實驗過程中對細胞活力的影響。此外，它具有受認證的生物安全功能和生物隔離設計，能確保使用者可以對危險樣本進行安全處理。該系統兼容各種樣本收集設備，包括單細胞沉積等。它有助於免疫學、幹細胞生物學和癌症的研究，有助研究人員的下游研究作出分析。



Cell Culturing
細胞培養

Cell Culture Facilities
細胞培養室

Class II Type A2 Biosafety Cabinet
第二等級 Type A2生物安全櫃

Our Cell Culture Facilities are equipped with seven certified Class II Type A2 Biosafety Cabinets. Animal and human cell lines are cultured in the biosafety cabinets. A recent expansion of our Facilities has accelerated and assisted the research of our Institute.

我們的細胞培養設施共配備七個獲得認證的二級A2型生物安全櫃。無論動物細胞以及人類細胞皆可以在生物安全櫃中培養。有賴於近期細胞培養設施的擴建，所內的研究效率得以加速提升。

RESEARCH ACTIVITIES AND OUTPUTS
科研動態

Research Areas and Teams
研究領域隊伍

Research teams within the Institute can be grouped under two main areas, namely, "Diseases and Pathobiology" and "New Technologies".

研究所內的研究隊伍可大致分為兩大研究範疇，是為「疾病及病理生物」和「創新技術」。

Diseases and Pathobiology
疾病及病理生物

Research Area 研究領域	Principal Investigator 首席研究員
Digestive Diseases 消化疾病研究	Jun Yu 于君
Emerging Infectious Diseases and Microbiota 防疫研究及腸道微生物學	Siew Ng 黃秀娟
	Renee Chan 陳韻怡
	Peter Cheung 張栢恒
	Hein Min Tun 黃世萬
	Chris Mok 莫家斌
Cancers 癌症研究	Jessie Liang 梁巧儀
	Andreas Möeller
Cardiovascular Medicine 心血管疾病研究	Xiaoqiang Yao 姚曉強
	Alex Lee 李沛威
Diabetes and Obesity 糖尿病與肥胖症研究	Juliana Chan 陳重娥
	Ronald Ma 馬青雲
Inflammatory Diseases 炎症性疾病研究	Hui-yao Lan 藍輝耀
Neuroscience and Neurotechnology 神經科學及神經技術	Owen Ko 高浩
	Hei Ming Lai 黎曦明
	Vincent Mok 莫仲棠
Reproduction and Development 生殖與發育研究	Ronald Wang 黃志超
Nephrology 腎臟疾病研究	Cheuk Chun Szeto 司徒卓俊

New Technologies
創新技術

Research Area 研究領域	Principal Investigator 首席研究員
Molecular Diagnostics 分子診斷學	Dennis Lo 盧煜明
	Nelson Tang 鄧亮生
	Allen Chan 陳君賜
	Jacky Lam 林偉棋
Stem Cells and Tissue Regeneration 幹細胞及組織再生研究	Gang Li 李剛
	Kathy Lui 呂愛蘭
	Wayne Lee 李郁偉
Biomaterial, Chemical Biology and Drug Translational Research 生物材料，化學生物學及藥物轉譯研究	Ling Qin 秦嶺
	Billy Ng 吳濰龍
Genomics and Bioinformatics 基因組學與生物訊息學	Hao Sun 孫昊
	Peiyong Jiang 江培勇
	Ken Sung 宋永健
Non-coding RNAs and Cellular Signalling 非編碼核糖核苷酸研究及細胞訊號轉導	Huating Wang 王華婷
	William Wu 胡嘉麒
Robotics & AI 人工智能	Zheng Li 李崢

PUBLICATIONS AND OTHER RESEARCH OUTPUTS

學術著作及其他研究成果

A summary of the publications and other research outputs of individual teams for the reporting period can be found in Appendix: Reports on Research Activities.

In 2023, a total of 267 publications from these teams were published.

Among the publications, 111, 37 and 73 were published in journals with impact factors greater than 4, 10 and 15, respectively. Highlighted below are several major ones:

各小組的研究成果及著作詳列於附錄：科研活動報告部分。過去一年，研究所屬下各研究小組共發表267篇學術論文，當中有111、37及73篇分別刊登於影響分子高於4、10及15的學術刊物。

NEJM Evidence

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NEJM Evid 2023; 2 (7)
DOI: 10.1056/EVIDoa2200309

ORIGINAL ARTICLE

Plasma Epstein–Barr Virus DNA and Risk of Future Nasopharyngeal Cancer

K.C. Allen Chan, F.R.C.P.A.,[1,2,3,4] W.K. Jacky Lam, F.R.C.S.,[1,2,3,4,5] Ann King, F.R.C.R.,[6] Vivien S. Lin, B.Sc.,[1,2,3,4] Patrick P.H. Lee, B.Sc.,[1,2,3,4] Benny C.Y. Zee, Ph.D.,[7] Stephen L. Chan, F.R.C.P.,[3,8] Irene O.L. Tse, B.N.,[1,2,3,4] Amy F.C. Tsang, B.N.,[1,2,3,4] Maggie Z.J. Li, B.N.,[1,2,3,4] Peiyong Jiang, Ph.D.,[1,2,3,4] Qi Yong H. Ai, Ph.D.,[6,9] Darren M.C. Poon, F.R.C.R.,[8] K.H. Au, F.R.C.R.,[10] Edwin P. Hui, F.R.C.P.,[3,8] Brigette B.Y. Ma, M.D.,[3,8] Andrew C. Van Hasselt, F.R.C.S.,[5] Anthony T.C. Chan, F.R.C.P.,[3,8] John K.S. Woo, F.R.C.S.,[5] and Y.M. Dennis Lo, F.R.S.[1,2,3,4]

Author(s): Dennis Lo, Allen Chan, Jacky Lam, Peiyong Jiang et al.
Journal: *NEJM Evidence*, June 2023

Detection of cancer-derived DNA in blood plasma, or liquid biopsy, has become an important tool for cancer diagnostics. In particular, such utility for cancer screening is a hot research topic. However, in some tested positive individuals, no cancer could be found despite thorough investigations. The significance of a positive cancer DNA test in individuals without an immediately identifiable cancer is unclear. The research team led by Professor Dennis Lo used nasopharyngeal cancer (NPC) as a model to address this question. They carried out two rounds of NPC screening, separated by a median of 4 years, for 20,000 volunteers using plasma Epstein-Barr virus (EBV) DNA analysis. They first demonstrated that liquid biopsy for cancer screening is a feasible concept that could bring about a clinical impact. Screening by plasma EBV DNA, as cancer-derived DNA in NPC, could identify early asymptomatic cancer and lead to a 90% reduction in mortality. Remarkably, they further showed that individuals with positive results but no identifiable cancer in the first round would have an elevated risk of up to 16.8 folds of having NPC at the second-round. Their findings revealed, for the first time, that the presence of cancer-associated DNA changes not only can detect a current concealed cancer but also reflect the risk of future cancer development. These findings have important implications for the future development of plasma DNA-based tumour markers. This study is published in the *NEJM Evidence*, a publication of the New England Journal of Medicine Group (*NEJM Evid* 2023;2(7)).

分析血漿中來自於癌症的游離DNA，或液體活檢，已成為癌症診斷的重要工具。其應用於癌症篩查更加是一個熱門的研究課題。然而，在一些檢測呈陽性的人士中，經過徹底調查後並未發現癌症。究竟血漿中出現癌症DNA而未能立即發現癌症的長遠臨床意義是什麼? 盧煜明教授領導的研究團隊以鼻咽癌為模型來解答這個問題。 他們使用血漿Epstein-Barr病毒(EBV)DNA分析，對 20,000名志願者在四年間進行了兩輪鼻咽癌篩查。他們首先證明液體活檢是一個可行的方案，可帶來臨床上的影響。通過血漿EBV DNA，即癌症釋放的DNA分析，可以篩查出早期無症狀的鼻咽癌，並使治療後的死亡率降低 90%。他們更發現在第一輪篩查中出現陽性結果而沒有鼻咽癌的人士，在 4 年後進行的第二輪篩查中確診鼻咽癌的風險將增加，達陰性結果參加者的16.8倍。他們的研究結果顯示，於血漿中檢測與癌症相關的DNA變化不僅可以偵測當前隱藏的癌症，還可以反映未來罹患癌症癌症的風險。這些發現對於發展血漿DNA腫瘤標誌物具有重要意義。這項研究發表在新英格蘭醫學雜誌集團的出版物《*NEJM Evidence*》上（*NEJM Evid* 2023；2(7)）。

nature microbiology

Article

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Parabacteroides distasonis uses dietary inulin to suppress NASH via its metabolite pentadecanoic acid

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Author(s): Jun Yu et al.

Journal: *Nature Microbiology*, June 2023

Parabacteroides distasonis uses dietary inulin to suppress NASH via its metabolite pentadecanoic acid

In recent decades, overnutrition and obesity have led to the dramatic rise in the incidence of non-alcoholic fatty liver disease (NAFLD), which has become a global health burden. A proportion of patients with NAFLD develops non-alcoholic steatohepatitis (NASH), with inflammation and hepatocyte damage. The team led by Professor Jun Yu undertook this study to ask whether dietary fibre might be preventives for NASH, and discovered that soluble fibre is more effective than insoluble fibre in preventing NASH in mice. A distinct feature of soluble fibre vs insoluble fibre is the ability of gut microbes to metabolize the former for energy. They thus hypothesize that soluble fibre-associated gut microbes and metabolites play an important role in NASH prevention. To answer this question, they employed ^{13}C-labeled inulin as a tracer, which will be assimilated by gut microbes and incorporated into their genomic DNA and metabolites. Integrated metagenomic and metabolomic analyses identified ^{13}C-labeled bacteria such as *Bacteroides uniformis*, *Bacteroides acidifaciens*, and *Parabacteroides distasonis*, and ^{13}C-labeled metabolites including long chain fatty acids, that are enriched as a consequence of microbial fermentation. Validation work revealed that *P. distasonis* is the most effective in suppressing NASH in mice. Mechanistically, ^{13}C-tracing revealed that *P. distasonis* exerts its protective effect by producing the metabolite pentadecanoic acid, which in turn restores gut barrier function and suppresses hepatic inflammation. Taken together, the team identified an inulin *P. distasonis*-pentadecanoic

狄氏副擬桿菌利用菊粉產生十五烷酸抑制非酒精性脂肪肝炎

近年來，肥胖和營養過剩導致非酒精性脂肪肝(NAFLD)發生率顯著升高。其中一部分NAFLD病人進而發展成為非酒精性脂肪肝炎(NASH)，伴隨發炎和肝細胞損傷。為此，于君教授及其研究團隊進行了利用膳食纖維預防NASH的研究，發現可溶性纖維比不可溶性纖維在小鼠中更能有效預防NASH。透過追蹤13碳標記的菊粉(可溶性纖維)在小鼠腸道中的代謝路徑，以及綜合分析宏基因組和代謝組的結果，發現了一系列13C標記的細菌例如單形擬桿菌、產酸擬桿菌、狄氏副擬桿菌及其代謝物如長鏈脂肪酸。進一步實驗顯示狄氏副擬桿菌在預防小鼠NASH效果最為顯著。他們發現狄氏副擬桿菌透過產生代謝物十五烷酸起到保護作用，後者可以修復腸道黏膜屏障功能，抑制肝臟發炎。綜上，狄氏副擬桿菌透過利用菊粉產生十五烷酸，可以抑制NASH。

A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (RECOVERY): a randomised, double-blind, placebo-controlled trial

Raphaela I Lau, Qi Su*, Ivan S F Lau, Jessica Y L Ching, Martin C S Wong, Louis H S Lau, Hein M Tun, Chris K P Mok, Steven W H Chau, Yee Kit Tse, Chun Pan Cheung, Moses K T Li, Giann T Y Yeung, Pui Kuan Cheong, Francis K L Chan†, Siew C Ng†*

Author(s): Siew Ng, Hein Min Tun, Chris Mok et al.

Journal: *The Lancet Infectious Diseases*, December 2023

Post-acute COVID-19 syndrome (or post-COVID conditions) refers to the long-term symptoms that persist after acute SARS-CoV-2 infection, with no effective treatment. CUHK Medicine conducted a large-scale, double-blind, randomised, placebo-controlled trial (RECOVERY) to confirm that treatment with an oral synbiotic preparation (SIM01) could lead to significant alleviation in various symptoms of post-acute COVID-19 syndrome (PACS). Clinical assessments confirmed that the SIM01 group had significantly higher alleviation rates in five PACS symptoms, including fatigue, difficulty in concentration, memory loss, gastrointestinal upset and general unwellness, than the placebo group. Treatment with SIM01 significantly enhanced the diversity and richness of gut microbiota, promoted the growth of multiple beneficial bacteria, and inhibited potentially pathogenic bacteria, thereby maintaining microbial balance. Additionally, SIM01 has improved the functions of gut microbiota, potentially promoting the release of short-chain fatty acids and inhibiting the production of urea. These findings have been published in *The Lancet Infectious Diseases*, a world-leading journal in infectious diseases, offering important directions for the treatment of PACS globally.

香港中文大學醫學院進行了大型雙盲、隨機、安慰劑對照研究 (RECOVERY)，證實口服合生製劑 (SIM01) 能有效緩解多種長新冠症狀，包括疲倦、注意力下降、記憶力減退、腸胃不適及整體不適。在維護腸道微生態平衡方面，SIM01能顯著提升腸道菌群的多樣性和豐富度，促進益菌的生長並抑制多種害菌。此外，SIM01能改善腸道菌群的功能，以促進短鏈脂肪酸的釋放並抑制尿素的生成。這些嶄新的臨床研究結果將為全球治療長新冠提供重要的指引。

nature communications

Article

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DNA methylation markers for kidney function and progression of diabetic kidney disease

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Check for updates

Kelly Yichen Li[1,2], Claudia Ha Ting Tam[3,4,5], Hongbo Liu[6,7], Samantha Day[8,9], Cadmon King Poo Lim[3,5], Wing Yee So[3,4], Chuiguo Huang[3], Guozhi Jiang[3,10], Mai Shi[3], Heung Man Lee[3], TRANSCEND Consortium*, Hui-yao Lan[3,11], Cheuk-Chun Szeto[3,11], Robert L. Hanson[8], Robert G. Nelson[8], Katalin Susztak[6,7], Juliana C. N. Chan[3,4,11], Kevin Y. Yip[1,2,4,12] & Ronald C. W. Ma[3,4,5]

Author(s): Ronald Ma et al.

Journal: *Nature Communications*, May 2023

DNA methylation markers for kidney function and progression of diabetic kidney disease

Diabetic kidney disease (DKD) has become the leading cause of kidney failure, and can be prevented through treatment intensification and the use of renoprotective drugs. However, how to identify those at risk of developing kidney failure remains challenging. Leveraging on their cohort with prospective follow-up and associated biosamples, this study utilized a novel method to interrogate methylation markers in blood and showed that blood methylation markers are strongly associated with kidney function. Furthermore, by identifying a panel of methylation markers most strongly associated with kidney function as well as subsequent decline in kidney function during follow-up, the research team led by Professor Ronald Ma was able to develop prediction models for future decline in kidney function and development of kidney failure. The prediction models also predicted kidney function and decline in kidney function in an external cohort. Interestingly, some of the key genes identified to show differential methylation in DKD also showed differential methylation in the kidney in kidney biopsies, highlighting functional relevance of the genes in the kidney. The methylation signature was found to be superior to clinical risk factors to predict risk of kidney failure. A calculator has been developed by the research team based on the methylation markers, to help identify high-risk patients for early intervention to reduce risk of progression to kidney failure. The patented invention also received a Silver Medal at the 49th International Exhibition of Inventions Geneva.

腎功能和糖尿病腎病變進展的 DNA 甲基化標記物

糖尿病腎病變 (DKD) 已成為腎衰竭的主要原因，可以透過強化治療和使用保護腎臟的藥物來預防。然而，如何識別那些較高風險腎衰竭的患者仍然具挑戰性。利用他們的前瞻性追蹤隊列和相關生物樣本，本研究採用了一種新方法來查考血液中的甲基化標記物，並表明血液甲基化標記物與腎功能密切相關。此外，透過鑑定一組與腎功能以及後續腎功能下降最密切相關的甲基化標記物，馬青雲教授及其團隊能夠開發未來腎功能下降和腎衰竭發展的預測模型。該預測模型還預測了外部隊列中的腎功能和腎功能下降。有趣的是，一些在 DKD 中顯示出甲基化差異的關鍵基因在腎臟活檢中也顯示出腎臟中的甲基化差異，突出了這些基因腎臟功能的相關性。研究發現，甲基化特徵在預測腎衰竭風險方面優於臨床危險因子。研究團隊基於甲基化標記物開發了一種計算器，以幫助識別高風險患者進行早期幹預，以降低進展為腎衰竭的風險。該專利發明也曾在第49屆日內瓦國際發明展上獲得銀牌。

ORIGINAL RESEARCH

Annals of Internal Medicine

Acupuncture and Doxylamine–Pyridoxine for Nausea and Vomiting in Pregnancy

A Randomized, Controlled, 2 × 2 Factorial Trial

Xiao-Ke Wu, MD, PhD; Jing-Shu Gao, MSc; Hong-Li Ma, MD; Yu Wang, MD; Bei Zhang, MD; Zhao-Lan Liu, PhD; Jian Li, MD; Jing Cong, PhD; Hui-Chao Qin, MSc; Xin-Ming Yang, MD; Qi Wu, PhD; Xiao-Yong Chen, MD; Zong-Lin Lu, MD; Ya-Hong Feng, MD; Xue Qi, MD; Yan-Xiang Wang, MD; Lan Yu, MD; Ying-Mei Cui, MD; Chun-Mei An, MD; Li-Li Zhou, MD; Yu-Hong Hu, MD; Lu Li, PhD; Yi-Juan Cao, MD; Ying Yan, MD; Li Liu, MD; Yu-Xiu Liu, MD; Zhi-Shun Liu, MD, PhD; Rebecca C. Painter, MD, PhD; Ernest H.Y. Ng, MD; Jian-Ping Liu, MD; Ben Willem J. Mol, MD; and Chi Chiu Wang, MD, PhD

Author(s): Ronald Wang et al.

Journal: *Annals of Internal Medicine*, June 2023

Nausea and vomiting impacts up to 85% of pregnant women. While 80 to 90% of those cases are mild, severe nausea and vomiting, or hyperemesis gravidarum, develops in 10% of cases. In addition, up to 10% of wanted pregnancies that are complicated by HG are terminated because of intolerable symptoms and complications. Despite the need for an effective treatment and hesitation of medication amongst pregnant women, very few recommendations can be made with regard to optimal and alternative treatments because of inadequate sample sizes and poor study quality.

In this study, Professor Ronald Wong and his team randomly assigned 352 women in early pregnancy with moderate to severe nausea and vomiting to receive daily active or sham acupuncture for 30 minutes and/or doxylamine-pyridoxine or placebo for 14 days to assess the efficacy and safety of either intervention or the combination of both. They found that active acupuncture and doxylamine–pyridoxine were modestly superior to sham acupuncture and placebo, respectively, in reducing the severity symptoms and improving quality of life among pregnant women. However, combination of both treatments offered numerically larger benefits than each treatment alone. It is noted that antinausea drugs may be underprescribed by general practitioners because of concerns about potential risks for birth defects. Acupuncture could serve as an alternative for patients who are unwilling to use pharmacologic treatments during pregnancy. This novel RCT is socially important area with senior involvement, high impact and widely spread generalisability.

有研究發現高達 85% 的孕婦在懷孕期間會感到噁心和嘔吐。雖然大多數病例症狀輕度，但仍有10% 的病例會出現嚴重妊娠劇吐。此外，高達 10% 孕婦因無法忍受症狀和併發症而無奈終止妊娠。儘管孕婦需要有效的治療和高質量的臨床證據，但樣本量不足和研究設計差，關於替代治療的建議很少。

在這項研究中，黃志超教授及其團隊隨機分配352 名患有中度至重度妊娠噁心嘔吐的早期妊娠婦女接受每日針灸或假針灸30 分鐘和/或多西拉敏-吡哆醇或安慰劑14 天，以評估針灸或聯合療法的有效性和安全性。他們發現，在減輕孕婦嚴重症狀和改善生活品質方面，針灸和多西拉敏-吡哆醇分別優於假針灸和安慰劑。然而，兩種治療方法的結合所帶來的益處比單獨使用的治療方法益處要大得多。值得注意的是，目前由於擔心出生缺陷的潛在風險，醫生可能會開出較少的抗噁心藥物。對於不願在孕期使用藥物治療的患者，針灸可以作為一種替代方法。這項臨床隨機對照試驗是具有社會重要性的領域，具有高度參與、高影響力和廣泛的普遍性。



GRANTS
補助金及其他資助

Our Principal Investigators and their teams affiliated with the Institute have received grants of over HK$1.994 billion during this reporting period. In particular, grants under the General Research Fund (GRF) scheme of the Research Grants Council (RGC) of HK$50 million are listed below:

此外，在本報告年度期間，研究所各項目負責人及其小組成員所取得的補助金及其他資助合計逾港幣十九億九千四百萬，其中研究資助局的優配研究金共逾港幣五千萬，獲資助研究項目的詳情如下：

Project Title 研究題目	Principal Investigators / Research Team 研究所首席研究員 / 小組	Amount (HK$)
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) SLC25A22 Drives Immune Suppression In KRAS-Mutant Colorectal Cancer through Metabolic Regulation of CXCL1/CXCR2 Axis	Jun Yu	1,155,532
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) RNA Demethylase AlkB Homolog 5 (ALKBH5) Drives Immune Suppression in Colorectal Cancer via Epitranscriptome Regulation of AXIN2-WNT-DKK1 Axis		1,325,732
Research Grants Council – General Research Fund (1/10/2022 – 30/9/2025) Role of Intestine TM6SF2 in Protecting Non-Alcoholic Fatty Liver Disease through the Maintenance of Gut Barrier Function		1,120,716
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Dissecting the Role of RNA N6-Methyladenosine Modification in Mutant KRAS-Driven Colorectal Cancer: Molecular Mechanisms and Targeted Therapy	Jun Yu	1,158,188
Research Grants Council – General Research Fund (1/10/2023 – 30/9/2026) Elucidating the Role and Mechanism of TM6SF2 in Suppressing Fatty Liver Disease-Associated Liver Cancer through Regulating Anti-Tumor Immunity		1,462,000
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Development of a Single-cell Full-length Mitochondrial Genome Sequencing Platform Based on Droplet Microfluidics	Nelson Tang	970,181
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Characterization on The Role of Proteus Mirabilis-Derived Cadaverine in Regulation of Proinflammatory Phenotype and Immune Response in Crohn's Disease	Siew Ng	1,151,224
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Evolution and Determinants of Population Mental Health during the Myanmar Conflict: A Nationwide Longitudinal Study from 2021 to 2025	Hein Min Tun	881,339
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Role of TRPA1 channels in regulating the functions and maturation of embryonic stem cell-derived cardiomyocytes through mediating mitochondrial biogenesis and/or dynamics	Xiaoqiang Yao	996,285
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) LETM-domain Containing Protein 1 as a New Player in Adipose Thermogenesis		1,178,251
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Delineating the Metabolic Architecture and Response to Anti-hyperglycaemic Drug Treatment in Lean Type 2 Diabetes in Chinese	Juliana Chan Ronald Ma	1,178,778
Research Grants Council – General Research Fund (1/1/2020 – 30/6/2023) The Effect of In Utero Hyperglycaemia, Maternal Overnutrition and Interaction with Postnatal Lifestyle on Cardiometabolic Risk at Young Adulthood – Extension of HAPO Follow Up Study	Ronald Ma Ronald Wang	1,158,019

Project Title 研究題目	Principal Investigators / Research Team 研究所首席 研究員 / 小組	Amount (HK$)
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) Metformin as a Neuroprotective Therapy for Glaucoma – a Randomized Controlled Trial	Ronald Ma	1,160,564
Research Grants Council – General Research Fund (1/7/2021 – 31/12/2023) Regulatory Role of Smad3 in SARS-CoV-2 N Protein-Induced Acute Kidney Injury in db/db Mice	Hui-yao Lan	1,125,732
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Mechanisms of Cognitive Aging Repair via Targeting GLP-1 Signaling	Owen Ko Vincent Mok	1,155,631
Research Grants Council – General Research Fund (1/1/2019 – 30/6/2023) Design of Synchronized Pairing Peripheral Nerve Stimulation and Cortical Polarization to Promote Poststroke Neuroplasticity for Hand Function Recovery	Vincent Mok	495,086
Research Grants Council – General Research Fund (1/11/2021 – 31/10/2024) Progression of Prodromal Markers of A-Synucleinopathy Neurodegeneration in the First-Degree Relatives of Patients with REM Sleep Behavior Disorder: A 7-Year Prospective Study		1,154,476
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Design of Elastomer-based Soft Actuator and Flexible Electronic Polymers Sensor for Rehabilitation of Hand Function After Stroke	Vincent Mok Zheng Li	844,415
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Transcranial Direct Current Stimulation in Post-stroke Fatigue: A Double-blind Randomised Control Trial	Vincent Mok	1,090,616
Research Grants Council – General Research Fund (1/9/2021 – 29/2/2024) Epithelium Caveolin and its Calcium Signaling Pathway in Endometrium of Recurrent Miscarriage	Ronald Wang	775,732
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Engineering the Biomimetic Structural Mechanical Heterogeneity of Cell-adaptable Nanocomposite Hydrogels for Biomedical Applications	Gang Li	1,185,400
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) The Role of Lgr5 in Cartilage Development and Mesenchymal Stem Cells Mediated Cartilage Repair		996,285
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) Mechanistic Studies on Treatment of Diabetic Foot Ulcers by Novel Tibial Cortex Transverse Transport Surgery		1,125,732

Project Title 研究題目	Principal Investigators / Research Team 研究所首席 研究員 / 小組	Amount (HK$)
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Studying the Functional Mechanism of Endothelial YY1 in Postischemic Angiogenesis	Kathy Lui Huating Wang	1,195,542
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) Studying the Functional Mechanism of YY1 in the Regulation of Glucose Metabolism in Pancreatic Beta Cells through O-GlcNAcylation	Kathy Lui	1,325,732
Research Grants Council – General Research Fund (1/1/2021 – 31/1/2023) Exploration of Effects and Molecular Mechanism of Ginkgolide B in Treating Ageing-related Osteoporosis	Wayne Lee	920,567
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) Enhancing the Therapeutic Effect of Bracing for Adolescent Idiopathic Scoliosis with a Hybrid Bracing Protocol: A Randomized-Controlled Trial		977,708
Research Grants Council – General Research Fund (1/8/2022 – 31/7/2025) lncRNA H19 Modulates Osteoarthritis Development via Subchondral Bone Remodeling and Osteocyte Responses to Mechanical Stimulation?		1,172,904
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Identification of a Central to Sympathetic Neural Circuit in Magnesium-promoted Bone Regeneration using Retrograde Tracing and Single-cell RNA-seq	Ling Qin	1,126,379
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) Magnesium Activated Progenitor Cells in Synovial Fluid to Regenerate Articular Cartilage		1,174,492
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2023) An Innovative Strategy Recapitulates the Neuropeptide-Guided Angiogenic-Osteogenic Coupling for Functional Repair of Segmental Bone Defect		1,175,052

Project Title 研究題目	Principal Investigators / Research Team 研究所首席研究員 / 小組	Amount (HK$)
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) 3D Genome Rewiring During Muscle Stem Cell Lineage Development and Ageing	Hao Sun Huating Wang	1,194,637
Research Grants Council – General Research Fund (1/8/2023 – 31/7/2026) In Vivo RNA Structure Probing Unveils DHX36 Binding-structure Interplay in Regulation of mRNA Abundance		1,600,000
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Investigating the Functional Significance of Three-Dimensional Structures of Topologically Associating Domains	Huating Wang	1,195,542
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) Functional Characterization of Atf3 in Skeletal Muscle Stem Cells and Muscle Regeneration		1,394,799
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) YY1 Deficiency in Satellite Cell Exacerbates Fibrosis in Dystrophic Muscle: Elucidation of Satellite Cell/Macrophage/Fibro-adipogenic Progenitor Crosstalk in Duchenne Muscular Dystrophy Mice		1,525,732
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Elucidating the Novel Regulatory Function of RNA Binding Proteins in 3D Genome Organization		1,425,114
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) m6A Modification Controls the Autophagic Response to Helicobacter Pylori Infection	William Wu	1,195,290
Research Grants Council – General Research Fund (1/1/2022 – 31/12/2024) Elucidating the Role and Mechanism of RNA N6-Methyladenosine m6A Regulator METTL3 in Promoting Colorectal Cancer Through Modulating Gut Microbiota		1,150,352
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2024) Delineating the Sensorimotor Cortex-Spinal Cord Descending Pain Pathway and Its Interaction with Gut Microbiota		1,114,323
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Elucidating the Role of RNA N1-Methyladenosine Modifications in Colorectal Cancer		1,130,669
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Sex Differences in the Gut Colonization of Carnobacterium Maltaromaticum for Suppressing Colorectal Tumorigenesis	William Wu	1,180,120
Research Grants Council – General Research Fund (1/1/2021 – 31/12/2023) DNA Structure Inspired Multi-helix Continuum Mechanism for Minimally Invasive Surgical Robots	Zheng Li	873,995
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Intelligent Magnetic Anchored and Guided Endoscope with Surgeon Preference Embedded Autonomous View Control		965,158
Research Grants Council – General Research Fund (1/1/2023 – 31/12/2025) Design and Synthesis of Novel Carbocyclic Nucleoside Analogues as Antiviral Agents	Billy Ng	464,000
	Total:	**50,324,021**

SCIENTIFIC EXCHANGE AND VISITORS

學術交流及訪客

During the reporting period, the Institute received a number of renowned academicians, experts and delegations from within and beyond the Territory. Some of them are highlighted as follows:

過去一年，研究所接待多位本港及海外著名學者、專家及訪問團，進行學術交流及參觀，詳列如下：

23 March 2023

Visit to the Institute and the State Key Laboratory of Translational Oncology by Professor John Chai, Council Chairman of the Chinese University of Hong Kong.

香港中文大學校董會主席查逸超教授參觀研究所及轉化腫瘤學國家重點實驗室。





14 September 2023

Visit to the Institute by Professor Arieh Warshel, 2013 Nobel Laureate in Chemistry.

2013年諾貝爾化學獎得主Professor Arieh Warshel參觀研究所。



15 September 2023

Seminar by Dr Steve Mao, Editor-in-Chief of *Cancer Cell* on "Cell Press and Cancer Cell: Advancing with the Community".

Steve Mao博士（*Cancer Cell*期刊主編）舉行研討會，題目為「Cell Press and Cancer Cell: Advancing with the Community」。

21 September 2023

Visit to the Faculty of Medicine and the Institute by Professor Chung-mau Lo, Secretary for Health, Health Bureau of the Government of the Hong Kong Special Administrative Region.

香港特別行政區政府醫務衞生局局長盧寵茂教授參觀醫學院及研究所。



Appendix 附錄

REPORTS ON RESEARCH ACTIVITIES

科研活動報告

01 Digestive Diseases
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- Jun Yu

02 Molecular Diagnostics
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- Nelson Tang
- Allen Chan
- Jacky Lam

03 Emerging Infectious Diseases and Microbiota
防疫研究及腸道微生物學
- Siew Ng
- Renee Chan
- Peter Cheung
- Hein Min Tun
- Chris Mok

04 Cancers
癌症研究
- Jessie Liang
- Andreas Möller

05 Cardiovascular Medicine
心血管疾病研究
- Xiaoqiang Yao
- Alex Lee

06 Diabetes and Obesity
糖尿病與肥胖症研究
- Juliana Chan
- Ronald Ma

07 Inflammatory Diseases
炎症性疾病研究
- Hui-yao Lan

08 Neuroscience and Neurotechnology
神經科學及神經技術
- Owen Ko
- Hei Ming Lai
- Vincent Mok

09 Reproduction and Development
生殖與發育研究
- Ronald Wang

10 Stem Cells and Tissue Regeneration
幹細胞及組織再生研究
- Gang Li
- Kathy Lui
- Wayne Lee

11 Biomaterial, Chemical Biology and Drug Translational Research
生物材料，化學生物學及藥物轉譯研究
- Ling Qin
- Billy Ng

12 Genomics and Bioinformatics
基因組學與生物訊息學
- Hao Sun
- Peiyong Jiang
- Ken Sung

13 Non-coding RNAs and Cellular Signalling
非編碼核糖核苷酸研究及細胞訊號轉導
- Huating Wang
- William Wu

14 Nephrology
腎臟疾病研究
- Cheuk Chun Szeto

15 Robotics and AI
機械人與人工智能
- Zheng Li

01

Digestive Diseases
消化疾病研究

Gastrointestinal (GI) diseases, including GI tract cancers and non-alcoholic fatty liver disease (NAFLD), are major diseases in Hong Kong and they cause significant morbidity and mortality. **Jun Yu** and the multidisciplinary team of scientists and clinicians at Institute of Digestive Diseases specialise in GI basic research, focusing on: 1) understanding the role of gut microbiome dysbiosis in GI cancers and NAFLD; 2) genetic, epigenetic and epitranscriptomic mechanisms in the pathogenesis of GI cancers and NAFLD; as well as translational research including 3) identification of probiotic bacteria that prevents disease development; and 4) the discovery of molecular diagnostic markers and therapeutic targets of GI cancers and NAFLD.

消化道疾病如消化道腫瘤和脂肪性肝病是香港常見病。**于君**及其團隊專注於基礎和轉化研究包括：1）研究腸道微生態與消化道腫瘤和脂肪性肝病的關係；2）闡明消化道腫瘤和脂肪性肝病的分子機制；3）益生菌防治消化道腫瘤和脂肪性肝病；及4）開發新的診斷標誌和治療靶標。

Jun Yu
于君



Nelson Tang is the Principal Investigator of the Laboratory for Genetics of Disease Susceptibility. The research team led by Nelson specialised in complex traits and genetic statistics. His research covers genetic association studies, expression quantitative traits and post-genome-wide association study (GWAS) analysis. A patent has been recently granted for gene expression analyses. He is also teaching a bioinformatics course in the Faculty of Engineering.

The research team has a long-standing cooperation with international researchers, Nelson is the Associate Director of the joint laboratory with the Kunming Institute of Zoology of the Chinese Academy of Sciences (CAS). Recently, the team explored the genetic mechanism of Adolescent idiopathic scoliosis and Ageing.

鄧亮生是疾病易感性遺傳學實驗室的首席研究員，由他帶領的研究小組專門從事複雜性狀的遺傳學和統計分析。他的研究涵蓋遺傳關聯研究、表達數量性狀和後全基因組關聯分析 (GWAS)，並於最近獲得了一項用於基因表達分析的專利。鄧亮生另亦在工程學院教授生物信息學課程。

研究小組長期與國際研究人員合作，包括中國科學院昆明動物研究所，而鄧亮生是該聯合實驗室的副主任。最近，團隊發表了一個持續了10年的研究結果，使人開始了解青少年特發性脊柱側彎的遺傳機制。

Nelson Tang
鄧亮生



02

Molecular Diagnostics
分子診斷學

Dennis Lo
盧煜明



Dennis Lo is globally renowned as a pioneer and leader in liquid biopsy. The team led by Dennis has developed novel approaches for analysing circulating nucleic acids that have impacted the diagnostics of fetal diseases, cancer, autoimmune disorders and transplantation monitoring. In 2023, he was elected as a member of the Chinese Academy of Sciences, in recognition of his success and contribution in medical research. He was also received the inaugural Tengchong Science Award.

盧煜明作為液體活檢領域的先驅和領軍人物，在全球享負盛名。由他帶領的團隊開發了嶄新的方法，用於分析循環核酸，對胎兒疾病、癌症、自身免疫疾病和移植監測的無創診斷產生了重大影響。於2023年，盧煜明獲選為中國科學院院士，以表彰他在醫學研究方面重大的成就和貢獻，同時他亦獲頒首屆「騰衝科學大獎」。

Allen Chan
陳君賜



Allen Chan and his team have established the clinical utility of plasma Epstein-Barr virus (EBV) DNA for screening of nasopharyngeal carcinoma (NPC). They have carried out a re-screening of their screening cohort of about 20,000 Chinese men and discovered that those who had detectable plasma EBV DNA 4 years before (at the first round) suffered a higher risk of NPC identified at the second round. Such result illuminated that, for cancer types other than NPC, the presence of cancer-associated DNA changes not only can detect a current concealed cancer but also reflect the risk of future cancer development.

陳君賜及其團隊立了血漿EB病毒DNA用於鼻咽癌篩查的臨床用途。他們對約2萬名中國男性的篩檢族群進行了再篩檢，發現在4年前第一輪檢測中，檢測到血漿EBV DNA的人在第二輪中發現患鼻咽癌的風險更高。這項結果揭示了除鼻咽癌外，癌症相關DNA的存在不僅可以檢測出當前隱藏的癌症，還可以反映未來癌症發展的風險，這對於其他類型的癌症具有重要意義。

Jacky Lam and his research team focus on the potential clinical application of cell-free DNA in cancer diagnostics. Using nasopharyngeal cancer (NPC) as a model, the team has investigated the differentiating molecular characteristics of plasma Epstein-Barr virus (EBV) DNA between NPC and non-NPC subjects. Such discoveries have been translated into the development of novel diagnostic assays for NPC screening and prognostication, with improved performance compared to the conventional testing. Plasma EBV DNA serves as an archetypal type of circulating tumour DNA. The team continues to explore ways to enhance accuracy and efficiency of NPC screening modalities.

林偉棋及其研究團隊的研究集中於游離DNA在癌症檢測的臨床應用。以鼻咽癌作模型，研究隊伍分析血漿EB病毒DNA在癌症及非癌症患者的分子特徵，藉此開發用以鼻咽癌篩查及預後的嶄新檢測技術，較傳統方法的表現更佳。

Jacky Lam
林偉棋



03

Emerging Infectious Diseases and Microbiota

防疫研究及腸道微生物學

Siew Ng
黃秀娟



Siew Ng and her team are pioneers in the field of gut microbiome. They discovered and translated microbiome signatures into novel diagnostics and therapeutics for human diseases. They showed that microbiome modulation with an oral microencapsulated live bacteria (SIM01) improved long COVID symptoms. They also developed a multi-kingdom technology (MOZAIC™) to improve success after faecal microbiota transplant (FMT) for life-threatening gut infections. This technology is implemented in all hospitals within the Hospital Authority in Hong Kong. In 2023, Siew became the first clinician-scientist in Hong Kong to be selected as a New Cornerstone Investigator.

黃秀娟及其團隊是腸道微生物領域的先驅。團隊發現了微生物菌群特徵，並將其轉化為人類疾病的新型診斷和治療方法。團隊證明，使用口服微膠囊活菌配方(SIM01)調節微生物菌群，可以改善長新冠症狀。團隊還開發了一種多界技術(MOZAIC™)，提高微生物菌群移植(FMT)治療危及性命的腸道感染的成功率。這項技術已在香港醫院管理局轄下所有醫院進行。2023年，黃秀娟成為香港第一位被選為新基石研究員的臨床醫生科學家。

In **Renee Chan**'s laboratory, they pioneer research that is crucial in advancing the understanding and treatment of paediatric respiratory diseases. They have implemented nasal strips, revolutionising paediatric research by enabling the study of nasal immunity from neonates to school-age children. It has provided significant insights into basic immunology, vaccine efficacy measurement, and local inflammatory studies of allergies and obstructive sleep apnea. They conduct the epidemiological study of respiratory virus infections in children, shedding light on virus diversity and co-infections, particularly after the SARS-CoV-2 pandemic. They have developed respiratory organoid models from individuals with obstructive respiratory diseases including chronic obstructive pulmonary disease (COPD) and also from different age groups, providing a valuable tool for studying disease mechanisms and antiviral drug screening. In collaboration with chemists and structural biologist, they have created an antiviral drug screening platform, opening new avenues for the development of novel therapeutics against respiratory viruses. Their collective efforts have the potential to significantly impact the prevention and treatment of respiratory diseases in children.

陳韻怡及其團隊開創了採用鼻紙條對於兒科呼吸系統疾病理解和治療作縱向研究。通過這收集鼻腔黏液的方法，他們便能研究兒童，甚至新生兒的呼吸道免疫學，為兒科研究提供了對基礎免疫學、疫苗效能測量以及過敏和阻塞性睡眠呼吸暫停的局部發炎性調查的重要數據。同時，他們進行呼吸道病毒的流行病學研究，揭示在新型冠狀病毒大流行後所出現的層疊感染，會在特定兒童的年齡層發生。通過培養不同年齡和患有不同阻塞性呼吸疾病人的呼吸道上皮類器官模型，他們探索其獨有的致病機制，同時亦可用作新抗毒藥物研發的篩選平台。

Renee Chan
陳韻怡



Peter Cheung
張栢恒



Peter Cheung and his team's research focus on understanding diseases at the molecular level using computational and structural biology approaches. Their work involves developing new methods to study how viruses like influenza and coronaviruses replicate and mutate. They also analyse clinical data to evaluate medical interventions. The team's ultimate goal is to gain insights that can help design better treatments and preventions. Through both basic science and applied research, they strive to advance human health and alleviate suffering from infectious diseases.

張栢恒與其團隊的研究專注於運用計算生物學和結構生物學方法，在分子層面上了解疾病。他們的工作涉及研發新方法去研究流感病毒和新冠病毒如何複製和變異。他們還分析了臨床數據來評估醫療干預措施。團隊的最終目標是獲得有助於設計更好的治療和預防措施的見解。他們通過基礎科學和應用研究，致力推進人類健康及緩解傳染病帶來的痛苦。

Hein Min Tun
黃世萬



The research team led by **Hein Min Tun** uses conventional microbiology and molecular biology techniques, cutting-edge sequencing technologies, coupled with bioinformatics, statistical and epidemiological approaches to study: 1) the composition, function, and dynamics of human and animal microbiomes in health and disease; and 2) monitoring antimicrobial resistance (AMR) bacteria and resistome in humans, animals, and the environment using a holistic One Health approach. Their goal is to contribute to improving scientific understanding on the impact of microbiome and AMR in public health.

由**黃世萬**領導的研究團隊運用傳統的微生物學和分子生物學技術，結合尖端的測序技術以及生物信息學、統計學和流行病學方法，開展以下的研究：1）人類和動物微生物群在健康和疾病中的組成、功能和動態；以及2）利用「One Health」方法，監測在人類、動物和環境中抗菌藥物耐藥性（AMR）細菌和耐藥基因組。團隊的目標是增強對微生物群和抗藥性的認識，理解公共衛生對科學的影響作出貢獻。

Chris Mok
莫家斌



The major objective of **Chris Mok** and his research team is to understand the interplay between the host adaptive immunity and the viral determinants of respiratory viruses such as influenza viruses and coronaviruses using a combination of clinical, virological, immunological and structural approaches. They are particularly interested in understanding how adaptive immunity is regulated and sharpened by the evolution of respiratory viruses, which will help further improve the current vaccines.

莫家斌及其研究團隊的主要研究方向是通過結合臨床、病毒學、免疫學，以及結構化方法，了解宿主適應性免疫與呼吸道病毒（如流感病毒和冠狀病毒）之間的相互作用。他們研究呼吸道病毒的進化是如何調節與增強宿主的適應性免疫，將有助於進一步優化疫苗。

04 Cancers
癌症研究

Jessie Liang
梁巧儀



Gut microbiota dysbiosis has been associated with colorectal tumorigenesis. One of the researches focuses of **Jessie Liang** and her team is to develop a microbiome-based test for the non-invasive diagnosis of colorectal cancer and adenoma. The diagnostic performance of the identified new microbial markers would be further validated by targeted quantification using qPCR. They are also working on developing targeted modulation of gut microbiota to reduce cancer risk. Further functional and mechanism research is conducted on the bacteria they are particularly interested in. The team also investigates the roles and functional mechanisms of cancer-related genes in gastrointestinal cancers, such as some Human endogenous retroviruses (HERV)-related genes, DDX5-PolG2, etc.

腸道菌群失調與結直腸腫瘤發生有關。**梁巧儀**及其團隊的研究重點之一是開發一種基於微生物組的測試，用於結直腸癌和腺瘤的無創診斷。已識別的新微生物標記物的診斷性能將通過使用 qPCR 的靶向定量進一步驗證。其團隊也致力於開發靶向調節腸道菌群以降低患癌風險。對於他們特別感興趣的菌株，也會進行進一步的功能和機制研究。此外，團隊還研究了一些癌症相關基因在胃腸道癌症中的作用和功能機制，例如一些人類內源性反轉錄病毒 (HERV)相關的基因和DDX5-PolG2等。

Andreas Möller



Andreas Möller and his research team focus on understanding cancer progression and how cancer cells communicate with the rest of the body. A focus here is how cancer influences the immune system to evade and inactivate anti-cancer immune responses, to facilitate cancer growth and spreading. Uncovering the mechanisms and factors responsible for the mediation of cancer communication allows the team to gain a greater understanding of cancer processes. The factors that act as cancer cell mediators can be found in the bloodstream, and not only provide information on how cancers grow, but also act as biomarkers for cancer detection.

Andreas Möller及其團隊專注於探討癌症發展以及癌細胞如何與身體其他部位溝通。他們的研究重點在於癌症和免疫系統如何產生相互作用而導致抗癌免疫反應失衡。研究目標是由個別病人血液中的癌症溝通上的協調介面，開發診斷癌症存在的生物標記。

05

Cardiovascular Medicine

心血管疾病研究

Xiaoqiang Yao and his research team have been working on Ca^{2+}-permeable ion channels and endoplasmic reticulum stress-related proteins in cardiovascular system and cancer. Recently, they have uncovered novel function of Orai1 channels in endothelium-dependent contraction and role of TRPM2 channels in atherosclerotic progress. They have been in the process of developing strategy of active immunisation with TRPM2 peptide in vaccine platform for potential treatment of atherosclerosis.

姚曉強和其團隊一直致力於心血管系統及癌症中的鈣離子通道的研究。他們近期的研究發現了Orai1離子通道在內皮依賴性血管收縮中的重要作用。他們還發現 TRPM2 離子通道在動脈粥樣硬化中有重要作用。他們現正開發TRPM2短肽用作疫苗，以治療動脈粥狀硬化。

Xiaoqiang Yao
姚曉強



Alex Lee, an esteemed cardiologist and physician-scientist, specialises in using advanced imaging techniques to study the heart, particularly echocardiography. The team led by Alex has made breakthroughs in 3D printing for minimally invasive heart treatments and incorporating artificial intelligence into cardiac imaging. Their work has influenced guidelines for conditions like mitral regurgitation. The team has published research in respected journals, received prestigious awards, and delivered impactful keynote lectures. Through collaborations and research grants, they advance heart disease imaging and intervention, prioritising exceptional patient care and education. Their goal is to achieve excellence in patient care, education, and research to positively impact society.

李沛威是一位傑出的心臟病學家和醫學科學家，專注於先進影像技術在心臟研究中的應用，特別是超聲心動圖。他的研究團隊在三維列印和人工智能的融合上取得突破，影響了二尖瓣逆流等疾病的治療。他還在知名期刊發表研究成果，獲得多項獎項，並發表重要演講。通過合作和研究的資助，使其能夠推進心臟疾病的影像和介入的研究，也能優先考慮給予患者卓越的護理和教育。不管是過去還是將來，其團隊的目標一直是以創新方法和專業知識改善心臟疾病診斷和治療，為患者帶來健康和希望，為社會帶來積極的作用。

Alex Lee
李沛威



06

Diabetes and Obesity

糖尿病與肥胖症研究

Led by five tenured research physicians with expertise in endocrinology and/or clinical pharmacology, **Juliana Chan** has assembled a 60-member team of knowledge workers in the field of basic, clinical, data and experimental science. They use a multi-method approach to redefine the causes, track trajectories, discover new mechanisms, and evaluate interventions for outcomes in people with or at risk of developing diabetes. Supported by HKD 84 million competitive/earmarked grants and 10 post-doctoral/research fellowships, in 2023, the team collectively published 67 papers with 4 PhD and 1 MPhil graduates and issued 6 press releases in their pursuit of precision diagnosis, prevention and management of diabetes.

在五位擁有內分泌學和/或臨床藥理學專業知識的終身研究醫生的領導下，**陳重娥**組建了一支由基礎、臨床、數據和實驗科學領域的知識工作者組成的60人團隊，採用多種方法重新定義糖尿病患者或高危人群的病因、追蹤其發病軌跡、發現新機制並評估干預措施的效果。在8,400萬港元的競爭性/專項撥款和10個博士後/研究獎學金的支援下，團隊在2023年共發表了67篇論文，分別培訓了4名博士和1名碩士畢業生，並發佈了6篇新聞稿，以追求糖尿病的精準診斷、預防和管理。

Juliana Chan
陳重娥



Ronald Ma and his research team focus on the causes and consequences of diabetes across the life course, and the identification of molecular biomarkers that would facilitate the diagnosis, stratification and treatment of individuals with diabetes. Their aim is to reveal novel understanding of the underlying pathogenesis of diabetes and its complications, identify biomarkers that can be used clinically, and to translate them to deliver precision medicine for diabetes. In particular, given that more than 60% of the global estimate of people affected by diabetes are from Asia, their studies provide an important Asian perspective to seek the best therapeutic strategies for patients in Asia.

馬青雲和他的研究團隊的研究側重於糖尿病在整個生命過程中的成因和後果，以及鑑定有助於糖尿病患者的診斷、分類和治療的分子生物標誌物。他們的目標是揭示對糖尿病及其併發症的潛在發病機理的新穎理解，確定可在臨床上使用的生物標誌物，將其轉化並用於提供糖尿病的精準醫療。鑑於全球估計有60%以上的糖尿病患者來自亞洲，他們的研究更提供了重要的亞洲視角，可以尋找最適合亞洲患者的解決方案。

Ronald Ma
馬青雲



07

Inflammatory Diseases
炎症性疾病研究

In 2023, research team led by **Hui-yao Lan** continued studying COVID-19 acute kidney injury (AKI) and discovered that SARS-CoV-2 N protein can bind and activate Smad3 directly to cause cell death via the G1 cell cycle arrest and necroptosis pathways, resulting in severe AKI. This is particularly severe with high mortality in those with diabetes, hypertension, and underlying kidney diseases. More importantly, targeting Smad3 with a pharmacological inhibitor SIS3 and a traditional Chinese medicine compound quercetin can protect kidneys from COVID-19 acute kidney injury.

在過去的一年裡，**藍輝耀**領導的研究團隊繼續積極開展新冠病毒COVID-19急性腎損傷的研究，發現COVID-19殼核蛋白(SARS-CoV-2 N)可以結合並激活Smad3，導致腎小管細胞死亡和急性腎損傷，特別在糖尿病與高血壓基礎疾病情況下更為嚴重。應用中藥槲皮素或小分子藥物靶向抑製Smad3可以保護腎臟免受 COVID-19引起急性腎損傷。

Hui-yao Lan
藍輝耀



08

Neuroscience and Neurotechnology
神經科學及神經技術

Owen Ko
高浩



Owen Ko's team seeks to uncover the pathogenesis of neurodegenerative diseases and develop disease-modifying therapeutics. To this end, they utilise a combination of molecular, chemical and optical tools to (1) study gliovascular dysfunction in aging and neurodegeneration; (2) develop biomedical methods for revealing the fundamental principles governing the operation of neural circuits, and their dysfunction in pathological conditions.

高浩團隊的研究目標是以揭示神經退行性疾病的發病機制去推進疾病療法的開發。為此，他們利用生物分子，化學和光學工具來 1) 研究衰老和腦部退化過程中的神經血管和膠質細胞功能障礙；和 2) 開發新的生物醫學工具，以揭示神經系統在病理情況下的神經迴路功能缺失。

Hei Ming Lai
黎曦明



The multidisciplinary laboratory led by **Hei Ming Lai** and his research team develops innovative solutions across research, clinical diagnostics, energy, and industry sectors. Currently, they are advancing the commercialisation of these cutting-edge technologies.

由**黎曦明**及其研究團隊帶領的跨學科實驗室開發創新解決方案，涵蓋研究、臨床診斷、能源和工業領域。他們正在推進這些尖端技術的商業化，讓更多人受惠。

Vincent Mok
莫仲棠



Vincent Mok's team focuses on Alzheimer's disease, stroke, cerebral small vessel disease, and Parkinson's disease. With the rapidly aging populations worldwide, developing innovative technologies to tackle aging-associated disorders is becoming a priority of the global societies. Given the complexity of cellular and physiological changes involved in aging, and the lack of easily targetable driving pathways, it remains a formidable challenge to develop therapeutic approaches that can slow, or even reverse, the age-related functional decline in any body organ system. To this end, they aim to develop novel diagnostic and prognostic methods, as well as treatment strategies of common age-related brain diseases among their local population.

莫仲棠的研究團隊專注於阿茲海默症、中風、腦小血管病和柏金遜症。由於全球人口老化問題日趨嚴重，以及衰老過程中細胞和生理變化的複雜性，團隊的研究目標旨在研發嶄新的診斷、預測與治療策略，以應對常見於本地華人的腦部退化性疾病。

09

Reproduction and Development

生殖與發育研究

Ronald Wang
黃志超



Ronald Wang and his team focus on research in reproduction and development, and are actively involved in clinical, basic and translational studies of reproductive medicine and maternal medicine, including but not limited to endometriosis, endometrium imaging, endometrial cancer, reproductive failure, polycystic ovary syndrome, preterm birth, preeclampsia, gestational diabetes mellitus, and cord blood stem cells, with significant research collaboration, excellent progress and fruitful research output.

黃志超及其團隊主要研究的工作以生殖和發育為主，積極參與生殖醫學和母胎醫學的臨床、基礎及轉化研究。團隊建立重大的研究合作，工作進展傑出，研究成果卓越。

10

Stem Cells and Tissue Regeneration

幹細胞及組織再生研究

Gang Li
李剛



Gang Li's research team continues their research efforts on novel therapies strategies for diabetic foot ulcers, ischemic stroke and Alzheimer's disease, and cartilage and menisci repair. They have published over 12 peer-reviewed papers and received over HKD 6 million research grants. Gang has been invited to give keynote speeches and lectures at various national and international conferences and meetings for more than 20 times in 2023. He also continuously served as visiting professors at many prestigious universities and research societies, and editorial board members for 6 international journals. He was on the list of the world's Top 2% Scientists in 2023.

2023年，**李剛**及其研究團隊繼續致力研究糖尿病足潰瘍、缺血性中風和阿茲海默症，以及軟骨和半月板修復的新治療策略。 團隊們發表了超過12篇論文，並獲得超過600萬港元的研究資助。2023年李剛受邀在各類國內外會議上做主題演講20餘次，並連續擔任多間著名大學和研究學會的客座教授或領導人，及6份國際期刊的編委。 他獲列入2023年度史丹福大學的全球首2%頂尖科學家名單。

Kathy Lui
呂愛蘭



Cardiovascular disease has been the leading cause of death worldwide in the past three decades. The research team led by **Kathy Lui** is interested in regenerating the aged or damaged cardiovascular system. They have studied the pathogenesis of cardiovascular diseases, and the crosstalk between cardiovascular diseases and inflammation. Recently, the team also studied the pathophysiological origin of diabetes which is one of the major risk factors leading to cardiovascular disorders. They have utilised human pluripotent stem cells as a platform; and mRNA as well as monoclonal antibodies as therapeutic agents for disease modelling and drug screening.

在過去三十年裡，心血管疾病是全世界人類死亡的主要原因。**呂愛蘭**帶領的研究團隊一直對老化或受損的心血管系統的再生研究感興趣。他們研究心血管疾病的發病機制，以及心血管疾病與炎症之間的相互作用。最近，研究團隊還研究作為導致心血管疾病主要危險因素的糖尿病的病理生理學起源。他們還利用人類多能幹細胞，使用信使核糖核酸及單株抗體作爲治療劑，來構建用於疾病建模和藥物篩選的平台。

Wayne Lee
李郁偉



Wayne Lee and his team's research can be divided into two major areas of orthopaedics with important clinical relevance. The first line focuses on the development of GMP-grade cell therapy to treat osteoarthritis (OA) and other musculoskeletal problems. Wayne is a registered authorized person for advanced therapy product in Hong Kong. In collaboration with orthopaedic surgeons and local GMP centre, they are preparing cell therapy clinical trial for OA. The second line is on the biological roles of osteocyte in adolescent idiopathic scoliosis (AIS) and age-related disorders. Recently, the team has identified a novel mechanism underlying the abnormal subchondral bone remodelling in OA which could be a potential new therapeutic target for OA.

李郁偉及其研究團隊的研究可分為兩個主要領域。第一個領域專注於開發GMP級細胞治療，用於治療骨關節炎(OA)和其他肌肉骨骼問題。他是香港授權進階治療產品的註冊授權人。團隊們正在和骨科醫生以及當地的GMP中心合作，研究一種細胞治療方法，為骨關節炎準備細胞治療臨床試驗。團隊們也在研究骨細胞在青少年特發性脊柱側彎(AIS)和年齡相關的疾病中的作用。最近，團隊們發現了一種新的機制，可以解釋為什麼在骨關節炎中，軟骨下骨的結構會出現問題，這個發現可能成為治療骨關節炎的新方法。

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Biomaterial, Chemical Biology and Drug Translational Research

生物材料，化學生物學與藥物轉譯研究

Ling Qin
秦嶺



Ling Qin and his research team have been dedicated to the research and development of innovative orthopaedic implants to address the high incidence of refractory musculoskeletal diseases associated with the aging society. Based on the basic research on bioactive and biodegradable magnesium (Mg), the team has developed various innovative products (e.g. Mg-based hybrid devices and magnesium-containing hydrogels) to facilitate musculoskeletal tissue regeneration and functional restoration. They are now committed to pushing forward pre-clinical research to clinical applications, aiming to shorten the rehabilitation period, decrease incidence and mortality, and reduce the healthcare and economic burden of related diseases.

秦嶺及其研究團隊多年專注於研究和開發創新型骨科植入物，以應對與社會老齡化相伴的高發難癒型肌肉系統疾病。該團隊以具有生物活性及生物可降解性鎂金屬為核心，開發用於促進肌肉骨骼組織再生及功能恢復的各類創新產品（例如鎂基組合臨床器械、骨缺損修復水凝胶等）。團隊現階段致力於推進研究成果由基礎研究向臨床應用轉化，期望縮短臨床康復時間，降低相關疾病發病率與死亡率，減輕社會醫療經濟負擔。

Billy Ng's research interests are chemical biology, drug discovery, and medicinal chemistry. The Ng's Lab uses chemical and biological tools to develop: (i) novel small molecules to target these dysregulated pathways and (ii) novel and safe medicines for the treatment of various dreadful diseases, including cancers, infectious and neurodegenerative diseases. They also collaborate closely with physicians and entrepreneurs to translate their findings from bench to bedside.

吳濰龍的研究興趣是利用合成化學、生物化學和分子生物學來研究疾病的分子機制，從而開發出新型的安全藥物，用於治療癌症、傳染病和神經退行性等疾病。他們更致力於與醫生和企業密切合作，將研究成果轉化到臨床應用。

Billy Ng
吳濰龍



12

Genomics and Bioinformatics

基因組學與生物訊息學

Hao Sun
孫昊



A research team led by **Hao Sun** has committed to using integrative genomic approaches to study the transcriptional regulation mechanism during different stages of stem cell development, as well as developing computational approaches for sequencing-based disease diagnosis.

生物資訊學和基因組學是一門正在迅速興起的邊緣學科，它位於分子生物學、計算機、數學等多個領域的交叉點上。隨著第二代基因測序技術的普及，生物資訊和基因組學已經成為生物醫學研究的重要領域。由**孫昊**所領導的生物資訊學和基因組學研究小組致力於運用基因組學的研究的方法來研究幹細胞的分化過程及其分子機理、二代測序數據的算法和數據挖掘，及開發二代測序技術在轉化醫學中的應用。

Peiyong Jiang
江培勇



In this academic year, **Peiyong Jiang** and his team have made several important scientific achievements, for example, uncovering the novel biological properties of long cell-free DNA (cfDNA) and developing novel deconvolutional analysis of end motifs for assessing different DNA nuclease activities. The team has dedicated great efforts to pushing the frontiers of cfDNA fragmentomics and assiduously pursued clinical applications. In particular, the team has applied a non-negative matrix factorisation (NMF) algorithm to deconvolute a total of six distinct types of cfDNA cleavages. These cleavage patterns shed mechanistic insights into the processes in cfDNA fragmentation, which may open new possibilities for liquid biopsy of cancers and immune diseases.

在本學年中，**江培勇**和他的團隊取得了多項重要的科學成果，例如揭示了長游離DNA（cfDNA）新的生物學特性，以及基於游離DNA末端模序，開發了用於評估不同DNA核酸酶活性的新方法。該團隊致力於推動cfDNA片段組學的前沿發展，並孜孜不倦地追求臨床應用。尤其該團隊應用非負矩陣分解（NMF）演算法解析了六種不同類型的cfDNA斷裂模式。這些裂解模式為 cfDNA 片段化過程提供了機制性見解，可能為癌症和免疫疾病的液體活檢開闢新的可能性。

Ken Sung
宋永健



In this academic year, **Ken Sung** and the Laboratory of Computational Genomics have made a number of important achievements. With the recent development of genomic sequencing technologies, the team continues to develop novel frontier bioinformatics algorithms and software so that it is possible to sequence an individual genome cost-effectively and rapidly. He and his team have further used genomic data to learn the relationship between genomic variants and diseases and developed methods that can accurately call genomic variations (particularly structural variations). In addition, the team developed methods that can predict disease-causing mutations and applied them to Hong Kong patients successfully, which may open new possibilities for discovering important pathogenic variants for Hong Kong people.

本學年，**宋永健**及其計算基因組實驗室取得了多項重要成果。隨著基因組測序技術的不斷發展，該團隊致力於開發新穎生物信息算法及軟件，使其能以更加經濟有效的快速對單個基因組進行測序。他和他的團隊進一步使用基因組數據來了解基因組變異於疾病之間的關係，並且開發了可以準確識別基因組變異(尤其是結構變異)的方法。此外，該團隊還開發了預測致病突變的方法，並將其成功的應用在香港患者中，這可能為香港人發現重要致病性變異開闢新的可能。

13

Non-coding RNAs and Cellular Signalling

非編碼核糖核苷酸研究及細胞訊號轉導

Skeletal muscle has the remarkable ability to regenerate after injury, owing to adult muscle stem cells (MuSC). These cells are normally in a quiescent stage but can be rapidly activated upon injury, followed by proliferative expansion and differentiation into multinucleated myofiber to repair the damaged muscle tissues. Understanding how each phase of stem cell activities is regulated is the first step toward harnessing their regenerative potential for therapeutic treatments of many skeletal muscle-related diseases, such as ageing-inflicted Sarcopenia and Duchenne Muscular Dystrophy. **Huating Wang** and her research team thus dedicate their efforts to deciphering both intrinsic and extrinsic mechanisms governing MuSC activity in both physiological and pathological settings.

骨骼肌俱有強大的再生能力，這是由於成年肌肉幹細胞的存在。這些細胞通常處於靜息狀態期，但是在受傷時可以被快速激活，然後進行增殖性擴張並分化為多核肌纖維，以修復受損的肌肉組織。研究肌肉幹細胞活性如何在每個階段被調控，才能使我們有可能將它們用於衰老引起的肌少症等肌肉相關疾病的治療。因此，**王華婷**的研究團隊致力於解密在生理和病理條件下調控肌肉幹細胞活性的內源和外源機制。

Huating Wang
王華婷



William Wu
胡嘉麒



William Wu and his research team are devoted to the pursuit of excellence in research on the molecular mechanisms of diseases of public health significance, including infection/sepsis, chronic pain and cancer. They are particularly interested in the role of gut microbes and the use of omics platforms and big data.

胡嘉麒及其研究團隊致力於開展與公眾健康密切相關的前沿性科學研究，包括感染/敗血症、慢性疼痛、癌症等的分子機制研究。團隊尤其對腸道微生物及利用誇組學平台和大數據發掘與疾病相關的治療靶點感興趣。

14

Nephrology

腎臟疾病研究

Cheuk Chun Szeto
司徒卓俊



The research team, led by **Cheuk Chun Szeto**, investigates the use of urinary biomarkers for the diagnosis and monitoring of chronic kidney diseases such as diabetic kidney disease, IgA nephropathy, and lupus nephritis. They explore the potential of various urinary biomarkers, including cytokines, transcription factor mRNA, nucleic acid fragments, and podocyte-associated molecules. In addition, they analyse the adipokine and metabolomic signature in obesity and diabetic nephropathy, as well as the role of circulating bacterial and nucleic acid fragments as cardiovascular risk factors in kidney diseases.

由**司徒卓俊**帶領的研究團隊，重點研究尿液生物標誌物在慢性腎臟疾病的診斷和監測中的應用，包括糖尿病腎病、IgA腎病和紅斑狼瘡性腎炎。他們探索了各種尿液生物標誌物，包括細胞因子、轉錄因子核酸、核酸片段和足細胞相關分子的臨床應用。此外，他們也有研究肥胖和糖尿病腎病中的脂聯素和代謝組學的特徵，以及循環細菌和核酸片段在腎臟疾病中作為心血管風險因素的角色。

15

Robotics & AI

機械人與人工智能



Zheng Li
李崢

Zheng Li and his research team mainly focus on the research and development of innovative medical robots and devices, including intelligent flexible surgical robots for minimally invasive surgery, soft medical robots for gastrointestinal tract inspection, soft medical robots for rehabilitation, a magnetic anchored and guided system for Video-Assisted Thoracic Surgery (VATS), semi-autonomous robots for stereotactic brain biopsy, a semi-autonomous robotic system for transperineal prostate biopsy, and real-time surgical instrument detection and tracking with AI-assistance.

李崢及其研究團隊致力於研究醫療機械人和手術設備的創新和開發，包括用於微創手術的智能柔性機械人、用於胃腸道檢查的軟體機械人、用於胸腔內視鏡影像輔助手術的智能磁錨定內窺鏡、幫助進行腦內立體定位術的半自動機械人、用於會陰前列腺刺穿活檢的半自動機械人，以及利用人工智能進行實時探測和追蹤手術工具。



DIGESTIVE DISEASES

消化疾病研究

PRINCIPAL INVESTIGATOR
Jun Yu

TEAM MEMBERS
Vincent Wong, Dennis Wong, Jennifer Zhang, Hongyan Gou

RESEARCH PROGRESS SUMMARY

Gut microbiota in Colorectal Cancer

Probiotics are potential chemopreventive agents against colorectal cancer (CRC). The team led by **Jun Yu** has identified a number of novel probiotics effective in CRC prevention. The first one, *Carnobacterium maltaromaticum* (*C. maltaromaticum*), was found to be depleted in female patients with CRC. A series of animal studies showed that *C. maltaromaticum* reduces intestinal tumour formation in 2 murine CRC models in a female-specific manner. Mechanistically, *C. maltaromaticum* surface protein DD-CPase binds to estrogen-dependent SLC3A2 in colon epithelial cells. *C. maltaromaticum* then co-operates with *Faecalibacterium prausnitzii* to increase vitamin D and augment host vitamin D receptor (VDR) signalling, leading to tumour suppression. This paper is published in *Cancer Cell*, the top journal in Oncology (*Cancer Cell*, 2023).

The research team unravelled two probiotics as potential adjuvants for CRC immunotherapy. *Roseburia intestinalis* (*R. intestinalis*) is significantly depleted in CRC patients, and its administration suppressed tumour formation in *Apc*$^{Min/+}$ and AOM-induced CRC in mice, and restored gut barrier function in these models. They further identified that *R. intestinalis* produced abundant butyrate. *R. intestinalis*-derived butyrate activated anti-tumour immunity by binding to TLR5 receptor on CD8^{+} T cells to increase granzyme B, interferon-γ and tumour necrosis factor (TNF)-α expression. Accordingly, *R. intestinalis* improved anti-PD1 immunotherapy efficacy in immune-cold CRC models (*Gut*, 2023).

Another promising probiotic candidate is *Lactobacillus gallinarum* (*L. gallinarum*). *L. gallinarum* significantly improved anti-PD1 efficacy in 2 syngeneic mouse models with different microsatellite instability (MSI) statuses,



and in spontaneous CRC tumourigenesis. Metabolomic analyses revealed that *L. gallinarum* generated indole-3-carboxylic acid (ICA) as the functional metabolite. ICA inhibited indoleamine 2,3-dioxygenase (IDO1) expression to suppress kynurenine (Kyn) in tumours, and also antagonised Kyn-dependent activation of aryl hydrocarbon receptor in $CD4^+$ T cells, thereby inhibiting T_{reg} differentiation. Suppressed T_{reg} by *L. gallinarum* or ICA in turn activated $CD8^+$ T cell function, thus augmenting anti-PD1 efficacy (*Gut*, 2023).

Besides probiotics, the team investigated the interaction of diet and microbiome in CRC pathogenesis. They found that, to their surprise, a diet high in soluble fibre (but not insoluble fibre) promoted the development of CRC in mouse models, an effect abolished by the use of antibiotics. They further demonstrated that soluble fibre induced gut dysbiosis with enrichment of *Bacteroides uniformis* and depletion of *Bifidobacterium pseudolongum* depletion, accompanied by increased faecal butyrate and serum bile acids and decreased inosine. Pro-tumourigenic effect of soluble fibre-modulated microbiota was validated by faecal microbiota transplantation to germ-free mice. Hence, excess soluble fibre consumption may promote CRC via gut microbiota and metabolites (*Gastroenterology*, 2023).

Molecular Mechanism of Colorectal Cancer

M^6A is the most abundant RNA modification in humans. The research team showed that YTH N6-methyladenosine RNA binding protein 1 (YTHDF1), an m^6A reader, contributes to the tumour immune microenvironment. Single cell-sequencing of tumours with YTHDF1 knockout showed that YTHDF1 loss down-regulated myeloid-derived suppressor cells (MDSCs), together with reactivated cytotoxic T $CD8^+$ cells. Integrated MeRIP-seq, RNA-seq and Ribo-seq identified p65/Rela as a YTHDF1 target, leading to upregulation of CXCL1 cytokine, which increased MDSC migration via CXCL1-CXCR2 axis. Targeting of YTHDF1 by CRISPR or VNPs-siYTHDF1 boosted anti-PD1 efficacy in multiple CRC models, suggesting YTHDF1 is an attractive drug target to improve immunotherapy efficacy in CRC (*Gut*, 2023).

Further investigation revealed that an m^6A eraser, AlkB homolog 5 (ALKBH5), also fosters an immune suppressive microenvironment in CRC. ALKBH5 induced MDSC accumulation but reduced natural killer cells and cytotoxic $CD8^+$ T cells in tumour allografts, $CD34^+$ humanised mice, and intestine-specific *Alkbh5* knockin mice. Integrated sequencing efforts identified that ALKBH5 targets AXIN2 to activate oncogenic Wnt/β-catenin signalling, leading to increased secretion of Dickkopf-related protein 1 (DKK1). ALKBH5-induced DDK1 recruits MSDCs to drive immunosuppression in CRC. Targeting ALKBH5 using VNP-siALKBH5 thus potentiated anti-PD1 treatment in suppressing CRC growth (*Gastroenterology*, 2023).

Rewiring of tumour metabolism plays an important role in tumorigenesis. In this study, the team showed that SLC25A22, a metabolic gene upregulated in *KRAS*-mutant CRC, induces immunosuppression. In tumour allografts, humanised mice and transgenic *Slc25a22* knockout mice, SLC25A22 depletion restored anti-tumour immunity by repressing MDSCs and subsequent reactivation of $CD8^+$ T cells. Mechanistically, they find that SLC25A22 plays a central role in promoting asparagine, which binds and activates SRC-ERK-ETS2-CXCL1 cascade. CXCL1 in turn recruits MDSCs to impair $CD8^+$ T cells. Targeting SLC25A22 or asparagine impaired MDSC infiltration in *KRAS*-mutant CRC, and synergised with anti-PD1 to suppress the growth of KRAS-mutant CRC (*Nature Communications*, 2023).

Non–Alcoholic Fatty Liver Disease (NAFLD) and its associated Hepatocellular Carcinoma (HCC)

Non-alcoholic steatohepatitis (NASH) is a severe form of NASH. This study investigated the role of dietary intervention on NASH development in mice and identified soluble fibre inulin to be more effective than insoluble fibre cellulose in suppressing NASH progression in mice. The team devised an innovative ^{13}C-inulin stable-isotope tracing to track inulin metabolism into gut microbes and metabolites. Integrated analysis of ^{13}C-inulin metagenomes and metabolomes first demonstrated that *Parabacteroides distasonis* (*P. distasonis*) and its metabolite pentadecanoic acid was enriched by inulin. Mechanistically, *P. distasonis* and pentadecanoic acid restored gut barrier function and suppressed liver pro-inflammatory cytokine expression. This study suggests that inulin-derived gut microbes and metabolites could alleviate NASH (*Nat Microbiol*, 2023).

NAFLD-HCC is an emerging malignancy with few therapeutic options. As gut dysbiosis is a hallmark of NAFLD-HCC, the team sought to identify bacterial species as prophylactic for the prevention of NAFLD-HCC. They demonstrated that *Bifidobacterium pseudolongum* (*B. pseudolongum*) is the top depleted bacterium in mouse models of NAFLD-HCC. *B. pseudolongum* significantly suppressed NAFLD-HCC formation in two mouse models, and its conditioned medium inhibited cell proliferation *in vitro*. Acetate was identified as the critical anti-cancer metabolite of *B. pseudolongum*. Acetate travels to the liver via the gut-liver axis, binds and activates the GPR43 receptor on hepatocytes, leading to repressed IL-6/JAK1/STAT3 oncogenic signalling. Together, *B. pseudolongum* is a novel probiotic that protects against NAFLD-HCC by secreting anti-tumour metabolite acetate (*J Hepatol*, 2023).

Cancer chemoprevention

Pien Tze Huang (PZH) is a well-established Traditional Chinese Medicine with beneficial effects against inflammation and cancer. In this study, the research explored the chemopreventive effect of PZH in CRC. In $Apc^{Min/+}$ and AOM-DSS models of CRC, PZH dose-dependently suppressed tumorigenesis. PZH altered the gut microbiota, with increased levels of probiotics *Pseudobutyrivibrio xylanivorans* and *Eubacterium limosum*, while pathogenic bacteria *Aeromonas veronii*, *Campylobacter jejuni*, *Collinsella aerofaciens*, and *Peptoniphilus harei* were depleted. In addition, PZH promoted beneficial metabolites and restored gut barrier function. Pathway analysis further revealed that PZH inhibited PI3K-Akt and pro-inflammatory signalling. Notably, faecal microbiota transplantation from PZH-treated mice to germ-free mice recapitulated the chemopreventive effects of PZH. Collectively, they showed that PZH could prevent CRC by virtue of its effect on the gut microbiota and metabolites (*Gastroenterology*, 2013).

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Jun Yu	Distinguished Research Awards for Gene and Cell Therapy	Molecular Cloud
	Academician of European (Life Science)	Academy of Europe
	Ranked Top 2 in Female Scientist in All Field and Top 8 Scientist in the Field of Medicine in China	Research.com
	Highly Cited Researchers	Clarivate
	Academician of Hong Kong	Hong Kong Academy of Sciences
	Wu Jieping-Paul Janssen Prize in Medicine and Pharmacy	The International Exchange and Cooperation Center of the National Health Commission
	First-class Higher Education Outstanding Scientific Research Output Award (Natural Science Award)	Ministry of Education
Jennifer Zhang	First-class Higher Education Outstanding Scientific Research Output Award (Natural Science Award)	Ministry of Education

Fellowships

Name	Details	
	Fellowship	Organisation
Jun Yu	Academician	Academia Europaea
		Academia Hong Kong
	學部委員	中國醫學科學院
	Fellow	American Gastroenterology Association, USA
	Vice President	China Medical Women's Association Division of Digestive Disease
		Guangdong-Hong Kong-Macao Greater Bay Area Gastroenterology Association
	Vice Chairman	Cancer and Gut Microbiome Committee of China Anti-Cancer Association
		Chronic Disease Management Branch of China Medical Biotechnology Association
		Hong Kong Scientist Association, HK
		Digestive Disease Branch of the Cross-Strait Medicine and Health Exchange Association
	Council member	Hong Kong Immunology Association, HK
		Microecology Branch of Chinese Preventive Medicine Association
	Member	International Cancer Genome Consortium, USA
		American Association for Cancer Research, USA
		Australian Medical Association, Australia
	Expert member	Expert Committee of the Collaborative Development Center of Gastroenterology Department of Beijing Hospital Administration
	Executive Committee	Hong Kong Cancer Institute
	Admission Panel Member	The incubation programmes run by the Hong Kong Science & Technology Park under the category "Biomedical Technology–Medical Devices/ Diagnostics"
	CPPCC member	Hebei Committee of the Chinese People's Political Consultative Conference
	Committee member	Professional Committee of Cancer Screening, Early Diagnosis and Early Treatment of China Anti-Cancer Association
	Advisory Board Member	Oncology & Cancer Research, Regional Advisory Board
Vincent Wong	Council Member	AsiaHep Hong Kong
		Hong Kong Association for the Study of Liver Diseases
	Member	American Association for the Study of Liver Diseases
		European Association for the Study of the Liver
Dennis Wong	Member	American Gastroenterology Association, USA
		Tumor microecology of China anti-Cancer Association
		China Anti-Cancer Association
Jennifer Zhang	Youth Vice Chairman	Cross-Strait Medical and Health Exchange Association Gastroenterology Branch
	Member	American Gastroenterology Association, USA
		Tumor microecology of China anti-Cancer Association
		Chronic Disease Management of China Medicinal Biotech Association
		Hong Kong Immunology Association
Hongyan Gou	Youth Vice Member	Cross-Strait Medical and Health Exchange Association Gastroenterology Branch
	Member	Hong Kong Immunology Association

Academic Editorships

Name	Details	
	Role	Journal
Jun Yu	Associate Editor	Gut
		Oncogene
		Life Sciences
		Journal of Digestive Diseases
		Journal of Pathology Research
		World Journal of Gastroenterology
		Hepatoma Research
	Advisory board	Cancer Cell
		eBioMedicine
	Regional Advisory Board	Springer Nature
	Deputy Chief Editor	Journal of Gastroenterology and Hepatology
		Chinese Medical Journal (English)
	Editor	Gut
		Oncogenesis
		Scientific Reports
		The Open Hepatology Journal
		Pragmatic and Observational Research

Name	Details	
	Role	Journal
Jun Yu	Editor	ISRN Gastroenterology
		International Journal of Clinical Medicine
		Insight Knowledge
		The Open Gastroenterology Journal
		Journal of Gastroenterology & Hepatology Research
Vincent Wong	Editorial Board Member	JHEP Reports
		Hepatology Communications
		Alimentary Pharmacology & Therapeutics
	Associate Editor	Clinical Gastroenterology and Hepatology
Dennis Wong	Editorial Board Member	Frontiers in Medicine
		Oncogene
	Guest Editorial Member	Cells
	Guest Associate Editor	Biomedicine
Jennifer Zhang	Editorial Board Member	Frontiers in Oncology
		Frontiers in Cell and Developmental Biology
		Frontiers in Microbiology
		International Journal of Medical Sciences

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Jun Yu	Chair	AGA Abstract Review Committee – Microbiome
	Reviewer	Advanced Science
		Alimentary Pharmacology & Therapeutics
		American Journal of Gastroenterology
		American Journal of Pathology
		Annals of Internal Medicine
		Annals of Oncology
		BioMed Research International
		BMC Cancer
		BMC Gastroenterology
		British Journal of Cancer
		Cancer
		Cancer Cell

Name	Details	
	Role	Journal / Conference
Jun Yu	Reviewer	Cancer Discovery
		Cancer Letters
		Cancer Research
		Carcinogenesis
		Cell
		Cell & Bioscience
		Cell Death & Disease
		Cell Host & Microbe
		Cell Metabolism
		Cell Reports
		Cellular and Molecular Gastroenterology and Hepatology
		Clinical and Experimental Pharmacology and Physiology
		Clinical Cancer Research
		Clinical Gastroenterology and Hepatology
		Digestion
		Digestive Diseases and Sciences
		EBioMed
		FEBS Letters
		Gastroenterology
		Genomics Proteinomics & Bioinformatics
		BioMed Research International
		Gut
		Gut Microbes
		Hepatology
		HPDI
		Human Molecular Genetics
		International Journal of Biochemistry & Cell Biology
		International Journal of Cancer
		International Journal of Oncology
		ISRN Gastroenterol
		Journal of Clinical Investigation
		Journal of Current Pharmaceutical Design
		Journal of Gastroenterology and Hepatology
		Journal of Hepatology
		Lancet
		Microbiome

Name	Details	
	Role	Journal / Conference
Jun Yu	Reviewer	Nature Communication
		Nature Medicine
		Nature Methods
		Nature Microbiology
		Nature Reviews Clinical Oncology
		Nature Reviews Gastroeneterology and Hepatology
		New England Journal of Medicine
		Oncogene
		Science
		Signal Transduction and Targeted Therapy
Vincent Wong	Reviewer	Gastroenterology
		Gut
		Hepatology
		Journal of Hepatology
Dennis Wong	Reviewer	Gut
		Oncogene
		Pathology
		Pharmacological Research
		Pharmaceutics
		Theranostics
		Expert Opinion on Investigational Drugs
		Journal of Gastroenterology & Hepatology
		Molecules
		Metabolites
		Nature Communications
Jennifer Zhang	Reviewer	Cell Metabolism
		Gastroenterology
		Advanced Sciences
		Frontiers in Oncology
		Journal of Gastroenterology & Hepatology
		Journal of Leukocyte Biology
		Cancer Letters
		Gut
		Oncogene
		Life Sciences
		Frontiers in Immunology
		Alimentary Pharmacology & Therapeutics
		Experimental Cell Research

Name	Details	
	Role	Journal / Conference
Jennifer Zhang	Reviewer	Cell & Bioscience
		Cell Reports
		Engineering
		Health Sciences Report
Hongyan Gou	Reviewer	Oncogene
		Cancer Research
		Frontiers in Pharmacology

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jun Yu	Exploiting Epitranscriptome Dysregulation in Colorectal Carcinogenesis and Metastasis: Mechanisms and Novel Therapeutic Approaches	Research Grants Council – Collaborative Research Fund	01/07/2020	30/06/2023	6,158,384
	RNA Demethylase AlkB Homolog 5 (ALKBH5) Drives Immune Suppression in Colorectal Cancer via Epitranscriptome Regulation of AXIN2-WNT-DKK1 Axis	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,325,732
	Evaluation of SQLE as a Novel Therapeutic Target in Non-Alcoholic Fatty Liver Disease	Health Bureau – Health and Medical Research Fund	01/07/2020	30/06/2023	1,498,772
	The Role and Mechanism of Methylation Modification and Its Regulatory Genes in the Development of Colorectal Cancer	National Natural Foundation of China	01/01/2020	31/12/2023	RMB 2,000,000
	Developing Probiotics into High-Efficacy and Safe Prophylactics and Adjuvant Therapies for Colorectal Cancer	Research Grants Council – General Research Fund, Research Impact Fund	30/06/2022	29/06/2027	9,790,000
	Non-Invasive Diagnosis of Colorectal Cancer Using Microbiome Markers	Shenzhen-Hong Kong-Macau Technology Scheme	30/04/2022	30/04/2024	RMB 1,000,000
	Evaluation of the Combination of Mebendazole Plus Navitoclax for the Treatment of Non-Alcoholic Fatty Liver Disease Associated-Hepatocellular Carcinoma	Health Bureau – Health and Medical Research Fund	01/05/2022	30/04/2025	1,499,880

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jun Yu	Developing Mechanism-Driven Probiotics for Improving Response to Immunotherapy in Colorectal Cancer	Innovation and Technology Commission – Innovation and Technology Fund Research Talent Hub	01/11/2022	30/10/2024	3,994,999
	Fighting Disease Recurrence and Promoting Tissue Repair after Liver Transplantation: Translating Basic Discoveries to Clinical Excellence	Research Grants Council – Theme-based Research Scheme	01/12/2019	30/11/2024	45,000,000
	The Interaction of Key Intestinal Pathogens and Host Factors in Promoting the Development of Colorectal Cancer	National Key R&D Program of China	01/11/2020	30/10/2025	RMB 22,000,000
	Assess Antibiotic Resistome Flows from Pollution Hotspots to Environments and Explore the Control Strategies	Research Grants Council – Theme-based Research Scheme	01/12/2020	31/11/2025	29,000,000
	The Mechanism and Clinical Translation of the Gut Microbiota in Non-Alcoholic Fatty Liver Disease	Guangdong-Hong Kong Technology Cooperation Scheme	01/07/2023	30/06/2025	2,200,000
Dennis Wong	Branched Chain Amino Acids (BCAA) Restriction to Alleviate Colorectal Cancer Metastasis	Health Bureau – Health and Medical Research Fund	01/12/2021	30/11/2024	1,499,880
	SLC25A22 Drives Immune Suppression In KRAS-Mutant Colorectal Cancer through Metabolic Regulation of CXCL1/CXCR2 Axis	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,155,532
	SLC25A22 Drives Oncometabolite Succinate to Promote Cancer Stemness in KRAS-Mutant Colorectal Cancer	Research Grants Council – Early Career Scheme	01/01/2021	31/12/2023	936,520
	Dissecting the Role of RNA N6-Methyladenosine Modification in Mutant KRAS-Driven Colorectal Cancer: Molecular Mechanisms and Targeted Therapy	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,158,188
	Functional Investigation of Novel Oncogenic Bacterium Peptostreptococcus Stomatis in Colorectal Carcinogenesis and Chemoresistance	Health Bureau – Health and Medical Research Fund	01/08/2023	31/07/2026	1,499,880

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jennifer Zhang	Mechanism of Dietary Cholesterol-Induced Mitochondrial Dysfunction in Fatty Liver Associated Liver Cancer	National Natural Science Foundation of China	01/01/2022	31/12/2024	RMB 300,000
	Selective Blockade of p38α Alternative Activation in T Cells as a Novel Therapeutic Strategy for Non-Alcoholic Steatohepatitis	Health Bureau – Health and Medical Research Fund	01/01/2022	31/12/2024	1,288,600
	Role of Intestine TM6SF2 in Protecting Non-Alcoholic Fatty Liver Disease through the Maintenance of Gut Barrier Function	Research Grants Council – General Research Fund	01/10/2022	30/09/2025	1,120,716
	Basic and Translational Research of Non-Alcoholic Fatty Liver Disease	National Natural Science Foundation of China – Excellent Young Scientists Fund (HK and Macao)	01/01/2023	31/12/2026	RMB 2,000,000
	Evaluation of *Bifidobacterium Pseudolongum* as Prophylaxis against Fatty Liver Disease-Associated Liver Cancer through Gut-Liver Axis	National Natural Science Foundation of China	01/01/2023	31/12/2026	RMB 520,000
	Establishing an Optimal Biomarker Panel for Non-Invasive Diagnosis of Non-Alcoholic Steatohepatitis	Health Bureau – Health and Medical Research Fund Research Fellowship Scheme, Hong Kong	01/04/2023	31/12/2025	1,080,920
	Elucidating the Role and Mechanism of TM6SF2 in Suppressing Fatty Liver Disease-Associated Liver Cancer through Regulating Anti-Tumor Immunity	Research Grants Council – General Research Fund	01/10/2023	30/09/2026	1,462,000
Hongyan Gou	Study on the Mechanism of TRIP6 Promoting Colorectal Cancer Metastasis by Regulating Cancer Stem Cells	National Natural Science Foundation of China	01/01/2022	31/12/2024	RMB 300,000
	The Immune Mechanism of TRIP6 to Promote Colorectal Cancer Liver Metastasis by Interacting with Tumor Microenvironment	Shenzhen Basic Research	01/06/2020	30/05/2025	RMB 300,000

Publications

A. Journal Papers

1. Wong CC, Fong W, Yu J. Gut microbes promote chemoradiotherapy resistance via metabolic cross-feeding. *Cancer Cell*. 2023;41(1):12-14. doi:10.1016/j.ccell.2022.11.017. (Preview)

2. Yu J. Gut microbiome and metabolome: The crucial players in inflammatory bowel disease. *Journal of Gastroenterology and Hepatology*. 2023;38(1):5-6. doi:10.1111/jgh.16098. (Editorial)

3. Liu Y, Lau HCH, Cheng WY, Yu J. Gut microbiome in colorectal cancer: Clinical diagnosis and treatment. *Genomics, Proteomics and Bioinformatics*. 2023;21(1):84-96. doi:10.1016/j.gpb.2022.07.002. (Review)

4. Qian Y, Zhou L, Luk STY, Xu J, Li W, Gou H, Chen H, Kang W, Yu J, Wong CC. The sodium channel subunit SCNN1B suppresses colorectal cancer via suppression of active c-Raf and MAPK signaling cascade. *Oncogene*. 2023;42(8):601-612. doi:10.1038/s41388-022-02576-4.

5. Chen Y, Qiu Q, She J, Yu J. Extrachromosomal circular DNA in colorectal cancer: Biogenesis, function and potential as therapeutic target. *Oncogene*. 2023;42(13):941-951. doi:10.1038/s41388-023-02640-7. (Review)

6. Wang X, Wong CC, Chen H, Fu K, Shi L, Su H, Guo S, Gou H, Hu X, Zhang L, Ji J, Yu J. The N6-methyladenine DNA demethylase ALKBH1 promotes gastric carcinogenesis by disrupting NRF1 binding capacity. *Cell Reports*. 2023;42(3). doi:10.1016/j.celrep.2023.112279.

7. Yang Z, Gao S, Wong CC, Liu W, Chen H, Shang H, Wu ZY, Xu L, Zhang X, Wong N, Kuang M, Yu J. TUBB4B is a novel therapeutic target in non-alcoholic fatty liver disease-associated hepatocellular carcinoma. *Journal of Pathology*. 2023;260(1):71-83. doi:10.1002/path.6065.

8. Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. *Nature Reviews Clinical Oncology*. 2023;20(7):429-452. doi:10.1038/s41571-023-00766-x. (Review)

9. Zhou X, Zhang X, Yu J. Gut mycobiome in metabolic diseases: Mechanisms and clinical implication. *Biomedical Journal*. Published online June 2023:100625. doi:10.1016/j.bj.2023.100625. (Review, Epub ahead of print)

10. Zhang X, Ha S, Lau HCH, Yu J. Excess body weight: Novel insights into its roles in obesity comorbidities. *Seminars in Cancer Biology*. 2023;92:16-27. doi:10.1016/j.semcancer.2023.03.008. (Review)

11. Wong CC, Yu J. Colorectal cancer subtyping with microbiome - A game changer for personalized medicine? *Gastroenterology*. 2023;165(1):25-27. doi:10.1053/j.gastro.2023.04.023. (Editorial)

12. Kang X, Ng SK, Liu C, Lin Y, Zhou Y, Kwong TNY, Ni Y, Lam TYT, Wu WKK, Wei H, Sung JJY, Yu J, Wong SH. Altered gut microbiota of obesity subjects promotes colorectal carcinogenesis in mice. *eBioMedicine*. 2023;93. doi:10.1016/j.ebiom.2023.104670.

13. Yu J. Bifidobacterium triple viable powder/capsule: How effective it is against gastrointestinal diseases? *Journal of Gastroenterology and Hepatology*. 2023;38(7):1013-1014. doi:10.1111/jgh.16283. (Editorial)

14. Bao Y, Zhai J, ChenH, Wong CC, Liang C, Ding Y, Huang D, Gou H, ChenD, Pan Y, Kang W, To KF, Yu J. Targeting m^6A reader YTHDF1 augments antitumour immunity and boosts anti-PD-1 efficacy in colorectal cancer. *Gut.* 2003;72(8):1497-1509. doi:10.1136/gutjnl-2022-328845.

15. Zhai J, Chen H, Wong CC, Peng Y, Gou H, Zhang J, Pan Y, Chen D, Lin Y, Wang S, Kang W, To KF, Chen Z, Nie Y, He HH, Sung JJY, Yu J. ALKBH5 drives immune suppression via targeting AXIN2 to promote colorectal cancer and is a target for boosting immunotherapy. *Gastroenterology*. 2023;165(2):445-462. doi:10.1053/j.gastro.2023.04.032.

16. Wei W, Wong CC, Jia Z, Liu W, Liu C, Ji F, Pan Y, Wang F, Wang G, Zhao L, Chu ESH, Zhang X, Sung JJY, Yu J. Parabacteroides distasonis uses dietary inulin to suppress NASH via its metabolite pentadecanoic acid. *Nature Microbiology*. 2023;8(8):1534-1548. doi:10.1038/s41564-023-01418-7.

17. Zhou Q, Peng Y, Ji F, Chen H, Kang W, Chan LS, Gou H, Lin Y, Huang P, Chen D, Wei Q, Su H, Liang C, Zhang X, Yu J, Wong CC. Targeting of SLC25A22 boosts the immunotherapeutic response in KRAS-mutant colorectal cancer. *Nature Communications*. 2023;14(1). doi:10.1038/s41467-023-39571-6.

18. Li Q, Chan H, Liu WX, Liu CA, Zhou Y, Huang D, Wang X, Li X, Xie C, Liu WYZ, Wang XS, Ng SK, Gou H, Zhao LY, Fong W, Jiang L, Lin Y, Zhao G, Bai F, Liu X, Chen H, Zhang L, Wong SH, Chan MTV, Wu WKK, Yu J. Carnobacterium maltaromaticum boosts intestinal vitamin D production to suppress colorectal cancer in female mice. *Cancer Cell*. 2023;41(8):1450-1465.e8. doi:10.1016/j.ccell.2023.06.011.

19. Pan Y, Chen H, Zhang X, Liu W, Ding Y, Huang D, Zhai J, Wei W, Wen J, Chen D, Zhou Y, Liang C, Wong N, Man K, Cheung AHK, Wong CC, Yu J. METTL3 drives NAFLD-related hepatocellular carcinoma and is a therapeutic target for boosting immunotherapy. *Cell Reports Medicine*. 2023;4(8). doi:10.1016/j.xcrm.2023.101144.

20. Kang X, Liu C, Ding Y, Ni Y, Ji F, Lau HCH, Jiang L, Sung JJY, Wong SH, Yu J. Roseburia intestinalis generated butyrate boosts anti-PD-1 efficacy in colorectal cancer by activating cytotoxic $CD8^+$ T cells. *Gut*. 2023;72(11):2112-2122. doi:10.1136/gutjnl-2023-330291.

21. Fong W, Li Q, Ji F, Liang W, Lau HCH, Kang X, Liu W, To KKW, Zuo Z, Li X, Zhang X, Sung JJY, Yu J. Lactobacillus gallinarum-derived metabolites boost anti-PD1 efficacy in colorectal cancer by inhibiting regulatory T cells through modulating IDO1/Kyn/AHR axis. *Gut*. 2023;72(12):2272-2285. doi:10.1136/gutjnl-2023-329543.

22. Gou H, Su H, Liu D, Wong CC, Shang H, Fang Y, Zeng X, Chen H, Li Y, Huang Z, Fan M, Wei C, Wang X, Zhang X, Li X, Yu J. Traditional medicine Pien Tze Huang suppresses colorectal tumorigenesis through restoring gut microbiota and metabolites. *Gastroenterology*. 2023;165(6):1404-1419. doi:10.1053/j.gastro.2023.08.052.

23. Wong CC, Zhai J, Yu J. Reply to “ALKBH5 in colorectal cancer: An insufficiently explored and controversial research area”. *Gastroenterology*. 2023;165(6):1581-1582. doi:10.1053/j.gastro.2023.09.018. (Reply)

24. Liu Y, Lau HCH, Yu J. Microbial metabolites in colorectal tumorigenesis and cancer therapy. *Gut Microbes*. 2023;15(1). doi:10.1080/19490976.2023.2203968. (Review)

25. Gou H, Wong CC, Chen H, Shang H, Su H, Zhai J, Liu W, Liu W, Sun D, Wang X, Yu J. TRIP6 disrupts tight junctions to promote metastasis and drug resistance and is a therapeutic target in colorectal cancer. *Cancer Letters*. 2023;578. doi:10.1016/j.canlet.2023.216438.

26. Song Q, Zhang X, Liu W, Wei H, Liang W, Zhou Y, Ding Y, Ji F, Cheung HKA, Wong N, Yu J. Bifidobacterium pseudolongum-generated acetate suppresses non-alcoholic fatty liver disease-associated hepatocellular carcinoma. *Journal of Hepatology*. 2023;79(6):1352-1365. doi:10.1016/j.jhep.2023.07.005.

27. Yang J, Wei H, Lin Y, Chu ESH, Zhou Y, Gou H, Guo S, Lau HCH, Cheung AHK, Chen H, To KF, Sung JJY, Wang Y, Yu J. High soluble fiber promotes colorectal tumorigenesis through modulating gut microbiota and metabolities in mice. *Gastroenterology*. 2024;166(2):323-337.e7. doi:10.1053/j.gastro.2023.10.012.

28. Ding Y, Zhao L, Wang G, Shi Y, Guo G, Liu C, Chen Z, Coker OO, She J, Yu J. PacBio sequencing of human fecal samples uncovers the DNA methylation landscape of 22 673 gut phages. *Nucleic Acids Research*. 2023;51(22):12140-12149. doi:10.1093/nar/gkad977.

29. Li S, Zhu S, Yu J. The role of gut microbiota and metabolites in cancer chemotherapy. *Journal of Advanced Research*. Published online November 26, 2023. doi:10.1016/j.jare.2023.11.027. (Review, Epub ahead of print)

30. Ha S, Zhang X, Yu J. Probiotics intervention in colorectal cancer: From traditional approaches to novel strategies. *Chinese Medical Journal*. 2024;137(1):8-20. doi:10.1097/cm9.0000000000002955. (Review)

B. Patents

1. The United States Patent:

   Title: Fecal Bacterial Markers for Colorectal Cancer
   Inventors: Jun Yu, Joseph Sung, Qiaoyi Liang
   Patent No.: US 11603567 B2
   Issue Date: 14 March 2023

   Title: Therapeutic and Prophylactic Treatment for Colorectal Cancer
   Inventors: Ka Kei Wu, Jun Yu
   Patent No.: US 11554145 B2
   Issue Date: 17 January 2023

   Title: Compositions for Enhancing Immunotherapy Efficacy in Colorectal Cancer Treatment
   Inventors: Jun Yu, Ka Kei Wu, Winnie Fong, Xing Kang, Qing Li
   Application No.: US63/464,325
   File Date: 5 May 2023

2. European Patent:

   Title: Fecal Bacterial Markers for Colorectal Cancer
   Inventors: Jun Yu, Joseph Sung, Qiaoyi Liang
   Patent No.: EP 3504346B1
   File Date: 21 March 2019
   Issue Date: 16 August 2023

3. China PCT:

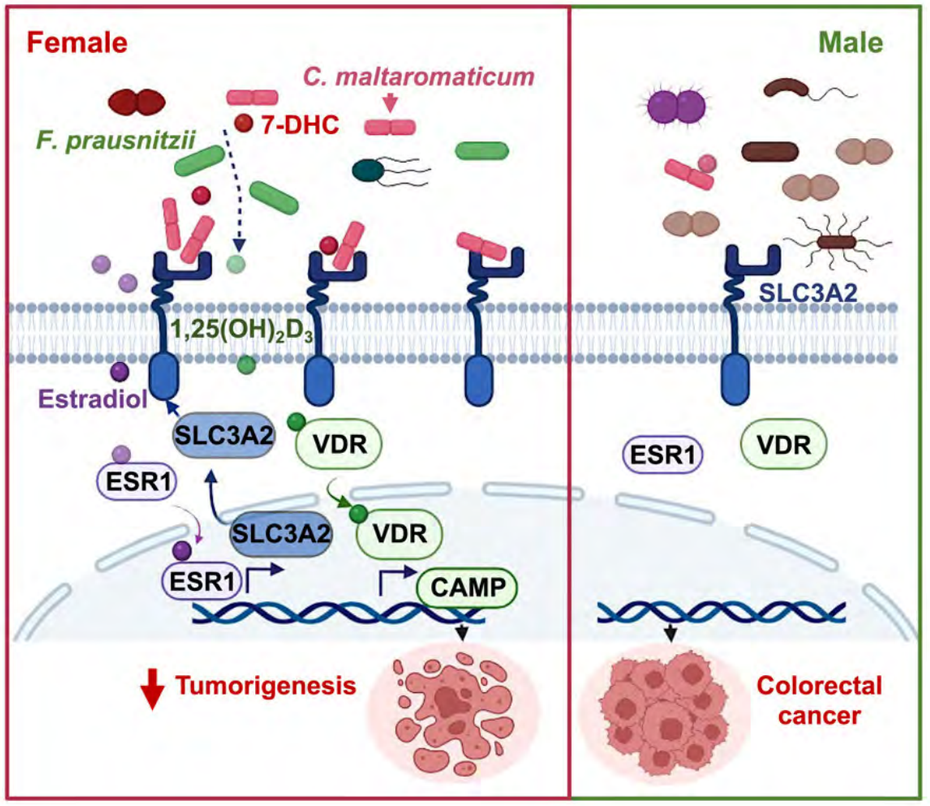
   Title: Fecal Bacterial Markers for Colorectal Cancer
   Inventors: Jun Yu, Joseph Sung, Qiaoyi Liang
   Patent No.: CN 107779505 B
   Issue Date: 6 June 2023

   Title: Markers for Diagnosis of Non-Alcoholic Steatohepaitis
   Inventors: Jun Yu, Xiang Zhang, Guijun Zhao
   Application No.: PCT/CN2023/075430
   File Date: 10 February 2023

4. China Patent:

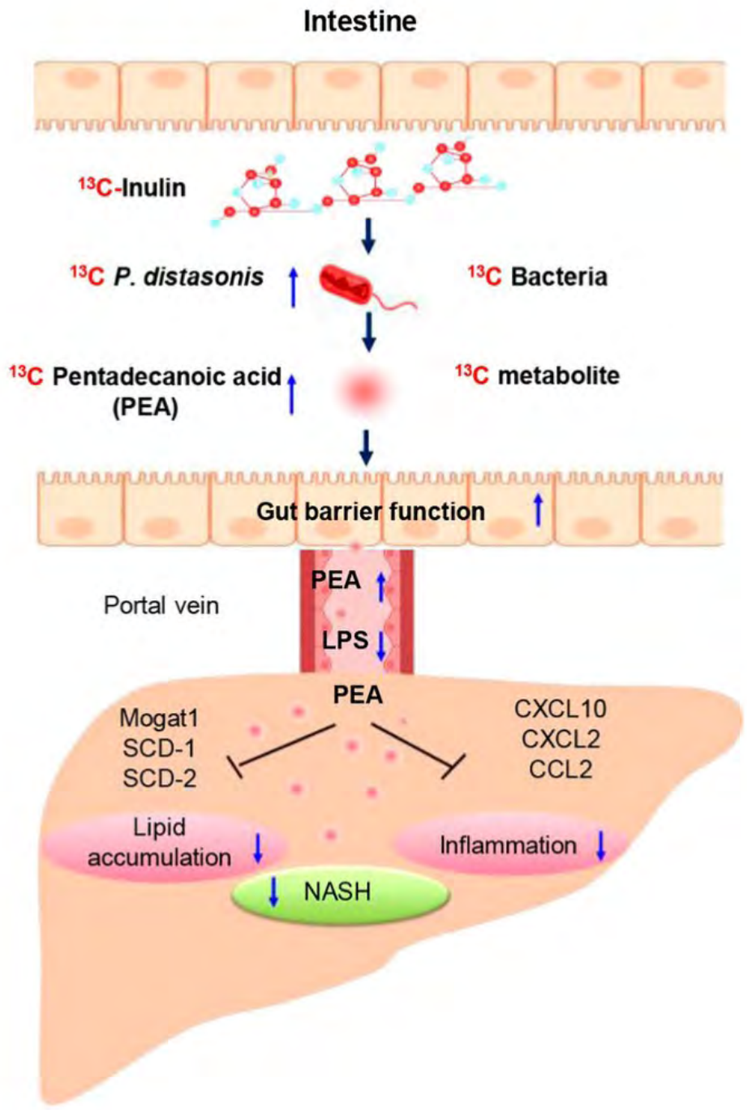
   Title: Method and Comptions for Nucleic Acid Analysis
   Inventors: Jun Yu, Yiping Ho, Guoping Wang, Liuyang Zhao, Fuyang Qu
   Application No.: CN202310290106.9A
   File Date: 23 March 2023

   Title: Fecal Combination Diagnostic Markers and Kit for Colorectal Cancer and Advanced Adenoma
   Inventors: Jun Yu, Hongyan Gou
   File Date: 18 June 2023



C. maltaromaticum colonises the gut in an estrogen-dependent manner and acts along with other microbes to augment the intestinal vitamin D production to activate the host VDR for suppressing CRC.

Source: Li Q, Chan H, Liu WX, Liu CA, Zhou Y, Huang D, Wang X, Li X, Xie C, Liu WYZ, Wang XS, Ng SK, Gou H, Zhao LY, Fong W, Jiang L, Lin Y, Zhao G, Bai F, Liu X, Chen H, Zhang L, Wong SH, Chan MTV, Wu WKK, Yu J. Carnobacterium maltaromaticum boosts intestinal vitamin D production to suppress colorectal cancer in female mice. Cancer Cell. 2023;41(8):1450-1465.e8. doi:10.1016/j.ccell.2023.06.011.



By ^{13}C stable isotype labeling in mice, the research team provided the direct link between dietary inulin and its target bioactive intestinal bacteria *P. distasonis* and its metabolite pentadecanoic acid. *P. distasonis* recaptitulated the beneficial effect of inulin by restoring gut barrier function and inhibiting pro-inflammatory signalling.

Source: Wei W, Wong CC, Jia Z, Liu W, Liu C, Ji F, Pan Y, Wang F, Wang G, Zhao L, Chu ESH, Zhang X, Sung JJY, Yu J. Parabacteroides distasonis uses dietary inulin to suppress NASH via its metabolite pentadecanoic acid. Nature Microbiology. 2023;8(8):1534-1548. doi:10.1038/s41564-023-01418-7.



MOLECULAR DIAGNOSTICS

CIRCULATING FETAL NUCLEIC ACIDS

分子診斷學

PRINCIPAL INVESTIGATOR

Dennis Lo

TEAM MEMBERS

Allen Chan, Rossa Chiu, Peiyong Jiang, Jacky Lam, Peter Cheung, Guanhua Zhu, Qing Zhou, Diana Han, Stephanie Yu, Lois Choy, Alice Cheng, Rebecca Chan, Charles Chan, Lu Ji, Huimin Shang, Wenlei Peng, Vicky Lee, Spencer Ding, Sherwood Fung, Wanxia Gai, Mary Jane Ma, Guangya Wang, Dongyan Xiong, Qian Qian Mou, Irene Tse, Patty Tse, Vivien Lin, Amy Tsang, Maggie Li, Saravanan Ramakrishnan, Angel Lai, Lilian Zhong, Manna Law, West Choi, Xingqian Li, Winsome Wong, Harry Chan, Chris Kum, Patrick Tin, Xingfu Qin, Zejia Lin, Zilong Wang, Zhiyang Ge, Yao He

RESEARCH PROGRESS SUMMARY

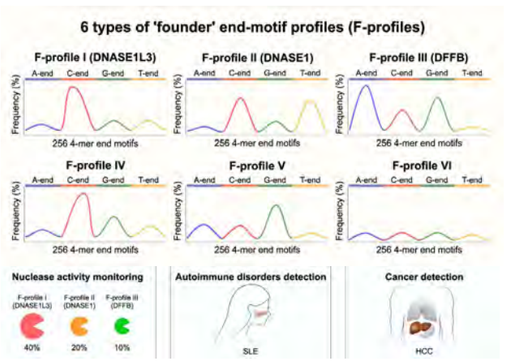
Detection of cancer-derived DNA in blood plasma, or liquid biopsy, for cancer screening is a hot research topic. However, in some tested positive individuals, no cancer could be found despite thorough investigations. The significance of a positive cancer DNA test in individuals without an immediately identifiable cancer is unclear. The research team led by **Dennis Lo** used nasopharyngeal cancer (NPC) as a model to address this question. They carried out two rounds of NPC screening, separated by a median of about 4 years, for 20,000 volunteers using plasma Epstein-Barr virus (EBV) DNA analysis. They first demonstrated that liquid biopsy for cancer screening is a feasible concept that could bring about a clinical impact. Screening by plasma EBV DNA, as cancer-derived DNA in NPC, could identify early asymptomatic cancer and lead to a 90% reduction in mortality. Remarkably, they further showed that individuals with positive results but no identifiable cancer in the first round would have an elevated risk of up to 16.8 folds of having NPC at the second-round. Their findings revealed, for the first time, that the presence of cancer-associated DNA changes not only can detect a current concealed cancer but also reflect the risk of future cancer development. These findings have important implications for the future development of plasma DNA-based tumour markers. This study is published in the *NEJM Evidence*, a publication of the New England Journal of Medicine Group (Chan et al. *NEJM Evid* 2023;2(7)).

The realisation of nonrandom fragmentation patterns exhibited by cell-free DNA (cfDNA) has prompted the research team to delve deeper into the biology of DNA fragmentation, now known as 'fragmentomics' analysis. In the pursuit of understanding DNA fragmentation, the team has successfully developed a range of fragmentomics

markers that hold diagnostic implications for cancer detection and determination of tissue of origin. These markers include factors such as fragment size, preferred end, end motif, and jagged end (Lo et al. *Science* 2021;372:eaaw3616). In addition, they have identified several key nucleases that contribute in the generation and fragmentation of circulating DNA, including deoxyribonuclease1-like 3 (DNASE1L3), deoxyribonuclease1 (DNASE1) and DNA fragmentation factor subunit beta (DFFB, also known as caspase-activated DNase) (Han et al. *Am J Hum Genet* 2020;106:202-214).

The team continued their work on linking nucleases and cfDNA fragmentation. Specifically, they have attempted to decipher the relative contributions of cfDNA cleavage patterns related to underlying fragmentation factors through a mathematical model known as non-negative matrix factorization (NMF), they deconvoluted cfDNA cleavage and identified 6 distinct types of cfDNA cleavage patterns, referred to as 'founder' end-motif profiles (F-profiles), named F-profiles I, II, III, IV, V, and VI. F-profiles I, II, and III were linked to DNASE1L3, DNASE1, and DFFB, respectively through the deconvolution analysis in knockout mice deficient in the corresponding nucleases. Such analysis of the relative contributions of F-profiles in cfDNA were subsequently shown to be useful to inform a wide spectrum of pathological states including cancer.

To demonstrate the potential applications in cancer diagnostics, the team has used the hepatocellular cancer (HCC) model. They analysed the contributions of distinct types of cfDNA cleavages in a cohort consisting of healthy controls, hepatitis B virus (HBV) carriers without HCC, and patients with HCC. Compared with healthy controls, F-profile I level was found to be decreased in HCC patients, whereas no appreciable change was observed in HBV carriers. Interestingly, among the 6 F-profiles, the most discriminative power in detecting patients with HCC was F-profile VI (AUC: 0.97). As F-profile VI showed a promising differentiation power between the patients with and without HCC, they explored whether any biological process was linked to F-profile VI. Because of the lack of obvious preference in the frequencies across 4-mer motifs in the F-profile VI, the team hypothesised that cfDNA fragmentation occurring in patients with cancer might in part be induced by DNA damages via a mechanism which was distinct from the known apoptotic pathways, for example, DFFB and/or DNASE1L3-mediated DNA fragmentation. They proposed that F-profile VI might be associated with oxidative stress, given the implication of oxidative stress in many steps in carcinogenesis. It was known that the increase of oxidative stress could be observed during chemotherapy and radiotherapy. Using the model of patients with NPC who were subjected to cisplatin- or carboplatin-based chemoradiotherapy, the F-profile VI contributions in plasma were shown to be elevated, in contrast to cfDNA from the same patient collected before the treatment. The results of this study have been published in the *Proceedings of the National Academy of Sciences of the United States of America.* (Zhou et al. *Proc Natl Acad Sci U S A* 2023;120(17): e2220982120).



RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Dennis Lo	Tengchong Science Award	Tengchong Scientists Forum
	China's major medical achievements of the 21st century	Chinese Academy of Medical Sciences
	ILCHUN Molecular Medicine Award	Korean Society for Biochemistry and Molecular Biology
	The Global Impact Award	Tatler Asia

Fellowships

Name	Details	
	Fellowship	Organisation
Dennis Lo	Fellow of the National Academy of Inventors (NAI)	National Academy of Inventors (NAI)
	Member of the Chinese Academy of Sciences	Chinese Academy of Sciences
	Member of Beijing Municipal Committee of the Chinese People's Political Consultative Conference (CPPCC)	Chinese People's Political Consultative Conference (CPPCC)

Academic Editorships

Name	Details	
	Role	Journal
Peiyong Jiang	Editorial Board Member	Extracellular Vesicles and Circulating Nucleic Acids
Jacky Lam		BMC Medical Genomics

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Dennis Lo	Centre for Novostics	Innovation and Technology Commission – InnoHK Scheme	01/05/2020	30/04/2023	Not to be disclosed

Publications

A. Journal Papers

1. Wang G, Lam WKJ, Ling L, Ma MJL, Ramakrishnan S, Chan DCT, Lee WS, Cheng SH, Chan RWY, Yu SCY, Tse IOL, Wong WT, Jiang P, Chiu RWK, Allen Chan KC, Lo YMD. Fragment ends of circulating microbial DNA as signatures for pathogen detection in sepsis. *Clinical Chemistry*. 2023;69(2):189-201. doi:10.1093/clinchem/hvac197.

2. Yu SCY, Deng J, Qiao R, Cheng SH, Peng W, Lau SL, Choy LYL, Leung TY, Wong J, Wong VWS, Wong GLH, Jiang P, Chiu RWK, Chan KCA, Lo YMD. Comparison of single molecule, real-time sequencing and nanopore sequencing for analysis of the size, end-motif, and tissue-of-origin of long cell-free DNA in plasma. *Clinical Chemistry*. 2023;69(2):168-179. doi:10.1093/clinchem/hvac180.

3. Lam WKJ, King AD, Miller JA, Liu Z, Yu KJ, Chua MLK, Ma BBY, Chen MY, Pinsky BA, Lou PJ, Woo JKS, Hsu WL, Simon J, Doolan DL, Waterboer T, Hui EP, Li H, Tsang RK, Wong KCW, Goh JP, Vlantis AC, Ai QY, Wong LM, Abdullah V, Lin JC, Chen CJ, Pfeiffer RM, Le QT, Lee AWM, Ji M, Cao S, Ma J, Chan ATC, Chan KCA, Hildesheim A. Recommendations for Epstein-Barr virus–based screening for nasopharyngeal cancer in high- and intermediate-risk regions. *JNCI: Journal of the National Cancer Institute*. 2023;115(4):355-364. doi:10.1093/jnci/djad012. (Review)

4. Zhou Z, Ma MJL, Chan RWY, Lam WKJ, Peng W, Gai W, Hu X, Ding SC, Ji L, Zhou Q, Cheung PPH, Yu SCY, Teoh JYC, Szeto CC, Wong J, Wong VWS, Wong GLH, Chan SL, Hui EP, Ma BBY, Chan

ATC, Chiu RWK, Chan KCA, Lo YMD, Jiang P. Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(17):e2220982120. doi:10.1073/pnas.2220982120.

5. 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;72(9):1758-1773. doi:10.1136/gutjnl-2022-328364.

6. Chan A, Lam WKJ, King A, Lin VS, Lee PPH, Zee BCY, Chan SL, Tse IOL, Tsang AFC, Li MZJ, Jiang P, Yong Q, Ai H, Poon DMC, Au KH, Hui EP, Ma BBY, Hasselt AC Van, Chan ATC, Woo JKS, Lo YMD. Plasma Epstein–Barr virus DNA and risk of future nasopharyngeal cancer. *NEJM Evidence*. 2023;2(7). doi:10.1056/evidoa2200309.

7. Yu SCY, Choy LYL, Lo YMD. 'Longing' for the next generation of liquid biopsy: the diagnostic potential of long cell-free DNA in oncology and prenatal testing. *Molecular Diagnosis and Therapy*. 2023;27(5):563-571. doi:10.1007/s40291-023-00661-2.

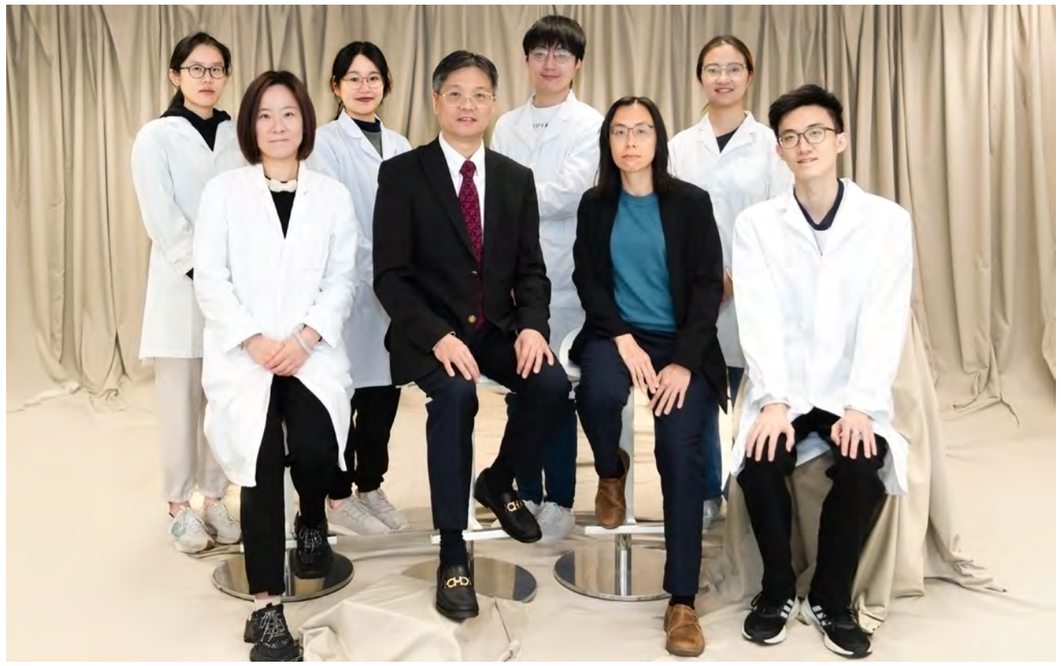
8. Gai W, Yu SCY, Chan WTC, Peng W, Lau SL, Leung TY, Jiang P, Chan KCA, Lo YMD. Droplet digital PCR is a cost-effective method for analyzing long cell-free DNA in maternal plasma: Application in preeclampsia. *Prenatal Diagnosis*. 2023;43(11):1385-1393. doi:10.1002/pd.6432.

9. Mattox AK, Douville C, Wang Y, Popoli M, Ptak J, Silliman N, Dobbyn L, Schaefer J, Lu S, Pearlman AH, Cohen JD, Tie J, Gibbs P, Lahouel K, Bettegowda C, Hruban RH, Tomasetti C, Jiang P, Chan KCA, Lo YMD, Papadopoulos N, Kinzler KW, Vogelstein B. The origin of highly elevated cell-free DNA in healthy individuals and patients with pancreatic, colorectal, lung, or ovarian cancer. *Cancer Discovery*. 2023;13(10):2166-2179. doi:10.1158/2159-8290.cd-21-1252/728398.



Dennis Lo received the inaugural Tengchong Science Award.

Source: Dennis Lo



MOLECULAR DIAGNOSTICS

GENETICS OF DISEASE SUSCEPTIBILITY

分子診斷學

PRINCIPAL INVESTIGATOR
Nelson Tang

TEAM MEMBERS
Paul Chan, Linda Lam, Suk Ling Ma

RESEARCH PROGRESS SUMMARY

Research Directions:

1. Genetics of complex traits: To identify prevalent genetic variants causing common diseases in Han Chinese;
2. Statistical genetics and computational statistical analysis of big genetic and biological datasets;
3. Analysis of variation of the transcriptome using the latest technology of next-generation sequencing.

Research into Biology of Aging:

The mission of the GDS laboratory is to identify disease predisposition genes and biomarkers for common diseases, particularly focusing on complex traits. One of the most important traits for general well-being is ageing. The laboratory led by **Nelson Tang's** team has a long track record in the study of biomarkers for healthy ageing. Telomere undergoes natural attrition with age. The research group is involved in the development of various analysis methods of telomere length. They also participate in international consortiums in studies of natural attrition of telomere length and found that their telomere is long enough for natural aging. However, environmental hazards, like smoking or diseases may accelerate the attrition process. Despite these findings, it is not fully understood if such accelerated shortening of telomeres will lead to any significant health consequences.

RESEARCH AND SCHOLARSHIP

Academic Editorships

Name	Details	
	Role	Journal
Nelson Tang	Editorial Board Member	Pathology
		Frontiers in Pediatrics
		Journal of Pediatric Biochemistry (Official journal of World Society of Child Science)
		Genes – Open Access Journal of Genetics & Genomics
		Frontiers in Genetics

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Nelson Tang	Reviewer	Hong Kong Medical Journal
		Union World Conference
		Human Genetics
		Journal of Orthopaedic Surgery

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Nelson Tang	Development of a Single-cell Full-length Mitochondrial Genome Sequencing Platform Based on Droplet Microfluidics	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	970,181
	Paediatric Biomonitoring Reference Values for Metals and Trace Elements in Urine: A Survey of Hong Kong Children	Health Bureau	04/10/2021	03/10/2024	1,009,167
	Establishment Hong Kong Branch of CAS Center for Excellence in Animal Evolution and Genetics	The Chinese University of Hong Kong – Vice-Chancellor's One-off Discretionary Fund	01/06/2020	31/05/2023	12,000,000

Publications

A. Journal Papers

1. Yeung SSY, Ma SL, Wang X, Chen Y, Tsui SKW, Tang NLS, Woo J. Telomere length among Chinese aged 75+ years. *Gerontology*. 2023;69(12):1414-1423. doi:10.1159/000534644.

2. Xiao FH, Wang HT, Chen XQ, Ge MX, Yan D, Yang XL, Yang LQ, Lin R, Guo RH, Zhang W, Tang NLS, He Y, Zhou J, Cai WW, Kong QP. Hypermethylation in H3K9me3 regions characterizes the centenarian methylomes in healthy aging. *National Science Review*. 2023;10(6). doi:10.1093/nsr/nwad067. (Editorial)

3. Tam CHT, Lim CKP, Luk AOY, Shi M, Cheung Hm, Ng ACW, Lee H, Lau ESH, Fan B, Jiang G, Kong APS, Ozaki R, Chow EYK, Lee KF, Siu SC, Hui G, Tsang CC, Lau KP, Leung JYY, Cheung EYN, Yu G, et al. Identification of a common variant for coronary heart disease at PDE1A contributes to individualized treatment goals and risk stratification of cardiovascular complications in Chinese patients with type 2 diabetes. *Diabetes Care*. 2023;46(6):1271-1281. doi:10.2337/dc22-2331.

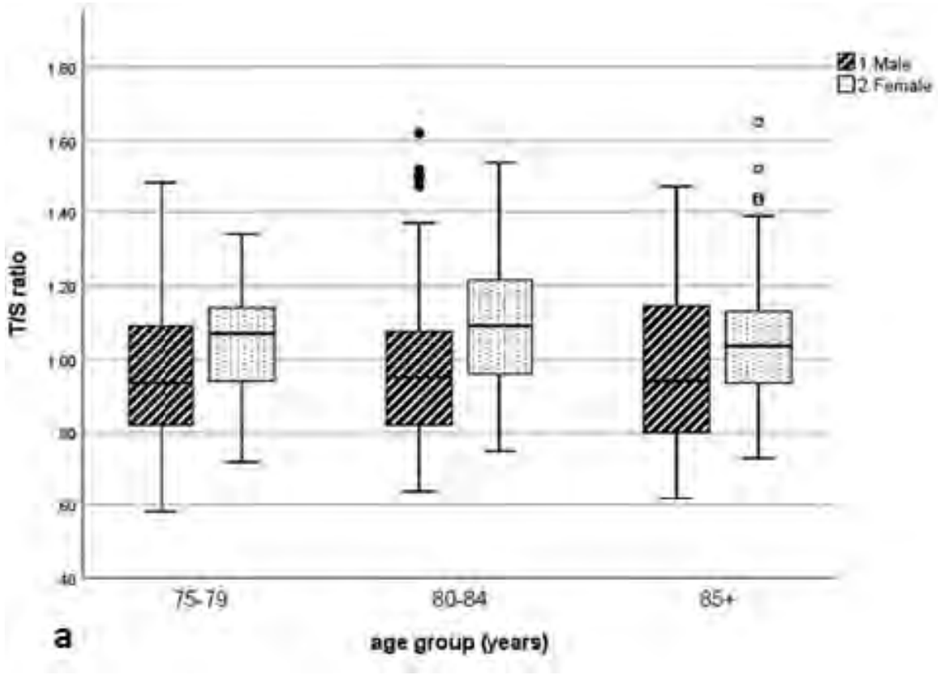
B. Patents

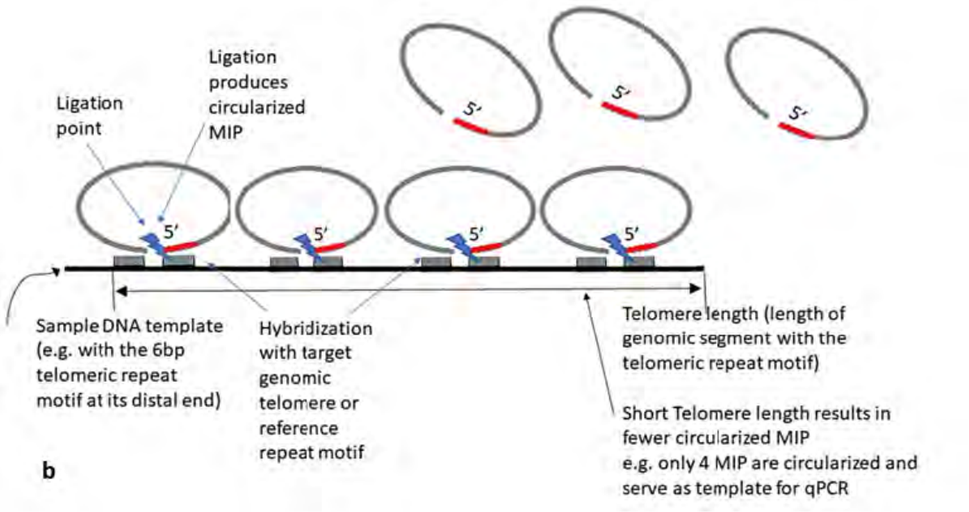
1. The United States Patent:

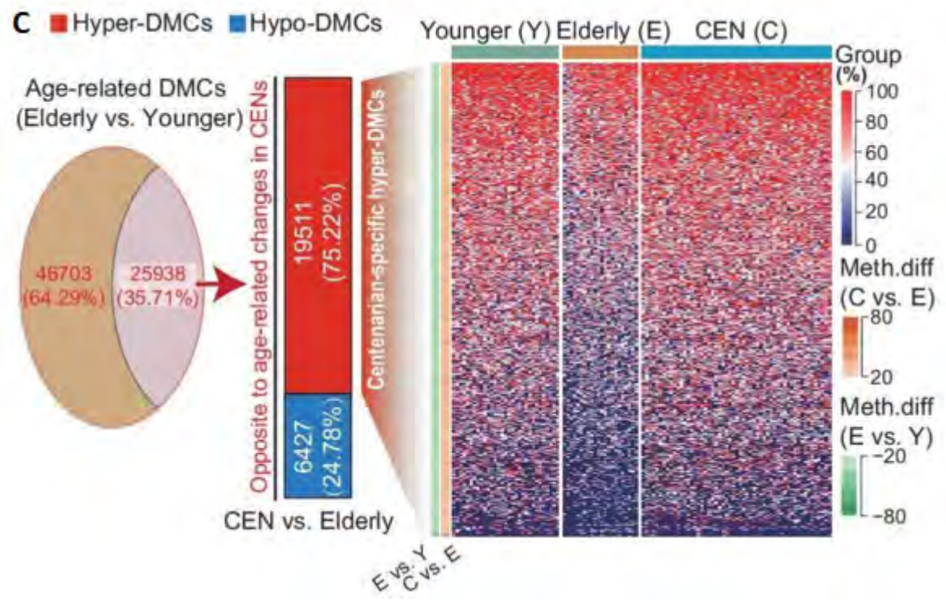
   Title: Method for Determining The Copy Number of A Tandem Repeat Sequence
   Inventors: Tang NLS, Ma SL, Woo J
   National Application No.: 16/891,452
   Patent No.: US11639521B2
   Filing Date: 2 May 2023

2. Hong Kong Patent:

   Title: Methods for Determining Gene Expression in A Single Cell Subpopulation and Associated Kits and Uses
   Inventors: Huang D, Leung KS, Tang NLS
   Patent No.: HK30087169
   Filing Date: 1 September 2023







The research team led by Nelson Tang reported how the environment influenced telomere length among ageing-well individuals (Woo J, Tang N, Suen E, Leung J, Wong M. Green space, psychological restoration, and telomere length. *Lancet*. 373:299-300.). In their recent study, they confirmed that lifestyle habit has a stronger effect on telomere length than chronic age (Figure A) by a new high-sensitive assay of telomere length (Figure B), a figure from their patent document). In an analysis of epigenetic markers, Centenarians who were individuals exceptionally successful in healthy ageing were more alike to youngsters than the elderly in a heatmap analysis (Figure C).

Sources:
Yeung SSY, Ma SL, Wang X, Chen Y, Tsui SKW, Tang NLS, Woo J. Telomere length among Chinese aged 75+ years. Gerontology. 2023;69(12):1414-1423. doi:10.1159/000534644.

Nelson Tang's patent

Xiao FH, Wang HT, Chen XQ, Ge MX, Yan D, Yang XL, Yang LQ, Lin R, Guo RH, Zhang W, Tang NLS, He Y, Zhou J, Cai WW, Kong QP. Hypermethylation in H3K9me3 regions characterizes the centenarian methylomes in healthy aging. National Science Review. 2023;10(6). doi:10.1093/nsr/nwad067.



MOLECULAR DIAGNOSTICS

PLASMA NUCLEIC ACIDS RESEARCH

分子診斷學

PRINCIPAL INVESTIGATOR
Allen Chan

TEAM MEMBERS
Jacky Lam, Wanxia Gai, Charles Chan, Sherwood Fung, Vicky Lee, Irene Tse, Amy Tsang, Maggie Li, Vivien Lin, Kaede Chau, Olive Wong, Sze Wan Wong

RESEARCH PROGRESS SUMMARY

A large-scale prospective clinical study carried out by **Allen Chan** and his team has laid the foundation for the use of plasma Epstein-Barr virus (EBV) DNA analysis for screening of nasopharyngeal carcinoma (NPC) (Chan et al. *N Engl J Med* 2017; 513-522). They have recently completed a rescreening of the original cohort of about 20,000 participants recruited into the study. The rescreening efforts reveal the future risk of NPC among those positive for plasma EBV DNA with implications on the optimal screening intervals for subjects with different risk profiles.

In the Phase 2 study, the same screening protocol which involves a two-time-point testing of plasma EBV DNA by real-time polymerase-chain-reaction (PCR) was adopted. In total, 17,838 out of the original cohort of 20,174 subjects (88.4%) participated in the second-round screening. In this round of re-screening, twenty-four subjects were diagnosed with NPC, with 17 (67%) having early-stage disease (stages I or II). The proportion of early-stage patients was similar to that identified from the first-round screening (71%) but much higher than that of the control historical cohort (20%). NPC patients identified at the second round of screening also had superior survival compared to patients in the historical cohort (3-year progression-free survival: 100% vs 70%, respectively; hazard ratio: 0.11). This illustrated that interval screening by plasma EBV DNA testing could also enable early cancer detection and bring about survival improvements.

Specifically, the team has analysed the plasma EBV DNA positivity status at initial recruitment (samples collected 4 years ago) of the 24 newly diagnosed NPC cases identified in this Phase 2 re-screening study. Such analysis was aimed at dissecting the long-term risk of NPC among subjects positive for plasma EBV DNA. Among the 24 NPC patients, 17 had negative results, 3 had transiently positive and 4 had persistently positive plasma EBV DNA results in the Phase 1 study. Compared to subjects with undetectable first-round EBV DNA (i.e. relative risk = 1), the relative risks of

developing an NPC identified at the second round were 4.4 (95% confidence interval: 1.3 – 15.0) and 16.8 (95% confidence interval: 5.7 – 49.6), respectively, for subjects with transiently positive and persistently positive EBV DNA results. The study findings have been published in *The New England Journal of Medicine Evidence* (Chan et al. *NEJM Evid* 2023; 2(7)). Therefore, this rescreening study has illuminated that plasma EBV DNA positivity represents a strong risk factor for NPC. This finding would have implications for formulating a personalised screening protocol based on the plasma EBV DNA status, such as different screening intervals would be applied to different risk groups.

RESEARCH AND SCHOLARSHIP

Research Award and Recognition

Name	Details	
	Award	Organisation
Allen Chan	2023 Positive Droplet Award	Bio-rad

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Allen Chan	Centre for Novostics	Innovation and Technology Commission	01/05/2020	30/04/2025	Not to be disclosed
	Prospective 20,000-Person Nasopharyngeal Carcinoma (NPC) Screening Programme using Plasma Epstein-Barr Virus (EBV) DNA Analysis	Kadoorie Charitable Foundation	01/04/2013	31/03/2023	9,400,000

Publications

A. Journal Papers

1. Wang G, Lam WKJ, Ling L, Ma MJL, Ramakrishnan S, Chan DCT, Lee WS, Cheng SH, Chan RWY, Yu SCY, Tse IOL, Wong WT, Jiang P, Chiu RWK, Chan KCA, Lo YMD. Fragment ends of circulating microbial DNA as signatures for pathogen detection in sepsis. *Clinical chemistry*. 2023;69(2):189-201. doi:10.1093/clinchem/hvac197.

2. Yu SCY, Deng J, Qiao R, Cheng SH, Peng W, Lau SL, Choy LYL, Leung TY, Wong J, Wong VWS, Wong GLH, Jiang P, Chiu RWK, Chan KCA, Lo YMD. Comparison of single molecule, real-time sequencing and nanopore sequencing for analysis of the size, end-motif, and tissue-of-origin of long cell-free DNA in plasma. *Clinical chemistry*. 2023;69(2):168-179. doi:10.1093/clinchem/hvac180.

3. Lam WKJ, King AD, Miller JA, Liu Z, Yu KJ, Chua MLK, Ma BBY, Chen MY, Pinsky BA, Lou PJ, Woo JKS, Hsu WL, Simon J, Doolan DL, Waterboer T, Hui EP, Li H, Tsang RK, Wong KCW, Goh JP, Vlantis AC, Ai QY, Wong LM, Abdullah V, Lin JC, Chen CJ, Pfeiffer RM, Le QT, Lee AWM, Ji M, Cao S, Ma J, Chan ATC, Chan KCA, Hildesheim A. Recommendations for Epstein-Barr virus-based screening for nasopharyngeal cancer in high- and intermediate-risk regions. *Journal of the National Cancer Institute*. 2023;115(4):355-364. doi:10.1093/jnci/djad012.

4. Mahajan S, Balcioglu HE, Oostvogels A, Dik WA, Chan KCA, Lo KW, Hui EP, Tsang A, Tong J, Lam WKJ, Wong K, Chan ATC, Ma BBY, Debets R. Frequency of peripheral CD8+ T cells expressing chemo-attractant receptors CCR1, 4 and 5 increases in NPC patients with EBV clearance upon radiotherapy. *Cancers*. 2023;15(6). doi:10.3390/cancers15061887.

5. Zhou Z, Ma MJL, Chan RWY, Lam WKJ, Peng W, Gai W, Hu X, Ding SC, Ji L, Zhou Q, Cheung PPH, Yu SCY, Teoh JYC, Szeto CC, Wong J, Wong VWS, Wong GLH, Chan SL, Hui EP, Ma BBY, Chan ATC, Chiu RWK, Chan KCA, Lo YMD, Jiang P. Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(17). doi:10.1073/pnas.2220982120.

6. 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;72(9):1758-1773. doi:10.1136/gutjnl-2022-328364.

7. Chan A, Lam WKJ, King A, Lin VS, Lee PPH, Zee BCY, Chan SL, Tse IOL, Tsang AFC, Li MZJ, Jiang P, Yong Q, Ai H, Poon DMC, Au KH, Hui EP, Ma BBY, Hasselt AC Van, Chan ATC, Woo JKS, Lo YMD. Plasma Epstein-Barr virus DNA and risk of future nasopharyngeal cancer. *NEJM Evidence*. 2023;2(7). doi:10.1056/evidoa2200309.

8. Lou PJ, Lam WKJ, Hsu WL, Pfeiffer RM, Yu KJ, Chan CML, Lee VCT, Chen TC, Terng S Der, Tsou YA, Leu YS, Liao LJ, Chang YL, Chien YC, Wang CP, Lin CY, Hua CH, Lee JC, Yang TL, Hsiao CH, Wu MS, et al. Performance and operational feasibility of Epstein-Barr virus-based screening for detection of nasopharyngeal carcinoma: Direct comparison of two alternative approaches. *Journal of Clinical Oncology*. 2023;41(26):4257-4266. doi:10.1200/jco.22.01979.

9. Gai W, Yu SCY, Chan WTC, Peng W, Lau SL, Leung TY, Jiang P, Chan KCA, Lo YMD. Droplet digital PCR is a cost-effective method for analyzing long cell-free DNA in maternal plasma: Application in preeclampsia. *Prenatal Diagnosis*. 2023;43(11):1385-1393. doi:10.1002/pd.6432.

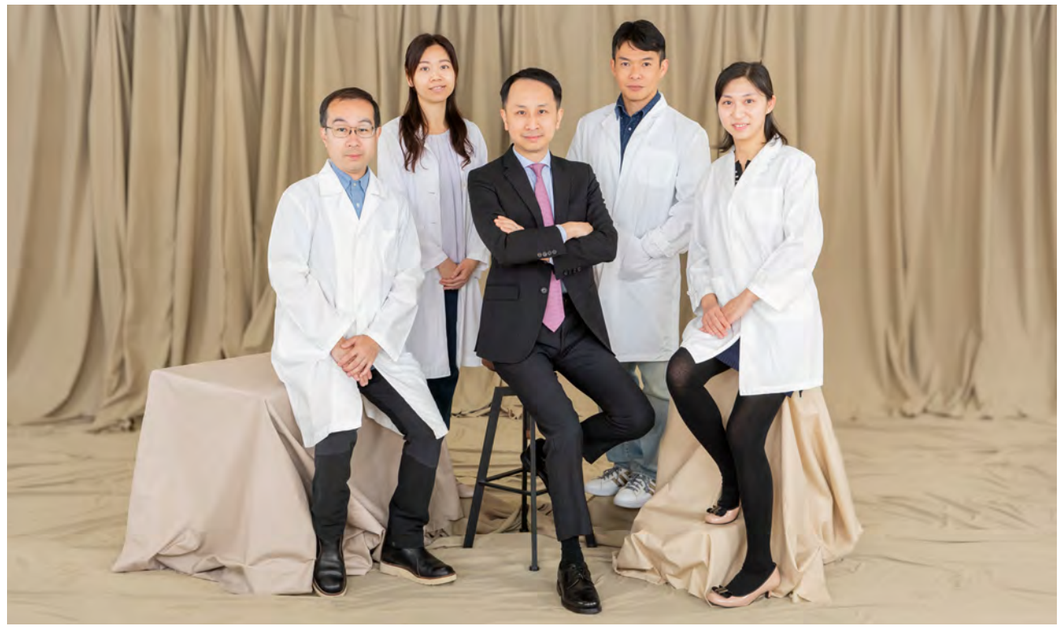
10. Mattox AK, Douville C, Wang Y, Popoli M, Ptak J, Silliman N, Dobbyn L, Schaefer J, Lu S, Pearlman AH, Cohen JD, Tie J, Gibbs P, Lahouel K, Bettegowda C, Hruban RH, Tomasetti C, Jiang P, Chan KCA, Lo YMD, Papadopoulos N, Kinzler KW, Vogelstein B. The origin of highly elevated cell-free DNA in healthy individuals and patients with pancreatic, colorectal, lung, or ovarian cancer. *Cancer Discovery*. 2023;13(10):2166-2179. doi:10.1158/2159-8290.cd-21-1252.

11. Lai R, Yeung DCM, Yeung ZWC, Hui TSC, Lam WKJ, Chan KCA, Ng CWK, To ZWH, Cho RHW, Chan CPL, Lai CCF, Leung NMW, Wong EWY, Chung JCK, Tsang RKY, Li KWS, Chow JCH, Cheung KKM, Chan JYK. Combining transoral nasopharyngeal brush and plasma Epstein-Barr virus DNA in detecting locally recurrent nasopharyngeal carcinoma. *Otolaryngology - Head and Neck Surgery (United States)*. 2023;169(5):1208-1214. doi:10.1002/ohn.380.



Inaugural Lecture of Tony Mok Shu Kam Professorship in Medicine by Professor Allen Chan

Source: Allen Chan



MOLECULAR DIAGNOSTICS

PLASMA NUCLEIC ACIDS RESEARCH

分子診斷學

PRINCIPAL INVESTIGATOR
Jacky Lam

TEAM MEMBERS
Irene Tse, Vivien Lin, Man Na Law

RESEARCH PROGRESS SUMMARY

Jacky Lam and his research team have previously identified the distinct nasopharyngeal cancer (NPC) associated molecular profiles of plasma Epstein-Barr virus (EBV) DNA through targeted next-generation sequencing (NGS), including quantitation, size and methylation. Based on the discovery, they have developed novel diagnostic approaches that allow better differentiation of NPC and non-NPC samples. Through the quantitative and size analysis, the team could reduce the false positive rate of NPC detection from 5.4% to 0.7% with a modelled positive predictive value (PPV) of 19.6% in our prospective screening cohort, that is, almost double of that two time-point PCR-based testing reported before (11.0%) (Lam et al. *Proc Natl Acad Sci U S A* 2018;115(22):E5115-E5124). Importantly, the improvement in the specificity and PPV could be achieved through a single time-point analysis and this could facilitate population-wide testing.

To validate the performance of the team developed NGS-based NPC screening test, they have conducted a collaborative study with the National Cancer Institute (NCI) of the United States. In this collaborative study, they have evaluated the diagnostic performances of plasma EBV DNA (using their targeted NGS test) versus EBV antibody (using combined VCA-IgA and EA-IgA testing) for NPC detection. This is the first head-to-head comparison study to evaluate and compare the two screening modalities in a large cohort. The study cohort included archived NPC samples and age and sex-matched controls from a multi-centred, hospital-based study conducted in Taiwan between 2010 and 2014. A total of 797 prospectively collected NPC cases and 1,745 controls were subject to PCR-based EBV DNA testing. Plasma EBV DNA testing (by their targeted NGS test) yielded significantly higher sensitivity and specificity than EBV antibody testing. For plasma EBV DNA analysis, the reported sensitivity was 93.2% and specificity was 98.1%. In contrast, for EBV antibodies analysis, the sensitivity was 88.4% and specificity was 94.9%. The EBV DNA-based screening approach exhibited substantially higher PPVs than the EBV antibody-based approach. The finding of this collaborative study validates the performances of their proposed NGS-based EBV DNA test for screening of NPC. This also demonstrates the superior performance compared to EBV antibody. The manuscript of this study has been published in the *Journal of Clinical Oncology* (Lou et al. *J Clin Oncol*. 2023; 41(26): 4257–4266).

To translate research findings into clinical practice and promote NPC screening in the population level, Allen Chan and Jacky have organised the Nasopharyngeal Cancer Screening Conference. In the meeting, 40 experts from various disciplines (including otorhinolaryngologists, radiologists, oncologists, pathologists, primary care physicians, virologists, epidemiologists and statisticians) gathered to review and discuss available data on EBV-based screening for NPC. Through the meeting, they led the development of the first international recommendation document on the use of EBV-based biomarkers for screening of NPC. The recommendation document would be useful to guide public health programs in order to translate research findings into well-proven clinical benefits of morbidity and mortality reduction. In particular, it would be of strategic importance for enhancing NPC screening adoption in Hong Kong and the Greater Bay Area. The document has been published in *The Journal of National Cancer Institute* (Lam et al. *J Natl Cancer Inst* 2023;115(4):355-364).

RESEARCH AND SCHOLARSHIP

Research Award and Recognition

Name	Details	
	Award	Organisation
Jacky Lam	Lo Ying Shek Chi Wai Foundation Meritorious Research Award	Lo Ying Shek Chi Wai Foundation

Academic Editorship

Name	Details	
	Role	Journal
Jacky Lam	Editorial Board Member	BMC Medical Genomics

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jacky Lam	Investigating the Molecular Characteristics of Epstein-Barr Virus DNA in Plasma to Enhance Surveillance of Recurrence of Nasopharyngeal Carcinoma	Research Grants Council – Early Career Scheme	01/09/2021	31/08/2023	648,491
	Analysis of Plasma Epstein-Barr Virus (EBV) DNA and EBV Antibody for Early Detection of Nasopharyngeal Carcinoma and Protocol Optimisation	National Natural Science Foundation of China/ Research Grants Council Joint Research Scheme 2022/23	01/01/2023	31/12/2026	662,366

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jacky Lam	Magnetic Resonance Imaging Screening for Nasopharyngeal Carcinoma: Artificial Intelligence for Automatic Detection	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,125,732
	Evaluation of Intra-treatment Response: Is the RECIST Guideline Applied to Nasopharyngeal Carcinoma Treated with Induction Chemotherapy?	Health Bureau – Health and Medical Research Fund	01/08/2023	31/10/2024	327,500
	Molecular Analysis of Plasma Epstein-Barr Virus DNA by Targeted Sequencing in Virus-associated Lymphoma	The Chinese University of Hong Kong Research Committee – Direct Grant	30/06/2023	29/06/2024	50,000

Publications

A. Journal Papers

1. Wang G, Lam WKJ, Ling L, Ma MJL, Ramakrishnan S, Chan DCT, Lee WS, Cheng SH, Chan RWY, Yu SCY, Tse IOL, Wong WT, Jiang P, Chiu RWK, Chan KCA, Lo YMD. Fragment ends of circulating microbial DNA as signatures for pathogen detection in sepsis. *Clinical Chemistry*. 2023;69(2):189-201. doi:10.1093/clinchem/hvac197.

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3. Mahajan S, Balcioglu HE, Oostvogels A, Dik WA, Chan KCA, Lo KW, Hui EP, Tsang A, Tong J, Lam WKJ, Wong K, Chan ATC, Ma BBY, Debets R. Frequency of peripheral CD8+ T cells expressing chemo-attractant receptors CCR1, 4 and 5 increases in NPC patients with EBV clearance upon radiotherapy. *Cancers*. 2023;15(6):1887. doi:10.3390/cancers15061887.

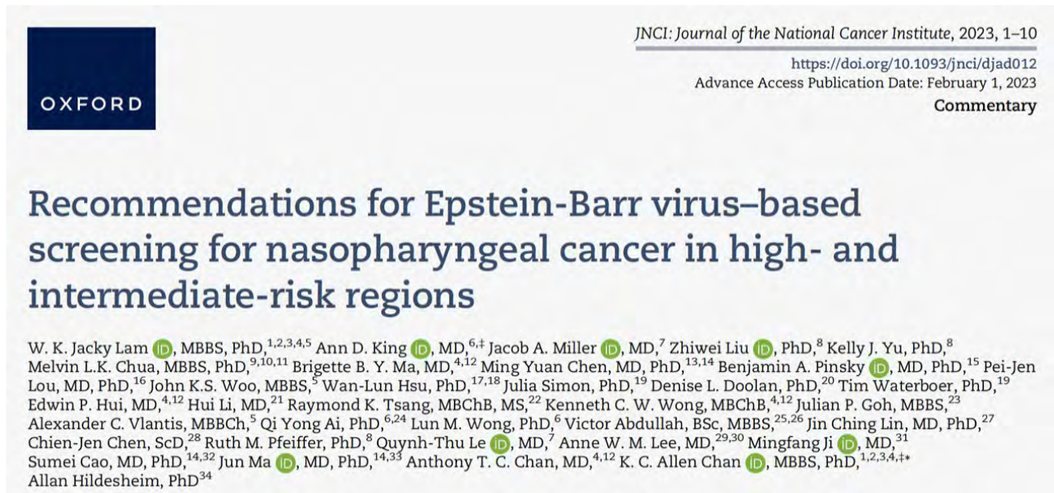
4. Zhou Z, Ma MJL, Chan RWY, Lam WKJ, Peng W, Gai W, Hu X, Ding SC, Ji L, Zhou Q, Cheung PPH, Yu SCY, Teoh JYC, Szeto CC, Wong J, Wong VWS, Wong GLH, Chan SL, Hui EP, Ma BBY, Chan ATC, Chiu RWK, Chan KCA, Lo YMD, Jiang P. Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(17):e2220982120. doi:10.1073/pnas.2220982120.

5. Chan A, Lam WKJ, King A, Lin VS, Lee PPH, Zee BCY, Chan SL, Tse IOL, Tsang AFC, Li MZJ, Jiang P, Yong Q, Ai H, Poon DMC, Au KH, Hui EP, Ma BBY, Hasselt AC Van, Chan ATC, Woo JKS, Lo YMD. Plasma Epstein-Barr virus DNA and risk of future nasopharyngeal cancer. *NEJM Evidence*. 2023;2(7). doi:10.1056/evidoa2200309.

6. Lou PJ, Lam WKJ, Hsu WL, Pfeiffer RM, Yu KJ, Chan CML, Lee VCT, Chen TC, Terng S Der, Tsou YA, Leu YS, Liao LJ, Chang YL, Chien YC, Wang CP, Lin CY, Hua CH, Lee JC, Yang TL, Hsiao CH, Wu MS, et al. Performance and operational feasibility of Epstein-Barr virus-based screening for detection of nasopharyngeal carcinoma: Direct comparison of two alternative approaches. *Journal of Clinical Oncology*. 2023;41(26):4257-4266. doi:10.1200/jco.22.01979.

7. Lam WKJ, Kang G, Wong WSW. Circulating tumour DNA for detection of minimal residual disease in head and neck squamous cell carcinoma: A new hope. *Annals of Oncology*. 2023;34(12):1080-1081. doi:10.1016/j.annonc.2023.10.693. (Editorial)

8. Lai R, Yeung DCM, Yeung ZWC, Hui TSC, Lam WKJ, Chan KCA, Ng CWK, To ZWH, Cho RHW, Chan CPL, Lai CCF, Leung NMW, Wong EWY, Chung JCK, Tsang RKY, Li KWS, Chow JCH, Cheung KKM, Chan JYK. Combining transoral nasopharyngeal brush and plasma Epstein-Barr virus DNA in detecting locally recurrent nasopharyngeal carcinoma. *Otolaryngology–Head and Neck Surgery*. 2023;169(5):1208-1214. doi:10.1002/ohn.380.



OXFORD

JNCI: Journal of the National Cancer Institute, 2023, 1–10
https://doi.org/10.1093/jnci/djad012
Advance Access Publication Date: February 1, 2023
Commentary

Recommendations for Epstein-Barr virus–based screening for nasopharyngeal cancer in high- and intermediate-risk regions

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The first international recommendation document on the use of Epstein-Barr virus-based biomarkers for screening of NPC was published by the Meeting Group after the Nasopharyngeal Carcinoma Screening Conference.

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EMERGING INFECTIOUS DISEASES AND MICROBIOTA

FAECAL MICROBIOTA TRANSPLANTATION

防疫研究及腸道微生物學

PRINCIPAL INVESTIGATOR
Siew Ng

TEAM MEMBERS
Francis Chan, Hein Min Tun, Lin Zhang, Jielun Hu, Jingwan Zhang, Zhilu Xu, Qi Su, Ye Peng, Wenyi Zhu, Yating Wan, Chun Pan Cheung, Whitney Tang, Jessica Ching, Alicia Chan, Clinical FMT Team

RESEARCH PROGRESS SUMMARY

In 2023, **Siew Ng** and her team further translated their microbiome knowledge and innovations into clinical applications. They conducted a randomised, double-blind, placebo-controlled trial (RECOVERY STUDY) to test the efficacy of an oral microencapsulated live bacteria preparation (SIM01), developed by the team during the COVID-19 pandemic. Their study found that SIM01 improved gut microbiota composition and alleviated symptoms of long COVID. More patients who received SIM01 had significant improvements in five key symptoms including gastrointestinal upset, fatigue, difficulty in concentration, memory loss, and general unwellness. This is the world's first clinical trial to demonstrate that modulation of the gut microbiota can improve long COVID symptoms (Lau et al. *The Lancet Infectious Diseases*. 2023, online). The study also highlighted important mechanisms underlying the benefits of SIM01. The intervention not only led to increased gut microbiota diversity, richness and microbial function, but also enhanced the production of metabolites from beneficial gut bacteria, including short-chain fatty acids, which can circulate to the brain. These findings provide new insights and support the importance of the gut-brain axis, and that modulation of the gut microbiota represents a novel approach to improving neurological symptoms. These findings also suggest that maintaining a balanced gut microbiota is important in preventing infectious diseases and long-term symptoms.

Recently, Siew and her team developed a novel technology, MOZAIC™ (Multi-kingdom OptimiZAtIon for microbiota Consortia), that led to improved clinical outcomes after faecal microbiota transplantation (FMT). The clinical success rate was improved from 70% to over 90% in patients with recurrent Clostridioides difficile infection (CDI). In the first FMT registry that spans 8 years, the team demonstrated that patients' median survival doubled from 2.1 to 4.7 years (Yau et al. *Clinical Gastroenterology and Hepatology,* 2023 Sep 19:S1542-3565(23)00712-7).

This MOZAIC™ platform was driven by machine-learning analysis, utilising over 800 FMT datasets and over 2000 metagenomic sequenced samples to dissect the complex network of multi-kingdom microbiota, their genes and functions to facilitate personalised donor selection and donor-recipient-matching for better long-term outcomes and safety. The successful implementation of the MOZAIC™ technology demonstrates the immense potential of gut microbiota in curing diseases and saving lives.

Since October 2023, this patented technology has been adopted by the Hospital Authority to provide a territory-wide FMT service to all patients with CDI in public hospitals in Hong Kong. This partnership serves as a successful example of how innovations can be translated into clinical applications.

In the reporting period, the team filed 10 patents in Hong Kong, China, the United States and the United Kingdom, and published over 20 peer-reviewed papers. Siew was awarded the New Cornerstone Investigator Award. She is the first and only Hong Kong scholar in the field of Biology and Biomedical Sciences to receive this honour. She was also awarded the Highly Cited Researcher by Clarivate for the fourth consecutive year.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	**Organisation**
Siew Ng	Highly Cited Researcher 2023	Clarivate
	New Cornerstone Investigator, in Biology and Biomedical Sciences	New Cornerstone Investigator Foundation
	APAGE - World Gastroenterology Organization (WGO) Distinguished Global Lecture Award	The Asian Pacific Digestive Week 2023 Scientific Committee
	Gold Medal	International Invention Fair in the Middle East
	High Flyer Innopreneur Award	Hong Kong Innopreneur Awards by Federation of Hong Kong Industries
	Most Popular Innopreneur Award	Hong Kong Innopreneur Awards by Federation of Hong Kong Industries
Siew Ng Francis Chan Qi Su	Gold Medal with Congratulation of the Jury	International Exhibition of Inventions Geneva 2023
	Silver Medal	International Exhibition of Inventions Geneva 2023
Francis Chan	Highly Cited Researcher 2023	Clarivate
	AGA Institute Council Section Research Mentor Award 2023	American Gastroenterological Association
Qi Su	First Prize	China Gut Conference 2023
	Gold Medal	3rd Aisa Exhibition of Innovations and Inventions Hong Kong
	Excellent Presentation	Hospital Authority – Infectious Disease and Infection Control Theme Based Training Seminar
	Excellent Academic Award	Shanghai Youth Forum – Virology
	Micro Ecological Emerging Award	Lion Lake International Microbiome Conference
	E-Academic Award	Korea Digestive Disease Week

Fellowships

Name	Details	
	Fellowship	Organisation
Yingzhi Liu	Faculty Postdoctoral Fellowship	The Chinese University of Hong Kong
Wenye Xu		
Qianru Sun		

Academic Editorships

Name	Details	
	Role	Journal
Siew Ng	Associate Editor	GUT
		BMC Gastroenterology
	Review Editor	Frontiers in Gastroenterology
	Editorial Board Member	Journal of Gastroenterology and Hepatology
		Gastroenterology
		World Journal of Gastroenterology
		Inflammatory Intestinal Disease
		Journal of Crohn's and Colitis
		Alimentary Pharmacology & Therapeutics
	International Editorial Board Member	Indonesian Journal of Gastroenterology
Francis Chan	Senior Associate Editor	Gastroenterology
Jingwan Zhang	Editorial board member	World Journal of Gastroenterology
Lin Zhang	Editorial Board Member	Frontiers in Oral Health (Infections and Microbes)
		Frontiers in Nutrition and Microbes
		iMeta
Qi Su	Associate Editor	Frontiers in Veterinary Science
	Guest Associate Editor	Frontiers in Food Science and Technology

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Siew Ng	IBD GIVES-21: Global IBD Visualization of Epidemiology Studies (GIVES) in the 21st Century	The Leona M. & Harry B. Helmsley Charitable Trust	01/11/2020	31/10/2023	15,564,946
	Health@InnoHK: Microbiota I-Center (MagIC)	Innovation and Technology Commission	08/05/2020	07/05/2025	Not to be disclosed
	Midstream Research Programme: A Microbiome-Based Noninvasive Diagnostic Test for Early Colorectal Cancers	Innovation and Technology Commission – Innovation and Technology Fund	01/04/2021	30/09/2023	4,600,000
	Exposomics for Early Life Crohn's Disease	Yale University	01/05/2021	31/12/2023	1,506,426
	Mother-to-Infant Transfer of Bacteriome, Virome, Fungome and Metabolome in health and Crohn's disease (Mommy-CD)	The Leona M. & Harry B. Helmsley Charitable Trust	01/12/2019	30/11/2023	19,740,477
	Recurrence Rates in High-risk Subjects with Baseline Advanced Colorectal Adenomas Followed up at Different Surveillance Intervals: A Multi-center Randomised Controlled Trial in Four Chinese Cities	Health Bureau – Health and Medical Research Fund	09/2020	09/2023	1,460,388
	Early Detection and Surveillance of COVID-19 Infection by Non-invasive Ophthalmic Evaluations	Health Bureau – Commissioned Studies	01/08/2020	30/04/2023	4,822,810
	HKSTP-KingMed Co-Incubation Scheme	Hong Kong Science and Technology Parks Corporation	01/2021	12/2024	4,000,000
	Croucher Senior Medical Research Fellowships	Croucher Foundation	01/03/2021	31/03/2027	1,000,000
	Establishment of the Hub of Advanced Technology for Child Health (HATCH)	D.H. Chen Foundation	10/2021	09/2024	48,240,000
Lin Zhang	Targeting H3K27me3 by EZH2 Inhibitors in Control of Drug-Resistant Helicobacter Pylori Colonization	Health Bureau – Health and Medical Research Fund	01/09/2020	31/08/2023	1,494,292
	Effects of Ketamine and Cannabis on Antimicrobial Peptide Expression and Infection Susceptibility: An In Vitro and Animal Study	Beat Drugs Fund Association – Beat Drugs Fund	01/08/2019	31/12/2023	3,086,661
	Gut Microbiota Activates the Impaired Lysosome Acidification Against SARS-CoV-2 Non-structural Protein 6 Triggered NLRP3-dependent Pyrolosis	The Chinese University of Hong Kong Research Committee – Direct Grant	30/06/2023	29/06/2024	75,000
	Optimisation of Clinical Treatment of Severe Influenza to Reduce Morbidity and Mortality	Health Bureau – Commissioned Programme for Influenza Research	01/09/2019	31/08/2026	4,996,960

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jingwan Zhang	Developing Microbiome Risk Profiles as Biomarkers for Predicting Relapse in Crohn's Disease	Health Bureau – Health and Medical Research Fund	01/08/2023	31/07/2027	1,461,440
	Identification and Management of Toxic Metabolites Produced by *Proteus Mirabilis* to Improve Microbiota Dysbiosis in Crohn's Disease	National Natural Science Foundation of China	01/01/2022	31/12/2024	RMB 300,000
	Gut Microbiome in Inflammatory Bowel Disease	Startup Funding	02/11/2023	01/11/2025	1,450,760
Siew Ng Lin Zhang Jingwan Zhang	Translating Microbiome, Multi-Omics and Dietary Innovations to Enhance Inflammatory Bowel Disease Diagnosis and Outcome	Research Grants Council – Research Impact Fund	29/06/2023	28/06/2026	7,750,000
Jingwan Zhang Siew Ng	Characterization on The Role of Proteus Mirabilis-Derived Cadaverine in Regulation of Proinflammatory Phenotype and Immune Response in Crohn's Disease	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,151,224
Siew Ng Francis Chan Lin Zhang	Gut Microbiota in Adults with Chronic Widespread Pain	Peter Hung Pain Research Institute – Peter Hung Pain Research Institute Research Grant	01/12/2022	30/11/2024	602,810
Siew Ng Francis Chan	Modulation of Gut Microbiota to Enhance Health and Immunity in Vulnerable Individuals during COVID-19 Pandemic	Health Bureau – Health and Medical Research Fund	01/04/2021	31/03/2024	9,980,840
Francis Chan Siew Ng Lin Zhang	Novel Strategies to Facilitate Early Detection, Prevention and Intervention for Long-Term Health Problems Related to COVID-19 (NovITor-COVID study)	Health Bureau – Health and Medical Research Fund	01/04/2021	31/03/2026	45,991,725

Publications

A. Journal Papers

1. Lau RI, Su Q, Lau ISF, Ching JYL, Wong MCS, Lau LHS, Tun HM, Mok CKP, Chau SWH, Tse YK, Cheung CP, Li MKT, Yeung GTY, Cheong PK, Chan FKL, Ng SC. A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (RECOVERY): A randomised, double-blind, placebo-controlled trial. *The Lancet Infectious Diseases*. 2024;24(3):256-265. doi:10.1016/s1473-3099(23)00685-0. (Epub ahead of print)
2. Zhang L, Agrawal M, Ng SC, Jess T. Early-life exposures and the microbiome: Implications for IBD prevention. *Gut*. 2024;73(3):541-549. doi:10.1136/gutjnl-2023-330002.
3. Schreiber S, Rubin DT, Ng SC, Peyrin-Biroulet L, Danese S, Modesto I, Guo X, Su C, Kwok KK, Jo H, Chen Y, Yndestad A, Reinisch W, Dubinsky MC. Major adverse cardiovascular events by baseline cardiovascular risk in patients with ulcerative colitis treated with tofacitinib: Data from the OCTAVE clinical programme. *Journal of Crohn's and Colitis*. 2023;17(11):1761-1770. doi:10.1093/ecco-jcc/jjad104.
4. Yau YK, Su Q, Xu Z, Tang W, Ching JYL, Mak JWY, Cheung CP, Fung M, Ip M, Chan PKS, Wu JCY, Chan FKL, Ng SC. Randomised clinical trial: Faecal microbiota transplantation for irritable bowel syndrome with diarrhoea. *Alimentary Pharmacology & Therapeutics*. 2023;58(8):795-804. doi:10.1111/apt.17703.
5. Zhao S, Lok KYW, Sin ZY, Peng Y, Fan HSL, Nagesh N, Choi MSL, Kwok JYY, Choi EPH, Zhang X, Wai HKF, Tsang LCH, Cheng SSM, Wong MKL, Zhu J, Mok CKP, Ng SC, Chan FKL, Peiris M, Poon LLM, Tun HM. COVID-19 mRNA vaccine-mediated antibodies in human breast milk and their association with breast milk microbiota composition. *NPJ Vaccines*. 2023;8(1):1-11. doi:10.1038/s41541-023-00745-4.
6. Liu Y, Chan MTV, Chan FKL, Wu WKK, Ng SC, Zhang L. Lower gut abundance of eubacterium rectale is linked to COVID-19 mortality. *Frontiers in Cellular and Infection Microbiology*. 2023;13:1249069. doi:10.3389/fcimb.2023.1249069.
7. Peng Y, Zhang L, Mok CKP, Ching JYL, Zhao S, Wong MKL, Zhu J, Chen C, Wang S, Yan S, Qin B, Liu Y, Zhang X, Cheung CP, Cheong PK, Ip KL, Fung ACH, Wong KKY, Hui DSC, Chan FKL, Ng SC, Tun HM. Baseline gut microbiota and metabolome predict durable immunogenicity to SARS-CoV-2 vaccines. *Signal Transduction and Targeted Therapy*. 2023;8(1):1-11. doi:10.1038/s41392-023-01629-8.
8. Yau YK, Lau LHS, Lui RNS, Wong SH, Guo CL, Mak JWY, Ching JYL, Ip M, Kamm MA, Rubin DT, Chan PKS, Chan FKL, Ng SC. Long-term safety outcomes of fecal microbiota transplantation: Real-world data over 8 years from the Hong Kong FMT registry. *Clinical Gastroenterology and Hepatology*. 2023;22(3):611-620.e12. doi:10.1016/j.cgh.2023.09.001. (Epub ahead of print)
9. Liu Q, Xu Z, Dai M, Su Q, Leung Chan FK, Ng SC. Faecal microbiota transplantations and the role of bacteriophages. *Clinical Microbiology and Infection*. 2023;29(6):689-694. doi:10.1016/j.cmi.2022.11.012. (Review)
10. Wu CY, Liang LL, Ho HJ, Hsu CT, Hsu HT, Ao CK, Wu CY, Lin YH, Chuang YF, Hsu YC, Chen YJ, Ng SC. Physical fitness and inflammatory bowel disease risk among children and adolescents in Taiwan. *JAMA Pediatrics*. 2023;177(6):608-616. doi:10.1001/jamapediatrics.2023.0929.
11. Huang J, De LP, Zhang L, Xu W, Wong SH, Ng SC, Wong MCS. Updated epidemiology of gastrointestinal cancers in East Asia. *Nature Reviews Gastroenterology & Hepatology*. 2023;20(5):271-287. doi:10.1038/s41575-022-00726-3. (Review)
12. Liang JQ, Zeng Y, Lau EYT, Sun Y, Huang Y, Zhou T, Xu Z, Yu J, Ng SC, Chan FKL. A probiotic formula for modulation of colorectal cancer risk via reducing CRC-associated bacteria. *Cells*. 2023;12(9):1244. doi:10.3390/cells12091244/s1.
13. Lin Y, Xu Z, Yeoh YK, Tun HM, Huang W, Jiang W, Chan FKL, Ng SC. Combing fecal microbial community data to identify consistent obesity-specific microbial signatures and shared metabolic pathways. *iScience*. 2023;26(4):106476. doi:10.1016/j.isci.2023.106476.
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15. Xu Z, Wing J, Mak Y, Lin Y, Yang K, Liu Q, Zhang F, Lau L, Tang W, Ching JY, Tun HM, Chan P, Chan FKL, Ng SC, We A, Lin W, Lam T, Lam P, Mok A, Chan T, Long T, Wong M, Hey C, Chan H, Chan J, Fung M, Chin L, Lui RN, Wong SH, Wong VW, Kong AP, Cw Ma R, Chow EY, Wong SK, Chak I, Ho H. Mixed-donor faecal microbiota transplantation was associated with increased butyrate-producing bacteria for obesity. *Gut*. 2023;0(0). doi:10.1136/gutjnl-2022-328993. (Letter)
16. Loayza JJJ, Kang S, Schooth L, Teh JJ, de Klerk A, Noon EK, Zhang J, Hu J, Hamilton AL, Wilson-O'Brien A, Trakman GL, Lin W, Ching J, Or L, Sung JJY, Yu J, Ng SC, Kamm MA, Morrison M. Effect of food additives on key bacterial taxa and the mucosa-associated microbiota in Crohn's disease. The ENIGMA study. *Gut Microbes*. 2023;15(1). doi:10.1080/19490976.2023.2172670.
17. Nagata N, Takeuchi T, Masuoka H, Aoki R, Ishikane M, Iwamoto N, Sugiyama M, Suda W, Nakanishi Y, Terada-Hirashima J, Kimura M, Nishijima T, Inooka H, Miyoshi-Akiyama T, Kojima Y, Shimokawa C, Hisaeda H, Zhang F, Yeoh YK, Ng SC, Uemura N, Itoi T, Mizokami M, Kawai T, Sugiyama H, Ohmagari N, Ohno H. Human gut microbiota and its metabolites impact immune responses in COVID-19 and its complications. *Gastroenterology*. 2023;164(2):272-288. doi:10.1053/j.gastro.2022.09.024.
18. Yao J, Fekadu G, Ng SC, You JHS. Fecal microbiota transplantation for patients with active ulcerative colitis: A cost-effectiveness analysis. *Journal of Gastroenterology and Hepatology*. 2023;38(1):70-78. doi:10.1111/jgh.16015.

19. Li Q, Chan H, Liu WX, Liu CA, Zhou Y, Huang D, Wang X, Li X, Xie C, Liu WYZ, Wang XS, Ng SK, Gou H, Zhao LY, Fong W, Jiang L, Lin Y, Zhao G, Bai F, Liu X, Chen H, Zhang L, Wong SH, Chan MTV, Wu WKK, Yu J. *Carnobacterium maltaromaticum* boosts intestinal vitamin D production to suppress colorectal cancer in female mice. *Cancer Cell*. 2023;41(8):1450-1465.e8. doi:10.1016/j.ccell.2023.06.011.

20. Chen H, Zhang X, Su H, Zeng J, Chan H, Li Q, Liu X, Zhang L, Wu WKK, Chan MTV, Chen H. Immune dysregulation and RNA N6-methyladenosine modification in sepsis. *Wiley Interdisciplinary Reviews: RNA*. 2023;14(3):e1764. doi:10.1002/wrna.1764. (Review)

B. Conference Papers

1. Panés J, D'Haens GR, Sands BE, Ng SC, Lawendy N, Kulisek N, Guo X, Wu J, Vranic I, Panaccione R, Vermeire S. S1194 Tofacitinib for the treatment of ulcerative colitis: Up to 9.2 years of safety data from the global clinical program. *American Journal of Gastroenterology*. 2023;118(10S):S911-S911. doi:10.14309/01.ajg.0000954416.69032.a8.

2. Chevarin C, Xu Z, Martin L, Robin F, Beyrouthy R, Colombel JF, Sulakvelidze A, Bonnet R, Ng SC, Buisson A, Barnich N. Mo1799 Comparison of Crohn's disease-associated Adherent-Invasive Escherichia Coli (AIEC) from France and Hong-Kong: Results from the pacific study. *Gastroenterology*. 2023;164(6):S-915. doi:10.1016/s0016-5085(23)03109-8.

3. Dai M, Xiao X, Guo CL, Yip HC, Chu S, Hon SS, Ng SS, Chiu PWYW, Ng SC, Chan FK, Lau LHS. Tu1101 The long-term risk of metachronous advanced adenoma recurrence after endoscopic submucosal dissection for colorectal neoplasia: A longitudinal propensity-score matched analysis. *Gastroenterology*. 2023;164(6):S-978. doi:10.1016/s0016-5085(23)03258-4.

4. Kang S, Teh JJ, Zhang J, Hu J, Hamilton AL, Wilson-O'Brien A, Trakman GL, Lin WY, Ching JY, Sung JJ, Yu J, Ng SC, Kamm MA, Morrison M. Mo1815 Characterization of the colonic mucosa-associated metagenome reveals novel microbes and geographically distinct communities in health and Crohn's disease. The ENIGMA study. *Gastroenterology*. 2023;164(6):S-921. doi:10.1016/s0016-5085(23)03125-6.

5. Lau RI, Ching JY, Wong MC, Lau LHS, Lau SFI, Leung YTR, Chin WY, Chau WHS, Yeung TYG, Chu HY, Cheong PK, Chan FK, Ng SC. 913a Modulation of gut microbiome alleviates post-acute COVID-19 syndrome: A randomised, triple-blind, placebo-controlled trial (recovery study). *Gastroenterology*. 2023;164(6):S-1571. doi:10.1016/s0016-5085(23)04756-x.

6. Lau RI, Lau SFI, Ching JY, Tang W, Chiu KCJ, Cheong PK, Pak MHA, Siu WY, Ng SC, Chan FK. Sa1060 Gastrointestinal involvement in post-acute COVID-19 syndrome: Results from a population-based study of 8,156 subjects. *Gastroenterology*. 2023;164(6):S-278. doi:10.1016/s0016-5085(23)01630-x.

7. Lin Y, Xu ZL, Dong X, Huang W, Sun Y, Zhang F, Chevarin C, Buisson A, Barnich N, Colombel JF, Miao Y, Chan FK, Ng SC. Mo1794 Dietary factors affect the presence of Adherent-Invasive Escherichia Coli (AIEC) in Crohn's disease: Results from the pacific study. *Gastroenterology*. 2023;164(6):S-914. doi:10.1016/s0016-5085(23)03104-9.

8. Sun Q, Zhu W, Lin WY, Trakman GL, Ching JY, Hamilton AL, Brien AWO, Morrison M, Kamm MA, Chan FK, Zhang J, Ng SC. 271 Polysorbate-80 exacerbates proteus mirabilis-induced intestinal inflammation via stimulation of enzyme X secretion. The ENIGMA study. *Gastroenterology*. 2023;164(6):S-48. doi:10.1016/s0016-5085(23)01072-7.

9. Teh JJ, Kang S, Leonard A, Zhang J, Hu J, Hamilton AL, Wilson-O'Brien A, Trakman GL, Lin WY, Ching JY, Sung JJ, Yu J, Ng SC, Kamm MA, Morrison M. Mo1811 Characterization of the key anti-inflammatory bacterium *Faecalibacterium prausnitzii* internationally in health and Crohn's disease. The ENIGMA study. *Gastroenterology*. 2023;164(6):S-920. doi:10.1016/s0016-5085(23)03121-9.

10. Teh JJ, Kang S, Zhang J, Hu J, Hamilton AL, Wilson-O'Brien A, Trakman GL, Lin WY, Ching JY, Sung JJ, Yu J, Ng SC, Kamm MA, Morrison M. Mo1807 The secretomes of colonic mucosa-associated microbiota in Crohn's disease and health identify key bacteria driving pro- and anti-inflammatory responses. The ENIGMA study. *Gastroenterology*. 2023;164(6):S-919. doi:10.1016/s0016-5085(23)03117-7.

11. Windsor JW, Hracs L, Gorospe J, Coward S, Buie MJ, Quan J, Markovinovic A, Caplan L, Cummings M, Gearry R, Kotze PG, Abreu MT, Rubin DT, Dotan I, Bernstein CN, Panaccione R, Ng SC, Kaplan G. Sa1770 The global evolution of inflammatory bowel disease across four epidemiologic stages: A systematic review of incidence and prevalence studies over the past century. *Gastroenterology*. 2023;164(6):S-423. doi:10.1016/s0016-5085(23)01984-4.

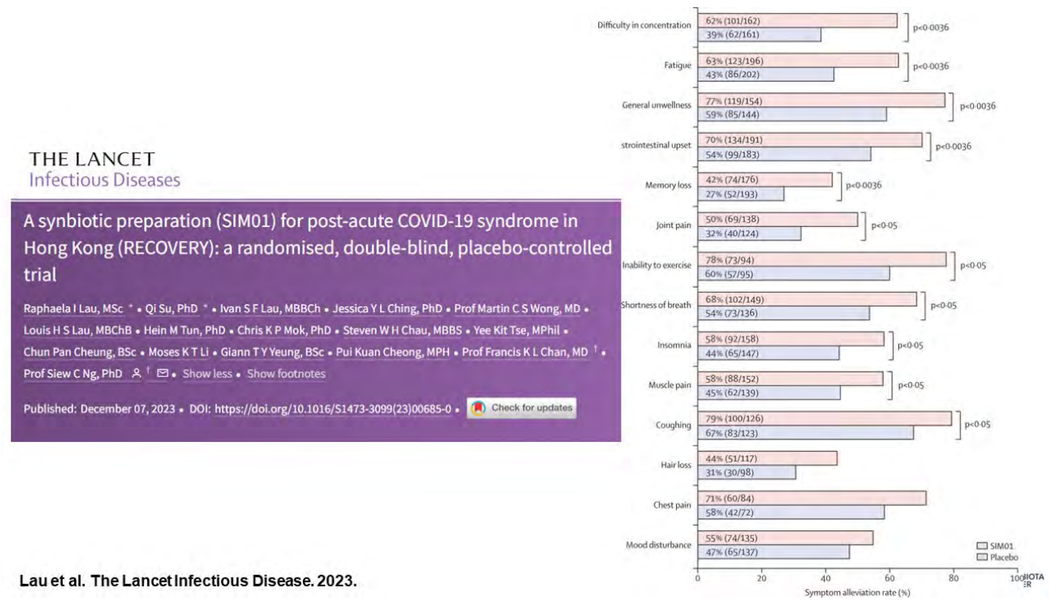
12. Wong MC, Zhang L, Ching JY, Mak JWY, Wong YM, Chiu E, Chan FK, Ng SC. 119 Effects of gut microbiome modulation on clinical outcomes and gut dysbiosis among elderly and diabetes patients after COVID-19 vaccination: A randomized, double-blind, placebo-controlled trial. *Gastroenterology*. 2023;164(6):S-19. doi:10.1016/s0016-5085(23)00999-x.

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15. Zhang L, Xu W, Meng HYH, Liu Y, Wang S, Ching JY, Cheung CP, Leung TF, Leung AS, Tam WH, Leung TY, Chan PK, Tun HM, Chang EB, Rubin DT, Claud EC, Chan FK, Ng SC. 874 The impact of COVID-19 on early life gut microbiome: Implications from two independent mother-baby dyad cohorts in the Greater Bay Area of China. *Gastroenterology*. 2023;164(6):S-194. doi:10.1016/s0016-5085(23)01426-9.

16. Dai M, Lau LHS, Lui RN, Yip HC, Chu S, Hon SF, Ng SSM, Chiu PWY, Ng SC, Chan FKL. Incidence and risk factors of metachronous adenoma recurrence after endoscopic submucosal dissection for colorectal neoplasia. *Journal of Gastroenterology and Hepatology*. 2023;38.



Lau et al. The Lancet Infectious Disease. 2023.

Modulation of the gut microbiome using oral microencapsulated live bacteria (SIM01) developed by Siew Ng and her team led to improvement in post-acute COVID-19 syndrome. More patients in the SIM01 group compared with the placebo group had alleviations of fatigue, memory loss, and difficulty in concentration by 6 months.

Source: Lau RI, Su Q, Lau ISF, Ching JYL, Wong MCS, Lau LHS, Tun HM, Mok CKP, Chau SWH, Tse YK, Cheung CP, Li MKT, Yeung GTY, Cheong PK, Chan FKL, Ng SC. A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (RECOVERY): A randomised, double-blind, placebo-controlled trial. The Lancet Infectious Diseases. 2024;24(3):256-265. doi:10.1016/s1473-3099(23)00685-0.



Novel microbiome technology MOZAIC™ enhances treatment success of faecal microbiota transplantation. The success rate is over 90% in patients with recurrent *Clostridioides difficile* infection (CDI). The team led by Siew Ng collaborates with the Hospital Authority to provide this new technology to treat patients with refractory or recurrent CDI at public hospitals across Hong Kong.

Source: Press conference on 16 November 2023



EMERGING INFECTIOUS DISEASES AND MICROBIOTA

防疫研究及腸道微生物學

PRINCIPAL INVESTIGATOR
Renee Chan

TEAM MEMBERS
Kathy Chan, Kin Pong Tao, Joseph Tsun, Chun Sang Pun, Joan Marie Javillo Baguio, Stacy Yam, Ben Wong, Shaojun Liu, Behzad Nasiri Ahmadabadi, Chun Hei Lei, Shuo Wang

RESEARCH PROGRESS SUMMARY

The nasal strip application in various paediatric research

With the implementation of the nasal strip as the standardised nasal epithelial lining fluid sampling tool since 2020, numerous research outputs on the aspect of nasal immunity have been delivered, ranging from the initial nasal antibody monitoring to the development of nasal IgA in neonates, the nasal IgE detection and its association with allergies in school-age children and the circadian nasal inflammatory mediators profile in children with obstructive sleep apnea.

The epidemiological study of respiratory virus infection in children

Respiratory viruses have long been recognised as a significant cause of morbidity and mortality in children. With the support of the General Research Fund, they conducted a comprehensive study on the epidemiology and viral dynamics in the hospitalised children. Specifically, they explored respiratory virus diversity in the pre-SARS-CoV-2 era, identified the monopoly of minor group rhinoviruses (RV-A47 and RV-A49) during the mid of SARS-CoV-2 pandemic with a shrinkage of respiratory virus diversity. Additionally, they revealed the increased respiratory co-infections in specific age groups (3 to 5 years old) of children, possibly a reflection of the immune debt inherited from the lack of respiratory virus exposure in the past three years of SARS-CoV-2 pandemic.



The establishment of respiratory organoid model for obstructive airway disease from preterm babies to the elderlies

Their team successfully developed airway organoids using clinical materials from subjects with obstructive respiratory diseases, including neonates, infants, children with bronchopulmonary dysplasia (BPD) or BPD history, children with asthma and the elderlies with chronic pulmonary obstruction disease, COPD. These individuals are vulnerable and at higher risk in a respiratory virus outbreak. They have characterised these disease-group and age-group specific organoids, which will be used in ongoing research on disease mechanisms and antiviral drug screening.

The antiviral drug screening platform

In the search for novel therapeutics against the continuous emergence of respiratory virus, they team up with Billy Ng (School of Pharmacy, CUHK) who synthesised novel antiviral drug candidates and bring new opportunities for exploration and development of antiviral therapy. Respiratory syncytial virus (RSV) is one of leading causes of bronchiolitis and pneumonia in infants and young children, while there was no dedicated drug for RSV infection. They screened and identified drug candidates belong to the class of nucleoside analogues, which are known for their antiviral properties. The anti-RSV drug prototype was created by utilising a readily available sugar as the key starting material, while it possesses extraordinary antiviral effectiveness.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Behzad Nasiri Ahmadabadi	Dragon Culture PhD Scholarships for Medical Study	Dragon Culture Charity Fund
Chun Sang Pun	Hong Kong Special Administrative Region Government Scholarship	The Government of the Hong Kong Special Administrative Region

Academic Editorships

Name	Details	
	Role	Journal
Renee Chan	Invited Editor – Special Issue	Journal of Virological Methods
	Associate Editor	Frontiers in Infectious Diseases – Pathogenesis and therapy
	Review Editor	Frontiers for Young Minds – Human Health
	Academic Editor	PLoS One

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Renee Chan	Reviewer	Frontiers in Medicine
		Emerging Microbes & Infections
		Journal of Virological Methods
		The Lancet Infectious Diseases
		PLoS Pathogens
		Frontiers for Young Minds
		Microbiology Spectrum
	Abstract reviewer	Joint Annual Scientific Meeting in Child Health

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Renee Chan	The Construction of Chronic Obstructive Pulmonary Disease (COPD) Organoid Model to Screen	The Chinese University of Hong Kong Research Committee – Direct Grant	19/06/2023	18/06/2024	30,000
	The Construction of Lung Cancer Organoid Using Fine Needle Aspirate or Trucut Biopsy	The Chinese University of Hong Kong Research Committee – Direct Grant	30/06/2023	29/06/2024	25,645
	A Study to Investigate the Effect of Antibiotics on Respiratory Microbiomes and Outcome in Preterm Neonates	The Chinese University of Hong Kong Research Committee – Direct Grant	30/06/2023	29/06/2024	25,645
	A Study to Assess the Efficacy of Plasma and Urine Biomarkers for Early Detection of Necrotizing Enterocolitis (NEC)	The Chinese University of Hong Kong Research Committee – Direct Grant	15/06/2023	14/06/2024	149,700
	Mucosal Inflammation in Children with OSA – Potential Biomarkers of OSA Complications	Health Bureau – Commissioned Programmes for Influenza Research	01/01/2023	31/12/2025	3,049,191

Publications

A. Journal Papers

1. Chang X, Ismail NI, Rahman A, Xu D, Chan RWY, Ong SG, Ong SB. Long Covid-19 and the heart: is cardiac mitochondria the missing link? *Antioxidants and Redox Signaling*. 2023;38(7-9):599-618. doi:10.1089/ars.2022.0126.

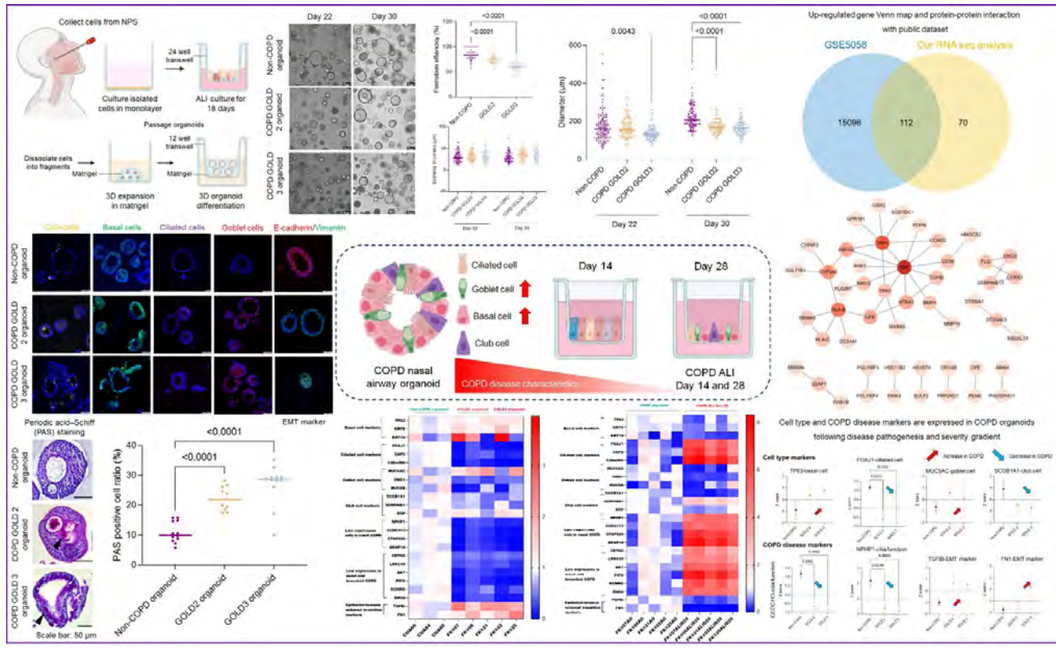
2. Liu S, Tsun JGS, Fung GPG, Lui GCY, Chan KYY, Chan PKS, Chan RWY. Comparison of the mucosal and systemic antibody responses in Covid-19 recovered patients with one dose of mRNA vaccine and unexposed subjects with three doses of mRNA vaccines. *Frontiers in Immunology*. 2023;14. doi:10.3389/fimmu.2023.1127401.

3. Scheeff S, Wang Y, Lyu MY, Ahmadabadi BN, Hau SCK, Hui TKC, Zhang Y, Zuo Z, Chan RWY, Ng BWL. Design and synthesis of bicyclo[4.3.0]nonene nucleoside analogues. *Organic Letters*. Published online December 22, 2023. doi:10.1021/acs.orglett.3c03590.

4. Song YP, Tang MF, Leung ASY, Tao KP, Chan OM, Wong GWK, Chan PKS, Chan RWY, Leung TF. Interactive effects between CDHR3 genotype and rhinovirus species for diagnosis and severity of respiratory tract infections in hospitalized children. *Microbiology Spectrum*. 2023;11(5). doi:10.1128/spectrum.01181-23.

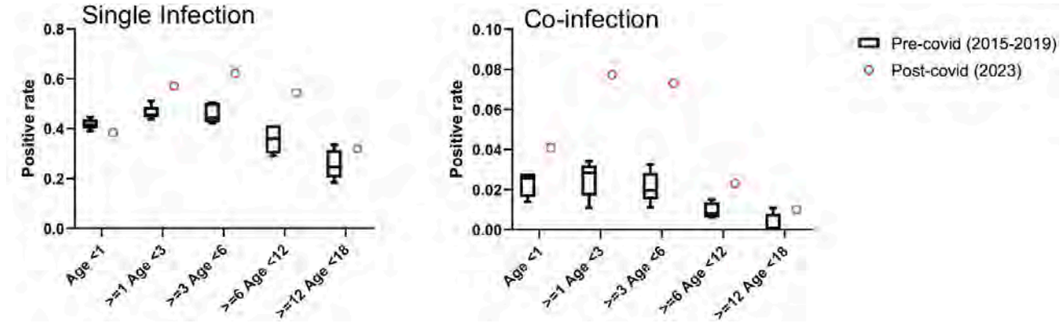
B. Conference Paper

1. Wong BKS, Wang Y, Tsun JGS, Chan LLY, Chan RWY. Comparison of rhinovirus A16 and C15 induced transcriptomic profiles in airway epithelia.



Construction and characterisation of COPD nasopharyngeal epithelial organoid. Patient specific nasopharyngeal epithelial organoid culture was culture from the patient specific clinical sample. The organoid was characterised by its morphological and structural feature under light microscopy. The cellular composition was evaluated using cell type specific marker using immunofluorescent staining while the COPD phenotype was assessed by epithelial-mesenchymal transition (EMT) marker, periodic acid-Schiff (PAS) staining, and transcriptomic analysis.

Source: Renee Chan



Epidemiological study of respiratory viral infection in paediatric population before and after COVID-19 stratified into developmental age-groups.

Source: Renee Chan



EMERGING INFECTIOUS DISEASES AND MICROBIOTA

防疫研究及腸道微生物學

PRINCIPAL INVESTIGATOR
Peter Cheung

TEAM MEMBERS
Xinzhou Xu, Ka Man Tse, Cheuk Wang Fung, Sin Yu Yeung, Buyu Zhang, Wing Ying Au, Lin Yang, Yiqiong Zhang, Liuli Dong, Zhinbin Liang, Zhitong Zhu, Zhouran Gao, Sirui Li

RESEARCH PROGRESS SUMMARY

Peter Cheung's research interests are diverse and multidimensional. He focuses on various areas, including structural biology and computational biology, statistics on large clinical datasets, molecular mechanisms of RNA virus replication and transcription, analysing of the evolution and antigenic properties of influenza and coronaviruses, and the impact of polymerase fidelity on viral evolution and host adaptation.

Peter has published a significant number of research articles and creative works. According to the Web of Science, he has a total of 32 publications, with a citation count of 1,386. Some notable publications include studies on the transcription and replication pathways of SARS-CoV-2 RNA polymerase, rapid microfluidics prototyping for multiplex diagnostics, predicting the antigenic evolution of SARS-CoV-2 using deep learning, and the effectiveness of heterologous and homologous COVID-19 vaccine regimens.

In terms of knowledge transfer activities, Peter has actively engaged in sharing his research findings. He has participated in academic conferences and public forums to present his work and exchange knowledge with fellow researchers and the wider scientific community. His research collaborations have also been instrumental in advancing his work. He has collaborated with researchers from different institutions, both locally and internationally, to enhance the scope and impact of his research.

Overall, Peter has made significant contributions to the field of biomedical research, particularly in the areas of virology, molecular biology, and computational biology. His dedication to multidimensional academic pursuits and his collaborations with other researchers have been instrumental in advancing scientific knowledge and understanding.

RESEARCH AND SCHOLARSHIP

Research Award and Recognition

Name	Details	
	Award	Organisation
Wing Ying Au	Postgraduate Research Output Award	The Chinese University of Hong Kong

Fellowships

Name	Details	
	Fellowship	Organisation
Wing Ying Au	Dragon Culture Doctoral Scholarship for Medicine	Dragon Culture Charity Fund
Xinzhou Xu	Postdoctoral Fellowship Scheme	University Grants Committee
Sirui Li	Hong Kong PhD Fellowship Scheme	University Grants Committee

Academic Editorship

Name	Details	
	Role	Journal
Peter Cheung	Reviewing Editor	Frontiers in Microbiology

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Peter Cheung	Reviewer	BMJ
		Emerging Microbes and Infections
		The Lancet Regional Health – Western Pacific
		International Journal of Infectious Diseases
		Vaccine

Publications

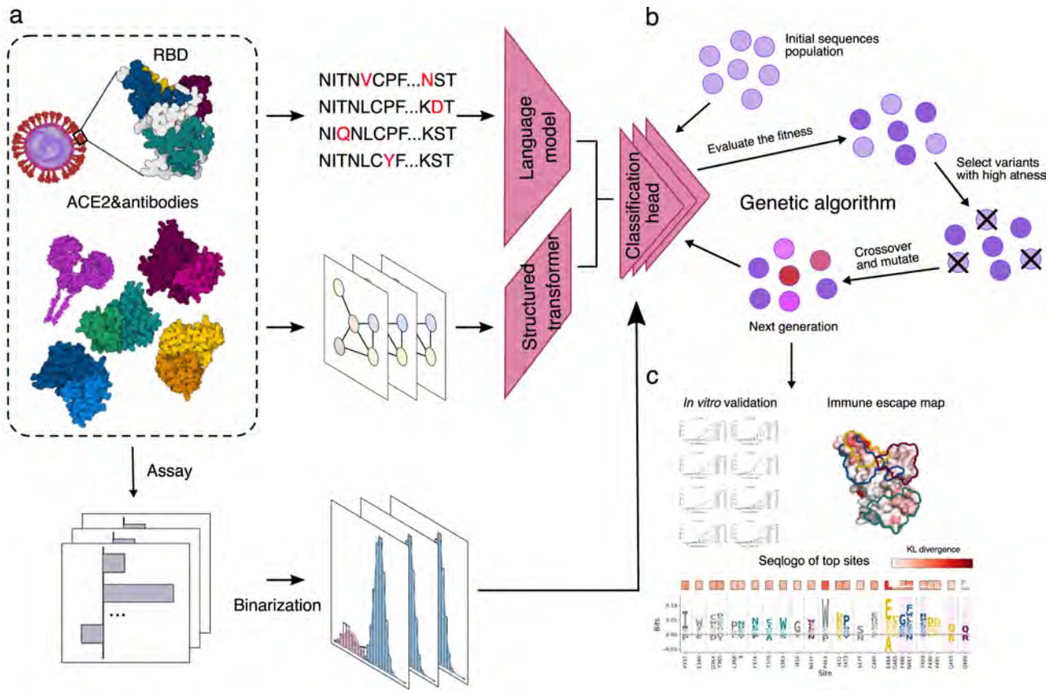
A. Journal Papers

1. Wang X, Xu T, Yao Y, Cheung PPH, Gao X, Zhang L. SARS-CoV-2 RNA-dependent RNA polymerase follows asynchronous translocation pathway for viral transcription and replication. *Journal of Physical Chemistry Letters*. 2023;14(45):10119-10128. doi:10.1021/acs.jpclett.3c01249.

2. Han W, Chen N, Xu X, Sahil A, Zhou J, Li Z, Zhong H, Gao E, Zhang R, Wang Y, Sun S, Cheung PPH, Gao X. Predicting the antigenic evolution of SARS-CoV-2 with deep learning. *Nature Communications*. 2023 14:1. 2023;14(1):1-14. doi:10.1038/s41467-023-39199-6.

3. Huang J, Zhao S, Chong KC, Zhou Y, Lu W, Fang F, Cheung PPH, Lai KC, Hui DS, Mok CKP. Infection rate in Guangzhou after easing the zero-COVID policy: Seroprevalence results to ORF8 antigen. *The Lancet Infectious Diseases*. 2023;23(4):403-404. doi:10.1016/S1473-3099(23)00112-3.

4. Zhou Z, Ma MJL, Chan RWY, Lam WKJ, Peng W, Gai W, Hu X, Ding SC, Ji L, Zhou Q, Cheung PPH, Yu SCY, Teoh JYC, Szeto CC, Wong J, Wong VWS, Wong GLH, Chan SL, Hui EP, Ma BBY, Chan ATC, Chiu RWK, Chan KCA, Lo YMD, Jiang P. Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(17):e2220982120. doi:10.1073/pnas.2220982120.



a. The multi-task learning model. The team led by Peter Cheung collected and cleaned the RBD variant sequences and their corresponding binding specificity to the ACE2 and eight antibodies. Then, the sequences and the structures of their binding partners were fed into the deep learning model with the multi-task learning objective.

b. The genetic algorithm. In silico-directed evolution was performed to navigate the virtual fitness landscape defined by the nine scores from the multi-task model. The generation loop was repeated multiple times until the desired functionality was reached.

c. These generated sequences were then subjected to validation experiments to evaluate their functional attributes.

Source: Han W, Chen N, Xu X, Sahil A, Zhou J, Li Z, Zhong H, Gao E, Zhang R, Wang Y, Sun S, Cheung PPH, Gao X. Predicting the antigenic evolution of SARS-CoV-2 with deep learning. Nature Communications. 2023 14:1. 2023;14(1):1-14. doi:10.1038/s41467-023-39199-6.



EMERGING INFECTIOUS DISEASES AND MICROBIOTA

SYSTEM MICROBIOLOGY, MICROBIOME & ANTIMICROBIAL RESISTANCE

防疫研究及腸道微生物學

PRINCIPAL INVESTIGATOR
Hein Min Tun

TEAM MEMBERS
Xi Zhang, Ye Peng, Suisha Liang, Chendi Sam Zhu, Yu Ying Bai, Shilin Zhao, Juelei Yu, Guanwen Huang, Xueqi Wu, Yuzhou Chen, Gailin Yang, Brian Ho, Jie Zhu, Xin Liu, Hang Li, Ingrid Chan

RESEARCH PROGRESS SUMMARY

Hein Min Tun and his research team study the composition, function, and dynamics of human and animal microbiomes in health and disease; and antimicrobial resistance (AMR) bacteria and the resistome in humans, animals, and the environment using a holistic One Health approach. He has been invited as an expert by the Quadripartite (WHO/OIE/FAO/UNEP) for the development of the One Health priority research agenda on antimicrobial resistance and by the STAR-IDAZ International Research Consortium (IRC) for the research roadmap development for alternatives to antibiotics. Additionally, this year he has been invited as a speaker at the 2nd RAPID Symposium by Institut Pasteur Korea to discuss AMR policies and practices. Through using the holistic One Health approach to strengthen the knowledge of AMR, the research team has highlighted the increasing concern and characterised dominant Salmonella serovars in humans, poultry, and aquaculture with emerging resistances in Sri Lanka. The findings of this study play an important role in informing public health policies to government bodies globally, not limited to Sri Lanka, in tackling and monitoring foodborne diseases (*Journal of Infection and Public Health*, IF: 6.700). Furthermore, Hein Min and his research team have emphasised the importance of longitudinal monitoring and surveying the

resistances of pathogens from downstream waste water close to hospital sites and from patients tested positive for resistant pathogens, such as carbapenemase-producing Enterobacteriaceae, which this could reflect the local and global spread of antimicrobial resistance (*Science of The Total Environment*, IF: 9.800). Moreover, the carriage of carbapenemase-producing Enterobacteriaceae has been found with an increasing trend in Hong Kong, where the use of beta-lactam antibiotics is a risk factor of the spread of carbapenem resistant Enterobacteriaceae (*Journal of Global Antimicrobial Resistance*, IF: 4.394).

Over the last seven years, Hein Min's team has revealed a series of seminal findings of the succession and development of keystone gut bacteria, the influencing environmental factors, and their association with health outcomes. The team's research into host-microbiome interaction highlights the important roles of our gut microbiome in our health and has conducted several landmarks research, ranging from early life microbiome research to the role of the microbiota gut-brain-axis in mental health. Through the state-of-the-art microbiome analysis with other omics and exposome data, his team and investigators from the Canadian Healthy Infant Longitudinal Development (CHILD) highlighted key findings on the importance of preserving natural green space in urban settings to prevent sensitisation to environmental allergens and promote early-life gut microbiota pathways. These findings reflect a mediating role of gut microbiome compositions in health and disease susceptibility (*Journal of Applied and Environmental Microbiology*, IF: 5.005). The role of the gut-microbiome-brain axis in our mental health has also been reflected in his team's research into the mechanistic roles of the gut microbiota in epileptogenesis among children with cerebral palsy. Through combined metagenomic and metabolomic analyses, evidence of gut dysbiosis amongst children with cerebral palsy and epilepsy were found and have shed insights on the potential roles of gut microbiota species, functional pathways, and metabolites in neuroprotection (*Frontiers in Neurology*, IF: 4.086).

In response to tackling the spread of COVID-19 and its effects on human health globally, the team has published key research in high impact factor journals that highlight the role of gut microbiota species in alleviating symptoms of post COVID-19 infection and their immunogenicity to the SARS-CoV-2 virus causing the COVID-19 pandemic. A randomised, double-blind, placebo-controlled trial was conducted by the team to assess a synbiotic preparation (SIM01) for the alleviation of post-acute COVID-19 syndrome (PACS) symptoms in patients in Hong Kong. This study made important implications on the management of PACS through gut microbiome modulation where treatment with a symbiotic preparation SIM01 alleviates multiple PACS symptoms (*The Lancet Infectious Diseases*, IF: 71.421). In a cohort study assessing the blood and stool samples of COVID-19 vaccinees, the collaboration between the team and Siew Ng's team identified potential microbiota-based adjuvants in extending the durability of COVID-19 vaccine immunity, including gut microbiota species *Bifidobacterium adolescentis*, *Bifidobacterium bifidum*, and *Roseburia faecis* (*Signal Transduction and Targeted Therapy*, IF: 38.120). These studies have significant implications not only for research into microbiome modulated immunity against viral infections but also for the general public by attracting the attentions of general news media on monitoring and safeguarding public health.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Hein Min Tun	Social Impact Team Award 2023	Distinguished Research Awards for Gene and Cell Therapy
Xueqi Wu	Hong Kong PhD Fellowship Scheme Award	The Research Grants Council of Hong Kong

Fellowships

Name	Details	
	Fellowship	Organisation
Shilin Zhao	HKU-Pasteur Research Pole Fellowship	School of Public Health, The University of Hong Kong
Ye Peng	Postdoctoral Fellowship Scheme	Research Committee, The Chinese University of Hong Kong
Chendi Sam Zhu	Faculty Postdoctoral Fellowship Scheme 2023/24	Faculty of Medicine, The Chinese University of Hong Kong

Academic Editorships

Name	Details	
	Role	Journal
Hein Min Tun	Associate Editor	Frontiers in Microbiology
	Editorial Board Member	Cellular and Molecular Life Sciences
	Guest Editor	Toxics
	JournalScan Contributors and Gut Ambassadors	Gut

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Hein Min Tun	Abstract Reviewer	7th World One Health Congress
	Reviewer	Lancet Microbes
		Gut
		Gastroenterology
		Gut Microbes
		JAMA Network Open
		Nature Communications
		Microbiome
		Cellular and Molecular Life Sciences
		mSystems
		FEMS Microbes
		Frontiers in Microbiology

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hein Min Tun	Translating Microbiome, Multi-Omics and Dietary Innovations to Enhance Inflammatory Bowel Disease Diagnosis and Outcome	Research Grants Council – Research Impact Fund	01/01/2023	31/12/2025	7,750,000
	Investigating the Gut Microbiota Associated Depression and its Modifiable Effect	Research Grants Council – Early Career Scheme	01/01/2023	31/12/2025	1,220,550
	Discovery and Construction of a Bacteriophage Isolate Collection to Target Antibiotic-Resistant Bacteria	The Chinese University of Hong Kong – Direct Grant for Research	19/06/2023	18/06/2024	150,000
	Characterization of Heteroresistance in Commensal *Escherichia Coli* Isolates in Relation to Therapeutic Use of Antibiotics	Health Bureau – Health and Medical Research Fund Health and Health Services	01/11/2022	30/10/2025	1,105,092
	Evolution and Determinants of Population Mental Health during the Myanmar Conflict: A Nationwide Longitudinal Study from 2021 to 2025	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	881,339
	Assess Antibiotic Resistome Flows from Pollution Hotspots to Environments and Explore the Control Strategies	Research Grants Council – Theme-based Research Scheme	01/01/2021	31/12/2025	18,905,000

Publications

A. Journal Papers

1. Lau RI, Su Q, Lau ISF, Ching JYL, Wong MCS, Lau LHS, Tun HM, Mok CKP, Chau SWH, Tse YK, Cheung CP, Li MKT, Yeung GTY, Cheong PK, Chan FKL, Ng SC. A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (recovery): A randomised, double-blind, placebo-controlled trial. *The Lancet Infectious Diseases*. 2024;24(3):256-265. doi:10.1016/s1473-3099(23)00685-0. (Epub ahead of print)

2. Tun HM, Peng Y, Massimino L, Sin ZY, Parigi TL, Facoetti A, Rahman S, Danese S, Ungaro F. Gut virome in inflammatory bowel disease and beyond. *Gut*. 2023;73(2):350-360. doi:10.1136/gutjnl-2023-330001. (Review, Epub ahead of print)

3. Peng Y, Tun HM. Meet the extended segatella copri complex. *Cell Host and Microbe*. 2023;31(11):1766-1769. doi:10.1016/j.chom.2023.10.009. (Review)

4. Ubeyratne KH, Madalagama RP, Liu X, Pathirage S, Ariyawansa S, Wong MKL, Tun HM. Phenotypic and genotypic characterization of antibiotic-resistant Salmonella isolated from humans, aquaculture, and poultry in Sri Lanka: A retrospective study. *Journal of Infection and Public Health*. 2023;16:203-209. doi:10.1016/j.jiph.2023.10.028.

5. Zhao S, Lok KYW, Sin ZY, Peng Y, Fan HSL, Nagesh N, Choi MSL, Kwok JYY, Choi EPH, Zhang X, Wai HKF, Tsang LCH, Cheng SSM, Wong MKL, Zhu J, Mok CKP, Ng SC, Chan FKL, Peiris M, Poon LLM, Tun HM. COVID-19 mRNA vaccine-mediated antibodies in human breast milk and their association with breast milk microbiota composition. *npj Vaccines*. 2023;8(1):151. doi:10.1038/s41541-023-00745-4.

6. Peng Y, Zhang L, Mok CKP, Ching JYL, Zhao S, Wong MKL, Zhu J, Chen C, Wang S, Yan S, Qin B, Liu Y, Zhang X, Cheung CP, Cheong PK, Ip KL, Fung ACH, Wong KKY, Hui DSC, Chan FKL, Ng SC, Tun HM. Baseline gut microbiota and metabolome predict durable immunogenicity to SARS-CoV-2 vaccines. *Signal Transduction and Targeted Therapy*. 2023;8(1):373. doi:10.1038/s41392-023-01629-8.

7. Liu X, Wong MKL, Zhang D, Chan DCL, Chan OSK, Chan GPL, Shum MHH, Peng Y, Lai CKC, Cowling BJ, Zhang T, Fukuda K, Lam TTY, Tun HM. Longitudinal monitoring reveals the emergence and spread of blages-5-harboring carbapenem-resistant Klebsiella quasipneumoniae in a Hong Kong hospital wastewater discharge line. *Science of the Total Environment*. 2023;903:166255. doi:10.1016/j.scitotenv.2023.166255.

8. Yang X, Zhang M, Zhang Y, Wei H, Guan Q, Dong C, Deng S, Tun HM, Xia Y. Ecological change of the gut microbiota during pregnancy and progression to dyslipidemia. *npj Biofilms and Microbiomes*. 2023;9(1). doi:10.1038/s41522-023-00383-7.

9. Peng Y, Chiu ATG, Li VWY, Zhang X, Yeung WL, Chan SHS, Tun HM. The role of the gut-microbiome-brain axis in metabolic remodeling amongst children with cerebral palsy and epilepsy. *Frontiers in Neurology*. 2023;14. doi:10.3389/fneur.2023.1109469.

10. Buchholz V, Bridgman SL, Nielsen CC, Gascon M, Tun HM, Simons E, Turvey SE, Subbarao P, Takaro TK, Brook JR, Scott JA, Mandhane PJ, Kozyrskyj AL. Natural green spaces, sensitization to allergens, and the role of gut microbiota during infancy. *mSystems*. 2023;8(2). doi:10.1128/msystems.01190-22.



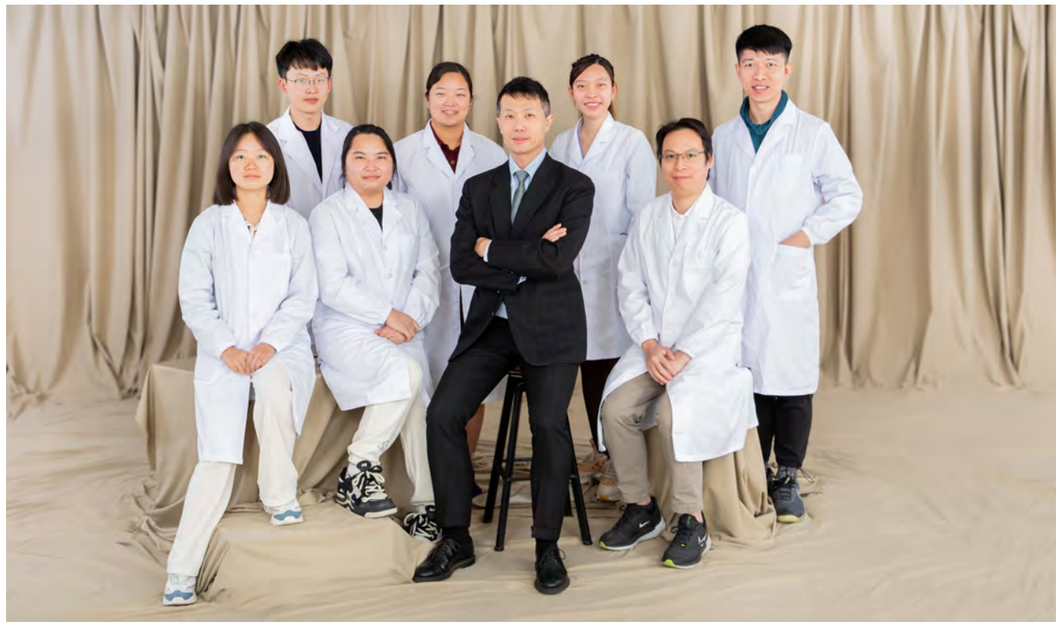
Contribution to the One Health Priority for Antimicrobial Resistance (AMR) report by Hein Min Tun (31st July, 2023).

Source: https://www.sphpc.cuhk.edu.hk/post/contribution-to-the-one-health-priority-research-agenda-for-amr-by-prof-hein-min-tun-1



The Faculty of Medicine at The Chinese University of Hong Kong conducted a study and published in the journal *Signal Transduction and Targeted Therapy*, led by Hein Min Tun, found that in people's gut microbiome, they have a secret weapon in the fight against COVID – and it lives inside many of them (11th December 2023).

Source: https://cuhkintouch.cpr.cuhk.edu.hk/2023/12/28515/



EMERGING INFECTIOUS DISEASES AND MICROBIOTA

防疫研究及腸道微生物學

PRINCIPAL INVESTIGATOR
Chris Mok

TEAM MEMBERS
Yun Sam Tang, Chunke Chen, Siu Lok Fung, Qihong Gao, Ka Man Lau, Jianxun Li, Yuanxin Sun

RESEARCH PROGRESS SUMMARY

Chris Mok and his research team mainly focus on understanding how the virus infection or vaccination determines the pathogenesis and immunity in the host. With experience in the related topic, they have established solid platforms for molecular, clinical, virologic as well as immunological studies.

Research on Coronaviruses

Over 600 million COVID-19 infections including more than 7 million deaths have been reported to the World Health Organization. Many COVID-19 vaccines have been rapidly developed, evaluated and widely used. These include inactivated whole virus, lipid nanoparticle (LNP)-encapsulated mRNA, adenovirus-vectored and protein sub-unit vaccines. The safety, immunogenicity and efficacy of these vaccines have been evaluated in separate clinical trials but there are few "head-to-head" comparisons of different vaccines. The team found that two doses of either CoronaVac or BNT162b2 elicited significant numbers of SARS-CoV-2 specific CD4 and CD8 responses compared to the pre-vaccinated baseline control. Vaccine-induced T-cell responses to the wild-type and Omicron BA.1 viruses were comparable in each of the vaccines. However, BNT162b2 induced higher Omicron-specific CD4 and CD8 T-cell responses in adults aged ≥60 years compared to CoronaVac. A third dose of either BNT162b2 or CoronaVac boosted waning T-cell responses compared to pre-third dose levels, but levels did not exceed those seen 1 month after the second dose. Memory phenotypes were found in both CD4 and CD8 T-cells in the two vaccine groups. Their study provides scientific evidence to explain good field vaccine efficacy of the CoronaVac vaccine against severe Omicron subvariant disease in spite of poor neutralising antibody responses.

Four seasonal coronaviruses, including HCoV-229E and HCoV-OC43, HCoV-NL63 and HCoV-HKU1 cause approximately 15-30% of common colds in adults. However, the full landscape of the immune trajectory to these viruses that covers the whole childhood period is still not well understood.

They evaluated the serological responses against the four seasonal coronaviruses in 1886 children aged under 18 years old by using Enzyme-linked immunosorbent assay (ELISA). Generalised Additive Models (GAM) were constructed to determine the relationship between the age and seroprevalence of the four seasonal coronaviruses throughout the whole childhood period. Specific antibody levels against the four seasonal coronaviruses were also tested from the plasma samples of 485 pairs of postpartum women and their newborn babies. The IgG levels of the four seasonal coronaviruses in the mother and the newborn babies were highly correlated. The seroprevalences in children showed a similar trajectory in that the levels of IgG in the neonates dropped significantly and reached the lowest level after the age of around 1 year and then resurgence in the children who aged older than 1-year-old. Using the lowest level from the GAMs as the team cutoff, the seroprevalences for HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1 were 98.11%, 96.23%, 96.23% and 94.34% at the age of 16-18 years old. They demonstrated that mothers share HCoV-specific IgGs with their newborn babies and the level of maternal IgGs waned at around one year after birth. A resurgence of the HCoV-specific IgGs was found thereafter with the increase of the age suggesting repeated infection occurred in children.

Research on influenza viruses

While neuraminidase (NA) is a re-emerging target for influenza vaccine development, its antigenicity remains poorly characterised. They isolated three broadly reactive N2 antibodies from the plasmablasts of a single vaccinee, including one that cross-reacts with NAs from seasonal H3N2 strains spanning five decades. Although these three antibodies have diverse germline usages, they recognise similar epitopes that are distant from the NA active site and involve the underside of the NA head domain, which is highly conserved among human H3N2 strains. Furthermore, the epitopes of these antibodies have minimal overlap with other structurally defined NA epitopes. They also showed that all three antibodies have *in vivo* protection activity, due to both Fc effector functions and NA inhibition through steric hindrance. Overall, the team's findings advance the understanding of NA antibody response and provide important insights into the development of a broadly protective influenza vaccine.



RESEARCH AND SCHOLARSHIP

Fellowships

Name	Details	
	Fellowship	Organisation
Chris Mok	Visiting Scientist	Nanyang Technological University
		National University of Singapore
	Honorary Assistant Professor	The University of Hong Kong

Academic Editorships

Name	Details	
	Role	Journal
Chris Mok	Associate Editor	Frontier of Immunology
		Virology Journal
	Guest Editor	PLOS Pathogens

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Chris Mok	Reviewer	Lancet Planetary Health
		Molecular Therapy
		PLOS Pathogens
		Virology Journal
		Influenza and Other Respiratory Viruses

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Chris Mok	Commissioned Research on the Novel Coronavirus Disease (COVID-19) – Long-term Longitudinal Comparisons of Health Status and Immune Response in Convalescent COVID-19 and Vaccinated Cohorts in Hong Kong	Health Bureau – Commissioned Studies	01/04/2021	31/03/2025	13,672,000
	Investigation on the T Cell Response against Omicron in Human Subjects after Receiving COVID-19 Vaccine	The Chinese University of Hong Kong – Direct Grant	30/06/2022	29/05/2023	150,000
	Guangdong-Hong Kong-Macau Joint Laboratory for Infectious Disease	Department of Science and Technology of Guangdong Province	01/01/2022	28/03/2023	RMB 1,000,000
	Long-term Longitudinal Comparisons of Immune Responses in Vaccinated Cohorts in Hong Kong	The National Laboratory of Hong Kong	01/01/2022	31/12/2023	RMB 1,200,000

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Chris Mok	From Structural to Genomic Biology: A Multi-scale Approach Tightly Integrating Structural Biology and Novel Genomics Platform to Quantitatively Analyze the Transcription and its Regulation of SARS-CoV-2 Viral RNA Polymerase	Research Grants Council – Collaborative Research Fund	30/06/2022	29/06/2025	300,000
	RAC-Establishment of a Joint Laboratory between CUHK and The Guangzhou National Laboratory	Joint Laboratory between The Chinese University of Hong Kong and The Guangzhou National Laboratory	28/09/2022	27/09/2025	7,316,000
	COVID-19: A Seroprevalence Study and a Fourth Dose Vaccination Study	S. H. Ho Foundation Limited – Donation	01/06/2022	31/05/2024	2,000,000
	Identification of Monoclonal Antibodies Targeting to the Spike Protein for the Therapeutic Treatment of Omicron BA.1 and BA.2 Infections	Health Bureau – Health and Medical Research Fund	01/09/2023	31/08/2025	1,500,000

Publications

A. Journal Papers

1. Lei R, Kim W, Lv H, Mou Z, Scherm MJ, Schmitz AJ, Turner JS, Tan TJC, Wang Y, Ouyang WO, Liang W, Rivera-Cardona J, Teo C, Graham CS, Brooke CB, Presti RM, Mok CKP, Krammer F, Dai X, Ellebedy AH, Wu NC. Leveraging vaccination-induced protective antibodies to define conserved epitopes on influenza N2 neuraminidase. *Immunity*. 2023;56(11):2621-2634.e6. doi:10.1016/ j.immuni.2023.10.005.

2. Lau RI, Su Q, Lau ISF, Ching JYL, Wong MCS, Lau LHS, Tun HM, Mok CKP, Chau SWH, Tse YK, Cheung CP, Li MKT, Yeung GTY, Cheong PK, Chan FKL, Ng SC. A synbiotic preparation (SIM01) for post-acute COVID-19 syndrome in Hong Kong (RECOVERY): A randomised, double-blind, placebo-controlled trial. *The Lancet Infectious Diseases*. Published online December 7, 2023. doi:10.1016/s1473-3099(23)00685-0. (Epub ahead of print)

3. Zhao S, Lok KYW, Sin ZY, Peng Y, Fan HSL, Nagesh N, Choi MSL, Kwok JYY, Choi EPH, Zhang X, Wai HKF, Tsang LCH, Cheng SSM, Wong MKL, Zhu J, Mok CKP, Ng SC, Chan FKL, Peiris M, Poon LLM, Tun HM. COVID-19 mRNA vaccine-mediated antibodies in human breast milk and their association with breast milk microbiota composition. *npj Vaccines*. 2023 8:1. 2023;8(1):1-11. doi:10.1038/s41541-023-00745-4.

4. So RTY, Chu DKW, Hui KPY, Mok CKP, Shum MHH, Sanyal S, Nicholls JM, Ho JCW, Cheung M, Ng K, Yeung H-W, Chan MCW, Poon LLM, Zhao J, Lam TTY, Peiris M. Amino acid substitution L232F in non-structural protein 6 identified as a possible human-adaptive mutation in clade B MERS coronaviruses. *Journal of Virology*. 2023;97(12). doi:10.1128/jvi.01369-23/suppl_file /jvi.01369-23-s0006.fasta.

5. Peng Y, Zhang L, Mok CKP, Ching JYL, Zhao S, Wong MKL, Zhu J, Chen C, Wang S, Yan S, Qin B, Liu Y, Zhang X, Cheung CP, Cheong PK, Ip KL, Fung ACH, Wong KKY, Hui DSC, Chan FKL, Ng SC, Tun HM. Baseline gut microbiota and metabolome predict durable immunogenicity to SARS-CoV-2 vaccines. *Signal Transduction and Targeted Therapy*. 2023 8:1. 2023;8(1):1-11. doi:10.1038/s41392-023-01629-8.

6. Liang W, Lv H, Chen C, Sun Y, Hui DS, Mok CKP. Lack of neutralizing antibodies against influenza A viruses in adults during the 2022/2023 winter season - A serological study using retrospective samples collected in Hong Kong. *International Journal of Infectious Diseases*. 2023;135:1-4. doi:10.1016/ j.ijid.2023.07.008.

7. Wei Y, Jia KM, Zhao S, Hung CT, Mok CKP, Poon PKM, Man Leung EY, Wang MH, Yam CHK, Chow TY, Guo Z, Yeoh EK, Chong KC. Estimation of vaccine effectiveness of CoronaVac and BNT162b2 against severe outcomes over time among patients with SARS-CoV-2 Omicron. *JAMA Network Open*. 2023;6(2):e2254777-e2254777. doi:10.1001/jamanetworkopen.2022.54777.

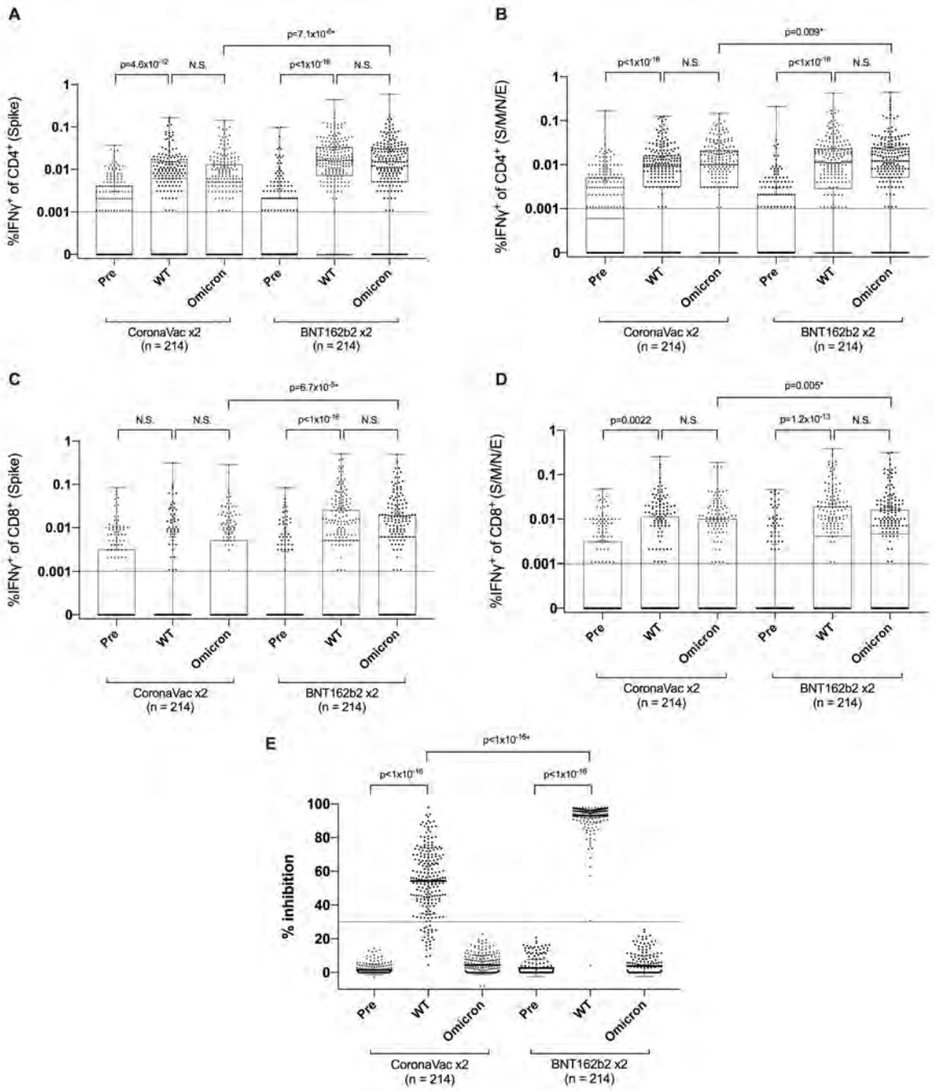
8. Mok CKP, Qin K. Mink infection with influenza A viruses: An ignored intermediate host? *One Health Advances*. 2023;1(1). doi:10.1186/S44280-023-00004-0.

9. Liu D, Chen C, Chen D, Zhu A, Li F, Zhuang Z, Mok CKP, Dai J, Li X, Jin Y, Chen Z, Sun J, Wang Y, Li Y, Zhang Y, Wen L, Zhang Z, Zhuo J, Wang J, Ran W, Wang D, Zhang S, Tang Y, Li S, Lai X, Wei P, Yuan J, Chen F, Huang S, Sun F, Qian Z, Tan W, Zhao J, Peiris M, Zhao J. Mouse models susceptible to HCoV-229E and HCoV-NL63 and cross protection from challenge with SARS-CoV-2. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(4). doi:10.1073/pnas.2202820120.

10. Guo Z, Zhao S, Mok CKP, So RTY, Yam CHK, Chow TY, Chan TCP, Wei Y, Jia KM, Wang MH, Chong KC, Yeoh EK. Comparing the incubation period, serial interval, and infectiousness profile between SARS-CoV-2 Omicron and Delta variants. *Journal of Medical Virology*. 2023;95(3):e28648. doi:10.1002/ jmv.28648.

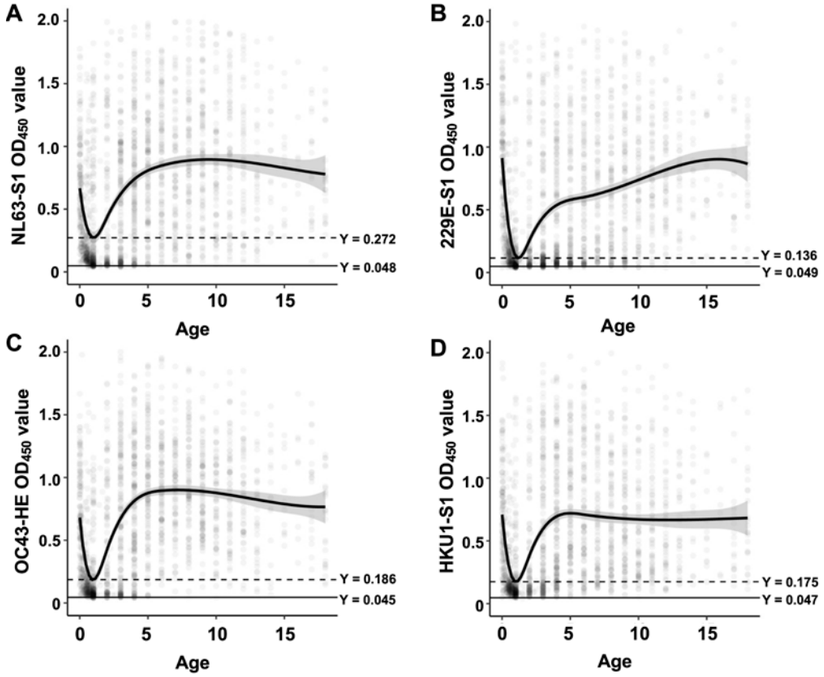
11. Luo Y, Lv H, Zhao S, Sun Y, Liu C, Chen C, Liang W, Kwok K on, Teo QW, So RT, Lin Y, Deng Y, Li B, Dai Z, Zhu J, Zhang D, Fernando J, Wu NC, Tun HM, Bruzzone R, Mok CKP, Mu X. Age-related seroprevalence trajectories of seasonal coronaviruses in children including neonates in Guangzhou, China. *International Journal of Infectious Diseases*. 2023;127:26-32. doi:10.1016/j.ijid.2022.11.044.

12. Mok CKP, Chen C, Zhao S, Sun Y, Yiu K, Chan TO, Lai HL, Lai KC, Lau KM, Ling KC, Chan KKP, Ng SS, Ko FW, Peiris M, Hui DS. Omicron BA.1-specific T-cell responses in adults vaccinated with CoronaVac or BNT162b2 in Hong Kong: An observational cohort study. *The Lancet Microbe*. 2023;4(6):e418-e430. doi:10.1016/s2666-5247(23)00006-x.



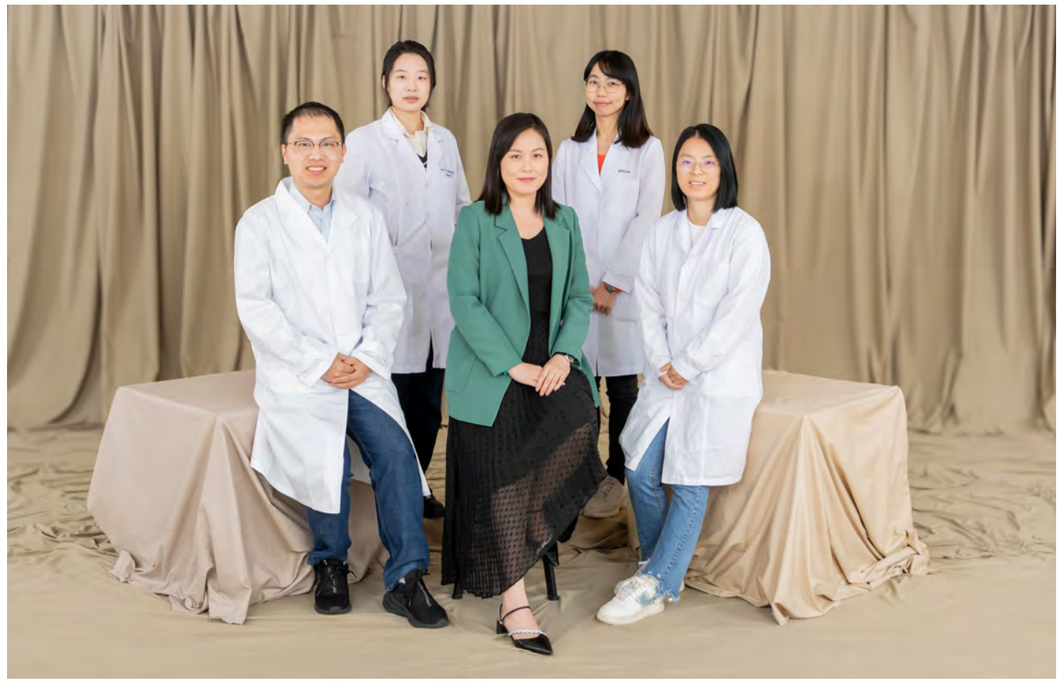
T-cell and antibody responses against SARS-CoV-2 in adults who received two doses of CoronaVac or BNT162b2 vaccines. PBMCs collected 1 month after two doses of CoronaVac (n=214) and BNT162b2 (n=214) vaccines were stimulated with pooled spike or structural (S/M/N/E) peptide pools. The percentage of (A and B) IFNγ+CD4+ and (C and D) IFNγ+CD8+ T-cells against WT or Omicron BA.1 were measured by flow cytometry. Dotted lines represent the limit of detection following background (DMSO) subtraction. (E) The percentage of inhibition detected by the surrogate neutralization test (sVNT) in plasma of the two vaccine groups detected by surrogate virus neutralisation test (sVNT) using the RBD of the wild type and Omicron BA.1, respectively. The dashed line at 30% indicates the positive threshold of the sVNT. Box-and-whisker plots show the minimum, IQRs, median and maximum of the data. Cross (+) represents the mean. Data within the same vaccine group was compared by Friedman multi-comparisons test followed by post hoc with pairwise Wilcoxon rank sum test paired with Benjamini-Hochberg correction. Wilcoxon rank-sum test was used to test between different subgroups. N.S. represented P<0.05 and was defined as statistically non-significant. *P was generated by a multiple linear regression model adjusting by age and gender.

Source: Mok CKP, Chen C, Zhao S, Sun Y, Yiu K, Chan TO, Lai HL, Lai KC, Lau KM, Ling KC, Chan KKP, Ng SS, Ko FW, Peiris M, Hui DS. Omicron BA.1-specific T-cell responses in adults vaccinated with CoronaVac or BNT162b2 in Hong Kong: An observational cohort study. The Lancet Microbe. 2023;4(6):e418-e430. doi:10.1016/s2666-5247(23)00006-x.



Seroprevalence trajectory of the four seasonal coronaviruses in children. The plasma samples were collected from 1886 children aged from 0 (neonates) to 18 years old. Each sample was tested by ELISA against either S1 (HCoV-229E, HCoV-NL63 or HCoV-HKU1) or hemagglutinin-esterase (HCoV-OC43) protein. Generalised additive models (GAM) were used to model the association between the serological data and the age. The black lines showed the fitted values and the gray areas showed the 95% confidence intervals. Each sample was tested in duplicate, and the results were represented by the mean of the two values. The solid line represents the cutoff of the negative control (PBS). The dashed lines represent the cutoff of the lowest point in GAMs and the solid lines represent the background (PBS) of the assay.

Source: Luo Y, Lv H, Zhao S, Sun Y, Liu C, Chen C, Liang W, Kwok K on, Teo QW, So RT, Lin Y, Deng Y, Li B, Dai Z, Zhu J, Zhang D, Fernando J, Wu NC, Tun HM, Bruzzone R, Mok CK, Mu X. Age-related seroprevalence trajectories of seasonal coronaviruses in children including neonates in Guangzhou, China. International Journal of Infectious Diseases. 2023;127:26-32. doi:10.1016/j.ijid.2022.11.044.



CANCERS

癌症研究

PRINCIPAL INVESTIGATOR
Jessie Liang

TEAM MEMBERS
Yuting Sun, Yao Zeng, Effie Lau, Silin Ye, Tingyu Zhou, Aijin Xie

RESEARCH PROGRESS SUMMARY

With the support of an Innovation and Technology Fund project, **Jessie Liang** and her research team developed a microbiome-based method for the non-invasive diagnosis of colorectal cancer (CRC) and adenoma. An invention patent and a utility model have been filed. The identified new microbial markers are under assessment of their diagnostic value by targeted quantification. Patent filing on some of the markers is under processing.

Probiotics can exert beneficial effects on gut microbiota and help maintain homeostasis. With probiotics that efficiently decrease the abundance of pathogenic bacteria that are associated with CRC, it is anticipated that the microbial risk for developing CRC would be reduced. Therefore, they also develop new probiotic formula for modulating gut microbiota, especially for reducing pathogenic bacteria, which may be ultimately beneficial for the prevention of CRC. Patents have been filed and licensed to a biotech company. The relevant probiotic product has been launched in the market. The findings have been presented in The 5th International Meeting on Intestinal Diseases in Conjunction with the Annual Congress of the Korean Association for the Study of Intestinal Diseases (IMKASID 2022), BEXCO, Busan, Korea (Best Poster Award), The 6th Korean Digestive Disease Week, Korea, Dec 1-3, 2022 (Oral presentation; Young Investigate Award), UEG Week 2022 (poster presentation) and Digestive Disease Week 2022 (poster presentation), The 16th International Gastrointestinal Consensus Symposium (IGICS), Tokyo, Japan, Feb 04, 2023 (Oral presentation; Young Investigate Award) and have been published in Cells in 2023.

Fusobacterium nucleatum (Fn) is a well-known bacterium contributing to colorectal tumorigenesis, but its functional mechanism remains to be fully elucidated. They have recently discovered a new role of Fn in inducing cholesterol production in host cells and the effectiveness of butyrate in inhibiting this process. This work has been presented in UEG Week 2023.

The team previously identified a faecal bacterial gene marker 'm3' from an unclassified bacterium to be significantly increased in patients with colorectal cancer and adenoma (Liang et al. *Gut* 2020). They have recently successfully isolated and characterised this m3-carrying bacterium and investigated its role in colorectal tumorigenesis (to be published).

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Jessie Liang	First class, Higher Education Outstanding Scientific Research Output Awards (Science and Technology)	Ministry of Education (MOE), China
	Young Investigators Award	16th International Gastrointestinal Consensus Symposium (IGICS)
Yao Zeng	First Prize for Excellent Paper	National Natural Science Foundation of China – Research Grant Council Youth Forum 2023
Yuting Sun	Young Investigator Travel Award	United European Gastroenterology Week 2023

Academic Editorships

Name	Details	
	Role	Journal
Jessie Liang	Guest Editor	Cells
	Editorial Board Member	Molecular Medicine Reports
		International Journal of Translational Research
		Journal of Gastroenterology, Liver & Pancreatic Diseases

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Jessie Liang	Reviewer	Gut
		Gut Microbes
		Gastroenterology
		International Journal of Cancer
		BMC Gastroenterology

Name	Details	
	Role	Journal / Conference
Jessie Liang	Reviewer	Heliyon
		Cancer Communications
		Clinical and Translational Medicine
		Pharmacological Research
		Cellular and Molecular Gastroenterology and Hepatology
		Journal of Gastroenterology and Hepatology
	Organising Committee	Hong Kong Society for Immunology Forum 2022
	Grant Reviewer	National Natural Science Foundation of China
		College Research Grant, Tung Wah College
		Israel Ministry of Health

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Jessie Liang	A Microbiome-based Non-invasive Diagnostic Test for Early Colorectal Cancers	The Innovation and Technology Commission Midstream Research Programme	01/04/2021	30/09/2023	4,600,000
	Organoid-based Investigations of COVID-19: Assess Infectivity of Mutant Viruses, Evaluate Vaccine Efficacy and Explore Disease Pathogenesis	Research Grants Council – Collaborative Research Fund (2nd round one-off CRF Coronavirus Disease and Novel Infections Diseases Research Exercise)	08/04/2022	07/05/2025	Amount not to be disclosed
	Function and Mechanism of Bacterium Fx in Suppressing Colorectal Tumorigenesis via Inhibiting Fusobacterium Nucleatum	Research Grants Council Research Grant – Direct Allocation	01/12/2023	30/11/2026	20,000
	Establishment of A Near-patient Test for Colorectal Cancer Screening Based on LAMP Detection of CRC-Related Fecal Bacterial Markers	University Grants Committee – Research Matching Grant Scheme	01/09/2022	31/08/2023	104,347
	Further Optimizing M3CRC Test and Evaluating its Performance in Diagnosing Colorectal Adenoma and Cancer	GenieBiome	01/08/2022	24/08/2024	300,000

Publications

A. Journal Paper

1. Liang JQ, Zeng Y, Lau EYT, Sun Y, Huang Y, Zhou T, Xu Z, Yu J, Ng SC, Chan FKL. A probiotic formula for modulation of colorectal cancer risk via reducing CRC-associated bacteria. *Cells*. 2023;12(9). doi:10.3390/cells12091244.

B. Conference Papers

1. Sun Y, Liang JQ. Fusobacterium nucleatum promotes cholesterol biosynthesis which is reversed by butyrate. In: *United European Gastroenterology (UEG) Week*. Copenhagen, Denmark. 2023 October 17.
2. Liang JQ, Zeng Y, Xu Z, Ng SC, Chan FK. A probiotic formula for modulation of colorectal cancer risk via reducing CRC-associated bacteria. In: *16th IGICS*. Tokyo. 2023 February 4. (Oral presentation)

C. Patents

1. China Patent:

   Title: Faecal Bacterial Markers for Colorectal Cancer
   Patent No.: ZL 201710261558.9
   Date of Patent: 6 June 2023

   Title: Novel Microbial Marker for the Prediction of Colorectal Cancer Risk
   Patent No.: 116042827
   Date of Patent: 22 December 2023

   Title: Assessing Risk for Colorectal Adenoma Recurrence by Noninvasive Means
   Application No.: 202180077828.5
   Filing date: 18 May 2023

   Title: 一种粪便采样装置
   Application No.: 202322110274.3
   Filing date: 7 August 2023

   Title: A Synbiotic Composition for Prevention of Colorectal Cancer
   Application No.: 202280007454.4
   Filing date: 15 May 2023
   Publication No.: CN 116615213 A
   Publication date: 18 August 2023

2. The United States Patent:

   Title: Faecal Bacterial Markers for Colorectal Cancer
   Patent No.: US 11603567
   Date of Patent: 14 March 2023

   Title: A Microbiome-based Test for Non-invasive Diagnosis of Colorectal Cancer and Adenoma
   US Provisional Application No.: 63/443,001
   Filing date: 02 February 2023

   Title: Assessing Risk for Colorectal Adenoma Recurrence by Noninvasive Means
   Application No.: 18/037,693
   Filing date: 18 May 2023

3. European Patent:

Title: Faecal Bacterial Markers for Colorectal Cancer
Patent No.: EP3504346
Grant date: 16 August 2023

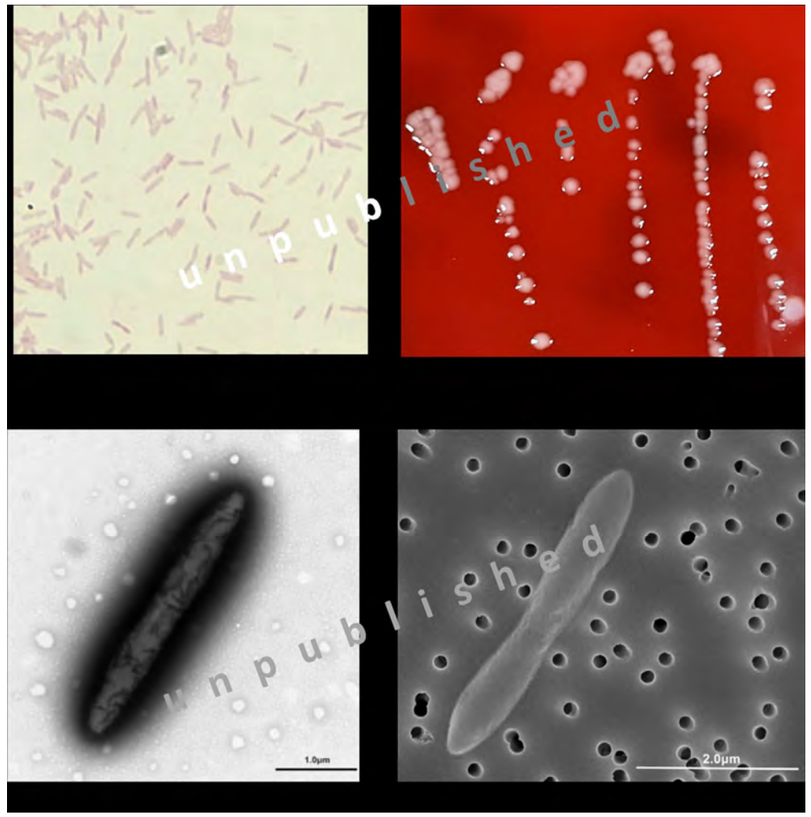
Title: Assessing Risk for Colorectal Adenoma Recurrence by Noninvasive Means
Application No.: 21893982.5
Filing date: 16 June 2023

4. Macau Patent:

Title: Faecal Bacterial Markers for Colorectal Cancer
Application No.: J/007317(182)
Filing date: 18 August 2023

5. Patent Cooperation Treaty Patent:

Title: Novel Microbial Marker for the Prediction of Colorectal Cancer Risk
Application No.: 22C53507
Filing date: 15 September 2022



Photos of their new M3 bacterium.

Source: Jessie Liang - Unpublished data



CANCERS
癌症研究

PRINCIPAL INVESTIGATOR
Andreas Möller

TEAM MEMBERS
Su-Ho Park, Sunyoung Ham, Keko'olani Visan, Sarah Voss, Li-Ying Wu, Yue Su

RESEARCH PROGRESS SUMMARY

With international collaborations spanning the globe from Asia to Oceania, to North America and to Europe, **Andreas Möller** and his team have identified key factors in the blood that not only contribute to cancer progression, but also act as biomarkers for early cancer detection and prognostication. Extracellular vesicles (EVs) play a crucial role in cancer development. These nanosized (30-200 nm) cell-derived particles contain various genetic materials such as proteins, DNA and RNA, encased by a stable lipid bilayer. Their composition facilitates their stability in bodily fluids in which they are omnipresent. As EVs are found in bodily fluids, their collection is non-invasive, easily accessible, highly efficient, and repeatable in nature. Hence EVs are great alternatives to traditional methods as biomarkers for cancer detection and prognostication.

Despite undergoing curative-intent treatments, many early-stage cancer patients develop therapy-resistant and metastatic tumours, demonstrating the inefficiency of current, traditional methods as a prognosticator. With this, Andreas and his team have identified four prognostic EV proteins, capable of predicting the response of lung (non-small cell lung cancer) cancer patients to therapy, before its start. This finding, published recently, has the capacity to personalise cancer therapy for patients based on the most successful treatment approach for the individual.

Conference presentations:

- Roles of extracellular vesicles in cancer progression and diagnostics

  2023 Chinese Society of Extracellular Vesicles Meeting, Shanghai, China, October 2023, Invited Keynote Speaker

- Approaches to discover extracellular vesicle-based biomarkers

  EV-based biomarkers: Commercialisation and clinical implementation, ISEV workshop, Denmark, October 2023, Speaker

- Roles of extracellular vesicles in cancer progression and diagnostics in SBS Research Day 2023

  Organised by School of Biomedical Sciences, The Chinese University of Hong Kong, Hong Kong, June 2023, Keynote Speaker

- Roles of extracellular vesicles in cancer progression and diagnostics

  IAMS Lecture (IAMS: Institute of Atomic and Molecular Sciences, Academia Sinica) organised by Center for Condensed Matter Sciences, National Taiwan University, Taiwan, March 2023, Invited Speaker

- Roles of extracellular vesicles in cancer progression and diagnostics

  Asia Pacific Societies of Extracellular Vesicles Conference, Taipei, Taiwan, 31 March - 1 April 2023, Plenary Speaker

- Cytokines bound to Cancer-derived Extracellular Vesicles impact immune cell phenotypes and metastasis

  5th International Conference on Cytokines in Cancer, Greece, 14 - 19 May 2023, Invited Speaker

Research Collaborations

- Biostability of exosomes, The Chinese University of Hong Kong, Hong Kong
- Cancer biology and exosomes, Tsinghua University, China
- Lung cancer exosomes, QIMR Berghofer MRI, Australia
- Clinical studies of lung exosomes, Royal Brisbane and Women's Hospital, Australia
- Prognostic biomarker in lung cancer, University of Applied Sciences Geneva HES-SO, Switzerland
- Exosomes in nanotech, University of Queensland, Australia
- Exosome biomarker, University of Queensland, Australia
- Exosomes in NSCLC prospective trial, Peter MacCallum Cancer Centre, Australia
- Timeline of NSCLC and exosomes as biomarker, Peter MacCallum Cancer Centre, Australia
- NSCLC samples for exosomes biomarker, Prince Charles Hospital Brisbane, Australia
- Blood and saliva exosomes in Head and neck cancer, Griffith University QLD, Australia
- Exosome tracking in cells, National Taiwan University, Taiwan
- Exosomes in NK cells, Cha University Korea, Korea
- Mitochondria detection of NK and T cells, Cha University Korea, Korea
- Exosome isolation and analysis in cancer, Thomas Jefferson University Philadelphia, United States of America
- CD155 and exosomes in melanoma, University of Bonn, Germany
- Exosomal miRNA in cancer detection, Tokyo Medical University, Japan
- Exosomes and secretome in Melanoma, Monash University, Australia
- Exosomes as biomarker in gastric cancer, Monash University, Australia

RESEARCH AND SCHOLARSHIP

Research Award and Recognition

Name	Details	
	Award	Organisation
Andreas Möller	Global STEM Scholar, Global STEM Professorship Scheme	The Goveronment of the Hong Kong Special Adminstrative Region

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Andreas Möller	Reviewer	Nature Communications
		Journal of Extracellular Biology
		Communications Medicine
		Nature Communications

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Andreas Möller	An Early Diagnostic and Prognostic Blood-based Biomarker for Head-and-neck Cancer	The Chinese University of Hong Kong – IdeaBooster Fund 2023/24	30/06/2023	30/06/2025	100,000
	JC STEM Lab of Personalised Cancer Medicine	Hong Kong Jockey Club Charities Trust	01/02/2023	31/01/2028	9,900,000
	To Support for Research Staff Cost in Association with Global STEM Professorship and Directorship for the JC STEM Lab of Personalised Cancer Medicine	Innovation and Technology Commission – Research Talent Hub	01/02/2023	31/01/2028	5,000,000

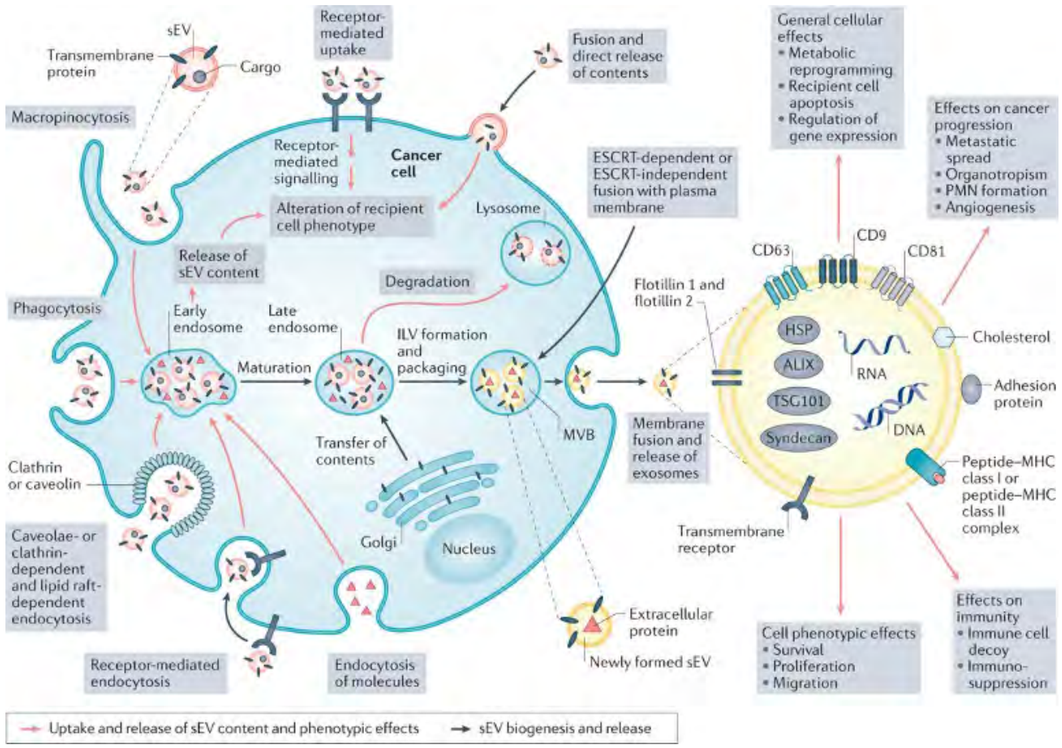
Publications

A. Journal Papers

1. Chee TM, O'farrell HE, Lima LG, Möller A, Fong KM, Yang IA, Bowman RV. Optimal isolation of extracellular vesicles from pleural fluid and profiling of their microRNA cargo. *Journal of Extracellular Biology*. 2023;2(10):e119. doi:10.1002/jex2.119.

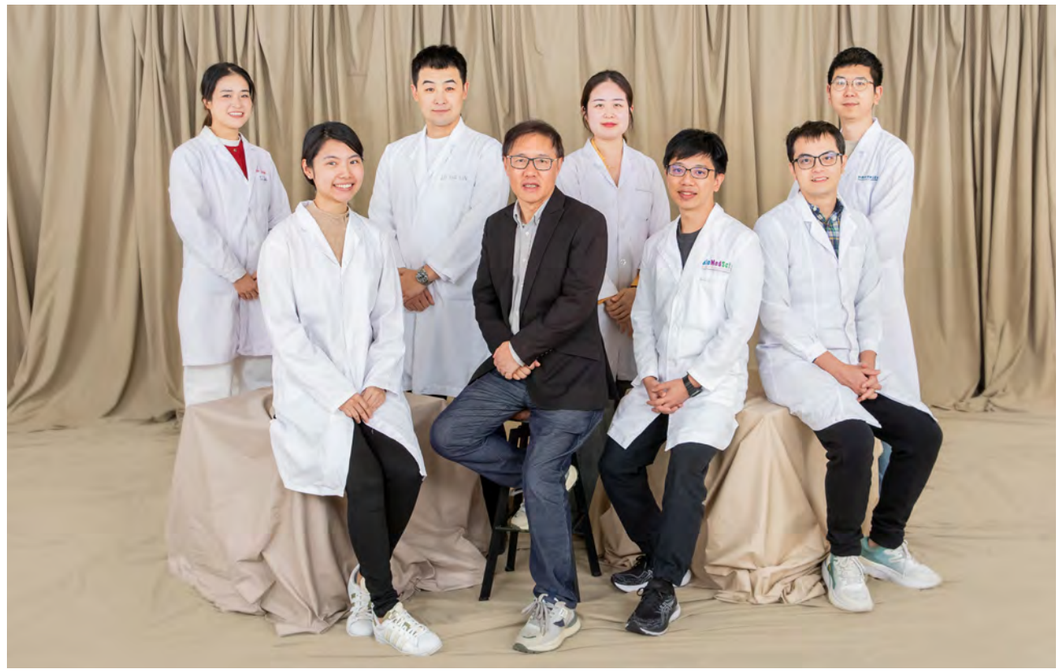
2. Jangholi A, Bark JM, de Lima LTF, Lima LG, Möller A, Kenny L, Vasani S, Rao S, Dolcetti R, Punyadeera C. Method optimisation to enrich small extracellular vesicles from saliva samples. *Clinical and Translational Medicine*. 2023;13(8):e1341. doi:10.1002/ctm2.1341. (Letter)

3. Rani S, Lai A, Nair S, Sharma S, Handberg A, Carrion F, Möller A, Salomon C. Extracellular vesicles as mediators of cell-cell communication in ovarian cancer and beyond - A lipids focus. *Cytokine & Growth Factor Reviews*. 2023;73:52-68. doi:10.1016/j.cytogfr.2023.06.004. (Review)



There are several biological mechanisms that small extracellular vesicles (sEVs) use to bind and/or be internalised by recipient cells (steps involved in sEV uptake and content release are denoted by red arrows). Cancer-derived sEVs can be taken up by receptor-mediated endocytosis. The sEV tetraspanins (CD9, CD63 and CD81) and other sEV molecules initiate recipient cell binding of sEVs. Certain ligands found on cancer-derived sEVs, for example, PDL1, FASL and tumour necrosis factor (TNF)-related apoptosis-inducing ligand (TRAIL; also known as TNFSF10), have been described to activate receptor-induced intracellular signalling in recipient cells. sEV internalisation through caveola-dependent or clathrin-dependent and lipid raft-dependent endocytosis seems to be independent of sEV ligands. Phagocytosis of preferably opsin-enriched sEVs is connected mostly to macrophages and other myeloid cell lineages and likely results in the intracellular destruction of the sEVs. Ligands activating macropinocytosis (an important cancer mechanism) through, for example, EGFR binding, enable unspecific sEV uptake of sEV and extracellular material. The sEVs are then released to the cytosolic space and could alter, depending on their cargo, the phenotype of the cell. Endocytosis leads to the formation of the early endosome and subsequent late-endosome maturation. Intraluminal vesicles (ILVs) are generated through the inward budding of the endosomal limiting membrane and form multivesicular bodies (MVBs). This process is coordinated via multiple proteins responsible for sEV biogenesis (steps involved in sEV biogenesis are denoted by black arrows), including ALIX, TSG101 and L domain-containing proteins. The late endosomes or MVBs either fuse with the lysosome for degradation of sEV content and release into the cytosol or undergo fusion with the plasma membrane for release of newly formed sEVs, which is coordinated by several Rab GTPases. These biogenic mechanisms result in distinct protein, nucleic acid and lipid content of sEVs. Canonical surface proteins, including tetraspanins, adhesion molecules (EPCAM, ephrin, integrins and lactadherin), MHC class I or class II molecules and proteoglycans can be used to isolate sEVs experimentally. Some of these proteins (ALIX, syndecan and TSG101) also characterise the biogenic origin of sEVs. sEVs are enriched, compared with their cell of origin, in various lipids, including cholesterol, sphingolipids and glycosphingolipids. The contents of sEVs can mediate intercellular communication that impacts a variety of cellular and tissue functions. ESCRT, endosomal sorting complexes required for transport; HSP heat shock protein; PMN, polymorphonuclear neutrophil.

Source: Möller A, Lobb RJ. 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.



CARDIOVASCULAR MEDICINE

VASCULAR MEDICINE – BASIC RESEARCH

心血管疾病研究

PRINCIPAL INVESTIGATOR
Xiaoqiang Yao

TEAM MEMBERS
Xiao Li, Jun Zhang, Zhenchuan Lei, Wentao Peng, Man Gu , Jan Tsz Yau, Chun-Yin Lo

RESEARCH PROGRESS SUMMARY

Xiaoqiang Yao and his research team has been working on Ca^{2+}-permeable ion channels and endoplasmic reticulum stress-related proteins in cardiovascular system and cancer. Recently, they have uncovered novel function of Orai1 channels in endothelium-dependent vascular contraction and role of TRPM2 channels in atherosclerotic progress. They have been in the process of developing the strategy of active immunisation with TRPM2 peptide in vaccine platform for potential treatment of atherosclerosis. In addition, they identified novel functional role of Orai1 channels in colorectal cancer. The research is supported by Hong Kong Innovation and Technology Fund, Hong Kong Research Grants Council Research Impact Fund, General Research Fund, and Health and Medical Research Fund.

Academic Editorships

Name	Details	
	Role	Journal
Xiaoqiang Yao	Associate Editor	Frontiers in Pharmacology
	Guest Editor	Cells

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Xiaoqiang Yao	Reviewer	Circulation Research
		Science Advances
		Cell Reports
		Cells

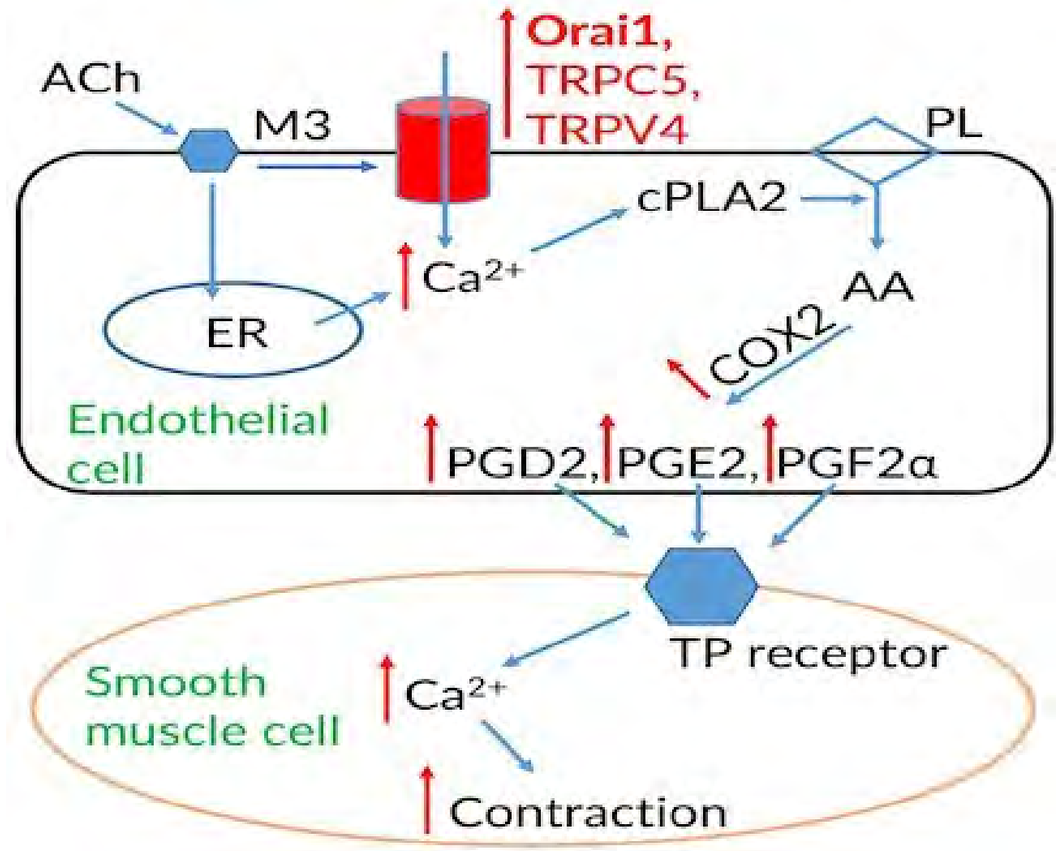
Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Xiaoqiang Yao	Orai1 Inhibitors as Potential Therapeutic Drugs against Colorectal Cancer Stem Cells	Innovation and Technology Commission – Innovation and Technology Fund	01/12/2022	31/05/2024	1,100,000
	Plant Bioreactor for Pharmaceutical Proteins	Research Grants Council – Research Impact Fund	01/06/2019	29/12/2024	5,000,000
	LETM-domain Containing Protein 1 as a New Player in Adipose Thermogenesis	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,178,251
	Role of TRPA1 Channels in Regulating the Functions and Maturation of Embryonic Stem Cell-Derived Cardiomyocytes Through Mediating Mitochondrial Biogenesis and/or Dynamics	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	996,285

Publications

A. Journal Paper

1. Zhang J, Yuan H, Li W, Chen S, Liu S, Li C, Yao X. Fusaric acid inhibits proliferation and induces apoptosis through triggering endoplasmic reticulum stress in MCF-7 human breast cancer cells. *Mycotoxin Research*. 2023;39(4):347-364. doi:10.1007/s12550-023-00497-z.



A schematic figure showing that the mechanism of how Orai1 channel contributes to endothelium-dependent vascular smooth muscle contraction together with two other channels (TRPC5 and TRPV4).

Sources: Xiaoqiang Yao



CARDIOVASCULAR MEDICINE

HEART DISEASES – CARDIAC IMAGING AND INTERVENTION

心血管疾病研究

PRINCIPAL INVESTIGATOR

Alex Lee

TEAM MEMBERS

Tsz Kin Tam, Guangming Tan, Man Fai Sim, Kevin Kam, Leo Lai, Andrew Li, Kent So, Geri Wong, Ken Wong, Alexandersson Anja, Tiffany Chung, Natalie Kwong, Crystal Tao, Xue Ting Wang, Xiaoyu Zhang, Tao Geng, Kitty Leung, Sophia Leung, Stella Luk, Lily Zhao, Raymond Chan, Robert Chan, Andy Lai, Tong Ding, Jamie Chan, Lavender Yeung

RESEARCH PROGRESS SUMMARY

In 2023, the research group led by **Alex Lee** marked significant advancements in their research efforts in the field of heart disease imaging and intervention. The research progress report highlights the key achievements and collaborations that have contributed to the advancement of their knowledge and the development of innovative solutions.

Clinical Trials and Research

The group established the Asian-Pacific 3D Echo Biobank for atrioventricular valve regurgitation and transcatheter repair, in collaboration with researchers from South Korea, Singapore, Taiwan, Mainland China, and India. They also took on national leadership roles in two major multi-centre clinical trials. The first was a multi-centre, randomised, double-blind, parallel-group, placebo-controlled study to evaluate the efficacy and safety of finerenone on morbidity and mortality in participants with heart failure (NYHA II-IV) and left ventricular ejection fraction ≥ 40% (FINEARTS-HF). The second was a pivotal phase 3 randomised, placebo-controlled clinical study to evaluate the efficacy and safety of the soluble guanylate cyclase stimulator vericiguat in adults with chronic heart failure with reduced ejection fraction (VICTOR).

The group also collaborated and consulted with AI industry leaders, including US2.AI and Echonous Kosmos, in applying AI to echo image acquisition, measurement, and reporting. They engaged in interdisciplinary collaboration with computer engineers to develop new 3D dynamic fusion imaging techniques for structural heart intervention, resulting in a research article published in Medical Physics. Additionally, they collaborated and consulted with device companies, Huihe Healthcare, Dawneo Healthcare, and Shenqi Healthcare, for the development of transcatheter tricuspid annuloplasty and TEER devices, which are undergoing clinical trials in Mainland China and Europe. The group also had consultancy and research agreements with major imaging device companies, Philips Healthcare and Abbott Healthcare, to develop and validate a novel 3D echo software and intracardiac echo technology.

In terms of research, the group collaborated on 3D physical replica for cardiac structure with partners in the USA and mainland China. They also initiated several investigator-driven drug clinical trials, such as the VALENTINO study investigating the effect of Vericiguat on cardiac remodeling in patients with heart failure and reduced ejection fraction (HFrEF), using novel echocardiographic imaging techniques. Additionally, the group conducted research programs related to Fabry disease, including the Asian Fabry Cardiomyopathy High-Risk Screening Program - Valve disease, the Prevalence of Fabry Disease Among Chinese Patients with Left Ventricular Hypertrophy in Hong Kong (HK-FAME), and the Natural History in Fabry Disease with IVS4+919G>A Mutations: A Longitudinal Study (FABULOUS). They also conducted a cost-effectiveness analysis of COVID-19 vaccines among the older adult population with pre-disposed comorbidities in Hong Kong.

Publication

The research group has published original and review articles in esteemed journals, including Clinical Cardiology, Frontiers in Cardiovascular Medicine, Frontiers in Medicine, Ultrasound in Medicine & Biology, JACC Cardiovascular Intervention, and Circulation: Cardiovascular Imaging. They also have a patent publication titled "3D physical replica of a cardiac structure and a method for manufacturing the same" in the United Kingdom and Mainland China.

Academic Conferences and Public Forums

The group has delivered lectures at international conferences on cardiac imaging and 3D printing for structural heart intervention, covering groundbreaking research topics. They have also been invited as international abstract graders for the European Society of Cardiology Congress 2023. The group successfully organised five events, including live cases, providing insights into tricuspid edge-to-edge repair. Additionally, they organised point-of-care ultrasound (POCUS) workshops to train Hong Kong doctors on POCUS image acquisition, interpretation, and management of pulmonary arterial hypertension and heart failure.

RESEARCH AND SCHOLARSHIP

Research Award and Recognition

Name	Details	
	Award	Organisation
Alex Lee	Asia's Outstanding Researcher Award	Asia Research Awards & Times of Research & the World Research Council

Fellowship

Name	Details	
	Fellowship	Organisation
Alex Lee	Fellowship of the Royal College of Physicians (London)	Royal College of Physicians

Academic Editorships

Name	Details	
	Role	Journal
Alex Lee	Reviewer	JACC: Asia
	Associate Editor	Frontiers in Cardiovascular Medicine
		Cardiovascular Ultrasound
		Frontiers in Cardiovascular Medicine
	Editor	JACC: Asia

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Alex Lee	Reviewer	Cardiovascular Ultrasound
		Heart
		Circulation
		Abstract grader for ESC Congress 2023
		Echocardiography
		IEEE Journal of Biomedical and Health Informatics
		JACC: Asia
		Journal of the American Society of Echocardiology (JASE)
		Journal of Asian Pacific Society of Cardiology

Grants and Consultancies

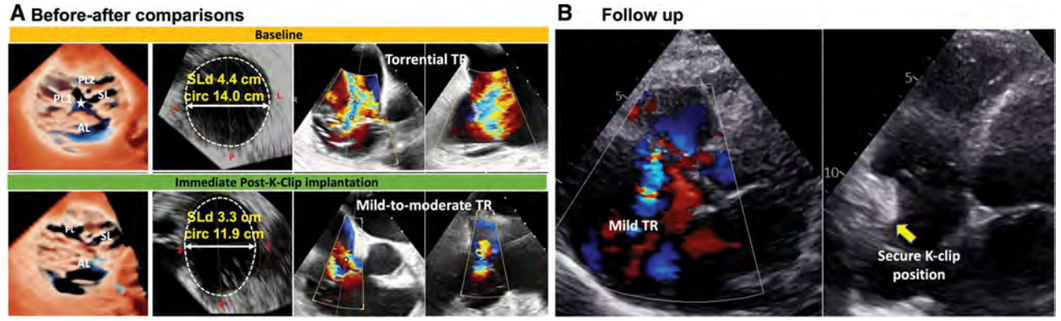
Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Alex Lee	Patient and Family Educational Training and Diagnostic Programme on Fabry Disease	Takeda Pharmaceuticals (Hong Kong) Limited	01/02/2023	31/01/2024	400,000
	Effect of Vericiguat on Cardiac Remodeling in Patients with Heart Failure and Reduced Ejection Fraction (Hfref): A Prospective Study Using Novel Echocardiographic Imaging Techniques (VALENTINO)	Bayer HealthCare Limited	19/10/2023	31/03/2025	450,000
	Cost Effectiveness Analysis of COVID-19 Vaccines Amongst Older Adult Population with Pre-disposed Comorbidities in Hong Kong	Fosun Industrial Co., Limited	01/01/2023	30/06/2025	500,000
Alex Lee	AI Echo Right Heart Project	Janssen, a division of Johnson & Johnson (HK) Limited	01/09/2022	31/08/2024	99,595
	Vascular Effects of Achieving Low Disease Activity in Axial Spondyloarthritis - A 2 Year Prospective Cohort Study	Health Bureau – Health and Medical Research Fund	01/09/2021	28/02/2025	1,505,615
	A Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Evaluate the Efficacy and Safety of Finerenone on Morbidity and Mortality in Participants with Heart Failure (NYHA II-IV) and Left Ventricular Ejection Fraction≥ 40%	Bayer HealthCare Limited	01/12/2020	30/11/2026	1,999,080
	Prevalence of Fabry Disease Among Chinese Patients with Left Ventricular Hypertrophy in Hong Kong (HK-FAME)	Sanofi-aventis Hong Kong Limited	28/05/2020	27/08/2023	846,125
	A Multinational, Multicenter Study to Assess the Effects of Oral Sildenafil on Mortality in Adults with Pulmonary Arterial Hypertension (PAH)	Pfizer Corporation Hong Kong Limited	25/10/2018	31/8/2023	2,399,028
	Clinical Trial of Atrial Fibrillation Patients Comparing Left Atrial Appendage Occlusion Therapy to Non-vitamin K Antagonist Oral Anticoagulants (CATALYST Trial)	Abbott Cardiovascular Systems Inc.	01/07/2021	31/12/2028	442,000
	3D Echo Biobank for Atrioventricular Valve Regurgitation and Transcatheter Repair	Abbott Medical (Hong Kong) Limited	01/09/2021	31/08/2023	900,000
	Study of Transthyretin Cardiac Amyloidosis Prevalence in Heart Failure Patients in Hong Kong (TAP-HK)	The University of Hong Kong	01/10/2021	30/09/2023	426,343.75
	Fabry Disease Research and Education 2022-2023	Takeda Pharmaceuticals (Hong Kong) Limited	01/01/2022	30/04/2023	330,000
	A Pivotal Phase 3 Randomised, Placebo-controlled Clinical Study to Evaluate the Efficacy and Safety of the sGC Stimulator Vericiguat/MK-1242 in Adults with Chronic Heart Failure with Reduced Ejection Fraction	Merck Sharp & Dohme (Asia) Limited	17/02/2022	01/04/2025	2,045,131.35

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Alex Lee	Natural History in Fabry Disease with IVS4+919G>A Mutations: A Longitudinal Study (FABULOUS)	Sanofi Hong Kong Limited	01/04/2022	31/08/2026	2,664,033
	Speeding Up Examination of Heart Diseases Through the Use of 3D Echocardiography and Machine Learning, Innovation & Technology Commission	Midstream Research Programme for Universities	01/04/2021	31/03/2024	1,251,200
	Asian Fabry Cardiomyopathy High-risk Screening Program – Valve disease	Sanofi Hong Kong Limited	13/12/2022	12/12/2025	955,118
	Artificial Intelligence and Deep Learning for Precision Heart Failure Management: A Pilot Study	Novartis Pharmaceuticals (HK) Limited	01/12/2020	31/12/2024	504,446.93

Publications

A. Journal Papers

1. Raja Shariff RE, Soesanto AM, Scalia GM, Ewe SH, Izumo M, Liu L, Li WCW, Kam KKH, Fan Y, Hong GR, Kinsara AJ, Tucay ES, Oh JK, Lee APW. Echocardiographic imaging in transcatheter structural intervention: An AAE review paper. *JACC Asia*. 2023;3(4):556-579. doi:10.1016/j.jacasi.2023.05.012. (Review)
2. Kam KKH, Lee APW. Radiation exposure of interventional echocardiographers: Protecting and nurturing a new subspecialty. *JACC Asia*. 2023;3(2):310. doi:10.1016/j.jacasi.2023.01.003.
3. Lui G, Leung HS, Lee J, Wong CK, Li X, Ho M, Wong V, Li T, Ho T, Chan YY, Lee SS, Lee APW, Wong KT, Zee B. An efficient approach to estimate the risk of coronary artery disease for people living with HIV using machine-learning-based retinal image analysis. *PLoS ONE*. 2023;18(2 February). doi:10.1371/journal.pone.0281701.
4. Mao Z, Zhao L, Huang S, Jin T, Fan Y, Lee APW. Complete region of interest reconstruction by fusing multiview deformable three-dimensional transesophageal echocardiography images. *Medical Physics*. 2023;50(1):61-73. doi:10.1002/mp.15910.
5. Chan JSK, Lau DHH, Fan Y, Lee APW. Fragmented vortex in heart failure with reduced ejection fraction: A prospective vector flow mapping study. *Ultrasound in Medicine and Biology*. 2023;49(4):982-988. doi:10.1016/j.ultrasmedbio.2022.12.001.
6. Lee APW, Ni Y, Lam YY. Imaging for transcatheter tricuspid annuloplasty using the K-Clip device. *Circulation: Cardiovascular Imaging*. 2023;16(6):518-520. doi:10.1161/circimaging.122.015033.
7. Fernandes R, Torres HR, Oliveira B, Azevedo J, Fan K, Lee AP, Vilaca JL, Morais P. Deep learning networks in the segmentation of the left atrial appendage in 2D ultrasound: a comparative analysis. *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, EMBS*. Published online 2023. doi:10.1109/embc40787.2023.10340937.



Postprocedural imaging. A, Intraprocedural echocardiography showing immediate reduction of the annular dimensions, coaptation gap, and tricuspid valve regurgitation (TR) severity; the P1 leaflet was excluded resulting in a 3-leaflet morphology (tricuspidization of the 4-leaflet valve). B, Three-month follow-up echocardiography showing mild residual TR and secure device position. yellow arrow=endothelialized K-Clip; dotted lines=tricuspid annulus. AL indicates anterior leaflet; Ao, aorta; circ, annular circumference; PL1, first posterior leaflet; PL2, second posterior leaflet; RCA, right coronary artery; SL, septal leaflet; and SLd, septolateral annular diameter.

Source: Lee APW, Ni Y, Lam YY. Imaging for transcatheter tricuspid annuloplasty using the K-Clip device. Circulation: Cardiovascular Imaging. 2023;16(6):518-520. doi:10.1161/circimaging.122.015033.



DIABETES AND OBESITY
糖尿病與肥胖症研究

PRINCIPAL INVESTIGATOR

Juliana Chan

TEAM MEMBERS

Ronald Ma, Alice Kong, Elaine Chow, Wing Yee So, Hongjiang Wu, Aimin Yang, Juliana Lui, Risa Ozaki, Kitty Cheung, Cadmon Lim, Stephanie Cheung, Phyllis Kwong, Eric Lau, Heung Man Lee, Claudia Tam, Donna Chen, Natural Chu, Baoqi Fan, Noel Ng, Mei Shi, Alex Ng, Emily Poon, Hester Lee, Abby Li, Kelly Wong, Jane Ho, Tony O, Ho Lam Hui, Hou Yong, Zhengli Bai, Jamie Cheung, Sandra Choi, Yingnan Fan, Yidan Hao, Jia He, Yintang Huang, Wang Ke, James Ling, Tsz Fung Choi, Gechang Yu, Tianjiao Yuan, Rebecca Yue, Yingchai Zhang, Xinge Zhang, Andy Kuo, Chun Hei Tam, Chuiguo Huang, Kit Ying Tsoi

RESEARCH PROGRESS SUMMARY

Using data science to monitor trends and evaluate outcomes
Hong Kong Diabetes Surveillance Database and Hong Kong Diabetes Register

Using the Hong Kong Diabetes Surveillance Database (HKDSD) curated from the Hospital Authority (HA) Electronic Medical Record (EMR) system, consisting of 4 million people with at least one blood glucose measurement (2000-2019), **Juliana Chan** and her research team identified 0.8 million people with diabetes. Between 2000 and 2016, they observed 50-70% decline in incidence of major events and death. Although Hong Kong ranked the world with the lowest death rate in people with diabetes, people with young-onset diabetes, diagnosed before the age of 40 years, had 5-8 fold higher risk of death than their peers without diabetes. This trend had not changed during the same period. In this territory-wide database, patients with diabetes had 3-6 fold higher incidence ratio of hospitalisation due to multiple causes than their age-sex matched counterparts without diabetes. Whilst most hospitalsations occurred in the above 40-year-old age group in people without diabetes, young patients with diabetes had high incidence of hospitalisation due to mental illness before the age of 40 years.

In the Hong Kong Diabetes Register (HKDR) established at the Prince of Wales Hospital since 1995, 1 in 5 adult patients had depressive symptoms often with somatisation, notably, lack of energy. These negative emotions were particularly prevalent in young people, women and patients with poor glycemic control and co-morbidities. After adjusting for multiple risk factors, depression was associated with 2-3 fold increased risk of major events and all-cause death. While it is well known that patients with complications had poor quality of life, for the first time, they reported residual impaired quality of life years after the occurrence of events in patients with diabetes. In elderly patients with diabetes, they reported high prevalence of insomnia and cognitive dysfunction, the latter risk being attenuated with insulin treatment. These multidimensional data highlight the burden of diabetes on physical, emotional and social health calling for patient-centred holistic care.

On a more positive note, using real-world evidence, they reported the benefits of persisting with highly affordable medications such as metformin and renin-angiotensin-system inhibitors (RASi) in reducing vascular, cancer, non-vascular, non-cancer death. Despite their life-saving nature, these drugs were often discontinued in patients when advanced chronic kidney disease (CKD) developed despite their high risk for developing multiple complications. Using advanced analytical methods to emulate a randomised controlled trial (RCT), they first reported that discontinuation of RASi and metformin in patients with advanced CKD was associated with increased risk of cardiovascular-renal events and all-cause death compared to those who persisted with these drugs.

The data granularity of HKDSD which captured laboratory results and medications allowed them to evaluate the impacts of treatment especially in low-risk patients where RCT data are far and between. Dipeptidyl peptidase inhibitor (DPP4i) is an oral glucose lowering drug which lowers fasting and post-prandial blood glucose with low risk of hypoglycaemia. Using propensity score matching, they reported that initiation of DPP4i within 2 years of diagnosis or at low HbA1c (<7.5%), compared to late intervention, improved glycemic durability, delayed insulin use and reduced all major events, mediated largely by reduced glycemic variability. In the same vein, early use of sodium glucose transporter 2 inhibitor (SGLT2i) at low HbA1c (<7.5%) was associated with reduced rate of decline in kidney function especially in high-risk patients. In RCT setting, weight loss of 15 kg in obese patients with type 2 diabetes induced remission of diabetes for up to 2 years. However, their real-world evidence indicated that during a 8-year follow up period, less than 6% of patients were able to stay in remission without use of drugs, although any period of remission was associated with improved outcomes. These data emphasise the importance of early detection, prevention, treatment to low glycemic targets and persistent use of organ protective drugs to reduce the burden of diabetes.

Joint Asia Diabetes Evaluation (JADE) Register

The web-based JADE portal enables delivery of technologically-assisted and data-driven care to promote quality assurance and shared decision-making. Using the JADE Register with over 120,000 patients enrolled from 11 countries/ regions in Asia established since 2007, they were the first to report the high prevalence of young-onset diabetes affecting 1 in 5 adults with diabetes in Asia. Compared to patients with later-onset diabetes, these young patients who had worse control of risk factors and less frequent use of organ protective drugs. In this multi-ethnic population, they reported different risk profiles and health behaviors between male and female patients with type 2 diabetes. Women had less physical activity and more central obesity, kidney disease and cancer events and were less likely to be at glycemic control and treated with organ protective drugs then men. Apart from these age and gender-related differences, they also evaluated the impact of family history on age of diagnosis in light of the high lifetime risk of complications in patients with young-onset diabetes. Diabetes is known to have strong familial clustering which may be due to shared genetics, environment and/or lifestyles. Using the JADE Register, they reported the associations of positive family history and number of affected family members with younger age of diagnosis, which was delayed by healthy lifestyles. They also demonstrated how patients with family history of diabetes benefitted disproportionately from self-management in achieving treatment goals. These data highlight how nature and nurture may contribute to the phenotypic heterogeneity of diabetes in Asian population.

Precision medicine, multi–omic analysis and personalised care in PRISM Study

The ongoing PRISM Project (**P**recision Medicine to **R**edefine **I**nsulin **S**ecretion and **M**onogenic Diabetes in Chinese Patients with Young Onset Diabetes) commissioned by the Health and Medical Research Fund (HMRF) commenced in 2020. In this 3-part study, they assessed the beta-cell function and auto-antibodies using samples in the biobank of the HKDR. They also used whole genome sequencing to discover co-segregation of genetic variants with diabetes traits in the Hong Kong Diabetes in Family Study (HKDFS) Cohort, the majority of index patients having young-onset diabetes. In the 3-year RCT, they randomised 441 patients with YOD to receive multidisciplinary care guided by biogenetic markers and facilitated by information technology for 1 year before returning to usual care while 441 patients received usual care. The study will complete in September 2024 with the primary outcome being all diabetes-related endpoints.

The implementation of PRISM Project has provided enormous insights regarding the many lifecourse factors as well as psychosocial-behavioral needs in addition to the phenotypic and genetic heterogeneity of these young patients. In the cohort analysis, they had reported that 5-8% of patients had latent autoimmune diabetes in adults (LADA). Compared to acute-onset autoimmune type 1 diabetes, these patients with LADA had 2.8-fold increased risk of end stage kidney disease (ESKD), likely due to delayed insulin treatment despite their superior response to insulin compared to non-LADA patients. They measured serum C peptide in their various biobanks and derived HOMA indexes to assess beta-cell function and insulin resistance. They reported the additive interactions of insulin resistance and deficiency on predicting onset of diabetes as well as early insulin requirement in patients with type 2 diabetes. In the PRISM cohort,

they confirmed that 5% of these young patients had antibodies, suggestive of LADA while 3.8% had rare variants of one or more of the 34 genes of monogenic diabetes, with many of them carrying variants of uncertain significance.

Collaboration with Hong Kong Genome Institute

To further unravel the complex aetiologies of young-onset diabetes, they are collaborating with the Hong Kong Genome Institute where they shall apply whole genome sequencing to the PRISM and HKFDS cohorts as well as family members of the PRISM cohort to elucidate the familial clustering of common and rare variants of genes associated with young-onset diabetes and related traits. Leveraging the available sequence and genome-wide array data in multiple cohorts established since 1995, they are using multiple methods to discover causal genes associated with young onset diabetes and complications, especially diabetic kidney disease (DKD). Importantly, they shall use big data analytics to segment patients based on genotype-phenotype-treatment outcomes in pursuit of prediction, prevention and treatment with precision

From multiomic analysis to discovery of path–ways with biomarkers and drug targets

In their ongoing multiomic project, they continue to use their biobanks and databases to apply for research grants and develop their students and fellows with academic output aimed at elucidating the genetic regulation of diabetic complications (see Ronald Ma's report in Lab 602). In brief, they have now gained considerable experiences and developed pipelines to decode the genomes including sequences and single nucleotide polymorphisms (SNPs) of 30,000 individuals at different stages of the development of diabetes and its complications continuously followed up since 1995. By integrating these multiomic data with clinical variables including laboratory, drug and hospitalisation data, they have discovered novel biomarkers and molecular signatures in both coding and non-coding regions associated with diabetes and its complication for risk stratification and early intervention. These molecular pathways provide opportunities for further investigations related to drug discovery or repurposing, accompanied by companion diagnostics.

In their collaborative project with a leading pharmaceutical company, they have used long-read and short-read whole genome sequencing data to study genetic causes of DKD with internal and external validation. Using bioinformatics and network analysis, computational biology and Mendelian Randomisation, they have discovered a list of novel loci for which they are developing kidney organoids, in collaboration with CUHK stem cell biologists, to confirm their functional significance. In collaboration with other basic scientists within and outside CUHK, they continue to use experimental models to elucidate the role of specific pathway (e.g. SIRT3) including the use of single cell sequencing in the development of diabetes and fatty liver. They have applied other *state-of-the-art* methods to their various biobanks and cohorts aimed at integrating the phenome, genome, epigenome, proteome, metabolome, and biomarkers, such as telomeres, to provide a lifecourse and individualised profile for explaining the heterogeneity in diabetes.

Technologies and therapeutics

In collaboration with the CUHK Phase 1 Clinical Trial Centre, they have established the insulin/glucose clamp techniques, a gold standard, to evaluate insulin secretory function and its actions in people with or without diabetes in controlled settings. Using this technique, they have confirmed the reduced beta-cell function in patients with young-onset diabetes, especially in those with lean body mass index, compared to age and sex-matched individuals without diabetes. These findings confirmed the inter-ethnic differences in the genetic associations of diabetes where genes implicated in beta-cell function played a more important role than insulin resistance compared to Europeans. These findings have therapeutic implications given the superior efficacy of drugs that promote insulin secretion including incretin mimetics such as DPP4i and glucagon-like-peptide 1 in reducing blood glucose in East Asian compared to European patients

Although more than 10 classes of glucose lowering drugs have been developed, one of the major unmet needs is defective glucose sensing by beta-cells as the first step in triggering insulin secretion. To this end, they have developed a strategic partnership with a China-based pharmaceutical company which has developed the first glucokinase activator (GKA). In 2022, this novel class of drug was approved by, and in 2024 reimbursed by regulatory agency in China for treatment of hyperglycaemia. Using clamp studies, they first demonstrated that GKA reduced the threshold of blood glucose level in triggering insulin level in patients with monogenic diabetes due to GK mutation, supported by functional studies. These award-winning results published in top journal have opened a new avenue for using molecular genetics and targeted treatment as an example of precision medicine in monogenic diabetes.

In a multicentre phase 3 study, they evaluated the efficacy and safety of a novel aldose reductase inhibitor in patients with type 2 diabetes and heart failure with preserved ejection fraction (HFpEF). In collaboration with their cardiologist, they set up the *state-of-the-art* facilities including echocardiogram, cardiopulmonary exercise testing and metabolomic platform to explore the mechanistic effects of this novel drug. With the completion of the trial, the top line results had shown its efficacy in preserving ejection fracture compared to deterioration in the control group. Given the genetic association of aldose reductase with diabetic complications, this new class of drug may be another candidate for precision medicine.

Continous glucose moitoring system and devices

The launching of continuous glucose monitoring (CGM) system lasting for 7-14 days has transformed diabetes care by providing immediate feedback to help both patients and providers to make shared decisions including medications and lifestyles. Supported by a local biotechnological company, their group has the opportunity to evaluate a novel CGM system lasting for 28 days, supported by the Innovation and Technology Commission (ITC). Through this project, their group has developed expertise in evaluating CGM systems and since then, supported by competitive grants to use CGM systems on top of lifestyle modification to prevent progression from prediabetes to diabetes. They have also evaluated the effects of using CGM to reduce risk of hypoglycemia in patients with DKD. Along the way, for the first time, they have examined the accuracy of CGM in patients with advanced DKD including those on peritoneal dialysis for which data are scarce. Hypoglycaemia remains a major unmet need in patients with type 1 diabetes treated with intensive insulin treatment. In many high-income countries, CGM proven to reduce risk of hypoglycaemia in patients with type 1 diabetes, is reimbursable or subsidised to improve quality of care. In a territory-wide program, the Hong Kong Jockey Club Charitable Trust is providing free CGM to patients with type 1 diabetes through a patient organisation with their group being commissioned to evaluate the effectiveness and cost-effectiveness of this 3-year program.

Modernisation of Chinese Medicine and drug–food–micriobiota interactions

Their previous animal-based mechanistic studies have revealed the multiomic effects of Chinese Medicine (CM) with improved beta-cell function and insulin resistance. Supported by a CUHK strategic grant, they confirmed the glucose-lowering effect of a novel CM formulation (JM) with possible remission in people with prediabetes. Taking this project forward and in colloaboration with School of Chinese Medicine, supported by the Hong Kong Insititue of Biotechnology, CU School of Pharmacy and CU Phase 1 Clinical Trial Centre, they have been funded by the ITC to use western methodologies and to evaluate the clinical and multiomic effects of JM in people with early type 2 diabetes. This study will be supplemented by a pharmacokinetic (PK) and pharmacodynamic (PD) study in volunteers for evaluating possible drug-herb interaction. By using standard methodologies employed in western medicine, they aim to develop JM into an evidence-based CM therapy for prevention, treatment and possible remission of type 2 diabetes. In the same vein, given the importance of nutrition in health and disease, they are also evaluating the effects of functional foods and drug-food interactions on metabolic health including changes in microbiota and their impacts on internal milieu and energy metabolism

Knowledge transfer, international profile and people development

As an International Diabetes Federation (IDF) Centre of Excellence in Diabetes Care, they continue to build professional capacity through bi-annual Master, Diploma and Certificate Courses in Endocrinology, Diabetes and Metabolism and their annual Hong Kong Diabetes and Cardiovascular Risk Factor – East Meets West Symposium organised by the Hong Kong Institute of Diabetes and Obesity to promulgate the latest advances, share best practices and foster collaborations. Supported by multiple parties including the Hong Kong Jockey Club and Asia Diabetes Foundation, a subsidiary of CUHK Foundation, they have been organising activities including on-line webinars by professionals and patient stories to educate and empower lay people and patients to protect their health and prevent disease through self-management and informed decision-making (http://hkido.cuhk.edu.hk/; https://www.adf.org.hk/).

By combining research, practice and education, their team has secured multiple competitive grants, set up strategic academic-industrial collaborations, established international collaborations, trained postgraduate students and fellows. Many of their graduates went on to become leaders in academic institutions or industry. Their contributions have been recognised with Ronald Ma receiving an endowment chair while other members are being supported by research assistant professorship and postdoctoral fellowship schemes. Their principal investigators are regular reviewers and serve on editorial boards of top medical journals. Some of them are also committees of international organisations in the field of diabetes, obesity and kidney disease where they contribute to guideline development and position statements to create regional and global impacts.

Apart from serving on Food and Health Bureau and HA committees to advise on matters related to diabetes, noncommunicable disease, drug utilisation and development, most PIs are members of grant review committees of ITC, Research Grant Committee (RGC), HMRF and Professional

Services Advancement Support Scheme to contribute to the development of knowledge workers in Hong Kong. Given the importance of industry in translating research findings to clinical use, some members also serve on steering committees of international projects including outcome trials and/or provide consultancy to global and regional advisory boards of multinational companies including Amgen, Astra Zeneca, Bayer, Boehringer Ingelheim, Merck, MSD, Novo Nordisk, Sanofi, Pfizer, Viatris and Zuelig Pharma.

Publicity and press release

In 2023, their productive research has led to award of multiple grants and publications whilst at the same time, they have shared key findings with the public to raise awareness. Some examples include:

- CUHK study shows few patients with type 2 diabetes can achieve diabetes remission in real-world settings through weight loss at early stage and eventually stop medications

  https://www.med.cuhk.edu.hk/press-releases/cuhk-study-shows-few-patients-with-type-2-diabetes-can-achieve-diabetes-remission-in-real-world-settings-through-weight-loss-at-early-stage-and-eventually-stop-medications

- CUHK study shows prediabetes in young people predicts a 90% lifetime risk of diabetes and is linked to nearly 70% higher risks of cardiovascular diseases

  https://www.med.cuhk.edu.hk/press-releases/cuhk-study-shows-prediabetes-in-young-people-predicts-a-90-lifetime-risk-of-diabetes-and-is-linked-to-nearly-70-higher-risks-of-cardiovascular-diseases

- New algorithm can predict diabetic kidney disease A simple blood sample could help doctors catch kidney disease earlier in type 2 diabetes patients

  https://www.med.cuhk.edu.hk/press-releases/new-algorithm-can-predict-diabetic-kidney-disease

- CUHK identifies a new genetic marker to predict heart disease risk in people with diabetes. Study finding highlights the potential of precision medicine in diabetes

  https://www.med.cuhk.edu.hk/press-releases/cuhk-identifies-a-new-genetic-marker-to-predict-heart-disease-risk-in-people-with-diabetes-study-finding-highlights-the-potential-of-precision-medicine-in-diabetes

- ADA 2023: Discontinuing Metformin Tied to Worse Cardio-Renal, Survival Outcomes - Outcomes poor at eGFR less than 30 mL/min/1.73m2 irrespective of cardiovascular status

  https://www.practiceupdate.com/content/ada-2023-discontinuing-metformin-tied-to-worse-cardio-renal-survival-outcomes/154118

- Few patients successfully treat their type 2 diabetes through weight loss. People with the most weight loss in the first year were most likely to achieve sustained remission

  https://www.eurekalert.org/news-releases/1031292
  https://www.upi.com/Health_News/2024/01/23/diabetes-weight-loss-study/5941705953836/

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Ronald Ma	SH Ho Professor of Diabetes	The Chinese University of Hong Kong
Johnny Cheung	The First Publication Prize of IDF -WPR Early Mid Career Researchers (EMCR), 2023, Q4 Original research paper: Cheung JTK, Yang A, Wu H, Lau ESH, Kong APS, Ma RCW, Luk AOY, Chan JCN, Chow E. Early treatment with dipeptidyl-peptidase 4 inhibitors reduces glycaemic variability and delays insulin initiation in type 2 diabetes: A propensity score-matched cohort study. Diabetes/Metabolism Research and Reviews. 2023: e3711. DOI: 10.1002/dmrr.3711	Western Pacific Region, International Diabetes Federation
Tony O	East Meets West Symposium Young Investigator Award (1st runner up)	Hong Kong Institute of Diabetes and Obesity
Jamie Cheung	Travel grant for oral presentation of abstract	Hong Kong Institute of Diabetes and Obesity
Yidan Hao	Best oral presentation (clinical)	40th Anniversary Annual Scientific Meeting, Hong Kong Society and Endocrinology, Metabolism and Reproduction
Natural Chu	East Meets West Symposium Young Investigator Award	Hong Kong Institute of Diabetes and Obesity
	Hong Kong & Macau Microbial SMRT Grant award winner	Pacific Biosciences

Fellowships

Name	Details	
	Fellowship	Organisation
Kit Ying Tsoi Shi Mai Donna Chen	Faculty Postdoctoral Fellowship	Faculty of Medicine, The Chinese University of Hong Kong
Chuiguo Huang	Postdoctoral Fellowship Scheme	Faculty of Medicine, The Chinese University of Hong Kong
Noel Ng	RGC Posdoctoral Fellowship	Research Grant Committee
Natural Chu Stephanie Cheung Baoqi Fan Phyllis Kwong Eric Lau	Research Talent Hub Scheme	Innovation and Technology Committee

Academic Editorships

Name	Details	
	Role	Journal
Juliana Chan	International Advisor	The Lancet Diabetes and Endocrinology
	Editorial Board Member	Diabetes Metabolism Research Review
		Journal of Diabetes
Ronald Ma	Expert Editor	Journal of Diabetes Investigation
	Associate Editor	Diabetologia
	Editorial Board Member	PLoS Medicine
		Obesity Reviews
Alice Kong	Editor-in-chief	Primary Care Diabetes
	Associate Editor	Obesity Reviews
	Section Editor	Current Diabetes Reports
	Editorial Board Member	Diabetes Care
		Diabetes Technology & Therapeutics
		International Medical Education
Andrea Luk	Associate Editor	Diabetic Medicine
	Editorial Board Member	Diabetes Care
Elaine Chow	Associate Editor	Primary Care Diabetes
		Diabetes Research and Clinical Practice
Hongjiang Wu	Associate Editor	Cardiovascular Diabetology
	Editorial Board Member	BMC Medicine
	Young Editorial Board Member	Journal of Zhejiang University-SCIENCE B
		Military Medical Research
Aimin Yang	Guest Editor	Frontiers in Nutrition
		Frontiers in Public Health

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Juliana Chan Ronald Ma Alice Kong Andrea Luk Elaine Chow	Reviewer Editorial Board Member	The Lancet
		The Lancet Endocrinology and Diabetes
		The Lancet Regional Health Western Pacific
		Nature Review
		Nature Medicine
		Nature Communication
		Nature Metabolism
		BMJ
		PLoS Medicine
		PLoS One
		BMC Medicine
Juliana Chan Ronald Ma Alice Kong Andrea Luk Elaine Chow	Reviewer Editorial Board Member	Diabetes Care
		Diabetologia
		Diabetes Obesity Metabolism
		Diabetes Rsearch and Clinical Practice
		Diabetic Medicine
		Primary Care Diabetes
		Acta Diabetologia
		Environment International
		International Journal of Epidemiology
		American Journal of Clinical Nutrition
		Chemosphere
		Environmental Pollution
		Science of The Total Environment
		Environmental Research
		Ecotoxicology and Environmental Safety
		Journal of Occupational and Environmental Medicine
		Annals of Academy of Medicine (Singapore)
		Frontiers in Public Health
		Biomolecules
		Biomedical and Environmental Sciences and British Journal of Cancer

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Juliana Chan	Empower our Youth and Transform our Future	The Chinese University of Hong Kong CUHK, ORKTS – Knowledge Transfer Project Fund	01/04/2023	30/09/2024	399,840
	Clinical Safety, Efficacy And Multiomic Evaluation of A Novel Chinese Medicine (cm) Formula in Type 2 Diabetes (T2D): Effects On Beta-Cell Function And Insulin Resistance	Innovation and Technology Commission – Midstream Research Programme for Universities	01/06/2022	30/05/2025	4,966,735
Juliana Chan Ronald Ma	Using Whole Genome Sequencing, Computational Biology and Functional Analysis to Discover Biological Pathways Implicated in Diabetic Kidney Disease	Astra Zeneca Investigator Initiated Study	30/10/2019	30/09/2023	8,918,060

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Juliana Chan Andrea Luk	Precision Medicine to Redefine Insulin Secretion and Monogenic Diabetes (PRISM) in Chinese Patients with Young Onset Diabetes	Health Bureau – Health and Medical Research Fund	01/09/2019	31/08/2024	8,457,718
Juliana Chan	Self-managing Healthy Eating & Active Lifestyle for impeding 3-Highs (High Blood Glucose, High Blood Pressure and High Cholesterol) Mobile Application (SHEALF3 APP) (renamed as Citybite APP and Chatbot)	Innovation and Technology Fund for Better Living via Asia Diabetes Foundation	01/10/2018	30/09/2023	4,247,006
	Real World Evidence of Sulphonlyureas Usage in Asian Patients with Type 2 Diabetes – The Joint Asia Diabetes Evaluation (JADE) Register	Servier via Asia Diabetes Foundation	01/03/2021	31/12/2023	1,200,000
	Using Modern and Traditional Technologies to Redefine and Prevent Young Onset Diabetes	The Chinese University of Hong Kong – Strategic Grant	01/09/2019	30/6/2023	500,000
Juliana Chan Elaine Chow	Effects of Dorzagliatin on 1st Phase Insulin and Beta-Cell Glucose Sensitivity in Individuals with Impaired and Normal Glucose Tolerance	Hua Medicine Investigator Initiated Study	03/03/2022	03/2023	1,221,800
Juliana Chan	Aldose Reductase Inhibition for Stabilization of Exercise capacity in Heart Failure (ARISE-HF): A Multicenter, Randomized, Placebo-Controlled Study to Evaluate the Safety and Efficacy of AT-001 in Patients with Diabetic Cardiomyopathy / Stage B Heart Failure at High Risk of Progression to Overt Heart Failure (Stage C Heart Failure)	Applied Therapeutics	01/11/2020	31/12/2025	1,500,000
Ronald Ma	Improving Diabetes Care for Young Patients	Hong Kong Jockey Club Charities Trust	01/07/2023	30/06/2027	10,900,000
	Translating Multi-Omic Discoveries to Transform Diabetes Care and Reduce Diabetic Complications	Research Committee Funding for Research Sustainability of Major Research Grants Council Funding Schemes	01/05/2019	30/04/2024	500,000
	Translating Multi-Omic Discoveries to Transform Diabetes Care and Reduce Diabetic Complications	Research Grants Council – Research Impact Fund	01/05/2019	30/04/2024	8,400,000
	A Nanotechnology Platform for Profiling Diabetes-related MiRNA for Precision Medicine	Innovation Technlogy Commision – Midstream Research Programme for Universities	01/06/2021	30/11/2023	4,201,853
	Genomic Medicine in Diabetic Kidney Disease - RMG01	University Grants Committee – Research Matching Grant Scheme	01/06/2020	31/08/2024	3,499,675

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ronald Ma	Croucher Senior Medical Research Fellowships, Research Project	Croucher Foundation	01/05/2021	30/04/2023	2,000,000
Alice Kong	The Impact of Cognitive Behavioral Therapy (CBT-i) on Glycemic Control in Older Type 2 Diabetes (T2D) Comorbid with Insomnia	Health Bureau – Health and Medical Research Fund	01/09/2021	31/08/2023	1,484,694
Andrea Luk	Delineating the Metabolic Architecture and Response to Anti-Hyperglycaemic Drug Treatment in Lean Type 2 Diabetes in Chinese	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,178,778
Elaine Chow	Continuous Glucose Monitoring as an Adjunct to Lifestyle Modification in Individuals with Impaired Glucose Tolerance: A Randomised Controlled Trial	Health Bureau – Health and Medical Research Fund	01/10/2020	30/09/2023	1,344,796
	Effectiveness and Safety Study of the Continuous Glucose Monitoring System (Fibersense) for Home Use (Including In-Clinic Sessions) in Patients with Diabetes	Innovation and Technology Commission – Guangdong – Hong Kong Technology Cooperation Funding Scheme	17/08/2020	16/11/2024	5,674,000
	A Phase 1b/2a Ascending Dose Study of the Safety, Tolerability and Preliminary Efficacy of Sublingual Liraglutide in Patients with Type 2 Diabetes	Innovation and Technology Commission – Partnership Research Programme	01/09/2020	31/05/2023	3,680,203
	Effect of Glucagon-like Peptide 1 Receptor Agonist in Combination with Insulin on Glycaemic Variability and Time-in-Range in Diabetic Kidney Disease: A Randomised Controlled Trial	Health Bureau – Health and Medical Research Fund	03/01/2022	02/01/2025	1,361,740
	The Impact of High or Low FODMAP Diets on Postprandial Glucose Response and Gut Microbiota in Individuals with Prediabetes Treated with Metformin: A Randomized Crossover Controlled-Feeding Trial	Merck Investigator Initiated Clinical Trial	01/11/2022	01/01/2024	669,575
Aimin Yang	Detecting People at High-risk of Progression from Prediabetes to Diabetes for Early Intervention - A Machine Learning Approach Using Electronic Health Records	Health Bureau – Health and Medical Research Fund Fellowship Scheme	01/2023	31/03/2025	1,100,000
Juliana Lui	Using Clinical-trials and Simulation-models to Estimate Cost-effectiveness of Non-steroidal Mineralocorticoid Antagonists, Rasi, SGLT2i as Triple Therapy in Patients with Type-2 Diabetes and Chronic-kidney Disease	Health Bureau – Health and Medical Research Fund	01/12/2023	31/07/2026	1,352,000

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Juliana Lui	Health Economic Analysis on the NT-ProBNP Guided Cardiovascular Risk Assessment and Treatment in Patients with Type-2 Diabetes in Hong Kong	Roche Diagnostics Hong Kong Investigator Initiated Study	01/08/2023	01/08/2026	300,000
Baoqi Fan	Clinical Utility of Anti-Islet Autoantibodies and Their Seroconversion in the Detection of Autoimmune Diabetes in Chinese	Health Bureau – Health and Medical Research Fund	18/09/2023	17/09/2025	934,000
Noel Ng	Long-term Health Impact of Polycystic Ovary Syndrome	Research Grants Council – Postdoctoral Research Fellowship Scheme	02/07/2020	01/07/2023	1,225,800
	Evaluation of the Long-Term Healthcare Impact of Polycystic Ovary Syndrome	Health Bureau – Health and Medical Research Fund	1/10/2021	30/09/2023	1,304,136

Publications

A. Journal Papers

1. Wu H, Lau ESH, Yang A, Fan B, Ma RCW, Kong APS, Chow E, So WY, Chan JCN, Luk AOY. Real world evidence of clinical predictors of glycaemic response to glucose-lowering drugs among Chinese with type 2 diabetes. *Diabetes/Metabolism Research and Reviews*. 2023;39(4):e3615. doi:10.1002/dmrr.3615.

2. Wu H, Lau ESH, Yang A, Zhang X, Fan B, Ma RCW, Kong APS, Chow E, So WY, Chan JCN, Luk AOY. Age-specific population attributable risk factors for all-cause and cause-specific mortality in type 2 diabetes: An analysis of a 6-year prospective cohort study of over 360,000 people in Hong Kong. *PLOS Medicine*. 2023;20(1):e1004173. doi:10.1371/journal.pmed.1004173.

3. Wu H, Yang A, Lau ESH, Zhang X, Fan B, Shi M, Huang C, Ma RCW, Kong APS, Chow E, So WY, Chan JCN, Luk AOY. Age- and sex-specific hospital bed-day rates in people with and without type 2 diabetes: A territory-wide population-based cohort study of 1.5 million people in Hong Kong. *PLOS Medicine*. 2023;20(8):e1004261. doi:10.1371/journal.pmed.1004261.

4. Yang A, Shi M, Lau ESH, Wu H, Zhang X, Fan B, Kong APS, Luk AOY, Ma RCW, Chan JCN, Chow E. Clinical outcomes following discontinuation of renin-angiotensin-system inhibitors in patients with type 2 diabetes and advanced chronic kidney disease: A prospective cohort study. *eClinicalMedicine*. 2023;55:101751. doi:10.1016/j.eclinm.2022.101751.

5. Zhang X, Wu H, Fan B, Shi M, Lau ESH, Yang A, Chow E, Kong APS, Chan JCN, Ma RCW, Luk AOY. The role of age on the risk relationship between prediabetes and major morbidities and mortality: Analysis of the Hong Kong diabetes surveillance database of 2 million Chinese adults. *The Lancet Regional Health – Western Pacific*. 2023;30:100599. doi:10.1016/j.lanwpc.2022.100599.

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7. Suzuki K, Hatzikotoulas K, Southam L, Taylor HJ, Yin X, Lorenz KM, Mandla R, Huerta-Chagoya A, Rayner NW, Bocher O, Arruda ALSV, Sonehara K, Namba S, Lee SSK, Preuss MH, Petty LE, Schroeder P, Vanderwerff B, Kals M, Bragg F, Lin K, Guo X, Zhang W, Yao J, Kim YJ, Graff M, Takeuchi F, Nano J, Lamri A, Nakatochi M, Moon S, Scott RA, Cook JP, Lee JJ, Pan I, Taliun D, Parra EJ, Chai JF, Bielak LF, Tabara Y, Hai Y, Thorleifsson G, Grarup N, Sofer T, Wuttke M, Sarnowski C, Gieger C, Nousome D, Trompet S, Kwak SH, Long J, Sun M, Tong L, Chen WM, Nongmaithem SS, Noordam R, Lim VJY, Tam CHT, Joo YY, Chen CH, Raffield LM, Prins BP, Nicolas A, Yanek LR, Chen G, Brody JA, Kabagambe E, An P, Xiang AH, Choi HS, Cade BE, Tan J, Broadaway KA, Williamson A, Kamali Z, Cui J, Adair LS, Adeyemo A, Aguilar-Salinas CA, Ahluwalia TS, Anand SS, Bertoni A, Bork-Jensen J, Brandslund I, Buchanan TA, Burant CF, Butterworth AS, Canouil M, Chan JCN, Chang LC, Chee ML, Chen J, Chen SH, Chen YT, Chen Z, Chuang LM, Cushman M, Danesh J, Das SK, de Silva HJ, Dedoussis G, Dimitrov L, Doumatey AP, Du S, Duan Q, Eckardt KU, Emery LS, Evans DS, Evans MK, Fischer K, Floyd JS, Ford I, Franco OH, Frayling TM, Freedman BI, Genter P, Gerstein HC, Giedraitis V, González-Villalpando C, González-Villalpando ME, Gordon-Larsen P, Gross M, Guare LA, Hackinger S, Han S, Hattersley AT, Herder C, Horikoshi M, Howard AG, Hsueh W, Huang M, Huang W, Hung YJ, Hwang MY, Hwu CM, Ichihara S, Ikram MA, Ingelsson M, Islam MT, Isono M, Jang HM, Jasmine F, Jiang G, Jonas JB, Jørgensen T, Kandeel FR, Kasturiratne A, Katsuya T, Kaur V, Kawaguchi T, Keaton JM, Kho AN, Khor CC, Kibriya MG, Kim DH, Kronenberg F, Kuusisto J, Läll K, Lange LA, Lee KM, Lee MS, Lee NR, Leong A, Li L, Li Y, Li-Gao R, Lithgart S, Lindgren CM, Linneberg A, Liu CT, Liu J, Locke AE, Louie T, Luan J, Luk AO, Luo X, Lv J, Lynch JA, Lyssenko V, Maeda S, Mamakou V, Mansuri SR, Matsuda K, Meitinger T, Metspalu A, Mo H, Morris AD, Nadler JL, Nalls MA, Nayak U, Ntalla I, Okada Y, Orozco L, Patel SR, Patil S, Pei P, Pereira MA, Peters A, Pirie FJ, Polikowsky HG, Porneala B, Prasad G, Rasmussen-Torvik LJ, Reiner AP, Roden M, Rohde R, Roll K, Sabanayagam C, Sandow K, Sankareswaran A, Sattar N, Schönherr S, Shahriar M, Shen B, Shi J, Shin DM, Shojima N, Smith JA, So WY, Stančáková A, Steinthorsdottir V, Stilp AM, Strauch K, Taylor KD, Thorand B, Thorsteinsdottir U, Tomlinson B, Tran TC, Tsai FJ, Tuomilehto J, Tusie-Luna T, Udler MS, Valladares-Salgado A, van Dam RM, van Klinken JB, Varma R, Wacher-Rodarte N, Wheeler E, Wickremasinghe AR, van Dijk KW, Witte DR, Yajnik CS, Yamamoto K, Yamamoto K, Yoon K, Yu C, Yuan JM, Yusuf S, Zawistowski M, Zhang L, Zheng W; VA Million Veteran Program; AMED GRIFIN Diabetes Initiative Japan; Biobank Japan Project; Penn Medicine BioBank; Regeneron Genetics Center; eMERGE Consortium; International Consortium for Blood Pressure (ICBP); Meta-Analyses of Glucose and Insulin-Related Traits Consortium (MAGIC); Raffel LJ, Igase M, Ipp E, Redline S, Cho YS, Lind L, Province MA, Fornage M, Hanis CL, Ingelsson E, Zonderman AB, Psaty BM, Wang YX, Rotimi CN, Becker DM, Matsuda F, Liu Y, Yokota M, Kardia SLR, Peyser PA, Pankow JS, Engert JC, Bonnefond A, Froguel P, Wilson JG, Sheu WHH, Wu JY, Hayes MG, Ma RCW, Wong TY, Mook-Kanamori DO, Tuomi T, Chandak GR, Collins FS, Bharadwaj D, Paré G, Sale MM, Ahsan H, Motala AA, Shu XO, Park KS, Jukema JW, Cruz M, Chen YI, Rich SS, McKean-Cowdin R, Grallert H, Cheng CY, Ghanbari M, Tai ES, Dupuis J, Kato N, Laakso M, Köttgen A, Koh WP, Bowden DW, Palmer CNA, Kooner JS, Kooperberg C, Liu S, North KE, Saleheen D, Hansen T, Pedersen O, Wareham NJ, Lee J, Kim BJ, Millwood IY, Walters RG, Stefansson K, Goodarzi MO, Mohlke KL, Langenberg C, Haiman CA, Loos RJF, Florez JC, Rader DJ, Ritchie MD, Zöllner S, Mägi R, Denny JC, Yamauchi T, Kadowaki T, Chambers JC, Ng MCY, Sim X, Below JE, Tsao PS, Chang KM, McCarthy MI, Meigs JB, Mahajan A, Spracklen CN, Mercader JM, Boehnke M, Rotter JI, Vujkovic M, Voight BF, Morris AP, Zeggini E. Multi-ancestry genome-wide study in >2.5 million individuals reveals heterogeneity in mechanistic pathways of type 2 diabetes and complications. *medRxiv*. Published online 2023. doi:10.1101/2023.03.31.23287839. (Epub ahead of print)

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11. Ng JKC, Ling J, Luk AOY, Lau ESH, Ma RCW, Li PKT, Szeto CC, Chan JCN, Chow E. Evaluation of a fourth-generation subcutaneous real-time continuous glucose monitor (CGM) in individuals with diabetes on peritoneal dialysis. *Diabetes Care*. 2023;46(6):1191-1195. doi:10.2337/dc22-2348.

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During a 4-year follow-up period, in 1816 patients with type 2 diabetes mainly treated with metformin and sulphonylureas, early DPP4i intensification within 2 years of diagnosis was associated with 30% risk reduction while low HbA1c Variability Score (HVS)* was associated with 60% reduced risk of insulin initiation compared to those initiated DPP4i at 3-5 years. The early DPP4i plus low HVS group had 70% reduced risk of insulin initiation compared to late DPP4i plus high HVS group. Despite having similar HbA1c at baseline, the late DPP4i group had higher HbA1c (8.2%) than the early DPP4i intensification group (7.7%) throughout the follow-up period. These data demonstrate the benefits of early DPP4i intensification in delaying insulin initiation, partially due to reduced glycaemic variability.

*HVS-percentage of HbA1c values different from previous value by 0.5%

Source: Cheung JTK, Yang A, Wu H, Lau ESH, Kong APS, Ma RCW, Luk AOY, Chan JCN, Chow E. Early treatment with dipeptidyl-peptidase 4 inhibitors reduces glycaemic variability and delays insulin initiation in type 2 diabetes: A propensity score-matched cohort study. Diabetes/Metabolism Research and Reviews. 2024;40(1). doi:10.1002/dmrr.3711.

Selected as the First Publication Prize of IDF -WPR Early Mid Career Researchers (EMCR), 2023, Q4
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DIABETES AND OBESITY

糖尿病與肥胖症研究

PRINCIPAL INVESTIGATOR
Ronald Ma

TEAM MEMBERS
Andrea Luk, Risa Ozaki, Wing Yee So, Hongjiang Wu, Cadmon Lim, Claudia Tam, Raymond Wan, Ming Wai Poon, Guozhi Jiang, Mai Shi, Noel Ng, Kit Ying Tsoi, Eric Lau, Baoqi Fan, Vince Chan, Alex Ng, Yong Hou, Atta Tsang, Chuiguo Huang, Yingnan Fan, Tsz Fung Tsoi, Xinge Zhang, Chun Hei Tam, Yingchai Zhang, Gechang Yu, Charmaine Lee, Yuzhi Deng, Kelly Wong, Chris Hui

RESEARCH PROGRESS SUMMARY

Epidemiology of diabetes and diabetes complications in Asians

They have continued to generate novel insights on the epidemiology of diabetes and diabetic complications in Asians, to help inform formulation of strategies and policies to address this important public health burden. With recent support from the Theme-based Research Scheme (TRS) on Diabetes Complications and ongoing support from a Research Impact Fund (PC: **Ronald Ma**), they have charted the natural history of diabetic kidney disease and the progressive decline in renal function using various novel analytic approaches, including latent trajectory analysis. This work has highlighted the heterogeneity of decline in renal function, and identified subgroups at particular risk of renal dysfunction. They are recently used proteomics, metabolomics and other omics approach to identify predisposing factors and markers associated with rapid renal function decline and the development of diabetic kidney disease. They have also conducted studies to examine sub-phenotype in diabetic kidney disease, and the long-term impact of acute kidney injury on progression of diabetic kidney disease. They are also using big-data analytics to examine the epidemiology of diabetes complications based on population-based administrative data. Both Ronald and Andrea Luk were major contributors to the recent International Diabetes Federation (IDF) Diabetes Atlas, leading subgroups on Type 1 Diabetes in Adults and Young-onset diabetes, respectively. The systematic review on Type 1 Diabetes in Adults was published in *Diabetes Care*, and the data formed the basis of the newly launched Type 1 Diabetes Index (https://www.t1dindex.org/), the first comprehensive resource on the global burden of type 1 diabetes, in an international effort led by the Juvenile Diabetes Research Foundation.

In work led by Andrea, they continue to use population-based data to provide novel insights on the epidemiology of diabetes and its complications in Asia. Recent advances include establishing the lifetime risk of diabetes among Chinese people with normoglycaemia and pre-diabetes, as well as the impact of age on diabetes-related complications and impact of different drugs on diabetes outcomes. They have examined age-specific associations and population attributable fractions of risk factors for all-cause and cause-specific mortality in people with type 2 diabetes. Another major analysis undertaken established the hospital bed-days for a variety of medical conditions for people with or without diabetes, as well as highlighting the burden of mental health disorders for people diagnosed with diabetes at a young age.

Earlier work has also highlighted the burden of young-onset diabetes, and conditions that predispose to young-onset diabetes. Having published one of the longest follow-up studies to investigate the impact of Polycystic Ovary Syndrome (PCOS) on development of glucose intolerance and diabetes among young women, they have been invited to contribute to co-lead a systematic review on this topic, as well as lead the related section in the recently completed International evidence-based guideline for the assessment and management of PCOS 2023. Their work in this area has also extended to the long-term follow-up of cardiovascular complications and metabolic outcomes in women with PCOS and their offspring, as well as analyses based on population-based data. Recent work on the offspring of women with PCOS, led by Noel Ng and supported by a Health and Medical Research Fund, was selected by the Androgen Excess-PCOS Society for the Azziz-Baumgartner Family Early Career Investigator Award in 2022.

Genetics of diabetes and gestational diabetes

Work from their group has contributed significantly to advance the understanding of the genetic basis of type 2 diabetes. Together with colleagues across Asia, they have completed one of the largest genome-wide association studies (GWAS) for type 2 diabetes, and identified 61 novel loci for type 2 diabetes. This study has considerably expanded the number of genetic loci associated with type 2 diabetes in Asians, and would form the basis of future translation towards clinical prediction and care. They are currently investigating the role of these markers in the development of glucose intolerance and other metabolic abnormalities among adolescents and children.

In a project supported by Research Grants Council (RGC) General Research Fund, Andrea completed an analysis to identify monogenic forms of diabetes among our cohort of patients with young-onset diabetes. This represents one of the largest studies on monogenic diabetes among Asian populations, and the work will provide complementary information on rare genetic variation that contributes to the heritability of diabetes in Asians, and help to advance precision medicine in diabetes.
Gestational diabetes has become a common major complication of pregnancy, and has long-term adverse effects for the mother and offspring. In collaboration with Xilin Yang from Tianjin Medical University, China, they have conducted a meta-analysis of genome-wide association study to identify novel genetic variants associated with gestational diabetes in the Chinese population, as well as search for metabolomic markers associated with GDM.

Long–term consequences of gestational dia–betes and related biomarkers

In a long-term collaborative study together with Wing Hung Tam from the Department of Obstetrics and Gynaecology, they have investigated the long-term health impact of gestational diabetes. This *include* the long-term follow-up of a GDM mother-offspring cohort over more than 2 decades to follow their long-term progression to metabolic abnormalities as well as diabetes (supported by several RGC grants), and the multi-centre Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) Follow Up Study. The latter has highlighted the long-term risk of diabetes among women with gestational diabetes, as well as the independent association between maternal GDM and offspring adiposity. In order to unravel the link between maternal hyperglycaemia and offspring metabolic abnormalities, in work supported by the RGC, they have applied epigenomic profiling to identify methylation changes to offspring DNA following exposure to maternal hyperglycaemia. They are also conducting a long-term follow-up off offspring of mothers with GDM as they now enter adulthood, to evaluate their metabolic profile as well as skeletal health. The recognition of the long-term risks of mothers with GDM and their offspring has led to completion of an interventional study to evaluate how to reduce this risk of future diabetes, and they have incorporated some elements of the intervention into tools to facilitate scaling up such efforts.

Genetic and novel biomarkers of diabetes complications

In work supported by the Research Grants Council Theme-based Research Scheme, they have completed one of the largest genome-wide association study for diabetes complications globally, and identified a number of genomic regions associated with diabetic kidney disease in Asians. In addition, through the TRS, they have established the multi-centre Hong Kong Diabetes Biobank (HKDB), which forms a unique dataset with detailed clinical phenotyping, multi-omics profiling and long-term follow-up which would serve to advance future epidemiology research as well as biomarker discovery. Ongoing work include investigating the biological mechanisms whereby the new genes impact on development of diabetes complications, with views to develop novel

treatments to target diabetes complications. With ongoing support from the Research Grants Council Research Impact Fund, they are continuing their work on biomarkers for diabetes complications, and have expanded that effort to incorporate methylation and metabolomic profiling to integrate into their multi-omics analyses to obtain a better picture of key disease pathways. Their GWAS for CHD risk in type 2 diabetes has identified a novel variant associated with risk of CHD in diabetes, with novel insights on risk factors control. They have developed novel methylation signatures for diabetic kidney disease, providing new strategies to identify those at risk of kidney failure.

Precision medicine in diabetes

Through support from the RGC Research Impact Fund and the Croucher Foundation, they aim to bring some of the discoveries generated from their work to translate to the bedside to impact on clinical care. This includes incorporating our biomarkers into clinical management of patients with diabetes, development of various polygenic risk scores, as well as pharmacogenomics studies to stratify patients based on treatment response for better selection of glucose-lowering and other treatments. They are also developing genetic risk scores for stratifying risk of type 1 diabetes in Chinese. Their group has played a major role in the recent global initiative on Precision Medicine in Diabetes, including leading a systematic review of biomarkers for predicting diabetes cardiovascular complications. This series of work will deliver tools that can facilitate personalised treatment of people with diabetes, and hopefully improve long-term outcome.

COVID–19 and diabetes

Since the pandemic began, COVID-19 has impacted on every aspect of daily life. People with diabetes have increased susceptibilities to COVID-19 and adverse outcomes following COVID-19 infections. Their group has been conducting epidemiological analyses relating to diabetes and COVID-19, including the impact of diabetes treatments on outcome, as well as genetic studies relating to adverse outcome in COVID-19.

Much of their research is highly multidisciplinary and collaborative, with ongoing collaborations with more than 20 research groups across the world.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
The Chinese University of Hong Kong Endocrine and Diabetes Team	Number 1 in Asia for Endocrinology and Metabolism 2022-2023	U.S. News Best Global Universities Rankings
Ronald Ma	Plenary Lecture	Japanese Society of Diabetes and Pregnancy 2023
	Top Cited Article 2021-2022	Obesity Reviews
Yingchai Zhang	Travel Grant	IDF-WPR Congress 2023/15th Scientific Meeting of AASD, Kyoto, Japan

Fellowships

Name	Details	
	Fellowship	Organisation
Noel Ng	Postdoctoral Fellowship	Research Grants Council
Kit Ying Tsoi		Faculty of Medicine, The Chinese University of Hong Kong
Chuiguo Huang		Research Committee, The Chinese University of Hong Kong

Academic Editorships

Name	Details	
	Role	Journal
Roanld Ma	Expert Editor (from 11/2020)	Journal of Diabetes Investigation
	Member of Editorial Board	PLoS Medicine
		Obesity Reviews
		Diabetes
	Associate Editor	Diabetologia
Andrea Luk	Associate Editor	Diabetic Medicine
	Member of Editorial Board	Diabetes Care

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Ronald Ma	Reviewer	Nature Medicine
		Cell Metabolism
		PLoS Medicine
		BMJ
		Diabetes Care
		Diabetologia
		Diabetes
		Diabetic Medicine
		Journal of Diabetes Investigation
		Diabetes/ Metabolism Research and Reviews
		Diabetes Research and Clinical Practice
		Journal of Clinical Endocrinology and Metabolism
		Journal of American College of Cardiology
		Circulation
		Genome Medicine
		American Journal of Clinical Nutrition
		Obesity Reviews
		Obesity
		International Journal of Obesity

Name	Details	
	Role	Journal / Conference
Andrea Luk	Reviewer	Diabetes Care
		Diabetologia
		Diabetic Medicine
		Diabetes
		Obesity and Metabolism
		Journal of Diabetes
		Diabetes/Metabolism Research and Reviews
		Diabetes Research and Clinical Practice
		Cardiovascular Diabetology
		Journal of Clinical Endocrinology and Metabolism
		Lancet Regional Health Western Pacific

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ronald Ma	Improving Diabetes Care for Young Patients	Hong Kong Jockey Club Charities Trust	01/07/2023	30/06/2027	10,900,000
	A Nanotechnology Platform For Profiling Diabetes-related MiRNA For Precision Medicine	Innovation and Technology Commission–Midstream Research Programme for Universities	01/06/2021	31/05/2024	5,998,400
	Research Talent Hub – PiH/198/21	Innovation and Technology Commission	01/06/2021	31/05/2024	1,388,000
	Research Talent Hub – PiH/313/21	Innovation and Technology Commission	10/11/2021	22/03/2023	86,584.02
	Research Talent Hub – PiH/247/22	Innovation and Technology Commission	12/08/2022	31/05/2024	438,493.54
	Research Talent Hub – PiH/377/22	Innovation and Technology Commission	15/11/2022	31/05/2024	438,060
	Research Talent Hub – PiH/199/23	Innovation and Technology Commission	04/05/2023	31/05/2024	600,145.16
	Precision Medicine in Diabetes	Croucher Foundation	01/05/2021	30/04/2023	2,000,000
	Translating Multi-omic Discoveries to Transform Diabetes Care and Reduce Diabetic Complications	Research Grants Council – Research Impact Fund	01/05/2019	30/04/2024	8,400,000
	Translating Multi-omic Discoveries to Transform Diabetes Care and Reduce Diabetic Complications	The Chinese University of Hong Kong Research Committee – Research Impact Matching Fund	01/05/2019	30/04/2024	3,401,550
Ronald Ma	Translating Multi-omic Discoveries to Transform Diabetes Care and Reduce Diabetic Complications	The Chinese University of Hong Kong Research Committee – Funding for Research Sustainability of Major Research Grants Council Funding Schemes	27/05/2019	30/04/2024	500,000
	Genomic Medicine in Diabetic Kidney Disease	University Grants Committee – Research Matching Grant Scheme	01/06/2020	31/12/2026	3,579,544.10
	Precision Medicine in Diabetes	University Grants Committee – Research Matching Grant Scheme	10/12/2021	9/12/2024	520,762.27
	A Phase 3b, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of TRC101 in Delaying Chronic Kidney Disease Progression in Subjects with Metabolic Acidosis	Tricida Inc	01/04/2019	31/12/2024	1,605,460
	PIONEER 12 China Multi-regional Clinical Trial: Efficacy and Safety of Oral Semaglutide Versus Sitagliptin in Subjects with Type 2 Diabetes Mellitus Treated with Metformin	Novo Nordisk Hong Kong Limited	01/08/2019	06/04/2023	2,332,500
	Semaglutide Cardiovascular Outcomes Trial in Patients with Type 2 Diabetes (SOUL)	Novo Nordisk Hong Kong Limited	29/08/2019	29/07/2024	9,424,000
	FAME 1 EYE - The Fenofibrate and Microvascular Events in Type 1 Diabetes Eye. A Randomised Trial to Evaluate the Efficacy on Retinopathy and Safety of Fenofibrate in Adults with Type 1 Diabetes; A Multicenter Double-blind Placebo-controlled Study in Australia and Internationally	University of Sydney	01/08/2019	31/12/2024	348,160
	Effect and Safety of Semaglutide 2.4mg Once - weekly on Weight Management in Subjects with Overweight or Obesity	Novo Nordisk Hong Kong Limited	08/12/2020	31/12/2024	2,309,170
	A Non-blinded Retrospective Biomarker Add-on Study to FIGARO-DKD for Bioprofiling the Pharmacodynamic Response to Finerenone in FIGARO-DKD Subjects (FIGARO-BM)	Bayer HealthCare Limited	15/10/2021	31/12/2023	105,000
	The Use of NT-proBNP for Stratifying Risk of Cardio-renal Complications in Chinese Patients with Type 2 Diabetes	Roche Diagnostics (Hong Kong) Limited	01/02/2022	01/07/2023	360,000

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ronald Ma	Novel Biomarkers for Glycaemic Progression in Diabetes	The Chinese University of Hong Kong – Direct Grant	30/6/2022	29/06/2023	75,000
	Developing an e-Health Platform to Improve Maternal Health and Reducing Long-term Risk of Chronic Diseases for Women with Gestational Diabetes	Knowledge Transfer Project Fund	01/04/2023	31/03/2025	400,000
	Translating Multi-omics Analyses for Precision Medicine in Diabetes	Research Committee – Postdoctoral Fellowship Scheme 2021 – 22	12/05/2022	30/04/2026	750,000
	Evaluation of the Long-Term Healthcare Impact of Polycystic Ovary Syndrome	Research Grants Council – Postdoctoral Fellowship Scheme 2020 – 21	02/07/2020	01/07/2023	1,198,540
Noel Ng	Evaluation of the Long-Term Healthcare Impact of Polycystic Ovary Syndrome	Health Bureau – Health and Medical Research Fund	01/10/2021	31/03/2024	1,304,136
Ronald Ma	Precision Medicine to Redefine Insulin Secretion and Monogenic Diabetes (PRISM) in Chinese Patients with Young Onset Diabetes	Health Bureau – Health and Medical Research Fund	01/09/2019	31/08/2024	8,457,718
	The Effect of in Utero Hyperglycaemia, Maternal Overnutrition and Interaction with Postnatal Lifestyle on Cardiometabolic Risk at Young Adulthood – Extension of HAPO Follow Up Study	Research Grants Council – General Research Fund	01/01/2020	30/06/2023	1,158,019
	Metformin as a Neuroprotective Therapy for Glaucoma – A Randomised Controlled Trial	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,160,564
Andrea Luk	Delineating the Metabolic Architecture and Response to Anti-hyperglycaemic Drug Treatment in Lean Type 2 Diabetes in Chinese	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,178,778
	A Pilot Program to Establish a Laboratory Service Hub for Multi-National Clinical Trials (396203964) sponsored by Teddy Clinical Research Laboratory (Hong Kong) Limited	Teddy Clinical Research Laboratory (Hong Kong) Limited	01/06/2023	30/09/2024	1,104,000
	A Phase 2 Randomised, Placebo-controlled, Double-blind, Dose-ranging Study to Evaluate the Efficacy, Safety and Tolerability of AMG 133 in Adult Subjects with Overweight or Obesity, with or without Type 2 Diabetes Mellitus	Amgen Asia Holding Limited	01/06/2023	31/05/2026	1,322,633

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Andrea Luk	A Multicenter, Double-blind, Randomised, Placebo-controlled, Phase II/III Study to Evaluate the Efficacy, Safety and Pharmacokinetics of JT001 (VV116) for the Early Treatment of Coronavirus Disease 2019 (COVID-19) in Participants with Mild to Moderate COVID-19	Shanghai JunTop Biosciences Co., Ltd	01/05/2022	31/12/2023	15,035,468
	A Multicenter, Double-blind, Randomised, Placebo-controlled, Phase II/III Study to Evaluate the Efficacy, Safety and Pharmacokinetics of JT001 (VV116) for the Early Treatment of Coronavirus Disease 2019 (COVID-19) in Participants with Mild to Moderate COVID-19	Shanghai JunTop Biosciences Co., Ltd	01/05/2022	31/12/2023	3,437,350
	A Trial Investigating the Pharmacokinetic Properties of Fast-acting Insulin Aspart in Chinese Subjects with Type 1 Diabetes or Type 2 Diabetes	Novo Nordisk Hong Kong Limited	01/12/2020	31/12/2023	2,672,830
	ReFineDR: Observational Study of Routine Ophthalmological Examinations of Patients Included in the 2 Bayer Sponsored Phase 3 Clinical Trials FIDELIO and FIGARO to Investigate the Effect of Finerenone on Delaying the Progression of Diabetic Retinopathy	Bayer Healthcare Limited	16/2/2021	31/12/2023	80,500
	Clinical Safety, Efficacy and Multiomic Evaluation of a Novel Chinese Medicine (CM) Formula in Type 2 Diabetes (T2D) : Effects on Beta-Cell Function and Insulin Resistance	Innovation and Technology Commission – Innovation and Technology Support Programme	01/06/2022	31/05/2025	4,966,735
	Innovative Diagnosis and Treatment for Shrimp Allergy	The Chinese University of Hong Kong Research Committee – Research Impact Matching Fund	01/06/2020	31/05/2025	8,397,098
	Precision Medicine to Redefine Insulin Secretion and Monogenic Diabetes (PRISM) in Chinese Patients with Young Onset Diabetes	Health Bureau – Health and Medical Research Fund	01/09/2019	31/08/2024	8,457,718
	Commissioned Programme on Early Phase Testing of Novel Pharmaceutical Products in the Phase 1 Clinical Trial Centre, the Chinese University of Hong Kong	Health Bureau – Health and Medical Research Fund	02/05/2019	01/05/2024	50,000,000

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Andrea Luk	Effect of Glucagon-like Peptide 1 Receptor Agonist in Combination with Insulin on Glycaemic Variability and Time-in-range in Diabetic Kidney Disease: A Randomised Controlled Trial	Health Bureau – Health and Medical Research Fund	03/01/2022	02/01/2025	1,361,740
	Effectiveness and Safety Study of the Percutaneous Optical Fibre Glucose Sensor (FiberSense) for Home Use in Diabetic Individuals	Innovation and Technology Commission – Guangdong – Hong Kong Technology Cooperation Funding Scheme	17/08/2020	17/11/2023	2,838,000
	Clinical Utility of Anti-islet Autoantibodies and Their Seroconversion in the Detection of Autoimmune Diabetes in Chinese	Health Bureau – Health and Medical Research Fund	18/09/2023	17/09/2025	934,000

Publications

A. Journal Papers

1. Chu NHS, He J, Leung KHT, Ma RCW, Lee JYS, Varney J, Chan JCN, Muir JG, Chow E. Higher short-chain fermentable carbohydrates are associated with lower body fat and higher insulin sensitivity in people with prediabetes. *Nutrients*. 2023;15(24). doi:10.3390/nu15245070.

2. Mao D, Yuen LY, Ho CS, Wang CC, Tam CHT, Chan MHM, Lowe WL, Ma RCW, Tam WH. The association of prenatal vitamin D status with pregnancy and neonatal outcomes. *Journal of the Endocrine Society*. 2024;8(1). doi:10.1210/jendso/bvad142.

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4. Lui JNM, Lau ESH, Yang A, Wu H, Fu A, Lau V, Loo K, Yeung T, Yue R, Ma RCW, Kong APS, Ozaki R, Luk AOY, Chow EYK, Chan JCN. Temporal associations of diabetes-related complications with health-related quality of life decrements in Chinese patients with type 2 diabetes: A prospective study among 19 322 adults — joint Asia diabetes evaluation (jade) register (2007–2018). *Journal of Diabetes*. Published online 2023. doi:10.1111/1753-0407.13503.

5. Fan Y, Fan B, Lau ESH, Lim CKP, Wu H, Ma RCW, Ozaki R, Kong APS, Chow E, Luk AOY, Chan JCN. Comparison of beta-cell function between Hong Kong Chinese with young-onset type 2 diabetes and late-onset type 2 diabetes. *Diabetes Research and Clinical Practice*. 2023;205. doi:10.1016/j.diabres.2023.110954.

6. Misra S, Aguilar-Salinas CA, Chikowore T, Konradsen F, Ma RCW, Mbau L, Mohan V, Morton RW, Nyirenda MJ, Tapela N, Franks PW. The case for precision medicine in the prevention, diagnosis, and treatment of cardiometabolic diseases in low-income and middle-income countries. *The Lancet Diabetes and Endocrinology*. 2023;11(11):836-847. doi:10.1016/s2213-8587(23)00164-x. (Review)

7. Leslie RD, Ma RCW, Franks PW, Nadeau KJ, Pearson ER, Redondo MJ. Understanding diabetes heterogeneity: Key steps towards precision medicine in diabetes. *The Lancet Diabetes and Endocrinology*. 2023;11(11):848-860. doi:10.1016/s2213-8587(23)00159-6. (Review)

8. Tobias DK, Merino J, Ahmad A, Aiken C, Benham JL, Bodhini D, Clark AL, Colclough K, Corcoy R, Cromer SJ, Duan D, Felton JL, Francis EC, Gillard P, Gingras V, Gaillard R, Haider E, Hughes A, Ikle JM, Jacobsen LM, Franks PW, et al. Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine. *Nature Medicine*. 2023;29(10):2438-2457. doi:10.1038/s41591-023-02502-5.

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10. Cheung JTK, Yang A, Wu H, Lau ESH, Kong APS, Ma RCW, Luk AOY, Chan JCN, Chow E. Early treatment with dipeptidyl-peptidase 4 inhibitors reduces glycaemic variability and delays insulin initiation in type 2 diabetes: a propensity score-matched cohort study. *Diabetes/Metabolism Research and Reviews*. 2024;40(1). doi:10.1002/dmrr.3711/v1/review2.

11. Wu H, Yang A, Lau ESH, Zhang X, Fan B, Shi M, Huang C, Ma RCW, Kong APS, Chow E, So WY, Chan JCN, Luk AOY. Age- and sex-specific hospital bed-day rates in people with and without type 2 diabetes: A territory-wide population-based cohort study of 1.5 million people in Hong Kong. *PLoS Medicine*. 2023;20(8). doi:10.1371/journal.pmed.1004261.

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13. Fan Y, Lau ESH, Wu H, Yang A, Chow E, Kong APS, Ma RCW, Chan JCN, Luk AOY. Incident cardiovascular-kidney disease, diabetic ketoacidosis, hypoglycaemia and mortality in adult-onset type 1 diabetes: A population-based retrospective cohort study in Hong Kong. *The Lancet Regional Health - Western Pacific*. 2023;34. doi:10.1016/j.lanwpc.2023.100730.

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23. Ng NYH, Wu H, Lau ESH, Zhang X, Yang A, Tsang AYT, Yau TTL, Kong APS, Ng K, Chung JPW, Chow EYK, Chan JCN, Cheung LP, Luk AOY, Ma RCW. Young-onset diabetes in women with polycystic ovary syndrome: A territory-wide retrospective analysis in Hong Kong. *Diabetes Research and Clinical Practice*. 2023;199. doi:10.1016/j.diabres.2023.110640.

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26. Wu H, Lau ESH, Yang A, Zhang X, Fan B, Ma RCW, Kong APS, Chow E, So WY, Chan JCN, Luk AOY. Age-specific population attributable risk factors for all-cause and cause-specific mortality in type 2 diabetes: An analysis of a 6-year prospective cohort study of over 360,000 people in Hong Kong. *PLoS Medicine*. 2023;20(1). doi:10.1371/journal.pmed.1004173.

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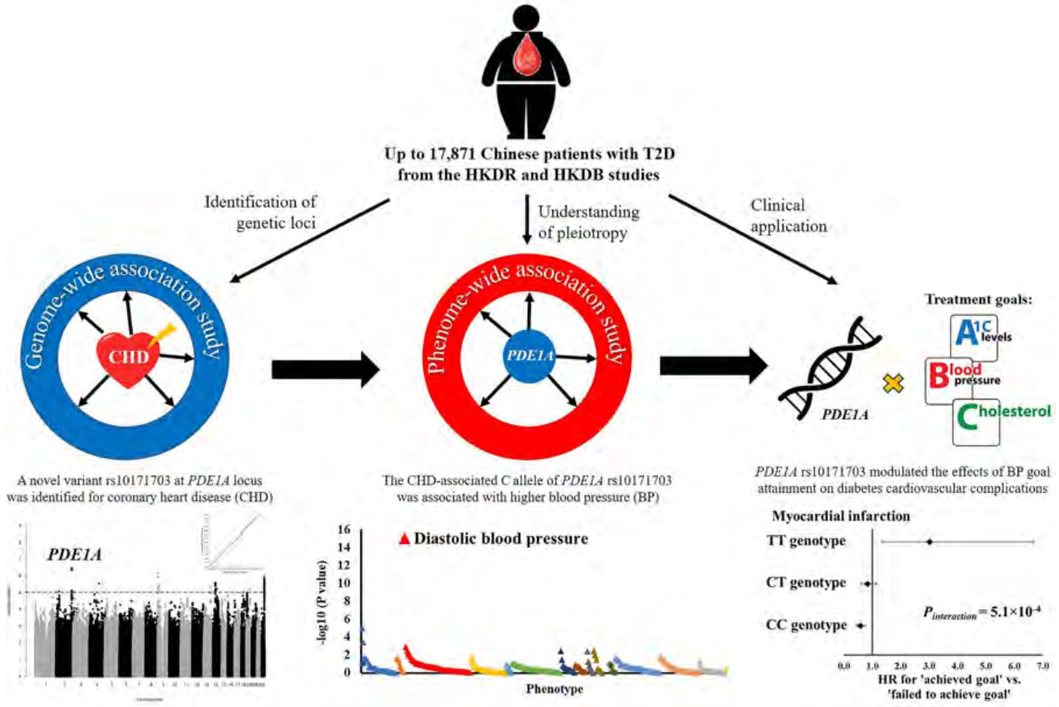
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29. Cheung JTK, Yang A, Wu H, Lau ESH, Shi M, Kong APS, Ma RCW, Luk AOY, Chan JCN, Chow E. Initiation of sodium-glucose cotransporter-2 inhibitors at lower HbA1c threshold attenuates eGFR decline in type 2 diabetes patients with and without cardiorenal disease: A propensity-matched cohort study. *Diabetes Research and Clinical Practice*. 2023;195. doi:10.1016/j.diabres.2022.110203. (Epub ahead of print)

30. Yang A, Shi M, Lau ESH, Wu H, Zhang X, Fan B, Kong APS, Luk AOY, Ma RCW, Chan JCN, Chow E. Clinical outcomes following discontinuation of renin-angiotensin-system inhibitors in patients with type 2 diabetes and advanced chronic kidney disease: A prospective cohort study. *eClinicalMedicine*. 2023;55. doi:10.1016/j.eclinm.2022.101751. (Epub ahead of print)

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32. Shi M, Yang A, Chow E, Lau ESH, Tam CHT, Kong APS, Luk AOY, Ma RCW, Cheung CMT, Chan JCN, Chan AWS. Genetic susceptibility of dipeptidyl peptidase-4 inhibitor associated bullous pemphigoid in Chinese patients with type 2 diabetes. *Journal of the European Academy of Dermatology and Venereology*. 2023;37(3):e375-e377. doi:10.1111/jdv.18762.



Conclusion: We discovered a novel CHD- and BP-related variant at *PDE1A* that interacted with BP goal attainment with divergent effects on CHD risk in Chinese patients with type 2 diabetes (T2D). Incorporating this information may facilitate individualised treatment strategies for precision care in diabetes only when our findings are validated.

GWAS identified novel loci for CHD in type 2 diabetes in Chinese for precision medicine treatment

Sources: **Tam CHT, Lim CKP, Luk AOY, Shi M, Cheung HM, Ng ACW, Lee HM, Lau ESH, Fan B, Jiang G, Kong APS, Ozaki R, Chow EYK, Lee KF, Siu SC, Hui G, Tsang CC, Lau KP, Leung JYY, Cheung EYN, Tsang MW, Kam G, Lau IT, Li JKY, Yeung VTF, Lau E, Lo S, Fung S, Cheng YL, Chow CC, Fan X, Chan TF. Yip KYL, Lok S, Yu W, Tsui SKW, Lan HY, Szeto CC, Tang NLS, Tomlinson B, Huang Y, Jenkins AJ, Keech A, So WY, Chan JCN, Ma RCW. Identification of a common variant for coronary heart disease at PDEIA contributes to individualized treatment goals and risk stratification of cardiovascular complications in Chinese patients with type 2 diabetes. *Diabetes* Care. 2023;46(6):1271-1281. doi:10.2337/dc22-2331.**



INFLAMMATORY DISEASES

炎症性疾病研究

PRINCIPAL INVESTIGATOR
Hui-yao Lan

TEAM MEMBERS
Guangyu Lian, Shiu-Kwong Thomas Mak, Sifan Sun, Huijun He, Wenjiang Wu, Biao Wei, Yu Zhong, Jiaxiao Li, Kaixiang Liu, Xiaoru Lan, Choilai Chung

RESEARCH PROGRESS SUMMARY

In the past year, the research team led by **Hui-yao Lan** continued studying the mechanisms of COVID-19 acute kidney injury (AKI) and TGF-β/Smad signalling in chronic kidney diseases with several important findings.

The research team is continuously studying the mechanisms of TGF-β/Smad signalling in chronic kidney diseases and found that TGF-β is a master regulator of diabetic complications including cardiopathy, nephropathy, and fatty liver. They discovered that TGF-β signals through its downstream mediator of Smad3 to mediate hypertensive cardiopathy, diabetic nephropathy and fatty liver. Specifically, they found that db/db lacking Smad3 are protected from diabetes and fatty liver and that targeting Smad3 specifically with a pharmacological inhibitor SIS3 or traditional Chinese medicine compounds Asiatic acid and naringenin is capable of inhibiting diabetes, diabetic nephropathy, and fatty liver.

More excitingly, they identified that one of SARS-CoV-2 proteins, SARS-CoV-2 N protein is a key mediator for AKI and induces AKI via the Smad3-dependent G1 cell cycle arrest and necroptosis mechanisms, which becomes much more severe under diabetes and hypertension conditions. Targeting Smad3 with a Smad3 inhibitor SIS3 and a traditional Chinese medicine compound quercetin can inhibit SARS-CoV-2 N protein-induced AKI. These findings are highly significant both scientifically and clinically and may lead to the development of novel therapy for COVID-19 AKI.

RESEARCH AND SCHOLARSHIP

Academic Editorships

Name	Details	
	Role	Journal
Hui-yao Lan	Editor-in Chief	Integrative Medicine in Nephrology and Andrology
	Editor	Clinical and Experimental Pharmacology and Physiology
	Executive Editor	International Journal of Biological Sciences
	Associate Editor	Journal of Clinical and Molecular Medicine
		Frontiers in Psychology
		Molecular Therapy

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Hui-yao Lan	Editorial Board Member	Journal of American Society of Nephrology
		Kidney International
		Scientific Reports
		Kidney Disease
		Diabetic Nephropathy

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hui-yao Lan	Regulatory Role of Smad3 in SARS-CoV-2 N Protein-induced Acute Kidney Injury in db/db Mice.	Research Grants Council – General Research Fund	01/07/2021	31/12/2023	1,125,732
	Translating Multi-Omic Discoveries to Transform Diabetes Care and Reduce Diabetic Complications	Research Grants Council – General Research Fund	01/03/2019	28/02/2024	12,000,000

Publications

A. Journal Papers

1. Chung JYF, Tang PCT, Chan MKK, Xue VW, Huang XR, Ng CSH, Zhang D, Leung KT, Wong CK, Lee TL, Lam EWF, Nikolic-Paterson DJ, To KF, Lan HY, Tang PMK. Smad3 is essential for polarization of tumor-associated neutrophils in non-small cell lung carcinoma. *Nature Communications*. 2023;14(1). doi:10.1038/S41467-023-37515-8.

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5. Tan RZ, Zhong X, Han RY, Xie KH, Jia J, Yang Y, Cheng M, Yang CY, Lan HY, Wang L. Macrophages mediate psoriasis via Mincle-dependent mechanism in mice. *Cell Death Discovery*. 2023;9(1). doi:10.1038/s41420-023-01444-8.

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7. Liang L, Wang W, Chen J, Wu W, Huang XR, Wei B, Zhong Y, Ma RCW, Yu X, Lan HY. SARS-CoV-2 N protein induces acute kidney injury in diabetic mice via the Smad3-Ripk3/MLKL necroptosis pathway. *Signal Transduction and Targeted Therapy*. 2023;8(1). doi:10.1038/s41392-023-01410-x. (Letter)

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9. Wu W, Wang W, Liang L, Chen J, Wei B, Huang XR, Wang X, Yu X, Lan HY. Treatment with quercetin inhibits SARS-CoV-2 N protein-induced acute kidney injury by blocking Smad3-dependent G1 cell-cycle arrest. *Molecular Therapy*. 2023;31(2):344-361. doi:10.1016/j.ymthe.2022.12.002.

10. Cao R, Su W, Sheng J, Guo Y, Su J, Zhang C, Wang H, Tang Y, Chen L, Qiao R, Chen X, Huang X, Zhou Y, Zhu L, Bai Z, Zhang X, Gustafsson JA, Wan Q, Lan HY, Guan Y. Estrogen receptor β attenuates renal fibrosis by suppressing the transcriptional activity of Smad3. *Biochimica et Biophysica Acta - Molecular Basis of Disease*. 2023;1869(6). doi:10.1016/j.bbadis.2023.166755.

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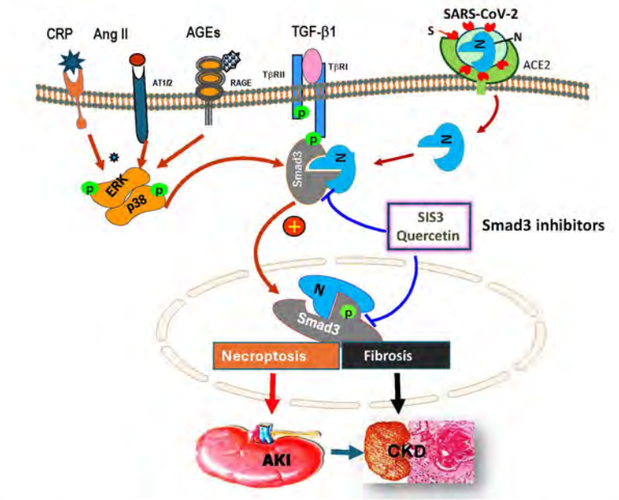
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22. He H, Wang H, Chen X, Zhong Y, Huang XR, Ma RCW, Wang C, Lan HY. Treatment for type 2 diabetes and diabetic nephropathy by targeting Smad3 signaling. International Journal of Biological Sciences. 2024;20(1):200-217. doi:10.7150/ibs 87820.



Treatment of ARS-CoV-2 N protein-induced AKI by targeting Smad3 with SIS3 and quercetin.

Source: HY Lan draw



NEUROSCIENCE AND NEUROTECHNOLOGY

神經科學及神經技術

PRINCIPAL INVESTIGATOR
Owen Ko

TEAM MEMBERS
Danny Chan, Roy Chan, Junzhe Huang, Dorothy Ieong, Bonaventure Ip, Andrew Kwok, Nenghan Lin, Michelle Lo, Samuel Sy, Alice Tung, Derek Wang, Manyu Wang, Felicia Wong, Peng Xiao, Isabel Xiong , Leo Yan, Jenny Zhang

RESEARCH PROGRESS SUMMARY

Gliovascular Dysfunction in Aging and Neurodegeneration

Owen Ko and his team adopt a multimodal approach combining genetic manipulation, molecular assays, in vivo functional and structural imaging to uncover how aging and disease-related genetic mutations cause neurodegeneration. Based on the knowledge gained on pathophysiology, they seek to develop disease-modifying therapeutics for age-related neurovascular and neurological disorders. Building on their previous discovery that targeting glucagon-like peptide-1 receptor (GLP-1R) may repair the aging neurovasculature, they have extended the works to (*i*) demonstrate the potential of using GLP-1R agonists to combat body-wide aging (US Patent Application, 2023 Dec 22;US 18/394,367), and (*ii*) conduct a pilot clinical trial in close collaboration with the clinical team (the GAPP-SVD trial, NCT05356104), on using GLP-1RA to slow the progression of cerebral small vessel disease (cSVD) – a strong manifestation of neurovascular aging and a leading cause of cognitive impairment. Under this research theme, they have successfully acquired new funding support and recognition over the past year. These include an inaugural Asian Young Scientist Fellowship (AYSF) from the Future Science Awards Foundation, and invited lectures at several conferences, including the Annual conference of the AYSF, the 10th Singapore International Parkinson Disease and Movement Disorders Symposium, as well as the 1st Greater Bay Area Life and Health Science Forum.

Development of Tools and Methods

Bottlenecks in neural circuit and brain disorder investigations are often due to methodological limitations. The team is actively developing imaging tools for pre-clinical investigations and potential clinical applications, emphasising new methods for high-throughput, three-dimensional neuronal activity and molecular profiling in the brain. These techniques will not only empower investigations of neural circuit functions in health and disease, but also benefit other fields of biomedical sciences. Notable advancement by the team this year included (i) publishing an optofluidic system for assaying whole-brain chemosensory responses (Sy et al., *Nature Communications*, 2023), and (ii) a review article providing an outline for the technical approaches and future roadmaps for volumetric histology (Yau et al., *Cell Reports Methods*, 2023). These works have been presented at an invited lecture at the 16th Annual Meeting of Chinese Neuroscience Society (CNS 2023) & the 2nd China-Japan-Korea International Meeting, and the Brain on Chips Symposium, Technical University of Braunschweig, Germany.

Other Collaborations

The team widely collaborates with other basic science and clinical research teams on several projects. Examples include (i) a preclinical study reporting how microglia recruits a subset of cytotoxic T cells to mediate detrimental neuroinflammation in the brain with radiation-induced injury (Shi et al., *Neuron*, 2023) in collaboration with Yamei Tang and Wei-Jye Lin (SYSU), (ii) a clinical study that established the role of combining a machine learning & MRI-based with a blood biomarker for the diagnosis of Alzheimer's disease pathology (Cai et al., *Alzheimer's and Dementia*, 2023) in collaboration with Vincent Mok (CUHK), (iii) ongoing development of a computed tomography perfusion (CTP) imaging analysis method for the clinical prognostication of acute ischemic stroke patients in collaboration with Bonaventure Ip (CUHK), and (iv) modelling of brain pathology with 3D-printed neural tissues in collaboration with Francis Szele and Linna Zhou (Oxford).

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Owen Ko	Life Science Fellow	Asian Young Scientist Fellowship, Future Science Awards Foundation

Academic Editorships

Name	Details	
	Role	Journal
Owen Ko	Editorial Board Member and Associate Editor	BioMed Central Biology

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Owen Ko	Reviewer	Alzheimer's and Dementia
		Journal of Neurology, Neurosurgery and Psychiatry
		Translational Neurodegeneration

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Owen Ko	Research Grant for Awardees of Asian Young Scientist Fellowship	Asian Young Scientist Fellowship, Future Science Awards Foundation	01/12/2023	30/11/2025	780,000
	Mechanisms of Cognitive Aging Repair via Targeting GLP-1 Signaling	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,155,631
	Development and Preclinical Test of Optical Pumping-based Hyperpolarized Carbon-13 Magnetic Resonance Spectroscopic Imaging for Diagnosis of Neurological Diseases	Innovation and Technology Commission – Partnership Research Programme	01/12/2022	30/11/2025	3,921,592
	Unveiling Neural Activities through Spatiotemporally Optimized Multiphoton (STOMP) Microscopy	Research Grants Council – Collaborative Research Fund	01/04/2022	31/03/2025	7,883,046
	Anti-aging Effects of GLP-1R Agonism and Companion Non-invasive Diagnostics	National Natural Science Foundation of China – Excellent Young Scientist Fund (Hong Kong and Macau)	01/01/2022	31/12/2024	2,430,000
	Novel MRI-based Machine Learning Tool to Detect Mild Cognitive Impairment Associated with Alzheimer's Disease	Health Bureau – Health and Medical Research Fund Advanced Medical Research	05/02/2022	04/02/2024	911,140
	Investigating Neurovascular and Astrocyte Dysfunction in Neurodegenerative Diseases	The Croucher Foundation	01/07/2020	30/06/2025	5,000,000
	Cellular Mechanisms of Synaptic Functions and Plasticity in Health and Neurodegenerative Diseases	Research Grants Council – Areas of Excellence Scheme	01/06/2017	31/05/2025	77,516,000

Publications

A. Journal Papers

1. Ip YMB, Lau KK, Ko H, Lau L, Yao A, Wong GLH, Yip TCF, Leng X, Chan H, Chan H, Mok V, Soo YOY, Seiffge D, Leung TW. Association of alternative anticoagulation strategies and outcomes in patients with ischemic stroke while taking a direct oral anticoagulant. *Neurology*. 2023;101(4):E358-E369. doi:10.1212/wnl.0000000000207422.

2. Cai Y, Fan X, Zhao L, Liu W, Luo Y, Lau AYL, Au LWC, Shi L, Lam BYK, Ko H, Mok VCT. Comparing machine learning-derived MRI-based and blood-based neurodegeneration biomarkers in predicting syndromal conversion in early AD. *Alzheimer's and Dementia*. 2023;19(11):4987-4998. doi:10.1002/alz.13083.

3. Yau CN, Lai HM, Lee K, Kwok AJ, Huang J, Ko H. Principles of deep immunohistochemistry for 3D histology. *Cell Reports Methods*. 2023;3(5). doi:10.1016/j.crmeth.2023.100458.

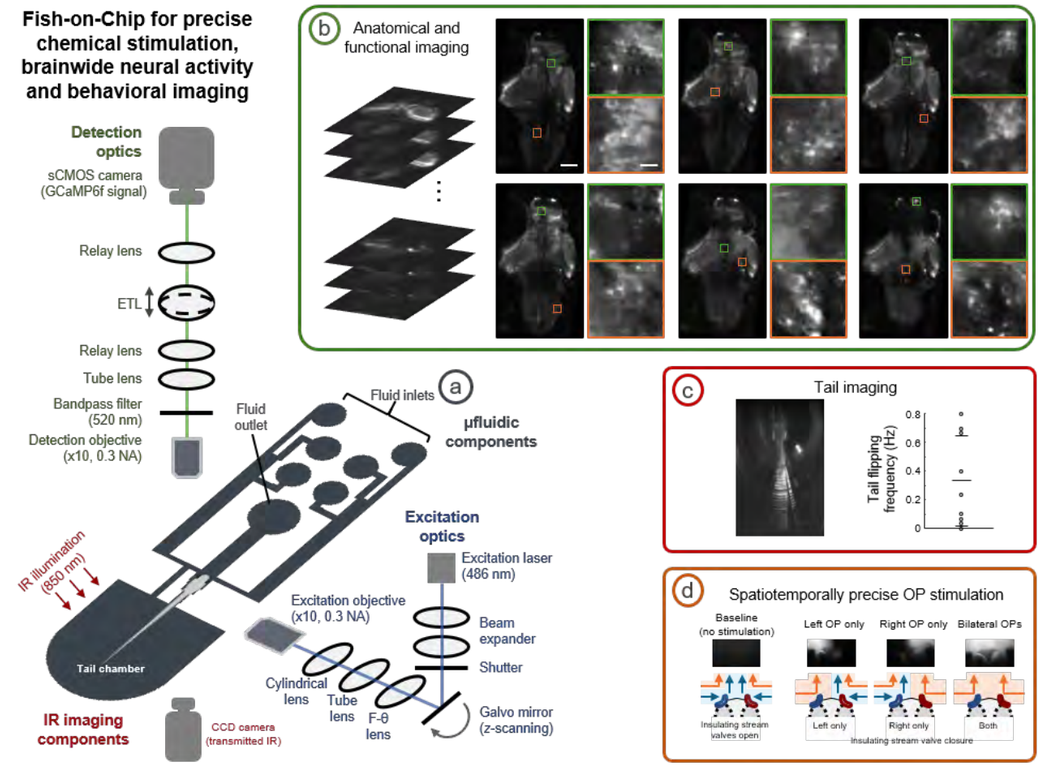
4. Shi Z, Yu P, Lin WJ, Chen S, Hu X, Chen S, Cheng J, Liu Q, Yang Y, Li S, Zhang Z, Xie J, Jiang J, He B, Li Y, Li H, Xu Y, Zeng J, Huang J, Mei J, Cai J, Chen J, Wu LJ, Ko H, Tang Y. Microglia drive transient insult-induced brain injury by chemotactic recruitment of CD8+T lymphocytes. *Neuron*. 2023;111(5):696-710.e9. doi:10.1016/j.neuron.2022.12.009.

5. Sy SKH, Chan DCW, Chan RCH, Lyu J, Li Z, Wong KKY, Choi CHJ, Mok VCT, Lai HM, Randlett O, Hu Y, Ko H. An optofluidic platform for interrogating chemosensory behavior and brainwide neural representation in larval zebrafish. *Nature Communications*. 2023;14(1). doi:10.1038/s41467-023-35836-2.

B. Patents

1. The United States Patents:

   Title: A method for reversing body-wide aging-associated functional changes
   National Application No.: US 18/394,367
   Filing date: 22 December 2023



Fish-on-Chip: An optofluidic system for in vivo imaging of chemosensory-evoked neuronal activity and behaviour in larval zebrafish – a popular model organism for neuroscience.
(a) In the system, the microfluidic (μfluidic) module is integrated with a scanning light sheet microscope. On the excitation path, a light sheet is formed by using a cylindrical lens and underfilling the back aperture of the excitation objective, with z-scanning achieved by a galvo mirror. On the detection arm of the optics, an electrically tunable lens (ETL) synchronised to the galvo mirror focuses the calcium reporter (GCaMP6f) signals from different planes of the larval zebrafish brain onto the sCMOS camera.
(b) Example images acquired from different planes of the whole brain. For each image set, the two images on the right are enlarged and contrast-adjusted images from the outlined areas of the corresponding large field-of-view (FOV) images. Scale bars: 100 μm for the large FOV images and 10 μm for the zoomed-in images.
(c) Tail flipping behaviour monitoring by an IR imaging module with 850-nm illumination and a CCD camera to capture the transmitted IR (also shown in (a)). Left panel: Temporally overlaid images of an example larva's tail. Right panel: Spontaneous tail flipping frequency of 9 assayed larval zebrafish that were behaviourally active. Horizontal lines indicate mean ± 1 SD.
(d) During functional imaging, the μfluidic module provides chemical delivery with sufficient accuracy for stimulating unilateral nasal cavity.

Source: Ko Lab



NEUROSCIENCE AND NEUROTECHNOLOGY

神經科學及神經技術

PRINCIPAL INVESTIGATOR
Hei Ming Lai

TEAM MEMBERS
Jacky Hung, Ben Wong, Carmen Chan, Thomas Wong, Juno Yau, Eldric Tsoi, Nick Chow

RESEARCH PROGRESS SUMMARY

Hei Ming Lai and his research team are at the forefront of tissue mapping innovation, developing Next Generation Histology technologies. They have pioneered a 3D spatial proteomics approach that merges deep, uniformly penetrating iterative multiplexed immunohistochemistry, tissue clearing, light-sheet microscopy, and advanced image analysis. Their method stand out as the fastest – achieving speeds 5 to 7 times quicker than current alternatives – and boosts the most extensive validation with ten times more antibodies validated. It excels in scalability, setting a new standard for both research and clinical applications that is accessible to all laboratories.

The limitations of traditional 2D histology, which relies on multiple machines and samples just 0.1% of the tissue, lead to significant diagnostic guesswork. In contrast, their 3D imaging technology reveals comprehensive tissue structure, clarifying ambiguous formations, detecting rare events, and quantifying molecular markers with single-cell resolution. This holistic view is transforming the team understanding and analysis of biopsy and surgical specimens, enabling precision medicine through deep phenotyping.

Their innovative technologies are already gaining traction within the scientific community, even before formal publication submission. Word of mouth has led to early adoption by researchers and collaboration with esteemed institutions and individuals, including The Human Protein Atlas and Nobel Laureate Eric Betzig. These partnerships are instrumental in tackling biological mysteries and developing novel tissue-based diagnostics.

Knowledge transfer

In 2023, they established Illumos Limited with the goal of commercialising their Next Generation Histology technology. Their company is dedicated to integrating 3D histology into precision diagnostics, enhancing the clinical workflow. By providing an additional layer of detail, they equip doctors and AI systems with the critical information necessary for accurate patient management plans. The result is a significant improvement in diagnostic precision and a profound impact on subsequent treatment decisions.

To accelerate and elevate the remarkable biological research, they have also opened their light sheet microscopy (MesoSPIM) to all Hong Kong researchers, providing a one-stop tissue-to-image infrastructures. This reduces the barriers to entry for 3D tissue imaging and analysis, which is advantageous in the data-driven era of biomedical and clinical research, and the shift in focus from single-cell technologies to spatially resolved biology that put omics back in context.

Invention exhibitions

Recognition of the team technological advances extends to the global stage. Their scalable 3D histology and alpha-phase $CsPbI_3$ perovskite nanocrystal synthesis technologies garnered accolades at the 48th International Exhibition of Inventions in Geneva and the 3rd Asia Exhibition of Innovations and Inventions, earning three gold medals or higher. These awards are a testament to the pioneering work their lab is conducting.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Hei Ming Lai	Gold Medal with the Congratulations of the Jury	48th International Exhibition of Inventions Geneva
	Gold Medal	
Hei Ming Lai Jacky Hung Juno Yau	Gold Medal	3rd Asia Exhibition of Innovations and Inventions Hong Kong

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hei Ming Lai	Accelerated, Ultra-multiplexed, Signal-amplified 3D Immunofluorescence	Innovation and Technology Fund – Innovation and Technology Support Programme Seed Fund	01/10/2022	31/03/2024	1,398,584
	Multi-modal Approaches to Determine Digital Clinical Phenotyping, Novel Proteomic Biomarkers, and Microbiota-host Responses of REM Sleep Behaviour Disorder, a Prodromal Stage of Alpha-synucleinopathy Neurodegeneration, in a Prospective Family Cohort	Research Grants Council – Collaborative Research Fund	01/02/2022	31/01/2025	7,214,620
	A Comprehensive Survey on Alpha-synuclein Pathologies in Colonic Submucosal Biopsies of Prodromal Parkinson's Disease Patients – An Exploratory Study	Health Bureau – Health and Medical Research Fund Advanced Medical Research	01/09/2021	31/08/2023	965,803

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hei Ming Lai	Clearing the Way for Better Tissue Diagnostics – A Midstream Development Project on Accessible Three-dimensional Histology Methods and Platform	Innovation and Technology Commission – Midstream Research Programme for Universities	01/03/2021	31/08/2023	4,699,999

Publications

A. Journal Papers

1. Huang B, Chau SWH, Liu Y, Chan JWY, Wang J, Ma SL, Zhang J, Chan PKS, Yeoh YK, Chen Z, Zhou L, Wong SH, Mok VCT, To KF, Lai HM, Ng S, Trenkwalder C, Chan FKL, Wing YK. Gut microbiome dysbiosis across early Parkinson's disease, REM sleep behavior disorder and their first-degree relatives. *Nature Communications.* 2023 14:1. 2023;14(1):1-13. doi:10.1038/s41467-023-38248-4.

2. Sy SKH, Chan DCW, Chan RCH, Lyu J, Li Z, Wong KKY, Choi CHJ, Mok VCT, Lai HM, Randlett O, Hu Y, Ko H. An optofluidic platform for interrogating chemosensory behavior and brainwide neural representation in larval zebrafish. *Nature Communications.* 2023;14(1):1-18. doi:10.1038/s41467-023-35836-2.

3. Kwok AJ, Lu J, Huang J, Ip BY, Mok VCT, Lai HM, Ko H. High-resolution omics of vascular ageing and inflammatory pathways in neurodegeneration. *Seminars in Cell & Developmental Biology*. 2024;155:30-49. doi:10.1016/j.semcdb.2023.06.005.

4. Yau CN, Lai HM, Lee K, Kwok AJ, Huang J, Ko H. Principles of deep immunohistochemistry for 3D histology. *Cell Reports Methods*. 2023;3(5):100458. doi:10.1016/j.crmeth.2023.100458.

B. Patents

1. US Provisional Patent:

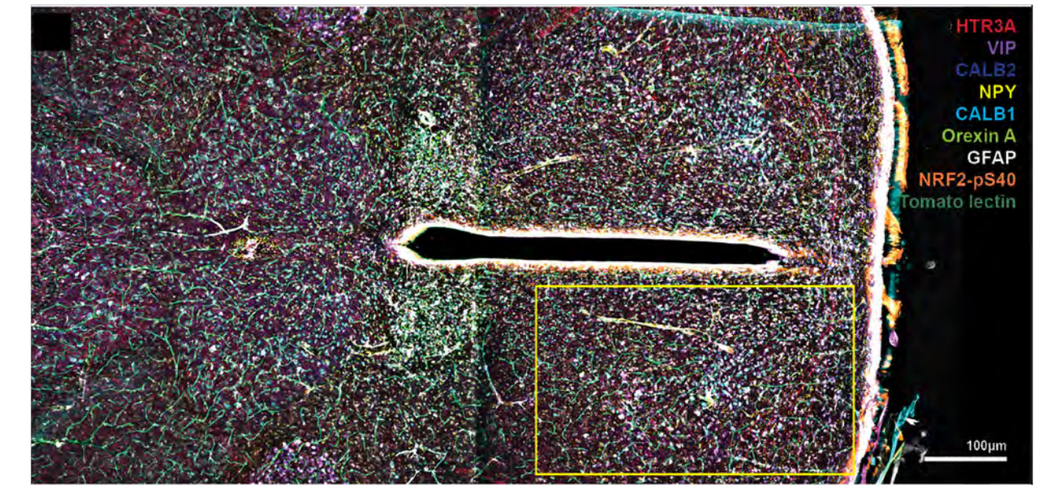
   Title: A General Chemical System for Universally Augmenting the Function of Proteins
   Inventors: Lai HM, Tsoi PLE
   National Application No.: 63/586,483

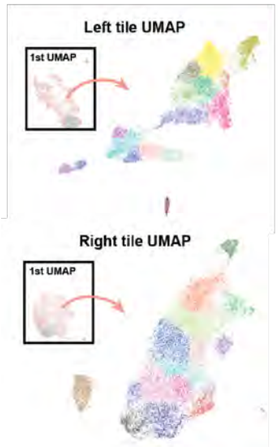
   Title: Non-denaturing, High-yield Method for Chromatographic Analysis and Purification of Proteins
   Inventors: Lai HM, Yau JCN
   National Application No.: 63/586,476

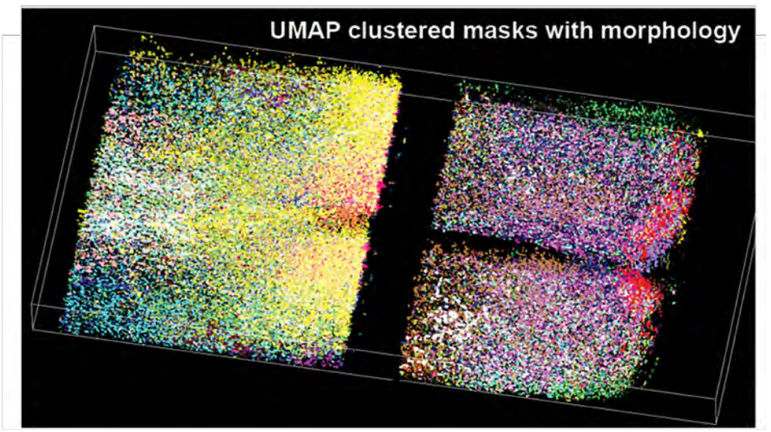
2. US Non-Provisional Patent:

   Title: Superchaotropes-assisted Deep Immunostaining
   Inventors: Lai HM, Yau JCN
   National Application No.: 18/477,775

High-dimensional clustering 192,075 cells based on expression levels & subcellular localization of 25 proteins, and their 3D coordinates + morphology







3D spatial proteomic profiling of a 1mm-thick mouse hypothalamus slice. A selected panel of 9 markers were shown.

Source: Hei Ming Lai



NEUROSCIENCE AND NEUROTECHNOLOGY

神經科學及神經技術

PRINCIPAL INVESTIGATOR
Vincent Mok

TEAM MEMBERS
Thomas Leung, Owen Ko, Bonaventure Ip, Lisa Au, Cindy Leng, Bonnie Lam, Andrew Kwok, Mandy Liu, Pauline Kwan, Elyia Han, Anthea Ng, Vincent Hui, Maverick So, Seraphina Lo, Cheryl Au, Suk Fung Tsang, Sangqi Pan, Trista Hung, Helen Chan, Huijing Zheng, Alison Wei, Katerina Chiu, Yvonne Lau, Ami Li, Dorothy Ieong, Junzhe Huang, Nathan Lin, Cici Zhao, Michelle Lo, Vera Cai, Angel Yung, Xuan Tian, Gillian Liang, Shuang Li, Yuying Liu, Yu Liu, Ziqi Li, Haipeng Li

RESEARCH PROGRESS SUMMARY

Research Studies

Vincent Mok and his team focus on Alzheimer's disease (AD), stroke, cerebral small vessel disease (SVD), and Parkinson's disease (PD). They made significant achievements in areas including:

1. Establish registries for Alzheimer's disease, intracranial large artery disease, sporadic cerebral small vessel disease (SVD), stroke, and Parkinson's disease (PD) in Chinese subjects respectively to develop precise biomarkers and diagnostics (e.g., AI-powered technologies based on MRI, retinal imaging, speech characteristics) for early diagnosis and to understand putative causative factors, as well as to predict and monitor disease progression of these brain diseases.

2. Development of a large population-based cohort (n=5000) in Hong Kong with longitudinal follow-up, consisting of healthy citizens and subjects at risk of brain diseases aged 45-74 years. Data on genomics/metabolomics, stool microbiota, cardiovascular risk profile, linguistics, cognition and psychology batteries, and brain imaging are being collected. The goal is to study how cultural, physical, psychological and environmental changes across the lifespan affect brain health.

3. Development of an animal model for sporadic SVD with utilisation of in-vivo multiphoton microscope and single cell-RNA sequencing for pathophysiology research and drug development.

4. Recent studies from the team have shown that a particular class of anti-diabetic drug, namely glucagon-like peptide 1 receptor agonist (GLP-1 RA) is able to reverse aging-related SVD. Clinical trial is urgently warranted to clarify whether re-purposing this anti-diabetic drug is able to slow down SVD progression. To this end, the research team has commenced a phase 2 open-label randomised controlled trial to investigate the effects and safety of GLP1-1 RA (exenatide) in slowing down the progression of early SVD.

Academic Conferences

Vincent and his team attended a number of conferences worldwide in 2023 with details as follows:

1. Mechanistic Investigations on How Targeting GLP-1 Signaling May Help in Age-Related Neurodegeneration. Asia Pacific Stroke Conference 2023. Hong Kong, 3 December 2023. (Owen Ko)

2. Cerebral Hemodynamics in Symptomatic ICAD and the Clinical Implications. Asia Pacific Stroke Conference 2023. Hong Kong, 3 December 2023. (Cindy Leng)

3. ICAD Endovascular Treatment Based on Pathogenesis. Asia Pacific Stroke Conference 2023. Hong Kong, 2 December 2023. (Thomas Leung)

4. Atrial Fibrillation & Dementia. Asia Pacific Stroke Conference 2023. Hong Kong, 2 December 2023. (Vincent Mok)

5. Advances in Treatment of Cerebral Small Vessel Disease. Asia Pacific Stroke Conference 2023. Hong Kong, 1 December 2023. (Bonaventure Ip)

6. Ischemic Stroke During DOAC Use. Asia Pacific Stroke Conference 2023. Hong Kong, 1 December 2023. (Bonaventure Ip)

7. Post-irradiation Carotid Stenosis. Asia Pacific Stroke Conference 2023. Hong Kong, 1 December 2023. (Thomas Leung)

8. Atrial Fibrillation Management in Elderly Patients. Geriatrics Society of Macau Annual Scientific Meeting 2023. Macau, 25 November 2023. (Bonaventure Ip)

9. The Quest to Extend Health Span: A Neuroscientific Approach. International Network of Neurodegenerative Disease Research, Global Alliance of Medical Excellence. Bologna, Italy, 22 November 2023. (Owen Ko)

10. Mechanistic Investigations on How Targeting Glp-1 Signalling May Help Parkinsonism and Other Age-Related Diseases. 10th Singapore International Parkinson Disease & Movement Disorders Symposium. Singapore, 28 September 2023. (Owen Ko)

11. Ischemic Stroke Despite DOAC – What Matters More Than the Subsequent Antithrombotic Regimen? Neurology Expert Gathering Tokyo 2023. Tokyo, Japan, 15 July 2023. (Bonaventure Ip)

12. Effective Translation of Endovascular Thrombectomy Trials into Real-World Practice in Hong Kong. Shandong Neurointerventional Surgery Workshop. Linyi, China, 16 June 2023. (Bonaventure Ip)

13. Is Anti-Amyloid Treatment Ready for Dementia? Advances in Medicine 2023. Hong Kong, 28 May 2023. (Lisa Au)

14. Never Too Early, Never Too Late. A Brief Update on Acute Ischemic Stroke Treatment. Advances in Medicine 2023. Hong Kong, 28 May 2023. (Sze Ho Ma)

15. Machine Learning Imaging Technology for the Diagnosis of Alzheimer's Disease. Advances in Medicine 2023. Hong Kong, 27 May 2023. (Vincent Mok)

16. Interrogating Chemosensory Behavior and Brainwide Neural Representation: An Optofluidic Approach. Brains on Chips Symposium: New Biomedical Research Tools for the Study of Neuronal Compartments in Health and Disease. Brunswick, Germany, 25 May 2023. (Owen Ko)

17. Plaque Remodelling and Stroke Relapse in Symptomatic Intracranial Atherosclerotic Disease: A Longitudinal 3D Rotational Angiography Study. Platform Presentation at the 9th European Stroke Organization Conference. Munich, Germany, 24-26 May 2023. (Thomas Leung)

18. Ageing Well: Breakthroughs and Investment Landscape in Longevity. Asia Summit on Global Health. Hong Kong, 17-18 May 2023. (Owen Ko)

19. Neuro-psychological Complications after Stroke-Dementia. Asia Pacific Stroke Organisation (APSO) 8th Webinar. Virtual, 22 May 2023. (Vincent Mok)

20. Paving the Way for Disease-Modifying Therapeutics for Cerebral Small Vessel Disease. The 19th Asia Pacific Multidisciplinary Meeting for Nervous System Diseases (BRAIN 2023). Hong Kong, 11 February 2023. (Owen Ko)

21. An Immune Cell Survey of Anti-NMDA Receptor Encephalitis. The 19th Asia Pacific Multidisciplinary Meeting for Nervous System Diseases (BRAIN 2023). Hong Kong, 11 February 2023. (Andrew Kwok)

22. Neuro-intensive Case for Stroke. The 19th Asia Pacific Multidisciplinary Meeting for Nervous System Diseases (BRAIN 2023). Hong Kong, 10 February 2023. (Vincent Ip)

23. Cerebral Hemodynamics in Stroke and Intracranial Atherosclerotic Disease. The 19th Asia Pacific Multidisciplinary Meeting for Nervous System Diseases (BRAIN 2023). Hong Kong, 9 February 2023. (Cindy Leng)

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Owen Ko	Life Science Fellow	Asian Young Scientist Fellowship, Future Science Awards Foundation
Bonaventure Ip	Distinguished Research Paper Award for Young Investigators 2023	Hong Kong College of Physicians
Vincent Mok	American Heart Association 2023 Paul Dudley White International Scholar Award	American Heart Association
Vera Cai	Tse Cheuk Ng Tai Prize in Dementia Research	Annual Chinese Dementia Research Association Symposium 2023

Fellowships

Name	Details	
	Fellowship	Organisation
Thomas Leung Lisa Au	First Fellow, Genetics and Genomics (Medicine)	Hong Kong College of Physicians

Academic Editorships

Name	Details	
	Role	Journal
Vincent Mok	Editorial Board Member	Cerebral Circulation – Cognition and Behavior (CCCB)
		Journal of Neurology, Neurosurgery and Psychiatry
		Movement Disorders Clinical Practice
		Frontiers in Neurology
Thomas Leung	Associate Editor	International Journal of Stroke
	Assistant Editor	Stroke
	Guest Associate Editor	Frontiers in Neurology
	Editorial Board Member	Interventional Neurology
		Journal of Cardiovascular Research
		Journal of Cardiac Circulation
		International Scholarly Research Network (ISRN) Radiology
		Precision Medicine
		Hong Kong Medical Journal
Owen Ko	Editorial Board Member and Associate Editor	BMC Biology
Cindy Leng	Associate Editor	Stroke and Vascular Neurology
	Editorial Board Member	Stroke
		International Journal of Stroke
		European Stroke Journal

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Vincent Mok Thomas Leung Cindy Leng	Reviewer	Neurology
Vincent Mok Cindy Leng		Stroke
Vincent Mok		Lancet Neurology
		Alzheimer's and Dementia
		Dementia and Geriatric Cognitive Disorders
		Alzheimer's Disease and Associated Disorders
		Parkinsonism and Related Disorders
		Journal of the Neurological Sciences
		Journal of Alzheimer Disease
		BMC Geriatrics
		Acta Pharmacologica Sinica
		Peritoneal Dialysis International
		Hong Kong Medical Journal
		CNS Neuroscience and Therapeutics

Name	Details	
	Role	Journal / Conference
Vincent Mok Bonaventure Ip	Reviewer	International Journal of Stroke
Vincent Mok Thomas Leung Bonaventure Ip		Frontiers Neurology
Thomas Leung Bonaventure Ip		The Lancet
Thomas Leung Cindy Leng		Journal of Neurology, Neurosurgery and Psychiatry
		European Journal of Neurology
		Hypertension
		Cerebrovascular Diseases
		The British Medical Journal
		Annals of Neurology
		Acta Neurologica Scandinavica
		Journal of Neuro-Interventional Surgery
		American Journal of Neuroradiology
		BMJ Open
Thomas Leung		European Neurology
		The Lancet Regional Health (Western Pacific)
		International Journal for Numerical Methods in Biomedical Engineering
		International Journal of Cardiology
		Clinical Medicine Insights: Therapeutics
		Cardiovascular Therapeutics
		Surgical Practice
		Clinical and Experimental Pharmacology and Physiology
Owen Ko		Alzheimer's and Dementia
		Journal of Neurology, Neurosurgery and Psychiatry
		Translational Neurodegeneration
Cindy Leng		Expert Review of Neurotherapeutics
		Scientific Reports
		Frontiers in Neurology
		Frontiers in Neural Circuits
		Annals of Pharmacotherapy
		Journal of Neuroimaging
		Neurological Research

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Cindy Leng	Secondary Stroke Prevention in Symptomatic Intracranial Atherosclerotic Stenosis: Will Cerebral Hemodynamics Alter the Optimal Target for Blood Pressure Management?	Health Bureau – Health and Medical Research Fund	01/08/2023	31/07/2026	1,498,112
Bonaventure Ip	Impact of COVID-19 Vaccines on Brain Health – A Community-based Study	Research Grants Council – Early Career Scheme	01/01/2023	31/08/2024	1,171,919
Cindy Leng	Residual Risk of Stroke in Symptomatic Intracranial Atherosclerotic Disease under Optimal Medical Treatment: The Role of Underlying Stroke Mechanisms	Research Grants Council – Early Career Scheme	01/01/2023	31/12/2025	1,003,200
Owen Ko	Mechanisms of Cognitive Aging Repair via Targeting GLP-1 Signaling	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,155,631
	Development and Preclinical Test of Optical Pumping-Based Hyperpolarized Carbon-13 Magnetic Resonance Spectroscopic Imaging for Diagnosis of Neurological Diseases	Innovation and Technology Commission – Partnership Research Programme	01/12/2022	30/11/2025	3,921,592
	Anti-aging Effects of GLP-1R Agonism and Companion Non-invasive Diagnostics	National Natural Science Foundation of China – Excellent Young Scientists Fund (Hong Kong and Macau)	01/01/2022	31/12/2024	2,175,447
	Novel MRI-based Machine Learning Tool to Detect Mild Cognitive Impairment Associated with Alzheimer's Disease	Health Bureau – Health and Medical Research Fund	05/02/2022	04/02/2024	911,140
	Investigating Neurovascular and Astrocyte Dysfunction in Neurodegenerative Diseases	The Croucher Foundation	01/07/2020	30/06/2025	5,000,000
Thomas Leung	Clinical Effectiveness Study for Integrated Chinese - Western Medicine Programme in Stroke Care	Hospital Authority	26/04/2023	31/03/2024	663,044
	A Phase 26, Multinational, Randomized, Double-blind Study to Investigate the Efficacy and Safety of Redasemtide (S-005151) Compared with Placebo in Adult Participants with Acute Ischemic Stroke Who are not Eligible for Tissue Plasminogen Activator or Thrombectomy	Shionogi & Co., Ltd	15/12/2023	14/12/2025	508,581

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Bonaventure Ip	A Phase 3, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Demonstrate the Efficacy and Safety of Milvexian, an Oral Factor Xla Inhibitor, for Stroke Prevention after an Acute Ischemic Stroke or High-risk Transient Ischemic Attack	Janssen Research & Development, LLC	01/11/2023	09/03/2027	2,168,466
Vincent Mok	Genetic Studies on Early Alzheimer's Disease	The Hong Kong University of Science and Technology – Hong Kong Center for Neurodegenerative Disease	01/05/2022	01/05/2025	650,000
	Neuroimaging Biomarkers in Parkinsonian Syndromes	Hong Kong Neurological Society	07/02/2022	06/02/2024	200,000
	Development and Clinical Application of Early Warning Platform for Cognitive Impairment in Parkinson's Disease	Innovation and Technology Commission – Guangdong-Hong Kong Technology Cooperation Funding Scheme	01/06/2021	31/05/2023	1,338,539
Thomas Leung	Identification of Atrial Fibrillation Patients at Risk of Intracerebral Haemorrhage with Advanced Retinal Imaging (I-SAVE Study)	Health Bureau – Health and Medical Research Fund	20/05/2019	19/02/2023	1,499,462
Owen Ko	Establishment of Spatial Multi-omics Core Facility	Research Grants Council – Collaborative Research Fund	30/06/2023	29/06/2026	4,000,000
	Cellular Mechanisms of Synaptic Functions and Plasticity in Health and Neurodegenerative Diseases	University Grants Committee – Areas of Excellence Scheme of the Research Grants Council	01/06/2017	31/05/2025	77,516,000
Vincent Mok	Research and Development of Artificial Intelligence in Extraction and Identification of Spoken Language Biomarkers for Screening and Monitoring of Neurocognitive Disorders	University Grants Committee – Theme-based Research Scheme	01/01/2020	31/12/2024	50,000,000
Thomas Leung	Neuropsychiatric 'Long-COVID' in Adult Patients	Collaborative Research Fund – 2021/22 One-off Collaborative Research Fund Coronavirus Disease and Novel Infectious Disease Exercise	10/05/2022	09/05/2023	3,251,480
Vincent Mok	Multi-modal Approaches to Determine Digital Clinical Phenotyping, Novel Proteomic Biomarkers, And Microbiota-host Responses of REM Sleep Behavior Disorder, a Prodromal Stage of Alpha-synucleinopathy Neurodegeneration, in a Prospective Family Cohort	Collaborative Research Fund – 2021/22 One-off Collaborative Research Fund Coronavirus Disease and Novel Infectious Disease Exercise	01/04/2022	31/03/2025	7,214,620
Owen Ko	Unveiling Neural Activities through Spatiotemporally Optimized Multiphoton (STOMP) Microscopy	University Grants Committee – Collaborative Research Fund of the Research Grants Council	01/04/2022	31/03/2025	7,883,046
Thomas Leung	Design of Elastomer-based Soft Actuator and Flexible Electronic Polymers Sensor for Rehabilitation of Hand Function After Stroke	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	844,415
Vincent Mok	Transcranial Direct Current Stimulation in Post-stroke Fatigue: A Double-blind Randomised Control Trial	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,090,616
	Multimodal Brain Connectomics Markers of Idiopathic Rapid Eye Movement (REM) Sleep Behavior Disorder and Their Prediction towards A-Synucleinopathy	Health Bureau – Health and Medical Research Fund	10/06/2023	09/06/2026	1,486,340
	AI-Based Day and Night Digital Phenotyping of Rapid Eye Movement (REM) Sleep Behaviors Disorder (RBD) and Its Prediction towards A-Synucleinopathy	Health Bureau – Health and Medical Research Fund	01/01/2023	30/06/2025	1,495,330
	Randomized Placebo- and Active-controlled Trial for Assessing the Efficacy of Bright Light Therapy for Sleep and Mood Symptoms in Patients with Parkinson's Disease	Health Bureau – Health and Medical Research Fund	01/08/2022	31/07/2025	413,200
	Progression of Prodromal Markers of A-Synucleinopathy Neurodegeneration in the First-Degree Relatives of Patients with REM Sleep Behavior Disorder: A 7-Year Prospective Study	Research Grants Council – General Research Fund	01/11/2021	31/10/2024	1,154,476
	Neural Correlates of Impulsivity in Idiopathic REM Sleep Behavior Disorder and Parkinson's Disease: A Functional Magnetic Resonance Imaging Case-control Study	Health Bureau – Health and Medical Research Fund	01/04/2021	31/03/2024	1,122,120

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Vincent Mok	Gut Microbiota in Major Depressive Disorders with And Without Rapid Eye Movement Behavior Disorder: Tracing A Subtype of Depression with Underlying Neurodegeneration	Health Bureau – Health and Medical Research Fund	01/07/2021	31/12/2023	1,104,304
Thomas Leung	Development of a Magnetically Enhanced TPA Accumulation (META) System to Enhance Endovascular Treatment for Elderly Patients with Acute Ischemic Stroke	Innovation and Technology Commission – Innovation and Technology Support Programme (Mid-stream, theme-based)	01/07/2019	30/06/2023	5,399,549
	Design of Synchronized Pairing Peripheral Nerve Stimulation and Cortical Polarization to Promote Poststroke Neuroplasticity for Hand Function Recovery	Research Grants Council – General Research Fund	01/01/2019	30/06/2023	495,086

Publications

A. Journal Papers

1. De Kort FAS, Coenen M, Weaver NA, Kuijf HJ, Aben HP, Bae H-J, Bordet R, Cammà G, Chen CPLH, Dewenter A, Duering M, Fang R, Van Der Giessen RS, Hamilton OKL, Hilal S, Huenges Wajer IMC, Kan CN, Kim J, Kim BJ, Köhler S, De Kort PLM, Koudstaal PJ, Lim J-S, Lopes R, Mok VCT, Staals J, Venketasubramanian N, Verhagen CM, Verhey FRJ, Wardlaw JM, Xu X, Yu K-H, Biesbroek JM, Biessels GJ. White matter hyperintensity volume and poststroke cognition: An individual patient data pooled analysis of 9 ischemic stroke cohort studies. *Stroke*. 2023;54(12):3021-3029. doi:10.1161/strokeaha.123.044297.

2. Mai Y, Cao Z, Zhao L, Yu Q, Xu J, Liu W, Liu B, Tang J, Luo Y, Liao W, Fang W, Ruan Y, Lei M, Mok VCT, Shi L, Liu J. The role of visual rating and automated brain volumetry in early detection and differential diagnosis of Alzheimer's disease. *CNS Neuroscience & Therapeutics*. 2023;00:1-12. doi:10.1111/cns.14492.

3. Huang J, Biessels GJ, de Leeuw FE, Ii Y, Skoog I, Mok V, Chen C, Hilal S. Cerebral microinfarcts revisited: Detection, causes, and clinical relevance. *International Journal of Stroke*. Published online January 1, 2023. doi:10.1177/17474930231187979. (Review, Epub ahead print)

4. Ip BYM, Ma SH, Yu SCH. Recent evidence of large-core thrombectomy in acute ischemic stroke-certainties and uncertainties. *CardioVascular and Interventional Radiology*. 2023;46(8):1111-1112. doi:10.1007/s00270-023-03499-7. (Commentary)

5. Kwok AJ, Lu J, Huang J, Ip BY, Mok VCT, Lai HM, Ko H. High-resolution omics of vascular ageing and inflammatory pathways in neurodegeneration. *Seminars in Cell and Developmental Biology*. 2024;155:30-49. doi:10.1016/j.semcdb.2023.06.005. (Review, Epub ahead print)

6. Tang EC hung, Lau AY lun, AU D, Ju Y, Lam BYK, Wong A, Au L, Mok VC tong. Effects of acupuncture upon cerebral hemodynamics in cerebral small vessel disease: A pilot study. *Cerebral Circulation - Cognition and Behavior*. 2023;4. doi:10.1016/j.cccb.2023.100168.

7. Duering M, Biessels GJ, Brodtmann A, Chen C, Cordonnier C, de Leeuw FE, Debette S, Frayne R, Jouvent E, Rost NS, ter Telgte A, Al-Shahi Salman R, Backes WH, Bae HJ, Brown R, Chabriat H, De Luca A, deCarli C, Dewenter A, Doubal FN, Duering M, Biessels GJ, Brodtmann A, Chen C, Cordonnier C, de Leeuw FE, Debette S, Frayne R, Jouvent E, Rost NS, ter Telgte A, Al-Shahi Salman R, Backes WH, Bae HJ, Brown R, Chabriat H, De Luca A, deCarli C, Dewenter A, Doubal FN, Ewers M, Field TS, Ganesh A, Greenberg S, Helmer KG, Hilal S, Jochems ACC, Jokinen H, Kuijf H, Lam BYK, Lebenberg J, MacIntosh BJ, Maillard P, Mok VCT, Pantoni L, Rudilosso S, Satizabal CL, Schirmer MD, Schmidt R, Smith C, Staals J, Thrippleton MJ, van Veluw SJ, Vemuri P, Wang Y, Werring D, Zedde M, Akinyemi RO, Del Brutto OH, Markus HS, Zhu YC, Smith EE, Dichgans M, Wardlaw JM. Neuroimaging standards for research into small vessel disease-advances since 2013. *The Lancet Neurology*. 2023;22(7):602-618. doi:10.1016/s1474-4422(23)00131-x.

8. Huang B, Chau SWH, Liu Y, Chan JWY, Wang J, Ma SL, Zhang J, Chan PKS, Yeoh YK, Chen Z, Zhou L, Wong SH, Mok VCT, To KF, Lai HM, Ng S, Trenkwalder C, Chan FKL, Wing YK. Gut microbiome dysbiosis across early parkinson's disease, REM sleep behavior disorder and their first-degree relatives. *Nature Communications*. 2023;14(1). doi:10.1038/s41467-023-38248-4.

9. Cai Y, Fan X, Zhao L, Liu W, Luo Y, Lau AYL, Au LWC, Shi L, Lam BYK, Ko H, Mok VCT. Comparing machine learning-derived MRI-based and blood-based neurodegeneration biomarkers in predicting syndromal conversion in early AD. *Alzheimer's and Dementia*. 2023;19(11):4987-4998. doi:10.1002/alz.13083.

10. Yau CN, Lai HM, Lee K, Kwok AJ, Huang J, Ko H. Principles of deep immunohistochemistry for 3D histology. *Cell Reports Methods*. 2023;3(5). doi:10.1016/j.crmeth.2023.100458. (Review)

11. Soo Y, Zietz A, Yiu B, Mok VCT, Polymeris AA, Seiffge D, Ambler G, Wilson D, Leung TWH, Tsang SF, Chu W, Abrigo J, Cheng C, Lee KJ, Lim JS, Shiozawa M, Koga M, Chabriat H, Hennerici M, Wong YK, Mak H, Collet R, Inamura S, Yoshifuji K, Arsava EM, Horstmann S, Purrucker J, Lam BY, Wong A, Kim YD, Song TJ, Lemmens R, Eppinger S, Gattringer T, Uysal E, Demirelli DS, Bornstein NM, Assayag EB, Hallevi H, Molad J, Nishihara M, Tanaka J, Coutts SB, Kappelle LJ, Al-Shahi Salman SR, Jager R, Lip GY, Goeldlin MB, Panos LD, Mas JL, Legrand L, Karayiannis C, Phan T, Bellut M, Chappell F, Makin S, Hayden D, Williams D, van Dam-Nolen DD, Nederkoorn PJ, Barbato C, Browning S, Wiegertjes K, Tuladhar AM, Mendyk AM, Köhler S, van Oostenburgge OR, Zhou Y, Xu C, Hilal S, Gyanwali B, Chen C, Lou M, Staals J, Bordet R, Kandiah N, de Leeuw LF, Simister R, Hendrikse J, Wardlaw J, Kelly P, Fluri F, Srikanth V, Calvet D, Jung S, Kwa VI, Smith EE, Hara H, Yakushiji Y, Orken DN, Fazekas F, Thijs V, Heo JH, Veltkamp R, Ay H, Imaizumi T, Lau KK, Jouvent E, Toyoda K, Yoshimura S, Bae HJ, Martí-Fàbregas J, Prats-Sánchez L, Lyrer P, Best J, Werring D, Engelter ST, Peters N. Impact of cerebral microbleeds in stroke patients with atrial fibrillation. *Annals of Neurology*. 2023;94(1):61-74. doi:10.1002/ana.26642.

12. Shi Z, Yu P, Lin WJ, Chen S, Hu X, Chen S, Cheng J, Liu Q, Yang Y, Li S, Zhang Z, Xie J, Jiang J, He B, Li Y, Li H, Xu Y, Zeng J, Huang J, Mei J, Cai J, Chen J, Wu LJ, Ko H, Tang Y. Microglia drive transient insult-induced brain injury by chemotactic recruitment of CD8+ T lymphocytes. *Neuron*. 2023;111(5):696-710.e9. doi:10.1016/j.neuron.2022.12.009.

13. Sy SKH, Chan DCW, Chan RCH, Lyu J, Li Z, Wong KKY, Choi CHJ, Mok VCT, Lai HM, Randlett O, Hu Y, Ko H. An optofluidic platform for interrogating chemosensory behavior and brainwide neural representation in larval zebrafish. *Nature Communications*. 2023;14(1). doi:10.1038/s41467-023-35836-2.

14. Lam BYK, Cai Y, Akinyemi R, Biessels GJ, van den Brink H, Chen C, Cheung CW, Chow KN, Chung HKH, Duering M, Fu ST, Gustafson D, Hilal S, Hui VMH, Kalaria R, Kim SY, Lam MLM, de Leeuw FE, Li ASM, Markus HS, Marseglia A, Zheng H, O'Brien J, Pantoni L, Sachdev PS, Smith EE, Wardlaw J, Mok VCT. The global burden of cerebral small vessel disease in low- and middle-income countries: A systematic review and meta-analysis. *International Journal of Stroke*. 2023;18(1):15-27. doi:10.1177/17474930221137019. (Review)

15. Wan EYF, Chui CSL, Ng VWS, Wang Y, Yan VKC, Lam ICH, Fan M, Lai FTT, Chan EWY, Li X, Wong CKH, Chung RKC, Cowling BJ, Fong WC, Lau AYL, Mok VCT, Chan FLF, Lee CK, Chan LST, Lo D, Lau KK, Hung IFN, Lau CS, Leung GM, Wong ICK. Messenger RNA coronavirus disease 2019 (COVID-19) vaccination with BNT162b2 increased risk of bell's palsy: A nested case-control and self-controlled case series study. *Clinical Infectious Diseases*. 2023;76(3):E291-E298. doi:10.1093/cid/ciac460.

B. Conference Papers

1. Leung TW, Ip BY, Yu SC, Leng X. Remodelling and stroke relapse in symptomatic intracranial atherosclerotic disease: A longitudinal 3D rotational angiography study. In: *The 9th European Stroke Organisation Conference (ESOC 2023)*. 2023.

2. Helen Meng, Brian Mak, Man-Wai Mak, Helene Fung, Xianmin Gong, Timothy Kwok, Xunying Liu, Vincent C. T. Mok, Patrick Wong, Jean Woo, Xixin Wu, Ka Ho Wong, Shensheng Xu, Naijun Zheng, Ranzo Huang, Jiawen Kang, Xiaoquan Ke, Junan Li, Jinchao Li, Yi Wang. Integrated and enhanced pipeline system to support spoken language analytics for screening neurocognitive disorders. In: *ISCA Interspeech2023*. 2023.

3. Xuan Tian, Bonaventure YM Ip, Shuang Li, Yuying Liu, Ka Lung Chan, Yu Liu, Shangmeng Huang, Karen KY Ma, Sze Ho Ma, Florence SY Fan, Vincent HL Ip, Yannie OY Soo, Alexander YL Lau, Howan Leung, Vincent CT Mok, Thomas WH Leung, Xinyi Leng. Prevalence and risk factors of intracranial and extracranial atherosclerotic stenosis in Chinese patients with acute minor stroke or transient ischemic attack. In: *91st European Atherosclerosis Society (EAS) Congress*. 2023.

4. Xuan Tian, Shuang Li, Yuying Liu, Bonaventure YM Ip, Jill Abrigo, Linfang Lan, Haipeng Liu, Sze Ho MA, Ka Yan Karen MA, Sin Ying Fan, Hing Lung Ip, Yannie OY Soo, Alexander Lau, Howan Leung, Vincent CT Mok, Thomas Leung, Xinyi Leng. Systemic inflammatory markers associated with progression of symptomatic intracranial atherosclerotic stenosis under medical treatment. In: *The 9th European Stroke Organisation Conference (ESOC 2023)*. 8(2). 2023 May 24.

5. X Leng, B Ip, SH Ma, KYK Ma, HL Ip, SY Fan, YYA Chan, WCL Au, YOY Soo, A Lau, H Leung, VCT Mok, S Yu, T Leung. Geometry at terminal internal carotid artery bifurcation associated with middle cerebral artery plaque ulceration: A three-dimensional rotational angiography study. In: *The 9th European Stroke Organisation Conference 2023 (ESOC 2023)*. 2023 May.

6. Shuang Li, Linfang Lan, Xuan Tian, Haipeng Liu, Bonaventure YM Ip, Sze Ho Ma, Jill Abrigo, Yuying Liu, Yu Liu, Karen KY Ma, Florence SY Fan, Vincent HL Ip, Yannie OY Soo, Alexander Y Lau, Howan Leung, Vincent CT Mok, Thomas W Leung, Xinyi Leng. Upstream high wall shear stress associated with artery-to-artery embolism and recurrent stroke in symptomatic intracranial atherosclerotic stenosis. In: *The 91st European Atherosclerosis Society Congress*. 2023.

7. Shuang Li, Xueyan Feng, Bonaventure Ip, Hing Lung Ip, Jill Abrigo, Linfang Lan, Haipeng Liu, Xuan Tian, Yuying Liu, Yu Liu, Karen KY Ma, Florence SY Fan, Sze Ho Ma, Hui Fang, Yuming Xu, Alexander Y Lau, Howan Leung, Yannie OY Soo, Vincent CT Mok, Ka Sing Wong, Xinyi Leng, Thomas W Leung. Internal and cortical borderzone infarcts in symptomatic intracranial atherosclerotic stenosis: Different hemodynamic impairment and risks of recurrent stroke. In: *European Stroke Organisation Conference 2023*. 2023.

8. Shuang Li, Xueyan Feng, Yuying Liu, Bonaventure Ip, Hing Lung Ip, Jill Abrigo, Xuan Tian, Yu Liu, Linfang Lan, Haipeng Liu, Lina Zheng, Karen KY Ma, Florence SY Fan, Sze Ho Ma, Alexander Y Lau, Howan Leung, Yannie OY Soo, Vincent CT Mok, Ka Sing Wong, Thomas W Leung, Xinyi Leng. Paradox effect of follow-up diastolic blood pressure on stroke recurrence according to the leptomeningeal collateral status in patients with symptomatic intracranial atherosclerotic stenosis. In: *European Stroke Organisation Conference 2023*. 2023.

9. X Leng, X Tian, T Leung. Evolution of symptomatic intracranial atherosclerotic disease under medical treatment: A systematic review. In: *The 9th European Stroke Organisation Conference 2023 (ESOC 2023)*. 2023 May.

10. B Ip, T Yip, G Wong, X Leng, T Leung. Risk of cerebrovascular events with intensive lipid control among direct oral anticoagulant users: A population-based analysis. In: *The 9th European Stroke Organisation Conference 2023 (ESOC 2023)*. 2023 May.

11. Zheng L, Abrigo J, Tian X, Li S, Liu Y, Ip HL, Fan SY, Ma SH, Ma KK, Ip BY, Mok VC, Wong KS, Liu L, Leung TW, Leng X. Cerebral small vessel disease in ipsilateral hemisphere to significance of intracranial atherosclerotic disease associated with stroke risk. In: *The 9th European Stroke Organisation Conference (ESOC 2023)*. 2023 May.

12. Yuying Liu, Xuan Tian, Shuang Li, Jill Abrigo, Yu Liu, Linfang Lan, Haipeng Liu, Sze Ho Ma, Ka Yan Karen Ma, Bonaventure Ym Ip, Sin Ying Fan, Hing Lung Ip, Yannie Oy Soo, Alexander Lau, Howan Leung, Vincent Ct Mok, K.S. Wong, Thomas Leung, Xinyi Leng. Evolution of leptomeningeal collaterals in middle cerebral artery stenosis possibly driven by the translesional pressure gradient. In: The 9th European Stroke Organisation Conference. *European Stroke Journal*. 8(2). 2023 May 24.

13. Leng X, Ip BYM, Ma SH, Miu A, Ma K, Au LWC, Fan FS, Ip VHL, Chan AYY, Lau AY, Soo YOY, Leung H, Mok VCT, Yu SCH, Leung TW. Symptomatic intracranial atherosclerotic plaques: Different morphological features in the anterior versus posterior circulation. In: *International Stroke Conference 2023 (ISC 2023)*. 54(1). 2023 February.

14. Y Cai, BYK Lam, X Fan, W Liu, L Shi, LWC Au, H Ko, VCT Mok. Machine-learning derived MRI-based atrophy biomarker predicts long-term cognitive decline in stroke or transient ischemic attack. In: *The 19th Asia Pacific Multidisciplinary Meeting for Nervous System Diseases (BRAIN 2023)*. 2023 February.

15. ST Fu, Y Cai, J Huang, W Liu, L Shi, LWC Au, H Ko, VCT Mok. Diagnostic performance of MRI-based Alzheimer's disease resemblance atrophy index and plasma-based biomarkers on Alzheimer's disease. In: *The 19th Asia Pacific Multidisciplinary Meeting for Nervous System Diseases (BRAIN 2023)*. 2023 February.

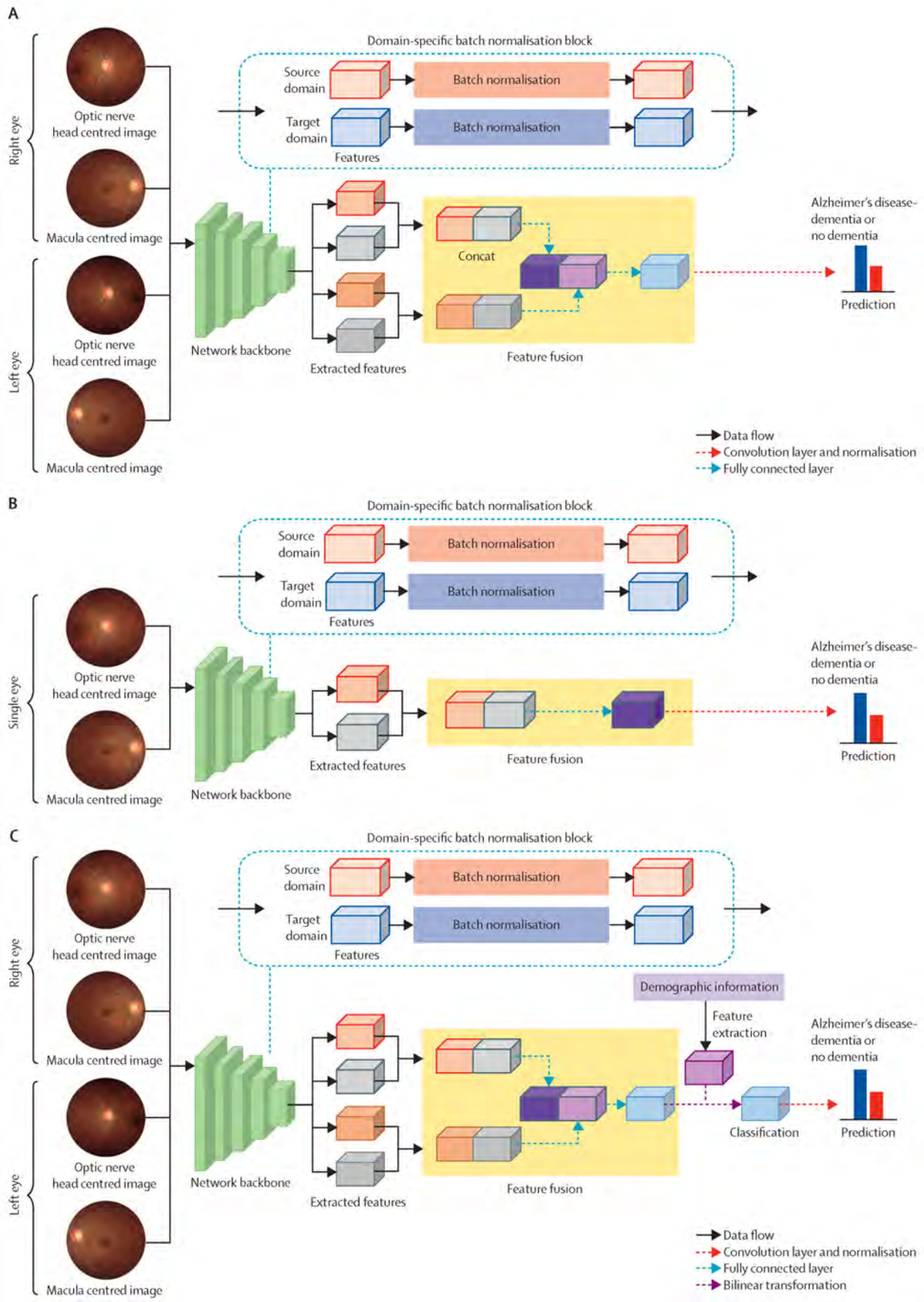
16. Janita Pak Chun Chau, Suzanne Hoi Shan Lo, Alexander Y Lau, Vivian Lee Wing Yan, Kai Chow Choi, Edward Wai Ching Shum, Sheung Sheung Hung, Vincent Chun Tong Mok, Kee Chen Elaine Siow, Jessica Yuet Ling Ching, Simon Kwun Yu Lam. Experiences of community-dwelling stroke survivors with a virtual multidisciplinary stroke clinic during the COVID pandemic. In: *International Stroke Conference 2023. Stroke, American Heart Association*. 54(1). 2023 February.

17. Janita Pak Chun Chau, Suzanne Hoi Shan Lo, Alexander Yuk Lun Lau, Vivian Wing Yan Lee, Kai Chow Choi, Edward Wai Ching Shum, Sheung Sheung Hung, Vincent Chung Tong Mok, Kee Chen Elaine Siow, Jessica Yuet Ling Ching, Simon Kwun Yu Lam. An evaluation of stroke survivors' self-efficacy in self-management using a stroke telehealth service. In: *International Stroke Conference 2023. Stroke, American Heart Association*. 54(1). 2023 February.

18. Hanna Lu, Sandra Sau Man Chan, Sukling Ma, Vincent Chung Tong Mok, Lin Shi, Defeng Wang, Arthur Dun-Ping Mak, Linda Chiu Wa Lam. Radiomic features for predicting the treatment response of repetitive transcranial magnetic stimulation in major neurocognitive disorder. In: *5th International Brain Stimulation Conference.* 2023 February.

19. Hanna Lu, Jing Li, Sandra Sau Man Chan, Sukling Ma, Vincent Chung Tong Mok, Lin Shi, Arthur Dun-Ping Mak, Linda Chiu Wa Lam. Predictive value of MRI-informed brain age matrices to rTMS effects in neurocognitive disorder with depression. In: *The 5th International Brain Stimulation Conference*. 2023 February.

20. Shuang Li, Lina Zheng, Xuan Tian, Yuying Liu, Xinyi Leng, Thomas W Leung. Identification of hub genes in endothelial cells under oscillatory flow. In: *International Stroke Conference 2023*. 54(1). 2023 February.



A deep learning model for detection of Alzheimer's disease based on retinal photographs.

Source: ***Cheung CY, Ran AR, Wang S, Chan VTT, Sham K, Hilal S, Venketasubramanian N, Cheng CY, Sabanayagam C, Tham YC, Schmetterer L, McKay GJ, Williams MA, Wong A, Au LWC, Lu Z, Yam JC, Tham CC, Chen JJ, Dumitrascu OM, Heng PA, Kwok TCY, Mok VCT, Milea D, Chen CLH, Wong TY. A deep learning model for detection of Alzheimer's disease based on retinal photographs: A retrospective, multicentre case-control study. The Lancet Digital Health. 2022;4(11):e806-e815. doi:10.1016/s2589-7500(22)00169-8.***



REPRODUCTION AND DEVELOPMENT

生殖與發育研究

PRINCIPAL INVESTIGATOR
Ronald Wang

TEAM MEMBERS
Judy Zhang, Max Wang, Tao Tang, Shirlly Deng, Tat Lau, Linda Wu, Nina Chu, Maran Leung, Yi Song, Alice Lin, Bekalu Alemu, Getnet Gedefaw Azeze, Iris Chen, Junshang Dai, Olena Getsko, Yang Ding, Helen Gong, Meilan Mo, Sophia Tan, Kenean Tlaye, Yifan Tu, Jinjiang Wang, Gashaw Garedew Woldeamanuel, Hanbin Wu, Feng Xiong, Kemin Yan, Ruqun Zheng, Xu Zheng, Michelle Yeung

RESEARCH PROGRESS SUMMARY

Ronald Wang and his team from the Department of Obstetrics & Gynaecology focus on the field of reproduction and development. The team covered a wide spectrum of clinical, basic and genetic studies of female and male reproduction, and embryo and fetal development in humans and mice. The team has many intradepartmental (TY Leung in fetal medicine and prenatal diagnosis; Liona Poon in maternal medicine; Jacqueline Chung in assisted reproductive technology), interdepartmental within the Faculty of Medicine (Simon Lam in neonatology; Ronald Ma in diabetes; Huating Wang, Kathy Chan, Tong Leung and Anna Tsan in stem cells, Alisa Shum in developmental biology), intrainstitutional with Faculty of Sciences (KM Kwan in developmental biology; Martin Tsui in environmental pollutants), interuniversity (HKU, Ernest Ng and Raymond Li in O&G; Thomas Leung and Bill Chan in drug development), and many other regional, national and international research collaboration in the field.

Ronald has worked on many research projects. He received a total of over 111 million research grants and owned 4 patents. He has published over 286 ISI articles in many acclaimed journals, including *JAMA, Annals of Internal Medicine, Nature Cell Biology, Nature Communications, Genes & Development, Cell Research, Proceedings of the National Academy of Sciences, Human Reproduction Update, Angiogenesis, Journal of Biological Chemistry, Free Radical Biology and Medicine, Molecular Human Reproduction, Human Reproduction,* and *Fertility and Sterility*. His success in O&G research has earned him multiple local and international scholarships and awards.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
黃志超 黃薇 裴天嬌 黃新 梁波 羅斌 伍芳蓉 譚婧	第五屆（2023 年）婦幼健康科學技術獎獲獎成果自然科學獎三等獎	中國婦幼健康研究會
黃志超 梁瑞寧 鄒陽 徐玲 李佩雙 范培 彭佳華 彭雪梅	2022 年度江西省科學技術進步獎一等獎	中國江西省人民政府
Ronald Wang Sze Wan Hung Gene Man Xiaoyan Chen Yiwei Zhao Tao Zhang Pui Wah Chung Tin Chiu Li	International Invention Fair in the Middle East 2023 Silver Medal	Kuwait Science Club

Fellowships

Name	Details	
	Fellowship	Organisation
Dan Wang	PhD Biomedical Sciences	The Chinese University of Hong Kong – Internal Examiner of Thesis Committee Board

Academic Editorships

Name	Details	
	Role	Journal
Ronald Wang	Associate Editor	Fertility & Reproduction
		Cell Press: Heliyon, section Women's Health
		Cell Press: Heliyon, section Genetics
	Editorial Board	Scientific Report

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Ronald Wang	Journal Reviewer	Cell Communication and Signaling
		Phytomedicine
		Reproductive Biology and Endocrinology
		Ultrasound in Obstetrics and Gynecology
		Frontiers in Aging Neuroscience
		Molecules
		Journal of Assisted Reproduction and Genetics
		BMC Pregnancy Childbirth
		Cell Communication and Signaling
		Acupuncture in Medicine
		BMC Pregnancy Childbirth
		Drug Design, Development and Therapy
		Journal of Clinical Medicine
		Reproductive BioMedicine Online
		Fertility and Sterility Science
		Life Sciences
		Biomedicine & Pharmacotherapy
		Journal of Clinical Medicine
		Heliyon
		Journal of Inflammation Research
		Frontiers in Cellular and Infection Microbiology
		Frontiers in Pharamcology
		Heliyon
		International Journal of Biological Sciences
		Journal of Ethnopharmacology
		Heliyon
		Genes & Diseases
		Theriogenology
	Abstract Reviewer	ASPIRE 2023 Congress in Australia

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ronald Wang	Chinese Medicines for Endometriosis: Pharmaceutical Efficacy, Targets and Mechanisms	The Chinese University of Hong Kong – Strategic Seed Funding for Collaborative Research Scheme	01/09/2022	31/08/2024	300,000
	Stem Cell-Niche Interactions in Tissue Maintenance and Engineering	Research Grants Council – Theme-based Research Scheme	01/01/2022	31/12/2026	66,438,000
	Disease Mechanism and Integrated Preventive Strategy of Preterm Preeclampsia 早發型子癇前期發病機制及整體化防控策略的研究 , Project 3: Multiomics and System Biology to Screen Biomarkers and Potential Target for Preeclampsia 利用多組學和系統生物學技術，篩選疾病生物標誌與潛在靶標	Ministry of Science of Technology Grant	01/12/2021	30/11/2025	RMB 27,777,000
	Epithelium Caveolin and its Calcium Signaling Pathway in Endometrium of Recurrent Miscarriage	Research Grants Council - General Research Fund	01/09/2021	29/02/2024	775,732
	Receptor Tyrosine Kinase Inhibitor Sunitinib as Novel Immunotherapy to Inhibit Myeloid-Derived Suppressor Cells for Treatment of Endometriosis	Health Bureau - Health and Medical Research Fund	01/09/2021	31/08/2023	1,360,000
	A Super-Resolution Fluorescence Microscopy Platform for Live – Cell and Animal-Tissue Imaging	Research Grants Council – Collaborative Research Fund	01/01/2021	31/12/2023	7,154,250
	The Effect of In Utero Hyperglycaemia, Maternal Overnutrition and Interaction with Postnatal Lifestyle on Cardiometabolic Risk at Young Adulthood – Extension of HAPO Follow Up Study	Research Grants Council – General Research Fund	01/01/2020	30/06/2023	1,158,019

Publications

A. Journal Papers

1. Shi Y, Wang CC, Wu L, Zhang Y, Xu A, Wang Y. Pathophysiological insight into fatty acid-binding protein-4: Multifaced roles in reproduction, pregnancy, and offspring health. *International Journal of Molecular Sciences*. 2023, Vol 24, Page 12655. 2023;24(16):12655. doi:10.3390/ijms241612655. (Review)

2. Chen X, Man GCW, Hung SW, Zhang T, Fung LWY, Cheung CW, Chung JPW, Li TC, Wang CC. Therapeutic effects of green tea on endometriosis. *Critical Reviews in Food Science and Nutrition*. 2023;63(18):3222-3235. doi:10.1080/10408398.2021.1986465. (Review)

3. Liang B, Dong R, Hung SW, Li Y, Lin Y, Wu L, Zhang T, Man GCW, Xu H, Chung JPW, Wang CC. Unique anti-angiogenic effects, pharmacological targets and therapeutic mechanisms of Chinese herbal medicines for endometriosis. *Genes & Diseases*. Published online November 11, 2023:101166. doi:10.1016/j.gendis.2023.101166. (Epub ahead of print)

4. Hung SW, Gaetani M, Li Y, Tan Z, Xu Z, Zhang R, Ding Y, Wai Man GC, Zhang T, Song Y, Wang Y, Wah Chung JP, Chan TH, Zubarev RA, Wang CC. Distinct molecular targets of ProEGCG from EGCG and superior inhibition of angiogenesis signaling pathways for treatment of endometriosis. *Journal of Pharmaceutical Analysis*. 2024;14(1):100-114. doi:10.1016/j.jpha.2023.09.005. (Epub ahead of print)

5. Tan Z, Gong X, Li Y, Hung SW, Huang J, Wang CC, Chung JPW. Impacts of endometrioma on ovarian aging from basic science to clinical management. *Frontiers in Endocrinology*. 2023;13:1073261. doi:10.3389/fendo.2022.1073261. (Review)

6. Mao D, Yuen LY, Ho CS, Wang CC, Tam CHT, Chan MHM, Lowe WL, Ma RCW, Tam WH. The association of prenatal vitamin D status with pregnancy and neonatal outcomes. *Journal of the Endocrine Society*. 2023;8(1):1-11. doi:10.1210/jendso/bvad142.

7. Alemu BK, Azeze GG, Wu L, Lau SL, Wang CC, Wang Y. Effects of maternal probiotic supplementation on breast milk microbiome and infant gut microbiome and health: A systematic review and meta-analysis of randomized controlled trials. *American Journal of Obstetrics & Gynecology MFM*. 2023;5(11):101148. doi:10.1016/j.ajogmf.2023.101148. (Review, Epub ahead of print)

8. Tian Y, Huang J, Wang CC, Lin H, Huang X, Zhao Y, Liu L, Zhang S. The impact of endometrial scratch performed in mid-luteal phase on the endometrium whole genome transcriptomic profiles in following menstrual cycle. *Human Fertility*. 2023;26(4):733-741. doi:10.1080/14647273.2023.2193909. (Epub ahead of print)

9. Qi R, Guan R, Cai S, Xu M, Yang WJ, Wang CC. Comprehensive molecular expression profiling of SARS-CoV-associated factors in the endometrium across the menstrual cycle and elevated susceptibility in women with recurrent pregnancy loss. *Frontiers in Genetics*. 2023;14:1246725. doi:10.3389/fgene.2023.1246725.

10. Qi R, Zhang T, Zhang Y, Chung JPW, Yang WJ, Wang CC. Association of angiotensin II and receptors in peri-implantation endometrium with microvessel density and pregnancy outcomes of women with recurrent implantation failure after embryo transfer. *Frontiers in Endocrinology*. 2023;14:1206326. doi:10.3389/fendo.2023.1206326. (Epub ahead of print)

11. Wu XK, Gao JS, Ma HL, Wang Y, Zhang B, Liu ZL, Li J, Cong J, Qin HC, Yang XM, Wu Q, Chen XY, Lu ZL, Feng YH, Qi X, Wang YX, Yu L, Cui YM, An CM, Zhou LL, Hu YH, Li L, Cao YJ, Yan Y, Liu L, Liu YX, Liu ZS, Painter RC, Ng EHY, Liu JP, Mol BWJ, Wang CC. Acupuncture and doxylamine–pyridoxine for nausea and vomiting in pregnancy. *Annals of Internal Medicine*. 2023;176(7):922-934. doi:10.7326/m22-2974. (Epub ahead of print)

12. Deng Y, Song Y, Du Q, Wang CC, Li H, Sui Y, Zhang Y, Tang T. Anti-HPV16 oncoproteins siRNA therapy for cervical cancer using a novel transdermal peptide PKU12. *Frontiers in Oncology*. 2023;13:1175958. doi:10.3389/fonc.2023.1175958.

13. Lin Y, Wu L, Zhao R, Chung PW, Wang CC. Chinese herbal medicine, alternative or complementary, for endometriosis-associated pain: A meta-analysis. *American Journal of Chinese Medicine*. 2023;51(4):807-832. doi:10.1142/s0192415x23500386.

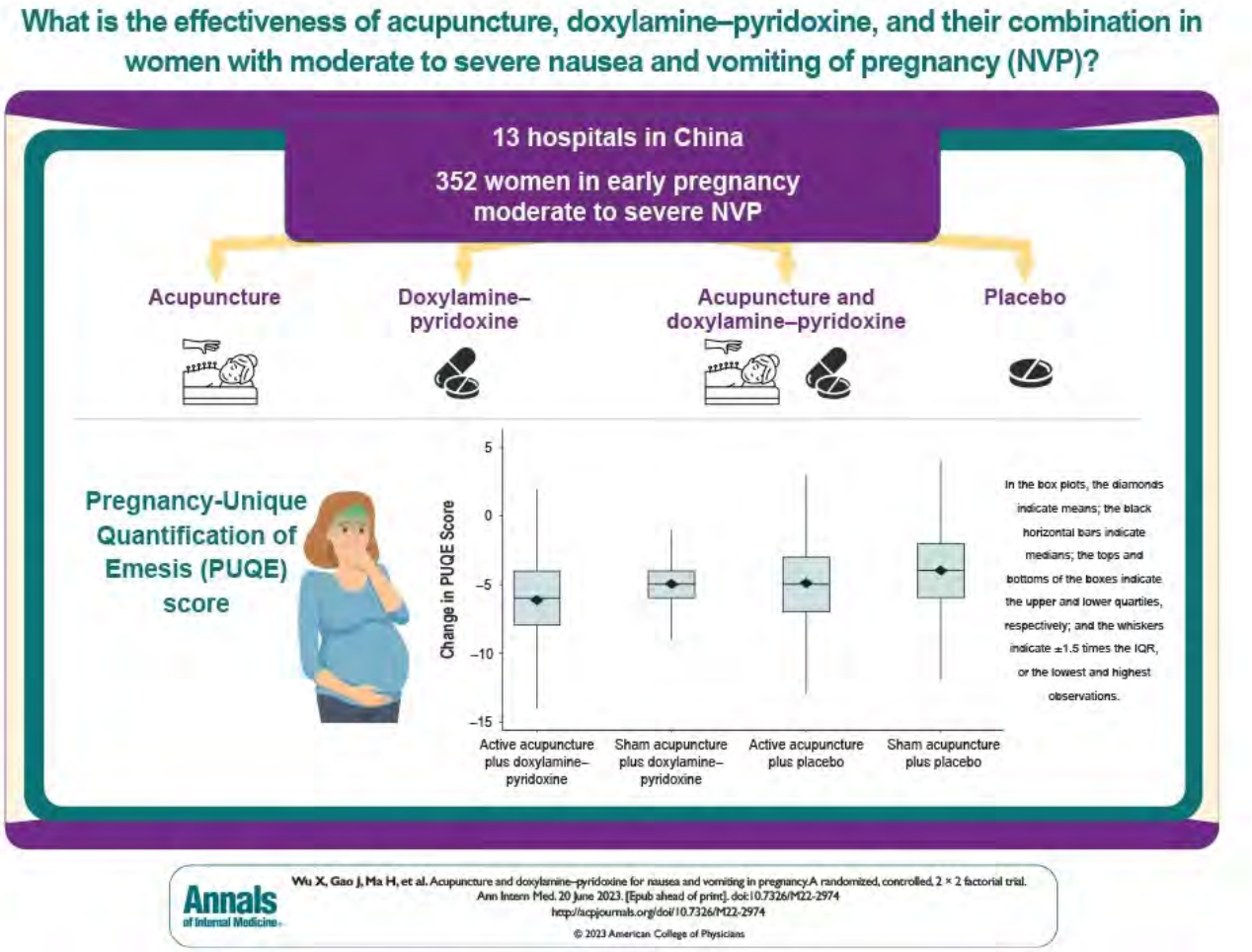
14. Woldeamanuel GG, Tlaye KG, Wu L, Poon LC, Wang CC. Platelet count in preeclampsia: A systematic review and meta-analysis. *American Journal of Obstetrics & Gynecology MFM*. 2023;5(7):100979. doi:10.1016/j.ajogmf.2023.100979. (Review)

15. Wu X, Wang CC, Cao Y, Li J, Li Z, Ma H, Gao J, Chang H, Zhang D, Cong J, Wang Y, Wu Q, Han X, Chung PWJ, Li Y, Zheng X, Chen L, Zeng L, Borchert A, Kuhn H, Chen ZJ, Ng EHY, Stener-Victorin E, Zhang H, Legro RS, Mol BWJ, Shi Y. Novel genetic risk and metabolic signatures of insulin signaling and androgenesis in the anovulation of polycystic ovary syndrome. *Engineering*. 2023;23:103-111. doi:10.1016/j.eng.2022.08.013.

16. Li PS, Peng XM, Niu XX, Xu L, Hung Yu Ng E, Wang CC, Dai JF, Lu J, Liang RN. Efficacy of acupuncture for endometriosis-associated pain: A multicenter randomized single-blind placebo-controlled trial. *Fertility and Sterility*. 2023;119(5):815-823. doi:10.1016/j.fertnstert.2023.01.034.

17. Chung JPW, Chan DYL, Song Y, Ng EYL, Law TSM, Ng K, Leung MBW, Wang S, Wan HM, Li JJX, Wang CC. Implementation of ovarian tissue cryopreservation in Hong Kong. *Hong Kong Medical Journal*. 2023;29(2):121-131. doi:10.12809/hkmj2210220. (Epub ahead of print)

18. Xie H, Zhang A, Mou X, He T, Li J, Wang CC, Fan X, Li L. Chinese herbal medicine for threatened miscarriage: An updated systematic review and meta-analysis. *Frontiers in Pharmacology*. 2023;14:1083746. doi:10.3389/fphar.2023.1083746.



The Pregnancy-Unique Quantification of Emesis (PUQE) score from 352 women who are in early pregnancy moderate to severe NVP collected in 13 hospitals in China.

Source: Wu XK, Gao JS, Ma HL, Wang Y, Zhang B, Liu ZL, Li J, Cong J, Qin HC, Yang XM, Wu Q, Chen XY, Lu ZL, Feng YH, Qi X, Wang YX, Yu L, Cui YM, An CM, Zhou LL, Hu YH, Li L, Cao YJ, Yan Y, Liu L, Liu YX, Liu ZS, Painter RC, Ng EHY, Liu JP, Mol BWJ, Wang CC. Acupuncture and doxylamine–pyridoxine for nausea and vomiting in pregnancy. Annals of Internal Medicine. 2023;176(7):922-934. doi:10.7326/m22-2974.



STEM CELLS AND TISSUE REGENERATION

ADULT STEM CELL BIOLOGY AND APPLICATIONS

幹細胞及組織再生研究

PRINCIPAL INVESTIGATOR

Gang Li

TEAM MEMBERS

Sien Lin, Lu Feng, Shanshan Bai, Yucong Li, Zhengmeng Yang, Linlong Li, Haixing Wang, Xiaoting Zhang, Xuan Lu, Ming Wang, Han Su, Yinuo Fan, Zhaowei Jiang, Yuejun Lin, Zhixian Zong, Jiakang Jin, Nan Hou, Jiaming Yang, Xu Yan

RESEARCH PROGRESS SUMMARY

In 2023, the research team has 17 members (1 Research Assistant Professor, 4 Postdoctoral Fellows, 1 Research Associates, 3 Research Assistants, 8 PhD Students) with the following research programmes carried out: (1) Development and mechanistic studies of tibial cortex transverse transport (TTT) surgery for the management of diabetic foot ulcers. (2) Development and mechanistic studies of cranial bone transport (CBT) surgery for the management of ischemic stroke and Alzheimer's disease. (3) Novel therapy strategies for osteoporotic bone fracture and chronic wounds. (4) Participation of InnoHK programme in Science Park with the Chinese Academy of Sciences. These research programmes have been progressed well as planned, with more than 12 peer-reviewed publications and over HK$6 million research grants income. **Gang Li** has been invited to give keynote speeches and lectures at various national and international conferences and meetings for more than 20 times in 2023, and continuously serves as visiting professors at many prestigious universities such as Monash University, Australia; University of Sains Malaysia; Nanjing Medical University China, etc. He also serves as the council member or vice chair for 4 prestigious national research societies, and editorial board members for 6 international journals. He served as the programme chair for 2023 Tissue Engineering and Regenerative Medicine Society (Asia-Pacific) Conference, October 19-22, Hong Kong Science Park, Hong Kong.

From 2020 to present, he has been on the list of the world's top 2% scientists (ranked among the 1% of the world's top scientists in 2022 and 2023). In 2023, he is ranked 9th of the top 100 scholars in the field of orthopedic surgery in PR China. In 2023, he is ranked 37th among the best CUHK Professors across all disciplines and ranked 2618th (world) and 50th national of the best scientists in the Biology and Biochemistry category (https://research.com/university/the-chinese-university-of-hong-kong).

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Jiaming Yang	Overseas PhD Student Scholarship	The Southern University of Science and Technology
Zhaowei Jiang	Best Poster Award	The Hong Kong Orthopaedic Association 43rd Annual Congress
	Golden Award	2023 TERMIS-AP Webinar Student Presentation Contest
Jiakang Jin	Hong Kong PhD Fellowship Award	Research Grant Counical, Hong Kong

Fellowships

Name	Details	
	Fellowship	Organisation
Gang Li	Adjunct Professor	Australian Regenerative Medicine Institute (ARMI), Monash University, Australia
	Visiting Professor and Assessor of Teaching Program	Department of Orthopaedic Surgery and Traumatology, University of Malaya, Malaysia
	Visiting Professor and Assessor of Teaching Program	Department of Orthopaedic Surgery, University of Sciences Malaysia
	Visiting Professor	Guang Dong Medical University, China
	Visiting Professor	Nanjing Medical University, China
	General Secretary	Division of Limb Deformity Correction and Reconstruction, Chinese Association of Orthopaedic Surgeons
	Co-Chairman of China Branch	International Limb Lengthening and Reconstruction Societies (ILLRS) and Association from Study and Application of the Methods of Ilizarov (ASAMI)
	副主任委員	中國骨科醫師協會 骨橫搬糖足學組
	香港科技工作者協會理事 (學術委員會委員)	Council Member of Academic Division, Hong Kong Association of Scientists
	中國材料學會 再生材料分會 副主任委員	Vice Chairman, Branch of Regenerative Biomaterials, Chinese Association of Materials
	Program Chairman	Tissue Engineering and Regenerative Medicine International Society (TERMIS) Asia Pacific (AP) 2023 Meeting, 19-22 October 2023, Hong Kong.
	Council and Funding Member	Hong Kong Society of Cell Biology

Name	Details	
	Fellowship	Organisation
Gang Li	Fellow	International Combined Orthopaedic Research Societies
	Fellow	American Orthopaedic Research Society

Academic Editorships

Name	Details	
	Role	Journal
Gang Li	Executive Associate Editor	Journal of Orthopaedic Translation
	Member of Editorial Board	Calcified Tissue International
		Bone and Joint Research
		Bone
		Journal of Orthopaedic Research
		China Medical Journal

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Gang Li	Reviewer	Stem Cells Research and Therapy
		Biomaterials
		Stem Cells
		Frontiers in Cell Biology
		Science Advances
		Bioactive Materials
		Journal of Physiology
		Journal of Chemical Engineering
		Journal of Orthopaedic Translation
		Bone and Joint Research
		Journal of Orthopaedic Research

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Gang Li	Studies of Cranial Bone Transport for Stroke Management	Research Grants Council – Research Matching Grant Scheme	01/01/2021	31/12/2025	800,000
	Mechanistic Studies of Tibial Cortex Transverse Transport (TTT) Surgery in Improving Diabetic Foot Ulcers Healing Outcomes	Health Bureau – Advanced Medical Research Fund	01/01/2023	31/12/2025	1,492,636
	Engineering the Biomimetic Structural Mechanical Heterogeneity of Cell-adaptable Nanocomposite Hydrogels for Biomedical Applications	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,185,400
	The Role of Lgr5 in Cartilage Development and Mesenchymal Stem Cells Mediated Cartilage Repair	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	996,285
	The Role and Mechanism of Focal Adhesion Protein Kindlin-2 in Distraction Osteogenesis	Natural Science Foundation and Research Grants Council Joint Fund	01/01/2023	31/12/2026	1,244,750
	Lgr5 陽性細胞在軟骨發育和修復中的作用及其機制研究	國家自然科學基金	01/01/2022	31/12/2025	623,699
	Mechanistic Studies on Treatment of Diabetic Foot Ulcers by Novel Tibial Cortex Transverse Transport Surgery	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,125,732
	Aging, skeletal degeneration and regeneration	Research Grants Council – Areas of Excellence Scheme	01/05/2021	30/04/2028	70,688,000
Sien Lin	Elucidation of Type 1 Innate Lymphoid Cells in Distraction Osteogenesis	Research Grants Council – General Research Fund	01/01/2024	31/12/2026	1,250,000
	Elucidation of Type 1 Innate Lymphoid Cells in Distraction Osteogenesis	The Chinese University of Hong Kong – Direct Grant	30/06/2023	29/06/2024	150,000
	KDM3A Regulates Bone Fracture Healing in Aging via the SIRT3-SOD2 Axis: From Mechanism to Intervention	Research Grants Council – General Research Fund	01/01/2024	31/12/2026	1,598,620

Publications

A. Journal Papers

1. Wang H, Lin S, Feng L, Huang B, Lu X, Yang Z, Jiang Z, Li YC, Zhang X, Wang M, Wang B, Kong L, Pan Q, Bai S, Li Y, Yang Y, Lee WYW, Currie PD, Lin C, Jiang Y, Chen J, Tortorella MD, Li H, Li G. Low-dose staphylococcal enterotoxin C2 mutant maintains bone homeostasis via regulating crosstalk between bone formation and host T-cell effector immunity. *Advanced Science.*. 2023;10(28). doi: 10.1002/advs.202300989.

2. Tao R, Mi B, Hu Y, Lin S, Xiong Y, Lu X, Panayi AC, Li G, Liu G. Hallmarks of peripheral nerve function in bone regeneration. *Bone Research*. 2023;11(1). doi:10.1038/s41413-022-00240-x. (Review)

3. Li Y, Li L, Wang M, Yang B, Huang B, Bai S, Zhang X, Hou N, Wang H, Yang Z, Tang C, Li Y, Lee WYW, Feng L, Tortorella MD, Li G. O-alg-THAM/gel hydrogels functionalized with engineered microspheres based on mesenchymal stem cell secretion recruit endogenous stem cells for cartilage repair. *Bioactive Materials.* 2023;28:255-272. doi:10.1016/j.bioactmat.2023.05.003.

4. Lin W, Wang M, Xu L, Tortorella M, Li G. Cartilage organoids for cartilage development and cartilage-associated disease modeling. *Frontiers in Cell and Developmental Biology.* 2023;11. doi:10.3389/fcell.2023.1125405. (Perspective)

5. Li Y, Li L, Li Y, Feng L, Wang B, Wang M, Wang H, Zhu M, Yang Y, Waldorff EI, Zhang N, Viohl I, Lin S, Bian L, Lee WYW, Li G. Enhancing cartilage repair with optimized supramolecular hydrogel-based scaffold and pulsed electromagnetic field. *Bioactive Materials.* 2023;22:312-324. doi:10.1016/j.bioactmat.2022.10.010.

6. Wu H, Tan J, Sun D, Wang X, Shen J, Wang S, Dai Q, Wei Z, Li G, Lin S, Luo F, Xie Z. Discovery of multipotent progenitor cells from human induced membrane: Equivalent to periosteum-derived stem cells in bone regeneration. *Journal of Orthopaedic Translation*. 2023;42:82-93. doi:10.1016/j.jot.2023.07.004.

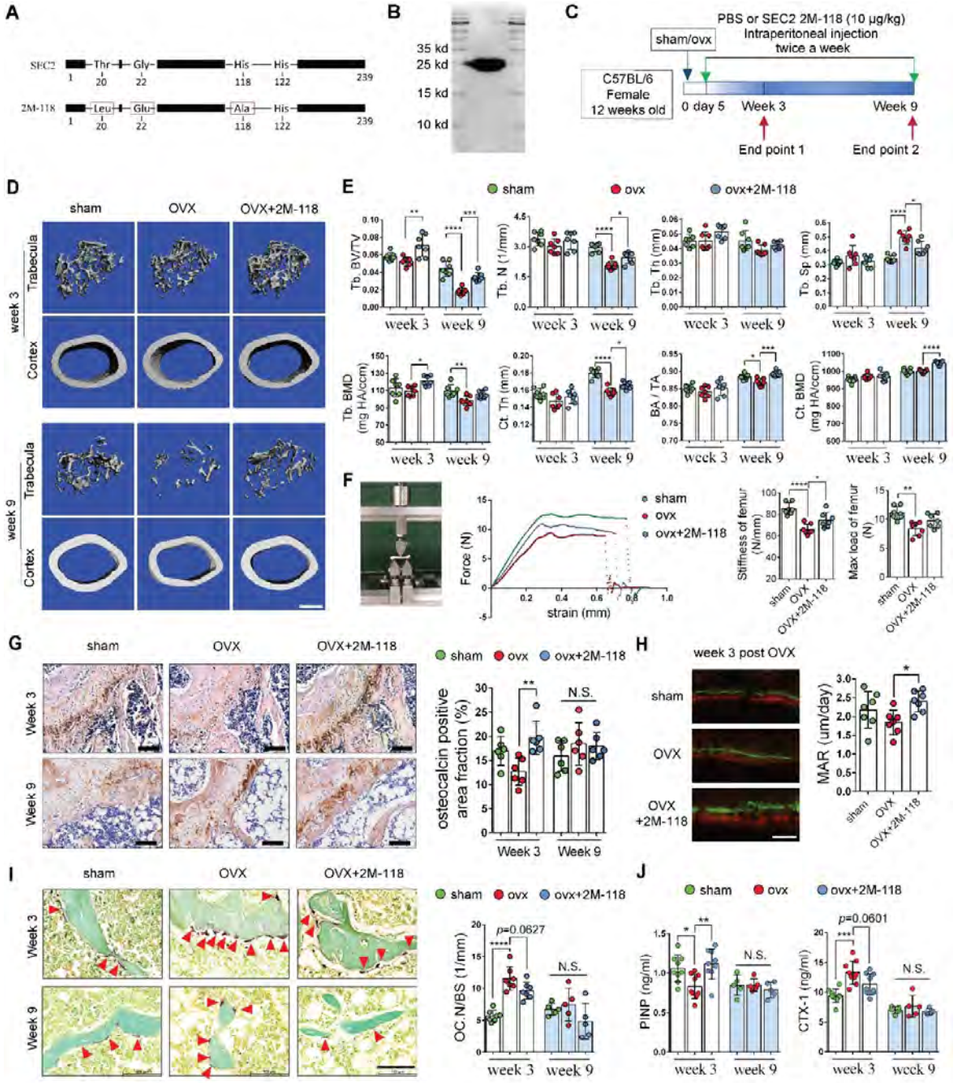
7. Hua J, Huang J, Li G, Lin S, Cui L. Glucocorticoid induced bone disorders in children: Research progress in treatment mechanisms. *Frontiers in Endocrinology.* 2023;14:1119427. doi:10.3389/fendo.2023.1119427/bibtex. (Review)

8. Peng X, Li Y, Liu M, Li Z, Wang X, Zhang K, Zhao X, Li G, Bian L. Complex coacervate-derived hydrogel with asymmetric and reversible wet bioadhesion for preventing UV light-induced morbidities. *Bioactive Materials*. 2023;30:62-72. doi:10.1016/j.bioactmat.2023.07.016.

9. Feng L, Yang Z, Hou N, Wang M, Lu X, Li Y, Wang H, Wang Y, Bai S, Zhang X, Lin Y, Yan X, Lin S, Tortorella MD, Li G. Long Non-Coding RNA Malat1 Increases the Rescuing Effect of Quercetin on TNFα-Impaired Bone Marrow Stem Cell Osteogenesis and Ovariectomy-Induced Osteoporosis. *International Journal of Molecular Sciences.* 2023;24(6). doi:10.3390/ijms24065965.

10. Chen J, Tan J, Li J, Cheng W, Ke L, Wang A, Wang Q, Lin S, Li G, Wang B, Chen J, Zhang P. Genetically Engineered Biomimetic Nanoparticles for Targeted Delivery of mRNA to Treat Rheumatoid Arthritis. *Small Methods*. 2023;7(11). doi:10.1002/smtd.202300678.

11. Chen J, Chen J, Tan J, Li J, Cheng W, Ke L, Wang Q, Wang A, Lin S, Li G, Zhang P, Wang B. HIF-1α dependent RhoA as a novel therapeutic target to regulate rheumatoid arthritis fibroblast-like synoviocytes migration in vitro and in vivo. *Journal of Orthopaedic Translation.* 2023;40:49-57. doi:10.1016/j.jot.2023.05.004.



Systemic administration of SEC2 2M-118 alleviates bone loss in OVX mice via promoting bone formation. A) Schematic diagram of SEC2 mutant protein 2M-118. Red boxes indicate mutations compared with the wild type SEC2. B) The purified SEC2 2M-118 was confirmed by western blot. C) OVX mice received systemic administration of SEC2 2M-118 and were terminated at two time points. D) 3-D reconstruction of trabecular bone in distal femur and cortical bone in midshaft. Scale bar, 500 μm. E) Quantitative analyses of trabecular parameters (BV/TV, Tb. N, Tb. Th, Tb Sp, and Tb. BMD) and cortical bone parameters (Ct. Th, BA/TA, Ct. BMD). n=7. F) Three-point bending test of femurs. Stiffness and max load of femurs were present. n=7. G) Representative microphotographs and quantitative analyses of immunohistochemistry (IHC) staining for osteocalcin (OCN) from femur sections. Scale bar, 100 μm. n=6. H) Representative images of calcein and xylenol orange double labeling of cortical bone in femur and quantification of mineral apposition rate (MAR). Scale bar, 50 μm. n=7. I) Representative images of TRAP staining of osteoclasts and quantification of osteoclast number per bone surface (Oc. N/BS) in femur at week 3 and week 9 post OVX surgery. The stained osteoclasts are indicated by arrows. Scale bar, 100 μm. n=5~7. J) Serum levels of procollagen type I intact N-terminal propeptide (PINP) and C-terminal telopeptide of type 1 collagen (CTX-1) at week 3 and week 9 post OVX surgery. n=5-9. Data were shown as Mean ± SD. One-way ANOVA was used with Bonferroni multiple comparisons test. *p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001. N.S.: not significant.

Source: Wang H, Lin S, Feng L, Huang B, Lu X, Yang Z, Jiang Z, Li YC, Zhang X, Wang M, Wang B, Kong L, Pan Q, Bai S, Li Y, Yang Y, Lee WYW, Currie PD, Lin C, Jiang Y, Chen J, Tortorella MD, Li H, Li G*. Low-Dose Staphylococcal Enterotoxin C2 Mutant Maintains Bone Homeostasis via Regulating Crosstalk between Bone Formation and Host T-Cell Effector Immunity. Advanced Science. 2023;10(28). doi: 10.1002/advs.202300989.



STEM CELLS AND TISSUE REGENERATION

STEM CELL AND VASCULAR REGENERATION

幹細胞及組織再生研究

PRINCIPAL INVESTIGATOR

Kathy Lui

TEAM MEMBERS

Zhangjing Ma, Wenchu Ye, Xiaoyun Cao, Lilin Li, Wentao Gao, Lei Cui, Panhong Liang, Hang Qu, Cheng Kiu Ho, Yangfeng Hou, Jitao Liu, Jiali Lin, Anna Chan, Jianfeng Pang, Binglin Lai

RESEARCH PROGRESS SUMMARY

Research on the molecular mechanisms underlying neonatal heart regeneration

The mammalian adult heart is notorious for its inability to regenerate; however, the neonatal one can transiently yet functionally regenerate after severe injuries within the first week after birth in both mice and humans. Therefore, it has been dreamed that one can recapitulate the cellular and molecular mechanisms underlying neonatal heart regeneration to promote cardiac repair in the adult counterpart after injuries. Neonatal cardiomyocytes are more immature and can re-enter the cell cycle after injury. Alongside heart development, other biological changes such as thyroid hormone level and maturation of heterogeneous immune cells such as macrophage and $CD4^+$ regulatory T cells (Tregs) as described by **Kathy Lui** and her team earlier (Li J et al., *Theranostics*, 2019) also take place that are reported to control cardiomyocyte proliferation and heart regeneration. Recently, Tregs have been demonstrated to drive the regeneration of multiple organ systems. For instance, they have shown that they can induce blood vessel regeneration by promoting apelin-mediated sprouting angiogenesis even in type-2 diabetic mice. In the heart, the team has also functionally demonstrated that $CD4^+$ but not $CD8^+$ T cells regulate its regeneration. In particular, Tregs are indispensable for promoting neonatal heart regeneration. In *Foxp3-hCD2* mice, $Foxp3^+$ Treg can be purified and subjected to lytic antibody-mediated ablation as they express human CD2 on the cell surface. They have demonstrated that adoptive transfer of splenic $hCD2^+$ Treg from *Foxp3-hCD2* mice contributes to neonatal heart regeneration as evidenced

by reduced cardiac fibrosis, increased fractional shortening and enhanced ejection fraction in Treg-deficient NOD/SCID mice. On the other hand, specific depletion of Treg via anti-hCD2 lytic antibody leads to increased cardiac fibrosis and impaired regeneration of the P3 heart of *Foxp3-hCD2* mice. These findings indicate a direct role of Treg in driving neonatal heart regeneration.

As a master regulator of immune tolerance, neonatal CD4+ T cells have an intrinsic "default" mechanism to become Tregs in response to T-cell receptor stimulations within 2 weeks after birth. They also function better than their adult counterparts in self-tolerance. While Tregs can be found in the neonatal heart, they are rarely found in the aging heart compared with other regenerative organs such as the liver as detected by their recent single-cell (sc)RNA-sequencing analysis (Journal Cover and highlighted article: Yang et al., *Journal of Leukocyte Biology*, 2024). Whether there are more resident Tregs in the neonatal than adult heart remains unclear. Tregs are recruited to the adult heart after myocardial infarction (MI) and the loss of which impairs heart repair. The infarcted heart and its draining lymph nodes also promote Tregs differentiation. Unlike in neonates, however, Tregs are insufficient to drive adult heart regeneration. Whether Tregs plasticity controls adult heart repair after MI, and their action mechanisms in heart repair and regeneration remain largely unknown. Altogether, these findings suggest that Tregs are important regulators of heart regeneration. In the meanwhile, they have been working to dissect the molecular mechanisms underlying Treg-mediated heart regeneration; and Treg residency and plasticity in the heart during development and disease.

Research on endothelial to hematopoietic transition

During embryonic development, endothelial cells (ECs) are differentiated into distinct endothelial subsets lining the arteries, veins, capillaries, and lymphatics of the vascular system through vasculogenesis and angiogenesis. In addition to maintenance of the vascular endothelial fate, a small subset of ECs termed hemogenic ECs (HE) acquire hemogenic potential and are converted to hematopoietic cells to support the generation of the first hematopoietic stem cells (HSCs) that sustain lifelong hematopoiesis. A landmark study has revealed that mouse embryos lacking *Flk1*, a tyrosine kinase required for endothelial development, die without both endothelial and hematopoietic cells. The generation of definitive erythro-myeloid progenitors (EMPs) and hematopoietic stem and progenitor cells (HSPCs), precursors of HSCs, are dependent on endothelial-to-hematopoietic transition (EHT), which takes place in the yolk sac (YS) at embryonic day (E)8.5-9.5 and the aorta-gonad-mesonephros (AGM) region at E10.5. Specifically, YS HE gives rise to definitive EMPs during transient definitive hematopoiesis, and AGM HE generates HSPCs during definitive hematopoiesis.

Recently, Mettl3-mediated m^{6}A RNA methylation has been reported to regulate HSPC generation through repressing Notch signaling in arterial ECs in zebrafish and mice (Lv et al., *Cell Research*, 2018; Zhang et al., *Nature*, 2017). Interestingly, the team found that the conclusion reported might not be entirely correct due to the fact that m^{6}A RNA methylation also regulates the process beyond EHT. The genetic tools used in previous work did not exclude the possibility of its regulation at the later stage. They have been finalising results for submission to clarify this important concept in the field. For review, they have also published a summary of the reported findings on m^{6}A contribution to normal and malignant hematopoiesis (Ma et al., *Journal of Leukocyte Biology*, 2024).

Research output and international recognition

In 2023, the team has been training 7 PhD and 1 MPhil students, 3 research assistants and 4 postdoctoral fellows, they have made significant progress and published 8 papers (listed in the below section) during the reporting period. Kathy has also secured 2 new grants as co-PI under the Research Grants Council Young Collaborative Research Fund and Research Grants Council Theme-based Research Scheme. In terms of serving the scientific community globally, she continues to serve as an Editorial Board Member for *Circulation Research* (American Heart Association) and *Cardiovascular Research* (European Society of Cardiology). She also helps in reviewing international grants under the Sir Henry Dale Fellowship for the Wellcome Trust of the United Kingdom; the Spark Funding Scheme for the Swiss National Science Foundation; the New Talent Programme for the Dutch Research Council; the Seed Fund for the United Kingdom Dunhill Medical Trust; the United Kingdom NC3R Grant; China's National Natural Science Foundation of China General Programme; Research Grants Council – General Research Fund as well as Macau University's General Research Grant. In terms of building an international reputation, Kathy has been invited to give lectures in person. She has given talks at the 1st Joint International Symposium on YY1 Research in Catania, Italy; the 34th Great Wall International Congress of Cardiology, Beijing, China; and the 15th Chinese Society of Immunology Annual Meeting in Suzhou, China. She has also given a few invited lectures including at Fudan University, Shanghai Jiaotong University and Tokyo University. Overall, their research work has attracted some international, regional and local recognition. They will continue to contribute to Science and serve their scientific community in 2024.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Zhangjing Ma	Young Investigator Award	The Hong Kong Society for Immunology

Academic Editorships

Name	Details	
	Role	Journal
Kathy Lui	Editorial Board Member	Circulation Research (American Heart Association)
		Cardiovascular Research (European Society of Cardiology)
		Immunology Letters (Journal for the European Federation of Immunology Societies)
	Review Editor	Frontiers in Immunology

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Kathy Lui	Journal Reviewer	Nature Cardiovascular Research
		Nature Communications
		European Heart Journal
		Circulation Research
		Cardiovascular Research
		Science China Life Science
	Abstract Reviewer	International Society for Stem Cell Research Annual Meeting

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Kathy Lui	Development of Therapeutic CRISPR-Cas Enzymes for Gene Therapy	Research Grants Council – Collaborative Research Fund	30/06/2023	29/06/2026	4,691,202
	Molecular Mechanisms Underlying T-cell Regulation of Vascular Disease, Repair and Regeneration	Research Grants Council – Research Fellowship Scheme	01/01/2023	31/12/2027	5,155,380

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Kathy Lui	Aging, Skeletal Degeneration and Regeneration	Research Grants Council – Areas of Excellence (AoE) Scheme	01/05/2021	30/04/2029	64,889,000
	Regulation of Insulin Synthesis in Pancreatic Beta Cells by Targeting Transcription Factor: A Preclinical and Translational Study	The Chinese University of Hong Kong – Research Committee Postdoctoral Fellowship Scheme	12/05/2022	10/05/2026	750,000
	Studying the Role of m6A RNA Modification in Vascular Diseases and Regeneration	National Natural Science Foundation of China – Research Fund	01/01/2021	31/12/2024	RMB 550,000
	Studying the Functional Mechanism of YY1 in the Regulation of Glucose Metabolism in Pancreatic Beta Cells through O-GlcNAcylation	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,325,732
	Unraveling the Impact of Hyperglycemia on Human Second Heart Field Development	Croucher Foundation – Croucher Innovation Awards	01/01/2017	31/12/2024	5,000,000
	Studying the Functional Mechanism of Endothelial YY1 in Postischemic Angiogenesis	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,195,542
	Studying the Role of m6A mRNA Modification in Endothelial to Hematopoietic Transition and Hematopoietic Cell Development	The Chinese University of Hong Kong – Research Committee Direct Grants	30/06/2022	29/06/2023	70,000

Publications

A. Journal Papers

1. Zhang S, Zhang Q, Liu Z, Liu K, He L, Lui KO, Wang L, Zhou B. Genetic dissection of intercellular interactions in vivo by membrane-permeable protein. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(1):e2120582120. doi:10.1073/pnas.2120582120.

2. Liu K, Tang M, Xu W, Meng X, Jin H, Han M, Pu J, Li Y, Jiao F, Sun R, Shen R, Lui KO, Lu L, Zhou B. An inducible hACE2 transgenic mouse model recapitulates SARS-CoV-2 infection and pathogenesis in vivo. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(25):e2207210120. doi:10.1073/pnas.2207210120.

3. Han M, Liu Z, Liu L, Huang X, Wang H, Pu W, Wang E, Liu X, Li Y, He L, Li X, Wu J, Qiu L, Shen R, Wang QD, Ji Y, Ardehali R, Shu Q, Lui KO, Wang L, Zhou B. Dual genetic tracing reveals a unique fibroblast subpopulation modulating cardiac fibrosis. *Nature Genetics*. 2023;55(4):665-678. doi:10.1038/s41588-023-01337-7. (Epub ahead of print)

4. Liu K, Jin H, Zhang S, Tang M, Meng X, Li Y, Pu W, Lui KO, Zhou B. Intercellular genetic tracing of cardiac endothelium in the developing heart. *Developmental Cell*. 2023;58(16):1502-1512.e3. doi:10.1016/j.devcel.2023.05.021.

5. Li X, Ma Z, Lui KO. A differentiation protocol for the generation of pancreatic beta-like cells from human embryonic stem cells. *STAR Protocols*. 2023;4(3):102407. doi:10.1016/j.xpro.2023.102407.

6. Ma Z, Sugimura R, Lui KO. The role of m^{6}A mRNA modification in normal and malignant hematopoiesis. *Journal of Leukocyte Biology*. 2024;115(1):100-115. doi:10.1093/jleuko/qiad061. (Review)

7. Yang KY, Liao J, Ma Z, Tse HF, Lu L, Graca L, Lui KO. Single-cell transcriptomics of Treg reveals hallmarks and trajectories of immunological aging. *Journal of Leukocyte Biology*. 2024;115(1):19-35. doi:10.1093/jleuko/qiad104. (Epub ahead of print)

8. Lui KO, Ma Z, Dimmeler S. SARS-CoV-2 induced vascular endothelial dysfunction: Direct or indirect effects? *Cardiovascular Research*. Published online December 30, 2023. doi:10.1093/cvr/cvad191. (Review, Epub ahead of print)



Cover of the January Issue 1, 2024 as a highlighted article by Yang et al., *Journal of Leukocyte Biology*, 2024.
Source: Journal of Leukocyte Biology



Kathy gave an invited talk at the 1st Joint International Symposium on YY1 Research in Catania, Italy.
Source: Kathy Lui



Kathy gave an invited talk at the 34th Great Wall International Congress of Cardiology, Beijing, China.

Source: Kathy Lui



Kathy gave an invited talk at the 15th Chinese Society of Immunology Annual Meeting in Suzhou, China.

Source: Kathy Lui



STEM CELLS AND TISSUE REGENERATION

幹細胞及組織再生研究

PRINCIPAL INVESTIGATOR

Wayne Lee

TEAM MEMBERS

Dorsa Dehghanbaniani, Belle Wang, Nicodemus Wong, Kenneth Yang, Tsz Lam Yiu, Ericsson Fung, Wei Ting Hsiao, Jessica Lo, Zhe Zhang, Gen Tang

RESEARCH PROGRESS SUMMARY

Wayne Lee and his research team study the roles of osteocyte in various musculoskeletal problems, including adolescent idiopathic scoliosis (AIS), and age-related disorders such as osteoarthritis and osteoporosis. For instance, the team has established various research platforms for the study of osteocytes, including FITC-Imaris imaging, acid-etched SEM, and human primary osteocyte culture model to study cellular response upon mechanical stimulation. In their AIS research, the team is employing multi-omics approach such as transcriptomic, proteomic and metabolomic to identify candidate genes that contribute to the progression of spinal deformity in AIS. Additionally, the team has developed a new mouse model of scoliosis which will aid in further understanding the underlying mechanism of this clinical problem. They have also discovered two potential drug candidates and are currently conducting pre-clinical validation studies to assess their effectiveness. In their cell therapy research, as a registered authorised person for advanced therapy product, Wayne also focuses on the development of cell therapy clinical trial for various neuro-musculoskeletal disorders. The team is working towards scaling up the production of mesenchymal stem cells while maintaining the quality and potency of the cell therapy product.

RESEARCH AND SCHOLARSHIP

Research Award and Recognition

Name	Details	
	Award	Organisation
Ashley Wong	The Best Paper Award for Trainee Member	The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA) 2023

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Wayne Lee	Reviewer	Journal of Orthopaedic Translation
		Stem Cell Research & Therapy
		Experimental & Molecular Medicine

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Wayne Lee	Exploration of Effects and Molecular Mechanism of Ginkgolide B in Treating Ageing-related Osteoporosis	Research Grants Council Hong – General Research Fund	01/01/2021	31/01/2023	920,567
	Enhancing Cell Therapy Efficacy by High-efficiency Quantitative Mitochondrial Transfer Technique	The Chinese University of Hong Kong – Strategic Seed Funding for Collaborative Research Scheme (SSFCRS)	01/11/2023	31/10/2025	500,000
	Exploring Bone Tissue Architecture Using Spatial Transcriptomics	The Chinese University of Hong Kong – Direct Grant	30/06/2023	29/06/2024	50,000
	lncRNA H19 Modulates Osteoarthritis Development via Subchondral Bone Remodelling and Osteocyte Responses to Mechanical Stimulation?	Research Grants Council – General Research Fund	01/08/2022	31/07/2025	1,172,904
	Can Honokiol, A Sirt3 Activator, Enhances the Effect of Vitamin D on Age-related Bone and Muscle Loss?	Health Bureau – Health and Medical Research Fund	01/08/2023	31/07/2025	1,131,368
	ASBMR 2020 Rising Star Award	The American Society for Bone and Mineral Research	01/11/2020	31/10/2023	466,800
	Bone Aging and Osteocyte Biology	The Chinese University of Hong Kong – Improvement on Competitiveness in Hiring New Faculties' Funding Scheme	01/08/2020	31/07/2023	1,106,667
	For the Acquisition and Maintenance of MARS Preclinical Spectral CT System	Research Grants Council – Research Matching Grant Scheme	22/05/2019	30/06/2025	2,001,104
	Enhancing the Therapeutic Effect of Bracing for Adolescent Idiopathic Scoliosis with A Hybrid Bracing Protocol: A Randomized-Controlled Trial	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	977,708
	Decellularized Scaffolds for Bone and Cartilage Regeneration	Innovation and Technology Commission – Innovation and Technology Fund	01/08/2021	31/01/2024	2,081,500
	Clinical Trials of Innovative Strategies for Musculoskeletal Regeneration	Innovation and Technology Commission – InnoHK Scheme	01/03/2022	28/02/2027	12,837,000
	Validation of A Novel Clinical Prognostic Model in Facilitating the Implementation of Risk Stratification Approach for Triaging Scoliosis Clinic Workflow During COVID-19 Pandemic	Health Bureau – Health and Medical Research Fund	01/10/2021	30/09/2024	1,174,472
	Aging, Skeletal Degeneration and Regeneration	Research Grants Council – Area of Excellence Scheme	01/05/2021	30/04/2029	70,688,000

Publications

A. Journal Papers

1. Wu Z, Yang KG, Lam TP, Cheng JCY, Zhu Z, Lee WY. Genetic insight into the putative causal proteins and druggable targets of osteoporosis: A large-scale proteome-wide mendelian randomization study. *Frontiers in Genetics*. 2023;14:1161817. doi:10.3389/fgene.2023.1161817.

2. Wang H, Lin S, Feng L, Huang B, Lu X, Yang Z, Jiang Z, Li YC, Zhang X, Wang M, Wang B, Kong L, Pan Q, Bai S, Li Y, Yang Y, Lee WYW, Currie PD, Lin C, Jiang Y, Chen J, Tortorella MD, Li H, Li G. Low-dose staphylococcal enterotoxin C2 mutant maintains bone homeostasis via regulating crosstalk between bone formation and host T-cell effector immunity. *Advanced Science*. 2023;10(28). doi:10.1002/advs.202300989.

3. Wang BYH, Hsiao AWT, Shiu HT, Wong N, Wang AYF, Lee CW, Lee OKS, Lee WYW. Mesenchymal stem cells alleviate dexamethasone-induced muscle atrophy in mice and the involvement of ERK1/2 signalling pathway. *Stem Cell Research and Therapy*. 2023;14(1). doi:10.1186/S13287-023-03418-0.

4. Li Y, Li L, Wang M, Yang B, Huang B, Bai S, Zhang X, Hou N, Wang H, Yang Z, Tang C, Li Y, Lee WYW, Feng L, Tortorella MD, Li G. O-alg-THAM/gel hydrogels functionalized with engineered microspheres based on mesenchymal stem cell secretion recruit endogenous stem cells for cartilage repair. *Bioactive Materials*. 2023;28:255-272. doi:10.1016/j.bioactmat.2023.05.003.

5. Li Y, Li L, Li Y, Feng L, Wang B, Wang M, Wang H, Zhu M, Yang Y, Waldorff EI, Zhang N, Viohl I, Lin S, Bian L, Lee WYW, Li G. Enhancing cartilage repair with optimized supramolecular hydrogel-based scaffold and pulsed electromagnetic field. *Bioactive Materials*. 2023;22:312-324. doi:10.1016/j.bioactmat.2022.10.010.

6. Wang BYH, Hsiao AWT, Wong N, Chen YF, Lee CW, Lee WYW. Is dexamethasone-induced muscle atrophy an alternative model for naturally aged sarcopenia model? *Journal of Orthopaedic Translation*. 2023;39:12-20. doi:10.1016/j.jot.2022.11.005.

7. Yang KG, Goff E, Cheng Klo, Kuhn GA, Wang Y, Cheng JCY, Qiu Y, Müller R, Lee WYW. Abnormal morphological features of osteocyte lacunae in adolescent idiopathic scoliosis: A large-scale assessment by ultra-high-resolution micro-computed tomography. *Bone*. 2023;166. doi:10.1016/j.bone.2022.116594.

B. Conference Papers

1. Yang GP, Lee WYW, Hung ALH, Cheng JCY, Lam TP. Prediction of Curve Progression in Adolescent Idiopathic Scoliosis with Bone Microarchitecture Phenotyping by an Unsupervised Machine Learning Protoco. Scoliosis Research Society (SRS) 58th Annual Meeting; Sep 6-9, 2023; Seattle, Washington, USA.

2. Yang GP, Kumar A, Cheng JCY, Lam TP. Unsupervised machine learning mediated clustering of bone microarchitecture phenotypes in the predicti on of curve progressionto surgical threshold in adolescent idiopathic scoliosis – A 6-year longitudinal study up to skeletal maturity. 2023 Annual Meeting of Pediatric Orthopaedics Society of North America (POSNA); Apr 26-29, 2023; Nashville, Tennessee.

3. Wang RL, Ong MTY, Chan VHF, Li G, Lee WYW. Novel Role of Lncrna H19 In Osteoarthritis Development Via Modulating Subchondral Bone Remodeling And Osteocyte Responses to Mechanical Stimulation. Orthopaedic Research Society; Feb 10-14, 2023; Dallas, Texas.

4. Wang R. Targeting lncRNA H19 by magnetic metal-organic frameworks to ameliorate abnormal subchondral bone remodeling and cartilage degradation in osteoarthritis. TERMIS-AP 2023 conference; Oct 16-19, 2023; Hong Kong.

5. Lo HTJ, Yiu TL, Mok KWD, Wong MS, Lee WYW. Cyp27b1 ablation in skeletal muscle impairs muscle regeneration. 16th International Conference; Jun 17-19, 2023; Cachexia, Sarcopenia & Muscle Wasting. Stockholm.

6. DehghanBaniani D, Mehrjou B, Chu PK, Lee WYW, Wu HK. A nanopatterned silk-based composite with sustained release of kartogenin for tissue engineering of articular cartilage superficial zone. Tissue Engineering and Regenerative Medicine International Society - European Chapter Meeting 2023 (TERMIS-EU 2023); Mar 28-31, 2023; Manchester, UK.

7. Zhang Z, Lau AYC, Yang GP, Hung ALH, Lam TP. Lower CYP27B1 expression in osteocytes increases the risk of scoliosis curve progression in a mouse model – A new insight to improve bone quality in Adolescent Idiopathic Scoliosis. The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

8. Yang GP, Lau AYC, Hung ALH, Lee WYW, Kumar A, Wan CWR, Lam TP, Cheng JCY. Can we predict curve progression in adolescent idiopathic scoliosis patients with Cobb angles < 10°: A pilot study with vertebra vector sequencing by recurrent neural networks (RNN)? The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

9. Yang GP, Lau AYC, Hung ALH, Lam TP, Cheng CY. Novel AI machine learning algorithm with volumetric bone quality and microarchitecture cluster phenotyping in the early prediction of curve progression and progression to surgical threshold in Adolescent idiopathic Scoliosis – A 6-year longitudinal study till skeletal maturity and beyond. The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

10. Wong C, Pak THC, Cheng JKH, He BY, Lau AYC. Online Mindfulness Intervention to Enhance Psychosocial Well-being for Adolescent IdiopathicScoliosis (AIS) – A Pilot Randomized Single-blinded Controlled Trial. The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

11. Wang R, Wong AYY, Mehrjou B, DehghanBaniani D, Ong MTY, Chan VHF, Li G, Chu PKH, Lee WYW. Targeting subchondral bone osteocytes by magnet guided anti-H19 delivery for osteoarthritis treatment: A preclinical study. The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

12. Sheng YA, Lau AYC, Yang GP, Hung ALH, Lee WYW. Role of sagittal plane malalignment on the etiopathogenesis of frontal plane deformity in idiopathic scoliosis - A prospective longitudinal study. The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

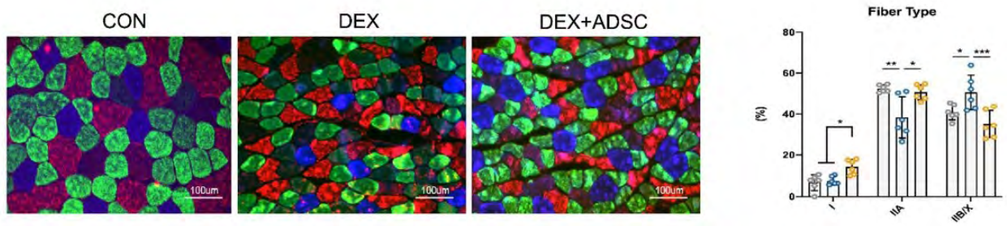
13. Lo HTJ, Yiu TL, Mok DKW, Wong MS, Lee WYW. A preclinical study exploring the Link between Vitamin D and Muscle Function in aging muscle. The 43rd Annual Congress of The Hong Kong Orthopaedic Association (HKOA 2023); Nov 4-5, 2023; Hong Kong.

14. Yang GP, Lau AYC, Hung ALH, Lee WYW, Kumar A, Wan CWR, Lam TP, Cheng JCY. Prediction of curve progression and progression to surgical threshold in adolescent idiopathic scoliosis with bone microarchitecture phenotyping by an unsupervised machine learning protocol – A 6-year longitudinal study till skeletal maturity and beyond. ASBMR 2023 Annual Meeting; Oct 13-16, 2023; Vancouver, Canada.

15. Wang R, Mehrjou B, DehghanBaniani D, Ong MTY, Chan HF, Li G, Chu PK, Lee WYW. Novel Role of IncRNA H19 in Osteoarthritis Subchondral Bone Remodeling and Treatment. ASBMR 2023 Annual Meeting; Oct 13-16, 2023; Vancouver, Canada.

16. Hsiao WT, Lee CW, Lee WYW. High-fat Diet Induced Skeletal Muscle Metabolic Memory and Its Implication in Hyperglycemia and Associated Muscle Atrophy. ASBMR 2023 Annual Meeting; Oct 13-16, 2023; Vancouver, Canada.

A.



Effect of adipose derived mesenchymal stem cells (ADSCs) treatment in controlling muscle fibre type switching (A-B) Immunofluorescence staining and quantification for fibre types in GA muscle sections. Blue: type I; green: type IIA; red: type IIB; black: type IIX staining (A). n = 6 per group. Statistical analysis are performed using one-way ANOVA test, with significance set at $P < 0.05$ (*$P < 0.05$, **$P < 0.01$, ***$P < 0.005$, #$P < 0.001$)

Source: ***Wang BYH, Hsiao AWT, Shiu HT, Wong N, Wang AYF, Lee CW, Lee OKS, Lee WYW. Mesenchymal stem cells alleviate dexamethasone-induced muscle atrophy in mice and the involvement of ERK1/2 signalling pathway. Stem Cell Research and Therapy. 2023;14(1). doi:10.1186/S13287-023-03418-0.***

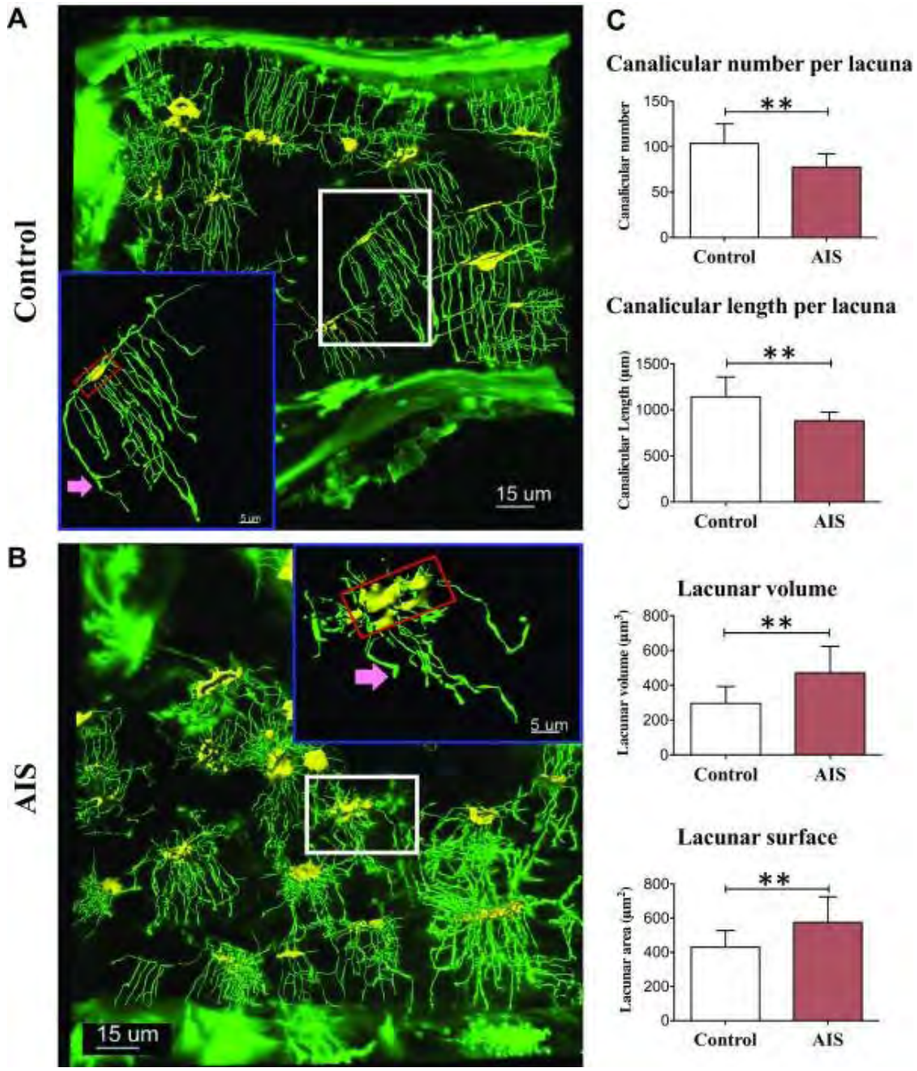


Illustration of the components of the osteocyte lacuno-canalicular network (LCN) visible in the confocal microscope. The lacunae are highlighted as yellow masses, and the canaliculi are displayed as green lines in the Imaris 3D images. Representative Imaris-aided visualisation of osteocyte cell body (yellow) and dendrite process (green) and volume rendering of FITC-stained undecalcified bone tissues with z-stack confocal images collected at 0.2-μm intervals. A, B) High magnification of boxed areas depicted individual LCN in the iliac bone tissues from control (A) and patients with AIS (B) (insert).

Source: Chen H, Zhang J, Wang Y, Cheuk KY, Hung ALH, Lam TP, Qiu Y, Fong JQ, Lee WYW, Cheng JCY. Abnormal lacuno-canalicular network and negative correlation between serum osteocalcin and Cobb angle indicate abnormal osteocyte function in adolescent idiopathic scoliosis. FASEB Journal. 2019;33(12):13882-13892. doi:10.1096/fj.201901227r.



BIOMATERIAL, CHEMICAL BIOLOGY AND DRUG TRANSLATIONAL RESEARCH

INNOVATIVE ORTHOPAEDIC BIOMATERIAL AND DRUG TRANSLATIONAL RESEARCH

生物材料，化學生物學及藥物轉譯研究

PRINCIPAL INVESTIGATOR

Ling Qin

TEAM MEMBERS

Jiankun Xu, Wenxue Tong, Delon Hsueh, Hao Yao, Lizhen Zheng, Bingyang Dai, Xu Li, Ziyi Chen, Qida Zhang, Li Zou, Liangbin Zhou, Xiaodan Chen, Liang Chang, Yuantao Zhang, Shunxiang Xu, Jiaxin Guo, Lei Lei, Yuanming An, Haozhi Zhang, Xin Chen, Tongzhou Liang, Shi'an Zhang, Junzheng Yang, Zheyu Jin, Naping Xiong, Zhenkang Wen, Hongwei Shao, Qing Lu, Weiyang Liu, Qinyu Tian, Zhengming Shan, Fanchu Zeng

RESEARCH PROGRESS SUMMARY

During the 2023 reporting period, **Ling Qin** was elected as a member of Academia Europaea (Clinical and Veterinary Section). He was also listed as the World's Top 2% Scientists and the Best Medicine Scientists (Top 5 in the field of Orthopaedics) in China, indicating that their study of magnesium-based orthopedic implants and tissue regeneration materials has been widely recognised both internationally and nationally.

Academic research achievements

The team is now working on more than 10 scientific programs, including projects of Areas of Excellence (AOE), National Natural Science Foundation of China – Research Grant Council Joint Research Scheme (NSFC-RGC), Innovation and Technology Commission-Mainland – Hong Kong Joint Funding Scheme (ITC-MHKJFS), etc. During 2023, they

published 25 peer-reviewed papers, 13 of them with impact factors over 10. Representative original research articles were published in (i) Advanced Functional Materials (burnt skin healing and tissue regeneration promoted by Magnesium Silicate); (ii) Advanced Science (arthritis alleviation by blocking infrapatellar fat pad Osteopontin-integrin β3 signalling); (iii) Advanced Materials (postsurgical osteosarcoma treatment using 3D printed MgO_2/PLGA Scaffold) and (iv) Materials Today (in-vivo characterisation of vacuum coacervate mediated bimodal control release for macromolecule drugs). Two representative review articles were published in Bioactive Materials (a. advanced hydrogel systems for mandibular; b. biochemical cues for articular cartilage repair)

Meanwhile, the research advances of Ling's team were presented at multiple international and local academic conferences, including the Orthopaedic Research Society Annual Meeting 2023 (ORS 2023, Feb, US); International Chinese Musculoskeletal Research Conference-Oxford (Oxford-ICMRS Symposium 2023, Aug, UK); Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Conference 2023 (TERMIS-AP 2023, Oct, HK); China Biomaterials Congress 2023 (CSBM 2023, Oct, China) and Hong Kong Orthopaedic Association conference 2023 (HKOA-2023, Nov, HK). Team members have received 6 oral or poster presentation awards during the conferences.

Translational research achievements

According to the study plan of the AOE project, to push forward the Class III medical device registration of magnesium-based orthopaedical implants at the National Medical Products Administration (NMPA), *Medical Magnesium Led. (Hong Kong)* and *CnMg Med Tech Ltd. (Shenzhen)* were established by the team this year and related patents were transferred out from the Chinese University of Hong Kong (CUHK). In the fourth quarter of 2023, *CnMg Med Tech Ltd.* signed contracts officially with the Original Equipment Manufacturer (OEM) *Ultracare Co. Ltd.* for the design and production of Magnesium-based hybrid devices. *CnMg Med Tech Ltd.* also officially signed contracts with third-party Contract Research Organisation (CRO) *RAMED (Beijing) Medical Technology Co., Ltd.* to promote multi-center clinical trials of magnesium-based hybrid devices, which was a milestone for the AOE project.

During the reporting period, translational research projects of Ling's team were exhibited in multiple international and national invention exhibitions. Invention of Magnesium-based hybrid device was awarded the gold medal at the Middle East International Invention Exhibition and the first-class prize in science and technology from the Chinese Society of Biomaterials. New magnesium-based implant designs also gained silver and bronze medals at the International Exhibition of Inventions Geneva 2023. Bioactive ligament initiated by their students won the gold medal in the 2023 9th "Internet +" China International College Student Innovation and Entrepreneurship Competition and champion in the 2023 10th "Creating Youth" Guangdong-Hong Kong-Macao Greater Bay Area Youth Innovation and Entrepreneurship Competition, suggesting the great translational potential of these projects.

National and international collaboration achievements

In March 2023, the Chinese University of Hong Kong (CUHK)-Shenzhen Innovation and Technology Research Institute (Futian) (FITRI) was officially launched with Ling as the Director of FITRI. Based on the cooperation between CUHK and the Shenzhen Futian Government, the main objective of FITRI is to facilitate Hong Kong's integration into the development of the Great Bay Area (GBA) and further promote national translational research collaborations.

In December 2023, taking the opportunity of Qin's election as a member of Academia Europaea (AE), he also joined the Translational Medicine Working Group of AE. Ling, as the Executive Director of TEA-NET, signed a memorandum of understanding to establish the Translational European-Asian Network (TEA-NET) initiative together with three other members of AE, András Varró, chairman of the National Academy of Scientist Education; Ole Petersen, representative of Academia Europaea and Béla Merkely, the rector of Semmelweis University. The mission of TEA-NET is to facilitate Europe-Asia collaborations and foster a vibrant platform for the training of outstanding research and clinical scientists dedicated to translational medicine research.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Ling Qin	2023 International Invention Fair in the Middle East Gold Medal	Kuwait Science Club
	2023 Special Edition of the Geneva International Exhibition of Inventions (Silver Medal)	International Exhibition of Inventions Geneva 2023
	中國生物材料學會科學技術獎一等獎	中國生物材料學會
Jiankun Xu	2023 Special Edition of the Geneva International Exhibition of Inventions (Bronze Medal)	International Exhibition of Inventions Geneva 2023
	2023 TERMIS-AP Best Poster Presentation Award (General)	Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter Conference 2023
	中國生物材料學會科學技術獎一等獎	中國生物材料學會
Yuantao Zhang	2023 ICMRS Webster Jee Young Investigator Award	International Chinese Musculoskeletal Research Society
	2023 ORS Best Poster Award	Orthopaedic Research Society
Bingyang Dai Shunxiang Xu	2023 TERMIS-AP Best Oral Presentation Award	Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter Conference 2023
Jiaxin Guo	2023 TERMIS-AP Virtual Student Paper Contest Golden Award	Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter Conference 2023
	Student Travel Achievement Recognition of Society for Biomaterials	Society for Biomaterials
Jiaxin Guo Liang Chang Xin Chen Naping Xiong Zheyu Jin	Professor Charles K. Kao Student Creativity Awards 2023, Merit Award, Postgraduate Group	The Office of Research and Knowledge Transfer Services & Centre for Entrepreneurship, The Chinese University of Hong Kong
張昊智 代冰洋 張元濤 安苑銘 陳鑫 雷蕾 溫鎮康	2023 年第九屆“互聯網 +”中國國際大學生創新創業大賽金獎	香港新一代文化協會
	2023 年第十屆“創青春”粵港澳大灣區青年創新創業大賽冠軍	廣東省青年聯合會

Fellowships

Name	Details	
	Fellowship	Organisation
Ling Qin	Membership	Academia Europaea
	Fellow	American Institute of Medical and Biological Engineering
		American Society for Bone and Mineral Research

Name	Details	
	Fellowship	Organisation
Ling Qin	Fellow	International Combined Orthopaedic Research Society
		International Union of Societies for Biomaterials Science and Engineering

Academic Editorships

Name	Details	
	Role	Journal
Ling Qin	Editor-in-Chief	Journal of Orthopaedic Translation
Ling Qin	Editorial Board Member	Journal of Bone and Mineral Research
		International Journal of Sports Medicine
		Journal of Neuro-musculoskeletal Interaction
		eCM (Switzerland)
Jiankun Xu	Editorial Board Member	Journal of Orthopaedic Translation
	Guest Associate Editor	Frontiers in Immunology

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Ling Qin	Reviewer	International Immunopharmacology
		ACS Applied Polymer Materials
		Bone Research
		Journal of Magnesium and Alloys
		Regenerative Biomaterials
		Bioactive Materials
		Advanced Materials
		American Journal of Sports Medicine
		Life Sciences
		Bioactive Materials
		Advanced Science
		Advanced Healthcare Materials
		Bioactive Materials
		Orthopaedic Journal of Sports Medicine
		Regenerative Biomaterials
		中華骨與關節外科雜誌
Jiankun Xu	Reviewer	Biomaterials
		Bioactive Materials
Jiankun Xu	Reviewer	Advanced Healthcare Materials
		Journal of Orthopaedic Translation
		Journal of Magnesium and Alloys
		Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter Conference 2023
Jiankun Xu Wenxue Tong	Judge for Selecting Best Oral/Poster Presentations	Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter Conference 2023
Wenxue Tong	Reviewer	Journal of Orthopaedics, Trauma and Rehabilitation
		Cartilage
		Frontiers in Medicine
		The Journal of Infection in Developing Countries
		Advanced Science
		Advanced Engineering Materials
		Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter Conference 2023
Lizhen Zheng	Reviewer	Frontiers in Genetics
		Materials Today Bio
		Heliyon
		International Journal of Biological Macromolecules
		Bioactive Materials
Bingyang Dai	Reviewer	Acta Biomaterialia
		MedComm
		Journal of Orthopaedic Translation
Xin Chen	Reviewer	Journal of Magnesium and Alloys

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ling Qin	Aging, Skeletal Degeneration and Regeneration	Research Grants Council – Areas of Excellence	01/05/2021	30/04/2029	70,680,000
	Magnesium Activated Progenitor Cells in Synovial Fluid to Regenerate Articular Cartilage	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,174,492
	Identification of a Central to Sympathetic Neural Circuit in Magnesium-promote Bone Regeneration using Retrograde Tracing and Single-cell RNA-seq	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,126,379
	Differential Roles of CGRP in Osteoarthritic Pain and Pathology	National Natural Science Foundation of China/Research Grant Council Joint Research Scheme	01/01/2022	31/12/2025	1,185,561
	Multifunctional Bioactive 3D-printed Scaffold as an All-in-one Platform for Postsurgical Osteosarcoma Treatment and Bone Defect Repair	Innovation and Technology Commission – Mainland-Hong Kong Joint Funding Scheme	01/11/2021	31/10/2023	1,900,000
Jiankun Xu	An Innovative Strategy Recapitulates the Neuropeptide-Guided Angiogenic-Osteogenic Coupling for Functional Repair of Segmental Bone Defect	Research Grants Council – General Research Fund	01/01/2022	31/12/2023	1,175,052
	Fibroblasts as a Novel Therapeutic Target for Enhancing the Healing of Challenging Bone Fractures	Health Bureau – Health and Medical Research Fund	01/08/2021	31/07/2024	1,499,980
	Role of Piezo1 in Tendon Healing	The Chinese University of Hong Kong – Direct Grant	30/06/2023	29/06/2024	30,000
	Magnesium Rescues Fibrosis in Bone Fracture Gap via Tuning the Spatial-temporal Interactions of Skeletal Stem Cells and Chemokines: Evidence at Single-cell Resolution	The Chinese University of Hong Kong – Direct Grant	30/06/2022	29/06/2023	75,000
	Targene Biotech (Hong Kong) Limited	The Innovation and Technology Commission – Technology Start-up Support Scheme for Universities	01/04/2020	31/03/2023	800,000
Wenxue Tong	Prevention and Treatment of Osteoarthritis by Screening a Novel Cartilage-targeting Adeno-associated Virus: A Gene Therapy Approach	Health Bureau – Health and Medical Research Fund	01/07/2022	30/06/2025	1,424,920

Publications

A. Journal Papers

1. Dai B, Zhu Y, Li X, Liang Z, Xu S, Zhang S, Zhang Z, Bai S, Tong W, Cao M, Li Y, Zhu X, Liu W, Zhang Y, Chang L, Yung PSH, Ho KKW, Xu J, Ngai T, Qin L. Blockage of osteopontin-integrin β3 signaling in infrapatellar fat pad attenuates osteoarthritis in mice. *Advanced Science*. 2023;10(22):2300897. doi:10.1002/advs.202300897.

2. Guo J, Yao H, Li X, Chang L, Wang Z, Zhu W, Su Y, Qin L, Xu J. Advanced hydrogel systems for mandibular reconstruction. *Bioactive Materials*. 2023;21:175-193. doi:10.1016/j.bioactmat.2022.08.001. (Review)

3. Innovation and translation of biological and biomaterial treatment for challenging musculoskeletal disorders. *Journal of Orthopaedic Translation*. 2023;40:A1. doi:10.1016/j.jot.2023.06.001. (Editorial)

4. Suen PK, Zheng L, Yang Q qing, Mak WS, Pak WY, Mo KY, Chan ML, Liu QQ, Qin L, Sun SSM. Lysine-rich rice partially enhanced the growth and development of skeletal system with better skeletal microarchitecture in young rats. *Nutrition Research*. 2024;121:67-81. doi:10.1016/j.nutres.2023.11.005.

5. Wei W, Tan B, Yan Y, Li W, Zeng X, Chen Q, Wang R, He H, Qin L, Li T, Chen W. Hip preservation or total hip arthroplasty? A retrospective case-control study of factors influencing arthroplasty decision-making for patients with osteonecrosis of the femoral head in China. *Orthopaedic Surgery*. 2023;15(3):731-739. doi:10.1111/os.13639. (Epub ahead of print)

6. Xu H, Zhu Y, Hsiao AWT, Xu J, Tong W, Chang L, Zhang X, Chen YF, Li J, Chen W, Zhang Y, Chan HF, Lee CW. Bioactive glass-elicited stem cell-derived extracellular vesicles regulate M2 macrophage polarization and angiogenesis to improve tendon regeneration and functional recovery. *Biomaterials*. 2023;294. doi:10.1016/j.biomaterials.2023.121998.

7. Xu S, Zhang Y, Dai B, Rao J, Deng F, Zhang S, Shao H, Li X, Jin Z, Liang T, Yang Y, Li Y, Chen Z, Tong W, Xu J, Ning C, Qin L. Green-prepared magnesium silicate sprays enhance the repair of burn-skin wound and appendages regeneration in rats and minipigs. *Advanced Functional Materials*. 2024;34(9):2307439. doi:10.1002/adfm.202307439.

8. Zhao P, Guo J, Jiang T, Xu X, Chen S, Li Z, Xu J, Li G, Bian L. Vacuolated coacervate mediates the bimodal release kinetics of diverse macromolecular drugs in vivo. *Materials Today*. 2023;66:26-35. doi:10.1016/j.mattod.2023.03.029.

9. Zhou L, Xu J, Schwab A, Tong W, Xu J, Zheng L, Li Y, Li Z, Xu S, Chen Z, Zou L, Zhao X, van Osch GJVM, Wen C, Qin L. Engineered biochemical cues of regenerative biomaterials to enhance endogenous stem/progenitor cells (ESPCs)-mediated articular cartilage repair. *Bioactive Materials*. 2023;26:490-512. doi:10.1016/j.bioactmat.2023.03.008. (Review)

10. Zhu WY, Yang WF, Wang L, Lan X, Tao ZY, Guo J, Xu J, Qin L, Su YX. The effect of drug holiday on preventing medication-related osteonecrosis of the jaw in osteoporotic rat model. *Journal of Orthopaedic Translation*. 2023;39:55-62. doi:10.1016/j.jot.2022.12.006.

11. Zhu Y, Guo J, Sheng Y, Xu J, Qin L, Ngai T. Injectable magnesium oxychloride cement foam-derived scaffold for augmenting osteoporotic defect repair. *Journal of Colloid and Interface Science*. 2023;640:199-210. doi:10.1016/j.jcis.2023.02.109.

B. Book Chapters

1. Ling Qin, Bingyang Dai, Lizhen Zheng. Adipose tissue: Endocrine functions, health implications, and future perspectives. In: *Contemporary Endocrinology*. Springer Nature.

C. Conference Papers

1. Yuantao Zhang, Lizhen Zheng, Wenxue Tong, Dick Ho Kiu Chow, Jiankun Xu, Ling Qin. Magnesium containing hybrid fixation system promotes the healing of long bone fractures: A large animal study. In: ORS 2023 Annual Meeting. Dallas, Texas, United Kingdom. 2023 February 10-14.

2. Yuantao Zhang, Lizhen Zheng, Wenxue Tong, Dick Ho Kiu Chow, Jiankun Xu, Ling Qin. Magnesium containing hybrid fixation system promotes the healing of long bone fractures: a large animal study. In: Oxford-ICMRS Symposium. United Kingdom. 2023 August 12-15.

3. Bingyang Dai, Yuwei Zhu, Jiankun Xu, To Ngai, Ling Qin. Targeting IL-6/MMP13 axis of infrapatellar fat pad to ameliorate osteoarthritis in mice. In: TERMIS-AP 2023 Conference. Hong Kong. 2023 October 16-19.

4. Bingyang Dai, Jiankun Xu, Ling Qin. Targeting IL-6/MMP13 axis in infrapatellar fat pad ameliorates osteoarthritis in mice. In: 中國生物材料大會 . Chong Qing, China. 2023 October 13-15.

5. Shunxiang Xu, Bingyang Dai, Hongwei Shao, Jiankun Xu, Ling Qin. Magnesium-containing dressings promote deep wound healing via activating fascia mobilization and neurovascular interaction. In: TERMIS-AP 2023 Conference. Hong Kong. 2023 October 16-19.

6. Wenxue Tong, Qiuli Qi, Jiankun Xu, Ling Qin. Optogenetic controlled tissue-targeting adeno-associated virus combination for osteoarthritis gene therapy and prevention. In: TERMIS-AP 2023 Conference. Hong Kong. 2023 October 16-19.

7. Wenxue Tong, Qiuli Qi, Jiankun Xu, Ling Qin. The application of direct evolution for gene therapy vector development and screening. In: Oxford-ICMRS Symposium. United Kingdom. 2023 August 12-15.

8. Wenxue Tong, Qiuli Qi, Jiankun Xu, Ling Qin. Optogenetic controlled tissue-targeting AAV combination for osteoarthritis gene therapy and prevention. In: The Hong Kong Orthopaedic Association. Hong Kong. 2023 November 4-5.

9. Jerry Jiankun Xu, Angel Yuk Wa Lee, Chi Ming Wong, Patrick Shu Hang Yung, Pauline Po Yee Lui. Protein X Knockout on Tendon-Derived Stem Dell Functions and Histopathology of Tendon. In: TERMIS-AP 2023 Conference. Hong Kong. 2023 October 16-19.

10. Florence Ou-Suet Pang, Michael Tim-yun Ong, Patrick Shu-hang Yung, Ling Qin, Jiankun Xu. Bilayer biomimetic membranes enhance tendon-bone healing. In: The Hong Kong Orthopaedic Association. Hong Kong. 2023 November 4-5.

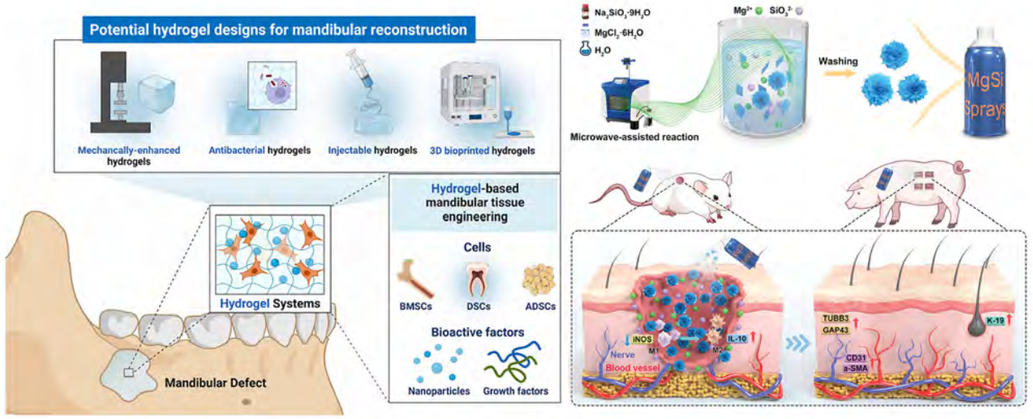
D. Patents

1. China Patent:

   Title: 生物活性水凝膠及其制備方法和應用
   Inventors: 秦嶺，許順祥，許建坤
   Patent Application No.: PCT/CN2023/078042
   Filing Date: 10 January 2023

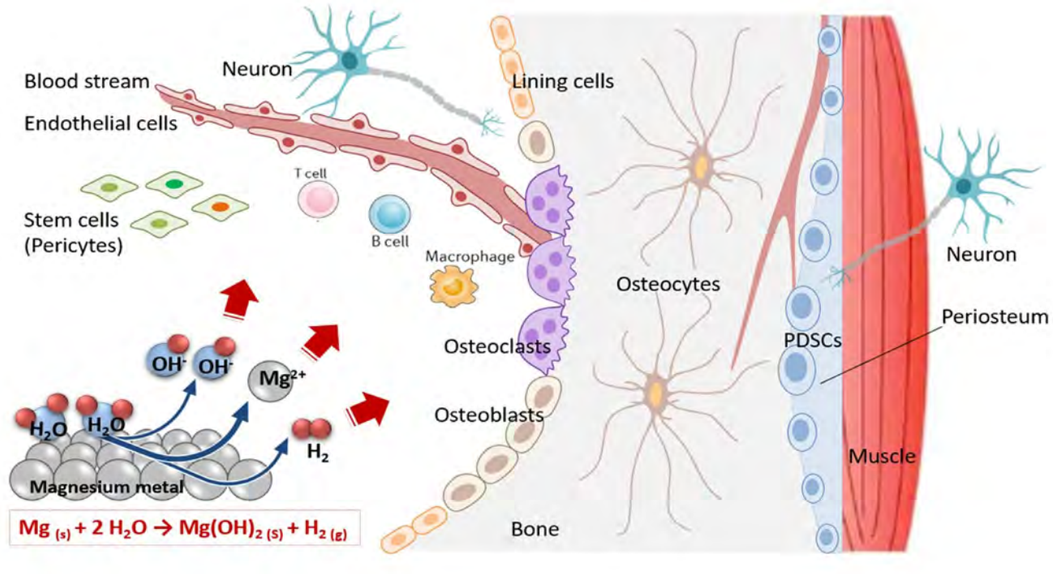
2. US Provisional Patent:

   Title: Injectable Magnesium Oxychloride Cement Foam (MOCF)-derived Scaffold for Treating Osteoporotic Bone Defects
   Inventors: T Ngai, L Qin, JK Xu, YW Zhu
   US Provisional Patent No.: 63/410,185
   PCT Patent Application No.: PCT/CN2023/078042



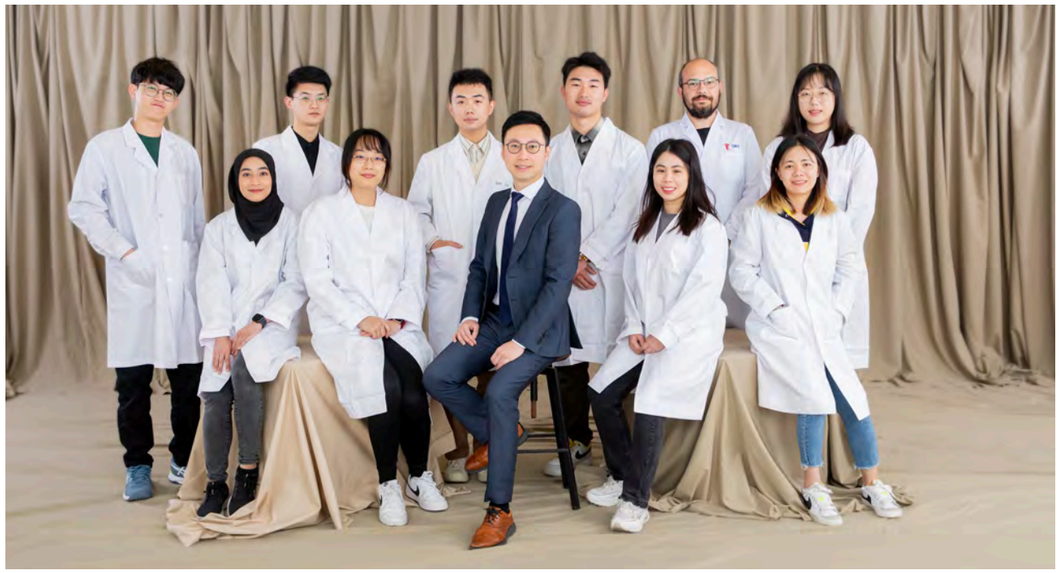
Advanced hydrogel systems for mandibular reconstruction and magnesium silicate sprays which could promote burn-wound repair and appendages regeneration, involving attenuated inflammation, promoted vascularisation, peripheral nerves, and hair follicles

Source: Ling Qin and his team



Further mechanistic studies on the bone and tissue regeneration stimulated by the bioactive magnesium and its biodegradation products (Mg^{2+}, H_2, and the alkaline environment)

Source: Ling Qin and his team



BIOMATERIAL, CHEMICAL BIOLOGY AND DRUG TRANSLATIONAL RESEARCH

CHEMICAL BIOLOGY AND DRUG DISCOVERY
生物材料，化學生物學及藥物轉譯研究

PRINCIPAL INVESTIGATOR
Billy Ng

TEAM MEMBERS
Stephan Scheeff, Bowen Ma, Khadija Shahed Khan, Xu He, Yao Qin, Josefina Xeque Amada, Tongyang Xu, Zhihao Guo, Richard Lo, Yunpeng Huang, Yating Guo

RESEARCH PROGRESS SUMMARY

Billy Ng and his team use modern chemical and biological tools to develop novel and safe medicines for the treatment of various dreadful diseases, including cancers, infectious and neurodegenerative diseases.

Billy's team has successfully used cutting-edge technologies to develop therapeutic molecules for combating viral infections and aging-related diseases. He has co-authored more than 30 papers in prestigious journals such as *Science*, *Nature Chemical Biology*, *Molecular Cell*, *J. Am. Chem. Soc.*, *Angew. Chem. Int. Ed.*, and *ACS Central Science*. His research has been funded by diverse sources, including the Bill & Melinda Gates Foundation, US National Academy of Medicine (NAM), the Innovation and Technology Fund (ITF), Health and Medical Research Fund (HMRF), and Research Grants Council (RGC) of Hong Kong. He was also honoured as a Young Global Leader (YGL) by the World Economic Forum.

Billy and his international team were the first to discover that an approved HCV drug can be repurposed for the treatment of COVID-19. He initiated a "crowd drug discovery" effort and led researchers from USA, UK, China, Germany, Japan, France, Korea, Taiwan and Hong Kong to develop antiviral agents for the pharmacological management of COVID-19 since its early outbreak. This discovery was published in *ACS Central Science* and highlighted by over 30 media reports, including SCMP, RTHK, HK01, Ta Kung Pao and Wen Wei Po.

He also launched a rapid "crowd" response to help other researchers to better understand the molecular biology and therapeutic targeting of various viral infections. As highlighted by the magazine *The Scientist*, this crowd drug discovery campaign has been very successful – its advanced antiviral research with over 500 citations (since 2020), and widely engaged the general public, with over 160,000 "shares, likes, and tweets" on Facebook and Twitter.

Recent increases in pneumonia cases have involved various respiratory pathogens. Besides influenza virus, coronavirus, and mycoplasma infections, the respiratory syncytial virus (RSV) also significantly contributes to severe respiratory infections. In the search for novel therapeutics against RSV, his team designed and synthesised novel antiviral drug candidates. As the continuous emergence of pathogenic viruses necessitates the development of novel and structurally diverse analogues, this research brings new opportunities for the exploration and development of antiviral therapy. The findings have been published in an international peer-reviewed scientific journal (*Org. Lett.* 2023).

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	**Organisation**
Billy Ng	Biomedicines Young Investigator Award	Biomedicines
	Young Global Leader (YGL)	World Economic Forum
Zhihao Guo	Vice-Chancellor's PhD Scholarship	The Chinese University of Hong Kong
Tongyang Xu		

Fellowship

Name	Details	
	Fellowship	**Organisation**
Josefina Xeque Amada	The Hong Kong PhD Fellowship Scheme (HKPFS)	Research Grants Council

Academic Editorship

Name	Details	
	Role	**Journal**
Billy Ng	Review Editor	Frontiers in Chemistry

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Billy Ng	Reviewer	72nd Lindau Nobel Laureate Meeting
		Science Translational Medicine
		Nature Biotechnology
		Nature Structural & Molecular Biology
		Nature Chemical Biology
		Nature Communications
		Science Advances
		eLife
		Journal of Biological Chemistry
		JCI Insight
		iScience

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Billy Ng	A Chemical Biology Approach to Probe Protein Glycosylation in Cancer	The Chinese University of Hong Kong – Faculty Innovation Award	01/10/2020	01/10/2025	2,500,000
	Exploring and Drugging the Cancer Glycome	Croucher Foundation	12/08/2019	12/08/2024	500,000
	Synthesis of Pseudo-natural Product Analogues of Bilobalide as Cardioprotective Agents	Research Grants Council – Early Career Scheme	01/01/2022	31/12/2024	491,303
	Development of Novel Therapeutic Drug for Niemann-pick Disease, Type C	Science, Technology and Innovation Commission of Shenzhen Municipality	30/07/2021	31/07/2023	1,200,000
	Development of Simeprevir Analogues as Anti-coronavirus Drugs	Health Bureau – Health and Medical Research Fund	01/09/2022	31/08/2025	1,500,000
	Design and Synthesis of Novel Carbocyclic Nucleoside Analogues as Antiviral Agents	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	464,000
	Bilobalide Analogues as Analgesics for Neuropathic Pain	Peter Hung Pain Research Institute Fund	01/10/2022	30/09/2025	1,750,000
	Bilobalide Derivatives as Therapeutics Against Ageing-related Neurodegenerative Diseases	United States National Academy of Medicine and Research Grants Council – Healthy Longevity Catalyst Awards	01/10/2022	30/09/2023	389,000
	Terpene Trilactone Derivatives as Therapeutics Against Ageing-related Neurodegenerative Diseases	The Chinese University of Hong Kong – Strategic Seed Funding for Collaborative Research Scheme	31/10/2023	31/10/2025	300,000
	Design of Carbobicyclic Nucleosides for Influenza	Bill & Melinda Gates Foundation	23/08/2023	30/09/2024	2,035,500

Publications

A. Journal Papers

1. Scheeff S, Wang Y, Lyu MY, Nasiri Ahmadabadi B, Hau SCK, Hui TKC, Zhang Y, Zuo Z, Chan RWY, Ng BWL. Design and synthesis of bicyclo[4.3.0]nonene nucleoside analogues. *Organic Letters*. Published online December 22, 2023. doi:10.1021/acs.orglett.3c03590. (Letter, Epub ahead of print)

2. Ma B, Khan KS, Xu T, Amada JX, Guo Z, Yan Y, Cheng ASL, Ng BWL. Targeted protein O-glcnacylation using bifunctional small molecules. *bioRxiv*. Published online January 1, 2023:2023.06.09.544275. doi:10.1101/2023.06.09.544275. (Epub ahead of print)

3. Ng BWL, Xu T, Guo Z. Discovery of chemical probes that perturb protein complexes using size exclusion chromatography and chemical proteomics. *Molecular Cell*. 2023;83(10):1544-1546. doi:10.1016/j.molcel.2023.04.028. (Commentary)

4. Ng BWL, Scheeff S, Amada JX. Making it hard to replicate understanding how to harden liquid condensates produced by influenza a virus could accelerate the development of novel antiviral drugs. *eLife*. 2023;12. doi:10.7554/elife.88044. (Commentary)

B. Patents

1. The United States Patents:

   Title: Bilobalide Derivative Compounds for Treating Cancers
   National Application No.: 63/610,394
   Date: 14 December 2023

   Title: Bilobalide Derivative Compounds for Treating Neurological Diseases
   National Application No.: 63/517,627
   Date: 4 August 2023

   Title: Compositions and Methods Related to Protein Labeling
   National Application No.: 63/467,875
   Date: 20 May 2023



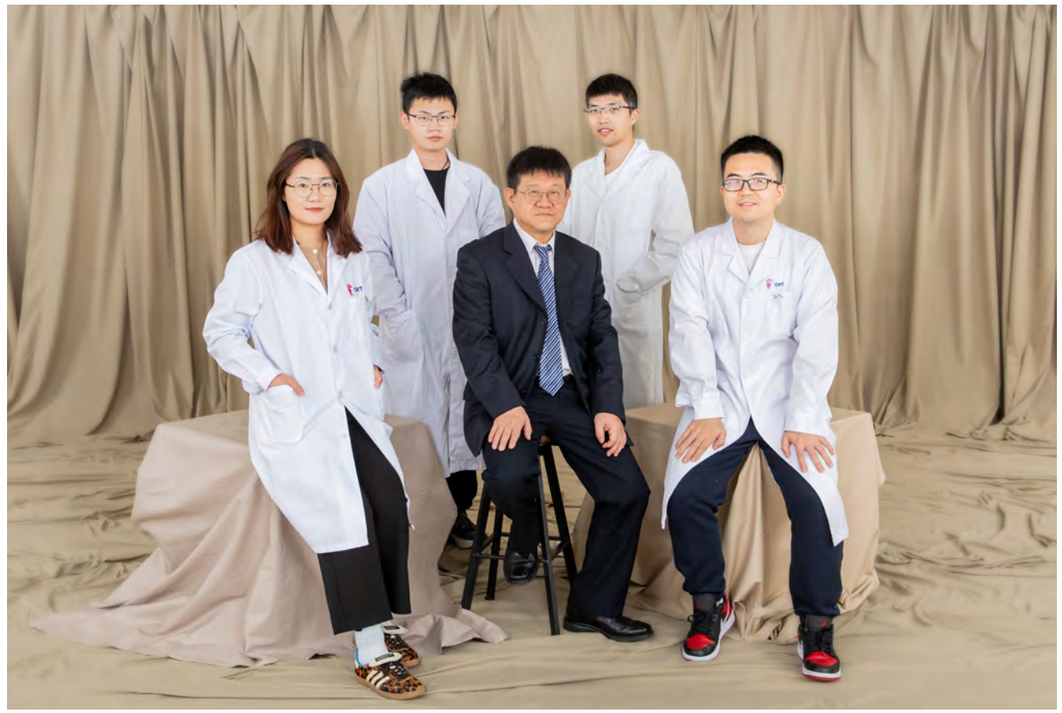
Chemical Inducers of Proximity
Source: Billy Ng



Carbohydrate-based Drug Discovery
Source: Billy Ng



Late-stage Modification of Drug-like Molecules
Source: Billy Ng



GENOMICS AND BIOINFORMATICS
基因組學與生物訊息學

PRINCIPAL INVESTIGATOR
Hao Sun

TEAM MEMBERS
Yulong Qiao, Xing Zhao, Manyi Wen, Chuhan Li, Qiang Sun, Feng Yang

RESEARCH PROGRESS SUMMARY

In the reporting period, **Hao Sun** and his team have 4 ongoing grants funded by Research Grants Council / General Research Fund, for studying transcriptional regulation mechanisms in muscle stem cells. His team also published 5 papers in some high-impact journals such as *Nature Communications* et al.

RESEARCH AND SCHOLARSHIP

Academic Editorship

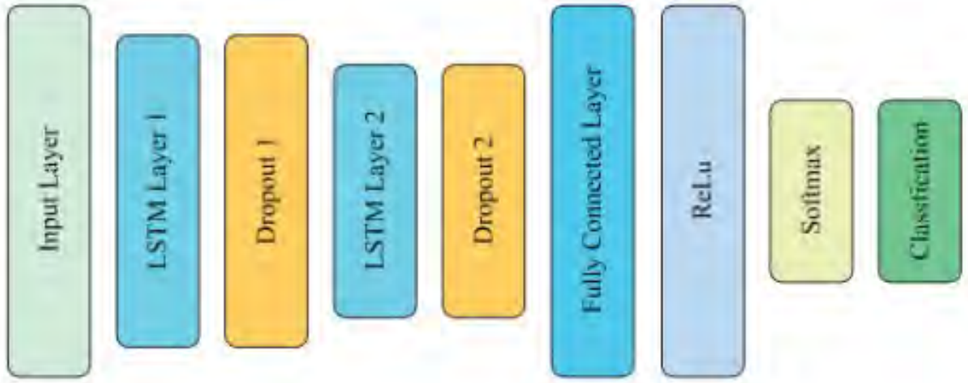
Name	Details	
	Role	Journal
Hao Sun	Academic Editor	PLoS One

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Hao Sun	Reviewer	Bioinformatics
		Clinical Biochemistry
		BMC Genomics

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Hao Sun	Elucidation of Intrinsic and Extrinsic Alterations Regulating Skeletal Muscle Stem Cell Aging: Mechanisms for Sarcopenia	Health Bureau – Health and Medical Research Fund	12/02/2021	01/12/2024	1,496,150
	In Vivo RNA Structure Probing Unveils DHX36 Binding-structure Interplay in Regulation of mRNA Abundance	Research Grants Council – General Research Fund	01/08/2023	31/07/2026	1,600,000
	3D Genome Rewiring During Muscle Stem Cell Linage Development and Aging	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,194,637



Name	Parameters
Input Layer	Size: 1x57584 (Z-score normalization)
LSTM Layer 1	Size: 120 LSTM cells (sequence mode)
Dropout 1	0.25 dropout probability
LSTM Layer 2	Size: 80 LSTM cells (last mode)
Dropout 2	0.25 dropout probability
Fully Connected Layer	Size: 1x28

Neural Network Architecture for Cancer Classification

Source:
Zhao X, Wang H, Sun H. GENESO a framework for pan-cancer classification and marker gene discovery by symmetrical occlusion method using deep learning. 2023;17. doi:10.21203/rs.3.rs-3550032/v1.



GENOMICS AND BIOINFORMATICS
基因組學與生物訊息學

PRINCIPAL INVESTIGATOR
Peiyong Jiang

TEAM MEMBERS
Guanhua Zhu, Qing Zhou, Lu Ji, Huiwen Che, Guangya Wang, Dongyan Xiong, Wenlei Peng, Xingqian Li, Hau Yuen Chan, Jiaen Deng, Guannan Kang, Jinyue Bai, Xi Hu, Rong Qiao, Zhidong Zhang, Yuwei Shi, Siyuan Huang, Wing Sum Wong, Wenshuo Li, Ruilong Zhou, Zilong Wang, Yao He

RESEARCH PROGRESS SUMMARY

Peiyong Jiang and his team continue their efforts to uncover new biological properties of cell-free DNA, and develop new diagnostic tools based on fragmentomics of cfDNA. For example, the team has applied a non-negative matrix factorisation algorithm to profile various DNA nuclease activities. The team has demonstrated that the use of fragmentomic features could facilitate the differentiation of underlying contaminating microbes from true pathogens in sepsis. The team filed a total of 6 patent applications in 2023.

RESEARCH AND SCHOLARSHIP

Fellowship

Name	Details	
	Fellowship	Organisation
Peiyong Jiang	Senior Member	National Academy of Inventors

Academic Editorship

Name	Details	
	Role	Journal
Peiyong Jiang	Editorial Board Member	Extracellular Vesicles and Circulating Nucleic Acids

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Peiyong Jiang	Reviewer	Nature Communications
		Molecular Cancer
		eBioMedicine

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Peiyong Jiang	Centre for Novostics	Innovation and Technology Commission – Innovation and Technology Fund	01/05/2020	01/05/2025	Amount not to be disclosed

Publications

A. Journal Papers

1. Mattox AK, Douville C, Wang Y, Popoli M, Ptak J, Silliman N, Dobbyn L, Schaefer J, Lu S, Pearlman AH, Cohen JD, Tie J, Gibbs P, Lahouel K, Bettegowda C, Hruban RH, Tomasetti C, Jiang P, Chan KCA, Lo YMD, Papadopoulos N, Kinzler KW, Vogelstein B. The origin of highly elevated cell-free DNA in healthy individuals and patients with pancreatic, colorectal, lung, or ovarian cancer. *Cancer Discovery*. 2023;13(10):2166-2179. doi:10.1158/2159-8290.cd-21-1252.

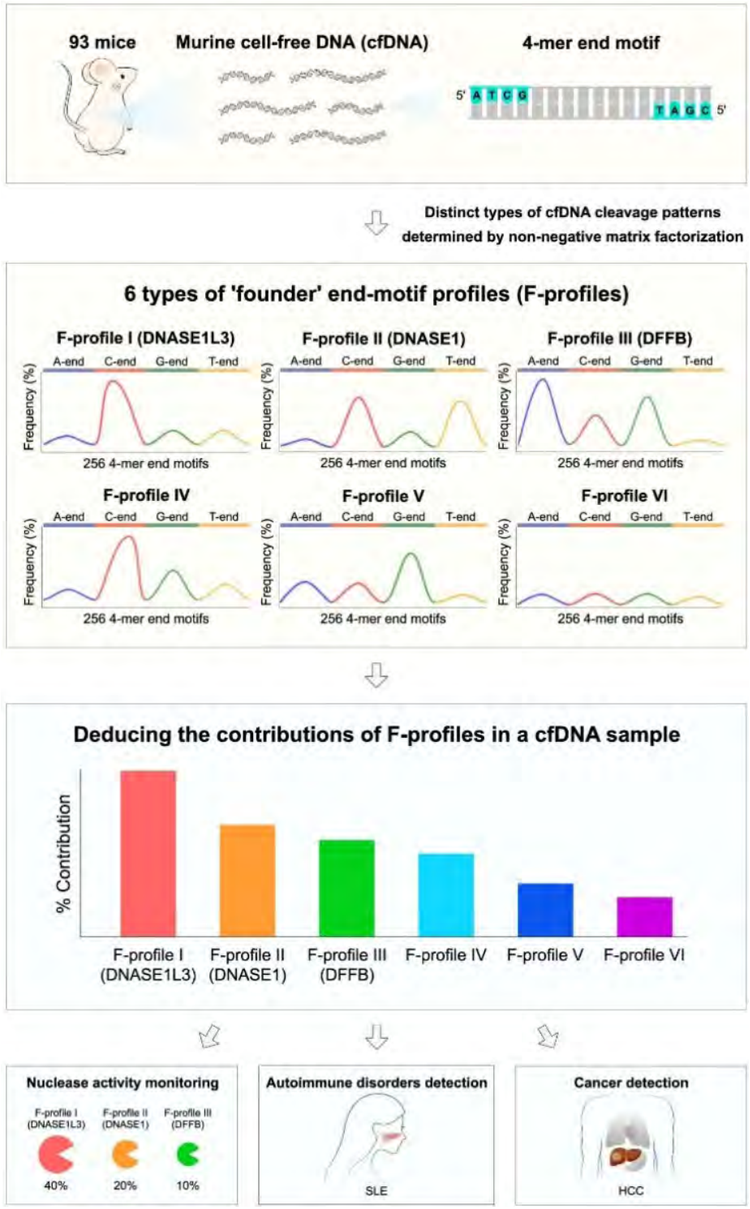
2. Gai W, Yu SCY, Chan WTC, Peng W, Lau SL, Leung TY, Jiang P, Chan KCA, Lo YMD. Droplet digital PCR is a cost-effective method for analyzing long cell-free DNA in maternal plasma: Application in preeclampsia. *Prenatal Diagnosis*. 2023;43(11):1385-1393. doi:10.1002/pd.6432.

3. Chan KCA, Lam WKJ, King A, Lin VS, Lee PPH, Zee BCY, Chan SL, Tse IOL, Tsang AFC, Li MZJ, Jiang P, Ai QYH, Poon DMC, Au KH, Hui EP, Ma BBY, Van Hasselt AC, Chan ATC, Woo JKS, Lo YMD. Plasma Epstein-Barr virus DNA and risk of future nasopharyngeal cancer. *NEJM Evidence*. 2023;2(7). doi:10.1056/evidoa2200309.

4. Zhou Z, Ma MJL, Chan RWY, Lam WKJ, Peng W, Gai W, Hu X, Ding SC, Ji L, Zhou Q, Cheung PPH, Yu SCY, Teoh JYC, Szeto CC, Wong J, Wong VWS, Wong GLH, Chan SL, Hui EP, Ma BBY, Chan ATC, Chiu RWK, Chan KCA, Lo YMD, Jiang P. Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs. *Proceedings of the National Academy of Sciences of the United States of America*. 2023;120(17). doi:10.1073/pnas.2220982120.

5. Yu SCY, Deng J, Qiao R, Cheng SH, Peng W, Lau SL, Choy LYL, Leung TY, Wong J, Wong VWS, Wong GLH, Jiang P, Chiu RWK, Chan KCA, Lo YMD. Comparison of single molecule, real-time sequencing and nanopore sequencing for analysis of the size, end-motif, and tissue-of-origin of long cell-free DNA in plasma. *Clinical Chemistry*. 2023;69(2):168-179. doi:10.1093/clinchem/hvac180.

6. Wang G, Lam WKJ, Ling L, Ma MJL, Ramakrishnan S, Chan DCT, Lee WS, Cheng SH, Chan RWY, Yu SCY, Tse IOL, Wong WT, Jiang P, Chiu RWK, Chan KCA, Lo YMD. Fragment ends of circulating microbial DNA as signatures for pathogen detection in sepsis. *Clinical Chemistry*. 2023;69(2):189-201. doi:10.1093/clinchem/hvac197.



Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs.

Schematic of distinct types of cfDNA cleavage analysis for cfDNA molecules. The terminal 4 nucleotides at each of the 5' fragment ends (i.e., 4-mer end motifs; n = 256) were determined from 93 murine cfDNA samples, including WT mice and nuclease-deficient mice. Six categories of distinct types of cfDNA cleavage patterns were found, referred to as "founder" end-motif profiles (i.e., F-profiles), by applying NMF analysis to the 4-mer end-motif profiles. F-profiles I, II, and III were associated with the cutting preference of DNASE1L3, DNASE1, and DFFB, respectively. The distinct types of cfDNA cleavage patterns learned from murine cfDNA could be extrapolated to human cfDNA for informing the proportional contributions of F-profiles in both mouse and human cfDNA samples (referred to as deconvolutional analysis of end motifs), allowing the detection of immune diseases and cancers.

Source:
Zhou Z, Ma MJL, Chan RWY, Lam WKJ, Peng W, Gai W, Hu X, Ding SC, Ji L, Zhou Q, Cheung PPH, Yu SCY, Teoh JYC, Szeto CC, Wong J, Wong VWS, Wong GLH, Chan SL, Hui EP, Ma BBY, Chan ATC, Chiu RWK, Chan KCA, Lo YMD, Jiang P. Fragmentation landscape of cell-free DNA revealed by deconvolutional analysis of end motifs. Proceedings of the National Academy of Sciences of the United States of America. 2023;120(17). doi:10.1073/pnas.2220982120.



GENOMICS AND BIOINFORMATICS
基因組學與生物訊息學

PRINCIPAL INVESTIGATOR
Ken Sung

TEAM MEMBERS
Sheng Cheng, Guangyi Chen, Chak Sum Anselm Au, Xingqian Li

RESEARCH PROGRESS SUMMARY

Ken Sung's team focused on developing methods to call genomic mutations through analysing next generation sequencing data. The team published one paper on calling insertions from the NGS dataset. This work is published in *Nature Communication.* They also published a method that calls structural variations from long reads. The work is published in *Computers in Biology and Medicine.* They also have a work on phylogenetic MUL-tree, which is published in the conference CPM.

His team started two research collaborations:

1. Work with China to perform genomic sequencing on K14-HPV16 mouse model to understand cervical cancer.
2. Work with University of Macau to perform T2T genome assembly for cancer genome.

He also gave 4 presentations :

1. (20 Oct 2023) Repeat-aware SV calling and its clinical application. ICBBS 2023, Singapore.
2. (10 Oct 2023) Repeat-aware insertion calling and its clinical application. Department of Computer Science, Hong Kong Baptist University, Hong Kong.
3. (28 May 2023) Repeat-aware insertion calling and its application in Human and Arabidopsis. ICBBT 2023, Xian, China.
4. (14 Apr 2023) Hong Kong Genome Project. University of Macau, Macau.

RESEARCH AND SCHOLARSHIP

Academic Editorships

Name	Details	
	Role	Journal
Ken Sung	Senior Editor	BMC Research Notes
	Associate Editor	Journal of Bioinformatics and Computational Biology
	Editor-in-Chief	Biomedical Informatics
	Steering Committee	International Workshop on Combinatorial Algorithms (IWOCA)

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Ken Sung	Conference Programme Committee	WALCOM
		RECOMB
		APBC
		IWBBIO
		RECOMB-CG
		BIBM

Grant and Consultancy

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ken Sung	JC STEM Lab of Computational Genomics	The Hong Kong Jockey Club Charities Trust	01/08/2023	31/07/2028	9,973,464

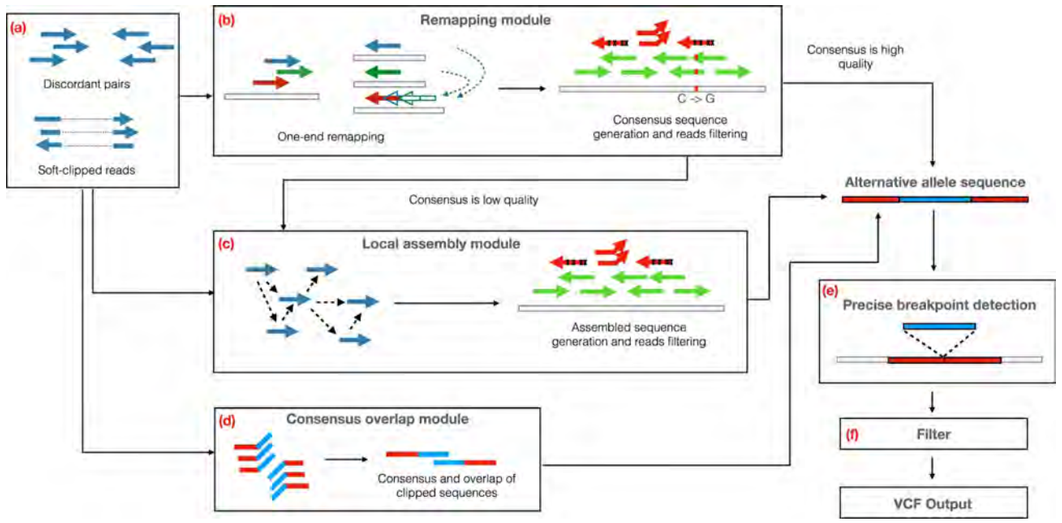
Publications

A. Journal Papers

1. Oner MU, Kye-Jet JMS, Lee HK, Sung WK. Distribution based MIL pooling filters: Experiments on a lymph node metastases dataset. *Medical Image Analysis*. 2023;87. doi:10.1016/j.media.2023.102813.
2. Rajaby R, Liu DX, Au CH, Cheung YT, Lau AYT, Yang QY, Sung WK. INSurVeyor: Improving insertion calling from short read sequencing data. *Nature Communications*. 2023;14(1):1-13. doi:10.1038/s41467-023-38870-2.
3. Zheng Y, Shang X, Sung WK. SVsearcher: A more accurate structural variation detection method in long read data. *Computers in Biology and Medicine*. 2023;158:106843. doi:10.1016/j.compbiomed.2023.106843.

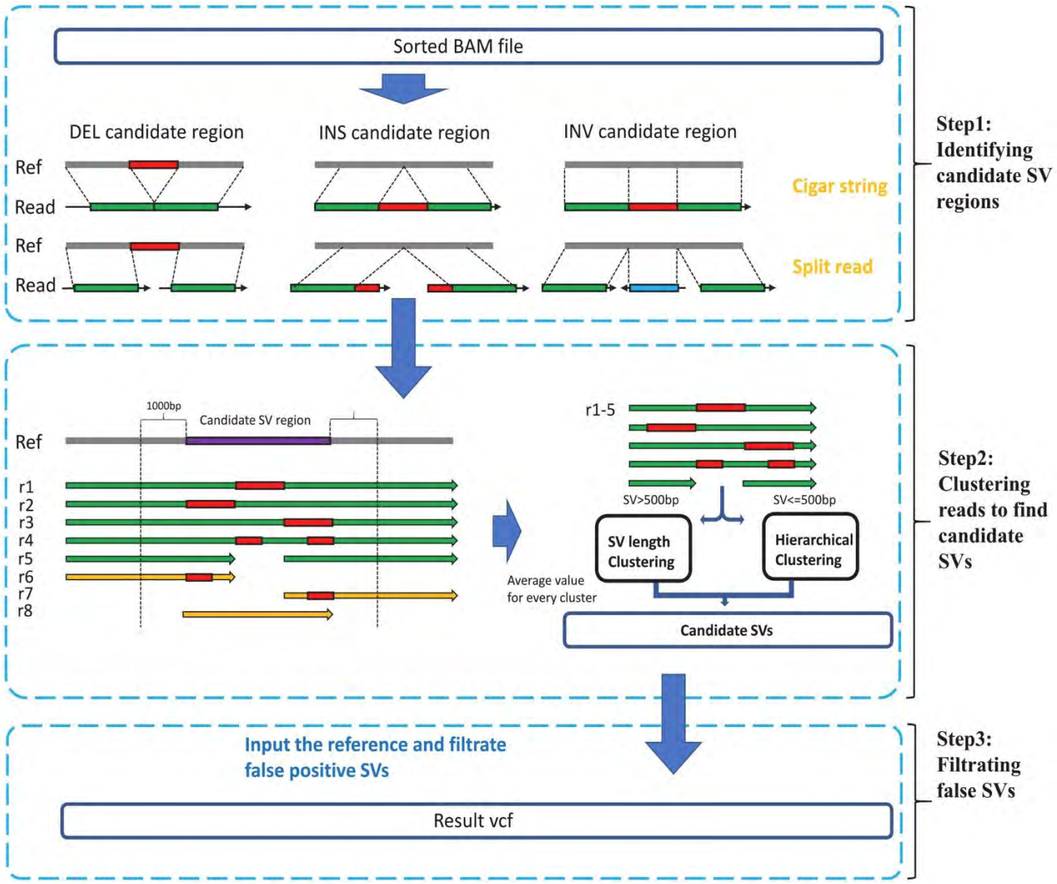
B. Conference Paper

1. Hampson C, Harvey DJ, Iliopoulos CS, Jansson J, Lim Z, Sung WK. MUL-tree pruning for consistency and compatibility. 34th Annual Symposium on Combinatorial Pattern Matching (CPM2023) doi:10.4230/lipics.cpm.2023.14/-/stats.



The method can be essentially divided into three blocks: (a) INSurVeyor extracts discordant pairs and clipped reads as possible evidence of insertions; (b–d) the evidence extracted by (a) is used to generate the alternative allele sequence, which consists of the predicted inserted sequence along with the two flanking regions shared with the reference genome. This is achieved by three separate modules: the remapping module (b) aims at predicting transpositions; the local assembly module (c) aims at predicting novel insertions, while the consensus overlap module (d) predicts small insertions. (e) This sequence is then remapped to the reference genome to identify the precise boundaries of the predicted insertion, which is finally passed through a series of filters (f) that aim at reducing the number of false positive calls.

Sources: Rajaby R, Liu DX, Au CH, Cheung YT, Lau AYT, Yang QY, Sung WK. INSurVeyor. Improving insertion calling from short read sequencing data. Nature Communications. 2023;14(1):1-13 doi:10.1038/s41467-023-38870-2.



The overview of SVsearcher. The input consists of a sorted BAM file and a reference file. There are three main steps in SVsearcher. Step 1 checks the CIGAR string and split read to get a list of candidate SV regions. Step 2 investigates every candidate SV region to detect candidate SVs. By clustering the reads, the team is able to detect multi-allelic SVs. Step 3 filters the false SVs and outputs the final list of SVs.

Sources: Zheng Y, Shang X, Sung WK. Ssearcher: A more accurate structural variation detection method in long read data. Computers in Biology and Medicine. 2023;158:106843. doi:10.1016/1.compbiomed.2023.106843.



NON-CODING RNAS AND CELLULAR SIGNALLING

NON-CODING RNAS

非編碼核糖核苷酸研究及細胞訊號轉導

PRINCIPAL INVESTIGATOR
Huating Wang

TEAM MEMBERS
Hao Sun, Xiaona Chen, Liangqiang He, Suyang Zhang, Yang Li, Yulong Qiang, Qiang Sun, Qin Zhou, Xingyuan Liu, Chuhan Li, Manyi Wen, Feng Yang, Gexin Liu, Ziliu Wang, Yang Fu, Xiaofan Guo

RESEARCH PROGRESS SUMMARY

During the past year, the team led by **Huating Wang** continued the work on understanding the intrinsic and extrinsic regulatory mechanisms orchestrating skeletal muscle stem cells and muscle regeneration. Specifically, they have been focusing on the following projects: (1) ATF3 induction prevents precocious activation of skeletal muscle stem cells by regulating H2B expression; (2) Multiscale 3D genome reorganization during skeletal muscle stem cell lineage progression and aging. Findings from their research were published on *Nature Communications* and *Science Advances* and are well accepted by peers among the scientific communities. As a result, they were invited to present their work at international and regional conferences such as Gordon Myogenesis Meeting, China Muscle Society Annual Meeting, etc. In addition, fruitful collaborations have been established with peer scientists from Hong Kong, China, the United States and Europe. Two patent applications have been submitted.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Gexin Liu	Best Poster Award, IAS-TRS Joint Symposium	The Hong Kong University of Science and Technology
Suyang Zhang	Best Poster Award	The 8th China Muscle Society Meeting
Yang Li	Oral Presentation Award, Myogenesis 2023	Gordon Research Conferences

Fellowships

Name	Details	
	Fellowship	Organisation
Yulong Qiao	Postdoctoral Fellowship	The Chinese University of Hong Kong
Suyang Zhang	Research Committee Postdoctoral Fellowship Scheme	The Chinese University of Hong Kong

Academic Editorships

Name	Details	
	Role	Journal
Huating Wang	Editorial Board Member	Life Medicine
		Skeletal Muscle
		Frontiers in Genetics

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Huating Wang	Reviewer	Science Advances
		Cell Reports
		Nature Communications
		iScience

Grants and Consultancies

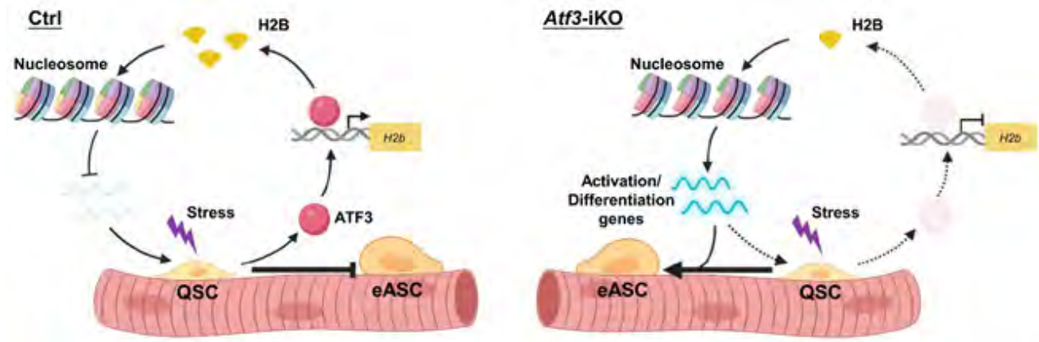
Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Huating Wang	Elucidating the Novel Regulatory Function of RNA Binding Proteins in 3D Genome Organization	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,425,114
	Dhx36 在骨骼肌幹細胞中基因調控的機制研究	National Natural Science Foundation of China	01/01/2022	31/12/2025	621,983
	Epigenomics Study of Aging Skeletal Muscle Stem Cells: Biology and Interventions for Sarcopenia	Innovation and Technology Commision – InnoHK Scheme	01/01/2022	31/12/2027	10,200,000
	Stem Cell-Niche Interactions in Tissue Maintenance and Engineering	Research Grants Council – Theme based Research Scheme	01/01/2022	31/12/2026	66,438,000
	Dissecting the Therapeutic Mechanism of an Effective Combination Treatment Targeting Neuromuscular Junction Degeneration and Myosteatosis to Combat Sarcopenia	Research Grants Council – Collaborative Research Fund	01/06/2022	31/05/2025	4,772,807
	YY1 Deficiency in Satellite Cell Exacerbates Fibrosis in Dystrophic Muscle: Elucidation of Satellite Cell/Macrophage/Fibro-Adipogenic Progenitor Crosstalk in Duchenne Muscular Dystrophy Mice	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,525,732
	Functional Characterization of Atf3 in Skeletal Muscle Stem Cells and Muscle Regeneration	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,394,799
	Elucidation of Intrinsic and Extrinsic Alterations Regulating Skeletal Muscle Stem Cell Aging: Mechanisms for Sarcopenia	Health Bureau – Health and Medical Research Fund Advanced Medical Research	02/12/2021	01/12/2024	1,496,150
	Aging, Skeletal Degeneration and Regeneration	Research Grants Council – Areas of Excellence Scheme	01/05/2021	30/04/2029	600,000
	Molecular Regulation of Quiescence and Early Activation in Muscle Stem Cells	Research Grants Council – Collaborative Research Fund	30/06/2020	29/06/2023	6,929,211
	Stem Cell Senescence in Skeletal Muscle Ageing: Mechanism and Treatment for Sarcopenia	Health Bureau – Health and Medical Research Fund Advanced Medical Research	19/08/2023	18/08/2026	1,491,150
	代謝微環境對骨骼肌發育和穩態維持的調控作用與機制	The Ministry of Science and Technology, People's Republic of China	01/12/2022	31/07/2027	4,220,599

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Huating Wang	Investigating the Functional Significance of Three-dimensional Structures of Topologically Associating Domains	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,195,542
	Studying the Functional Mechanism of Endothelial YY1 in Postischemic Angiogenesis	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,195,542
Xiaona Chen	Unraveling the Functional and Mechanistical role of DNA G-Quadruplex in Skeletal Muscle Stem Cells and Muscle Regeneration	The Chinese Univeristy of Hong Kong – Direct Grant	01/06/2023	31/05/2024	150,000
Huating Wang Hao Sun	3D Genome Rewiring During Muscle Stem Cell Lineage Development and Ageing	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,194,637
Hao Sun	In Vivo RNA Structure Probing Unveils DHX36 Binding-structure Interplay in Regulation of mRNA Abundance	Research Grants Council – General Research Fund	01/08/2023	31/07/2026	1,600,000

Publications

A. Journal Papers

1. Oprescu SN, Baumann N, Chen X, et al. Sox11 is enriched in myogenic progenitors but dispensable for development and regeneration of the skeletal muscle. *Skelet Muscle*. 2023;13(1):1-15. doi:10.1186/s13395-023-00324-0.
2. Zhang S, Yang F, Huang Y, et al. ATF3 induction prevents precocious activation of skeletal muscle stem cell by regulating H2B expression. *Nat Commun*. 2023;14(1):4978. doi:10.1038/s41467-023-41720-w.
3. Zhao Y, Ding Y, He L, et al. Multiscale 3D genome reorganization during skeletal muscle stem cell lineage progression and aging. *Sci Adv*. 2023;9(7): eabo1360. doi:10.1126/sciadv.abo1360.
4. Qiao Y, Sun Q, Chen X, et al. Nuclear m6A reader YTHDC1 promotes muscle stem cell activation/proliferation by regulating mRNA splicing and nuclear export. *Elife.* 2023;12. doi:10.7554/elife.82703.



H2B loss increases DNA damage and senescence in ATF3 iKO SCs.

Source: Zhang S, Yang F, Huang Y, et al. ATF3 induction prevents precocious activation of skeletal muscle stem cell by regulating H2B expression. Nat Commun. 2023;14(1):4978. doi:10.1038/s41467-023-41720-w.



NON-CODING RNAS AND CELLULAR SIGNALLING

CELLULAR SIGNALLING

非編碼核糖核苷酸研究及細胞訊號轉導

PRINCIPAL INVESTIGATOR
William Wu

TEAM MEMBERS
Matthew Chan, Lin Zhang, Xiaodong Liu, Huarong Chen, Likai Tan, Idy Ho, Chuan Xie, Qing Li, Judeng Zeng, Xiaoting Zhang, Xiansong Wang, Dan Huang, Zidan Zou, Fenfen Qin, Yingzhi Liu, Wenye Xu, Tingting Jin, Qian Li, Hao Su, Yanjun Jiang, Shuai Yan, Ling Lin, Shilan Wang, Dongjiao Chen, Hongyan Chen, Ziheng Huang, Na Qin, Jing Ren, Yushan Wang, Zemin Chen, Haiyun Shang, Yichen Yang, Xinyi Zhang, Ki Fung Suk

RESEARCH PROGRESS SUMMARY

Unravelling the link between Eubacterium rectale and COVID-19 mortality

The reduced abundance of two butyrate producers, namely *Eubacterium rectale* and *Roseburia intestinalis*, in the gut was found to be associated with COVID-19 mortality at the population level. The reduction of these species was also associated with severer COVID-19 manifestation.

Developing probiotics for cancer prevention

Carnobacterium maltaromaticum, a bacterium depleted in patients with colorectal cancer, was found to prevent intestinal tumorigenesis in a female-specific manner in mice. *C. maltaromaticum* cross-feeds with other gut microbes to produce vitamin D to protect against colorectal cancer formation via a vitamin D receptor-dependent manner.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
William Wu	Ranked 159th nationally based on D-index among the Best Scientists in the discipline of Medicine in China (Sep 2023)	Research.com
Huarong Chrn	Emerging Leader in the field of Oncology (May 2023)	The journal *Oncogene*
	2022 Top Reviewers (Jan 2023)	The journal *Oncogene*
Likai Tan	2023 EFIS-EJI Travel Grant	International γδ T cell conference

Fellowships

Name	Details	
	Fellowship	Organisation
William Wu	Fellowship of the Royal College of Physicians	The Royal College of Physicians, London, UK
Likai Tan	Youth Committee	The Chinese Association of Rehabilitation Medicine

Academic Editorships

Name	Details	
	Role	Journal
William Wu	Editorial Board Member	Oncogene
		Journal of Pharmacy and Pharmacology
	Associate Editor	Pharmacology of Anti-Cancer Drugs Section, Frontiers in Oncology / Frontiers in Pharmacology
	Topic Editor / Guest Associate Editor	Frontiers in Nutrition
		Frontiers in Microbiology
Lin Zhang	Editorial Board Member	Frontiers in Oral Health (Infections and Microbes)
		Frontiers in Nutrition and Microbes
Huarong Chen	Associate Editor	BMC Medicine
	Editorial Board Member	Experimental Cell Research
	Guest Editor	Diagnostics
Likai Tan	Review Editor	Frontiers in Immunology
Xiaodong Liu	Associate Editor	Frontiers in Molecular Neuroscience
	Review Editor	Frontiers in Pain Research Methods

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
William Wu	Peer Reviewer	Aging
		Gut (3 papers)
		Clinical and Translational Medicine
		MedComm
		Oncogene (2 papers)
		Obesity Reviews
		Journal of Gastroenterology and Hepatology (2 papers)
		Exploration of Digestive Diseases
		Bioorganic Chemistry
		Science of the Total Environment
		International Journal of Molecular Sciences
Lin Zhang	Peer Reviewer	Annals of Internal Medicine
		Gut
		Gastroenterology
		Journal of Pathology
		Oncogene
		International Journal of Molecular Sciences
		Inflammopharmacology
		Current Chemistry Medicine
		Scientific Report
		BMC Cancer
		Biomedicine & Pharmacotherapy
		Pediatric Allergy and Immunology
		Alimentary Pharmacology & Therapeutics
Huarong Chen	Peer Reviewer	BBA - Molecular Basis of Disease
		Advanced Science
		Clinical and Translational Medicine
		Cancer Medicine
		Clinical Epigenetics
		Frontiers of Medicine
		Heliyon
		Cell Cycle
		Cellular Oncology
		Gut Microbes
		Gut
		Experimental Cell Research
		BMC Medicine
		Molecular Cancer
		Oncogene
Likai Tan	Peer Reviewer	Journal of Leucocyte Biology
		Frontiers in Immunology
Xiaodong Liu	Peer Reviewer	CNS Neuroscience & Therapeutics
		Molecular Neurobiology

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
William Wu	Sex Differences in the Gut Colonization of *Carnobacterium Maltaromaticum* for Suppressing Colorectal Tumorigenesis	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,180,120
	Carnobacterium Maltaromaticum as a Novel Probiotic Treatment for Attenuating Gut Barrier Dysfunction and Systemic Inflammation in Sepsis	Health Bureau – Health and Medical Research Fund	13/11/2022	12/11/2025	1,499,960
	Developing Probiotics into High-Efficacy and Safe Prophylactics and Adjuvant Therapies for Colorectal Cancer	Research Grants Council – Research Impact Fund	30/06/2022	29/06/2027	9,790,000
	Mechanism of VitD3 Targeting Autophagy-Lysosomal Pathway Inhibiting C. *Difficile*-Related Inflammation	National Natural Science Foundation of China	01/01/2021	31/12/2024	RMB 550,000
	m6A Modification Controls the Autophagic Response to *Helicobacter Pylori* Infection	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	1,195,290
	A Mechanistic Study on the Influence of Cancers on Human Genome Evolution	Shenzhen Science and Technology Innovation Commission – Shenzhen Science and Technology Programme	18/03/2019	30/09/2023	RMB 3,000,000
	Molecular Characterization of the Ubiquitin-Proteasome System as a Host Defense Mechanism Against Intracellular Helicobacter Pylori Infection - RMG01	Research Grants Council – Research Matching Grant Scheme	01/06/2020	31/05/2023	1,419,234
	Developing Mechanism-driven Probiotics for Improving Response to Immunotherapy in Colorectal Cancer	Innovation and Technology Fund – Innovation and Technology Support Programme Seed Fund	26/02/2023	25/02/2025	3,994,999

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Lin Zhang	Targeting H3k27me3 By EZH2 Inhibitors in Control of Drug-Resistant Helicobacter Pylori Colonization	Health Bureau – Health and Medical Research Fund	01/09/2020	31/08/2023	1,494,292
	Effects of Ketamine and Cannabis on Antimicrobial Peptide Expression and Infection Susceptibility: An In Vitro and Animal Study	Beat Drugs Fund, Narcotics Division, Security Bureau	01/08/2019	31/12/2023	3,086,661 (including external audit fee)
	Translating Microbiome, Multi-omics and Dietary Innovations to Enhance Inflammatory Bowel Disease Diagnosis and Outcom	Research Grants Council – Research Impact Fund	29/06/2023	28/06/2026	7,750,000
	Gut Microbiota in Adults with Chronic Widespread Pain: A Pilot Case-Control Study	Peter Hung Pain Research Institute	01/12/2022	30/11/2024	602,810
	Novel Strategies to Facilitate Early Detection, Prevention and Intervention for Long-Term Health Problems Related to COVID-19 (NovITor-COVID Study)	Health Bureau – Commissioned Research on the Novel Coronavirus Disease (COVID-19)	01/04/2021	31/03/2026	45,991,725
	Optimisation of Clinical Treatment of Severe Influenza to Reduce Morbidity and Mortality	Health Bureau – Commisioned Programmes for Influenza Research	01/09/2019	31/08/2026	4,996,960
Xiaodong Liu	Screening of Botanic Ingredients for the Prevention or Treatment of Gout and the Mechanistic Study	Amway R&D China	28/04/2020	27/04/2023	RMB 600,000
	Screening of Botanic Ingredients for the Prevention or Treatment of Gout and the Mechanistic Study	Research Grants Council – Research Matching Grant Scheme	01/09/2020	27/04/2023	277,688.42
	Delineating the Sensorimotor Cortex-Spinal Cord Descending Pain Pathway and Its Interaction with Gut Microbiota	Research Grants Council – General Research Fund	01/01/2023	31/12/2024	1,114,323
	Bacteroides Uniformis as a Novel Probiotic Treatment for Attenuating Microglia Reactivation and Pain Hypersensitivity in Peripheral Neuropathy	Health Bureau – Health and Medical Research Fund	01/08/2022	30/07/2024	1,298,728
	Gut Microbiota Analysis for Identifying Prognostic Factors of Postherpetic Neuralgia and Pain-Alleviating Probiotics	Shenzhen Technology Innovation Committee	30/04/2022	30/04/2024	RMB 1,000,000
Xiaodong Liu	Costunolide Administration for the Treatment of Neuropathic Pain Via Blocking Microglia Mediated Synaptic Pruning in Spinal Cord	National Natural Science Foundation of China	01/01/2022	31/12/2025	RMB 550,000
Huarong Chen	Elucidating the Role of RNA N1-Methyladenosine Modifications in Colorectal Cancer	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	1,130,669
	RNA N6-Methyladenosine Methyltransferase-like 3 (METTL3) is a Potential Therapeutic Target for Immunotherapy in Colorectal Cancer	Health Bureau – Health and Medical Research Fund	01/09/2021	31/08/2023	1,475,400
	Elucidating the Role and Mechanism of RNA N6-Methyladenosine m6A Regulator METTL3 in Promoting Colorectal Cancer Through Modulating Gut Microbiota	Research Grants Council – General Research Fund	01/01/2022	31/12/2024	1,150,352
	Elucidating the Role of RNA N6-Methyladenosine Writer Methyltransferase Like 3 (METTL3) in Driving Immune Suppression in Colorectal Cancer	National Natural Science Foundation of China	01/01/2022	31/12/2024	RMB 300,000
	Defining the Role of TRNA Methyltransferase 61A (TRMT61A) in Colorectal Cancer	National Natural Science Foundation of China	01/01/2023	31/12/2026	RMB 520,000
	Elucidating the Role and Therapeutic Potential of RNA N1-methyladenosine (m1A) Modification in Sepsis	Health Bureau – Health and Medical Research Fund	01/04/2023	31/03/2026	1,499,808

Publications

A. Journal Papers

1. Li Q, Chan H, Liu WX, Liu CA, Zhou Y, Huang D, Wang X, Li X, Xie C, Liu WYZ, Wang XS, Ng SK, Gou H, Zhao LY, Fong W, Jiang L, Lin Y, Zhao G, Bai F, Liu X, Chen H, Zhang L, Wong SH, Chan MTV, Wu WKK, Yu J. Carnobacterium maltaromaticum boosts intestinal vitamin D production to suppress colorectal cancer in female mice. *Cancer Cell*. 2023;41(8):1450-1465.e8. doi:10.1016/j.ccell.2023.06.011.

2. Wu WKK. Parabacteroides distasonis: An emerging probiotic? *Gut*. 2023;72(9):1635-1636. doi:10.1136/gutjnl-2022-329386. (Editorial)

3. Liu Y, Chan MTV, Chan FKL, Wu WKK, Ng SC, Zhang L. Lower gut abundance of Eubacterium rectale is linked to COVID-19 mortality. *Frontiers in Cellular and Infection Microbiology*. 2023;13. doi:10.3389/fcimb.2023.1249069.

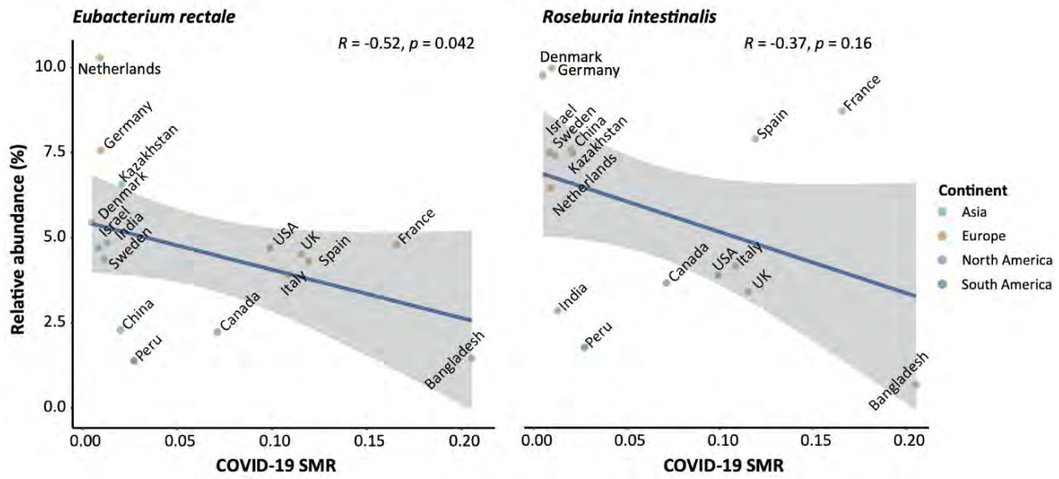
4. Kang X, Ng SK, Liu C, Lin Y, Zhou Y, Kwong TNY, Ni Y, Lam TYT, Wu WKK, Wei H, Sung JJY, Yu J, Wong SH. Altered gut microbiota of obesity subjects promotes colorectal carcinogenesis in mice. *eBioMedicine*. 2023;93. doi:10.1016/j.ebiom.2023.104670.

5. Su H, Cheung H, Lau HCH, Chen H, Zhang X, Qin N, Wang Y, Chan MTV, Wu WKK, Chen H. Crosstalk between gut microbiota and RNA N6-methyladenosine modification in cancer. *FEMS Microbiology Reviews*. 2023;47(4). doi:10.1093/femsre/fuad036. (Review)

6. Chen H, Zhang X, Su H, Zeng J, Chan H, Li Q, Liu X, Zhang L, Wu WKK, Chan MTV, Chen H. Immune dysregulation and RNA N6-methyladenosine modification in sepsis. *Wiley Interdisciplinary Reviews*: RNA. 2023;14(3). doi:10.1002/wrna.1764. (Review)

B. Conference Paper

1. Au-Doung PLW, Chan RH, Wu WKK, Li Q. Gut microbiota modulation: Probiotics and prebiotics in GI cancer. *Microbiome in Gastrointestinal Cancer* pp. 201-236. Singapore: Springer Nature



Negative correlations between the gut abundance of two bacterial species and COVID-19 mortality

Source:
Liu Y, Chan MTV, Chan FKL, Wu WKK, Ng SC, Zhang L (2023) Lower gut abundance of Eubacterium rectale is linked to COVID-19 mortality. Front Cell Infect Microbiol 13:1249069.



NEPHROLOGY

BIOMARKER AND TRANSLATIONAL RESEARCH
腎臟疾病研究

PRINCIPAL INVESTIGATOR
Cheuk Chun Szeto

TEAM MEMBERS
Jack Ng, Peter Poon, Ka Bik Lai, Cathy Luk, Chuanlei Li, Phyllis Cheng, Winston Fung, Gordon Chan

RESEARCH PROGRESS SUMMARY

Knowledge transfer and academic conferences

In 2023, **Cheuk Chun Szeto** and his team published the result of their research in a number of academic conferences in different countries outside Hong Kong, including Korea, Macau, and Mainland China. The topics of these conferences range from the management of common complications of chronic kidney disease, urinary podocyte markers, and the application of artificial intelligence to nephrology research. These conferences provide an opportunity for experts in the field to discuss strategies, share experiences and knowledge, and promote advancements in the management of kidney-related diseases and conditions. Specific conferences include:

1. New approaches to cardiorenal protection – Balancing RAASi Therapy and Potassium Levels. In: *New Horizons in Renal Innovations: Common, Rare and More* (symposium jointly organised by the Asian Pacific Society of Nephrology and Hong Kong Society of Nephrology), Hong Kong, March 2023.

2. Urinary podocyte markers in kidney disease. In: *Korean Society of Nephrology 2023 Meeting*, Seoul, April 2023.

3. Is artificial intelligence good for the kidney? In: *Hong Kong Society of Nephrology Annual Scientific Meeting,* Hong Kong, October 2023.

4. Update of the management of SIADH and hypervolemic hyponatremia. In: *The Society of Physician of Hong Kong Scientific Symposium*, Hong Kong, October 2023.

5. Primary glomerular diseases. In: *Macau Society of Nephrology Annual Scientific Meeting 2023*, Macau SAR, October 2023.

6. How to effectively manage hyperkalemia in the long term? In: *CKD Multidimensional Management Capability Enhancement Program - Hyperkalaemia Diagnosis and Treatment Advances Summit, Chinese Aging Well Association*, Guangzhou, China, November 2023.

7. AKI complicating cancer therapy. In: *4th International Congress of Chinese Nephrologists*, Guangzhou, China, December 2023.

8. Glycaemic control in CKD and dialysis patients – better index beyond HbA1c. In: *4th International Congress of Chinese Nephrologists*, Guangzhou, China, December 2023.

9. What should a young nephrologist know before starting research? In: *4th International Congress of Chinese Nephrologists*, Guangzhou, China, December 2023.

Organisation of academic conferences

In 2023, the team contributed to the organisation of two academic conferences, including the KDIGO Implementation Summit on Diabetes Management in CKD: From Primary to Collaborative Care in Hong Kong, and the 4th International Congress of Chinese Nephrologists in Guangzhou. These conferences serve as a valuable platform for renowned experts in the field to convene and engage in in-depth discussions regarding the latest advancements in the management of kidney diseases and dialysis. With a primary focus on fostering collaboration and knowledge exchange, these gatherings enable participants to share their valuable experiences, insights, and expertise, thereby contributing to the overall progress and development of collaborative research projects with other centres.

Research collaborations

Local collaborations

The group has extensive collaboration with various local investigators who are experts in artificial intelligence, 3-dimensional tissue imaging, and nano-particle therapy. They strive to facilitate progress in the field of kidney-related diseases management through innovative research and technology. Specific collaborations include:

1. With Owen Ko and Hei Ming Lai, Department of Psychiatry, The Chinese University of Hong Kong, on: 3D ultrastructural study of kidney
2. With I-Ming Hsing, Department of Chemical and Biological Engineering, The Hong Kong University of Science and Technology, on: Wearable device to measure biomarkers for kidney diseases
3. With Jonathan Choi, Department of Biomedical Engineering, The Chinese University of Hong Kong, on: Nanoparticle therapy for kidney disease
4. With Yan Xiaoyu, School of Pharmacy, The Chinese University of Hong Kong, on: Novel treatment of renal anemia.
5. With Nelson Tang, Department of Chemical Pathology, The Chinese University of Hong Kong, on: Immunological response of COVID vaccination
6. With Marques Ng, School of Nursing, The Chinese University of Hong Kong, on: Psychological health of patients with kidney disease
7. With Weitian Chen, Department of Diagnostic Radiology and Organ Imaging, The Chinese University of Hong Kong, on: Novel methods for the assessment of kidney fibrosis
8. With Ting-hsuan Chen, Department of Biomedical Engineering, City University of Hong Kong, on: Novel diagnostic tools for albuminuric kidney diseases

Overseas collaborations

The group also collaborates extensively with researchers from around the world in the field of nephrology and dialysis. These collaborations include experts from Canada, the United Kingdom, Austria, Germany, USA, and Israel. Their collaborative projects cover a wide range of areas, such as studying endotoxemia in chronic kidney disease, developing innovative technologies for rapid bacterial identification, and investigating the use of new peritoneal dialysis solutions. The main objective of these projects is to explore and develop novel technologies for the management of kidney diseases. Specific collaborative projects include:

1. With Chris McIntyre, Division of Nephrology, Schulich School of Medicine and Dentistry, The University of Western Ontario, Canada on: Endotoxemia in chronic kidney disease
2. With Stanley Fan, Barts Health NHS Trust, London, England, United Kingdom on: Polymerase Chain Reaction/Electrospray Ionisation-Mass Spectrometry (PCR/ESI-MS) for rapid bacterial identification in peritoneal dialysis effluent.
3. With Daniel March, Department of Infection, Immunity & Inflammation, University of Leicester, England, United Kingdom on: Endotoxemia and cardiovascular disease in dialysis patients
4. With Christoph Aufricht, The Medical University of Vienna, Austria on: Alanyl-Glutamine in Peritoneal Dialysis Fluids Improves Peritoneal Health and Systemic Inflammation
5. With Nelson Leung, Mayo Clinic College of Medicine, USA, on: Novel tools for the risk stratification of IgA nephropathy.
6. Zytoprotec GmbH, Germany on: Alanyl-Glutamine in Peritoneal Dialysis Fluids Improves Peritoneal Health and Systemic Inflammation
7. liberDi, The Trendlines Group, Israel on: The liberDi dialysis system

RESEARCH AND SCHOLARSHIP

Academic Editorships

Name	Details	
	Role	Journal
Cheuk Chun Szeto	Deputy Editor	Nephrology
	Associate Editor	Peritoneal Dialysis International
	Theme Editor (Peritoneal Dialysis)	Clinical Kidney Journal
	Editorial Board	Clinical Journal of American Society of Nephrology

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Cheuk Chun Szeto	Reviewer	Clinica Chimica Acta
		Kidney International
		American Journal of Kidney Diseases

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Cheuk Chun Szeto	Modified Creatinine Index as a Non-Invasive Tool for the Monitoring of Muscle Mass in Peritoneal Dialysis	Health Bureau – Health and Medical Research Fund	01/12/2023	30/11/2025	1,015,344
	Fluid Overload as the Cause of Gut Permeability Barrier Dysfunction in Chronic Kidney Disease	Lo's Family Charity Fund Limited	01/07/2022	30/06/2024	1,800,000
	Efficacy and Safety of Multiple Doses of Oral BI 690517 Over 14 Weeks, Alone and in Combination with Empagliflozin, in Patients with Diabetic and Non-diabetic Chronic Kidney Disease	Boehringer Ingelheim International GmbH	15/06/2022	13/02/2024	222,267
	A Randomized, Multicentre, Double-blind, Parallel-group, Active-control Study of the Efficacy and Safety of Sparsentan for the Treatment of Immunoglobulin a Nephropathy	Retrophin, Inc.	01/11/2018	30/06/2023	358,147
	Artificial Intelligent Methods and Technologies for Precise Diagnosis and Treatment of Cancer	Innovation and Technology Commission – Mainland-Hong Kong Joint Funding Scheme	01/01/2022	31/12/2024	2,136,125
	Randomised, Double-blind (Within Dose Groups), Placebo-controlled and Parallel Group Trial to Investigate the Effects of Different Doses of Oral BI 685509 Given Over 20 Weeks on UACR Reduction in Patients with Non-diabetic Kidney Disease	Boehringer Ingelheim International GmbH	01/06/2021	31/01/2023	358,988
	A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicentre Phase 3 Study to Investigate the Efficacy and Safety of Finerenone, in addition to Standard of Care, on the Progress	Bayer HealthCare Limited	01/08/2022	30/06/2023	174,458

Publications

A. Journal Papers

1. Chan GCK, Ng JKC, Cheng PMS, Chow KM, Szeto CC, Li PKT. Dietary micronutrient intake and its relationship with the malnutrition–inflammation–frailty complex in patients undergoing peritoneal dialysis. *Nutrients*. 2023;15(23). doi:10.3390/nu15234934.

2. Ling J, Ng JKC, Lau ESH, Luk AOY, Ma RCW, Vigersky RA, Li PKT, Chan JCN, Szeto CC, Chow E. Impact of body composition and anemia on accuracy of a real-time continuous glucose monitor in diabetes patients on continuous ambulatory peritoneal dialysis. *Diabetes Technology and Therapeutics*. Published online January 1, 2023. doi:10.1089/dia.2023.0349.

3. Zeng L, Chan GCK, Ng JKC, Fung WWS, Chow KM, Szeto CC. The effect of dipeptidyl peptidase 4 (DPP-4) inhibitors on hemoglobin level in diabetic kidney disease: A retrospective cohort study. *Medicine (United States)*. 2023;102(32):E34538. doi:10.1097/md.0000000000034538.

4. Jin Y, Cheng IT, So H, Wu D, Griffith JF, Hung VW, Qin L, Szeto CC, Chan AW, Tam LS. Role of inflammatory burden and treatment on joint space width in psoriatic arthritis—a high-resolution peripheral quantitative computed tomography study. *Arthritis Research and Therapy*. 2023;25(1). doi:10.1186/s13075-023-03124-5.

5. Fung WWS, Cheng PMS, Ng JKC, Chan GCK, Chow KM, Li PKT, Szeto CC. Pharmacokinetics of apixaban among peritoneal dialysis patients. *Kidney Medicine*. 2023;5(8). doi:10.1016/j.xkme.2023.100646.

6. Szeto CC, So H, Poon PYK, Luk CCW, Ng JKC, Fung WWS, Chan GCK, Chow KM, Lai FMM, Tam LS. Urinary long non-coding RNA levels as biomarkers of lupus nephritis. *International Journal of Molecular Sciences*. 2023;24(14). doi:10.3390/ijms241411813.

7. Than WH, Ng JKC, Chan GCK, Fung WWS, Chow KM, Szeto CC. Impact of weight gain on the subsequent survival of new peritoneal dialysis patients. *Kidney Diseases*. 2023;9(3):197-205. doi:10.1159/000529186.

8. Tian N, Meng H, Fung WWS, Ng JKC, Chan GCK, Kwong VWK, Pang WF, Chow KM, Li PKT, Szeto CC. Peritoneal dialysis after failed kidney allograft: Comparing patients with and without pd before transplant. *PLoS ONE*. 2023;18(7 July). doi:10.1371/journal.pone.0284152.

9. Than WH, Chan GCK, Kwan BCH, Lai KB, Chan RCK, Teoh JYC, Ng JKC, Fung WWS, Chow KM, Cheng PMS, Li PKT, Szeto CC. Plasma vaspin levels and clinical outcome in incident peritoneal dialysis patients. *BMC Nephrology*. 2023;24(1). doi:10.1186/s12882-023-03259-2.

10. Li KY, Tam CHT, Liu H, Day S, Lim CKP, So WY, Huang C, Jiang G, Shi M, Lee HM, Lan H, Szeto CC, Hanson RL, Nelson RG, Susztak K, Chan JCN, Yip KY, Ma RCW, Consortium T. DNA methylation markers for kidney function and progression of diabetic kidney disease. *Nature Communications*. 2023;14(1):2543. doi:10.1038/s41467-023-37837-7.

11. Lau LFS, Ng JKC, Fung WWS, Chan GCK, Cheng PMS, Chow KM, Leung CB, Li PKT, Szeto CC. Relationship between serial serum neutrophil-lymphocyte ratio, cardiovascular mortality, and all-cause mortality in Chinese peritoneal dialysis patients. *Kidney and Blood Pressure Research*. 2023;48(1):414-423. doi:10.1159/000530554.

12. Ng JKC, Ling J, Luk AOY, Lau ESH, Ma RCW, Li PKT, Szeto CC, Chan JCN, Chow E. Evaluation of a fourth-generation subcutaneous real-time continuous glucose monitor (CGM) in individuals with diabetes on peritoneal dialysis. *Diabetes Care*. 2023;46(6):1191-1195. doi:10.2337/dc22-2348.

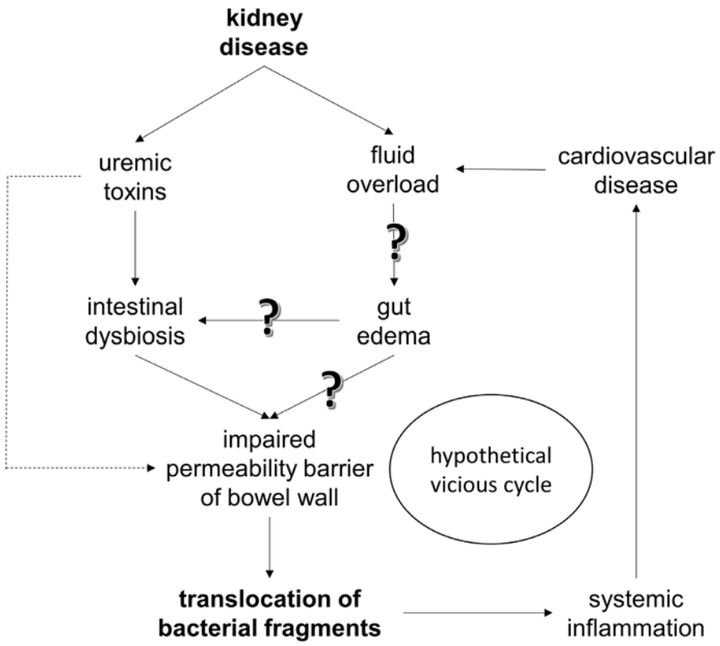
13. Zeng L, Ng JKC, Fung WWS, Chan GCK, Chow KM, Szeto CC. Intrarenal and urinary glycogen synthase kinase-3 beta levels in diabetic and nondiabetic chronic kidney disease. *Kidney and Blood Pressure Research*. 2023;48(1):241-248. doi:10.1159/000530210.

14. Than WH, Chan GCK, Kwan BCH, Lai KB, Chan RCK, Teoh JYC, Ng JKC, Fung WWS, Chow KM, Cheng PMS, Li PKT, Szeto CC. Omentin-1 levels and outcomes in incident peritoneal dialysis patients. *Kidney Medicine*. 2023;5(3). doi:10.1016/j.xkme.2023.100598.

15. Chan GCK, Fung WWS, Szeto CC, Ng JKC. From MIA to FIFA: The vicious matrix of frailty, inflammation, fluid overload and atherosclerosis in peritoneal dialysis. *Nephrology*. 2023;28(4):215-226. doi:10.1111/nep.14150. (Review)

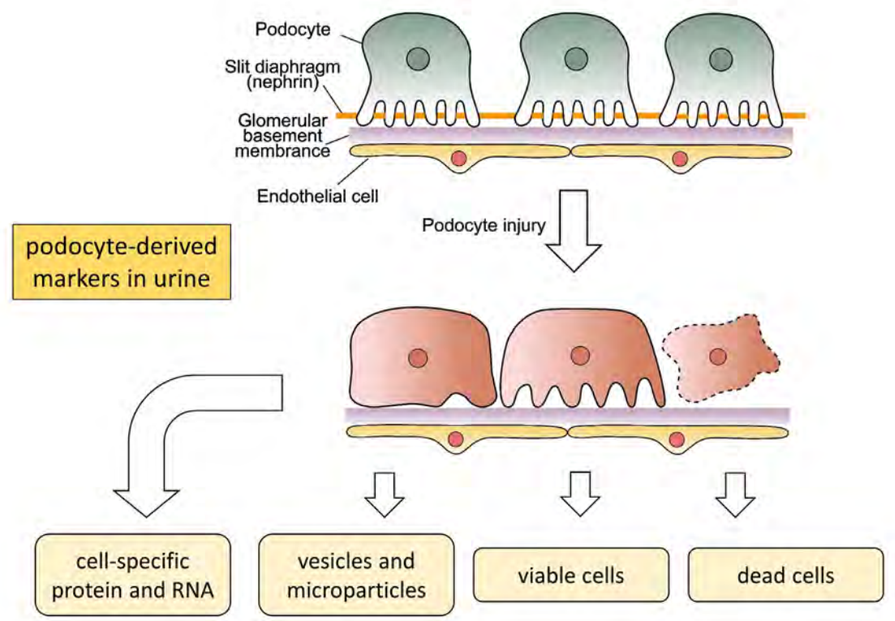
16. Chan GCK, Ng JKC, Chow KM, Szeto CC. SGLT2 inhibitors reduce adverse kidney and cardiovascular events in patients with advanced diabetic kidney disease: A population-based propensity score-matched cohort study. *Diabetes Research and Clinical Practice*. 2023;195. doi:10.1016/j.diabres.2022.110200.

17. Ng JKC, Kwan BCH, Chan GCK, Chow KM, Pang WF, Cheng PMS, Leung CB, Li PKT, Szeto CC. Predictors and prognostic significance of persistent fluid overload: A longitudinal study in Chinese peritoneal dialysis patients. *Peritoneal Dialysis International*. 2023;43(3):252-262. doi:10.1177/08968608221110491.



Pathogenic pathways of bacterial fragments translocation through the bowel and the hypothetical vicious cycle with cardiovascular disease.

Source: Cheuk Chun Szeto



Podocyte injury and potential podocyte-derived markers in urine. Injury to podocytes results in 3 inter-related pathological processes: morphological change, apoptosis, and detachment. Podocytes may remain viable but manifest as morphological changes that have functional downstream consequences, such as proteinuria and tubulointerstitial fibrosis. Podocyte apoptosis may develop as a result of cumulated morphological changes or directly from specific insults. Loss of podocyte in the glomeruli (i.e. podocytopenia) leads to architectural changes of the glomerular capillary loop and results in glomerulosclerosis. Podocytes, either apoptotic or viable ones due to loss of α3β1 integrin, may detach to the urinary space, be identified in the urine, and serve as markers of kidney disease. Vesicles, microparticles, or podocyte-specific molecules derived from injured or apoptotic podocyte may also be detected in the urine and serve as biomarkers. (GCBM, glomerular capillary basement membrane; AgII, angiotensin II; TGF-β, transforming growth factor beta; ROS, reactive oxygen species)

Source: Li C, Szeto CC. Urinary podocyte markers in diabetic kidney disease. Kidney research and clinical practice. Published online February 6, 2024. doi:10.23876/j.krcp.23.109.



ROBOTICS & ARTIFICIAL INTELLIGENCE

機械人與人工智能

PRINCIPAL INVESTIGATOR

Zheng Li

TEAM MEMBERS

Tao Zhang, Zhiwei Cui, Michael Lei, Truman Cheng, Zixiao Chen, Xuyang Ren, Ruoyu Xu, Yingbai Hu, Haochen Hu, Wai Shing Chan, Geoffrey Liu, Yuelin Zou, Zixin Jiang, Yisong Zhao, Yisen Huang, Jixiu Li, Yehui Li, Xiao Luo, Wing Yin Ng, Yichong Sun, Yitian Xian, Limin Zou, Jian Li, Ke Xie

RESEARCH PROGRESS SUMMARY

Zheng Li's team continued to explore the possibilities across different aspects of surgical robots including semi-autonomous transperineal prostatic biopsy robotic system, a multi-helical continuum mechanism for minimally invasive surgical robot inspired by DNA structure, a novel soft-tethered magnetic-pneumatic steered endoscope system for single-port video-assisted thoracic surgery (VATS), an intelligent magnetic anchored and guided endoscope (MAGS) embedded with autonomous view control from surgeon preference, a novel hybrid magnetic actuation and sensing system towards real-time capsule pan-endoscopy screening and a stereotactic brain biopsy robotic system with the incorporation of medical image processing and artificial intelligence. Some of the projects have progressed from conceptual design and prototype to clinically prepared systems for animal tests and clinical trials. Following the rapid recovery of on-site international conferences and events, the team members proactively presented their research results at top exhibitions and academic conferences such as the Geneva International Exhibition, IEEE International Conference on Robotics and Automation (ICRA), IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS) and IEEE International Conference on Robotics and Biomimetics (ROBIO). Meanwhile, their works were successfully published in leading journals. In particular, the prostate biopsy robotic system and the magnetically actuated capsule endoscope received the Silver Medals in the International Exhibition of Inventions of Geneva 2023. The former was selected as one of the featured projects from the showcase of The Chinese University of Hong Kong (CUHK) in the InnoCarnival 2023 exhibited in The Hong Kong Science Park. At least seven projects in the team are funded by General Research Fund, Innovation and Technology Fund, Research Grants Council and CUHK in which four of them initiated in 2023. The team will continue to strive to strengthen collaborations with long-term partners including ETH Zurich, Johns Hopkins University and Imperial College London meanwhile increasing participation in different academic and research activities in 2024.

RESEARCH AND SCHOLARSHIP

Research Awards and Recognitions

Name	Details	
	Award	Organisation
Zheng Li Michael Lei Xiao Luo Peter Chiu Philip Chiu Chi Fai Ng Yunhui Liu	Silver Medal	International Exhibition of Inventions Geneva 2023
Zheng Li Yehui Li Yichong Sun Philip Chiu James Lau	Silver Medal	International Exhibition of Inventions Geneva 2023

Academic Editorships

Name	Details	
	Role	Journal
Zheng Li	Associate Editor	IEEE Robotics and Automation Letters
		IEEE Transactions on Medical Robotics and Bionics
	Topic Editor	Frontiers in Robotics and AI

Reviewers of Journal / Conference

Name	Details	
	Role	Journal / Conference
Michael Lei	Reviewer	Transactions on Mechatronics (TMECH)
		2023 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS)
		2023 IEEE/ASME International Conference on Advanced Intelligent Mechatronics (AIM)
Zheng Li	Reviewer	Science Advances
		Advanced Science
		IEEE Transactions on Biomedical Engineering
		IEEE Transactions in Industrial Engineering

Name	Details	
	Role	Journal / Conference
Zheng Li	Reviewer	IEEE Transactions on Cybernetics
		IEEE Transactions on Robotics
		Transactions on Mechatronics (TMECH)
		IEEE Transactions on Medical Robotics and Bionics
		IEEE Robotics and Automation Letters
		IEEE Transactions on Neural Systems and Rehabilitation Engineering
		International Journal of Robotics Research
		Soft Robotics
		Sensors Journal
		Scientific Report
		Journal of Mechanisms and Robotics
		Biomedical Signal Processing and Control
		Science China Technological Sciences
		IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS)
		IEEE International Conference on Robotics and Automation (ICRA)
		Hamlyn Symposium on Medical Sciences
		IEEE International Conference on Robotics and Biomimetics (ROBIO)
		IEEE/EMBS International Conference on Biomedical Robotics and Biomechatronics (BioRob)

Grants and Consultancies

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Zheng Li	Intelligent Magnetic Anchored and Guided Endoscope with Surgeon Preference Embedded Autonomous View Control	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	965,158
	DNA Structure Inspired Multi-helix Continuum Mechanism for Minimally Invasive Surgical Robots	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	873,995
	Design of Elastomer-based Soft Actuator and Flexible Electronic Polymers Sensor for Rehabilitation of Hand Function after Stroke	Research Grants Council – General Research Fund	01/01/2023	31/12/2025	844,415
Zheng Li	Development of Lightweight, Intelligent, and Remote Ultrasound Robotic System	Innovation and Technology Commission – Innovation and Technology Fund	01/06/2022	31/05/2024	1,499,275
	Intelligent Surgical Robotic Assistant	The Chinese University of Hong Kong Resource Allocation Committee – Strategic Seed Funding for Collaborative Research Scheme	01/08/2022	31/07/2024	300,000
	Artificial Intelligence (AI)-assisted Risk-based Prostate Cancer Detection: A Synergy of Novel Biomarkers, Advanced Imaging, and Robotic-assisted Diagnosis	Research Grants Council – Young Collaborative Research Grant	01/06/2023	31/05/2024	1,661,542
	The Development of an Intelligent System for Real-time Automated Anatomical Recognition System during Endoscopic Ultrasound	Innovation and Technology Commission – Innovation and Technology Fund	01/03/2023	31/08/2024	1,377,079
	Soft Robotic Exosuit for Lower Limb Rehabilitation	Innovation and Technology Commission – Innovation and Technology Support Programme	01/09/2021	31/08/2023	2,948,600

Publications

A. Journal Papers

1. Huang Y, Li W, Zhang X, Li J, Li Y, Sun Y, Chiu PWY, Li Z. 4-DOF visual servoing of a robotic flexible endoscope with a predefined-time convergent and noise-immune adaptive neural network. *IEEE/ASME Transactions on Mechatronics.* Published online 2023. doi:10.1109/tmech.2023.3286850. (Epub ahead of print)

2. Cui Z, Li Y, Li W, Li J, Chiu PWY, Li Z. Hybrid vision/magnetic-force finite-time convergent neural network tracking control of electromagnetically actuated soft-tethered colonoscope robot with current constraints. *IEEE Transactions on Systems, Man, and Cybernetics: Systems*. 2023;53(10):6080-6093. doi:10.1109/tsmc.2023.3280588.

3. Li J, Huang Y, Zhang X, Xie K, Xian Y, Luo X, Chiu PWY, Li Z. An autonomous surgical instrument tracking framework with a binocular camera for a robotic flexible laparoscope. *IEEE Robotics and Automation Letters*. 2023;8(7):4291-4298. doi:10.1109/lra.2023.3281934.

4. Xian Y, Zhang X, Luo X, Li J, Zou L, Xie K, Li J, Li Y, Huang Y, Chan DTM, Chan DYC, Li Z. A semi-autonomous stereotactic brain biopsy robotic system with enhanced surgical safety and surgeon-robot collaboration. *IEEE Transactions on Biomedical Engineering*. 2023;70(12):3288-3299. doi:10.1109/tbme.2023.3281590.

5. Li Y, Ng WY, Li W, Huang Y, Zhang H, Xian Y, Li J, Sun Y, Chiu PWY, Li Z. Towards semi-autonomous colon screening using an electromagnetically actuated soft-tethered colonoscope based on visual servo control. *IEEE Transactions on Biomedical Engineering*. Published online January 1, 2023. doi:10.1109/tbme.2023.3292336. (Epub ahead of print)

B. Conference Papers

1. Ng WY, Wang HY, Li Z. Speech-image based multimodal AI interaction for scrub nurse assistance in the operating room. *2023 IEEE International Conference on Robotics and Biomimetics, ROBIO 2023*. Published online 2023. doi:10.1109/robio58561.2023.10354726.

2. Luo X, Xian Y, Lei M, Li J, Xie K, Zou L, Li Z. Robotic kinematic calibration with only position data and consideration of non-geometric errors using PoE-based model and gaussian mixture models. *IEEE International Conference on Intelligent Robots and Systems*. Published online 2023:1803-1809. doi:10.1109/iros55552.2023.10341731.

3. Sun Y, Li Y, Li J, Ng WY, Xian Y, Huang Y, Chiu PWY, Li Z. Model-based bending control of magnetically-actuated robotic endoscopes for automatic retroflexion in confined spaces. *IEEE International Conference on Intelligent Robots and Systems*. Published online 2023:8439-8445. doi:10.1109/iros55552.2023.10342414.

C. Patents

1. Title: System and Method for Automatic Stomach Screening
   Filing date: 16 February 2023

2. Title: Magnetic Anchored and Actuated System and Manufacturing Method Thereof
   Filing date: 20 April 2023

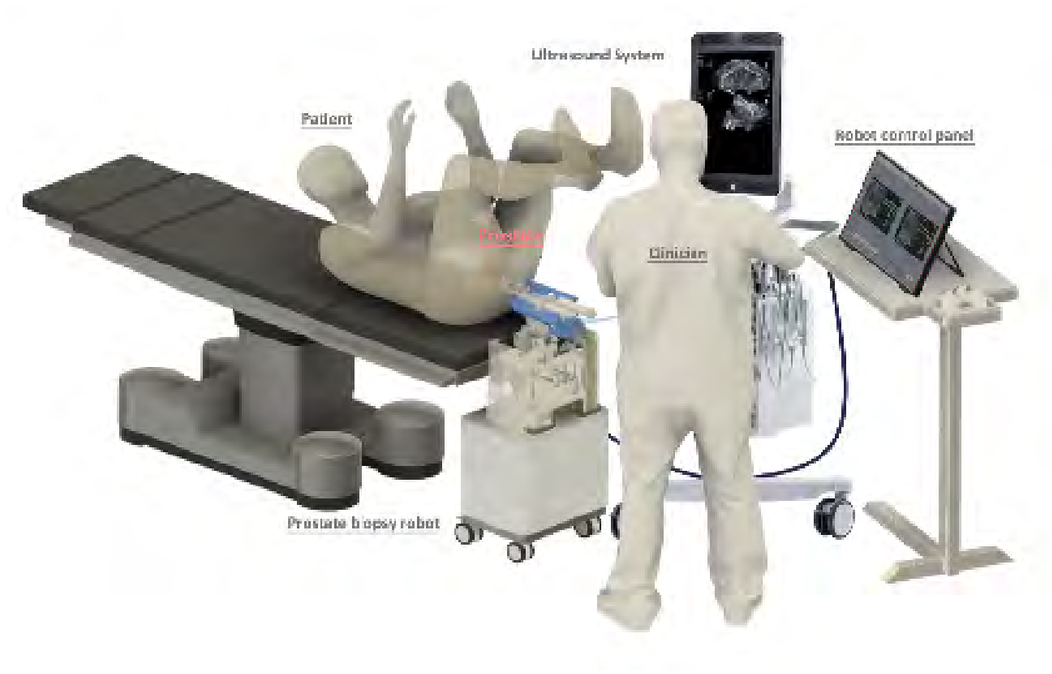
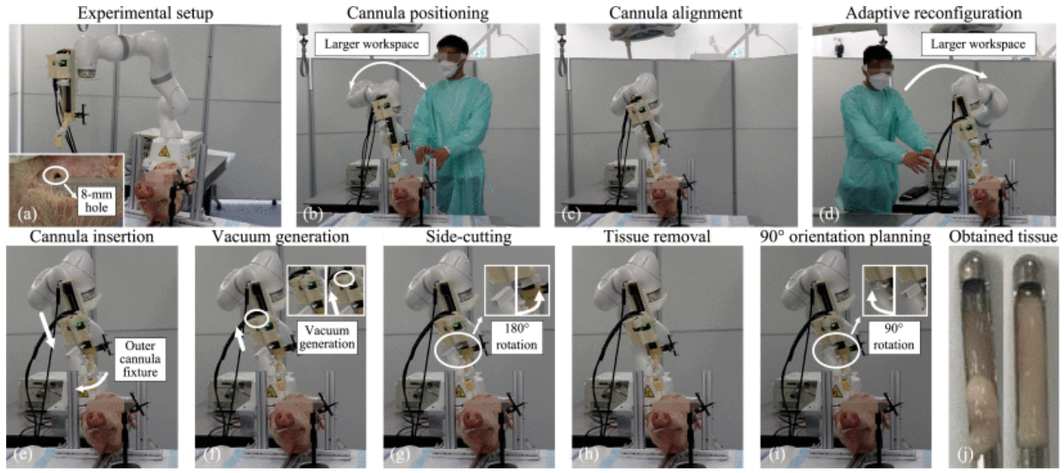


Illustration of the designed robotic prostate biopsy system with BK ultrasound system equipped with bi-planar transducer.

Source: Zheng Li's team



Brain biopsy test on swine head with the proposed robotic biopsy module: (a) Experimental setup, (b) Cannula positioning, (c) Cannula alignment, (d) Adaptive reconfiguration for workspace interference minimization, (e) Cannula insertion and outer cannula fixture, (f) Vacuum generation, (g) 180-degree side-cutting for tissue separation, (h) First tissue acqusition, (i) 90-degree orientation planning before the second biopsy, (j) Obtained samples.

Source: Xian Y, Zhang X, Luo X, Li J, Zou L, Xie K, Li J, Li Y, Huang Y, Chan DTM, Chan DYC, Li Z. A semi-autonomous stereotactic brain biopsy robotic system with enhanced surgical safety and surgeon-robot collaboration. IEEE Transactions on Biomedical Engineering. 2023;70(12):3288-3299. doi:10.1109/tbme.2023.3281590.



Hein Min Tun
黃世萬

INTERVIEW WITH PRINCIPAL INVESTIGATOR

與首席研究員對話

Hein Min Tun, trained in veterinary medicine, received his bachelor's degree in Myanmar in 2007 and his master's degree in Thailand in 2009. He furthered his studies at The University of Hong Kong, obtaining his PhD in 2014. In 2022, he joined The Jockey Club School of Public Health and Primary Care in CUHK as an Associate Professor and became the Associate Director of the Microbiota I-Center (MagIC) in 2023. His research focuses on the microbiome, antimicrobial resistance, and infectious diseases. With a diverse academic background spanning Myanmar, Thailand, and Canada, he brings a unique and valuable perspective to his research at CUHK.

Q1

What drew you to pursue your academic and research journey in Hong Kong after graduating from universities in Myanmar and Thailand and conducting research in Canada? How do you think the research environment and culture differ, and how does it support your research?

I did my PhD in Hong Kong, so I am familiar with the research infrastructure and culture here. During my PhD, I found many positive aspects of the research environment in Hong Kong. After spending my post-doctoral years in Canada under a prestigious CIHR fellowship, I felt that there was something significant I could contribute back in Hong Kong.



Group photo at the graduation of a PhD student.

When I returned in 2018, microbiome and antimicrobial resistance (AMR) research still needed to be improved in Hong Kong. I wanted to make Hong Kong a beacon for this area of research. Additionally, I was attached to esteemed professors like Keiji Fukuda and Malik Peiris, who were significant motivators. Hong Kong's research environment is unique due to its efficiency and productivity. The government's push towards translational research since 2018 was a game-changer, attracting me to set up my research career here.

Accessing cutting-edge technologies can be challenging in places like Thailand and Myanmar, whereas Hong Kong excels in this aspect. Researchers in Hong Kong are incredibly ambitious and hardworking, which differs from the more laid-back approach in some other countries. The focus in Hong Kong on short-term projects, like the General Research Fund (GRF) and Health and Medical Research Fund (HMRF) projects, promotes quick delivery and flexibility, which is advantageous, especially when adapting to new conditions like the COVID-19 pandemic.

Q2

What motivated you to specialise in studying infectious diseases and microbiota, given that you pursued a bachelor's and master's degree in veterinary science?

My background in veterinary science played a crucial role in my interest in infectious diseases. After my veterinary degree, I worked in a remote area between Burma and China, where I controlled two animal outbreaks, including one involving anthrax. This experience sparked my interest in infectious disease epidemiology. Many contagious diseases originate from animals, making the One Health approach essential, which I further explored during my master's in veterinary public health.

In 2010, during my PhD in Hong Kong, the advent of Next-Generation Sequencing opened up the field of microbiome research. The microbiome significantly impacts our immunity and overall health, aligning well with my background in ecology and infectious diseases. This interdisciplinary knowledge allowed me to delve deeper into microbiome research, unlocking numerous mysteries and contributing to our understanding of homeostasis and immunity.

Q3

Microbiome research is a relatively new health and medical research field. Could you please share the latest advancements in this area and their impact on health?

Microbiome research has advanced rapidly over the past two decades. Currently, three main areas are seeing significant progress:

1. *Microbiome-based testing:* This includes diagnostics and predicting treatment efficacy based on the microbiome.
2. *Therapeutics:* Initially focused on faecal microbiota transplantation (FMT), this area now explores more advanced therapeutic approaches, such as engineered microbiomes and live biotherapeutics.
3. *Personalised medicine and synthetic biology:* These fields are developing personalised treatments based on microbiome profiles and utilising synthetic biology to engineer beneficial microbiomes.

The gut-brain axis is another exciting area. We are studying how the gut microbiome influences mood and neural activities, potentially providing new treatments for mood disorders, neurodegeneration, and neurodevelopmental disorders like autism spectrum disorder (ASD) and Parkinson's disease. The aim is to develop precise microbiome-based therapeutics as an alternative to traditional treatments, which often have significant side effects and stigmas.



PhD graduation photo at the PhD lab office

Q4

What are the biggest challenges or unanswered questions in our field that researchers are currently working on?

One of the biggest challenges is defining what constitutes a healthy microbiome. Unlike blood parameters, there is no standardised reference range for a healthy microbiome due to its complexity and variability, which are influenced by numerous factors. My colleagues and I are working on identifying key microbial species essential for health, aiming to develop a reference framework that can guide future research and clinical practices.

Another challenge is understanding the microbiome's role in infectious diseases. The microbiome orchestrates our immune system, influencing our response to infections and vaccines. For instance, our research shows that missing specific bacteria in early life can increase susceptibility to infections like influenza. This highlights the critical window in early life for developing a healthy microbiome, which shapes long-term immunity and health outcomes.

Q5

How do lifestyle factors, such as diet and hygiene practices, impact the composition and diversity of the microbiota, and how does this influence the risk of emerging infectious diseases?

Lifestyle factors significantly impact the microbiome. For example, diet and hygiene practices can alter the composition and diversity of the microbiota. Countries with stringent hygiene practices often have populations with less diverse microbiomes, which can affect their immune responses and susceptibility to infections. On the other hand, exposure to diverse microbial environments, such as those in less hygienic conditions, can train the immune system and enhance infection resistance.

However, balancing hygiene and exposure is crucial. While extreme hygiene can limit microbial diversity and weaken immune responses, adequate hygiene practices are essential for preventing harmful infections. We aim to understand these dynamics better and promote practices that support a healthy microbiome while protecting against infectious diseases.



Hein Min Tun gave a keynote lecture at Microecology and Immunity Health Clinical Research (MIHC) Conference in 2023 at Shanghai, China.

The InnoHK initiative provides a unique environment focused on translational research, which is challenging to achieve within traditional university settings. At MagIC, we benefit from access to cutting-edge technologies and a supportive infrastructure that fosters innovation. For example, we recently established a germ-free facility, enabling advanced microbiome research that was previously impossible.

This initiative also allows us to bridge the gap between research and societal impact. We learn and practice bringing innovations to market, ensuring that our research effectively reaches patients and the public. The generous support from the Hong Kong government has been instrumental in these advancements, facilitating our progress and enhancing our research capabilities.

Q6

As the Associate Director of the Microbiota I–Center (MagIC), which is one of the InnoCentres established under the Hong Kong Government's InnoHK initiative, how do you and your fellow scientists benefit from this new initiative from a researcher's perspective?

Q7

Your team has won the Most Social Impact Team Award of the 2023 Distinguished Research Awards for Gene and Cell Therapy. Could you share more details about this award?

This award, organised by a biotech company, recognised research teams with significant social impact. Our team won the Most Social Impact Team Award for our work on furry pets and infant immune responses, as well as our research on the microbiome and COVID-19 vaccine responses. Our study on furry pets showed that exposure to pets during pregnancy benefits the baby's microbiome and reduces the risk of allergic diseases and obesity, gaining extensive international media coverage.

Our research on the microbiome's influence on COVID-19 vaccine efficacy demonstrated that a healthy microbiome enhances vaccine responses. This finding provided practical advice during the pandemic, helping people maintain vaccine immunity and informing public health strategies. The award reflects the societal relevance and real-world impact of our research.



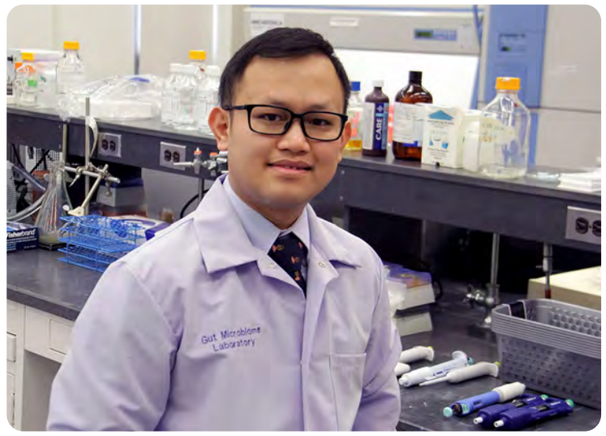
Hein Min Tun and his research group won the Gold Medal at the 3rd Asia Exhibition of Innovations and Inventions Hong Kong.

Q8

How do you stay motivated and maintain enthusiasm for your work in the face of setbacks or challenges?

Commitment to science is crucial. Believing in the value of our research helps us navigate challenges and setbacks. Perseverance is essential; we must consistently evaluate our science and adapt our approaches. Learning from setbacks is vital for future improvement.

Meeting renowned scientists and Nobel Laureates, like those at the Young Scientist Summit in Singapore, taught me that overcoming challenges is part of the scientific journey. Their experiences and perseverance inspire me to stay motivated. Viewing challenges as opportunities to learn, improve and keep our enthusiasm alive, driving us to continue our research.



Hein Min Tun at the Gut Microbiome Laboratory of the University of Manitoba, Canada



Photo with Ada E. Yonath, Nobel Laureate in Chemistry in 2009 at the Global Young Scientists Summit 2013, in Singapore

Q9

What advice would you like to give to the younger generations who are interested in research or pursuing a career in medical science?

My advice is threefold: commitment, perseverance, and passion for science. Research is not for everyone; it requires a strong commitment. I often joke with my team that choosing an experiment over leisure activities indicates a true dedication to science.

Perseverance is crucial; success in research requires persistence and resilience. Following the heart of science, rather than material gains, is essential for becoming a great scientist. If young researchers have these qualities, they will find success and fulfilment in their scientific careers.



Photo with Keiji Fukuda and his wife Holly at the Honorary Fellowship Ceremony of the University of Hong Kong.

Q10

As a new Principal Investigator of the Institute, what are your vision and goals in 5 years?

My vision is to make Hong Kong a global microbiome innovation, research, and development leader. Collaborating with my colleagues, I aim to establish Hong Kong as a beacon of microbiome research excellence.

Additionally, I want to enhance our role in antimicrobial resistance research and policy-making. A key goal is to establish a reference laboratory for AMR and microbiome research at the Institute. We have already made significant strides, such as receiving a GBP1.3 million Fleming Fellowship grant from the UK government for training officials from Bangladesh and Sri Lanka in AMR-related knowledge.

In the next five years, I aim to achieve these goals, substantially impacting microbiome and AMR research while positioning Hong Kong at the forefront of global scientific advancements.



Vincent Mok
莫仲棠

INTERVIEW WITH PRINCIPAL INVESTIGATOR

與首席研究員對話

Vincent Mok, completed his bachelor's degree of medicine in Sydney in 1993 and a doctoral degree at CUHK in 2005. He joined CUHK as Associate Professor in 2006 and became a Principal Investigator of the Li Ka Shing Institute of Health Sciences in 2023. His research focuses on the prevention and therapeutics of common age-related brain diseases (e.g. Alzheimer's Disease, Cerebral Small Vessel Disease and Parkinson's disease) as well as the employment of multi-modal neuroimaging aided by artificial intelligence technology in diagnosing, prognosticating and monitoring brain diseases. Currently, Professor Mok is the Director of CUHK's Therese Pei Fong Chow Research Centre for Prevention of Dementia, Margaret K.L. Cheung Research Centre for Management of Parkinsonism and Lau-Tat-chuen Research Centre of Brain Degenerative Diseases in Chinese. He has also committed deeply to nourishing the younger generations by serving as the Master of S.H. Ho College since 2022.

Q1

Why did you choose to become a clinician researcher and pursue your career in Hong Kong specialising in neurology? How does your work in both fields be mutually beneficial?

Honestly, during my first few years working as a doctor after graduation, I felt that research was a waste of time. There were so many patients in front of me requiring help. However, as I got involved in managing many patients suffering from neurodegenerative diseases, such as dementia and Parkinson's Disease, I have developed closer relationships with them. As I witnessed their continuous deterioration despite they were already receiving the best available treatments, my heart was greatly saddened. Since research provides hope of developing better treatments for them, I decided to delve deeper into research after completing my Neurology specialist training in 1999. With the encouragement and generous support of Professor Lawrence Wong, my boss then, I began to actively engage in research endeavours and successfully obtained a medical doctorate degree in 2005.

Q2

What is the situation of dementia in Hong Kong? In view of the aging population, what are the foreseen challenges in the early intervention and treatment of dementia and how should we get prepared to overcome them?

In Hong Kong, dementia poses a significant challenge due to the region's highest life expectancy globally, reaching 85 years old. At this age and above, almost a third of individuals will be affected by dementia. The primary challenge is that we need to raise public awareness that Alzheimer's dementia is preventable. Alzheimer's dementia is the most common cause of dementia, accounting 70% of cases. Tackling various modifiable risk factors proactively before development of cognitive symptoms is the most effective way of reducing the burden of dementia. Furthermore, another challenge is to educate the public about recognising early symptoms of Alzheimer's Disease. For instance, cognitive symptoms like short-term memory loss should not be dismissed as a normal part of aging but could indicate early-stage Alzheimer's Disease. As there are now effective pharmacological treatments (eg, anti-amyloid drugs) for slowing down the progression of early Alzheimer's disease. Early diagnosis and intervention are keys to slowing down the progression of the disease, emphasizing the importance of timely awareness and action.

Q3

Research reveals that non-genetic factors (e.g. central obesity, cardiovascular diseases, physical and cognitive inactivity, social isolation, educational attainment) also play an important role in the development of dementia, therefore an all-round preventive strategy should be adopted in patients. In many fast-paced and high-volume societies nowadays, what do you think various stakeholders could help with the prevention of dementia?

It is correct. Clinical studies conducted in the past 30 years have clearly demonstrated that maintaining a good brain health by optimising specific modifiable risk factors as listed out in the question can prevent up to 45% of dementia cases. I must appreciate the efforts of Health Bureau of our Hong Kong Government for taking proactive steps in the right direction by establishing District Health Centres across all 18 Districts in Hong Kong. The first centre was launched in 2019, focusing on enhancing the detection and management of conditions such as hypertension, diabetes, and promoting healthy lifestyles encompassing dietary habits and regular exercise within the community. It is paramount to recognize that every individual plays a crucial role in their health journey. While the government and doctors are vital stakeholders, each person bears the responsibility for their health. Encouraging regular health check-ups and adherence to healthy lifestyle practices are essential components of maintaining a good brain health.

Q4

What are the limitations of traditional amyloid PET imaging and magnetic resonance imaging (MRI) in the clinical assessment of Alzheimer's Disease? How does introduction of artificial intelligence (AI) technology revolutionize neuroimaging? Can you please also share with us how the MRI-derived Alzheimer's Disease- Resemblance Atrophy Index (AD-RAI) becomes a diagnostic biomarker for Alzheimer's Disease?

Alzheimer's Disease can be diagnosed at an early stage through amyloid PET imaging; however, their availability and cost present challenges for its widespread application. While MRI scans can pick up the pattern of atrophy and help identifying Alzheimer's Disease with 90% accuracy at later dementia stages, their accuracy diminishes to 60% in detecting early Alzheimer's Disease. In 2019, our team collaborated with computer scientist Dr. Shi Lin in developing a machine-learning model. This model enables the early detection of Alzheimer's Disease with an accuracy rate of almost 80% when combined with basic clinical information. By incorporating plasma biomarkers, the accuracy improves to 85%, with a sensitivity of 90%. We use the machine learning derived MRI index, namely AD-RAI, alongside blood biomarkers, to screen out high-risk cases before confirming with a PET scan. Radiographers can seamlessly upload MRI soft data to a cloud platform, generating a comprehensive report for users within 10 minutes.

Q5

You have recently developed a novel technology in the collaboration with the Department of Ophthalmology and Visual Sciences to detect a range of changes in the blood vessels and nerves of the retina that are associated with Alzheimer's disease. Can you please explain more about this technology? Do you think it can replace the traditional assessment tools in detecting Alzheimer's disease?

Retinal imaging emerges as a simpler method for screening people who are at risk of Alzheimer's dementia, surpassing even blood tests in terms of simplicity and non-invasiveness. Images captured can be uploaded to the cloud for analysis and rendering results within minutes. The rationale hinges on the concept that the retina serves as a direct extension of the brain. Studies conducted many years ago have already uncovered distinct retinal changes linked to Alzheimer's dementia, notably in retinal vasculature. Under the leadership of and partnership with Professors Carol Cheung and Clement Tham from the Department of Ophthalmology and Visual Sciences, a deep learning model was developed using training datasets of almost 3,000 cognitively healthy individuals and 500 Alzheimer's patients. This retinal measure exhibited an overall accuracy ranging from 70-90% when validated across various cohorts in distinguishing between Alzheimer's dementia and normal controls. Noteworthy discoveries emerged when implementing this method on elderly individuals without cognitive impairment. A positive finding as classified by this retinal measure indicates the presence of vascular anomalies akin to those observed in individuals with Alzheimer's dementia. Furthermore, these individuals display signs of accelerated biological aging in their brains. These findings suggest a potential for pre-emptively identifying subjects with suboptimal brain health and are at higher risk of developing Alzheimer's dementia in the future through retinal imaging screening.

Q6

Prevention is always better than cure of diseases, especially there is currently no cure for Alzheimer's disease. However, in case of diagnosis, what treatments would be most effective in reducing the symptoms? As a researcher, you would be very enthusiastic about exploring novel assessment tools and therapeutics. On the other hand, how would you encourage the frustrated caregivers as the memory of dementia patients cannot be reversed?

There are medications that may help to reduce or control some cognitive and behavioural symptoms of Alzheimer's dementia. However, those treatments may only address the symptoms for few years, rather than curing the disease. I fully understand the frustration of the caregivers, as I myself was once in their position caring for a close relative who passed away a few years ago because of dementia. It is important to share your frustrations and the burden of caregiving with close friends and relatives. Additionally, there are numerous reputable NGOs and professional healthcare organisations that provide comprehensive support through different stages of dementia.

Q7

Having been awarded the "Teacher of Year" for 7 times between 2005 and 2012, followed by the Master Teacher Award in 2012 and Education Awards (Collaborative Team) in 2023, you must have received many love and respects from students. Would you mind sharing your secrets of teaching? Have your mission in teaching been changed after becoming the Master of S.H. Ho College? What did the students inspire you the most during your teaching journey?

I have no secrets. When I was young, my parents taught me to do my best to serve the needs of others, to treat others with kindness, and to follow the golden rule of treating others as you wish to be treated. Recognising that students primarily require support in their learning and exam preparation, I consistently strive to share essential knowledge with them and encourage them along their journeys. Encouraging them to embrace a lifestyle of service remains a core belief that has remained unchanged even during my tenure as the Master of S.H. Ho College. I have been exposed to many non-medical and non-local students. I enjoy very much being with them and I learnt a lot from them. I have gained valuable insights from their passion and desire to create a positive impact. I have continually learnt and adapted from them, such as sharing stories in Instagram.

Q8

Clinician researchers devote their time and efforts not only in clinical practices but also in research. How do you stay motivated and maintain enthusiasm for your work in the face of setbacks or challenges? What advice would you give to the younger generations who would like to pursue this career, in particular those who are interested in neuroscience?

To stay motivated, several key factors come into play. Firstly, understanding the significance of your work, that your work is meaningful and not just for financial gain. Secondly, deriving a genuine enjoyment and passion from your work is crucial. I fell in love in doing research once I got involved in it and it's now hard for me not to keep doing it. Thirdly, it is important to recognise what your talents are. If you are talented in doing a particular thing, you should generally achieve more successes or satisfaction than failures as you are doing that particular thing. Lastly, staying connected with great people is of paramount importance. I am very fortunate to have been guided by a great boss, Professor Lawrence Wong, supported by esteemed colleagues such as Professor Thomas Leung, and buoyed by the friendships and partnerships of individuals like Professor Ko Ho, Dr. Adrian Wong, Dr Bonaventure Ip and all of my teammates from Neurology over the decades who have continuously kept me motivated.

Q9

As a new Principal Investigator of the Institute, what are your vision and goals in 5 years?

In the short term, my team's goal is to enhance the diagnostic accuracy of retinal imaging for the early detection of Alzheimer's Disease. We plan to incorporate another retinal imaging, namely, Optical Coherence Tomography (OCT) along with the fundus camera in the evaluation of various brain diseases. Our strategy is to leverage AI technology in developing better retinal and brain imaging diagnostic/prognostic methods for early detection of various brain diseases. In addition, we are currently conducting a phase 2 clinical trial to investigate the efficacy of GLP-1 receptor agonist, typically used in diabetes and obesity, for the treatment of cerebral small vessel disease, of which there is currently no specific treatment available. Our ultimate vision is to develop therapeutics that can tackle the age-related changes in the brain, considering aging as the strongest risk factor for various common brain diseases such as dementia, cerebrovascular diseases, and Parkinson's Disease. By slowing down the aging process of the brain, it is potentially possible to address multiple brain diseases simultaneously.



Dennis Lo
Allen Chan
Jacky Lam
Peiyong Jiang
盧煜明
陳君賜
林偉棋
江培勇

FROM SCIENCE TO IMPACTS

從科學到影響

Q1

Previously, your team has conducted an Hong Kong–wide screening for nasopharyngeal carcinoma (NPC) by the detection of plasma Epstein–Barr virus (EBV) DNA between 2013 and 2016 with a cohort of 20,174 ethnically Chinese men (first–round screening). What prompts your team to carry out a second–round screening based on the same cohort?

In the first-round screening, asymptomatic males were recruited for NPC screening. Plasma EBV DNA was detected with quantitative polymerase chain reaction (qPCR) with a two time-point testing protocol (4 weeks apart). Plasma EBV DNA-positive participants were classified into either the transiently positive (positive once) group and the persistently positive (positive twice) group. The latter group, defined as screen-positive, would be arranged for further investigations with nasoendoscopy and MRI. The majority of NPC identified were early-stage NPC and overall they were shown to have a 90% reduction in mortality.

However, there are a few questions remaining to be elucidated from the first-round screening.



1. In the previous study, the diagnostic value of plasma EBV DNA for NPC screening has been demonstrated. However, how often should screening be carried out to best improve the NPC patients' survival rate?
2. In the first-round screening, some volunteers were tested positive for plasma EBV DNA by qPCR with no detectable pathology by both nasoendoscopy and magnetic resonance imaging (MRI). Are they "genuinely" false positives? Or with a very early cancer being undetected due to current technology limitations? Or are they reflecting an ongoing process of accumulating genetic aberrations that would ultimately lead to the development of NPC? If yes, what are the increased risks of developing NPC amongst these people?

To address these questions, all the participants in the first-round screening were invited for a second-round screening. In between the two rounds of screening, we have arranged annual phone interviews to update their NPC status. In the first-round screening, 34 NPC cases were discovered, whereas only three cases were diagnosed over the 3-year period between the two rounds of screening. According to the local cancer registry, for our target screening population (i.e., men aged between 40 to 65 years), the annual incidence of NPC is 35 cases per 100,000 persons. Hence, approximately seven cases of NPC would be expected from the 20,000-person cohort each year. We previously hypothesized that the cases identified in the first round indeed included cases that would eventually present in the next 5 years but had been identified much earlier through the screening. This hypothesis is now supported by the fact that only three cases of NPC were diagnosed between the two rounds of screening, considering that approximately20 cases would be expected for a 3-year period.

The second-round screening has also demonstrated that NPC rescreening is effective for the detection of new asymptomatic NPC, and those who are identified to be NPC positive have superior survival compared with those not undergoing screening.

In the second-round screening, the previous" false positive" individuals from the first-round screening are shown to have higher risks of 4.4- and 16.8-fold of having NPC respectively in the transiently and persistently positive groups, compared with those with a negative plasma EBV DNA result.

Professor Allen Chan



Q2

What are the socioeconomic impacts for your discovery?

We have developed plasma EBV DNA as a new, effective screening tool of NPC. There is a strong need for early detection of NPC given the high disease burden of NPC in endemic regions including southern parts of China and Southeast Asia. In these regions, NPC ranks among the ten most common types of male cancer. Unfortunately, the majority of NPC patients present with advanced-stage disease with a 5-year overall survival rate of only 60%, while early-stage NPC is highly treatable and the 5-year overall survival rate is above 90%. The team has demonstrated that plasma EBV DNA testing could identify early-stage NPC. Importantly, the early detection could bring about survival benefits that is the ultimate goal of cancer screening, with a reduction of mortality by 90%. Screening with plasma EBV DNA could profoundly impact on the natural history of NPC. It is also now recognized as a cost-effective screening strategy in NPC-endemic regions.



Professor Dennis Lo

Q3

What are the recent advances in plasma EBV DNA analysis for NPC screening?

The NPC screening model serves as a proof of concept demonstrating the power of plasma DNA for cancer diagnostics especially early cancer detection. Apart from the detection of EBV DNA by qPCR, the molecular pattens of these EBV cfDNA fragments might also hold crucial information regarding the disease origin/status. It was later found out that the analysis of EBV DNA methylation pattern, size and quantitation by Next-Generation Sequencing (NGS) could further enhance the sensitivity and specificity for NPC detection. Now, with the combined strategy of qPCR and profiling these molecular features, a single round of blood sampling enable high performance for early NPC detection.

Q4

How can we apply what we have learnt to other viruses/cancers?

NPC is one of the commonest cancer types caused by an oncogenic virus. There exist other viruses that can also cause malignancies, e.g. Human Papilloma Virus (HPV) and Hepatitis B Virus (HBV). The NPC model could provide insights for screening of other virus-associated cancer.

In addition, the discovery is not limited to NPC or virus-associated cancer. Likewise, cancer-associated molecular patterns of plasma DNA are also found in other types of cancer, that could provide information regarding their disease status and progression. Our research team, led by Professor Dennis Lo, has been actively studying the biology of cell-free DNA. Recently, we have pioneered the 'fragmentomics' study of cell-free DNA developed a number of fragmentomics markers with diagnostic implications for cancer detection and informing tissue of origin.



Professor Jacky Lam

Q5

How can your discovery be adopted in the HK public health sector?

Conventionally, screening of NPC is done by analysing EBV Viral Capsid Antigen (VCA) or Early Antigen (EA) Immunoglobin A (IgA) levels, with comparatively lower sensitivity and specificity for NPC detection. Patients with high antibody levels are referred to Ear, Nose and Throat (ENT) specialists, for endoscopy, or MRI, if necessary. The inferior performance offered by the serological markers implies a high number of false positives, and therefore a heavy demand for ENT referrals and endoscopy. Recently the qPCR method for detection of plasma EBV DNA is being adopted by the Hospital Authority. Initial screening by plasma EBV DNA is offered at the general out-patient clinics. Such strategy could substantially reduce the ENT referral numbers and the overall patient waiting time for the first ENT consultation. There are also ongoing discussions with the government on launching community NPC screening projects.

Q6

How do you translate your scientific findings into commercial applications?

We have established biotechnology start-up companies, to which we have licensed our novel NPC and pan-cancer diagnostic technologies. Currently the start-up is providing the clinical service on NPC screening and prognostication/monitoring in Hong Kong. The company targets to extend the screening service to the Greater Bay Area. This would also help building up the local talent pool in biotechnology.



Jun Yu
于君

FROM SCIENCE TO IMPACTS
從科學到影響

Q1

What are NAFLD and NASH? How prevalent are these conditions in Hong Kong?



Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide, affecting billions globally, and it is a metabolic syndrome particularly prevailing in overweight, obese, and diabetic individuals. NAFLD can gradually progress to the more severe non-alcoholic steatohepatitis (NASH), which is a pathogenic condition with liver damage, steatosis (fat accumulation), inflammation, and fibrosis.

In Hong Kong, the prevalence of NAFLD was quite high, with 27% of the adult population were affected, ranging from 27.3% when diagnosed by advanced imaging techniques to 42.28% when diagnosed by ultrasound. The trend is expected to continue increasing in the coming ten years. Around 20% of NAFLD patients in Hong Kong have developed NASH.

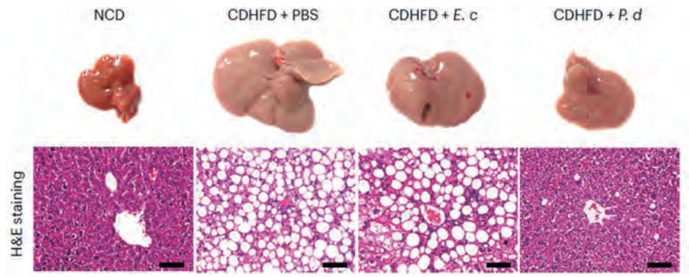
Q2

How do they lead to different stages of liver diseases and eventually liver cancer?

Without intervention, NASH can further progress to liver cirrhosis and eventually liver cancer. In fact, the incidence of NASH-related liver cancer has increased four-fold in the last decade, making NAFLD/NASH the fastest growing cause of liver cancer, especially with noticeable increasing trend in obese population.

The mechanism of progression of NAFLD and eventually liver is complex. Our team conducted in-depth and systematic studies, and have made important breakthroughs in the last five years in understanding the molecular mechanisms underlying from NAFLD to liver cancer.

These findings have been published in high-impact journals, including *Gastroenterology (Liu D, et al. 2021), Science Translation Medicine (Liu D, et al. 2018), Journal of Hepatology (Zhang X, et al. 2019 and Song Q, et al. 2023), Cell Reports Medicine (Pan Y, et al. 2023), Gut (Zhang X, et al. 2021)* and *Nature Microbiology (Wei W, et al. 2023).*



Q3

Currently how are NAFLD and NASH diagnosed and cured (From Steatohepatitis to Fibrosis)?

NAFLD is typically diagnosed through abnormal liver function tests, with the exclusion of other concomitant liver diseases, such as viral hepatitis and excess alcohol consumption. Liver biopsy has been the key standard for diagnosing NASH. A small piece of liver tissue is collected and examined by clinicians to determine any signs of inflammation, fibrosis, and scarring during the procedure. Our team have also established a blood-based biomarker panel with high selectivity and specificity for NASH diagnosis.

Currently, there is only one FDA approved drug, Resmetirom, for treatment of NASH with advanced fibrosis. All other therapeutic efforts to control NASH remained unsatisfactory in clinical trials unfortunately. Nevertheless, other non-interventional management strategies focusing on lifestyle changes, weight loss, and increase physical activity are encouraged.

Q4

Currently are there any food supplements/diets that can help prevent liver cancer (Fat/Cholesterol/Fibre)?

To help prevent liver cancer, dietary recommendations include consuming whole grains (e.g. brown bread, brown rice, oatmeal), fish rich in omega-3 fatty acids, fruits, and vegetables. In contrast, the intake of salty or preserved foods, fried foods, processed meat, and high-fat or high-cholesterol foods should be avoided for liver cancer.

Q5

What is the relationship between gut microbiota and liver cancer? How can the former affect the latter?

The relationship between gut microbiota and liver cancer is bidirectional. In liver cancer patients, their gut microbiota is significantly changed, with an enrichment of bacterial pathogens and a reduction of beneficial bacteria. This altered microbiota can in turn damage the intestinal barrier, allowing more microbial endotoxins to enter the circulation and reach the liver. This can cause hepatic inflammation and further accelerate liver cancer development.

Q6

Could you introduce to us P Distasonis? What is its natural habitat and how do people are acquire this bacterium? Are they culturable? Can they be used a biomarker for the disease instead of imaging (Biopsy/CT/Ultrasound/MRI)?

Parabacteroides distasonis (P. distasonis) is a gram-negative bacterium that is commonly present in human gastrointestinal tract. It can be acquired from human stools and is easily culturable under anaerobic conditions. P. distasonis is now considered an emerging probiotic that is effective in alleviating pain, metabolic syndromes, and inflammatory diseases such as inflammatory bowel disease and rheumatoid arthritis. Due to this beneficial bacterium is depleted in patients with NASH, it is not suitable to serve as a diagnostic biomarker for NASH.

Q7

What are inulin and its metabolite pentadecanoic acid? How does P Distasonis make use of them?

Inulin is a type of dietary soluble fiber particularly rich in wheat, onions, and garlic. After consumption, inulin cannot be digested by enzymes in human intestines. Instead, inulin is absorbed and degraded by various gut bacteria, including *P. distasonis*. *P. distasonis* can ferment inulin to produce different metabolic products, one of which is pentadecanoic acid.

Pentadecanoic acid is a saturated fatty acid with broad activities to protect cardiometabolic, immune, and liver health, and has been considered an essential fatty acid for humans. During experiments of using germ-free mice fed on an inulin diet, our study discovered that there was a substantial increase in Pentadecanoic acid levels with inoculation of *P. distasonis*.

Q8

How does inulin and P Distasonis protect against cancer? (Gut Immune Brain Axis/Inflammatory responses/Molecular pathways involved)?

Supplementation of inulin or *P. distasonis* has been found to significantly alleviate NASH development by reducing fat accumulation, steatosis, inflammation, and fibrosis in the mouse liver. Through ^{13}C-labeling, we found that *P. distasonis* can metabolise inulin to produce pentadecanoic acid. Pentadecanoic acid has been shown to restore the integrity of the intestinal barrier, limiting endotoxin translocation into the circulation, and suppressing the expression of pro-inflammatory cytokines and lipogenesis genes.

In our published study, we demonstrated the protective role of inulin and *P. distasonis* in NASH. Our ongoing research has also indicated that inulin plays a protective role in NAFLD associated liver cancer.

Q9

Are there any continuation projects based on this discovery?

Our team are now examining the effect of inulin on subsequent NASH-related liver cancer through modulation of the gut microbiome and its metabolites. We are also identifying more candidate probiotics and studying their role and underlying mechanism against NASH-related liver cancer in preclinical models. Additionally, we are planning to evaluate the prophylactic potential of *P. distasonis* and other probiotics against NAFLD and NASH in humans.

Q10

Are there any other gut bacteria that can also help protect against liver cancer?

Yes, our two publications in 2023 and 2024 identified that the consumption of probiotic *Bifidobacterium pseudolongum* or *Lactobacillus acidophilus* can markedly inhibit the development of NASH-related liver cancer. These two bacteria are presented in the gut microbiota. These research results have revealed new ways for the prevention and treatment of NASH and its associated liver cancer. Our findings have been published in *Journal of Hepatology (Song Q, et al. 2023)* and *eBioMedicine (Lau H, et al. 2024)*

Q11

Can your discovery be translated/patented into products that can be used as a prophylaxis or treatment as the first microbiota product that can be used to cure/ameliorate NASH/NAFLD (say e.g. different stages different formulations)?

Our findings are all based on pre-clinical mouse models. *P. distasonis* is now recognised as a safe probiotic for human consumption, so it can be translated as a prophylaxis against NAFLD and NASH. We are applying relevant patents for using *Lactobacillus* probiotics as novel prophylaxis to ameliorate, or even a cure to NASH/NAFLD. Human investigations are required before clinical application. Clinical interventional studies are needed to examine the efficacy and safety and efficacy of long-term consumption of inulin against NAFLD and NASH.

Q12

We have seen that you have used a lot of isotope work in your methodology, are there any platforms at LiHS that can help your research (Mass Spec/TOP)?

Our research needs to profile the metabolites in different sample types. To this end, we have been using the mass spectrometers at Li Ka Shing Translational Omics Platform (LKS TOP) to conduct untargeted and targeted metabolomics. LiHS has provided the ideal platform for our research with involvement of a substantial amount of bacteria culture at their bacteria culture facilities.

Q13

What is the outlook on microbiota research regarding gut cancer immunotherapy/immune–modulation?

The crosstalk between gut microbiota and host immunity is being heavily investigated. With an aim to improve patient outcomes, enormous efforts have been invested to develop strategies that utilize gut microbes as prognostic biomarkers or adjuvants of cancer immunotherapy.

With the rapid advance in microbiota research, harnessing the gut microbiota may be effective to enhance cancer immunotherapy efficacy in the near future. Our recent studies have shed light on the important role of the gut microbiome in shaping the tumor immune microenvironment and impacting the efficacy of cancer immunotherapies. We showed that *P. anaerobius* promotes a tumor-permissive immune microenvironment, whilst probiotics like *Lactobacillus gasseri (Lg)* and *Roseburia intestinalis (Ri)* can boost immunotherapy efficacy. Our findings have published in *Nature Microbiology (Liu Y, et al 2024)* and *Gut (Kang X, et al 2023).*

These studies will help promote the development of innovative immunotherapy approaches, and provide an important scientific basis for improving effective treatment of patients with gastrointestinal cancers.

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