LKS Faculty of Medicine
HKU-Pasteur Research Pole
香港大學-巴斯德研究中心

Annual Report
2022

Roberto Bruzzone, Co-Director
Leo Poon, Co-Director
Malik Peiris, Honorary Director

HKU-Pasteur Research Pole
7/F Jockey Club Building for Interdisciplinary Research
5, Sassoon Road, Hong Kong SAR

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INDEX

Summary

Mission

The HKU-Pasteur Research Pole is a joint laboratory, established by The University of Hong Kong (HKU) and the Institut Pasteur (IP), under the School of Public Health (SPH) of the Li Ka Shing Faculty of Medicine of the University of Hong Kong. HKU-Pasteur aims to confront the challenges posed by microbes by developing research and education programs that will contribute to mitigate the impact of infectious diseases.

Research

We focus on emerging and re-emerging infectious diseases (respiratory and mosquito-borne viruses) antimicrobial resistance (AMR) and computational approaches to investigate diversity and evolution of pathogens. An external review of the HKU-Pasteur was undertaken in 2021 to assess its overall performance at the mid-term of the 10-year agreement between HKU and IP (2016-2026). The review team recognized the continuing high quality and international impact of the scientific work as well as the teaching & training programs of HKU-Pasteur, which is organized around a core of Group Leaders engaged in competitive research projects aligned with the scientific priorities of HKU and IP. In 2022 two group leaders (Tun and Valkenburg) have departed to continue their careers elsewhere, a clear indication of our role as fertile soil to further careers of young scientists. They both keep a small group at HKU-Pasteur to continue collaborative research that is supported by long-term grants. We have recruited a new group leader, Soo-San Wong, whose laboratory is focused on understanding the determinants of robust antibody responses after respiratory virus infection and vaccination at a population as well as at the individual level. This research area is critical to our understanding of respiratory viruses' vaccine efficacy and disease pathogenesis. It will also improve our public health policies in managing the disease burden of seasonal respiratory viruses as well as pandemic risks of emerging viruses. We have published over 50 papers in 2022, many of whom have been published in high-impact journals and have received media coverage.

Teaching

HKU-Pasteur has pioneered a unique course series in Hong Kong and in the region that provides state of the art lectures and practical workshops in a "Master class" setting to outstanding postgraduate students and postdoctoral fellows coming from countries with markedly different resources. All HKU-Pasteur Courses have been approved by the Research Postgraduate Committee of HKU for inclusion in the coursework curriculum of MPhil/PhD students and have received the Pasteur International Course (OIC) label of the Institut Pasteur. The end to travel restrictions will allow resuming our educational program in 2023.

Perspectives

We have developed a strong identity to promote the missions of HKU, IP and the Institut Pasteur International Network, through research, teaching and public health activities. We have opened the Center for Immunology & Infection (C2I), the new collaborative project of HKU and the Institut Pasteur, funded with a major grant from the Innovation & Technology Commission. This translational research laboratory will address significant public healthcare challenges through novel technology platforms for biomarker discovery and the development of new vaccine and therapeutic strategies. We have planned the recruitment of a new Group Leader in 2023, to strengthen our research portfolio in the investigation of emerging and re-emerging viral infections and further enhance the role of HKU-Pasteur as a productive regional hub for the School of Public Health at HKU and the Pasteur Network.

2. Overview of the Programs

2.1 Research

The scientific activity of HKU-Pasteur encompasses wet lab and computational approaches to understand in mechanistic terms the interactions between microbes (pathogenic or commensals), hosts and the environment. The three main pillars of our research are: *Understanding how do viruses invade, replicate and escape infected cells*; *Understanding what makes a microbe pathogenic*; *Understanding how do microbes deal with the host immune response and the environment*.

Research in **the lab of Vijaykrishna Dhanasekaran** lab focuses on understanding the genetic and ecological factors that contribute to the emergence and spread of infectious diseases to improve disease control strategies through epidemiological studies, and computational and experimental methods. Recent research from the lab has concentrated on the impact of COVID-19 on respiratory diseases, including human influenza and RSV, and avian and swine influenza. Four research projects have highlighted the importance of continued surveillance of respiratory viruses, the need for strong border control and community surveillance to prevent local outbreaks during pandemics, the potential consequences of influenza lineage elimination, and the continued need for elimination strategies for highly pathogenic avian influenza H5N1 virus.

Leo Poon lab studies viruses at the animal and human interface, with a particular interest on influenza virus and coronaviruses. The Poon lab develops molecular diagnostic tests for these viruses and use multidisciplinary approach to study the ecology, transmission, and pathogenesis of these emerging viruses, with the overarching goal to generate experimental data to develop evidence-based control measures and/or inform public health policy. One important contribution has been the demonstration of transmission of SARS-CoV-2 delta variant from pet hamsters to humans, leading to onward human-to-human transmission. This study has expanded our understanding on the host range of SARS-CoV-2 and revealed the complexity of SARS-CoV-2 transmission in nature. Moreover, this work demonstrates the possibility of generating novel antigenic variants of SARS-CoV-2 in animals. This study has been well received by both scientific and public health communities (e.g., WHO, FAO and OIE) and was highlighted by Nature.

Sook-San Wong was appointed Assistant Professor in January 2022. The lab is focused on understanding the determinants of robust antibody responses after respiratory virus infection and vaccination at a population as well as at the individual level. This research area is critical to our understanding of respiratory viruses' vaccine efficacy and disease pathogenesis. Although vaccination remains one of the most effective public health strategies to control community transmission as well as to reduce the disease burden of respiratory viruses, some vaccinees may fail to mount sufficient protective antibody responses after primary or booster vaccination. Therefore, one of the lab's aims is to determine whether serum biomarkers can be used to identify poor vaccine responders in the older adults. This research can contribute towards precision vaccination in older adults, andwill also improve our public health policies in managing the disease burden of seasonal respiratory viruses.

Hein Min Tun and **Sophie Valkenburg** have left HKU-Pasteur to become Associate Professors at the Chinese University of Hong Kong and the Peter Doherty Institute, University of Melbourne, Australia, respectively. They remain actively involved in long-term funded projects that support smaller labs still working at HKU-Pasteur.

2.2 Teaching and Education

HKU-Pasteur offers three major international courses on an annual/biennial basis – Cell Biology, Virology and Immunology – which feature lectures from leading scientists. All HKU-Pasteur courses have been approved by the Research Postgraduate Committee of HKU for inclusion in the coursework curriculum of MPhil/PhD students and have received the Pasteur International Course (OIC) label of the Institut Pasteur. The coronavirus pandemic led to the cancellation of all HKU-Pasteur courses, which will gradually resume in 2023, owing to the end to travel restrictions. All Group Leaders are also actively engaged in the undergraduate and postgraduate curriculum of HKU.

We have continued our exchange program under the umbrella of the **HKU-Pasteur Research Pole Fellowship Program**, which provides a unique opportunity for postgraduate students and postdoctoral fellows in Hong Kong and Macau to pursue their research projects at the Institut Pasteur in Paris, France. This scheme is sponsored by The Légion d'Honneur Club Hong Kong Chapter, the Pasteur Foundation Asia, and the Consulate General of France. The HKU-Pasteur Research Pole Fellowship Program received the Knowledge Transfer award by the Grand Prix France Hong Kong, created by LePetitJournal.com and supported by the Consulate General of France to reward collaborations contributing positively to the influence, reputation or relationship of France and Hong Kong, in the fields of culture, entrepreneurship, gastronomy, human resources, education and sustainable development.

We have hosted **2 international student** for laboratory placement, from the University of Toronto (Canada) and University of Veterinary & Animal Sciences (Lahore - Pakistan), **4 interns** from the French International School, and **3 student interns** from School of Bio-Medical Sciences, the University of Hong Kong.

2.3 Other Major Activities

We retain leadership roles in several global projects. **Roberto Bruzzone** is the Chair of the Board of Directors of the International Severe Acute Respiratory and Emerging Infection Consortium (https://ww.isaric.org), a network of networks which aims at ensuring that clinical researchers have the open access protocols and data-sharing processes needed to facilitate a rapid response to emerging diseases. He is also the Co-Editor-in-Chief of *Cellular and Molecular Life Sciences*. **Malik Peiris** continues to serve on several WHO working groups in relation to both avian and swine origin influenza virus and is the Co-Director of the WHO H5 Reference Laboratory at HKU. **Leo Poon** currently is a committee member of the Coronavirus study group, ICTV, IUMS, and is an Advisor to the Hong Kong SAR for Food and Environmental Hygiene. He is also an Ad Hoc Expert of the WHO Influenza Molecular Diagnosis Working Group, and of the WHO Expert group for COVID-19 for clinical diagnosis and virus evolution. He is the Co-Editor-in-Chief of the *Virology Journal*. **The Center for Immunology & Infection (C2I),** funded by the Innovation and Technology Commission in April 2021, is now fully operational, with more than 40 staff. C2i represents a major development of an already successful and long-term collaboration between HKU and the Institut Pasteur. **Leo Poon is the Managing Director of C2I; Malik Peiris and Roberto Bruzzone are the Co-Directors**. C2i aims to validate a novel technology platform for biomarker discovery and development of new vaccine and therapeutic strategies. Overall, this program addresses major unmet needs with excellent potential for commercial exploitation, leading to the enhancement of Hong Kong's knowledge-based economy.

3. Progress Report

3.1 Vijay DHANASEKARAN Lab

Summary

The Pathogen Evolution Lab focuses on understanding the genetic and ecological factors that contribute to the emergence and spread of infectious diseases across One Health. The lab's research aims to improve disease control strategies through epidemiological studies, and computational and experimental methods. The lab's main research areas include developing interventions against viruses with epidemic and pandemic potential, vector-borne pathogens, and bacterial pathogens.

Recent research from the lab has concentrated on the impact of COVID-19 on respiratory diseases, including human influenza and RSV, and avian and swine influenza. Four research projects have highlighted the importance of continued surveillance of respiratory viruses, the need for strong border control and community surveillance to prevent local outbreaks during pandemics, the potential consequences of influenza lineage elimination, and the continued need for elimination strategies for highly pathogenic avian influenza H5N1 virus. These projects provide important insights into the complex interplay between COVID-19 and other respiratory diseases across One Health, emphasizing the need for ongoing research and surveillance.

The Pathogen Evolution Lab also engages in knowledge exchange and community impact, including providing commentary on Radio and Television, being interviewed by The Guardian, and designing and delivering a short course on Science in Action to underprivileged children in Hong Kong. In addition, Dr. Dhanasekaran is involved in several teaching roles and the lab has strong collaborations within and outside the Pasteur Network, including the World Health Organization, the University of Melbourne Peter Doherty Institute, Institut Pasteur Cambodia, St Jude Children's Research Hospital, Memphis, U.S.A., and Duke-NUS Medical School Singapore.

Research highlights

The episodic resurgence of highly pathogenic avian influenza H5 virus

[Funding: US National Institute of Allergy and Infectious Diseases (NIAID) (HHSN272201400006C)]

Highly pathogenic avian influenza (HPAI) H5N1 activity has intensified globally since 2021, replacing the dominant clade 2.3.4.4 H5N8 virus. H5N1 viruses have spread rapidly to four continents, causing increasing reports of mass mortality in wild birds and poultry. The ecological and virological properties required for future mitigation strategies are unclear. Using epidemiological, spatial and genomic approaches, we demonstrate changes in the source of resurgent H5 HPAI and reveal significant shifts in virus ecology and evolution (**Fig 1**). Outbreak data indicates key resurgent events in 2016/17 and 2020/21 that contributed to the panzootic spread of H5N1 in 2021/22, including an increase in virus diffusion velocity and persistence in wild birds. Genomic analysis reveals that the 2016/17 epizootics originated in Asia, where HPAI H5 reservoirs are documented as persistent. However, in 2020/21, 2.3.4.4b H5N8 viruses emerged in domestic poultry in Africa, featuring several novel mutations altering the HA structure, receptor binding, and antigenicity. The new H5N1 virus emerged from H5N8 through reassortment in wild birds along the Adriatic flyway around the Mediterranean Sea. It was characterized by extensive reassortment with low pathogenic avian influenza in domestic and wild birds as it spread globally. In contrast, earlier outbreaks of H5N8 were caused by a more stable genetic constellation, highlighting dynamic changes in HPAI H5 genomic evolution. These results

suggest a shift in the epicenter of HPAI H5 beyond Asia to new regions in Africa, the Middle East, Europe, and North and South America. The persistence of HPAI H5 with resurgence potential in domestic birds indicates that elimination strategies remain a high priority.

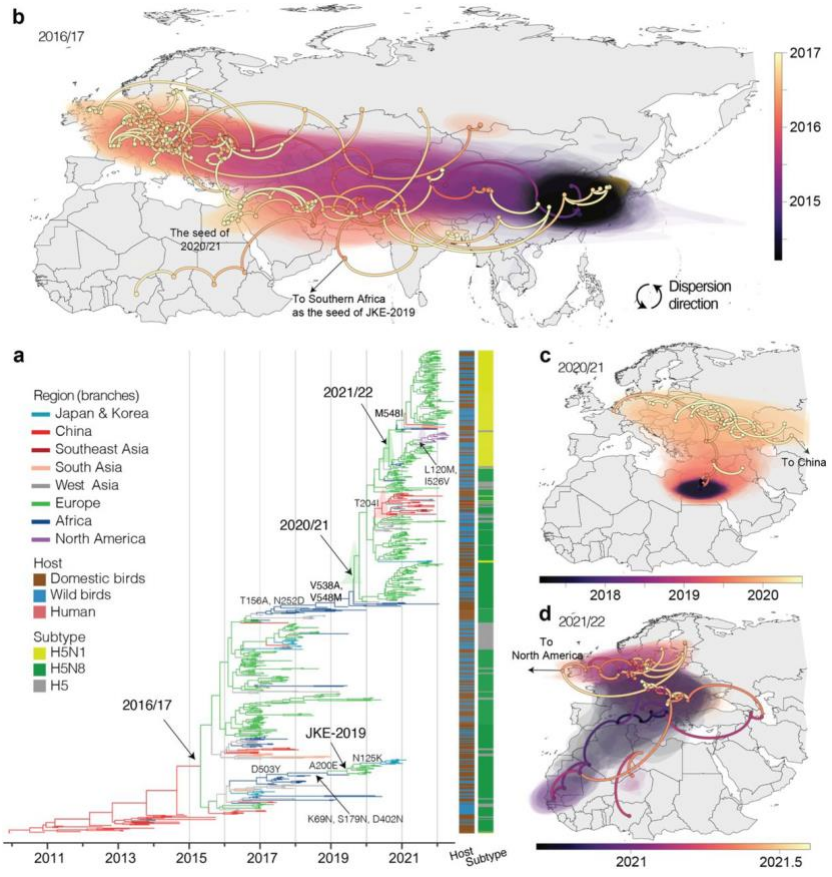

Figure 1. Evolution of clade 2.3.4.4b and early migration patterns of resurgence HPAI. (a) Maximum clade credibility tree with branches colored by geographic region. Colors on the right indicate host and virus subtype. The posterior distribution of the time to the most recent common ancestor (tMRCA) is shown as bar charts at specific nodes. (b) Continuous phylogeographic reconstruction of the spread of H5N8 from mid-2014 to 2017, (c) the early spread of H5N8 from 2017 to mid-2020 before the 2020/21 resurgence, and (d) the early spread of H5N1 from mid-2020 to 2021 before the 2021/22 resurgence. Circles represent nodes in the maximum clade credibility phylogeny, colored by the inferred time of occurrence. An interval of 95% higher posterior density is depicted by shaded areas, illustrating the uncertainty of the phylogeographic estimates.

Human seasonal influenza under COVID-19 and the potential consequences of influenza lineage elimination [Funding: US National Institute of Allergy and Infectious Diseases (NIAID) (HHSN272201400006C)]

Annual epidemics of seasonal influenza cause hundreds of thousands of deaths, high levels of morbidity, and substantial economic loss. Yet, global influenza circulation has been heavily suppressed by public health measures and travel restrictions since the onset of the COVID-19 pandemic. Notably, the influenza B/Yamagata lineage has not been conclusively detected since April 2020, and A(H3N2), A(H1N1), and B/Victoria viruses have since circulated with considerably less genetic diversity (**Fig 2**). Travel restrictions have largely confined regional outbreaks of A(H3N2) to South and Southeast Asia, B/Victoria to China, and A(H1N1) to West Africa. Seasonal influenza transmission lineages continue to perish globally, except in these select hotspots, which will likely seed future epidemics. Waning population immunity and sporadic case detection will further challenge influenza vaccine strain selection and epidemic control. We offer a perspective on the potential short- and long-term evolutionary dynamics of seasonal influenza and discuss potential consequences and mitigation strategies as global travel gradually returns to pre-pandemic levels.

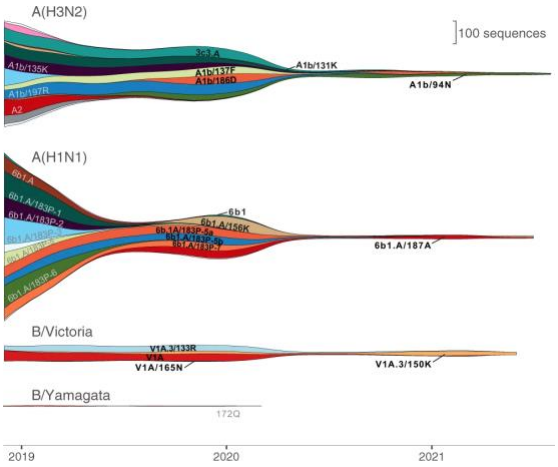

Figure 2. Streamgraph showing temporal changes in influenza lineage circulation. Lineage prevalence was estimated using sample collection dates of all sequences submitted to the Global Initiative for Sharing All Influenza Data (GISAID) from December 2018 to August 2021. Lineages detected since April 2020 are labeled in black; lineages that have not been detected since April 2020 are labeled in gray.

Genomic epidemiology of SARS-CoV-2 under an elimination strategy in Hong Kong [Funding: US National Institute of Allergy and Infectious Diseases (NIAID) (HHSN272201400006C)]

Hong Kong employed a strategy of intermittent public health and social measures alongside increasingly stringent travel regulations to eliminate domestic SARS-CoV-2 transmission. By analyzing 1899 genome sequences (>18% of confirmed cases) from 23-January-2020 to 26- January-2021, we reveal the effects of fluctuating control measures on the evolution and epidemiology of SARS-CoV-2 lineages in Hong Kong (**Fig 3**). Despite numerous importations, only three introductions were responsible for 90% of locally acquired cases. Community out- breaks were caused by novel introductions rather than a resurgence of circulating strains. Thus, local outbreak prevention requires strong border control and community surveillance, especially during periods of less stringent social restriction. Non-adherence to prolonged preventative measures may explain sustained local transmission observed during wave four in late 2020 and early 2021. We also found that, due to a tight transmission bottleneck, transmission of low-frequency single nucleotide variants between hosts is rare.

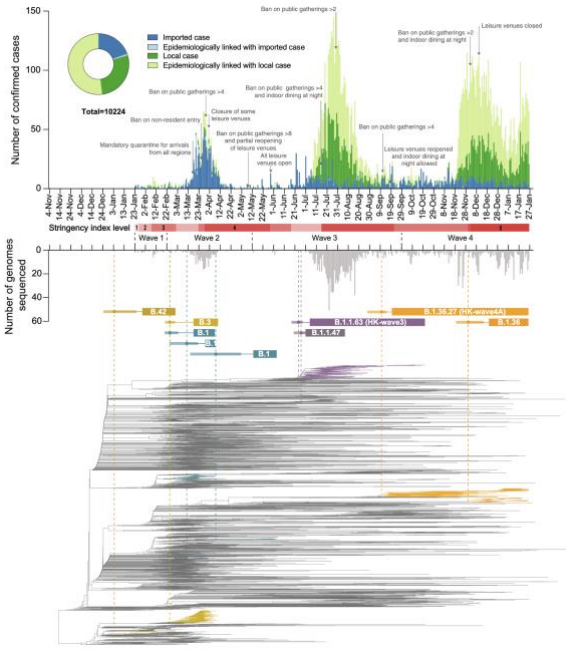

Figure 3. Epidemiological summary and time-scaled phylogeny of SARS-CoV-2 in Hong Kong. Confirmed cases (above) and sequenced genomes (below) are shown as bar charts across the four pandemic waves. Control-measure stringency applied in Hong Kong is based on the Oxford COVID-19 Government Response Tracker17. Red shaded bars delineate five levels of control-measure stringency in Hong Kong (Level 1: <40; level 2 : 40-50; level 3: 50-60; level 4: 60-70; level 5: >70). Time-scaled phylogeny of representative genomes from Hong Kong (n = 610) and overseas regions (n = 1,538) shows monophyletic clades containing at least five community cases in Hong Kong. The two largest Hong Kong lineages during HK-wave3 and HK-wave4A, B.1.1.63 and B.1.36.27, were subsampled to 100 and 65 sequences, respectively.

Off-season RSV epidemics in Australia after easing of COVID-19 restrictions

Human respiratory syncytial virus (RSV) is an important cause of acute respiratory infection with the most severe disease in the young and elderly. Non-pharmaceutical interventions and travel restrictions for controlling COVID-19 have impacted the circulation of most respiratory viruses including RSV globally, particularly in Australia, where during 2020 the normal winter epidemics were notably absent. However, in late 2020, unprecedented widespread RSV outbreaks occurred, beginning in spring, and extending into summer across two widely separated regions of the Australian continent, New South Wales (NSW) and Australian Capital Territory (ACT) in the east, and Western Australia. Through genomic sequencing we reveal a major reduction in RSV genetic diversity following COVID-19 emergence with two genetically distinct RSV-A clades circulating cryptically, likely localised for several months prior to an epidemic surge in cases upon relaxation of COVID-19 control measures (**Fig 4**). The NSW/ACT clade subsequently spread to the neighbouring state of Victoria and to cause extensive outbreaks and hospitalisations in early 2021. These findings highlight the need for continued surveillance and sequencing of RSV and other respiratory viruses during and after the COVID-19 pandemic, as mitigation measures may disrupt seasonal patterns, causing larger or more severe outbreaks.

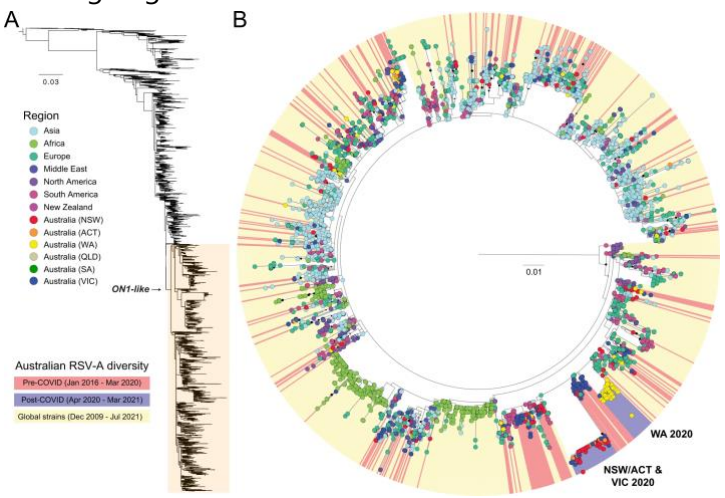

Figure 4. Phylogenetic analysis of global and Australian RSV-A glycoprotein sequences. (A) RSV-A sequences in this study were aligned with all available RSV-A sequences from NCBI GenBank. The glycoprotein coding region was extracted, and sequences less than 300 nt were removed. (B) A detailed examination of recently circulating ON1-like viruses showed only two pre-COVID-19 lineages (coloured red) survived into the post-COVID-19 period (blue). These two lineages were associated with outbreaks in NSW/ACT and WA in late 2020, and VIC in early 2021. No sequences sourced globally (yellow) were found to be related to these lineages, suggesting the sources remain unknown. Australian states—New South Wales (NSW), Australia Capital Territory (ACT), Western Australia (WA) and Victoria (VIC), South Australia (SA) and Queensland (QLD)—and globally-derived sequences are coloured according to the key provided. Diamonds at nodes indicate bootstrap support values >70%. Branches are proportional to the number of nucleotide substitutions per site.

Publications

1. Koszalka P, George A, Dhanasekaran V, Hurt AC, Subbarao K. 2022. Effect of Baloxavir and Oseltamivir in Combination on Infection with Influenza Viruses with PA/I38T or PA/E23K Substitutions in the Ferret Model. *mBio* 30;**13**(4):e0105622.
2. Xie R, Adam DC, Edwards KM, Gurung S, Wei X, Cowling BJ, Dhanasekaran V†. 2022. Genomic epidemiology of seasonal influenza circulation in China during prolonged border closure from 2020 to 2021. *Virus Evol* 13;**8**(2):veac062.
3. Eden J-S, Sikazwe C, Xie R, Deng Y-M, Sullivan SG, Michie A, Levy A, Cutmore E, Blyth C, Britton P, Crawford, Dong X, Dwyer D, Edwards K, Horsburgh B, Foley D, Kennedy K, Minney-Smith C, Speers D, Tulloch R, Holmes EC, Dhanasekaran V†, Smith D†, Kok J†, Barr IG† and the Australian RSV study group. 2022. Off-season RSV epidemics in Australia after easing of COVID-19 restrictions. *Nature Communications* **13**, 2884.
4. Dhanasekaran V†, Sullivan S, Edwards K, Xie R, Valkenburg S, Cowling B, Barr I. 2022. Human seasonal influenza under COVID-19 and the potential consequences of influenza lineage elimination. *Nat Commun* **13**, 1721.
5. Gu H, Xie R, Adam DC, Tsui JL, Chu DK, Chang LDJ, Cheuk SSY, Gurung S, Krishnan P, Ng DYM, Liu GYZ, Wan CKC, Cheng SSM, Edwards KM, Leung KSM, Wu JT, Tsang DNC, Leung GM, Cowling BJ, Peiris M, Lam TTY, Dhanasekaran V†, Poon LLM†. 2022. Genomic epidemiology of SARS-CoV-2 under an elimination strategy in Hong Kong. *Nat Commun* **13**,736.
6. Gu H, Cheng SSM, Krishnan P, Ng DYM, Chang LDJ, Liu GYZ, Cheuk SSY, Hui MMY, Fan MCY, Wan JHL, Lau LHK, Chu DKW, Dhanasekaran V, Peiris M, Poon LLM. 2022. Monitoring International Travelers Arriving in Hong Kong for Genomic Surveillance of SARS-CoV-2. *Emerg Infect Dis* 28: 247-250.

Seminars and Invited Presentations

Jan 2022 **Speaker**, presented a webinar "Human seasonal influenza under COVID-19 and the potential consequences of influenza lineage elimination" in the 1st Annual CEIRR Network Meeting, NIH, USA.

Aug 2022 **Speaker**, presented a webinar "Origins and spread of the 2020-2022 highly pathogenic avian influenza H5 panzootic" in the 1st Annual CEIRR Network Meeting, NIH, USA.

Sep 2022 **Invited Plenary Speakar**, OPTIONS XI for the control of Influenza, Belfast, UK (Declined due to COVID-19 travel restrictions)

Dec 2022 **Inivited Speaker**, presented a webinar "Changing epidemiology of respiratory viruses during COVID-19" at the 1st International Conference of Computational Antimicrobial Pharmacology, Melbourne, Australia

Dec 2022 **Invited Speaker**, presented a webinar "**Genomic epidemiology and phylodynamics of SARS-CoV-2 and other human respiratory viruses**" in the RGC Theme-based Research Scheme Seminar series, Hong Kong.

Knowledge Exchange activities

Radio. COVID-19 Science and policy communication through RHTK Radio 3 programs; *RTHK 3 Backchat* >25 appearances; *RTHK Morning News* 4 appearances

Newspaper. Interviewed by Guardian on the resurgent Omicron outbreak in Hong. Kong

Community-based teaching. Designed and delivered a short course on Science in Action to under-privileged children in Hong Kong, through Empower U. Planning additional activities for 2023/2024.

Teaching

1. CMED6000 – Capstone (Master of Public Health), The University of Hong Kong, Hong Kong SAR (**Supervisor and Examiner**).
2. Outbreak – Problem Based Learning (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Tutor**).
3. Health Research Projects (HRP) (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Supervisor and Examiner**)
4. Head Neck and Nervous system Block – Problem Based Learning (MBBS Year 2), The University of Hong Kong, Hong Kong SAR (**Tutor**).
5. Introduction to the Art and Science of Medicine, Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (**Tutor**).

Collaborations

1) **Ian Barr** (WHO Collaborating Centre for Reference and Research on Influenza, Peter Doherty Institute, Australia): Genomic epidemiology of influenza and RSV.
2) **Richard Webby** (St Jude Children's Research Hospital, USA): Evolutionary studies of influenza and SARS-CoV-2 viruses.
3) **Leo Poon** (School of Public Health, The University of Hong Kong): Genomic epidemiology of respiratory viruses.
4) **Ben Cowling** (School of Public Health, The University of Hong Kong): Genomic epidemiology of respiratory viruses.
5) **Edward Holmes** (Sydney University, Australia): Evolutionary dynamics of RNA viruses.
6) **Trevor Lithgow** (Monash University, Australia): Antimicrobial resistance of *Klebsiella*.
7) **Gavin Smith** (Duke-NUS Medical School, Singapore): Ecology and evolution of influenza and other respiratory viruses.
8) **Kanta Subbarao** (WHO Collaborating Centre for Reference and Research on Influenza, Peter Doherty Institute, Australia): Genomics of avian influenza viruses.
9) **Erik Karlsson** (Institute Pasteur Cambodia): Surveillnce of Avian influenza viruses in Southeast Asia

10) **Sebastian Duchene** (Peter Doherty Institute): Bayesian phylodynamics

11) **Ghazi Kayali** (Human Link, Saudi Arabia): Avian influnenza surveillance and policy in Africa and Middle East

Funding

1) Characterising the changing epidemiology of respiratory viruses through public health genomics. (**Principal Investigator**; HKU Seed Fund – Ends: 05/2023).
2) Control of Influenza: Individual and Population Immunity (**Sub PI** ; Research Grants Council of the Hong Kong Special Administrative Region, China – Ends 12/2023).
3) UHK Identity presence/absence of genetic markers of virulence. Centers for Influenza Research and Response (**Principal Investigator**; NIH UHK – Ends: 03/2028).

Personnel

Name	Position
Vijaykrishna DHANASEKARAN	Associate Professor
Kimberly E. EDWARDS	Project Manager
Xiaoman WEI	Postdoctoral Fellow
Sonia YOUNAS	PhD student
Ruopeng XIE	MPhil student
Shreya GURUNG	MPhil student
Yang ZHAO	Research Assistant I

3.2 Leo POON Lab

Summary

I have been researching on emerging infectious diseases for over 20 years. Zoonotic viruses, such as coronaviruses and influenza viruses, are my research topics. My team develops molecular diagnostic tests for these viruses. We also use multidisciplinary approach to study the ecology, transmission and pathogenesis of these emerging viruses. The overarching goal of my research is to generate experimental evidences to develop evidence-based control measures and/or inform public health policy.

Our research projects are mainly classified into 3 major areas:
1. Emerging Infectious Diseases
2. Basic Virology and vaccinology
3. Molecular diagnosis

Research highlights

Transmission of SARS-CoV-2 delta variant (AY.127) from pet hamsters to humans, leading to onward human-to-human transmission

Transmission of SARS-CoV-2 from humans to other mammals, including pet animals, has been reported. However, with the exception of farmed mink, there is no previous evidence that these infected animals can infect humans, resulting in sustained human-to-human transmission. Following a confirmed SARS-CoV-2 infection of a pet shop worker, animals in the shop and the warehouse supplying it were tested for evidence of SARS-CoV-2 infection (Yen et al., Lancet 2022).

In this investigation, 8 (50%) of 16 imported Syrian hamsters in the pet shop and seven (58%) of 12 Syrian hamsters in the corresponding warehouse were positive for SARS-CoV-2 infection in RT-qPCR or serological tests. None of the dwarf hamsters (n=75), rabbits (n=246), guinea pigs (n=66), chinchillas (n=116), and mice (n=2) were confirmed positive for SARS-CoV-2 in RT-qPCR tests. SARS-CoV-2 viral genomes deduced from human and hamster cases in this incident all belong to the delta variant of concern (AY.127) that had not been circulating locally before this outbreak. The viral genomes obtained from hamsters were phylogenetically related with some sequence heterogeneity. Phylogenetic dating suggests infection in these hamsters occurred around Oct 14, 2021 (95% CI Sept 15 to Nov 9, 2021). Multiple zoonotic transmission events to humans were detected, leading to onward human-to-human transmission.

This study has expanded our understanding on the host range of SARS-CoV-2 and revealed the complexity of SARS-CoV-2 transmission in nature (Figure 1). This work demonstrates the possibility of generating novel antigenic variants of SARS-CoV-2 in animals. Finding from this study have been well received by both scientific and public health communities (e.g. WHO, FAO and OIE). For example, this work was highlighted by Nature (https://www.nature.com/articles/d41586-022-00322-0).

This work reiterated the important of conducting SARS-CoV-2 surveillance in both humans and animals. Findings from this study and those from his previous work (e.g. SARS-CoV in civet cats, Science 302:276-8; SARS-CoV-2 in dogs, Nature. 586:776-778; Swine influenza virus in pigs: Science. 328:1529) have highlighted the importance of One Health in combating infectious diseases.

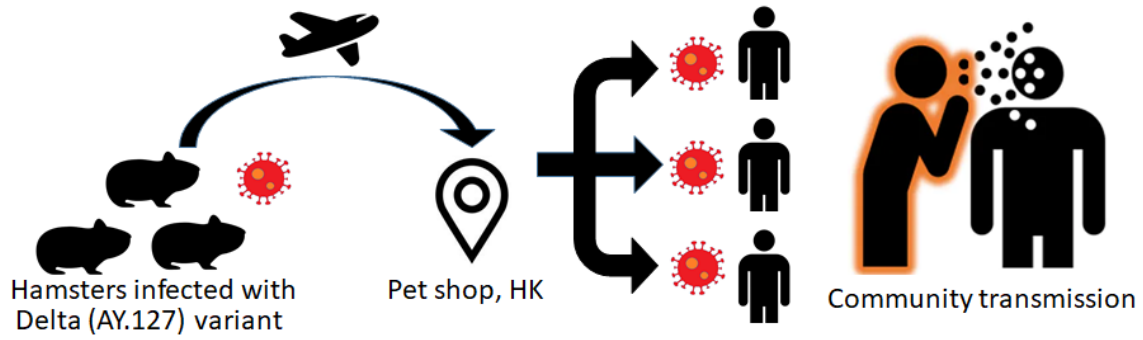

Figure 1. Zoonosis and reverse zoonosis of SARS-CoV-2 between human and hamster, leading to an outbreak of Delta (AY.127) in Hong Kong.

Because of the findings in hamsters, HK Government introduced early interventions to control hamster pets and successfully disrupted the transmission of this delta variant in Hong Kong. In addition, Food and Agriculture Organization (FAO), World Organisation for Animal Health (OIE) and World Health Organization (WHO) also issued a joint statement to urge for the prioritization of monitoring SARS-CoV-2 infection in animals for preventing the formation of animal reservoirs (https://www.who.int/news/item/07-03-2022-joint-statement-on-the-prioritization-of-monitoring-sars-cov-2-infection-in-wildlife-and-preventing-the-formation-of-animal-reservoirs).

Detection and characterization of SARS-CoV-2 variants in Hong Kong

Our next generation sequencing work of SARS-CoV-2 revealed possible sources of SARS-CoV-2 variants and transmission dynamics in Hong Kong (Gu et al., Nat Commun 2022, Gu et al., Emerg Infect Dis 2022a-2022d). My findings led to modifications/optimizations of COVID-19 control policies (e.g., quarantine hotel policy, guidelines on ventilation in gyms and mandatory RT-PCR testing). In addition, My lab is one of the very firsts which publish findings related to Omicron (Figure 2) and it recombinants (Figure 3).

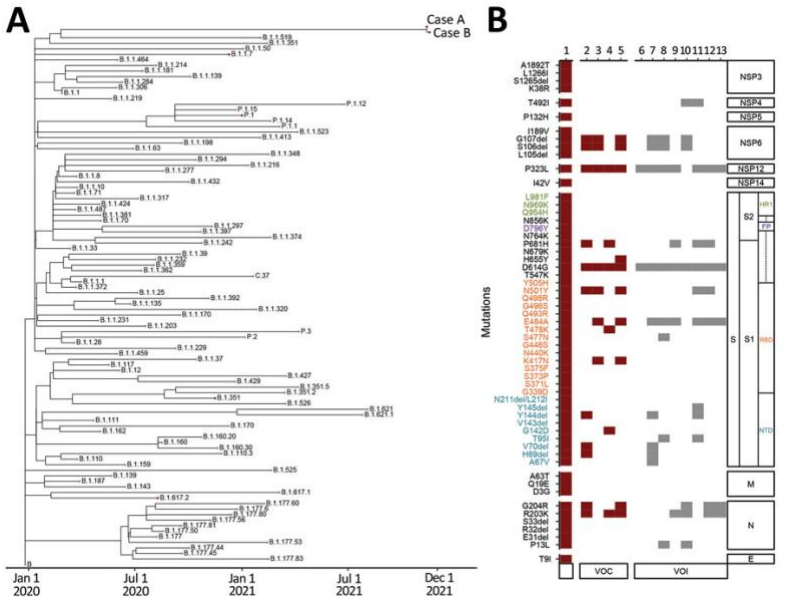

Figure 2. Detection of severe acute respiratory syndrome coronavirus 2 Omicron variant in 2 patients (cases A and B) in Hong Kong, China, November 2021. A) Phylogenetic time tree of Omicron nucleotide sequences using an early severe acute respiratory syndrome coronavirus sequence as a reference sequence (Wuhan-Hu-1/2019; GenBank accession no. MN908947.3). B) Comparison of Omicron variant mutations in case A to other variants; red indicates VOC and grey VOI (Appendix). Text colors indicate mutations found in NTD (blue), RBD (orange), FP (purple), and HR1 (green). Lane 1, case A; 2, Alpha (B.1.1.7); 3, Beta (B.1351); 4, Delta (B.1.617.2); 5, Gamma (P1); 6, Epsilon

(B.1.427/429); 7, Eta (B.1.525); 8, Iota (B.1.526); 9, Kappa (B.1.617.1); 10, Lambda (C.37); 11, Mu (B.1.1.621); 12, Theta (P.3); 13, Zeta (P.2). E, envelope; FP, fusion peptide; HR1, heptad repeat 1; M, matrix; NSP, nonstructural protein; NTD, N-terminal domain; RBD, receptor-binding domain; S, spike; VOC, variant of concern; VOI, variant of interest.

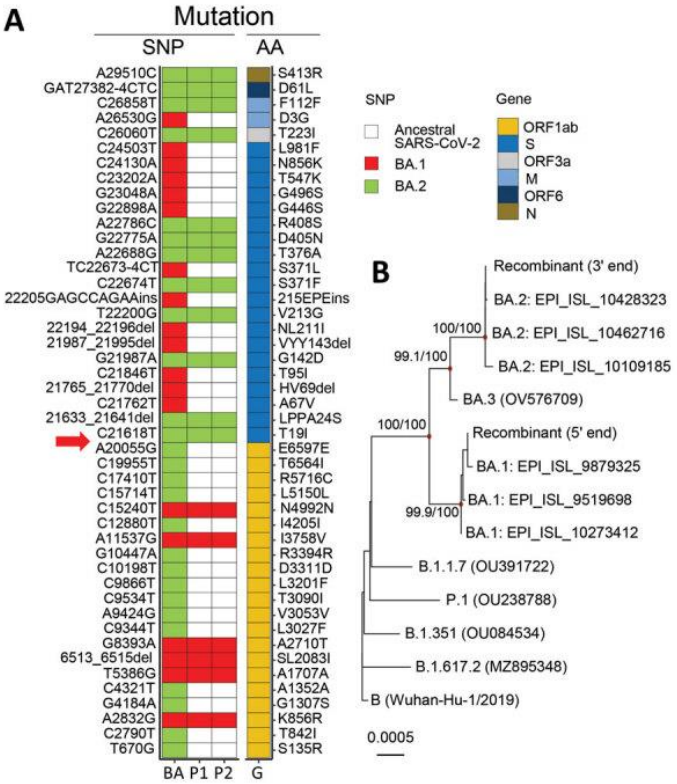

Figure 3. Detection of recombinant BA.1/BA.2 SARS-CoV-2 virus in arriving travelers, Hong Kong, China, February 2022. A) Mapping of BA.1- and BA.2-specific SNPs against the reference sequence genome (Genbank accession no. MN908947.3). Red boxes indicate BA.1-specific SNPs and green boxes indicate BA.2-specific SNPs found in samples from P1 and P2; the corresponding AA changes of these SNPs also are indicated. Red arrow indicates the putative breaking point. B) Phylogeny of viral RNA sequences at the 5′ and 3′ ends to the putative breakpoint. The maximum-likelihood tree was generated by using IQ-TREE (http://www.iqtree.org) and the transition plus empirical base frequencies plus proportion of invariable site nucleotide substitution model with Wuhan-Hu-1 (GenBank accession no. MN908947.3) as the outgroup. References sequences are shown with GISAID (https://www.gisaid.org) or GenBank accession numbers. Red node points show strongly supported branches as detected by SH-aLRT and ultrafast bootstrap values. Scale bar indicates nucleotide substitutions per site. AA, amino acid; BA, BA.1/BA.2 recombinant; G, gene; M, membrane; N, nucleocapsid; ORF, open reading frame; P1, patient 1; P2, patient 2; S, spike; SNP, single-nucleotide polymorphism.

The Omciron variants isolated from our surveillance was further studied in both in vitro and in vivo risk assessment platforms (Hui et al., Nature 2022; Su et al., J Infect Dis 2022). In addition, the antibody responses triggered by SARS-CoV-2 infection or COVID-19 vaccination against SARS-CoV-2 variants, including VOC Omicron, were studied (Cheng et al., Nat Med 2022; Cheng et al., Euro Surveill 2022).

With my expertise in coronavirus evolution and sequence analysis, I serve in several technical groups in WHO/FAO/OIE for controlling COVID-19. For example, I serve in the Technical Advisory Group on SARS-CoV-2 Virus Evolution to monitor SARS-CoV-2 evolution (Nat Microbiol. 6:821-823) and help to develop WHO guidelines for genomic surveillance of SARS-CoV-2 (https://www.who.int/publications/i/item/9789240018440).

In recognizing my contribution to control COVID-19 in Hong Kong, I received a research award (Outstanding Project Team on COVID-19) by the Food and Health Bureau, Hong Kong Government. In addition, I have recently receive an Distinguished Alumni Award from my alma mater (Hong Kong Baptist University) because of his contribution to in this pandemic.

Detection and characterization of influenza viruses

Several zoonotic influenza A viruses detected in humans contain genes derived from avian H9N2 subtypes. We uncovered a Eurasian avian-like H1N1 swine influenza virus with polymerase basic 1 and matrix gene segments derived from the H9N2 subtype, suggesting that H9N2 viruses are infecting pigs and reassorting with swine influenza viruses in China (Sun et a., Emerg Infect Dis 2022). We also conducted similar virus surveillance in poultry and detected a novel influenza A(H3N8) virus in chicken that have an internal genes derived from H9N2 viruses (Sit et al., Emerg Infect Dis 2022). This novel reassortant has been recently reported to cause human infections. These findings highlight the importance of systematic influenza virus surveillance in animals.

Publications

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2. Bull MB, Ma FN, Perera LP, Poon LL, Valkenburg SA. Early vaccine-mediated strain-specific cytokine imbalance induces mild immunopathology during influenza infection. *Immunol Cell Biol* 2022.
3. Burckhardt RM, Dennehy JJ, Poon LLM, Saif LJ, Enquist LW. Are COVID-19 Vaccine Boosters Needed? The Science behind Boosters. *J Virol* 2022; **96**(3): e0197321.
4. Cheng SM, Mok CKP, Chan KC, Ng SS, Lam BH, Luk LL, Ko FW, Chen C, Yiu K, Li JK, Chan KK, Tsang LC, Poon LL, Hui DS, Peiris M. SARS-CoV-2 Omicron variant BA.2 neutralisation in sera of people with Comirnaty or CoronaVac vaccination, infection or breakthrough infection, Hong Kong, 2020 to 2022. *Euro Surveill* 2022; **27**(18).
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9. Deng Y, Xu X, Zheng X, Ding J, Li S, Chui HK, Wong TK, Poon LLM, Zhang T. Use of sewage surveillance for COVID-19 to guide public health response: A case study in Hong Kong. *Sci Total Environ* 2022; **821**: 153250.

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Seminars and Invited Presentations

Feb 2022 **Invited Speaker**, presented a webinar "Molecular epidemiological study of COVID-19 cases in Hong Kong" in COVID-19 Scientific meeting organized by Pasteur, Paris.

April 2022 **Invited Speaker**, presented a webinar "Molecular epidemiology of SARS-CoV-2 in Hong Kong" in HKSGC and HKSMG – Joint Annual Scientific Meeting, Hong Kong.

May 2022 **Invited Speaker**, presented a webinar "Molecular surveillance of SARS-CoV-2 in Hong Kong: the discovery of zoonosis and reverse zoonosis of delta variant between humans and hamsters" organized by CREID-ESP, NIH, USA.

Aug 2022 **Speaker**, presented a webinar "Transmission of SARS-CoV-2 delta variant (AY.127) from pet hamsters to humans, leading to onward human-to-human transmission" in the 1st Annual CEIRR Network Meeting, NIH, USA.

Sept 2022 **Keynote Speaker**, presented a webinar "Stability of SARS-CoV-2 in different environmental conditions" in a conference "Respiratory virus transmission and non-pharmaceutical control measures" organized by ANRS Maladies Infectieuses Emergentes, Paris.

Sept 2022 **Invited Speaker**, presented a webinar "Stability of SARS-CoV-2 in different environmental conditions" in HK Tech Forum on Advanced Matter and Materials organized by the Hong Kong Young Academic of Science.
Sept 2022 **Invited Speaker**, presented a webinar "Application and effectiveness of genome sequencing of SARS-CoV-2 for contact tracing and control measures SARS-CoV-2" in the 2020 World Influenza Conference, Shenzhen, China
Sept 2022 **Invited Speaker**, presented a webinar "Molecular epidemiology of SARS-CoV-2 in Hong Kong" in "The Fight against COVID-19: Development, Prevention and Mutations" organized by the Hong Kong Young Academic of Science.
Sept 2022 **Invited Speaker**, presented a seminar "Molecular surveillance of SARS-CoV-2 in Hong Kong" in the Public Health Conference 2022 organized by the School of Public Heath, HKU.
Sept 2022 **Speaker**, presented a webinar "Use of molecular epidemiological, serological and experimental approaches to study COVID-19 transmission in Hong Kong" in the CREID Network 2022 Annual Meeting, NIH, USA.

Knowledge Exchange activities

April 2022 **Speaker**, presented a webinar "Molecular epidemiology of SARS-CoV-2 in Hong Kong" organized by the Hong Kong Young Academic of Science.

Teaching

1. CMED6105 – Infectious Diseases in Public Health (Master of Public Health), The University of Hong Kong, Hong Kong SAR (**Course director and lecturer**).
2. Life Science- (BNur Year 2 and BCMed Year 3), The University of Hong Kong, Hong Kong SAR (**Lecturer**).
3. Outbreak – Problem Based Learning (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Tutor**).
4. Musculoskeletal System Block– Problem Based Learning (MBBS Year 2), The University of Hong Kong, Hong Kong SAR (**Tutor**).
5. Introduction to the Art and Science of Medicine, Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (**Lecturer**).
6. Introduction to the Art and Science of Medicine (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (**Lecturer**).

Funding

1. Virological, immunological and epidemiological characterization of COVID-19 (**Principal Coordinator;** University Grants Committee/Theme-based Research Scheme – Ends 2026)
2. Molecular epidemiological study of COVID-19 cases in Hong Kong (**Principal Investigator**; Health and Medical Research Fund – Ends 2023).

3. Deciphering the role of RNA-RNA interactions between influenza viral segments on reassortment (**Principal Investigator**; Research Grants Council/General Research Fund – Ends 2023).
4. Control of influenza: individual and population immunity (**Co-Principal Investigator**; Research Grants Council/Theme based Research Scheme – Ends 2024).
5. Control of emerging, epidemic and endemic infectious diseases (**Co-Investigator**; HMRF - Commissioned Research on Control of Infectious Diseases – Ends 2025).
6. Replication-defective SARS-CoV-2 mutant vaccines with abnormal codon usages (**Principal coordinator**; University Grants Committee/Collaborative Research Fund – Ends 2024).
7. Airborne virus harvesting, detection and diagnostics inspired by origin of life (**Co-Principal Investigator**; University Grants Committee /Collaborative Research Fund – Ends 2024).

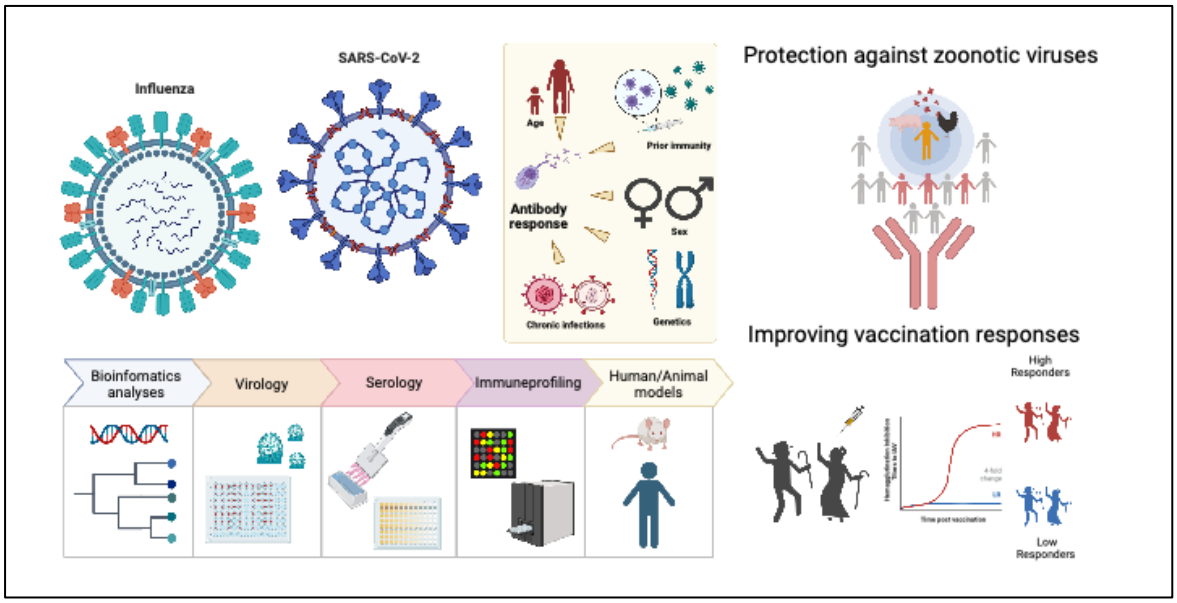
Personnel

Name	Position
Leo Poon	Professor
Alex Chin	Research Assistant Professor
Tenigeer	Post-doctoral Fellow
Alison Lai	Post-doctoral Fellow
Haogao Gu	Post-doctoral Fellow
Dana Wong	Technical Manager (Lab Manager)
Sylvia Lau	Senior Research Assistant
Yi Cao	Technical Officer
Kary Chan	Research Assistant I
Vincent Lei	Research Assistant II
Lau Ho Kan Leo	Research Assistant II
Nick Mak	Research Assistant II
Sammi Cheuk	Postgraduate Student
Lydia Chang	Postgraduate Student
Winnie Sun	Postgraduate Student
Daisy Ng	Postgraduate Student
Samuel Cheng	Postgraduate Student
Pavithra Krishnan	Postgraduate Student

3.3 Sook-San WONG Lab

Summary

My laboratory is focused on understanding the determinants of robust antibody responses after respiratory virus infection and vaccination at a population as well as at the individual level. Our interests also include studying population immunity to zoonotic viruses and how that contributes to our risk assessment process of such pathogens. This research area is critical to our understanding of respiratory viruses' vaccine efficacy and disease pathogenesis. It will also improve our public health policies in managing the disease burden of seasonal respiratory viruses as well as pandemic risks of emerging viruses.



Our research projects fall under the following themes:

1) Improving influenza vaccine responses
2) Evolution and population immunity to influenza neuraminidase (NA) antibodies
3) Understanding the antibody dynamics to influenza hemagglutinin (HA) and neuraminidase (NA) proteins
4) Impact of antibody cross-reactivity to seasonal coronaviruses on SARS-CoV-2 infection and vaccination responses

Research highlights

(a) Cytokine markers to predict vaccine responses

Vaccination remains one of the most effective public health strategy to control community transmission as well as to reduce the disease burden of respiratory viruses. However, some vaccinees may fail to mount sufficient protective antibody responses after primary or booster vaccination. In a collaboration with Guangdong Center for Disease Control and Prevention, we have discovered that serum cytokine levels, particularly IL-10

and TNF-α at time of vaccination were associated with subsequent antibody responses upon receipt of the inactivated influenza vaccines in older adults (Figure 1).

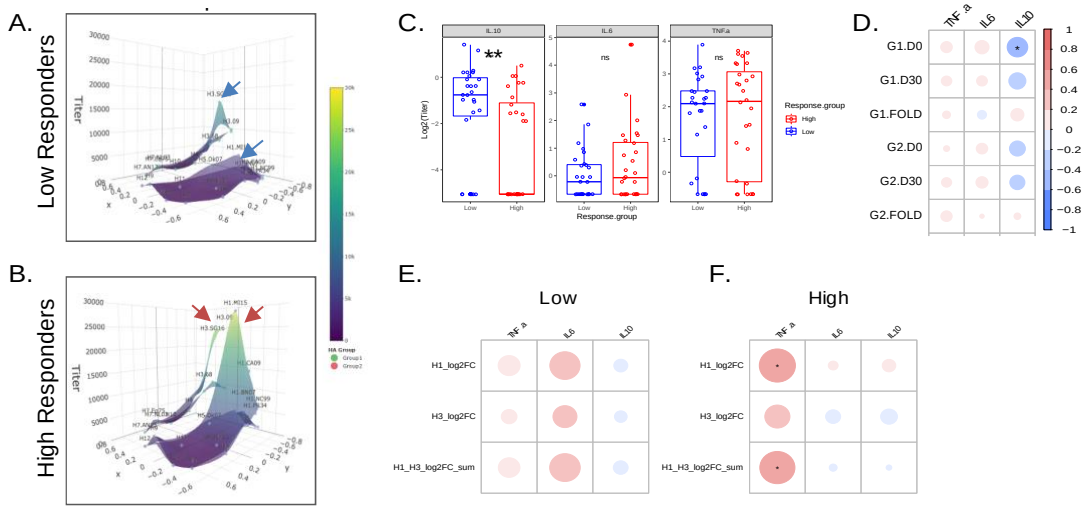


Figure 1. Preliminary data demonstrating the association between serum cytokine levels, pre-existing influenza antibodies and vaccine responses in older adults that received the 2018/2019 inactivated influenza vaccine. (A, B) Pre- (Day 0) and post-vaccination (Day 30) HA-IgG landscape to Group 1 and Group 2 influenza HAs in 29 low (LR) and 30 high-vaccine (HR) responders. Post-vaccination landscape is indicated by blue and red arrows respectively. (C) Differences in serum IL-10, IL-6 and TNF-α cytokine levels at Day 0 between LR (blue) and HR (red). Boxplots indicate the median and interquartile range (IQR) of log-transformed data. (D) Correlation between serum IL-10, IL-6 and TNF-α cytokine levels with total influenza HA-IgG, derived from the area-under-the curve (AUC) of antibody binding titers to 14 Group 1 and 8 Group 2 HA-antigens at Day 0 and Day 30. FOLD indicates AUC-fold change to the indicated group. (E) Correlation between TNF-α, IL-10 and IL-6 and HAI-antibody titers for LR and HR. Note that LR, by definition will not have any HAI-titer increase between Day 0 and Day 30. Color scale and the size of the circle in (B, C to F) are proportional to the Pearson's correlation, r-value and asterisks indicates statistical significance after adjustment for false-discovery rate using the Benjamini-Hochberg method. * indicates $p<0.05$, ** indicates $p<0.01$ and *** indicates $p<0.001$

In collaboration with Ben Cowling and Malik Peiris, we are developing a project to evaluate this in two randomized placebo-controlled influenza vaccine trials in older adults in Hong Kong; the 'Immunogenicity of Alternative Annual Influenza Vaccination Strategies in Older Adults in Hong Kong (PIVOT)' and the 'Randomized Immunogenicity trial in Elderly of Twice-Annual Influenza Vaccination (RETAIN)' study. PIVOT study was a head-to-head comparison on the immunogenicity of the standard-dose inactivated vaccine, MF59-adjuvanted vaccine, high-dose vaccine and recombinant-hemagglutinin (rHA) vaccine given in an alternating or non-alternating regimen over the course of four-years, while RETAIN assesses whether twice-annual influenza vaccination confers additional advantage over once-annual influenza vaccination in Hong Kong. Our primary goal for this project is to determine if these serum biomarkers can be used to identify poor vaccine responders in the older adults. Through PIVOT, we could also address if the enhanced vaccines are suitable for those with apparent immune deficiencies. The proposed study can contribute towards precision vaccination in older adults, identifying

optimal vaccine regimen that is suitable for the immune or health status of the vaccinee using already licensed vaccines.

(b) Neuraminidase (NA) immunity as correlates of protection against zoonotic influenza

NA-antibodies are more broadly cross-reactive compared to HA-antibodies and may provide better protection against antigenic variants. We have discovered that older adults exposed to the 1968 H3N2 pandemic viruses possess N2 antibodies that protects against H9N2 avian influenza viruses in a mouse challenge model (Figure 1). We hypothesize that early life exposure to the 1957 H2N2 and 1968 H3N2 pandemic viruses bearing avian origin NA could confer immune memory that cross-reacts with avian NA.

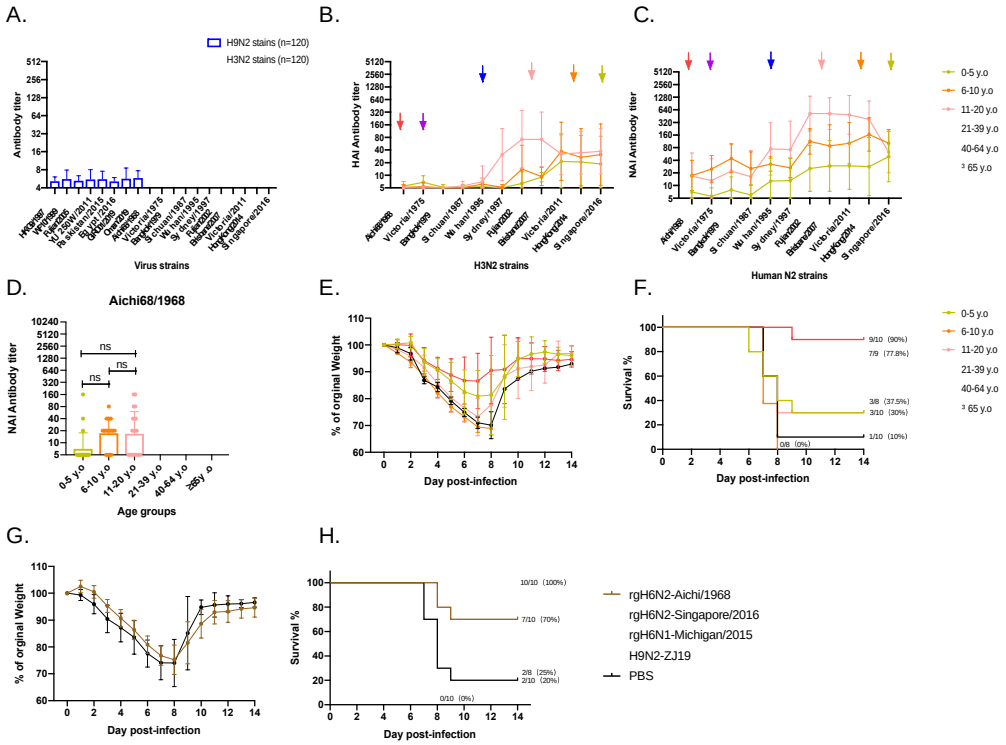


Figure 1. Cross-reactive and protective potential of human N2 antibodies against H9N2 viruses. (A) HAI-titers of study samples against representative H9N2 (blue) and H3N2 (red) viruses. Age-stratified (B) HAI and (C) NAI-antibody profile against select antigenically-distinct A/H3N2 strains in human circulation since 1968. (D) Age-stratified NAI-titers against 1968 pandemic strain, A/Aichi/2/1968 (H3N2). (E) Weight lost and (F) survival curve of mice that received 300 µl of the pooled human sera in the respective age-groups. Protective capacity of sera from mice were shown in (G) weight loss and (H) survival curve of mice that received of 300 µl of the pooled mice sera previously immunized with A/Aichi/2/1968, a recent H3N2 strain, A/Singapore/2018, as well as controls A/Michigan/45/2015 (H1N1) and A/chicken/Zhejiang/2019 (H9N2).

We currently have three projects in this program that is focused on i) understanding the molecular basis of the observed cross-reactivity (in collaboration with Dr. Mark Zanin), ii) systematically evaluating the breadth of cross-reactivity using phylogenetic approaches (in collaboration with Dr. Vijay Dhanasekaran) and iii) evaluating the cross-reactivity at the memory B cell level. The goal of this program is to identify the role of NA-antibodies in risk-assessments of zoonotic influenza viruses, in particular those posed by avian and

swine influenza viruses, and to discover therapeutics or vaccine candidate that are broadly protective against human and avian influenza infections. These projects have received partial funding from The University of Hong Kong Seed Funding and Start-Up Fund for New Staff.

(c) Molecular alterations in human milk in simulated maternal nasal mucosal infection with live attenuated influenza vaccination

The processes that regulate the induction of maternal antibodies in human milk after infection or vaccination by a respiratory pathogen is not well understood. In collaboration with Drs. Pia Pannaraj (University of Southern California) and Richard Webby, we reported on the transcriptomics changes in the breastmilk cells upon receipt of live-attenuated influenza vaccine (LAIV), as a proxy for influenza virus infection, compared to vaccination with standard inactivated influenza vaccines (IIV). We found that LAIV induced a greater degree of molecular perturbation in milk, particularly in the innate immune signalling pathways, whereas IIV induced greater changes in the blood cells (Figure 2). Both LAIV and IIV elicited influenza specific antibodies that lasted for at least 6 moths. Our study suggests that mucosal vaccination results in a rapid upregulation of innate immune responses in human milk not seen with intramuscular vaccination, providing timely protection until the antigen-specific immunity develops.

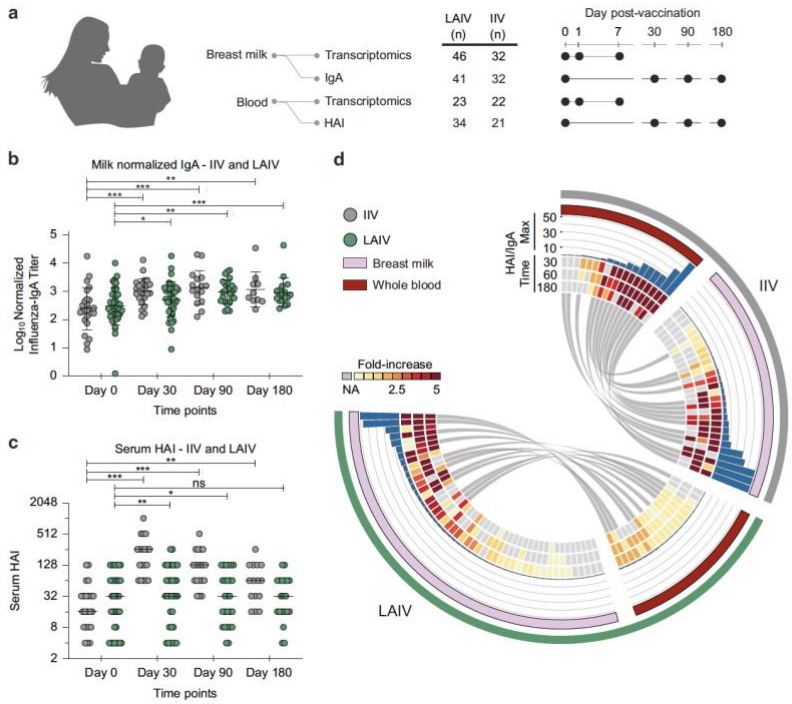


Figure 3. Study design and immune responses induced by vaccination. a Study overview: Total of 78 breastfeeding mothers were recruited and received doses of either LAIV (n = 46) or IIV (n = 32). b Human milk influenza-specific IgA increases by day 30 and persists above baseline (day 0) through at least 180 days in response to both LAIV and IIV. c Serum HAI increases by day 30 and persists through at least 180 days in serum after IIV but not LAIV. d Circos plot summarizing the antibody response induced by vaccination. Modified from Pannaraj et al.,. Mucosal Immunology. 2022 May;15(5):1040-1047.

Publications

1. Gass Jr. JD, Dusek RJ, Hall JS, Hallgrimsson GT, Vignisson SR, Ragnarsdottir SB, Halldórsson HP, Jónsson JE, Krauss S, **Wong SS**, Wan XF, Akter S, Sreevatsan S, Trovão NS, Nutter FB, Runstadler JA, Hill N (2023) Global dissemination of Influenza A virus is driven by wild bird migration through arctic and subarctic zones. Molecular Ecology, in press.
2. Pannaraj PS, da Costa-Martins AG, Cerini C, Li F, **Wong SS**, Webby RJ, Singh Y, Urbanski AH, Gonzalez-Dias P, Yang J, Nakaya H, Aldrovandi GM (2022) Molecular Alterations in Human Milk in Simulated Maternal Mucosal Infection with Live Attenuated Influenza Vaccination. Mucosal Immunology 15(5):1040-1047.
3. Kim HK, Kang JA, Lyoo KS, Le TB, Yeo YH, **Wong SS**, Na W, Song D, Webby RJ, Zanin M, Jeong DG, Yoon SW (2022) SARS-CoV-2 and influenza A virus co-infection alters viral tropism and hematological composition in Syrian hamsters. Transboundary and Emerging Diseases doi: 10.1111/tbed.14601. Online ahead of print
4. Lombarde JG, Pillai MR, Wehenkel M, Lin CY, Keating R, Brown SA, Crawford JC, Brice DC, Castellaw AH, Mandarano AH, Guy CS, Mejia JR, Carlessia DL, Chang TC, Oshansky CM, **Wong SS**, Webby RJ, Yan M, Li QZ, Marion TN, Thomas PG, McGargill MA (2022) Induction of broadly reactive influenza antibodies increases susceptibility to autoimmunity. Cell Reports 38(10):110482. doi: 10.1016/j.celrep.2022.110482.
5. Le TB, Kim HK, Ahn MJ, Zanin M, Lo VT, Ling S, Jiang Z, Kang JA, Bae PK, Kim YS, Kim S, **Wong SS**, Jeong DG, Yoon SW (2022) Diagnostic performance and clinical feasibility of a novel one-step RT-qPCR assay for simultaneous detection of multiple severe acute respiratory syndrome coronaviruses. Arch Virol doi: 10.1007/s00705-022-05383-0. Online ahead of print.
6. Chen Y, Lin T, Wang CB, Liang WL, Lian GW, Zanin M, **Wong SS**, Tian XG, Zhong JY, Zhang YY, Xie JH, Zheng LL, Chen FY, Dang R, Zhao MQ, Yang YY, Zhou R, Zhu B (2022) Human adenovirus (HAdV) infection in children with acute respiratory tract infections in Guangzhou, China, 2010-2021: a molecular epidemiology study. World J Pediatr. 2022 Aug;18(8):545-552.
7. Kang M., Zanin, M, **Wong, SS** (2022) Subtype H3N2 Influenza A Viruses: An Unmet Challenge in the Western Pacific. Vaccines 10, 112; https://doi.org/10.3390/vaccines10010112
8. Zhao F, Wang Y, Chen L, Zhang X, Ducatez M, He J, Wan Z, Ye J, Bai Z, Xia Y, Dong Z, Gu W, Huang Z, Liang T, Lin Z, Song W, Chen Z, Yang Z, **Wong SS**, Hao CL, Zanin M (2022) Critical influenza-like illness in a nine-year-old associated with a poultry-origin H9N2 avian influenza virus: risk assessment and zoonotic potential. Front. Virol. 1:727163. doi: 10.3389/fviro.2021.727163

Seminars and Invited Presentations

1. Wong SS. The impact of pre-existing antibodies and immune status on the influenza vaccine responses in older adults. Theme-based Research Seminar for Control of Influenza: Individual and Population Immunity (T11-712/19-N). Online. 25 March 2022. **Speaker**

2. Wong SS. The role of neuraminidase antibodies induced by human influenza N2 against avian influenza H9N2 infection. 2022 CEIRR Annual Network Meeting. 14 – 17 August 2022, Memphis, TN, USA. **Speaker**
3. Wong SS. The impact of pre-existing antibodies and immune status on the influenza vaccine responses in older adults. 2022 CEIRR Annual Network Meeting. 14 – 17 August 2022, Memphis, TN, USA. **Poster**
4. Wong SS. Update on the CARES project. Meeting on Immune Response to Influenza Infection and Vaccination, United States Center for Disease Control and Prevention on August 18-19, 2022, Atlanta, GA, USA. **Speaker**

Knowledge Exchange activities

1. Chair for online meeting "Recombinant Influenza Vaccine value in controlling influenza in Greater Bay Area Advisory Board Meeting" project on June 26th 2022, organized by China Association for Vaccines.
2. Chair for "Seminar on Zoonotic Disease and Climate Change", on 24 November 2022 at the HKU-Li Ka Shing Faculty of Medicine, co-organized by HKU-Pasteur Research Pole and the Centre for Immunology & Infection, in conjuction with the bicentenary celebration of Louis Pasteur and French Science Festival.
3. Speaker/Mentor for 2022 Korea Global Mentoring Conference, 8 July 2022, organized by University of Science and Technology (UST),
4. Hosted laboratory visits from the French International School, 22 November 2022.
5. Assistant Editor for Cellular and Molecular Life Sciences (Springer Journal)
6. Council Member of International Society for Influenza and Other Respiratory Virus Diseases
7. Abstract Adjudicator for 27th Research Postgraduate Symposium, HKU-Li Ka Shing Faculty of Medicine, 30 November 2022- 1 December 2022.

Teaching

1. Outbreak- Problem Based Learning (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (Tutor).
2. Cardiopulmonary Renal System– Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (Tutor)
3. Supervised two undergraduate students (Asra Sainju and Sukriti Gawali) for 6-weeks summer internship under the School of Biomedical Science (BBMS) Summer Local Research Internship Program 2022.

Collaborations

1. Benjamin Cowling (School of Public Health, The University of Hong Kong, Hong Kong SAR): The association of serum cytokine levels with responses to influenza vaccination in older adults receiving standard and enhanced influenza vaccines; Observational study on incidence and epidemiological characteristics of influenza virus infection in

adults aged 60 and over - understanding the potential preventive value of twice-yearly influenza vaccination.

2. JS Malik Peiris (School of Public Health, The University of Hong Kong, Hong Kong SAR): SARS-CoV-2 patient cohorts for immune characterisations.
3. Nancy Leung, (School of Public Health, The University of Hong Kong, Hong Kong SAR): Systematic investigation into the breadth of antibody and B-cell cross-reactivity to avian influenza neuraminidase (NA) proteins in humans.
4. Mark Zanin (School of Public Health, Center for Infection and Immunology, The University of Hong Kong): Systematic investigation into the breadth of antibody and B-cell cross-reactivity to avian influenza neuraminidase (NA) proteins in humans.
5. Sophie Valkenburg (Doherty Institute, The University of Melbourne): collaboration on mechanisms of vaccine failures in the PIVOT study.
6. Richard J Webby (Department of Infectious Diseases, St. Jude Children's Research Hospital): Mechanisms of avian influenza disease.
7. Ali Ellebedy (Washington School of Medicine, St. Louis): Systematic investigation into the breadth of antibody and B-cell cross-reactivity to avian influenza neuraminidase (NA) proteins in humans.
8. Maureen McGargill (Department of Immunology, St. Jude Children's Research Hospital): Mechanisms of avian influenza disease.
9. Mariette Ducatez (National Institute for Agriculture Research (INRA) and of the National Veterinary School of Toulouse (ENVT): Contribution of virological factors and herd immunity in H9N2 influenza transmission and human disease.
10. Kang Min (Guangdong Centers for Disease Control and Prevention): Characterizing the serological response in an influenza vaccination study in older adults in Guangdong Province.

Funding

1. Defining the breadth of antigenic cross-reactivity of human antibodies to influenza neuraminidase (NA) proteins derived from human and animal influenza viruses. Enhanced Start-Up Fund for New Staff, LKS Faculty of Medicine, The University of Hong Kong. 1/1/2023 – 31/12/2025. HK$380,000 ($48,000 USD). Sook-San Wong – PI
2. Defining the breadth of cross-reactive B-cells in older adults to influenza neuraminidase (NA) proteins derived from human and animal influenza viruses. Seed Fund for Basic Research for New Staff. The University of Hong Kong. 1/1/2023 – 31/12/2024. HK$149,851 ($19,000 USD). Sook-San Wong – PI
3. Virological, immunological and epidemiological characterization of COVID-19. Research Grants Council, TRS (T11-705/21-N). 1/1/2022 – 31/10/2022. HK$400,000 ($50,000 USD). Sook-San Wong – Co-PI
4. Control of influenza: individual and population immunity. Research Grants Council, TRS (T11-712/19/N). 1/1/2020 – 31/12/2024. HK$300,000 ($38,000 USD). Sook-San Wong – Co-PI.

Personnel

Name	Position
Sook-San WONG	Assistant Professor
Lewis SIU	Senior Technician
Cheng XIAO	Postgraduate Student
Zaolan LIANG	Postgraduate Student
Lihan YIN	Research Assistant I
Min LI	Research Assistant II
Cheryl LEUNG	Research Assistant II
Lisa Touyon	Research Assistant II

3.4 Hein Min TUN Lab

Summary

Our group 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) to monitor antimicrobial resistance (AMR) bacteria and resistome in humans, animals, and the environment using a holistic One Health approach. Our goal is to contribute to improving scientific understanding on the impact of microbiome and AMR in public health.

Our research projects are mainly classified into the following major areas:
1. Eearly-life microbiome for health and diseases
2. Microbiome and Allergy
3. Microbiome, Immunity and Infections
4. Microbiota-gut-brian axis
5. One Health antimcrobial resistance study

Research highlights

Gut microbiota composition is associated with SARS-CoV-2 vaccine immunogenicity and adverse events

The gut microbiota plays a key role in modulating host immune response. We conducted a prospective, observational study to examine gut microbiota composition in association with immune responses and adverse events in adults who have received the inactivated vaccine (CoronaVac; Sinovac) or the mRNA vaccine (BNT162b2; BioNTech; Comirnaty). We performed shotgun metagenomic sequencing in stool samples of 138 COVID-19 vaccinees (37 CoronaVac and 101 BNT162b2 vaccinees) collected at baseline and 1 month after second dose of vaccination. Immune markers were measured by SARS-CoV-2 surrogate virus neutralisation test and spike receptor-binding domain IgG ELISA.

We found a significantly lower immune response in recipients of CoronaVac than BNT162b2 vaccines ($p<0.05$). Bifidobacterium adolescentis was persistently higher in subjects with high neutralising antibodies to CoronaVac vaccine ($p=0.023$) and their baseline gut microbiome was enriched in pathways related to carbohydrate metabolism (linear discriminant analysis (LDA) scores >2 and $p<0.05$; Figure 1A). Neutralising antibodies in BNT162b2 vaccinees showed a positive correlation with the total abundance of bacteria with flagella and fimbriae including Roseburia faecis ($p=0.028$; Figure 1B) . The abundance of Prevotella copri and two Megamonas species were enriched in individuals with fewer adverse events following either of the vaccines indicating that these bacteria may play an anti-inflammatory role in host immune response (LDA scores>3 and $p<0.05$).

Our study has identified specific gut microbiota markers in association with improved immune response and reduced adverse events following COVID-19 vaccines. Microbiota-targeted interventions have the potential to complement effectiveness of COVID-19 vaccines. The study was published in the leading gastroenterology journal, Gut (Ng SC et al. Gut. 2022). The findings from this study were filed for a provisional patent (US patent application no. 63/273,088).

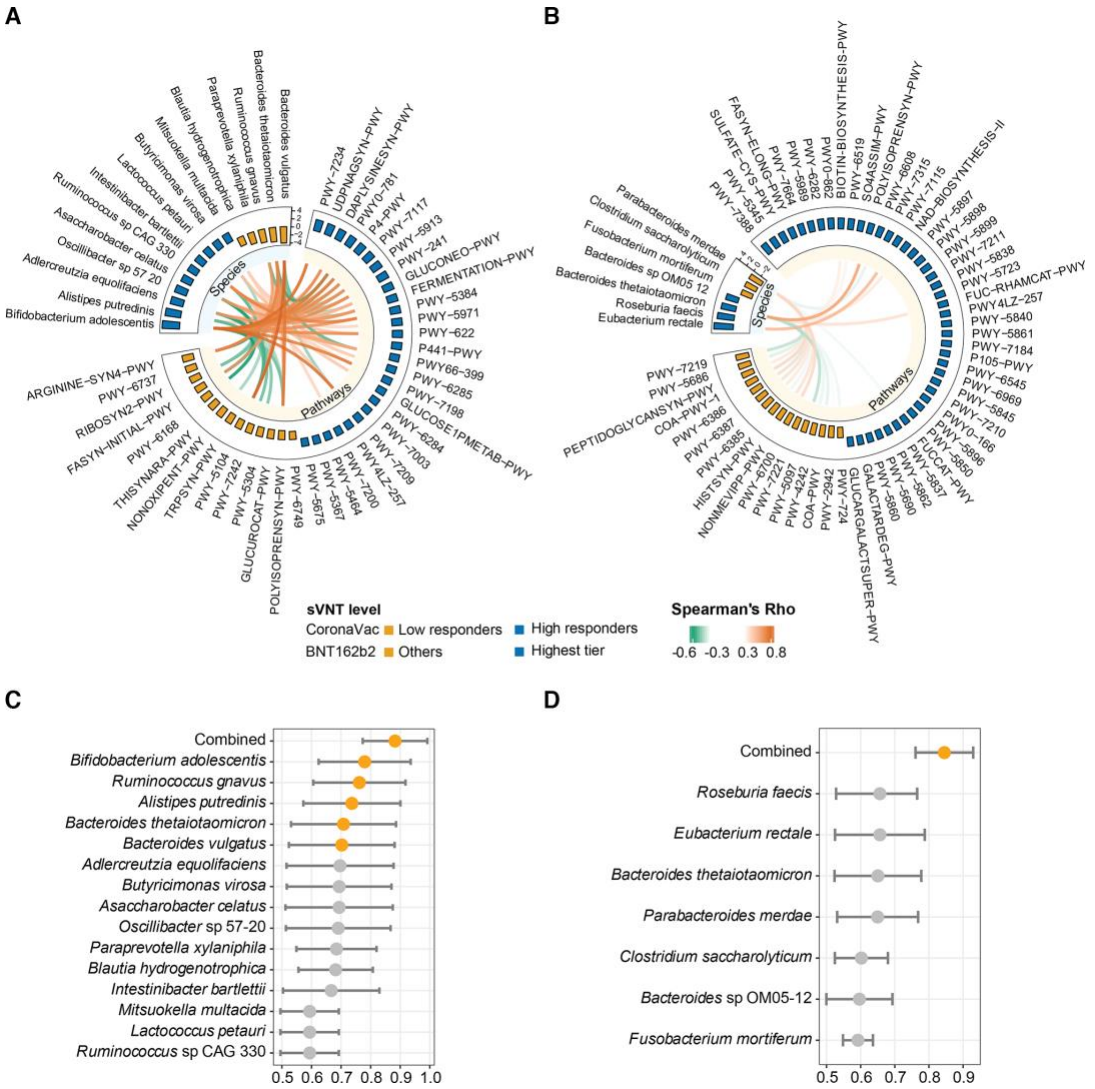


Figure 1. Baseline gut bacterial species and functions associated with high and low responders to vaccines at 1 month after second dose of vaccination. (A) Baseline bacterial species and pathways associated with high responders among CoronaVac vaccinees (n=37) (sVNT of 10-fold diluted plasma >60%). Differential baseline gut bacterial species and pathways were detected by LEfSe. Pairwise correlations between selected bacterial species and pathways markers with FDR corrected p<0.05 were shown. (B) Baseline bacterial species and pathways for highest-tier responders among BNT162b2 vaccinees (n=101) (the first quartile (Q1) of sVNT of 200-fold diluted plasma). sVNT-10: sVNT level of 10-fold diluted plasma; sVNT-200: sVNT level of 200-fold diluted plasma. Differential baseline gut bacterial species and pathways were detected by LEfSe. Pairwise correlations between selected bacterial species and pathways markers with FDR corrected p<0.05 were shown. Full names of differentially abundant pathways between high/low responders in (A,B) are described in online supplemental table S7C), AUROC (95% CI) values of models based on individual biomarkers and a combined model based on all biomarkers for high responders (n=16) vs low responders (n=21) among CoronaVac vaccinees. (D) AUROC (95% CI) values of models based on individual biomarkers and a combined model based on all biomarkers for the highest-tier responders (n=25) vs others (n=76) among BNT162b2 vaccines. each AUROC was presented as an orange dot with a bar showing the 95% CI. AUROC, area under the receiver operating characteristic curve; FDR, false discovery rate; LEfSe, linear discriminant analysis effect size; sVNT, surrogate virus neutralisation test.

Multi-cohort analysis of depression-associated gut bacteria sheds insight on bacterial biomarkers across populations

Gut microbes are associated with the development of depression based on extensive evidence. However, previous studies have led to conflicting reports on this association, posing challenges to the application of gut bacteria in the diagnostics and treatment of depression. To minimise heterogenicity in data analysis, the present meta-analysis adopted a standardised bioinformatics and statistical pipeline to analyse 16S rRNA sequences of 1827 samples from eight different cohorts.

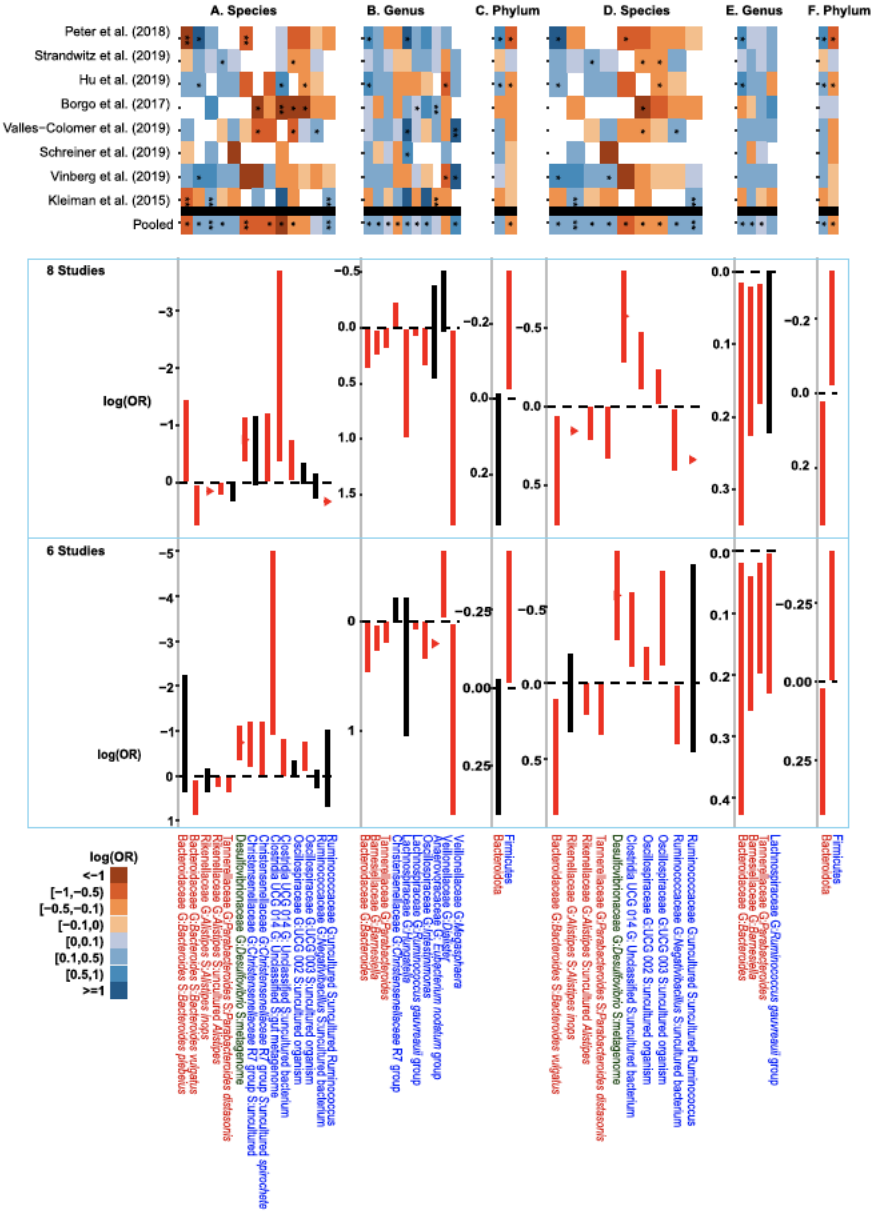


Figure 2. Differential bacterial biomarkers associated with depression. The adjusted model shown at the A Species level, B Genus level, C Phylum level. The crude model shown at the D Species level, E Genus level, F Phylum level. The colour in the heatmap indicates the log(OR) in each cohort. White indicates missing values. *p value < = 0.05, **p value < = 0.0001. The line in the forest plot indicates the 95%CI of pooled log(OR). Red indicates p value < = 0.05. Triangles indicate that the false discovery rate (FDR) adjusted p values < 0.1. Genera and species from the same phyla are labelled with the same colour.

Although changes in the overall bacterial community were identified by our meta-analysis, depressive-correlated changes in alpha-diversity were absent. Enrichment of *Bacteroidetes*, *Parabacteroides*, *Barnesiella*, *Bacteroides*, and *Bacteroides vulgatus*, along with depletion in Firmicutes, *Dialister*, *Oscillospiraceae UCG 003 and UCG 002*, and *Bacteroides plebeius*, were observed in depressive-associated bacteria. By contrast, elevated L-glutamine degradation, and reduced L-glutamate and L-isoleucine biosynthesis were identified in depressive-associated microbiomes. After systemically reviewing the data of these collected cohorts, we have established a bacterial classifier to identify depressive symptoms with AUC 0.834 and 0.685 in the training and external validation dataset, respectively. Moreover, a low-risk bacterial cluster for depressive symptoms was identified, which was represented by a lower abundance of *Escherichia-Shigella*, and a higher abundance of *Faecalibacterium*, *Oscillospiraceae UCG 002*, *Ruminococcus*, and Christensenellaceae R.7 group. This study has been published in Cellular and Molecular Life Sciences (Liang S et al. 2022. Cell Mol Life Sci).

A Universal LC-MS/MS Method for Simultaneous Detection of Antibiotic Residues in Animal and Environmental Samples

Detecting and monitoring the usage of antibiotics is a critical aspect of efforts to combat antimicrobial resistance. Antibiotic residue testing with existing LC-MS/MS methods is limited in detection range. Current methods also lack the capacity to detect multiple antibiotic residues in different samples simultaneously. In this study, we demonstrate a methodology that permits simultaneous extraction and detection of antibiotic residues in animal and environmental samples. A total of 30 different antibiotics from 13 classes could be qualitatively detected with our methodology. Further study to reduce analytes' matrix effect would allow for quantification of antibiotic residues. This study has been published in Antibiotics (Chan CL et al. 2022. Antibiotics).

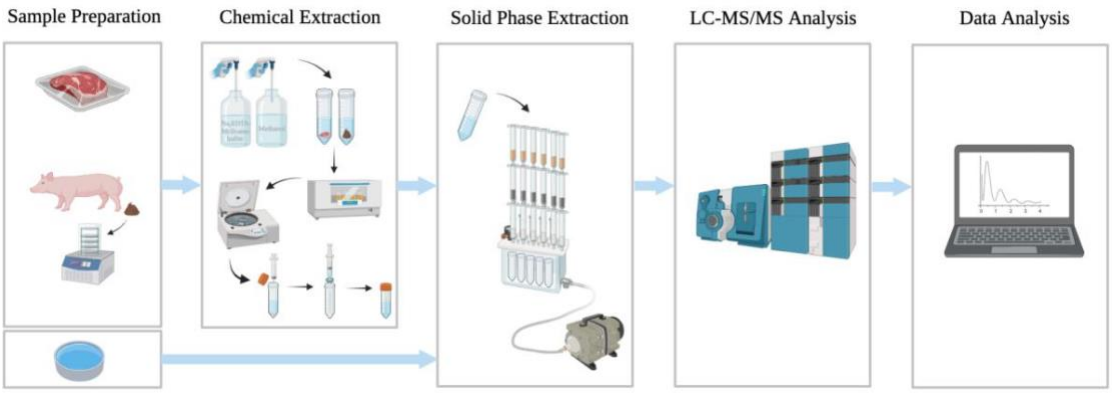


Figure 3. Flowchart showing the key steps in antibiotic residue testing.

Publications

1. **Tun HM**, Sanyal S. (2022). Proteomics-based approach for target disocovery in Zika virus infection: abridged secondary publication. ***Hong Kong Med J***. 6(6):29-32.
2. Liang S, Sin ZY, Yu J, Zhao S, Xi Z, Bruzzone R, **Tun HM**. (2022). Multi-cohort analysis of depression-associated gut bacteria sheds insight on bacterial biomarkers across populations. ***Cell Mol Life Sci***. 80(1):9.
3. Luo Y, Lv H, Zhao S, Sun Y, Liu C, Chen C, Liang W, Kwok KO, Teo QW, So RT, Lin Y, Deng Y, Li B, Dai Z, Zhu J, Zhang D, Fernando J, Wu NC, **Tun HM**. Bruzoone R, Mok CK, Mu X. (2022). Age-related seroprevalence trajectories of seasonal coronaviruses in children including neonates in Guangzhou, China. ***Int J Infect Dis***. S1201-9712(22)00636.
4. Su Q, Liu Q, Lau RI, Zhang J, Xu Z, Yeoh YK, Leung TWH, Tang W, Zhang L, Liang JQY, Yau YK, Zheng J, Liu C, Zhang M, Cheung CP, Ching JYL, **Tun HM**, Yu J, Chan FKL, Ng SC. (2022). Fecal microbiome-based machine learning for multi-class disease disgnosis. ***Nat Commun.*** 13(1): 6818.
5. Liu Q, Su Q, Zhang F, **Tun HM**, Mak JWY, Lui GC, Ng SSS, Ching JYL, Li A, Lu W, Liu C, Cheung CP, Hui DSC, Chan PKS, Chan FKL, Ng Sc. (2022). Multi-kingdom gut microbiota analyses define COVID-19 severity and post-acute COVID-19 syndrome. ***Nat Commun***. 13(1):6806
6. Chan OSK, Lam WWT, Fukuda K, **Tun HM**, Ohmagari N, Littmann J, Zhou XD, Xiao Y, Liu P, Wernli D. (2022). Antimicrobial resistance policy protagonists and processes-A qualitative study of policy adovacy and implementation. ***Antibiotics.*** 11(10):1434.
7. Chan OSK, Baranger-Ete M, Lam WWT, Wu P, Yeung M, Lee E, Bond H, Swan O, **Tun HM**. (2022). A retrospective study of antimicrobial resistant bacteria associated with feline and canine urinary tract infection in Hong Kong SAR, China- A case study on implication of first-line antibiotics use. ***Antibiotics***. 11(9):1140.
8. Xiao T, Zhang D, **Tun HM**, Shah NP. (2022). Cysteine protected cells from H_2O_2-induced damage and promoted long-chain fatty acids synthesis in vivo to improve γ-aminobutyric acid production in *Levilactobacillus brevis*. ***World J Microbiol Biotechnol***. 38(11)185.
9. Peng Y, Sin DZY, **Tun HM**. (2022). International travel, gut microbiome and ESBL-E. coli carriage. ***Lancet Microbe***. S2666-5247(22)00201.
10. Huang Y, Liu J, **Tun HM**, Stanton C, Chen T, El-Nezami H, Wei H, Wang M, Wu Q. (2022). Gut microbiota insights into human adaption to high-plateau diet. ***Imeta***. 1(1):e6.
11. Chan OS, Uchea C, **Tun HM**, Wu P, Fukuda K. (2022). What and where should the next antimicrobial resistance policies focus on? ***J Glob Antimicrob Resist*** 31:149-51.
12. Xiao T, Zhang D, **Tun HM**, Shah NP. (2022). Cysteine protected cells from H2O2-induced damage and promoted long-chain fatty acids synthesis in vivo to improve γ-aminobutyric acid production in *Levilactobacillus brevis*. ***World J Microbiol Biotechnol***. 38(11):185.

13. Obiakor CV, Parks J, Takaro TK, **Tun HM**, Morales-Lizcano N, Anzad MB, Mandhane PJ, Moraes TJ, Simons E, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL. (2022). Early life antimicrobial exposure: impact on Clostridioides difficile colonization in infants. ***Antibiotics.*** 11(7):981.

14. Chan CL, Wai HKF, Wu P, Lai SW, Chan OSK, **Tun HM**. (2022). A universal LC-MS/MS method for simultaneous detection of antibiotic residues in animal and environmental samples. ***Antibiotics***. 11(7):845.

15. Zheng X, Li S, Deng Y, Xu X, Ding J, Lau FTK, In Yau C, Poon LLM, **Tun HM**, Zhang T. (2022). Quantification of SARS-CoV-2 RNA in wastewater treatment plants mirrors the pandemic trend in Hong Kong. ***Sci Total Environ***. 844:157121.

16. Chan OSK, Wernli D, Liu P, **Tun HM**, Fukuda K, Lam W, Xiao YH, Zhou X, Grepin KA. (2022). Unpacking multi-level governance of antimicrobial resistance policies: the case of Guangdong, China. ***Health Policy Plan***. 37(9)1148-1157.

17. Xu X, Deng Y, Zheng X, Li S, Ding J, Yang Y, On HY, Yang R, Chui HK, Yau CI, **Tun HM**, Chin AWH, Poon LLM, Peiris M, Leung GM, Zhang T. (2022). Evaluation of RT-qPCR primer-probe sets to inform public health interventions based on COVID-19 sewage tests. ***Environ Sci Technol.*** 56(12)8875-8884.

18. Ng SC*, Peng Y*, Zhang L*, Mok CKP, Zhao S, Li A, Ching JYL, Liu Y, Yan S, Chan DLS, Zhu J, Chen C, Fung ACH, Wong KKY, Hui DS, Chan FKL[#], **Tun HM[#]**. (2022). Gut microbiota composition modulates SARS-CoV-2 vaccine immunogenicity and vaccine-related adverse events. ***Gut***. 71(6):1106-1116.

19. Zheng X, Deng Y, Xu X, Li S, Zhang Y, Ding J, On HY, Lai JCC, Yau CI, Chin AWH, Poon LLM, **Tun HM**, Zhang T. (2022). Comparison of virus concentration methods for SARS-CoV-2 sewage surveillance. ***Sci Total Environ***, 824:153687.

20. Zhang S, **Tun HM**, Zhang D, Chou H, Huang F, Kwok H, Wong DK, Mak L, Yuen M, Seto WK. (2022). Alleviation of Hepatic Steatosis: Dithizone-related gut microbiome restoration during Paneth Cell Dysfunction. ***Front Microbiol***. 13:813783.

21. Deng Y, Zheng X, Xu X, Chui HK, Lai WK, Li S, **Tun HM**, Poon LM, Ding J, Peiris M, Leung GM, Zhang T. Use of sewage surveillance for COVID-19: a large-scale evidence-based program in Hong Kong. ***Environ Health Perspect***. 130(5):57008.

Seminars and Invited Presentations

30/12/2022 Indispensable exposome-microbiome-immunity alliance in health and diseases. **Invited speaker** at departmental seminar of the Department of Chemical Pathology, The Chinese University of Hong Kong, Hong Kong.

3/12/2022 Antimicrobial comprehensive etiology study: from science to policies and practices. **Resource speaker** at the 58th Philippine Association of Medical Technologists Annual Convention, Manila, Philippine.

9/11/2022 AMR Interaction and transmission drivers between reservoirs in humans, animals , food and environment. **Session Chair** at the 7th World One Health Congress, Singapore.

7/10/2022 Antimicrobial comprehensive etiology study: from science to policies and practices. **Invited speaker** at the 1st RAPID Symposium, Insitut Pasteur Korea, Seoul, Korea.

4/09/2022 Gut microbiome and vaccine response. Invited speaker at the International Digestive Disease Forum (IDDF) 2022, Hong Kong.

21/06/2022 The mediation role of infant gut microbiome and immunity in the association between maternal smoking during pregnancy and childhood overweight. **Invited speaker and Session Chair** at Rising Stars in Exposure and Health Symposium, ISEE-AWPC & ISES-AC Joint Conference. Singapore.

Teaching

1. Hein Min Tun (2022) CMED6227 – Biological Basis of Disease (Master of Public Health), The University of Hong Kong, Hong Kong SAR (*Course Director and Lecturer*).
2. Hein Min Tun (2022) EBDM- Evidence-Based Decision Making for Patient Care and Public Health MBBS I and II, The University of Hong Kong, Hong Kong SAR (*Tutor*)
3. Hein Min Tun (2022) Fleming Fund Fellowship Program, Laboratory Fellows from Sri Lanka (*Mentor*)
4. Hein Min Tun (2022) BBMS2011/BPHM1121- Research Methods in Medicine and Health Sciences, The University of Hong Kong, Hong Kong SAR (*Course Coordinator*)

Collaborations

1. **Anita Kozyrskyj** (Department of Paediatrics, University of Alberta, Edmonton, Canada): Gut microbiota maturation during infancy.
2. **Andrea Haqq** (Department of Pediatrics, University of Alberta, Edmonton, Canada): Gut microbiota profile in children with Prader-Willi Syndrome.
3. **John Penders** (Department of Medical Microbiology, Maastricht University, Maastricht, The Netherlands): Antimicrobial dissemination in international travellers.
4. **Tanja Sobko** (School of Biological Sciences, The University of Hong Kong, Hong Kong SAR): Impact of nature connectedness on gut microbiome and mental health of children.
5. **Jincun Zhao** (Guangzhou Medical University, Mailand China): Multi-Platform Omics 1 Analysis Reveals Molecular Signature for COVID-19 Pathogenesis, Prognosis and Drug Target Discovery **&** Characterization of respiratory microbial dysbiosis in hospitalized COVID-19 patients.
6. **Wai-Kay Seto** (Department of Medicine, The University of Hong Kong, Hong Kong SAR): Functional role and therapeutic potential of Lactococcus lactis in non-alcoholic fatty liver disease **&** Investigating aerosol generation and transmissibility implications in upper and lower gastrointestinal endoscopy: a multicentre study.
7. **Tong Zhang** (Department of Civil Engineering, The University of Hong Kong, Hong Kong SAR): Grid monitoring of SARS-CoV-2 in sewage for an early-warning sign of community outbreak.
8. **Xudong Zhou** (School of Public Health, Zhejiang University, Mailand China): Antimicrobial resistance comprehensive etiology Study (ACES)-Mailand China.

9. **Rungtip Chuanchuen** (Department of Veterinary Public Health, Chulalongkorn University, Thailand): Antimicrobial resistance comprehensive etiology Study (ACES)-Thailand.
10. **Alongkorn Amonsin** (Department of Veterinary Public Health, Chulalongkorn University, Thailand): Coronavirus seroprevalence among bat exposure villagers in Thailand.
11. **Sophelia Chan** (Department of Paediatrics and Adolescent Medicine, Li Ka Shing Faculty of Medicine, University of Hong Kong): Microbiome in paediatric epilepsy.
12. **Siew C Ng** (Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong): Mommy Cohort and MiVac Cohort.

Funding

1. Translating microbiome, multi-omics and dietary innovations to enhance inflammatory bowel disease diagnosis and outcome (**Co-Principal Investigator;** RGC/Research Impact Fund – Ends: 06/2026)
2. Investigating the gut microbiota associated depression and its modifiable effects (**Principal Investigator;** RGC/Eearly Career Scheme – Ends: 12/2025)
3. Evolution and determinants of population mental health during the Myanmar conflict: a nationwide longitudinal study from 2021 to 2025 (**Co-Investigator;** RGC/GRF – Ends: 12/2025)
4. Characterization of heteroresistance in commensal Escherichia coli isolates in relation to therapeutic use of antibiotics (**Co-Investigator;** HMRF – Ends: 10/2025)
5. Fiber supplementation and metformin combination therapy in adolescents with severe obesity and insulin resistance: interactions with the gut microbiome (**Co-Principal Investigator**; Weston Family Microbiome Initiative Grant – Ends: 12/2024).
6. Strengthening sewage surveillance for SARS-CoV-2. (**Co-Investigator**; HMRF Commissioned Research on the Novel Coronavirus Disease (COVID-19) – Ends: 08/2024).
7. Assess antibiotic resistome flows from pollution hotspots to environments and explore the control startegies (**Co-Principal Investigator;** Theme-based Research Scheme – Ends: 12/2025).
8. Understanding aspects of common, complex chronic diseases in urban households: FAMILY Cohort (**Co-Investigator**; HMRF Commissioned Research – Ends: 09/2024)

Personnel

Name	Position
Hein Min Tun	Assistant Professor
Xi Zhang	Post-doctoral Fellow
Suisha Liang	PhD Student
Hogan Wai	PhD Student
Darren Chan	PhD Student
Ye Peng	PhD Student
Xiawan Zheng	PhD Student – Department of Civil Engineering, HKU
Shuxian Li	PhD Student – Department of Civil Engineering, HKU
Yulin Zhang	PhD Student – Department of Civil Engineering, HKU
Gary Chan	Mphil Student
Felice Pak	Research Assistant I
Shilin Zhao	Research Assistant I
Jie Zhu	Research Assistant I
Vivian Chan	Research Assistant II
Chloe Liu	Research Assistant II
Ingrid Chan	Research Assistant II
Xin Liu	Research Assistant II
Rista Shrestha	Research Assistant II
Daniel Sin	Research Assistant II
Jun Tao	Research Assistant II
Hilda On	Research Assistant II (P/T)
Thomas Chu	Research Assistant II (P/T)
Sandra Chiu	Research Assistant II (P/T)
Anxin Pan	Research Assistant – Department of Civil Engineering, HKU
Xianghui Shi	Research Assistant – Department of Civil Engineering, HKU
Mengying Wang	Research Assistant – Department of Civil Engineering, HKU

3.5 Sophie VALKENBURG Lab

Summary

I am Principal Investigator of viral immunology based at the University of Melbourne, at the Doherty Institute of Infection and Immunity since the start of 2022, and remain a honorary Assistant Professor at HKU-PRP, where I was based 2015-2021 as a Laboratory Head. My research program is devoted to investigating correlates of protection, specifically T and B cell responses, antibody quality and function for influenza viruses and SARS-CoV-2 from patients, randomised control vaccine trials and animal models (Figure 1). The aim of my research program is to define broadly reactive immune correlates from recovered patients, and how current vaccines stimulate or fail to stimulate these protective immune responses. Results are then further validated in animal models for protection from infection and incorporated to next generation universal vaccines for robust immunity.

In 2022, my team had 13 publications, which included influenza and SARS-CoV-2 studies. Specifcally for influenza, we characterised immunopathology in a T cell activating vaccine for influenza (Bull et al, ICB 2022) and sequence variation (Chu et al., Virus Research 2022). Whilst COVID-19 research focussed on comparing inactivated virion versus Spike mRNA vaccination by doses (Mu et al., STT 2022), teenagers (Duque et al., Nat Comms 2022), cross-reactivity to Omicron, and breadth to other Sarbecoviruses (Jia et al., Nat Comm 2022), and children (Hachim et al., Nat Comms 2022). I was also invited for presentations in the USA (Keystone and CEIRR), Ireland (Options for Influenza), Hong Kong (HKU) and Australia (Bio21) based on this work.

Other academic contributions include teaching by PhD examination in Norway and serve as a committee member for 3 PhD candidates at the Univeristy of Melbourne. I also gave a guest lecture to high school students as part of the Day of Immunology program at Federation Univeristy, Australia.

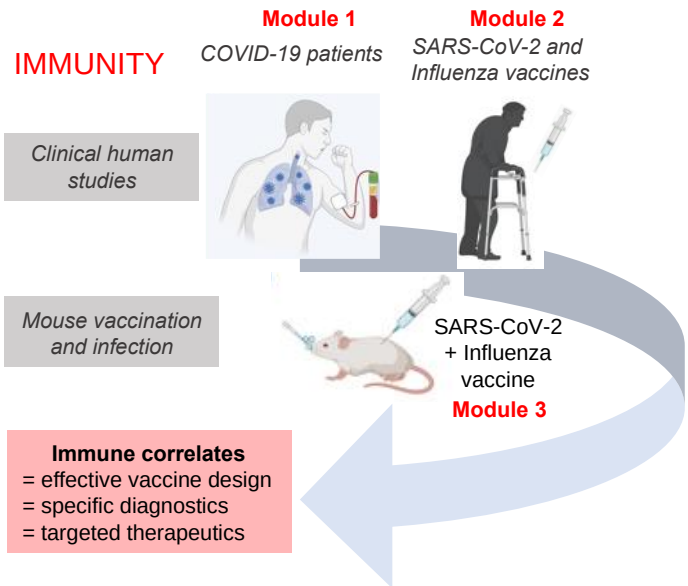


Figure 1: Overview of Valkenburg research program.

Research highlights

Vaccine mediated early cytokine imbalance for influenza

(*From Bull et al., ICB 2022*)

Influenza A viruses (IAV) exist as distinct serological subtypes, with limited antibody cross reactivity compared to T cell responses, leading to universal vaccines that elicit robust T cell responses entering clinical trials to combat pandemic and zoonotic outbreaks. Previously we have extensively characterized the viral vectored universal vaccine, Wyeth/IL-15/5flu, a group 1 HA, H5N1 based vaccine using a vaccinia backbone with IL-15. The vaccine elicits robust T cell responses to provide heterosubtypic protection from lethal infection, however we have also observed short term morbidity of vaccinated mice with a disparity between the effects of sublethal infection with group 1 and 2 IAV strains (Figure 2a-d), which did not cause increased infection by antibodies (Figure 2e). At day 3 of H3N2 (group 2 IAV) infection, there was a heavily skewed Th1 response in vaccinated infected mice with overproduction of cytokines (Figure 2f) and reduced chemokines, whilst H1N1 (group 1 IAV) infection had increased innate cellular responses.

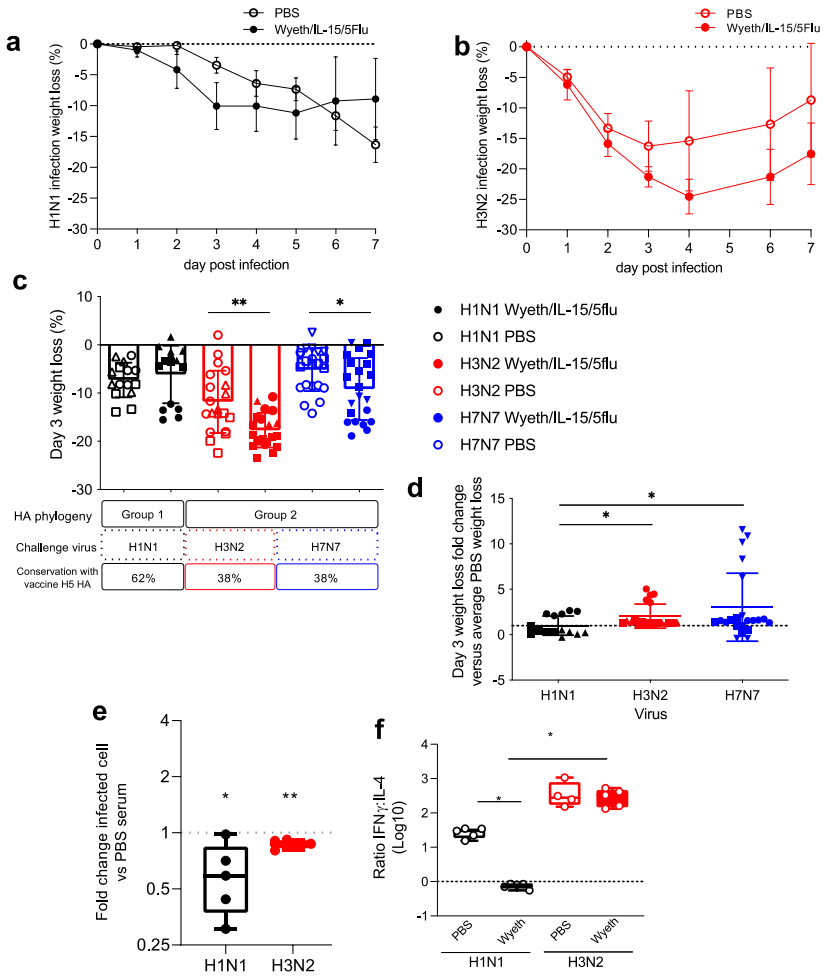


Figure 2: Early vaccine mediated weight loss driven by exuberant cytokine production. H1N1 (a) and H3N2 (b) weight loss in vaccine and placebo control, showed a group specific effect (c), for increased weight loss in group 2 viruses (d). The was not due to increased antibody mediated infection (e), but imbalanced cytokine production (f) in vaccinated mice. From Bull et al., ICB 2022.

These findings suggest that increased and early immune activation by T cell activating vaccines may induce mild immunopathology when there is a mismatch between non-neutralizing antibody and cross-reactive memory T cell responses leading to exuberant

cytokine production. Therefore, to avoid overstimulating proinflammatory immune responses upon infection, universal influenza vaccines that elicit strong T cell immunity will need a robust cross-reactive antibody response.

mRNA and prior immunity advantage for increased antibody breadth

(*From Jia et al., Nat Comms 2022*)

Vaccines that are broadly cross-protective against current and future SARS-CoV-2 variants of concern (VoC) or across the sarbecoviruses subgenus remain a priority for public health. Virus neutralization is the best available correlate of protection. To define the magnitude and breadth of cross-neutralization in individuals with different exposure to SARS-CoV-2 infection and vaccination, we here use a multiplex surrogate neutralization assay based on virus spike receptor binding domains of multiple SARS-CoV-2 VoC, as well as related bat and pangolin viruses.

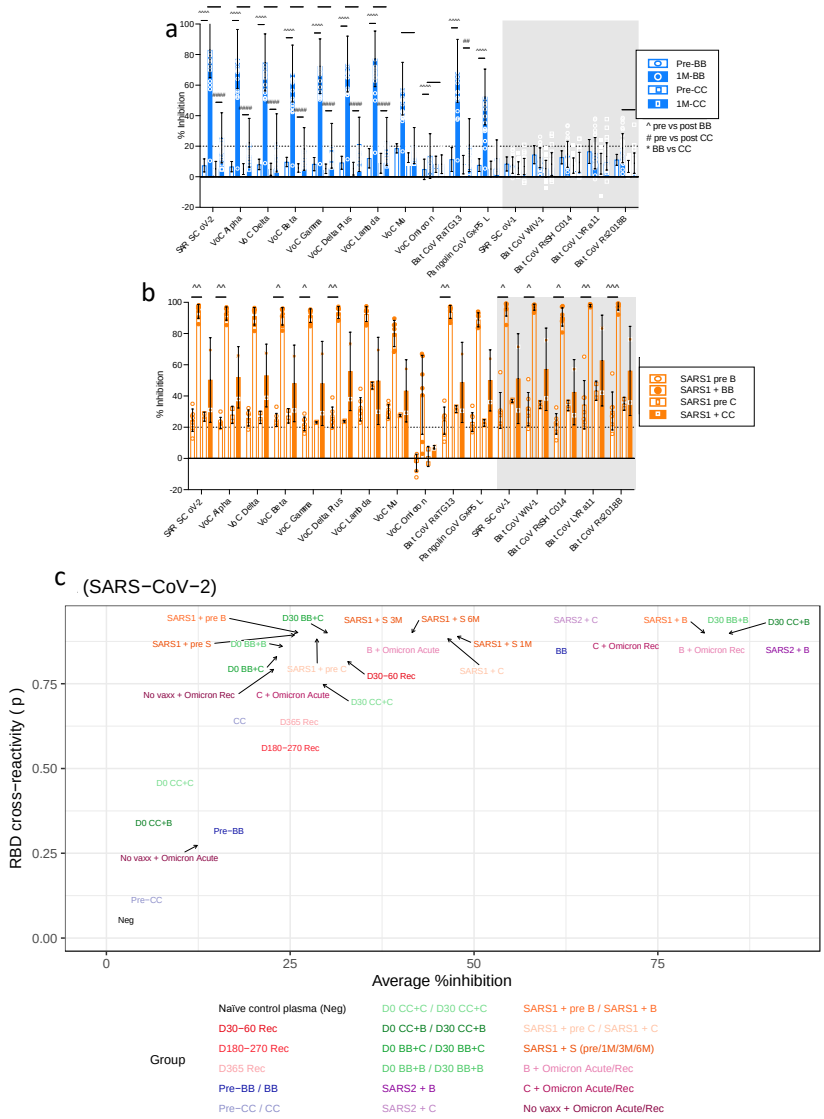


Figure 3: Antibody breadth by sVNT assay for vaccination (a), and prior SARS1 infection (b) shows increased magnitude and breadth of recognition (c). From Jia et al., Nat Comms 2022.

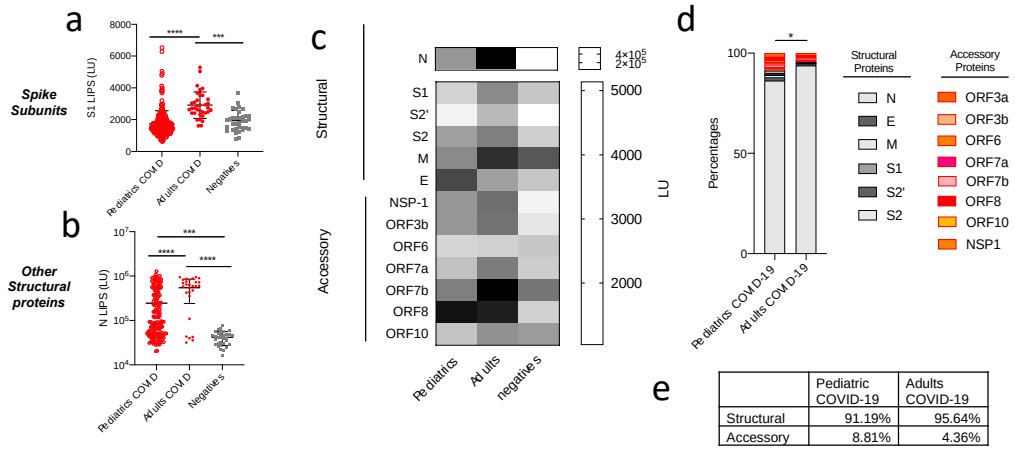
We include sera from cohorts of individuals vaccinated with two or three doses of RNA (BNT162b2) or inactivated SARS-CoV-2 (Coronavac or Sinopharm, Figure 3a)) vaccines

with or without a history of previous SARS-CoV-2 or SARS-CoV-1 infection (Figure 3b). SARS-CoV-2 or SARS-CoV-1 infection followed by BNT162b2 vaccine, Omicron BA.2 breakthrough infection following BNT162b2 vaccine or a third dose of BNT162b2 following two doses of BNT162b2 or CoronaVac elicit the highest and broadest neutralization across VoCs. For both breadth and magnitude of neutralization across all sarbecoviruses (Figure 3c), those infected with SARS-CoV-1 immunized with BNT162b2 outperform all other combinations of infection and/or vaccination. These data may inform vaccine design strategies for generating broadly neutralizing antibodies to SARS-CoV-2 variants or across the sarbecovirus subgenus.

Children have altered antibody specificity compared to adults for COVI19

From Hachim et al., Nat Comms 2022

The antibody response magnitude and kinetics may impact clinical severity, serological diagnosis and long-term protection of COVID-19, and children experience lower morbidity. We tested samples from 122 children in Hong Kong with symptomatic (n=78) and asymptomatic (n=44) SARS-CoV-2 infections up to 200 days post infection, relative to 71 infected adults (symptomatic n=61, and asymptomatic n=10), and negative controls (n=48). We assessed serum IgG antibodies to a 14-wide antigen panel of structural and accessory proteins by Luciferase Immuno-Precipitation System (LIPS) assay and circulating cytokines. Infected children have lower levels of Spike, Membrane, ORF3a, 7a, 7b antibodies, comparable ORF8 and elevated E-specific antibodies than adults. Combination of two unique antibody targets, ORF3d and ORF8, can accurately discriminate SARS-CoV-2 infection in children. Principal component analysis reveals distinct pediatric serological signatures, and the highest contribution to variance from adults are responses to non-structural proteins ORF3d, NSP1, ORF3a and ORF8. From a diverse panel of cytokines that can modulate immune priming and relative inflammation, the chemokines IL-8, MCP-1 and IL-6 correlate with the magnitude of pediatric antibody specificity and severity. Antibodies to SARS-CoV-2 internal proteins may become an important sero surveillance tool of infection with the roll-out of vaccines in the pediatric population.



	Pediatric COVID-19	Adults COVID-19
Structural	91.19%	95.64%
Accessory	8.81%	4.36%

Figure 4: Infected pediatric children have lower antibody responses to structural proteins than adults (a, b), across the SARS-CoV-2 proteome (c), with a greater proportion of antibodies targeting accessory proteins (d, e) compared to adults. From Hachim et al., Nat Comms 2022.

Publications

1. Lau JJ, Cheng SMS, Leung K, Lee CK, Hachim A, Tsang LCH, Yam KWH, Chaothai S, Kwan KKH, Chai ZYH, Lo THK, Mori M, Wu C, **Valkenburg SA**, Amarasinghe GK, Lau EHY, Hui DS, Leung GM, Peiris M, Wu JT. Population-based sero-epidemiological estimates of real-world vaccine effectiveness against Omicron infection in an infection-naive population, Hong Kong, January to July 2022. Nature Medicine, Jan 18. doi: 10.1038/s41591-023-02219-5, PMID: 36652990

2. Mu X[#], Cohen CA[#], Leung D[#], Rosa Duque JS[#], Cheng SMS[#], Chung Y, Wong HHW, Lee AMT, Li, WY Tam IYS, Lam JHY, Lee DHL, Chan SM, Tsang LCH, Chan KCK, Li JKC, Luk LLH, Chaothai S, Kwan KKH, Chu NC, Mori M, Jeevan T, Kandeil A, Tu WW*, **Valkenburg SA***, Peiris M*, Lau YL (# co-first, *co-last). Antibody and T cell responses against wild-type and Omicron SARS-CoV-2 after the third dose of BNT162b2 in healthy adolescents. Signal Transduction and Targeted Therapy. 7, 397 (2022). https://doi.org/10.1038/s41392-022-01282-7. PMID: 36517469

3. Bull MB, Ma FNL, Perera LP, Poon LLM, **Valkenburg SA.** Early vaccine mediated HA group directed cytokine imbalance induces mild immunopathology during influenza infection**.** Immunology Cell Biology, 2022 Nov 19. doi: 10.1111/imcb.12608, PMID: 36401824

4. Chu J, Gu H, Sun W, Fan R, Nicholls J, **Valkenburg SA**, Poon LLM. Heterosubtypic immune pressure accelerates emergence of influenza A virus escape phenotypes in mice. Virus Research. 2022 Oct 24;323:198991. PMID: 36302472

5. Jia JZ[#], Tan CW[#], Cheng SMS, Gu H, Yeoh AYY, Mok CKP, Wang Y, Zhao J, Leung NHL, Cowling BJ, Poon LLM, Hui DH, Wang L*, Peiris M*, **Valkenburg SA***. (# co-first, *co-last). Priming conditions shape breadth of neutralizing antibody responses to sarbecoviruses. Nature Communications. 2022 Oct 21;13(1):6285. doi: 10.1038/s41467-022-34038-6.PMID: 36271047

Featured blog: https://microbiologycommunity.nature.com/posts/spread-it-out-mrna-advantage-for-antibody-coverage-against-sars-type-viruses

6. Duque JSR[#], Wang X[#], Leung D[#], Cheng SMS[#], Cohen CA[#], Xiaofeng Mu, Hachim A, Yanmei Zhang, Chan SM, Chaothai S, Kwan KKH, Chan KCK, Li JKC, Luk LLH, Tsang LCH, Wong WHS, Cheang CH, Hung TK, Lam JHY, Chua GT, Tso WWY, Ip P, Mori M, Kavian N, Leung WH, **Valkenburg SA***, Peiris JSM*, Tu WW*, Lau YL* (# co-first, *co-last). Immunogenicity and reactogenicity of SARS-CoV-2 mRNA and inactivated vaccines in healthy adolescents. Nature Communications. 2022 Jun 28;13(1):3700. doi: 10.1038/s41467-022-31485-z. PMID: 35764637

7. Koutsakos M, **Valkenburg SA.** Special Issue-Immunity to Influenza Viruses. Viruses. 2022

8. **Valkenburg SA** and Poon LLM, Exploring the landscape of the immune responses to influenza infection and vaccination. (*invited commentary to LLMP*), Nature Medicine. 2022 Feb;28(2):239-240, doi: 10.1038/s41591-021-01656-4, PMID: 35177856

9. Hachim A, Gu H, Kavian O, Kwan MYW, Chan WH, Yau YS, Chiu SS, Tsang OTY, Hui DSC, Ma FNL, Cheng SMS, Poon LLM, Peiris JSM, **Valkenburg SA*** and Kavian N*. (*co-last) The SARS-CoV-2 antibody landscape is lower in magnitude for structural proteins,

diversified for accessory proteins and stable long-term in children. Nature Communications 2022. 13**,** 2951. PMID: 35618731 doi.org/10.1038/s41467-022-30699-5, medRixV PMID: 33655259)

Featured blog: https://healthcommunity.nature.com/posts/sars-cov-2-accessory-proteins-reveal-distinct-serological-signatures-in-children

10. **Valkenburg SA*** and Poon LLM. Universal influenza vaccines are futile when benchmarked for seasonal influenza vaccines. (*corresponding, *invited commentary to SAV*, Lancet Infectious Diseases. 2022. doi: 10.1016/S1473-3099(21)00749-0, PMID: 3530531.
11. Bull MB, Gu H, Ma FNL, Perera LP, Poon LLM, **Valkenburg SA**. Next-generation T cell-activating vaccination increases influenza virus mutation prevalence. Science Advances. 2022 Apr 8;8(14):eabl5209. doi: 10.1126/sciadv.abl5209. Epub 2022 Apr 6. PMID: 35385318.
12. Wan EYF, Chui CSL, Wang Y, Ng VWS, Yan VKC, Lai FTT, Li X, Wong CKH, Chan EWY, Wong CSM, Leung KSM, Ni MY, **Valkenburg SA**, Peiris JSM, Wu JTK, Cowling BJ, Ashcroft DM, Hung IFN, Leung GM, Wong ICK. Herpes zoster related hospitalization after inactivated (CoronaVac) and mRNA (BNT162b2) SARS-CoV-2 vaccination: A self-controlled case series and nested case-control study. Lancet Reg Health West Pac. 2022 Apr;21:100393. doi: 10.1016/j.lanwpc.2022.100393. PMID: 35128500
13. Dhanasekaran V, Sullivan S, Edwards KM, Xie R, Khvorov A, **Valkenburg SA**, Cowling BJ, Barr IG. Human seasonal influenza under COVID-19 and the potential consequences of influenza lineage elimination. Nature Communications. 2022 Mar 31;13(1):1721. doi: 10.1038/s41467-022-29402-5. PMID: 35361789

Seminars and Invited Presentations

1. The University of Hong Kong, Departmental seminar, Hong Kong, October 2022, *Invited Oral*
2. Bio21, The University of Melbourne, Departmental seminar, September 2022, *Invited Oral*
3. Options for the Control of Influenza XI, Belfast, Ireland, September 2022, *Selected Oral, Chair*
4. CEIRR 1st Annual meeting, Memphis, USA, August 2022, *Selected Oral, Chair*
5. Keystone, Viral Immunity, Keystone, USA, June 2022, *Invited Plenary Oral*
6. Victorian Infection and Immunity, Lorne, February 2022, *Selected Oral*

Knowledge Exchange activities

1. STEM mentoring program, Fatima Ganatra, University of Melbourne
2. Day of Immunology, Berwick High School at Federation University, *invited lecturer*

Teaching

1. PhD Thesis examiner, The University of Bergen, Norway
2. Third year BIOM003 project student, University of Melbourne, Australia

Collaborations

1. **Benjamin Cowling** (School of Public Health, The University of Hong Kong, Hong Kong SAR): Longitudinal impact of repeat influenza and combined COVID-19 vaccines.
2. **Leo LM Poon** (School of Public Health, The University of Hong Kong, Hong Kong SAR): Broadly reactive influenza and COVID-19 vaccines in mouse models.
3. **JS Malik Peiris** (School of Public Health, The University of Hong Kong, Hong Kong SAR): SARS-CoV-2 patient cohorts for immune characterisations.
4. **Amy Chung** (University of Melbourne, Australia): Antibody effector functions after influenza exposure by multiplex assay.
5. **Katherine Kedzierska** (University of Melbourne, Australia): T cell responses in vulnerable groups.
6. **Linfa Wang** (Duke NUS, Singapore): Sarbecovirus antibodies.

Funding

1. **VC2 COVID-19 Research Seed Funding grant**, 2022-2023
"Influence of antibody host genetics and imprinting upon COVID-19 immunity in the elderly". *Co-investigator (PI K Selva)*

2. **DMI Collaborative grant**, 2022-2023
"Dietary copper deficiency and immunological control of Streptococcus pneumoniae infection". *Co-investigator (PI S Neville)*

3. **NHMRC, Emerging Leader 2 fellowship**, 2022-2026
"Harnessing immunity for optimal SARS-CoV-2 and influenza vaccines". *Principal investigator*

4. **RGC, Theme based Research Scheme,** 2022-2026
"Virological, immunological and epidemiological characterization of COVID-19". *Co-investigator (PI LLM Poon)*

5. **RGC, Collaborative Research fund (CRF) grant,** 2021-2023
"Replication-defective SARS-CoV-2 mutant vaccines with abnormal codon usages". *Co-investigator (PI LLM Poon)*

6. **RGC, Theme based Research Scheme,** 2020-2024
"Control of influenza: individual and population immunity". *Co-investigator (PI BJ Cowling)*

7. **NIH, AR01, AI153700-01,** 2020-2024
"The dynamics of the immune response to repeat seasonal influenza vaccination and consequences for protection". *Co-investigator (PI BJ Cowling)*

Personnel

Name	Position
Prathanporn Kaewpreedee	Senior Technical Officer
Alan Cheung	Research Assistant I
Janice Zhirong Jia	Research Assistant I
Kelly Lee	Research Assistant II
Carolyn A Cohen	PhD student

3.6 Teaching and Education

HKU-Pasteur Course Series

HKU-Pasteur has pioneered a unique course series in Hong Kong and in the region that provides state of the art lectures and practical workshops in a "Master class" setting to outstanding postgraduate students and postdoctoral fellows coming from countries with markedly different resources. The ever-growing network of alumni around the world demonstrates that this educational program helps intensify human and scientific links between HKU-Pasteur, the School of Public Health at HKU, the Institut Pasteur International Network and the international scientific community, while continuing to attract to Hong Kong top scientists and highly motivated students. All HKU-Pasteur Courses have been approved by the Research Postgraduate Committee of HKU for inclusion in the coursework curriculum of MPhil/PhD students and have received the Pasteur International Course (OIC) label of the Institut Pasteur. The educational program of HKU-Pasteur is supported with external grants from the Institut Pasteur International Network, the French Consulate in Hong Kong and Macau, the Regional Health Cooperation Office of the French Ministry of Foreign Affairs the Pasteur Foundation Asia and other private donations. **All courses were cancelled for the past three years owing to the coronavirus pandemic. They will resume in 2023 with the Croucher Summer Course "Emerging Viral Infections – The One-Health Approach.**

Additional teaching and training

Besides their involvement in the HKU-Pasteur course series, the **Co-Directors and Group Leaders** at HKU-Pasteur are also teaching courses in the undergraduate and postgraduate curriculum and the Problem-Based Learning modules for MBBS students (see complete list at the end of this section). HKU-Pasteur regularly hosts undergraduate/ postgraduate students from overseas and local institutions for internships. In 2022 we welcome two international trainee and two local trainee for an internship period. In addition, we resumed our **training programs for high school students from the French International School (FIS) in Hong Kong.** We hosted four students from FIS.

Complete list of taught and international courses

1. Roberto Bruzzone (2022) Molecular Biology of the Cell Course, Institut Pasteur, Paris, France (**Course Director**).
2. Roberto Bruzzone (2022) Endocrine and Reproductive Systems, Problem Based Learning (MBBS Year 2), The University of Hong Kong, Hong Kong SAR (**Tutor**).
3. Vijay Dhanasekaran (2022) CMED6000 – Capstone (Master of Public Health), The University of Hong Kong, Hong Kong SAR (**Supervisor and Examiner**).
4. Vijay Dhanasekaran (2022) Outbreak – Problem Based Learning (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Tutor**).
5. Vijay Dhanasekaran (2022) Health Research Projects (HRP) (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Supervisor and Examiner**).
6. Vijay Dhanasekaran (2022) Head Neck and Nervous system Block – Problem Based Learning (MBBS Year 2), The University of Hong Kong, Hong Kong SAR (**Tutor**).

7. Vijay Dhanasekaran (2022) Introduction to the Art and Science of Medicine, Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (**Tutor**).
8. Leo Poon (2022) CMED6105 – Infectious Diseases in Public Health (Master of Public Health), The University of Hong Kong, Hong Kong SAR (**Course director and lecturer**).
9. Leo Poon (2022) Life Science- (BNur Year 2 and BCMed Year 3), The University of Hong Kong, Hong Kong SAR (**Lecturer**).
10. Leo Poon (2022) Outbreak – Problem Based Learning (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Tutor**).
11. Leo Poon (2022) Musculoskeletal System Block– Problem Based Learning (MBBS Year 2), The University of Hong Kong, Hong Kong SAR (**Tutor**).
12. Leo Poon (2022) Introduction to the Art and Science of Medicine (MBBS Year 1), Problem Based Learning, The University of Hong Kong, Hong Kong SAR (**Lecturer**).
13. Hein Min Tun (2022) CMED6227 – Biological Basis of Disease (Master of Public Health), The University of Hong Kong, Hong Kong SAR (**Course Director and Lecturer**).
14. Hein Min Tun (2022) EBDM- Evidence-Based Decision Making for Patient Care and Public Health MBBS I and II, The University of Hong Kong, Hong Kong SAR (**Tutor**).
15. Hein Min Tun (2022) Fleming Fund Fellowship Program, Laboratory Fellows from Sri Lanka (**Mentor**).
16. Hein Min Tun (2022) BBMS2011/BPHM1121- Research Methods in Medicine and Health Sciences, The University of Hong Kong, Hong Kong SAR (**Course Coordinator**).
17. Sook-San Wong (2022) Outbreak- Problem Based Learning (MBBS Year 4), The University of Hong Kong, Hong Kong SAR (**Tutor**).
18. Sook-San Wong (2022) Cardiopulmonary Renal System– Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (**Tutor**).

Complete list of interns

Name	
Juliette Clot	French International School, Hong Kong SAR
Lorenzo Godingen	French International School, Hong Kong SAR
Sarah Granveaud	French International School, Hong Kong SAR
Bertille Voets	French International School, Hong Kong SAR
Edward Ye	School of Public Health, HKU, Hong Kong SAR
Sukriti Gyawali	School of Biomedical Sciences, HKU, Hong Kong SAR
Asra Sainju	School of Biomedical Sciences, HKU, Hong Kong SAR
Tooba Latif	University of Veterinary and Animal Sciences, Pakistan
Yee Tsui	University of Toronto, Canada

3.7 Other Major Activities

International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)

Roberto Bruzzone was appointed as the Interim Chair in December of 2018 and became the Chair at the beginning of 2020, for a three-year term. ISARIC launched in 2011, is a consortium of over 40 clinical research networks operational in 131 countries (http://isaric.tghn.org/). ISARIC provides a collaborative platform through which global, patient-oriented clinical studies can be developed, executed, and shared. In response to the COVID-19 pandemic, ISARIC networks and scientists have been involved in many important clinical studies, including two randomized clinical trials with COVID-19 patients in China.

Center for Immunology & Infection (C2I)

We have been awarded a major 5-year grant, totaling over 40 million euros, from the Innovation and Technology Commission to establish the Center for Immunology & Infection (C2I) within the framework of InnoHK, a recent collaborative scientific research scheme set up set up by the Government of the Hong Kong Special Administrative Region. C2i represents a major development of an already successful and long-term collaboration between HKU and the Institut Pasteur. **Leo Poon is the Managing Director of C2I; Malik Peiris and Roberto Bruzzone are the Co-Directors**. C2i aims to validate a novel technology platform for biomarker discovery and development of new vaccine and therapeutic strategies. Overall, this program addresses major unmet global and local public health needs with excellent potential for commercial exploitation, leading to the enhancement of Hong Kong's knowledge-based economy and providing state-of-art training for the local population.

Other key actions

We retain leadership roles in international forums. **Malik Peiris** participates in WHO working groups in relation to both avian and swine origin influenza virus and is the Co-Director of the WHO H5 Reference Laboratory at HKU. **Roberto Bruzzone** is Co-Editor-in-Chief of *Cellular and Molecular Life Sciences*. **Leo Poon** is a committee member of the Coronavirus study group, ICTV, IUMS, and an Advisor to the Hong Kong SAR for Food and Environmental Hygiene. He is also an Ad Hoc Expert of the WHO Influenza Molecular Diagnosis Working Group, and of the WHO Expert group for COVID-19 for clinical diagnosis and virus evolution. He is the Co-Editor-in-Chief of the *Virology Journal*.

3.8 Knowledge Exchange

Zoonotic Diseases and Climate Change Workshop

To celebrate the bicentenary of Louis Pasteur's birth, the HKU-Pasteur Research Pole organized a workshop together with the Centre for Immunology & Infection (C2i), with the support of the Consulate General of France, focusing on the risks that climate change presents to zoonotic diseases.

Held at the Faculty of Medicine of the University of Hong Kong on November 24th the seminar kicked off with a keynote lecture by Nolwenn Jouvenet from Institut Pasteur, followed by a roundtable with local experts from HKU, HKU-Pasteur, C2i and CUHK. The panelists discussed the ongoing impact of long-term shifts in temperatures and weather patterns on ecology of vectors and animal reservoirs, as well as human behavior and lifestyles such as migration patterns and microbiome alteration and the global efforts to tackle those issues.

15:00	–	15:10	Welcome and Bicentenary introduction - *10 min*	**Prof. Roberto Bruzzone** *HKU-PRP / C2i* (*Online*)
15:10	–	15:15	Welcome speech - 5 *min*	**Christile Drulhe** *Consul General of France* (*In Person*)
15:15	–	15:50	Keynote Lecture with Q&A *(25+10) 35 min*	**Nolwenn Jouvenet**, *Institut Pasteur Keynnote speaker* (*Online*)
15:50	–	16:50	Panel Discussion with Q&A *(45+15) 60 min*	Moderator **Dr. Sook-San Wong,** *HKU-PRP* (*In Person*) Panelist 1 **Dr. Hein Min Tun,** *The Chinese University of Hong Kong* (*In Person*) Panelist 2 **Dr. Vijay Dhanasekaran,** *HKU-PRP,* (*In Person*) Panelist 3 **Dr. Tommy Lam,** *C2i,* (*In Person*) Panelist 4 **Dr. Linwei Tian**, HKU SPH (*In Person*)
16:50	–	17:00	Closing remarks - *10 min*	**Prof. Leo Poon** *HKU-PRP / C2i* (*In Person*)

Louis Pasteur Bicentenary Exhibition

As part of the Louis Pasteur bicentenary celebrations initiated by the Institut Pasteur (Paris, France) and the French Science Festival 2022, the HKU-Pasteur Research Pole

organized the exhibition *From Louis to Pasteur, 1822-1895* in collaboration with the Centre for Immunology & Infection (C2i) and with the support of the Consulate General of France in Hong Kong and Macau. The exhibition commemorated the bicentenary of Louis Pasteur's birth, tracing his major scientific works, as well as some significant episodes of his private life and his scientific legacy. The exhibition was held at the Faculty of Medicine of the University of Hong Kong from 10 to 25 November 2022, then at the French International School from 28 November to 16 December 2022 (in two different campuses) and Science Park from 9 to 20 January 2023.

HKU-Pasteur Research Pole Fellowship Program 2022

The objective of the HKU-Pasteur Research Pole Fellowship Program is to provide a unique opportunity for postgraduate students and postdoctoral fellows in Hong Kong and Macau to pursue their research projects in the outstanding scientific environment of the Institut Pasteur in Paris, France.

Following the success of the first round, a new call for application was launched in October 2021. Once more, despite the pandemic situation, the HKU-Pasteur Research Pole received many applications from Hong Kong and Macau candidates.

The Selection Committee of the HKU-Pasteur Research Pole fellowship selected 4 outstanding laureates for the 2022 round:

- **Ms SUN Wanying,** PhD student at the HKU Faculty of Medicine School of Biomedical Sciences, for an internship in the Infectious Disease Epidemiology and Analytics G5 Unit under the supervision of Dr Michael White.
- **Ms HE Weisi,** PhD student at the HKU Faculty of Medicine School of Biomedical Sciences, for an internship in the Biorganic Chemistry of Nucleic Acids Laboratory under the supervision of Dr Marcel Hollenstein. ***Ms HE unfortunately had to withdraw from the program for personal reasons.***
- **Mr SAPOZHNIKOV Georgy,** PhD student at the HKU Faculty of Medicine School of Biomedical Sciences, for an internship in the Cell Death and Epithelial Homeostasis Group (CEDH)under the supervision of Dr Romain Levayer.
- **Mr LAGNITON Philip**, PhD student at the University of Macau Faculty of Health Sciences, for an internship in the Statistical Genetics Laboratory under the supervision of Dr Hugues Aschard. ***Mr LAGNITON's internship was cancelled due to the Covid-19 related travel restrictions from Macau.***

A new call for application was launched on November 2022 with the aim to expand the program with additional fellowships.

The HKU-Pasteur Fellowship rewarded by the Grand Prix France Hong Kong

In 2022, the HKU-Pasteur Fellowship received the Knowledge Transfer award by the Grand Prix France Hong Kong during a ceremony hosted by the Consul General of France in Hong Kong and Macau. The *Grand Prix France Hong Kong* was created by LePetitJournal.com and supported by the Consulate General of France to reward collaborations contributing positively to the influence, reputation or relationship of France and Hong Kong, in the fields of culture, entrepreneurship, gastronomy, human resources,

education and sustainable development. The HKU-Pasteur Research Pole, represented by Professor Leo Poon, received the Knowledge Transfer award from Bouygues Construction, sponsor of the event, together with Mr Gerard Millet, Vice President & Honorary Secretary of The Légion d'Honneur Club Hong Kong Chapter, a major contributor to the Fellowship together with the Pasteur Foundation Asia and the Consulate General of France.

Laboratory visit with students from the French International School

Visit on 22 November 2022 of the HKU-Pasteur Research Pole laboratory organized in partnership with the French International School with 25 students from their establishment. Students were introduced by Sook-San Wong to the daily life of a researcher and shown around the work that is being done at HKU-Pasteur regarding influenza and coronaviruses.

Major Published Research News

The research conducted at the HKU-Pasteur Research Pole in 2022 has once again been of outstanding quality. Several publications from Leo Poon and Malik Peiris have been mentioned in the press and other media.

- https://www.med.hku.hk/en/news/press/20230207-comirnaty-coronavac-effectiveness
- https://www.med.hku.hk/en/news/press/20220311-omicron-surface-stability
- https://www.med.hku.hk/en/news/press/20220311-syrian-hamsters-sars-cov-2

Research conducted by Vijay Dhanasekaran and his team with the University of Sydney on the impact of COVID-19 on the patterns of winter viruses in Australia also received media attention.

- https://www.sydney.edu.au/news-opinion/news/2022/05/31/how-covid19-created-dramatic-changes--in-a-winter-virus.html

Additionally, Leo Poon has been interviewed by local media over the year and was featured in a Nature Portfolio podcast to discuss the significance of the connection and collaboration in the early hours of COVID-19.

4. Scientific Output

4.1 Publications

1. Bull MB, Gu H, Ma FNL, Perera LP, Poon LLM, Valkenburg SA (2022) Next Generation T cell-activating vaccination increases influenza virus mutation prevalence. *Sci Adv* 8(14):eabl5209.
2. Bull MB, Ma FN, Perera LP, Poon LL, Valkenburg SA. Early vaccine-mediated strain-specific cytokine imbalance induces mild immunopathology during influenza infection. *Immunol Cell Biol* 2022.
3. Burckhardt RM, Dennehy JJ, Poon LLM, Saif LJ, Enquist LW (2022) Are COVID-19 Vaccine Boosters Needed? The Science behind Boosters. *.J Virol* **96**:e0197321.
4. Chan CL, Wai HKF, Wu P, Lai SW, Chan OSK, Tun HM (2022). A universal LC-MS/MS method for simultaneous detection of antibiotic residues in animal and environmental samples. *Antibiotics* 11(7):845.
5. Cheng SM, Mok CKP, Chan KC, Ng SS, Lam BH, Luk LL, Ko FW, Chen C, Yiu K, Li JK, Chan KK, Tsang LC, Poon LL, Hui DS, Peiris M. SARS-CoV-2 Omicron variant BA.2 neutralisation in sera of people with Comirnaty or CoronaVac vaccination, infection or breakthrough infection, Hong Kong, 2020 to 2022. *Euro Surveill* 2022; **27**(18)
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7. Cheng SS, Mok CK, Li JK, Ng SS, Lam BH, Jeevan T, Kandeil A, Pekosz A, Chan KC, Tsang LC, Ko FW, Chen C, Yiu K, Luk LL, Chan KK, Webby RJ, Poon LL, Hui DS, Peiris M. Plaque-neutralizing antibody to BA.2.12.1, BA.4 and BA.5 in individuals with three doses of BioNTech or CoronaVac vaccines, natural infection and breakthrough infection. *J Clin Virol* 2022; **156**: 105273
8. Chu JT, Gu H, Sun W, Fan RL, Nicholls JM, Valkenburg SA, Poon LL. Heterosubtypic immune pressure accelerates emergence of influenza A virus escape phenotypes in mice. *Virus Res* 2022; **323**: 198991.
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13. Dhanasekaran V†, Sullivan S, Edwards K, Xie R, Valkenburg S, Cowling B, Barr I. 2022. Human seasonal influenza under COVID-19 and the potential consequences of influenza lineage elimination. *Nat Comm* **13**, 1721.

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5. Annexes

5.1 List of Staff

Name	Position
Malik Peiris	Honorary Director
Roberto Bruzzone	Co-Director
Leo Poon	Co-Director
Vijaykrishna Dhanasekaran	Associate Professor
Hein Min Tun	Assistant Professor
Sooksan Wong	Assistant Professor
Anne Li	Administration Manager
Wendy Yu	Laboratory Manager
Mathilde Boisserin	Communication Officer (ended Jan-2022)
Adrien Garnier	Communication Officer
Dilys Li	Executive Assistant
Christine Wong	Executive Assistant
Prathanporn Kaewpreedee	Post-doctoral Fellow
Xiaoman Wei	Post-doctoral Fellow (ended October-2022)
Xi Zhang	Post-doctoral Fellow (ended August-2022)
Carolyn Cohen	PhD Student
Suisha Liang	PhD Student
Weiwen Liang	PhD Student
Zaolan Liang	PhD student
Hogan Wai	PhD Student
Cheng Xiao	PhD student
Ruopeng Xie	PhD student
Sonia Younas	PhD Student
Darren Chan	PhD Student (dropped out July-2022)
Tomas Lyu	PhD Student (ended October-2022)
Ye Peng	PhD Student (ended December-2022)
Ray So	PhD Student (ended August-2021) Post-doctoral Fellow (September-2022)
Xiawan Zheng	PhD Student – Department of Civil Engineering, HKU
Shuxian Li	PhD Student – Department of Civil Engineering, HKU

Yulin Zhang	PhD Student – Department of Civil Engineering, HKU
Gary Chan	Mphil Student
Shreya Gurung	Mphil Student
Lewis Siu	Senior Technician
Kimberly Edwards	Senior Research Assistant
Janice Jia	Research Assistant I
Yihan Lin	Research Assistant I
Felice Pak	Research Assistant I (ended January-2022)
Shilin Zhao	Research Assistant I (ended July-2022)
Yang Zhou	Research Assistant I (ended April-2022)
Jie Zhu	Research Assistant I (ended July-2022)
Joy Adeoti	Research Assistant II
Vivian Chan	Research Assistant II
Kelly Lee	Research Assistant II
Cheryl Leung	Research Assistant II
Iris Li	Research Assistant II
Chloe Liu	Research Assistant II
Lisa Touyon	Research Assistant II
Ingrid Chan	Research Assistant II (ended November-2022)
Alan Cheung	Research Assistant II (ended July-2022)
Xin Liu	Research Assistant II (ended August-2022)
Hilda On	Research Assistant II (P/T) (ended June-2022)
Rista Shrestha	Research Assistant II (ended October-2022)
Daniel Sin	Research Assistant II (ended September-2022)
Jun Tao	Research Assistant II (ended November-2022)
Thomas Chu	Research Assistant II (P/T) (ended August 2022)
Sandra Chiu	Research Assistant II (P/T) (ended July-2022)
Anxin Pan	Research Assistant – Department of Civil Engineering, HKU
Xianghui Shi	Research Assistant – Department of Civil Engineering, HKU
Mengying Wang	Research Assistant – Department of Civil Engineering, HKU
Jieying Leung	Laboratory Assistant

Student Interns

Name	
Juliette Clot	French International School, Hong Kong SAR
Lorenzo Godingen	French International School, Hong Kong SAR
Sarah Granveaud	French International School, Hong Kong SAR
Bertille Voets	French International School, Hong Kong SAR
Edward Ye	School of Public Health, HKU, Hong Kong SAR
Sukriti Gyawali	School of Biomedical Sciences, HKU, Hong Kong SAR
Asra Sainju	School of Biomedical Sciences, HKU, Hong Kong SAR
Tooba Latif	University of Veterinary and Animal Sciences, Pakistan
Yee Tsui	University of Toronto, Canada

Visiting and Honorary Appointments

Name	Position	Apointment End date
James Di Santo	Visiting Research Professor	31-December-2022
Noël Tordo	Honorary Professor	31-December-2023
Jincun Zhao	Honorary Professor	31-December-2024
Ralf Altmeyer	Honorary Associate Professor	5-November-2022
Hein Min Tun	Honorary Associate Professor	18-August 2024
Chris Mok	Honorary Assistant Professor	30-April-2025
Sophie Valkenburg	Honorary Assistant Professor	10-November-2023
Iris Wai Sum Iris Li	Honorary Clinical Assistant Professor	30-June-2022
Barbara Gayraud-Morel	Honorary Research Associate	31-December-2023
Niloufar Kavian	Honorary Research Associate	31-December-2022
Yun Lan	Honorary Research Associate	30-April-2023
Qiwen Teo	Honorary Research Associate	31-October-2022
Simon Muller	Honorary Tutor	31-December-2023

5.2 Income & Expenses for the year ending June 2022 (Period: 1 July 2021 to 30 June 2022)

INCOME:

Central Fund	$ 2,750,000.00	18.3 %
Faculty in-kind	$ 2,125,000.02	14.2 %
Institut Pasteur	$ 2,200,669.33	14.7 %
External Grants**	**$ 7,798,464.63**	**51.9 %**
Teaching/Training	$ 139,372.00	0.9 %
TOTAL	**$ 15,013,572.68**	**100.0%**

EXPENSES:

Staff cost	$ 6,959,628.20	56.8 %
Research/Equipment/Maintenance	$ 4,962,168.53	40.5 %
Conference / Meeting	$ 82,940.79	0.7 %
Administration	$78,001.27	0.6 %
Teaching/Training	$ 164,982.62	1.3 %
TOTAL	**$ 12,247,721.41**	**100.0 %**

BALANCE CARRY FORWARD TO 2022/2023 **$ 2,765,851.27**

5.3 Forecast of Income & Expenditure for the year ending June 2023 (Period: 1 July 2022 to 30 June 2023)

INCOME:

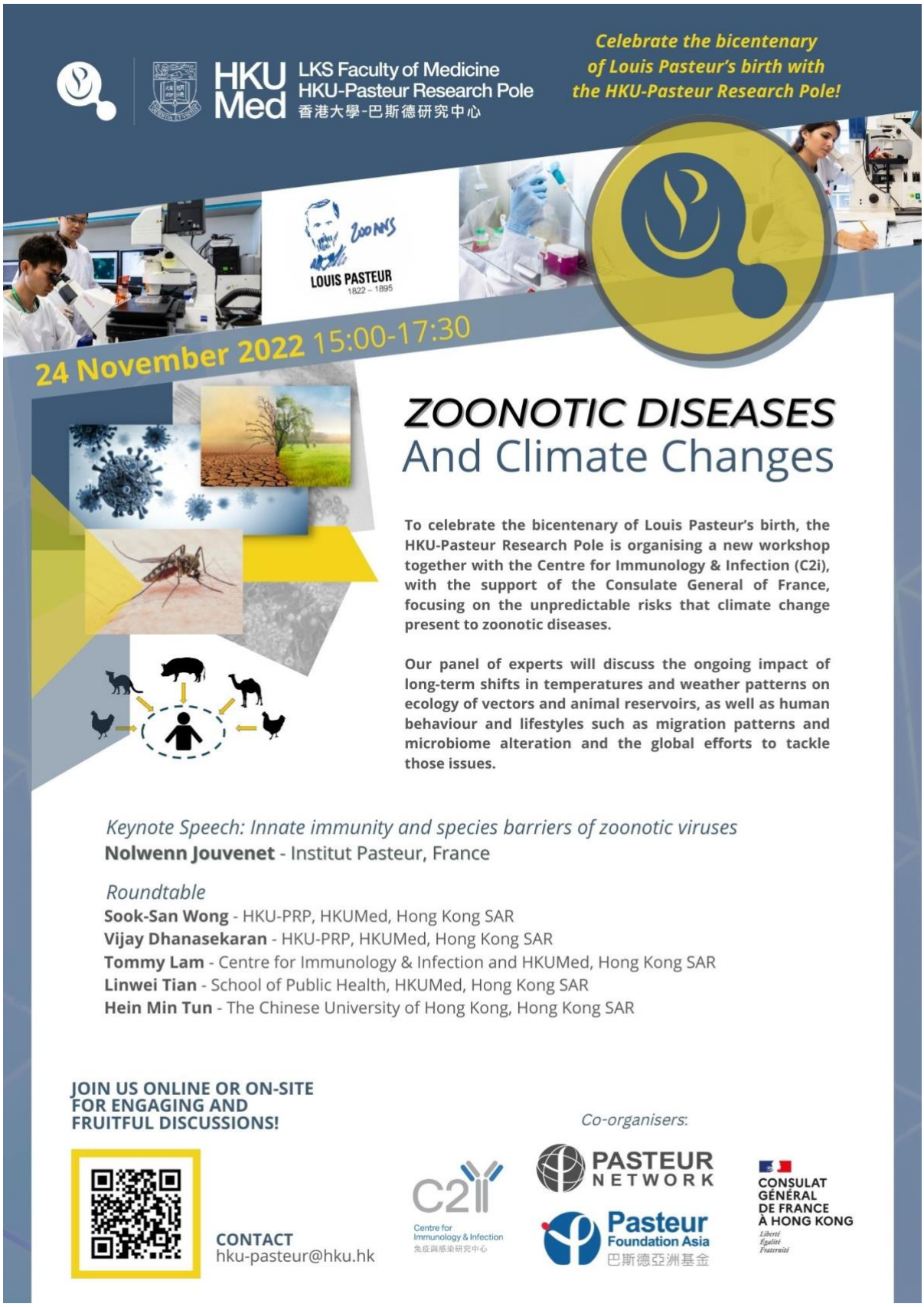
Central Fund	$2,500,000.00	17.2 %
Faculty in-kind	$2,375,000.00	16.3 %
Institut Pasteur (Euro 250,000.-)	$1,942,500.00	13.4 %
External Grants**	**$ 6,858,788.38**	**47.2 %**
Teaching/Training	$ 850,000.00	5.9 %
	$ 14,526,288.38	**100.0%**

EXPENSES:

Staff cost	$ 6,500,000.00	50.4 %
Research/Equipment/Maintenance	$ 5,000,000.00	38.8 %
Conference / Meeting	$ 300,000.00	2.3 %
Administration	$ 250,000.00	1.9 %
Teaching/Training	$ 850,000.00	6.6 %
TOTAL	**$ 12,900,000.00**	**100.0 %**

ESTIMATED BALANCE **$ 1,626,288.38**

5.4 Zoonotic Diseases and Climate Changes

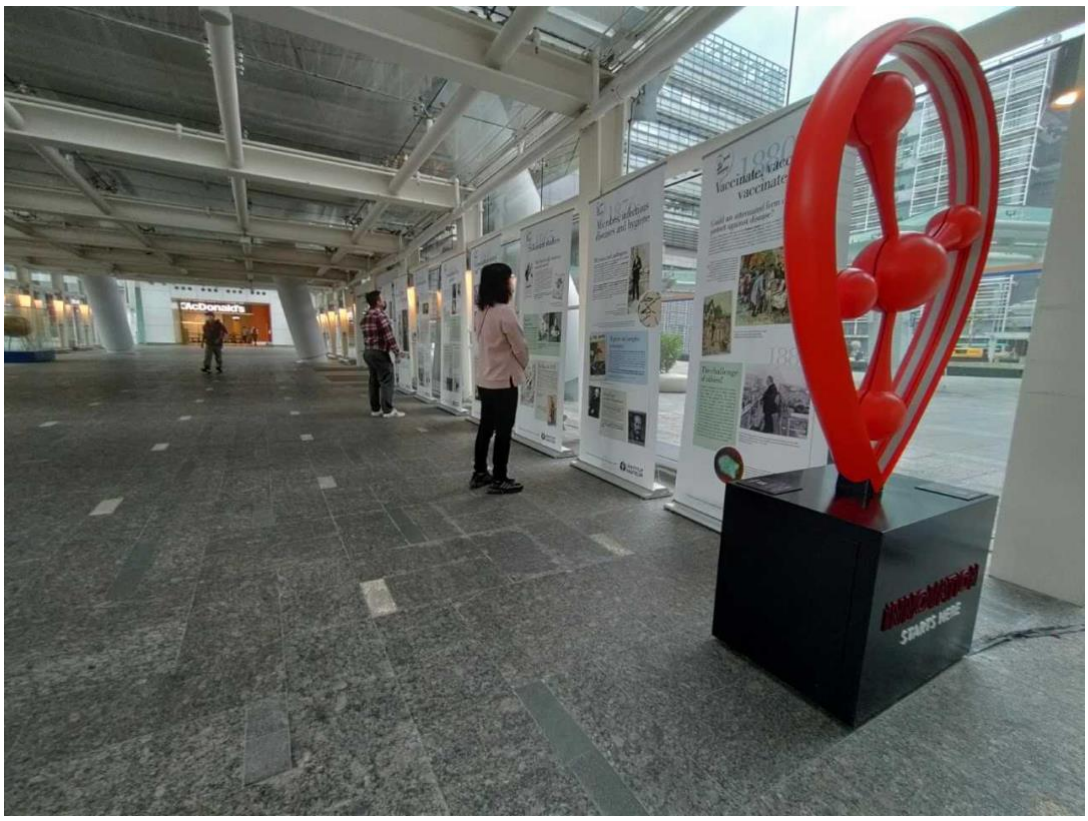


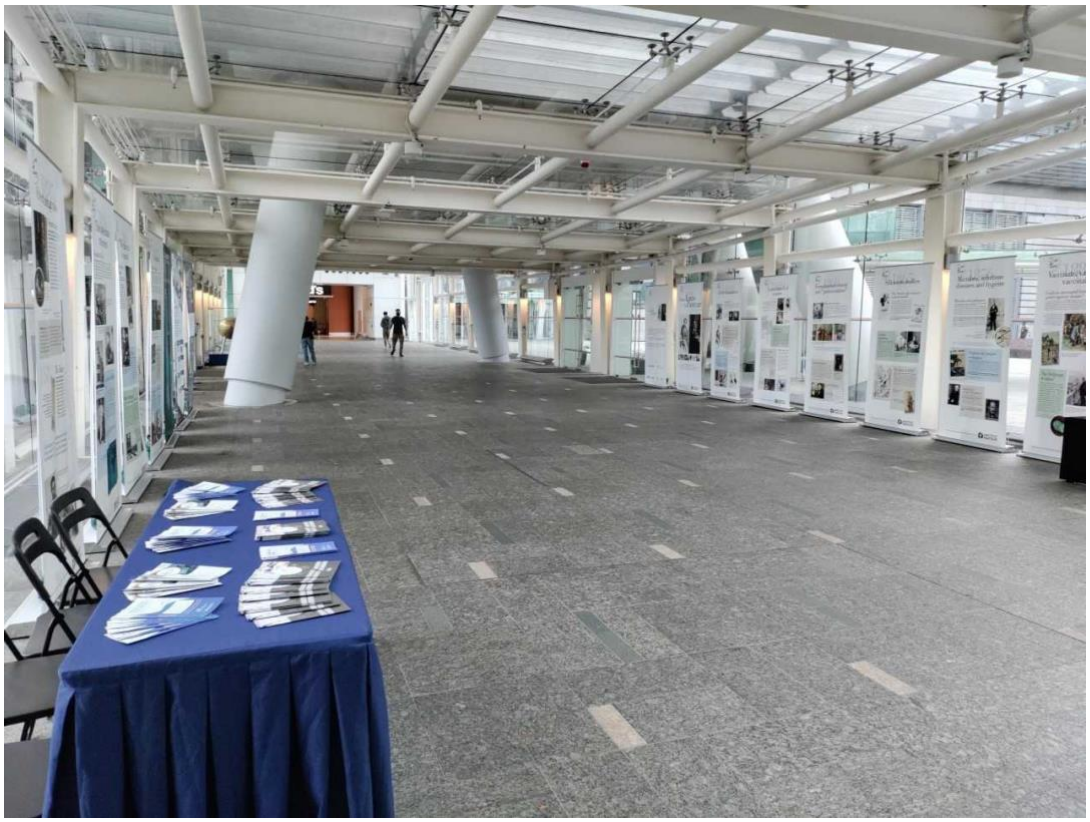
5.5 HKU-Pasteur Research Pole Fellowship

5.6 Louis Pasteur Bicentenary Exhibition

The University of Hong Kong Li Ka Shing Faculty of Medicine: -

Hong Kong Science Park: -





French International School: -

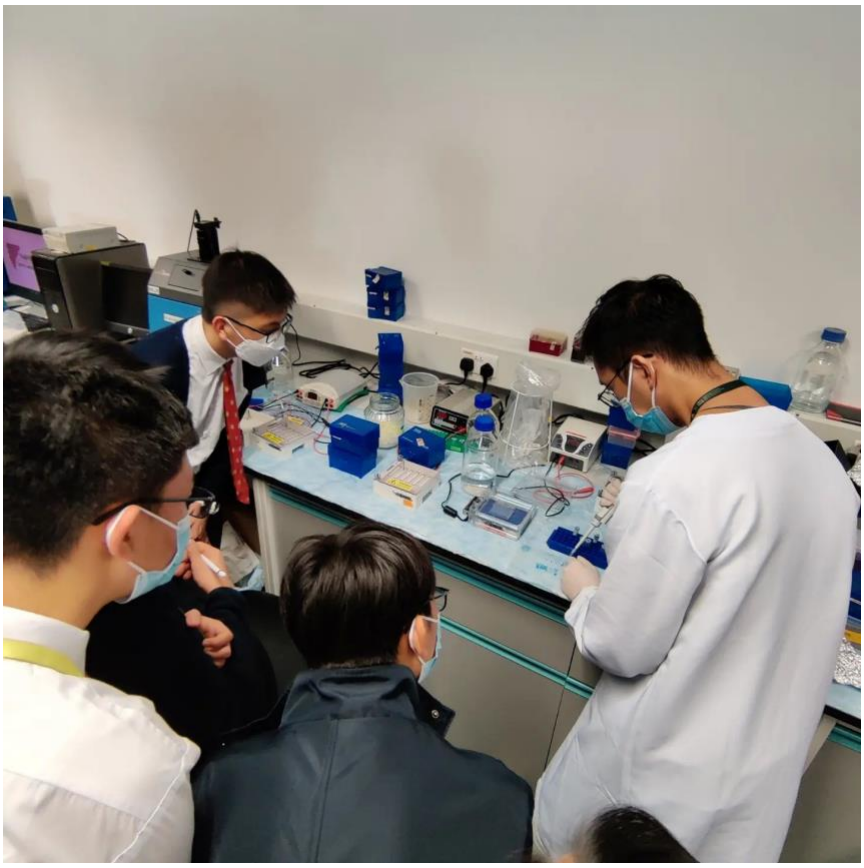
Main Campus

Tseung Kwan O Campus

5.7 Students Visit from French International School


EXIT 出口
From Louis to Pasteur
Birth of a scientist

5.8 Students Visit from Munsang College



LKS Faculty of Medicine
HKU-Pasteur Research Pole
香港大學-巴斯德研究中心

Annual Report 2022

Roberto Bruzzone, Co-Director
Leo Poon, Co-Director
Malik Peiris, Honorary Director

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