# Annual Report 2018

**HKU-Pasteur Research Pole**

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# Summary

## Mission

The HKU-Pasteur Research Pole (HKU-PRP) 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-PRP aims to improve global health through research and education by confronting the challenges posed by viral infections and provide solutions to treat infectious diseases.

## Research

We have organized our activity around Group Leaders who are engaged in competitive research projects aligned with scientific priorities of HKU and IP, namely on emerging and re-emerging infectious diseases (respiratory and mosquito-borne viruses) and, with the recruitment of a new Group Leader, anti-microbial resistance. With respect to influenza research, we have extended our exploration of virus-host interaction and host response to viral infection by combining clinical studies and basic research investigations to gain insight into the mechanistic aspects of disease pathogenesis and adaptive immunity for improved protection. Collaboration with the State Key Laboratory of Respiratory Disease of the Guangzhou Medical University, where laboratory space has been made available to HKU-PRP, has also been expanded with the signing of a cooperation project for a Respiratory Diseases Research Center in the framework of the second Guangdong-Hong Kong-Macao Greater Bay Area Hygiene and Health Cooperation Conference. We are studying both the innate and adaptive immune response to viral infection with a broad objective to investigate the underlining mechanisms relevant to disease pathogenesis and how this could be harnessed and optimized by vaccination to improve protection from diverse influenza virus infection. With respect to arboviruses, we have designed a functional screening strategy to identify novel host factors, which are co-opted by the virus to facilitate its replication, biogenesis, trafficking, and egress. This approach offers novel therapeutic possibilities by interfering with host factors, instead of viral components, as treatment targets. HKU-PRP has published over 25 papers since January 2018.

## Teaching

Our course series draw an increasing number of highly qualified applications from around the world and have generated a worldwide network of trainees. We have received a grant from the Croucher Foundation to organize a new series of courses on "Emerging Viral Infections". We have reached another major landmark with the 10$^{th}$ HKU-Pasteur Immunology course, concluded by a scientific symposium reuniting some of the course alumni. In collaboration with the C3BI at the Institut Pasteur, we have held a hands-on course on Molecular Phylogenetics. The 2018 edition of our Public Health Workshop series at the Pasteur Institute of Ho Chi Minh City (Vietnam), which is primarly aimed at public health professionals and academics in the region, focused on viral hepatitis and was supported by the French Regional Scientific Cooperation.

## 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. Together with the School of Public Health, we have recruited a new Group Leader, Dr. Hein Min TUN, to develop a research program on the role of human and animal microbiome in health and diseases, including surveillance of antimicrobial resistant bacteria, at the interface of human, animals and the environment. We plan to recruit another Group Leader in 2019, to spearhead computational biology research programs. We have coordinated the signing of a Memorandum of Understanding between IP, HKU and Hong Kong Science and Technology Parks to establish an interdisciplinary research centre for immunology, infection and personalized medicine. In summary, the results obtained in 2018 are clearly in line with our strategic objective to position HKU-PRP as a cluster of excellence within the School of Public Health and one of the hubs of the Institut Pasteur International Network.

# 2. Overview of the Programs

## 2.1 Research

The scientific activity of HKU-PRP is organized around three core research questions that meet the overarching goals of Internationalization, Innovation, Interdisciplinarity and Impact (HKU's 3+1):

1. *How do viruses invade, replicate and escape infected cells?* This question encompasses both the virus point of view of the infectious process – by studying molecules and machinery of the host cells that are hijacked during the viral life cycle, as well as the cellular view – to investigate counterstrategies employed by the host in order to prevent virus infection at various steps, including replication, assembly and release.
2. *What makes a microbe pathogenic?* This question interrogates the behavior and pathogenicity of emerging viruses and bacteria with a multi-layered approach that spans serology, epidemiology, microbiology and pathogenicity to delineate genetic determinants of virulence and the acquisition of traits that favor crossing of species barriers by zoonotic viruses and anti-microbial resistance at the human-animal-environment interface.
3. *How do microbes deal with the host immune response and the environment?* This question zooms in, on the one hand, on innate responses and the complex strategies devised by viruses to foil them and, on the other hand, on adaptive lines of defense of the host and how they could be harnessed and optimized by vaccination to improve protection. By using conventional microbiology, molecular biology and next-generation sequencing, coupled with bioinformatics, statistical and epidemiological approaches we will extend study the composition and function of human and animal microbiomes in health and disease.

**Research in the Suki Lee lab** focused on virus-host interaction and host innate immune response to viral infection, with a major objective to investigate the underlining mechanisms of innate immunity relevant to disease pathogenesis. Her lab revealed a novel role of Toll-like receptor (TLR)-10, an orphan receptor without well-characterized ligands or functions, in viral pathogenesis by showing that influenza virus infection increases TLR10 expression. They have now shown that TLR10 is predominantly localized to endosomes and binds dsRNA *in vitro* at endosomal pH, suggesting that dsRNA is a ligand of TLR10. Recognition of dsRNA by TLR10 activates a downstream signal cascade that suppresses interferon regulatory factor-7 dependent type I IFN production. They also demonstrate crosstalk between TLR10 and TLR3, as they compete with each other for dsRNA binding. Together, these results demonstrate that dsRNA is a ligand for TLR10 and lead to propose novel dual functions of TLR10 in regulating innate immune response and interferon signaling: first, recognition of dsRNA as a nucleotide-sensing receptor and second, sequestration of dsRNA from TLR3 to inhibit TLR3 signaling in response to dsRNA stimulation. The lab is also investigating the neuropathogenicity of avian influenza H7N9 virus. They have shown that that differentiated human astrocytic (T98G) and neuronal (SH-SY5Y) cells can be infected by avian H7N9 and pandemic H1N1 viruses. However, infectious progeny viruses can only be detected in H7N9 virus infected human neuronal cells. Furthermore, H7N9 virus triggered high pro-inflammatory cytokine expression, while pandemic H1N1 virus induced only low cytokine expression in either brain cell type. These experimental findings demonstrate that avian H7N9 virus can infect, replicate, induce cytokine upregulation and cause cytopathic effects in human brain cells, and thus may

potentially lead to profound central nervous system injury. **Suki Lee and her team left HKU-PRP at the end of 2018**.

**The lab of Chris Mok** uses a combination of clinical and experimental studies that span the areas of serology, epidemiology and molecular biology to understand the behavior and pathogenicity of emerging viruses. The major objective of the group is to understand the pathogenicity of respiratory viruses such as avian influenza viruses and coronaviruses through combining clinical, basic and epidemiological studies. In this context, the Mok lab has set up collaborations with different research partners to identify and investigate viral, host and environmental factors that influence the impact of the viral infection. During this year, the lab also established a collaboration team with the teams of Jincun Zhao (Guangzhou Medical University, PR China) and Ian Wilson (Scripps Research Institute, USA) to investigate adaptive immunity in humans upon infection/vaccination. Research to understand the pathogenicity of MERS-CoV is ongoing also in collaboration with Jincun Zhao lab, encompassing the investigation of viral determinants and immune response against the virus. In collaboration with Guangzhou Medical University, the Kunming University of Science and Technology and Guangdong Province Center for Disease Control (GDCDC), through our well-established platform "Guangdong-Hong Kong Joint Research Centre for Clinical and Preventive Medicine against Emerging Infectious Diseases", we are setting up new research projects on influenza virus research, with the validation of the tree shrew as a "low-level primate" new animal model, as well as bird surveillance system in Yunnan and Guangdong provinces (PR China), to monitor the activity of avian influenza virus in wildlife. The Mok lab is now obtaining evidence of cellular immune responses specifically against MERS-CoV from peripheral blood mononuclear cells isolated from the camel and non-camel workers in the same abattoir in Nigeria. This important observation challenges the currently held assumption that MERS-CoV infection is absent in Africa, where the majority of dromedary camels, which are presently the only known source of zoonotic MERS-CoV, reside.

**The main objectives of the Sumana Sanyal lab** are to combine methods of molecular biology and immunology to address aspects of host-pathogen interactions. Using influenza and dengue as model systems, the Sanyal lab aims to determine the identity and function of specific host factors that are exploited by these viruses to complete their intracellular life cycle. They also investigate counterstrategies employed by the host – either through upregulation of immune signaling pathways or expression of virus restriction factors – in order to prevent virus infection at various steps, including replication, assembly and release. A molecular understanding of host cellular factors involved in virus infections is crucial not only to provide novel insights into pathways hijacked by them, but also for development of effective antimicrobials against such pathogens. Among other factors, the lab is particularly interested in ubiquitin and ubiquitin-like post-translational modifiers of protein function, such as ISG15 that play a significant role in modulating different pathways, most of which are innate signaling pathways such as RIG-I, TLR7 and inflammasome activation. The ubiquitylation machinery is frequently exploited by a number of pathogens either to masquerade as host proteins or to inhibit immune signaling cascades. Sanyal and co-workers have employed a chemoenzymatic strategy to identify deubiquitylating enzymes (DUBs) that are specifically expressed upon influenza infection and are currently investigating the role of these DUBs. Their ongoing studies involve characterization and pharmacological intervention of these DUBs in order to attenuate influenza infection. Preliminary data in macrophages and

dendritic cells support the hypothesis that influenza takes advantage of DUBs to suppress signaling pathways such as RIG-I and inflammasome activation that require ubiquitin modification for recruitment of downstream effectors. In the near future the lab will test small molecules that target these DUBs both in vitro and in vivo. Identification of host factors that can be targeted for developing novel anti-viral compounds has the additional benefit of avoiding potential resistance acquired in viruses by mutation and selection. In this context, the complexity of the assembly and release of dengue virus provides a potentially rich source of host targets for interference. Propagation of dengue virus (DENV), Zika virus (ZIKV) and other members of the family appears to involve extensive membrane and lipid remodeling to facilitate virus replication, trafficking, assembly and egress. However, we have been severely limited in our understanding of the role of fundamental biological pathways typically hijacked by flaviviruses. We recently discovered that Aup1 – a lipid droplet associated protein – is upregulated upon dengue infection. Dengue NS4A interacted with Aup1 to exploit its acyltransferase function that in turn induced lipophagy. In addition, the sterol regulatory element binding proteins were activated to induce *de novo* sterol and fatty acid biosynthesis. We are currently extending our findings with dengue virus to explore similarities and differences that exist in Zika.

**The newly formed group of Hein Min Tun** uses conventional microbiology, molecular biology and cutting-edge sequencing, coupled with bioinformatics, statistical and epidemiological approaches to study the composition, function, and dynamics of human and animal microbiomes in health and diseases, and to monitor antimicrobial resistance (AMR) bacteria and resistome in humans, animals, and the environment using holistic One Health approach. The overarching goal is to contribute in improving scientific understanding on roles of microbiome and AMR in public health. Hein Min Tun is a public health veterinarian who received his Ph.D. degree from the University of Hong Kong. He then moved to Canada to pursue his postdoctoral research at the Gut Microbiome Laboratory of the University of Manitoba where he held an additional role as a lab manager. After 2 years working for microbiome and resistome research in food animals, human and the environment, he joined with the SyMBIOTA research team at the Department of Pediatrics in the University of Alberta to study roles of infant gut microbiome in health and diseases using the Canadian Healthy Infant Longitudinal Development (CHILD) birth cohort. He is an alumnus of the HKU-Pasteur Virology Course (2010).

**The main objectives of the group of Sophie Valkenburg** are to define immune correlates of protection for influenza viruses from infection and vaccination. Her research is centered on the role of protective heterologous T and B cell immunity in mouse and human systems, by investigating novel vaccines and immune correlates of protection for influenza. The primary focus of the lab is to study adaptive immunity to influenza, and how this could be harnessed and optimized by vaccination to improve protection from diverse influenza virus infection. Hemagglutinin (HA)-specific antibodies can block influenza infection, whilst T cells recognize influenza-infected cells. A vaccine which ultimately combines antibody and T cell based immunity for influenza will provide a full-proof immunological barrier to influenza infection, which our studies will ultimately help develop. The two mainresearch projects aim to elucidate how cross-reactive T and B cell responses to influenza provide broad immunity. The team has further grown over 2018 with the recruitment and training of three new research assistants. Sophie Valkenburg joined the international network of the NIH Centres of Excellence for Influenza Research

and Surveillance (CEIRS) in 2017, and in 2018 again attended their annual meeting in New York, and was awarded a second project of 2-year funding for a collaborative project with St Jude's Children's hospital (Memphis, USA). Progress is being made in the characterization of a T-cell based universal influenza vaccine by investigating DC trafficking, immune mediated pressure by Next Generation Sequencing and innate lymphoid cell recruitment to determine the impact of T cell activated vaccines. The Valkenburg has extended its observations to define the human correlates of protection from influenza in a long-term project carried out in collaboration with Benjamin Cowling (School of Public Health at HKU). Whilst T cell responses have been shown to be highly effective in mediating protection in mouse models, corresponding data in human influenza infection is not as robust. All adults have established influenza-specific memory T cell responses; however, we have repeated infections during our lifetime that can range from mild to life threatening. The half-life of T cell memory and cross reactivity may explain the variability in protection from repeated infection. In collaboration we aim to determine the correlation between higher baseline early effector T cell memory responses and protection from influenza infection or reduced symptom severity and viral shedding in a household transmission setting. Blood samples are obtained from infected index cases, and uninfected household contacts that are monitored for influenza transmission, at day 0 and day 28. The aim of the study is to find if there is an immunological difference between contacts positive and negative for influenza transmission during sampling. Sample collection has been ongoing since June 2013 due to the limited and specific nature of cases and intensity of monitoring households.

Research at HKU-PRP includes work by **Jimmy Lai** (joint appointment in the Department of Pathology), who studies the interactions between viruses with the host receptors and the interplay between different influenza surface proteins during viral infection, in order to have a better understanding on viral host adaptation and cell/tissue tropism. Work on the sero-epidemiology of MERS-CoV and Ebola virus is coordinated by **Malik Peiris**. His recent findings, obtained in collaboration with several teams worldwide, conclusively demonstrate that MERS-CoV infection is ubiquitous in dromedaries across Africa as well as in the Arabian Peninsula. Viruses from Africa, however, are phylogenetically distinct from contemporary viruses from the Arabian Peninsula and both genetic and phenotypic differences may be relevant to explain their zoonotic potential. **Barbara Gayraud-Morel** was a Visiting Scientist from the Institut Pasteur (until 08/18), who is working in collaboration with teams at HKU and HKUST to explore the consequences of respiratory virus infections on skeletal muscles and muscle stem cells in particular. Her results show that during influenza viral infection, muscle stem cells are subjected to several modifications at the protein and gene expression levels. The presence of **James Di Santo**, a Visiting Research Professor from IP since 2016, has stimulated ideas and exchanges in the field of immunology at several different levels within the LKS Faculty of Medicine, culminated in the preparation of a major project to understand the genetic and environmental determinants of immune responsiveness in normal individuals. The project has been submitted to the Innovation and Technology Commission within the framework of the Inno@Health scheme launched by the Hong Kong Government.

## 2.2 Teaching and Education

HKU-PRP has pioneered in Hong Kong a teaching program of excellence that has been established to train in biomedical sciences a selected group students coming from all over

the world. We offer three major international courses on an annual/biennial basis – Cell Biology, Virology and Immunology – which feature lectures from leading scientists and have received increasing support from extramural funding. All HKU-Pasteur courses have been approved by the Research Postgraduate Committee of HKU for inclusion in the coursework curriculum of MPhil/PhD students. The program is extremely competitive and has established the reputation of HKU-PRP for training in biomedical research. All Group Leaders are actively engaged in our international courses as well as in the undergraduate and postgraduate curriculum of HKU.

The **HKU-Pasteur Cell Biology Course**, which reached the 8th edition in 2018, focused on proteomics based approaches to probe the cell biology underlying human diseases. With the advent of more sophisticated technology and instrumentation in mass spectrometry, a strong interest has emerged to assess and interrogate biology at the level of protein networks along with the more conventional genomic and transcriptomic approaches. The ability to determine changes at the protein level, including post-translational modifications that dictate protein states and their corresponding function, is revealing a new texture to biology. The lectures, methods and technologies used during the practicum highlighted the power of using mass spectrometry and proteomics combined with quantitative analysis to probe signaling networks that are typically perturbed in various diseased states.

We have co-organized with **Christian Drosten of the Charite – Universitaetsmedizin** (Berlin, Germany), the first **Croucher Summer Course on Emerging Viral Infections**. This new course series aims to address the grand challenges of containing emerging viral infections with an inclusive One- Health approach combining the fields of animal and human health. The course consisted of lectures and a practical workshop designed to challenge participants to prepare a short grant proposal addressing major research questions related to the human-virus interaction.

To take into account the increasing demand for training in *omic* science, we have held an **Introduction to Molecular Phylogenetics Course**, in collaboration with **Olivier Gascuel and the Center of Bioinformatics, Biostatistcs and Integrative Biology of the Institut Pasteur.** This week-long course aimed to give the basic theoretical and practical concepts, best practices, and software necessary to start working on molecular phylogenetics and its applications to epidemiology. The course comprised theoretical morning sessions followed by hands-on workshops in the afternoons for a few selected students working with their own data.

**The HKU-Pasteur Immunology Course** reached a significant milestone with its 10th edition. We continued to delve into the theme of "**Quantitative Immunology**" with course lectures highlighting the latest advances in large-scale, quantitative data collection and computational analysis as applied to biochemical aspects of immune cell activation and function, multicellular behavior in tissues and model organisms, and human immune function in health and disease. While the Faculty covered various areas in systems immunology during the morning lectures, students were busy in the afternoons with two blocks of hands-on practical workshops, which comprised a "wet" laboratory experiment to determine the baseline immune status of healthy donors for various immune parameters in the first week, and a 'dry', bioinformatics data analysis using R-studio in the second week. The course was concluded by a **Scientific Symposium that celebrated the tenth edition of the HKU-Pasteur Immunology Course**. During this decade we have received more than 500 applications and trained more than 200 students and young

scientists, who are now continuing their own professional careers in science, education, private sector and other venues.

The **Public Health Workshop series at the Pasteur Institute of Ho Chi Minh City** is attracting increasing number of applications and has become a benchmark for a world-class training program for epidemiologists, researchers and public health officials in the region. The topic of the 2018 edition, organized in close partnership with the Pasteur Institute of Ho Chi Minh City, was "**Epidemiology, Surveillance and Elimination of Viral Hepatitis**". This workshop focused on how to integrate viral hepatitis strategic activities and indicators within national health information systems and tools, including for outbreak surveillance, and monitoring and evaluation of the hepatitis response plan. It discussed the hepatitis burden, assessing trends over time, and presented an update on normative guidance and tools on hepatitis surveillance, and monitoring. Training sessions covered the role of vaccines and antivirals to prevent and treat Hepatitis B disease and best practices towards elimination of hepatitis B. The course series has been generously supported from its inception by the Regional Health Cooperation Office of the French Ministry of Foreign Affairs.

**We have hosted seven international students for their laboratory placement**, from **France**, **Germany**, **The Netherlands**, **Singapore** and **United Kingdom**, as well as several interns from local institutions.

## 2.3 International Activity

We retain leadership roles in a number of global projects. **Roberto Bruzzone** is a member of the **Executive Committee and Interim Chair** of the **International Severe Acute Respiratory and Emerging Infection Consortium** (**www.isaric.tghn.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. **Malik Peiris** is the **Coordinator of the Theme-based Research Scheme**: "Viral, host and environmental determinants of influenza virus transmission and pathogenesis", which has been awarded a HK$75 million grant. This large-scale multidisciplinary project aims at enhancing global public health by identifying the viral and host determinants of influenza virus transmission and pathogenesis leading to evidence-based interventions. **Malik Peiris** continues to serve on a number of **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 an **Associate Editor of the Virology Journal** and **Member of the International Affairs Committee of the American Society for Cell Biology**. **Group Leaders** have actively participated in major international conferences (Keystone Symposia, EMBO meetings, Gordon Research Conferences) and are regularly invited to give lectures and seminars at major universities and research institutions worldwide. **Malik Peiris** was one of the co-organizers of the Keystone Symposium "Framing the Response to Emerging Virus Infections", which was held in Hong Kong, October 14-18, 2018 and **was named one of "Science stars of East Asia" by Nature magazine**.

# 3. Progress Report

# 3.1 Chris Ka Pun MOK Lab

## Main Objectives and Strategy

The major objective of our group is to understand the pathogenicity of respiratory viruses such as avian influenza viruses and coronaviruses through combining clinical, basic and epidemiological studies. In this context, we have set up collaborations with different research partners to identify and investigate viral, host and environmental factors that influence the impact of the viral infection. During this year, we also established a collaboration team with the teams of Jincun Zhao (Guangzhou Medical University, PR China) and Ian Wilson (Scripps Research Institute, USA) to investigate adaptive immunity in humans upon infection/vaccination. Research to understand the pathogenicity of MERS-CoV is ongoing also in collaboration with Jincun Zhao lab, encompassing the investigation of viral determinants and immune response against the virus. In collaboration with Guangzhou Medical University, the Kunming University of Science and Technology and Guangdong Province Center for Disease Control (GDCDC), through our well-established platform "Guangdong-Hong Kong Joint Research Centre for Clinical and Preventive Medicine against Emerging Infectious Diseases", we are setting up new research projects on influenza virus research, the validation of new animal models and bird surveillance system in Yunnan and Guangdong provinces (PR China), to monitor the activity of avian influenza virus in wildlife. Our major research projects are listed below.

### *Preventing an antigenically disruptive mutations in egg-based H3N2 seasonal influenza vaccines by mutational incompatibility*

Egg-based seasonal influenza vaccines are the major preventive countermeasure against influenza virus. However, their effectiveness can be compromised from antigenic changes arising from egg-adaptive mutations on influenza hemagglutinin (HA). The L194P mutation is commonly observed in egg-based H3N2 vaccine seed strains and significantly alters HA antigenicity. An approach to prevent occurrence of L194P would therefore be beneficial. We show that emergence of L194P during egg passaging can be impeded by pre-existence of a G186V mutation, revealing strong incompatibility between these mutations.

X-ray structures illustrate that, when both G186V and L194P are present, the receptor-binding site of HA is severely disrupted. Importantly, wild-type HA antigenicity is maintained in G186V, but not in L194P. Our results demonstrate once can take advantage of epistatic interactions to prevent emergence of mutations that adversely alter antigenicity during egg adaptation. Overall, this study provides important insight into the optimum selection of egg-based influenza vaccine seed strains.

### *Evidences of human infection with MERS-CoV in Africa*

Zoonotic transmission of Middle East Respiratory Syndrome-Coronavirus Virus (MERS-CoV) continues to occur in the Arabian Peninsula and remains a cause for global public health concern. Up to now, more than 2,000 laboratory cases have been confirmed with an approximately 35% fatality rate. Dromedary camels are presently the only known source of zoonotic MERS-CoV, with the evidences of high detection rate in swab and high seropositive in blood samples. Patients with MERS-CoV infection in Arabian Peninsula are strongly associated to either direct or indirect exposure to camels. However, no human zoonotic MERS has been documented in Africa thus far, despite the fact that over 60% of the global population of dromedaries is found in Africa.

The current notion that human infection by MERS-CoV is absent in Africa is mainly supported by the results of serology studies, which found no detectable neutralizing antibodies even from subjects with close contact with camels. In keeping with previous observations, we reported that there was no serological evidence of MERS-CoV infection in subjects working in a camel abattoir in Nigeria,

who were exposed to the virus (So RT et al, Euro Surveill, 2018). Detection of virus-specific T cell responses, however, is a more sensitive approach than the serological test to determine whether infections of MERS-CoV actually occur. In this study, we further detect the CD4 and CD8 T cell responses specifically against the Spike (S1 and S2), nucleoprotein (N) and envelope (E) proteins of MERS-CoV from peripheral blood mononuclear cells (PBMC) isolated from the camel and non-camel workers in the same abattoir. Our data provide strong evidence that a significant percentage of workers in a camel abattoir had been infected either by MERS-CoV or by an immunologically similar virus.

### *Tree shrew as a new animal model to study the pathogenesis of avian influenza virus infection*

Outbreaks of avian influenza virus continue to pose threats to human health. Animal models such as the mouse, ferret and macaque are used to understand the pathogenesis of avian influenza virus in humans. It was previously reported that tree shrew (*Tupaiabelangeri, family Tupaiidae*), which is regarded as a "low-level primate", exhibits a similar distributions of $\alpha$2,3 and $\alpha$2,6 linked sialic acid receptors as humans and is, therefore, a potentially useful mammalian model for studying human influenza virus infection. In this study, we use the tree shrew experimental model to investigate the pathogenesis of avian influenza A(H9N2) virus and the effect of the E627K mammalian-adapting mutation in the PB2 gene. Evidence of disease, virus titers in the upper and lower respiratory tract, histopathology and the induction of pro-inflammatory cytokines were recorded. We also established an *ex vivo* culture models of tree shrew respiratory tissues to study the tropism and replication of H9N2 virus. Our results demonstrate that the tree shrew is a novel *in vivo* experimental model for avian influenza research that provides results comparable with that observed in ferrets. The disease spectrum and pathogenesis correlated well with what is observed in humans.

## Publications


1) Tang YS, Lo CY, Mok CK, Chan PK, Shaw PC (2019) The extended C-terminal region of influenza C nucleoprotein is important for nuclear import and RNP activity. *J Virol*, in press.

2) Zhang J, Su R, Jian X, An H, Jiang R, Mok CK (2018) The D253N Mutation in the polymerase basic 2 gene in avian influenza (H9N2) virus contributes to the pathogenesis of the virus in mammalian hosts. *Virol Sin* 33:531-537.

3) Li R, Yuan B, Xia X, Zhang S, Du Q, Yang C, Li N, Zhao J, Zhang Y, Zhang R, Feng Y, Jiao J, Peiris M, Zhong N, Mok CK*, Yang Z* (2018) Tree shrew as a new animal model to study the pathogenesis of avian influenza (H9N2) virus infection. *Emerg Microbes Infect* 7:166. (*Co-corresponding authors)

4) Zhao X, Li R, Zhou Y, Xiao M, Ma C, Yang Z, Zeng S, Du Q, Yang C, Jiang H, Hu Y, Wang K, Mok CK, Sun P, Dong J, Cui W, Wang J, Tu Y, Yang Z, Hu W (2018) Discovery of highly potent pinanamine-based inhibitors against amantadine- and oseltamivir-resistant influenza A viruses. *J Med Chem* 61:5187-5198.

5) Zhang T, Xiao M, Wong CK, Mok KC, Zhao X, Ti H, Shaw PC (2018) Sheng Jiang San, a traditional multi-herb formulation, exerts anti-influenza effects in vitro and in vivo via neuraminidase inhibition and immune regulation. *BMC Complement Altern Med* 18:150.

6) Guan W, Wu NC, Lee HHY, Li Y, Jiang W, Shen L, Wu DC, Chen R, Zhong N, Wilson IA, Peiris M, Yang Z, Mok CK (2018) Clinical correlations of transcriptional profile in patients infected with avian influenza H7N9 Virus. *J Infect Dis* 218:1238-1248.

7) Huang J, Liang W, Chen S, Zhu Y, Chen H, **Mok CK**, Zhou Y (2018) Serum cytokine profiles in patients with dengue fever at the acute infection phase. *Dis Markers* **2018**:8403937.

8) Mak GCK, Kwan MY, **Mok CK**, Lo JYC, Peiris M, Leung CW (2018) Influenza A(H5N1) virus infection in a child with encephalitis complicated by obstructive hydrocephalus. *Clin Infect Dis* **66**:136-139.

9) Herfst S, **Mok CK**, van den Brand JMA, van der Vliet S, Rosu ME, Spronken MI, Yang Z, de Meulder D, Lexmond P, Bestebroer TM, Peiris JSM, Fouchier RAM, Richard M (2018) Human clade 2.3.4.4 A/H5N6 influenza virus lacks mammalian adaptation markers and does not transmit via the airborne route between ferrets. *mSphere* **3**. pii: e00405-17.

10) Chan MC, Chan RW, **Mok CK**, Mak NK, Wong RN (2018) Indirubin-3'-oxime as an antiviral and immunomodulatory agent in treatment of severe human influenza virus infection. *Hong Kong Med J* **24** (Suppl 6):45-47.

## Awards, Seminars, and Invited Lectures

1) Chris Mok (2018) 14th International Congress of Parasitology (ICOPA 2018), Daegu, South Korea.

2) Chris Mok (2018) Global Meeting on Avian Influenza East Asia Influenza Centre, Jeju, South Korea.

3) Chris Mok (2018) The Virus Research Symposium of Korea Research Institute of Bioscience and Biotechnology, Daejeon, South Korea.

## Presentations at meetings

1) Guan W, Wu NC, Liang W, Peiris M, Yang Z, Mok CK (2018) Clinical correlated transcriptional signatures in severe patients with the infection of avian influenza (H7N9) virus. *The 2nd International Meeting on Respiratory Pathogens, The International Society for Influenza and Other Respiratory Virus Diseases*, Singapore (**Poster**).

## Teaching

1) Chris Mok (2018) 1st Croucher Summer Course on Emerging Viral Infections, The University of Hong Kong, Hong Kong SAR (*Director, Tutor and Course Committee*).

2) Chris Mok (2018) Introduction to the Art and Science of Medicine – Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (*Tutor*).

3) Chris Mok (2018) Teaching course for Guangdong Center for Disease Control and Prevention, Guangzhou, PR China (*Lecturer*).

## Collaborations (local and international)

1) **Nan-Shan Zhong, Jin-cun Zhao, Zi-Feng Yang** (State Key Laboratory of Respiratory Disease, Guangzhou, PR China): Clinical and laboratory studies on emerging infectious diseases in Guangzhou.
2) **Michael Chan** (School of Public Health, The University of Hong Kong) and **Ron Fouchier** (Erasmus Medical Center, The Netherlands): Pathogenicity and transmissibility of influenza virus.
3) **Ian Wilson, Nicholas Wu (**The Scripps Research Institute, USA): Bioinformatic and structural study on influenza research.

## Funding

1) Investigation on a pinanamine derivative as an antiviral agent against influenza A virus infection (**Principal Investigator**; Health and Medical Research Fund – Ends: 05/2020).
2) Viral, Host and Environmental Determinants of Influenza Virus Transmission and Pathogenesis (**Co-Investigator**; GRC/GRF: Theme-based Research Scheme – Ends: 12/2019)
3) Investigation on the immunological cross-protection between different human coronaviruses (**Co-Investigator**; NSFC/RGC Joint Research Scheme – Ends: 12/2022).
4) Evaluation of anti-influenza properties of antrafenine and its analogs (**Co-Investigator**; Health and Medical Research Fund – Ends: 05/2021).
5) Study of Avian Influenza Variation Based on International Collaoration (**Collaborator**: Wonkwang University acting through Zoonosis Research Centre, South Korea – Ends: 12/2019)
6) Building Up Reverse Genetics Technique and Production of Recombinant Influenza Viruses (**Collaborator**: Korea Research Institute of Bioscience and Biotechnology, South Korea)

# Personnel

| Name | Position |
|---|---|
| Chris MOK | Research Assistant Professor |
| Gannon MAK | PhD student (graduated June 2018) |
| Fionn MA | MPhil student (graduated August 2018) |
| Garrick YIP | MPhil student |
| Tomas LYU | Research Assistant |
| Wilson NG | Research Assistant |
| Chung Lam MAK | Student Intern (Institute of Vocational Education) |

# 3.2 Sumana SANYAL LAB

## Main Objectives and Strategy

The main objectives of the lab are to combine methods of molecular biology and immunology to address aspects of host-pathogen interactions. Using influenza and dengue as model systems, we aim to determine the identity and function of specific host factors that are exploited by these viruses to complete their intracellular life cycle. We also investigate counterstrategies employed by the host – either through upregulation of immune signaling pathways or expression of virus restriction factors – in order to prevent virus infection at various steps, including replication, assembly and release. Among other factors, we are particularly interested in ubiquitin and ubiquitin-like post-translational modifiers of protein function, such as ISG15 that play a significant role in modulating different pathways, most of which are innate signaling pathways such as RIG-I, TLR7 and inflammasome activation. Our major research projects are listed below.

### *Characterization of host factors involved in virus infections*

A molecular understanding of host cellular factors involved in virus infections is crucial not only to provide novel insights into pathways hijacked by them, but also for development of effective antimicrobials against such pathogens. Identification of host factors that can be targeted for developing novel anti-viral compounds has the additional benefit of avoiding potential resistance acquired in viruses by mutation and selection.

**(a) *Exploitation of lipid metabolic pathways in flavivirus infection:*** The complexity of the assembly and release of dengue virus provides a potentially rich source of host targets for interference. Propagation of dengue virus (DENV), Zika virus (ZIKV) and other members of the family appears to involve extensive membrane and lipid remodeling to facilitate virus replication, trafficking, assembly and egress. However, we have been severely limited in our understanding of the role of fundamental biological pathways typically hijacked by flaviviruses. We recently discovered that Aup1 – a lipid droplet associated protein – is upregulated upon dengue infection. Dengue NS4A interacted with Aup1 to exploit its acyltransferase function that in turn induced lipophagy. In addition, the sterol regulatory element binding proteins were activated to induce *de novo* sterol and fatty acid biosynthesis. We are currently extending our findings with dengue virus to explore similarities and differences that exist in Zika.

**(b) *Role of Tsg101 in influenza virus infection:*** A major response of mammalian cells to viral infections is through upregulation of the interferon type I and II pathways. Viruses in turn implement counter strategies through either inhibition of IFN response or by activation of proteins that inhibit the function of interferon-stimulated genes (ISGs). The function of Tsg101 appears to be dictated by several post-translational modifications including ISG15, phosphorylation and ubiquitylation. Using a combination of CRISPR/Cas9 knockouts and protein interaction assays, we are currently exploring the functional relevance of these modifications during influenza infection, centered on (i)Tsg101 and (ii) MGRN1 - an E3-ligase that ubiquitylates Tsg101.

**(c) *Mechanism of Src-family kinase (SFK)-mediated signaling during flavivirus infections*:** Amongst the host factors that facilitate egress of dengue virus particles through the secretory pathway are the KDELR, class-II Arfs and several Src-family kinases. We recently screened a number of SFKs to determine their impact on intracellular transport of dengue and Zika. Deficiency of Lyn through siRNA-mediated suppression as well as pharmacological inhibition had a significant impact on release of both dengue and Zika virus particles. We are in the process of elucidating the mechanism through which

these SFKs activate the signaling cascade that is necessary for transport of flavivirus particles along the host secretory pathway.

## *Targeting deubiquitylases as therapeutic strategies against viral infections*

Influenza virus is responsible not only for annual epidemics, but also for frequent outbreaks of pathogenic avian flu strains that have become a serious public health issue worldwide. The ubiquitylation machinery is frequently exploited by a number of pathogens either to masquerade as host proteins or to inhibit immune signaling cascades. We have employed a chemoenzymatic strategy to identify deubiquitylating enzymes (DUBs) that are specifically expressed upon influenza infection and are currently investigating the role of these DUBs. Our ongoing studies involve characterization and pharmacological intervention of these DUBs in order to attenuate influenza infection. Preliminary data in macrophages and dendritic cells support the hypothesis that influenza takes advantage of DUBs to suppress signaling pathways such as RIG-I and inflammasome activation that require ubiquitin modification for recruitment of downstream effectors. We also propose to test small molecules that target these DUBs both in vitro and in vivo. Our current efforts are centered on OtuB1, which appears to interact with influenza PB2. Deficiency of OtuB1 results in a significant drop in release of both proinflammatory cytokines and virus particles from infected cells.

## *Regulation of immune signaling by deubiquitylases*

Signaling cascades require tight control over activation and suppression to maintain downstream activities for appropriate durations. Such regulation is often executed by post-translational modifications such as phosphorylation and ubiquitylation. We are interested in deciphering the role of deubiquitylases (DUB) in the context of a number of innate and adaptive immune responses. We have identified DUBs that are either specifically recruited or inactivated in the T-cell receptor-signaling cascade, presumably to optimize the length and magnitude of downstream activities. Usp12, which resides in the nucleus, is redistributed to the cytosol in a TCR stimulus specific manner. In the absence of Usp12 surface expression of the TCR is drastically reduced. This phenotype is recapitulated upon inhibition of Usp12 translocation from the nucleus to the cytosol. Using proximity based labeling we identified LAT and Trat1 to be substrates of Usp12. We are also pursuing a set of DUBs, including Usp4, identified through functional screening in mouse T-lymphocytes that function to suppress TCR signaling.

# Publications


1. Jahan AS, Biquand E, Munoz R, Le Quang A, Mok CK, Wong HH, Teo Q, Doak S, Chin AWH, Poon LLM, te Velthuis A, García-Sastre A, Demeret C, **Sanyal S** (2019) OTUB1 functions as a ubiquitin sensor for RIG-I activation and is targeted for proteasomal degradation by Influenza A virus NS1. *Immunity* (under review).
2. Wong HH, **Sanyal S** (2019) Viral strategies of manipulating autophagy to benefit infection. *Semin Cell Dev Biol (invited review).*
3. Fan Y, **Sanyal S**, Bruzzone R (2018) Breaking Bad: How viruses subvert the cell cycle *Front Cell Infect Microbiol* **8**:396.

4. Zhang J, Lan Y, Li MY, Lamers MM, Fusade-Boyer M, Klemm E, Thiele C, Ashour J, **Sanyal S** (2018) Flaviviruses exploit the lipid droplet protein AUP1 to trigger lipophagy and drive virus production. *Cell Host Microbe* **23**:819-831.
5. Pombo JP, **Sanyal S** (2018) Perturbation of cholesterol and fatty acid homeostasis during flavivirus infections. *Front Immunol* **9**:1276.
6. Zhang J, Lan Y, **Sanyal S** (2017) Modulation of lipid droplet metabolism – a potential target for therapeutic intervention in *Flaviviridae* infections. *Front Microbiol* **8**:2286.
7. Fan Y, Mok CK, Kein F, Bruzzone R, **Sanyal S** (2017) Cell-cycle independent role of CyclinD3 in host restriction of influenza infection. *J Biol Chem* **292**:5070-5088.

## Awards, Seminars, and Invited Lectures

1. Sumana Sanyal (Sept-Nov 2018) Doris Zimmern HKU-Cambridge Visiting Fellowship, University of Cambridge, UK.
2. Sumana Sanyal (Dec 2018) Keynote speaker at the Annual Influenza Update Meeting, Emmanuel College, University of Cambridge, UK.
3. Sumana Sanyal (Nov 2018) Sir William Dunn School of Pathology, University of Oxford, UK.
4. Sumana Sanyal (Oct 2018) Department of Pathology, University of Cambridge, UK.
5. Sumana Sanyal (Sept 2018) Cambridge Institute of Medical Research, University of Cambridge, UK.
6. Sumana Sanyal (May 2018) Karolinska Institutet, Stockholm, Sweden.
7. Sumana Sanyal (Jan 2018) California Institute of Technology, Pasadena, USA.
8. Sumana Sanyal (Jan 2018) Whitehead Institute for Biomedical Research/Massachusetts Institute of Technology, USA.

## Presentations at Meetings

1. Jahan A, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Oral**).
2. Li MY, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Oral**).
3. Lan Y, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Poster**).
4. Teo Q, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Poster**).
5. Pombo J, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Poster**).
6. Sanyal S (2018) *Keystone Conference: Ubiquitin Signaling.* Tahoe City, USA (**Oral**).

## Teaching

1. Sumana Sanyal (2018) Basic Metabolism (BSc Biochemistry Year 3 students) The University of Hong Kong, Hong Kong SAR.
2. Sumana Sanyal (2018) Essentials in Proteomics (BBMS Year 3) The University of Hong Kong, Hong Kong SAR.
3. Sumana Sanyal (2018) Recent Advances in Biotechnology (MMPH) The University of Hong Kong, Hong Kong SAR.
4. Sumana Sanyal (2018) Cancer Screening – Problem Based Learning (MBBS Year 4 students) The University of Hong Kong, Hong Kong SAR (*Tutor*).
5. Sumana Sanyal (2018) Introduction to the art and science of medicine – Problem Based Learning (MBBS Year 1 students) The University of Hong Kong, Hong Kong SAR (*Tutor*).
6. Sumana Sanyal (2018) Endocrine and Reproductive Systems – Problem Based Learning (MBBS Year II students) The University of Hong Kong, Hong Kong SAR (*Tutor*).
7. Sumana Sanyal (2018) 8$^{th}$ HKU-Pasteur Cell Biology Course, The University of Hong Kong, Hong Kong SAR (*Director, Lecturer and Tutor*).

## Collaborations

1. **Adolfo García-Sastre** (Mount Sinai School of Medicine, New York, USA): Function of ubiquitin like modifiers and their mode of restricting RNA virus infections.
2. **Leo Poon** (University of Hong Kong, Hong Kong SAR): Functional characterization of PB2 ubiquitylation.
3. **Christoph Thiele** (LIMES Institute, University of Bonn, Germany): Role of lipid droplets in virus infections.
4. **Caroline Demeret** (Institut Pasteur, Paris, France): Role of deubiquitylases in influenza virus infections.
5. **Joseph Ashour** (Boehringer Ingelheim/Mount Sinai School of Medicine, New York, USA): Manipulation of host factors in influenza and dengue infections.
6. **Hidde Ploegh** (The Whitehead Institute for Biomedical Research, MIT, Cambridge, MA, USA): Studying host factors and their mechanism of function during influenza virus biogenesis centered on ubiquitylation.

## Funding

1. Role of Tsg101 in influenza virus infection (**Principal Investigator**; Research Grants Council/General Research Fund – Ends: 11/2018).
2. Role of Usp4 in T Cell Receptor-signaling (**Principal Investigator**; Seed Funding for basic research – Ends: 12/2018).

3. Targeting lipid droplet metabolism as therapeutic intervention during dengue virus infections (**Principal Investigator**; Health and Medical Research Fund – Ends: 06/2019).
4. Regulation of dengue virus life cycle by KDEL receptor-dependent signaling pathway: a new target to interfere with viral infection and pathogenesis (**Co-Investigator**; Health and Medical Research Fund – Ends: 08/2019).
5. Mechanism of OtuB1 mediated regulation of influenza virus infection (**Principal Investigator**; Research Grants Council/General Research Fund – Ends: 12/2019).
6. A chemical proteomics-based strategy for target discovery in flavivirus infections (**Principal Investigator**; Health and Medical Research Fund – Ends: 09/2020).
7. Regulation of the intracellular life cycle of influenza A virus by E3 ubiquitin ligase Mgrn1 (**Co-Investigator**; Health and Medical Research Fund – Ends: 06/2020).
8. Host lipid metabolism as a potential target for Zika antiviral therapy (**Co-Investigator**; Health and Medical Research Fund – Ends: 09/2020).
9. Croucher Foundation (**Principal Investigator**; Ends: 02/2020).
10. Viral Host and Environmental Determinants of Influenza virus transmission and pathogenesis (**Co-investigator**; Research Grants Council/ Theme-based Research Scheme – Ends: 12/2019).
11. Broad-spectrum inhibition of RNA virus infections by targeting virus-triggered autophagy (**Principal Investigator**; Boehringer Ingelheim collaborative fund; pending approval).

# Personnel

| Name | Position |
|---|---|
| Sumana SANYAL | Assistant Professor |
| Mingyuan LI | Postdoctoral Fellow |
| Yun LAN | Postdoctoral Fellow |
| Tami ZHANG | Postdoctoral Fellow |
| Lewis SIU | Research Technician |
| Akhee Sabiha JAHAN | PhD Student (graduated November 2018) |
| Ho Him WONG | PhD Student |
| Julian Ho | Mphil Student |
| Joao POMBO | MPhil Student (graduated November 2018) |
| Qiwen TEO | MPhil Student |
| Lynn CHEN | Research Assistant |
| Trupti Shivaprasad NAIK | Research Assistant |
| Hiu Wah CHAN | Student Intern (Institute of Vocational Education) |
| Mike Zi Xi DAI | Student Intern (Hong Kong University Science and Technology) |
| Martin KAMPMANN | Student Intern (University of Heidelberg, Germany) |
| Marie LACLIDE | Student Intern (University of Bordeaux, France) |
| Sophie VAN LEUR | Student Intern (Erasmus Medical Center, Rotterdam, The Netherlands) |
| Karen Wai Sze CHAN | Executive Assistant |

## 3.3 Hein Min TUN LAB

### Main Objectives and Strategy

Our group uses conventional microbiology and molecular biology techniques, cutting-edge sequencing technologies, coupled with bioinformatics, statistical and epidemiological approaches to study the composition, function, and dynamics of human and animal microbiomes in health and diseases, and to monitor antimicrobial resistance (AMR) bacteria and resistome in humans, animals, and the environment using holistic One Health approach. Our goal is to contribute in improving scientific understanding on roles of microbiome and AMR in public health.

### *The impact of early-life antibiotic exposure on infant gut microbiome and resistome*

Neonates are exposed to antibiotics both before and after birth, often empirically due to risk factors for infection. Surprisingly limited data is available on the impact of early life antibiotics in the harboring antibiotic resistance (AR) genes by the gut microbiota. proof-of-concept study was employed to examine the impact of early life exposure to antibiotics on the gut resistome of 3 months old infants. Among ten randomly selected infants, five infants were e xposed to antibiotics/antifungal either at birth or during their first 3 months of life. History for antibiotic exposure was obtained from hospital records and/or questionnaires. Fecal samples were collected at 3 months for genomic DNA extraction and followed by shotgun metagenomics sequencing. Sequence data were subjected to quality check, trimming and then annotation based on AR genes database (CARD). The gut metagenome of infants harbored diverse AR genes mainly genes involved in RND, ABC, and MFS efflux pumps, tetracycline resistant, beta-lactams resistant, and polymyxin resistant. However, unsupervised clustering of AR genes population showed a clear separation between antibiotic-exposed infants and antibiotic-naïve infants, with the exception that an infant with rehospitalisation history, and one with history of antifungal use are clustered into high AR gene abundance group although they did not receive antibiotics. Moreover, the relative abundance of AR genes was significantly higher in the infant group which mostly had exposed to antibiotics in their early life ($P<0.01$). Our study indicated that early life exposure to antimicrobial drugs contributes selective pressure for the development of resistance genes. The presence of AR genes in antibiotic-naïve infants also suggested that the acquisition of antimicrobial resistance can be impacted by maternal and environmental microbes during and after delivery.

### *Antimicrobial resistant E. coli recovered from aero- and hydro-environment*

Antimicrobial resistance (AMR) is a threat to public and animal health on the global scale. The origin of the genes associated with resistance has long been unknown. Recently, there is a growing body of evidence demonstrating that environmental bacteria are resistant to a multitude of antibiotic substances and that this environmental reservoir of AMR is still growing. The analysis of the genomes of bacterial pathogens indicates that they have acquired their resistance profiles by incorporating different genetic elements through horizontal gene transfer. The ancestors of pathogenic bacteria, as well as the origin of resistance determinants, lay most likely in the environmental microbiota. Indeed, there is some evidence that at least some clinically relevant resistance genes have originated in environmental bacterial species. Thus, feasible measures are required to reduce the risks posed by AMR genes and resistant bacteria that occur in the environment. Our study aims to demonstrate antimicrobial resistant (AMR) phenotypes of E. coli isolated from air-

conditioner and seawater as a preliminary data to strengthen environmental surveillance of AMR bacteria. Dust samples from air conditioner (n=12) and seawater samples (n=6) were collected and subjected for E. coli isolation. Briefly, swabs from air conditioning filter and seawater filtrated membranes were pre-enriched with buffer peptone water (BPW) prior to isolation of Enterobacteriaceae on MacConkey agar and followed by specific identification of E.coli-on selective Eosin-Methylene Blue (EMB) agar. Identified E.coli- were tested for antimicrobial susceptibility using Kirby-Bauer Disk Diffusion method according to Clinical and Laboratory Standard Institude (CLSI) guideline. A total of 12 antimicrobial agents including ampicillin (AMP), chloramphenicol (CHP), ciprofloxacin (CIP), norfloxacin (NOR), tetracycline (TET), gentamicin (GEN), amoxycillin-clavulanate (AMC), tobramycin (TOB), ceftaxidime (CAZ), cafaxitin (FOX), azithromycin (AZM), and meropenem (MEP) were examined in this study. A total of 12 E.coli isolates were identified and tested for antimicrobial susceptibility. 91.6% of isolates (n=??) were phenotypically resistant to at least one antimicrobial compound and six resistance patterns were found. AMP resistant was the most prevalent resistant pattern, found in 50% of isolates, follow by AMP & TET resistance (16.6%). Three isolates showed resistant to at least three types of antimicrobial agents, thus they can be considered as Multidrug resistance (MDR) E. coli. Surprisingly, one out of three MDR isolates conferred resistance to MEP together with other antimicrobial agents such as AMP, AMC, TOB, CAZ, FOX, and AZM. Since MEP is the antimicrobial agent which is uncommon for outpatient uses, and related to hospital. This suggested the possible dissemination of hospital-related AMR bacteria in the environment. Our findings suggested that surveillance of AMR bacteria in Hong Kong's environment should be considered as an approach in One Health initiative of AMR surveillance.

### *Effects of exclusive breastfeeding on infant gut microbiota across populations: A Meta-analysis*

Previous studies on the differences in gut microbiota between exclusively breastfed (EBF) and non-EBF infants have provided highly variable results. Here we perform a meta-analysis of seven microbiome studies (1825 stool samples from 684 infants) to compare the gut microbiota of non-EBF and EBF infants across populations. In the first 6 months of life, gut bacterial diversity, microbiota age, relative abundances of Bacteroidetes and Firmicutes, and predicted microbial pathways related to carbohydrate metabolism are consistently higher in non-EBF than in EBF infants, whereas relative abundances of pathways related to lipid metabolism, vitamin metabolism, and detoxification are lower. Variation in predicted microbial pathways associated with non-EBF infants is larger among infants born by Caesarian section than among those vaginally delivered. Longer duration of exclusive breastfeeding is associated with reduced diarrhea-related gut microbiota dysbiosis. Furthermore, differences in gut microbiota between EBF and non-EBF infants persist after 6 months of age. Our findings elucidate some mechanisms of short and long-term benefits of exclusive breastfeeding across different populations. This is a multi-institutional collaborative research effort.

## Publications

1. Drall KM, **Tun HM**, Kozyrskyj AL (2018) Commentary: The influence of proton pump inhibitors on the fecal microbiome of infants with gastroesophageal reflux-a prospective longitudinal interventional study. *Front Cell Infect Microbiol* **8**:430.

2. Ho NT, Li F, Lee-Sarwar KA, **Tun HM**, Brown BP, Pannaraj PS, Bender JM, Azad MB, Thompon AL, Weiss ST, Azcarate-Peril MA, Litonjua AA, Kozyrskyj AL, Jaspan HB, Aldrovandi GM, Kuhn L (2018) Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations. *Nat Commun* **9**:4169.
3. Obiakor VC, **Tun HM**, Bridgman SL, Arrieta M, Kozyrskyj AL (2018) The association between early life antibiotic use and allergic disease in young children: recent insights and their implications. *Expert Rev Clin Immunol* **14**:841-855.
4. Tun MH, **Tun HM**, Mahoney JJ, Konya TB, Guttman DS, Becker AB, Mandhane PJ, Turvey SE, Subbarao P, Sears MR, Brook JR, Lou W, Takaro TK, Scott JA, Kozyrskyj AL, CHILD Study Investigators (2018) Postnatal exposure to household disinfectants, infant gut microbiota and subsequent risk of overweight in children. *CMAJ* **190**:E1097-E1107.

## Awards, Seminars, and Invited Lectures

1. Hein Min Tun (2018) School of Public Health, Nanjing Medical University, Nanjing, PR China.
2. Hein Min Tun (2018) BGI-Research, Shenzhen, PR China.
3. Hein Min Tun (2018) Guangzhou Medical University, PR China.
4. Hein Min Tun (2018) Pasteur Institute of Ho Chi Minh City, Vietnam.
5. Hein Min Tun (2018) Gut Health Congress: Asia, Hong Kong SAR.
6. Hein Min Tun (2018) University of Alberta, Edmonton, Canada.

# Presentations at Meetings

1. Kang LJ, Tun HM, Oberlander TF, Becker AB, Azad MB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL (2018) Maternal prenatal depressive symptoms, serotonergic antidepressant use and alterations to infant gut microbiota. *7th International Human Microbiome Congress* (IHMC 2018), Killarney, Ireland (**Poster**).
2. Poonsuk K, On H, Chan CL, Tun HM (2018) Antimicrobial resistant *E. coli* recovered from aero- and hydro- environments. Regional Symposium on AMR, Fighting AMR – Partnerships in Action, Hong Kong, Hong Kong SAR (**Poster**).
3. Tun HM, Konya T, Chari R, Field CJ, Guttman DS, Becker AB, Azad MB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL (2018) Delayed gut microbiota maturation during infancy is associated with food sensitization in children. *7th International Human Microbiome Congress* (IHMC 2018), Killarney, Ireland (**Poster**).

4. Tun HM, Tamana S, Chari R, Field CJ, Guttman DS, Becker AB, Azad MB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL (2018) Association between the infant gut microbiome and cognitive development in a general population. *7th International Human Microbiome Congress* (IHMC 2018), Killarney, Ireland (**Poster**).
5. Tun HM, Shum MHH, Lam TTY, Kozyrskyj AL (2018) Early life antibiotic exposure and infant gut resistome. *Institut Pasteur International Network Symposium*, Paris, France (**Oral**).

## Teaching

1. Hein Min Tum (2018) C3BI Courses: Introduction to Molecular Phylogenetics, HKU-Pasteur Research Pole, The University of Hong Kong, Hong Kong SAR (*Lecturer and Tutor*).

## Collaborations

1. Anita Kozyrskyj (Department of Paediatrics, University of Alberta, Edmonton, Canada): Gut microbiota maturation during infancy.
2. John Penders (Department of Medical Microbiology, Maastricht University, Maastricht, The Netherlands): Antimicrobial dissemination in international travellers.
3. Tanja Sobko (School of Biological Sciences, University of Hong Kong, Hong Kong SAR): Impact of nature connectedness on gut microbiome and mental health of children.

## Funding

1. Intergenerational transmission of antimicrobial resistance and microbiome during labour at home vs hospital: a proof-of-principle study (**Principal Investigator**; Calmette & Yersin Intra-Pasteur Network Grant – Ends: Dec/2019).
2. Unwanted souvenirs for Hong Kong travelers: a prospective epidemiological approach to study the emergence and dissemination of antimicrobial resistance (**Principal Investigator**; Seed Funding for basic research – Ends: 04/2020).
3. Cross-sectional study of antimicrobial use pattern, antimicrobial resistant pathogen and bacterial genomic association in urinary tract infection patients.(**Co-Investigator**; Seed Funding for basic research – Ends: 06/2021).
4. Bacterial carriage in the upper respiratory tract among community healthy subjects in Hong Kong and Guangzhou (**Co-Investigator**; Seed Funding for basic research – Ends: 01/2021).
5. Bacterial carriage in the upper respiratory tract among community healthy subjects in Hong Kong and Guangzhou (**Co-Investigator**; Enhanced New Staff Start-up Research Grant – Ends: 01/2021).

6. Childhood infections and pollution (CHIP): a UCL-HKU one health technology enabled citizen science approach to better manage and prevent infections in children in Jaipur's urban slums (**Co-Investigator**; HKU-UCL Strategic Partnership Fund – Ends: Dec/2019).
7. Antimicrobial resistance comprehensive etiology Study (ACES) (**Co-Principal Investigator**; Research Grants Council/Research Impact Fund – Ends: 06/2022).
8. Understanding aspects of common, complex chronic diseases in urban households: FAMILY Cohort. (**Co-Investigator**; Health and Medical Research Fund Commissioned Research – Ends: 06/2020).

# Personnel

| Name | Position |
|---|---|
| Hein Min TUN | Research Assistant Professor |
| Kanchana POONSUK | Postdoctoral Fellow |
| Darren Chak Lun CHAN | Research Assistant |
| Sylvian GHO | Student Intern (Erasmus Medical Center, Rotterdam, The Netherlands) |
| Hilda ON | Student Intern (Institute of Vocational Education) |

# 3.4 Sophie VALKENBURG Lab

## Main Objectives and Strategy

The main objectives of the lab are to define immune correlates of protection for influenza viruses from infection and vaccination. Our research is centered on the role of protective heterologous T and B cell immunity in mouse and human systems, by investigating novel vaccines and immune correlates of protection for influenza. Our primary focus is to study adaptive immunity to influenza, and how this could be harnessed and optimized by vaccination to improve protection from diverse influenza virus infection. Hemagglutinin (HA)-specific antibodies can block influenza infection, whilst T cells recognize influenza-infected cells. A vaccine which ultimately combines antibody and T cell based immunity for influenza will provide a full-proof immunological barrier to influenza infection, which our studies will ultimately help develop. Our major research projects, which aim to elucidate how cross-reactive T and B cell responses to influenza provide broad immunity, are listed below.

### *Broadly reactive influenza vaccines in mouse models*

A vaccine that is broadly protective against different strains and subtypes of influenza is needed in lieu of the current seasonal vaccine that requires yearly update and is not protective against pandemic or outbreak strains.

**(a) *A T-cell based universal vaccine:*** In collaboration with Leo LM Poon at HKU, and Liyange Perera and Thomas Waldmann at NIH, our group is determining the mechanism of protection of a Vaccinia Wyeth vaccine vector encoding 5 influenza proteins, HA, NA, NP and Matrix 1 and 2 proteins, with a molecular IL-15 adjuvant to enhance vaccine memory responses, termed Wyeth/5Flu/IL-15. The vaccine has been highly effective in mice providing protection against avian, pandemic and seasonal strains of influenza. The vaccine elicits effective influenza-specific T cell memory responses that establish early local T cell responses upon influenza challenge, significantly reducing viral lung titers and thus survival. Importantly, depletion of T cell subsets showed that memory CD4 T cell responses were necessary for vaccine mediated protection, an under-appreciated role of helper subset. The vaccine is being further investigated to determine the role T cell mediated immune pressure may play in viral escape for future vaccine strategies.

**(b) *An HA-stem based vaccine:*** In collaboration with Leo LM Poon at HKU. The HA protein contains a stem region with conserved conformational epitopes that are relatively conserved between different influenza strains, leading to the induction of broadly neutralizing antibodies that recognize influenza viruses of different subtypes, in some cases groups (group 1 or 2) or even both influenza A and B viruses. Using a protein minimization technique, the Varadarajan lab at the Indian Institute of Science developed an HA-mini stem recombinant protein vaccine that mimics the pre-fusion native form of the HA protein by utilizing a trimerization motif, Foldon. HA-stem specific antibodies are also assessed across vaccine our studies using this HA-stem mini-protein, such as the effect of adjuvant on seasonsal vaccination on older adults and mouse models.

### *Human correlates of protection from influenza*

**(a) *Protective pre-existing T cell responses*:** Whilst T cell responses have been shown to be highly effective in mediating protection in mouse models, corresponding data in human influenza infection is not as robust. All adults have established influenza-specific

memory T cell responses; however, we have repeated infections during our lifetime that can range from mild to life threatening. The half-life of T cell memory and cross reactivity may explain the variability in protection from repeated infection. In collaboration with Benjamin Cowling (School of Public Health at HKU), we aim to determine the correlation between higher baseline early effector T cell memory responses and protection from influenza infection or reduced symptom severity and viral shedding in a household transmission setting. Blood samples are obtained from infected index cases, and uninfected household contacts that are monitored for influenza transmission, at day 0 and day 28. The aim of the study is to find if there is an immunological difference between contacts positive and negative for influenza transmission during sampling. Sample collection has been ongoing since June 2013 due to the limited and specific nature of cases and intensity of monitoring households.

**(b) *ADCC avian cross-reactivity:*** H7N9-specific antibodies eliciting antibody-dependent cellular toxicity (ADCC) have been found from the blood of healthy unexposed adults, and therefore ADCC antibodies must target conserved epitopes of the HA protein. In collaboration with Joe Wu (School of Public Health at HKU), the level of H1 and H7-specific ADCC antibodies is being probed in a large community cohort study, using archived serum from Red Cross blood collection. This model was extended in to a mouse model of peptide vaccination to assess ADCC peptide mediated protection from lethal influenza challenge.

**(c) *Enhanced influenza vaccines for the susceptible elderly:*** The 2015 Northern hemisphere winter influenza season had excess mortality in over 65 year olds due to vaccine mismatch between the H3N2 circulating strain and vaccine strain (A/Texas/50/2012). The updated vaccine containing the A/Switzerland/9715293/2013 virus became available after the peak of the influenza season. In collaboration with Yat Hang Tam (School of Public Health at HKU), the benefit of re-vaccinating the elderly in establishing H3N2-Switzerland specific T and B cell and ADCC responses is being assessed by comparing subjects who received one dose of the updated vaccine versus two doses of vaccine. Further immune correlates such as the subjects HLA background and IgG subclasses is now being tested.

## Publications


1. **Valkenburg SA**, Li OTW, Li A, Bull M, Waldmann TA, Perera LP, Peiris M, Poon LLM (2018) Protection by universal influenza vaccine is mediated by memory CD4 T cells. *Vaccine* **36**:4198-4206.
2. Clemens EB, van de Sandt C, Wong SS, Wakim LM, **Valkenburg SA** (2018) Harnessing the Power of T Cells: The Promising Hope for a Universal Influenza Vaccine. *Vaccines* (*Basel*) **6**:pii:E18.
3. **Valkenburg SA**, Leung NHL, Bull MB, Yan LM, Li APY, Poon LLM, Cowling BJ (2018) The Hurdles From Bench to Bedside in the Realization and Implementation of a Universal Influenza Vaccine. *Front Immunol* **9**:1479.
4. Tam YH, **Valkenburg SA**, Perera RAPM, Wong JHF, Fang VJ, Ng TWY, Kwong ASK, Tsui WWS, Ip DKM, Poon LLM, Chau CKV, Barr IG, Peiris JSM, Cowling BJ (2018) Immune Responses to Twice-Annual Influenza Vaccination in Older Adults in Hong Kong. *Clin Infect Dis* **66**:904-912.

5. Nguyen THO, Sant S, Bird NL, Grant EJ, Clemens EB, Koutsakos M, **Valkenburg SA,** Gras S, Lappas M, Jaworowski A, Crowe J, Loh L, Kedzierska K (2018) Perturbed $CD8^+$ T cell immunity across universal influenza epitopes in the elderly. *J Leukoc Biol* **103**:321-339.

## Awards, Seminars, and Invited Lectures

1. Sophie Valkenburg (2018) St Jude Children's Research Hospital, Memphis, TN, USA.
2. Sophie Valkenburg (2018) CDC Atlanta, GA, USA.
3. Sophie Valkenburg (2018) Chinese Vaccinology Course, University of Chinese Academy of Sciences, Gates Foundation.

## Presentations at Meetings

1. Valkenburg SA, Kavian NT, Li APY i, Leung NHL, Poon LLM, Cowling BJ (2018) ADCC antibodies correlate with reduced infection in a household model of influenza transmission. *Keystone Symposia: Framing the response to emerging infectious diseases,* Hong Kong, Hong Kong SAR (**Oral**).
2. Valkenburg SA, Wang Y, Li APY, Fang VJ, Leung NHL, Ip DKM, Chu D, Perera RAPM, Peiris JSM, Poon LLM, Cowling BJ (2018) Determining baseline CMI and ADCC immune correlates in a household model of influenza transmission. *CEIRS Annual meeting*, New York, USA (**Oral**).
3. Valkenburg SA, Kavian NT, Li APY i, Leung NHL, Poon LLM, Cowling BJ (2018) ADCC antibodies correlate with reduced infection in a household model of influenza transmission. *5th European Congress of Immunology*, Amsterdam, The Netherlands (**Poster**).

## Teaching

1. Sophie Valkenburg (2018) $10^{th}$ HKU-Pasteur Immunology Course, The University of Hong Kong, Hong Kong SAR (*Director, Tutor and Course Committee*).
2. Sophie Valkenburg (2018) "Biological Basis of Disease" (Master of Public Health, CMED-6227), School of Public Health, The University of Hong Kong, Hong Kong SAR (*Lecturer*).
3. Sophie Valkenburg (2018) Croucher Summer Course: Vaccinology for Public Health and Clinical Practice in the 21st century, The University of Hong Kong, Hong Kong SAR (*Tutor*).
4. Sophie Valkenburg (2018) Research Integrity workshop for Postgraduate students (GRSC6031/MMPH7101, May 2018), The University of Hong Kong, Hong Kong SAR (*Lecturer*).
5. Sophie Valkenburg (2018) Health Research Project , The University of Hong Kong, Hong Kong SAR (*Tutor*).

## Collaborations

1. **Benjamin Cowling** (School of Public Health, The University of Hong Kong, Hong Kong SAR): Determining the correlation between baseline T cell responses and protection from transmission in a household transmission setting; Longitudinal impact of repeat vaccination in the Hong Kong Elderly.
2. **Leo LM Poon** (School of Public Health, The University of Hong Kong, Hong Kong SAR): Broadly reactive influenza vaccines in mouse models.
3. **Ragahavan Varadarajan** (Indian Institute of Science, Bangalore, India): Characterization of a headless-trimeric pre-fusion conformation HA recombinant protein vaccine in a mouse model to generate broadly reactive HA-stem antibodies.
4. **Joseph Wu** (School of Public Health, The University of Hong Kong, Hong Kong SAR): Probing ADCC antibody responses towards avian influenza viruses in the community.
5. **Yat Hang Tam** (School of Public Health, The University of Hong Kong, Hong Kong SAR): Two-dose vaccine immune effect in elderly for the H3N2-mismatch.
6. **Liyange Perera and Thomas Waldmann** (NIH, NAID, Bethesda, USA): Vaccinia vector H5N1 vaccine for broad T cell responses, with an emphasis on CD4 mediated heterologous protection.
7. **Katherine Kedzierska** (The University of Melbourne, Australia): Mutation rates in T cell epitopes during infection and human T cell responses towards influenza.

## Funding

1. Influenza virus escape is the double-edged sword of effective T cell immunity (**Principal Investigator**; RGC Seed Funding for basic research – Ends: 10/2018).
2. Research on the epidemiology, vaccine effectiveness and treatment of influenza and other respiratory viruses in Southeast Asia and the Western Pacific (**Co-Investigator**; US Center for Disease Control – Ends: 07/2021).
3. Detection and characterization of antibody-dependent cell-mediated cytotoxicity (ADCC) responses against human H7N9 virus in humans and mice (**Co-Investigator**; Health and Medical Research Fund – Ends: 04/2018).
4. Influenza viruses adapt to escape T cell responses (**Principal Investigator**; General Research Fund/Research Grants Council – Ends: 12/2020).
5. Influenza ADCC-antibody responses in vaccination and infection of children as a correlate of protection (**Principal Investigator**; Health and Medical Research Fund – Ends: 08/2020).
6. Repeated elderly influenza vaccination and establishing cellular immune responses (**Co-Investigator**; CEIRS NIH – Ends: 08/2019).
7. Repeated elderly influenza vaccination and underlying factors contributing to antibody quality and cellular immunity (**Co-Investigator**; CEIRS NIH – Ends: 08/2020).

8. The protective role of antibody effector functions for influenza in mice and humans (**Principal Investigator**; General Research Fund/Research Grants Council – Ends 12/2021).

# Personnel

| Name | Position |
|---|---|
| Sophie VALKENBURG | Research Assistant Professor |
| Niloufar KAVIAN | Post-doctoral fellow |
| Athena LI | PhD Student |
| Maireid BULL | MPhil Student |
| Jodi CHAN | Research Assistant |
| Carolyn COHEN | Research Assistant |
| Asmaa HACHIM | Research Assistant |
| Jordan CHUNG | Student Intern (Brunel University, London, UK) |
| Matthew KHONG | Student Intern (LKS Faculty of Medicine) |

# 3.5 Jimmy Chun Cheong LAI

## Main Objectives and Strategy

The main objective of my research is to study the interactions between viruses with the host receptors, in order to have a better understanding of viral host adaptation and tissue tropism. Main projects include the study of influenza virus-cell receptor interactions at the atomic level by a combination of chemical, biochemical and cell biological methods; and the investigation of the interplay between different influenza surface proteins during viral infection. In addition, in collaboration with the department of clinical oncology of HKU and QIMR Berghofer Medical Research Institute in Australia, we are performing a clinical trial to evaluate effectiveness of adoptive immunotherapy as treatment of nasopharyngeal carcinoma (NPC), which is caused by a combination of environmental, genetic and viral factors, being often linked to Epstein–Barr virus (EBV) infection. In 2018, we have summarized and published our exploration of the basis of influenza receptor specificity and the role O-linked sialylated glycans in influenza viral infection. We found that O-glycans are important receptors for some influenza strains, which challenges the dogma that N-glycans are the predominant cell receptor for influenza viruses. We characterized the role of HA-receptor bindings on the level of NA activity and the NA-substrate specificity.

### *Study of influenza virus-host receptor*

The objective of this project is to obtain a better understanding of the influenza viral tropism. Sialic acids are known to be the receptor molecules of influenza viruses, but the diversity of sialylated glycans is not equivalent in different animal species and organs. Therefore, it is likely that the interactions between influenza viral proteins and different sialylated glycans are involved in the viral adaptation to the host and one possible mechanism underlying species jump, e.g. from avian to human. In our study, we have produced influenza virions or virus-like particles (VLP) of different influenza subtypes. The interactions between hemagglutinin (HA), neuraminidase (NA) and a variety of sialylated glycans are being investigated using chemical methods. Functional studies of the virions are also carried out on cell/tissue cultures.

### *Interplays between influenza surface proteins in cell receptor interactions*

Influenza HA and NA are two major glycoproteins both interacting with sialic acid receptors at the cell surface. It has been long recognized that a balance between HA receptor-binding and NA receptor-cleaving functions is important for influenza virulence and transmission. However, interplays between the two viral proteins have not been clearly defined. In this project we aim to investigate the role of HA-receptor binding properties on the NA functions. The effect of HA inactivation on NA enzymatic activity will be tested with replication-competent virions. VLPs containing NA with or without corresponding HA will also be produced for the comparison of their NA activities.

### *Immunotherapy against nasopharyngeal carcinoma*

The aim of the project is to develop an effective immunotherapy treatment against Epstein-Barr virus (EBV)-associated nasopharyngeal carcinoma (NPC), which, differently from Western countries, is endemic in southern China, including Hong Kong. EBV is present in virtually all poorly differentiated and undifferentiated nonkeratinizing NPC (type II and III, according to the WHO classification), making the viral antigens expressed by tumor cells attractive targets for immunotherapy. Our strategy is to generate LMP/EBNA1-specific T

**cells from PBMC isolated from NPC patients using an adenoviral vector. The safety and efficacy of expanded T cells can be assessed upon adoptive CTL infusion as immunotherapy.**

## Publications


1. Mayr J, Lau K, **Lai JC**, Gagarinov I, Chan RW, von Itzstein M, Nicholls JN, Haselhorst T (2018) Unraveling the role of O-glycans in influenza A virus infection. *Sci Rep* **8**:1-12.
2. **Lai JC**, Karunarathna HM, Wong HH, Peiris JS, Nicholls JN (2019) Neuraminidase activity and specificity of influenza A virus are influenced by haemagglutinin-receptor binding. *Emerg Microbes Infect* **8**:327-338.


## Collaborations

1. **Xuechen Li** (Department of Chemistry, The University of Hong Kong): Molecular determinants of influenza virus tropism and binding; expertise in glycan synthesis, to produce glycans of interest as influenza receptor analogues.
2. **Guang Zhu** (Division of Life Science, The University of Hong Kong Science and Technology): Access to equipment and technical support regarding NMR spectroscopy.
3. **Mark von Itzstein and Thomas Haselhorst** (Institute for Glycomics, Griffith University, Australia): Study of O-linked sialylated glycans and synthesis of O-glycans analogue.
4. **Michael Chan** (School of Public Health, The University of Hong Kong): Comparison of native influenza virus and virus-like-particles in their receptor-binding properties using the *ex vivo* human culture model.
5. **Dora Kwong** (Department of Clinical Oncology, The University of Hong Kong ong): Clinical trials of immunotherapy against EBV-associated NPC.
6. **Rajiv Khanna** (Department of Immunology, Queensland Institute of Medical Research, Australia): Immunotherapy against EBV and technology transfer to develop methods of T cells expansion.

## Funding


1. Viral, Host and Environmental Determinants of Influenza Virus Transmission and Pathogenesis (**Co-Investigator**; RGC Theme-based Research Scheme – Ends: 12/2019).
2. Immunotherapy against nasopharyngeal carcinoma (**Co-Investigator**; Ester Lee and Chew Pik Foundation, Croucher Foundation and other donors – Ends: open).

# 3.6 Barbara GAYRAUD-MOREL (Visiting Scientist from the Institut Pasteur, Paris)

## Main Objectives and Strategy

### *Consequences of influenza infection on skeletal muscles*

Part of this research is related to skeletal muscle function, which is relevant to the subject of her work at the Institut Pasteur, in the Stem Cell and Development laboratory directed by Shahragim Tajbakhsh. This project aims to explore the consequences of respiratory virus infections on skeletal muscles and muscle stem cells in particular. This work is at the interface between my expertise about skeletal muscle biology and infectious diseases studied at HKU-PRP. The project relies on collaboration between HKU-PRP and several laboratories: Leo Poon (The University of Hong Kong), Tom Cheung (Hong Kong University of Science and Technology), Shahragim Tajbakhsh (Institut Pasteur, Paris). In August 2018, BGM ended her 3 years of attachment as Visiting Scientist at HKU-PRP and returned to the Stem Cells Unit at the Institut Pasteur. These 3 years (2015-2018) have allowed developing a fruitful collaboration between the two laboratories, broadening the scope and enhancing the impact of the HKU-Pasteur partnership. Our data led to interesting and surprising findings. First, we found that skeletal muscle stem cells respond to the systemic inflammation when mice are infected intranasally by the influenza virus. Within few days, they modulate their molecular properties, modify their repertoire of cell surface receptors, and have altered pathway signatures that are critical for maintenance of cellular quiescence and cell cycle entry. These results are striking and they open a new field of research that exposes physiological response of tissues and organs to pathogens. We are continuing this collaboration and a joint grant proposal has been submitted in the framework of the *Programmes transversaux de Recherche* scheme of the Institut Pasteur.

### *Establishment of a human lung epithelium derived from hESCs to study infectious diseases*

The second area of research aimed to establish a human lung epithelium model to study infectious diseases. For now, most experiments with influenza and other respiratory viruses are performed on cell lines more or less related to human epithelial lung cells. We aimed to take advantage of the growing human embryonic stem cell (hESC) and iPSC fields to establish a model of human lung epithelium to investigate respiratory infectious diseases. These past years, few laboratories have succeeded to generate efficient *in vitro* lung and airway epithelial cells from human pluripotent cells for applications in regenerative medicine, modeling lung diseases, or drug screening. To differentiate hESCs into pulmonary cells the Snoeck lab developed a protocol which consist in recapitulating embryonic stages of lung development by providing key signaling molecules (Activin A, BMP, FGF, Wnt...) in a sequential and controlled timing. Briefly, hESCs are induced into Definitive Endoderm (DE), and then specified to a more anterior foregut endoderm (AFE) fate. They are further directed to produce lung progenitors before being finally differentiated into mature epithelial cells (mostly distal type II alveolar epithelial cells). hESCs are also easily manipulated to perform editing (mutation, deletion, tagging) of genes relevant to biological questions concerning host-virus mechanisms of infection. The first attempts have been performed with hESCs, which are considered to be more homogeneous in their ability to proceed through differentiation. However, we aimed to apply such protocol to hiPSC lines that could be generated in the lab from patients more resistant or susceptible to influenza infection.

## Publications

1. **Gayraud-Morel** B, Le Bouteiller M, Commere PH, Cohen-Tannoudji M, Tajbakhsh S (2018) Notchless defines a stage-specific requirement for ribosome biogenesis during lineage progression in adult skeletal myogenesis. *Development* **145**. pii: dev162636.

2. Formicola L, Pannérec A, Correra RM, **Gayraud-Morel** B, Ollitrault D, Besson V, Tajbakhsh S, Lachey J, Seehra JS, Marazzi G, Sassoon DA (2018) Inhibition of the Activin Receptor Type-2B Pathway Restores Regenerative Capacity in Satellite Cell-Depleted Skeletal Muscle. *Front Physiol* **9**:515.
3. Chal J, Al Tanoury Z, Oginuma M, Moncuquet P, Gobert B, Miyanari A, Tassy O, Guevara G, Hubaud A, Bera A, Sumara O, Garnier JM, Kennedy L, Knockaert M, **Gayraud-Morel** B, Tajbakhsh S, Pourquié O (2018) Recapitulating early development of mouse musculoskeletal precursors of the paraxial mesoderm *in vitro*. *Development* **145**. pii: dev157339.
4. Castel D, Baghdadi MB, Mella S, **Gayraud-Morel** B, Marty V, Cavaillé J, Antoniewski C, Tajbakhsh S (2018) Small-RNA sequencing identifies dynamic microRNA deregulation during skeletal muscle lineage progression. *Sci Rep* **8**:4208.

## Collaborations

1. **Leo Poon** (School of Public Health, The University of Hong Kong, Hong Kong SAR).
2. **Thomas Cheung** (Division of Life Sciences, Hong Kong University of Science and Technology, Hong Kong SAR).
3. **Shahragim Tajbakhkh** (Institut Pasteur, Paris, France).

## Teaching

1. Barbara Gayraud-Morel (2018) Advances in Stem Cell Biology (*Tutor and Coordinator*).

# 3.7 Teaching and Education

## HKU-Pasteur Course Series

The main objective of our educational pillar is to further develop an advanced teaching program in life sciences that will train a highly selected group of students who will be at the forefront of biomedical research in their countries. Our courses are extremely competitive and comparable in quality to that of established benchmarks, such as EMBO and Cold Spring Harbor courses and, therefore, are solidifying the reputation of HKU-PRP and Hong Kong as the premier regional hub for biomedical education. In 2018 we have organized and co-organized five international courses, 4 in Hong Kong (Cell Biology, Immunology, Emerging Viral Infections, Introduction to Molecular Phylogenetics) and 1 in Ho Chi Minh City ,Vietnam (Epidemiology, Surveillance and Elimination of Viral Hepatitis). We received more than 300 applications from over 30 countries; 170 students with global geographic representation were selected for participation.

The **8th HKU-Pasteur Cell Biology Course** focused on proteomics based approaches to probe the cell biology underlying human diseases. With the advent of more sophisticated technology and instrumentation in mass spectrometry, a strong interest has emerged to assess and interrogate biology at the level of protein networks along with the more conventional genomic and transcriptomic approaches. The ability to determine changes at the protein level including post-translational modifications that dictate protein states and their corresponding function is revealing a new texture to biology. Both systems-wide as well as targeted proteomic strategies have proved critical for generating hypotheses in various cellular perturbations. Novel targets for drug development have emerged as a result of such methods that take into account active enzymatic states that can be specifically inhibited in the context of human pathologies. Hence a combination of genomic and transcriptomic approaches together with proteomics of cell biology has emerged as a holistic way to reveal how biological networks operate in normal physiology and human diseases. The program of the 8th HKU-Pasteur Cell Biology Course brought together scientific leaders in the integration of methods in biochemistry and mass spectrometry, spanning conventional to more advanced approaches, which enable the analysis of dynamic biological networks under normal physiology and during diseased states such as pathogen infection. The seminars, methods and technologies used during the course will highlight the power of using mass spectrometry and proteomics combined with quantitative analysis to probe signaling networks that are typically perturbed in various diseased states. We received 26 applications from 10 countries and selected 23 students (10 nationalities) coming from (in alphabetical order): Brazil (1), Canada (1), France (2), Hong Kong (14), India (1), Portuguese (1), PR China (1) and Tunisia (2). We acknowledge that there has been a progressive decrease in the number of applicants for this course series and are at a loss of fully understanding the underlying reasons, particularly considering that the 2018 edition focused on proteomics, which is one of the cutting-edge approaches to address in mechanistic fashion fundamental biological questions. The objective of the HKU-Pasteur Cell Biology course is to foster the development of this discipline, which is becoming the centerpiece of not just basic research, but also of studies that tackle a number of questions relevant to the quality of human life and public health. The HKU-Pasteur Cell Biology course has been approved by the Research Postgraduate Committee of HKU for inclusion in the coursework curriculum of MPhil/PhD students.

**The HKU-Pasteur Immunology Course**, an annual event that has become a reference for postgraduate students in immunology and life sciences from all over the world, reached a significant milestone with its 10th edition. We continued our exploration at the frontiers of quantitative immunology to describe the function of the immune system in health and disease. Individuals differ in many respects including in their response to stress and infection. While the question of human variability continues to be a focal point of scientific research, one of the big challenges to develop a precision medical care is to define the parameters (genetic, epigenetic or environmental) that constitute a "healthy" immune system. Lectures reviewd the ongoing transition from reductionist studies that have been the focus of number of studies based on the application of genetic approaches in animal models to a more integrated view of the physiology and pathology of the human immune system. Emphasis was placed on how biological function emerges from the interaction of multiple components in networks and pathways, how the construction of quantitative models permits predictions about systems behavior that can be tested experimentally, and how deep analysis of large-scale, multi-parameter data collection in humans can lead to identification of reliable biomarkers and bring insight into disease pathogenesis. We received 55 applications from 19 countries. We selected 24 students (11 nationalities) coming from (in alphabetical order): Australia (2), Bangladesh (1), France (1), Hong Kong (6), India (2), Italy (1), PR China (5), Singapore (3), Tunis (1) and United Kingdom (2). To celebrate the tenth birthday of the HKU-Pasteur Immunology Course we hosted a one-day Scientific Symposium with more than 100 persons in attendance. During this decade we received more than 500 applications and trained more than 200 students, who are now continuing their own professional careers in science, education, private sector and other venues. There were four sessions, featuring some of the brightest alumni of the course, who presented their current current work and personal paths, with two keynote lectures to open and close the day. **We thank the Pasteur Foundation Asia for its generous contribution to the 10th Anniversary Symposium**. The HKU-Pasteur Immunology course has been approved by the Research Postgraduate Committee of HKU for inclusion in the coursework curriculum of MPhil/PhD students.

## Additional teaching and training

We have co-organized with the Faculty Core Facility of HKU the first edition of the **Croucher Summer Course on Emerging Viral Infections**. This course series aims to address the grand challenges of containing emerging viral infections with an inclusive One- Health approach combining the fields of animal and human health. Recent epidemics (avian and pandemic influenza, chikungunya, SARS and MERS coronaviruses, Ebola, Zika virus etc.) have underscored not only the growing globalization of health issues, but also the intimate relationships among human health, animal health and our ecosystems. The course consisted of lectures and a practical workshop designed to challenge participants to prepare a short grant proposal addressing major research questions related to the human-virus interaction. Drawing examples from different viruses such as influenza, coronaviruses or arboviruses, lectures discussed how the environment, vectors and humans interact with the viruses and the main drivers contributing to their pathogenicity and transmissibility. Most of the speakers stayed for the whole week and actively discussed with the students during coffee breaks and lunches. We received 41 applications from 19 countries. We selected 24 students (14 nationalities) coming from (in alphabetical order): Australia (2), Bangladesh

(2), Burkina Faso (1), China (2), France (1), Germany (2), Hong Kong (3), Iran (1), Korea (1), Malaysia (1), Mexico (1), Netherlands (1), Philippines (1), Thailand (1), USA (1), Vietnam (2), Zimbabwe (1). The grant received by the Croucher Foundation will cover two additional courses in 2020 and 2022.

The **Public Health Workshop series at the Pasteur Institute of Ho Chi Minh City** is attracting increasing number of applications and has become a benchmark for a world-class training program for epidemiologists, researchers and public health officials in the region. The topic of the 2018 edition, organized in close partnership with the Pasteur Institute of Ho Chi Minh City, the School of Public Health at HKU and the International Network of Institut Pasteur, was "**Epidemiology, Surveillance and Elimination of Viral Hepatitis**". The WHO has emphasized the need for a global health sector strategy on viral hepatitis stems from the scale and complexity of the hepatitis pandemic, along with growing recognition of its massive public health burden and the huge opportunities for action. To date, few countries have seized these opportunities; action has tended to be fragmented and inadequate. The time has come for a strategy based on a public health approach that is concerned with preventing infection and disease, promoting health, and prolonging life among the population as a whole. This strategy aims to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized interventions and services that can readily be taken to scale and decentralized, including in resource-limited settings. The program discussed in critical fashion how to integrate viral hepatitis strategic activities and indicators within national health information systems and tools, including for outbreak surveillance, and monitoring and evaluation of the hepatitis response plan. The course was again oversubscribed and we selected 28 trainees (out of 86 applications) from 14 countries (in alphabetical order): Australia (2), Burkina Faso (1), Cambodia (2), China (1), Gambia (1), Indonesia (2), Korea (1), Lao PDR (1), Malaysia (1), Mongolia (1), Myanmar (3), Philippines (2), Thailand (3), Vietnam (7). The workshop provided basic theory of epidemiology of viral hepatitis, such as transmission and global distribution, as well as comparative analysis of health systems, and presented an update on normative guidance and tools on hepatitis surveillance and monitoring. Participants were trained about purpose and methods, optimizing screening strategies, risk reduction, management, data analysis for communication, and assessment of surveillance through interactive teaching carried out by expert faculty. Training sessions covered role of vaccines and antivirals to prevent and treat Hepatitis B disease and the key challenges that the health system is facing to achieve the goals of WHO 2030 Agenda for Sustainable Development, which include a vision of a world where viral hepatitis transmission is halted and everyone living with viral hepatitis has access to safe, affordable and effective care and treatment; and the elimination of viral hepatitis as a major public health threat by 2030. One of the assets of the course is its broad regional recruitment base of trainees, which is possible because it is entirely run in English. These week-long workshops have established the foundation of a top training program, based in the Pasteur Institute in Ho Chi Minh City, for epidemiologists working in research and public health in the region, in order to strengthen the ability to react to acute infectious threats. We are planning to organize thematic workshops on an annual basis to further enhance the visibility of this program in collaboration with colleagues in the School of Public Health at the University of Hong Kong, which allows assembling an international teaching team that includes local (Vietnamese) faculty and world-leading experts. An additional objective of this course series is to create a strong community of researchers, public health and

government staff and team leaders in South East Asia equipped with knowledge of best public health practices. Since 2012, when the first edition of this course series took place with the support of the French Regional Scientific Cooperation, we have received more than 500 applications and selected almost 200 applicants. We are keeping in contact with them through mails and advertisements and we have strong positive feed- backs from them. We plan to have a scientific meeting with some of the alumni in the future to celebrate the 10th anniversary of this course series. **The course series has been generously supported** from its inception by the **Regional Health Cooperation Office of the French Ministry of Foreign Affairs**. **We also thank the Pasteur Foundation Asia for its generous contribution** for the second consecutive year.

We have initiated in close **collaboration with the Center of Bioinformatics, Biostatistics and Integrative Biology (C3BI) of the Institut Pasteur** an additional targeted action around big data utilization, which takes into account the increasing demand for training in *omic* science. To contribute to, and to fully benefit from, opportunities in the emerging era of big data, we have held an **Introduction to Molecular Phylogenetics Course** in Hong Kong. This introductory course aimed to give the basic theoretical and practical concepts, best practices, and software necessary to start working on molecular phylogenetics and its applications to epidemiology. The course consisted of morning lectures followed by hands-on practical session in the afternoons for small groups of selected students working with their own data sets. Topics included: general principles for the inference, interpretation of trees, and application to infectious diseases; an introduction to the math behind the trees and evolutionary models; distance and parsimony methods; maximum likelihood and Bayesian methods, phylodynamics; branch supports, bootstrapping; selection of the best method and evolutionary model; tree dating, reconstructing and using character evolution; molecular epidemiology. We received almost 100 applications, confirming the growing interest for the field of bioinformatics. We selected a total of 56 students: 25 for the full course and 31 for theory sessions only, with an overwheleming majority being from Hong Kong. We are in talks with C3BI for a new course in 2020.

Besides their involvement in the HKU-Pasteur course series, the **Co-Directors and Group Leaders** at HKU-PRP are also teaching courses in the undergraduate and postgraduate curriculum and the Problem-Based Learning modules for MBBS students. HKU-PRP regularly hosts undergraduate/postgraduate students from overseas institutions for internships. In 2018 we welcomed seven international trainees for an internship period:

- Pedro FERNANDES GONCALVES from Institut Pasteur Paris, France
- Marie LACLIDE from Universite Bordeaux, France
- Martin KAMPMANN from Fakultat fur Biowissenschaften, Germany
- Sylvian GHO from Erasmus MC Rotterdam, The Netherlands
- Sophie VAN LEUR from Erasmus MC Rotterdam, The Netherlands
- Ida Lexin LIAN from Ngee Ann Polytechnic, Singapore
- Jordan CHUNG from Brunel University, London, United Kingdom

We continue our educational program for high school students from the French International School in Hong Kong and have hosted one for the week-long work experience laboratory placement. Moreover, four students from the Hong Kong Institute

of Vocational Education (IVE) have trained with us during the summer. We have partnered with IVE for many years and two of their students, after spending time in the lab, have previously joined HKU-PRP for MPhil research work. **This year Hilda ON received an award for "Outstanding Industrial Attachment Scholarship" for her work in the Tun lab**. Matthew Khong, a second year MBBS student, has continued his attachment to the Valkenburg lab for the second consecutive year.

- Oscar SAUTEDE Sautede from French International School
- Chun Kit CHAN from Institute of Vocational Education
- Hiu Wah CHAN from Hong Kong Institute of Vocational Education
- Chung Lam MAK from Hong Kong Institute of Vocational Education
- Hilda ON from Hong Kong Institute of Vocational Education
- Matthew Kawa KHONG from the LKS Faculty of Medicine at HKU
- Mike Zi Xi DAI from Hong Kong University of Science and Technology

## A decade of HKU-Pasteur Teaching Programs

HKU-PRP has pioneered a unique method in Hong Kong and in the region as we provide state of the art lectures and practical workshops in a "Master class" setting to outstanding students at the postgraduate and early postdoctoral level coming from countries with markedly different resources. Our alumni network demonstrates that this educational program helps intensify human and scientific links between HKU-PRP, the School of Public Health at HKU and the Institut Pasteur International Network, and will continue to attract to Hong Kong top scientists and highly motivated students. HKU-Pasteur courses are supported with external grants that are received, on a competitive basis, from Institut Pasteur International Network, the Li Ka Shing Faculty of Medicine at HKU, the French Consulate in Hong Kong and Macau and other private donations.

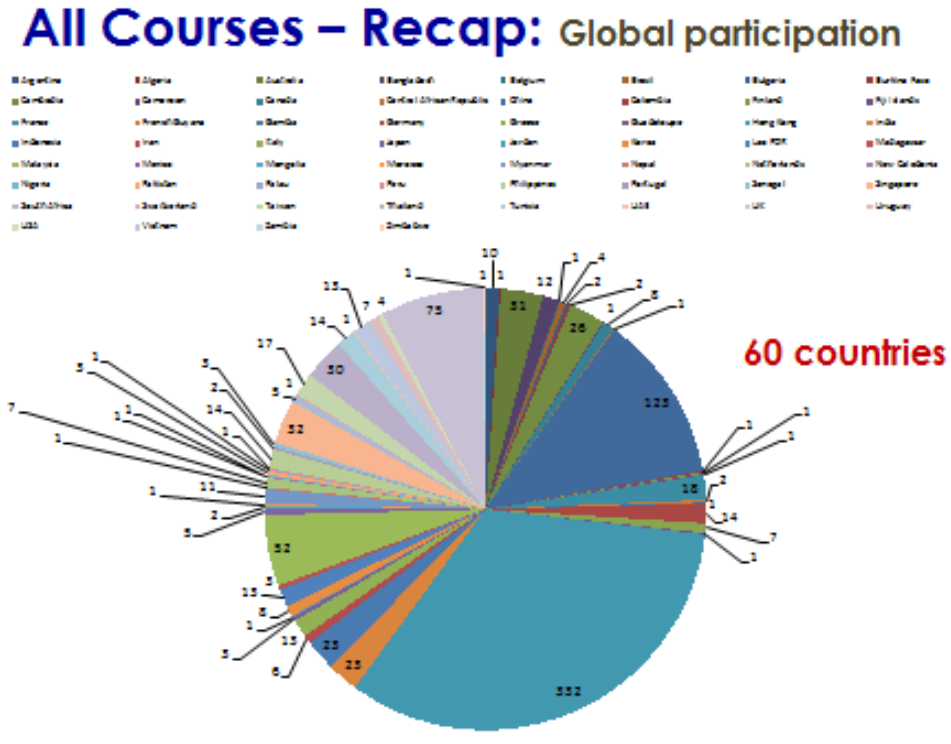



**Figure 1.** Geographical distribution of selected applicants of major courses organized by HKU-Pasteur (2009-2018).

Our budget covers advertising costs, travel and accommodation for all lecturers (except from industry). Selected students are expected to pay for their travel costs. Registration fees (HKD 1,500) include tuition, all course materials, accommodation (on sharing twin basis for overseas participants) and food (lunch and coffee breaks). Full reports of all events have been separately provided to the members of the HKU-PRP Advisory Committee. We have carried out a 10-year survey (2009-2018) of the training program at HKU-Pasteur, which over this decade has welcomed more than 1,000 students from 60 countries (**Figure 1**). The analysis clearly demonstrates the cost-effectiveness of our approach in comparison to the Croucher Summer Courses, which are entirely sponsored by the Croucher Foundation (**Figures 2-3**).

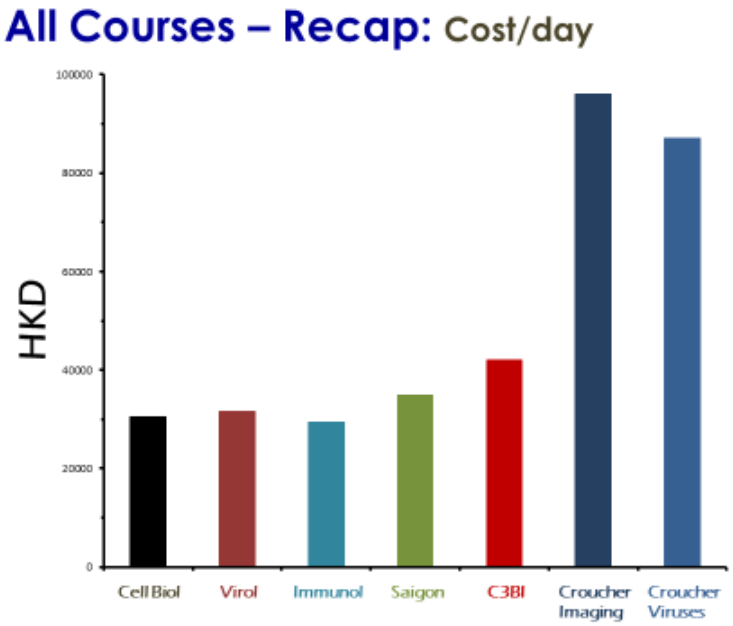



**Figure 2.** Comparative analysis of the cost/day of international courses organized by HKU-Pasteur (2009-2018).

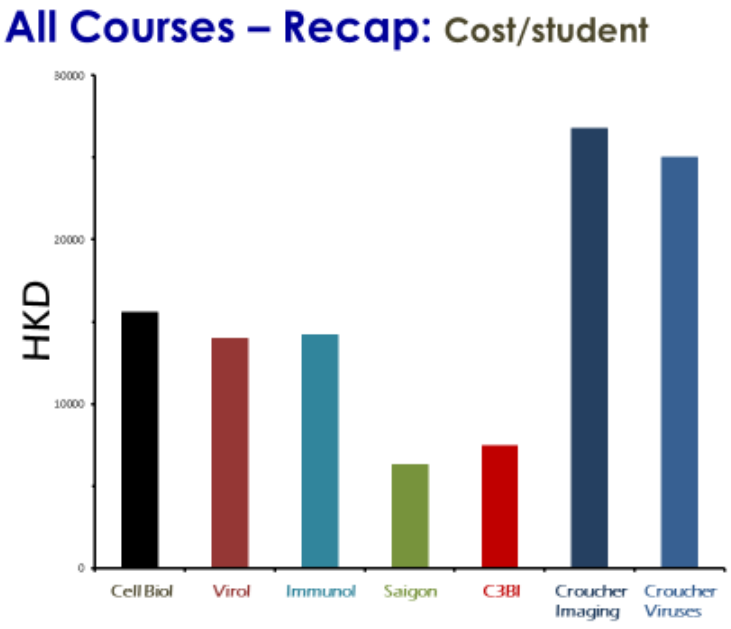



**Figure 3.** Comparative analysis of the cost/student of international courses organized by HKU-Pasteur (2009-2018).

## Complete list of taught and international courses

1. Roberto Bruzzone (2018) Molecular Biology of the Cell Course, Institut Pasteur, Paris, France (*Director*).
2. Roberto Bruzzone (2018) 8th HKU-Pasteur Cell Biology Course, The University of Hong Kong, Hong Kong SAR (*Director*).
3. Roberto Bruzzone (2018) 1st Croucher Summer Course on Emerging Viral Infections, The University of Hong Kong, Hong Kong SAR (*Director*).
4. Roberto Bruzzone (2018) 10th HKU-Pasteur Immunology Course, The University of Hong Kong, Hong Kong SAR (*Director*).
5. Roberto Bruzzone (2018) CMED6227 – Biological Basis of Disease (Master of Public Health), The University of Hong Kong, Hong Kong SAR.
6. Roberto Bruzzone (2018) Introduction to the Art and Science of Medicine, Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (*Tutor*).
7. Roberto Bruzzone (2018) Introduction to Molecular Phylogenetics, The University of Hong Kong, Hong Kong SAR (*Co-Organizer*).
8. Roberto Bruzzone (2018) Epidemiology, Surveillance and Elimination of Viral Hepatitis, Pasteur Institute of Ho Chi Minh City, Vietnam (*Director*).
9. Barbara Gayraud-Morel (2018) Advances in Stem Cell BiologyCourse, Institut Pasteur, Paris, France (*Tutor and Coordinator*).
10. Suki Lee (2017) Hematology and Immunology System – Problem Based Learning (MBBS Year 2), LKS Faculty of Medicine, The University of Hong Kong, Hong Kong SAR (*Tutor*).
11. Chris Mok (2018) 1st Croucher Summer Course on Emerging Viral Infections, The University of Hong Kong, Hong Kong SAR (*Director, Tutor and Course Committee*).
12. Chris Mok (2018) Introduction to the Art and Science of Medicine – Problem Based Learning (MBBS Year 1), The University of Hong Kong, Hong Kong SAR (*Tutor*).
13. Chris Mok (2018) Teaching course for Guangdong Center for Disease Control and Prevention, Guangzhou, PR China (*Lecturer*).
14. Malik Peiris (2018) Course Director, 1st Croucher Summer Course on Emerging Viral Infections, The University of Hong Kong, Hong Kong SAR.
15. Malik Peiris (2018) CMED6104 – Emerging infectious diseases: the "One Health" concept (Master of Public Health), The University of Hong Kong, Hong Kong SAR.
16. Sumana Sanyal (2018) Basic Metabolism (BSc Biochemistry Year 3 students) The University of Hong Kong, Hong Kong SAR.
17. Sumana Sanyal (2018) Essentials in Proteomics (BBMS Year 3) The University of Hong Kong, Hong Kong SAR.
18. Sumana Sanyal (2018) Recent Advances in Biotechnology (MMPH) The University of Hong Kong, Hong Kong SAR.
19. Sumana Sanyal (2018) Cancer Screening – Problem Based Learning (MBBS Year 4 students) The University of Hong Kong, Hong Kong SAR (*Tutor*).
20. Sumana Sanyal (2018) Introduction to the art and science of medicine – Problem Based Learning (MBBS Year 1 students) The University of Hong Kong, Hong Kong SAR (*Tutor*).

21. Sumana Sanyal (2018) Endocrine and Reproductive Systems – Problem Based Learning (MBBS Year II students) The University of Hong Kong, Hong Kong SAR (*Tutor*).
22. Sumana Sanyal (2018) 8th HKU-Pasteur Cell Biology Course, The University of Hong Kong, Hong Kong SAR (*Director, Lecturer and Tutor*).
23. Sophie Valkenburg (2018) 10th HKU-Pasteur Immunology Course, The University of Hong Kong, Hong Kong SAR (*Director, Tutor and Course Committee*).
24. Sophie Valkenburg (2018) "Biological Basis of Disease" (Master of Public Health), School of Public Health, The University of Hong Kong, Hong Kong SAR (*Lecturer*).
25. Sophie Valkenburg (2018) Croucher Summer Course: Vaccinology for Public Health and Clinical Practice in the 21st century, The University of Hong Kong, Hong Kong SAR (*Tutor*).
26. Sophie Valkenburg (2018) Research Integrity workshop for Postgraduate students (GRSC6031/MMPH7101, May 2018), The University of Hong Kong, Hong Kong SAR (*Lecturer*).
27. Sophie Valkenburg (2018) Health Research Project , The University of Hong Kong, Hong Kong SAR (*Tutor*).

# Complete list of interns

| | |
|---|---|
| Pedro Filipe FERNANDES GONCALVES | Institut Pasteur, Paris, France |
| Sylvian GHO | Erasmus Medical Center, Rotterdam, The Netherlands |
| Martin KAMPMANN | University of Heidelberg, Germany |
| Marie LACLIDE | University of Bordeaux, France |
| Sophie VAN LEUR | Erasmus Medical Center, Rotterdam, The Netherlands |
| Ida Lexin LIAN | Ngee Ann Polytechnic, Singapore |
| Jordan CHUNG | Brunel University, London, United Kingdom |
| Oscar SAUTEDE | French International School, Hong Kong SAR |
| Chun Kit CHAN | Institute of Vocational Education, Hong Kong SAR |
| Hiu Wah CHAN | Institute of Vocational Education. Hong Kong SAR |
| Chung Lam MAK | Institute of Vocational Education, Hong Kong SAR |
| Hilda ON | Institute of Vocational Education, Hong Kong SAR |
| Mike Zi Xi DAI | Hong Kong University of Science and Technology, Hong Kong SAR |
| Matthew Kawa KHONG | University of Hong Kong, Hong Kong SAR |

## 3.8 International Activity

HKU-PRP exerts a leadership role in a number of research and educational programs of global scope.

### International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)

Roberto Bruzzone has been on the Executive Committee of ISARIC since its official launching in 2012, Vice-Chair since 2014 and, in December of 2018 became the Interim Chair. ISARIC is a global consortium of over 50 clinical research networks with representatives in 111 countries, who are committed to working together to conduct world-class research on emerging infections to generate new knowledge to save lives. It exists because we all recognize the need for a rapid, coordinated and high quality clinical research response to epidemics. Over this period ISARIC has made a notable impact on the clinical research response to infectious diseases such as MERS-CoV and Ebola and has established itself as a well-known and key contributor to international outbreak research preparedness and response. The consortium mission is to ensure that clinical research is fully integrated and complementary to the 'public health' response in order to understand the causes of such infections and, how they develop and progress in patients, to identify the best treatment for individuals and prevent further transmission and hence save lives. ISARIC has played a major role in the Ebola virus crisis and has urged the deployment of alternative trial designs to fast-track the evaluation of new Ebola treatments. It has been involved in the coordination of two clinical trials in West Africa. ISARIC has assisted with the deployment of research on Zika virus and has set up a web site for shared resourced and information.

### Theme-based Research Scheme "Viral, host and environmental determinants of influenza virus transmission and pathogenesis"

Malik Peiris is the Coordinator of the Theme-based Research Scheme (TRS): "Viral, host and environmental determinants of influenza virus transmission and pathogenesis", which has been awarded a HK$75 million grant. The program addresses two outstanding "grand-challenge" research questions in influenza: i) the biological determinants of influenza virus transmission from animals-to-humans and from human-to-humans; and ii) the pathogenesis of severe influenza disease. The specific goals of the TRS are to:

- Understand the viral, host and environmental determinants of influenza virus transmission between humans, and from animals to humans;
- Understand the viral and host determinants of pathogenesis of severe influenza;
- Develop evidence based interventions to reduce transmission and novel therapeutic strategies targeting the host.

This research program, which promotes the implementation of the "One Health" concept to manage influenza risks, will end in 2019.

## Visiting Research Professors Scheme

Professor James Di Santo from the Institut Pasteur has been appointed as Visiting Professor in 2016 through the "Visiting Research Professors" scheme of the University Research Committee of HKU. James Di Santo is one of the leading scientists in the field of human innate immunity and his appointment has been an invaluable asset in building an even stronger program in human immunology. One of the tangible outcomes of his tenure has been the reinforcement of this strategic area of research with the signing of a Memorandum of Understanding between the LKS Faculty of Medicine of HKU and Institut Pasteur, to set up an interdisciplinary research center for immunology, infection and personalized medicine within the the framework of the Health@Inno scheme launched by the Hong Kong SAR government. The immune system is responsible for maintaining a healthy state and preventing infection in the majority of cases. However, dysfunction of the immune system can result in increased susceptibility to infections, inflammation, autoimmunity or even development of cancer in some individuals. Moreover, individual heterogeneity in the immune response can have an enormous impact on the likelihood to respond to therapy or the development of side effects secondary to vaccine administration. Thus, knowledge of these parameters in healthy humans, as envisaged in the Healthy Human Global Project (HHGP), is essential to establish personalized and precision medical care, and disease management. The project has been submitted to the Innovation and Technology Commission. James Di Santo plays also an active role in mentoring postgraduate students and early stage investigators involved in the project.

We have obtained additional funds through the PROCORE – France/Hong Kong Joint Research Scheme supported by the RGC to further explore the functions of human ILCs during the course of infection by respiratory pathogens.

## Other key actions

Malik Peiris continues to serve on a number of 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. He took part in the WHO Workshop "Efficacy trials of MERS-CoV Therapeutics and Vaccines: endpoints, trial design, site selection, held at WHO Headquarters in Geneva (30 November, 2018).

He was one of the co-organizers of the Keystone Symposium "Framing the Response to Emerging Virus Infections", which was held in Hong Kong, October 14-18, 2018. The symposium covered key themes, including the need to understand why zoonotic diseases matter, their association with agriculture, the importance of surveillance and early detection, and the difficulties of dealing with diseases that involve both medical and veterinary communities. The conference gathered experts in virology, immunology, vaccinology, epidemiology with those that seek to transfer knowledge between these groups, veterinarians, industry and government.

Other notable honors bestowed to Malik Peiris include the Allan Granoff Lecture at St Jude's Children's Research Hospital, Memphis, USA (June 2018) and the inivrtation to join the Scientific Advisory Boards of the Institut Pasteur (Paris, France) and the Peter Doherty Institute for Infection and Immunity at the University of Melbourne (Australia). Malik Peiris was named one of "Science stars of East Asia" by Nature magazine (https://www.nature.com/articles/d41586-018-05506-1).

# 4. Scientific Output

## 4.1 Publications


1. Babu TM, Perera R, Wu JT, Fitzgerald T, Nolan C, Cowling BJ, Krauss S, Treanor JT, Peiris M (2018) Population serologic immunity to human and avian H2N2 viruses in the United States and Hong Kong for pandemic risk assessment. *J Infect Dis* **218**:1054-1060.
2. Chan MC, Chan RW, Mok CK, Mak NK, Wong RN (2018) Indirubin-3'-oxime as an antiviral and immunomodulatory agent in treatment of severe human influenza virus infection. *Hong Kong Med J* **24** (Suppl 6):45-47.
3. Chu DKW, Hui KPY, Perera RAPM, Miguel E, Niemeyer D, Zhao J, Channappanavar R, Dudas G, Oladipo JO, Traoré A, Fassi-Fihri O, Ali A, Demissié GF, Muth D, Chan MCW, Nicholls JM, Meyerholz DK, Kuranga SA, Mamo G, Zhou Z, So RTY, Hemida MG,Webby RJ, Roger F, Rambaut A, Poon LLM, Perlman S, Drosten C, Chevalier V, Peiris M (2018) MERS coronaviruses from camels in Africa exhibit region-dependent genetic diversity. *Proc Natl Acad Sci USA* **115**:3144-3149.
4. Clemens EB, van de Sandt C, Wong SS, Wakim LM, Valkenburg SA (2018) Harnessing the power of T cells: The promising hope for a universal influenza vaccine. *Vaccines* (*Basel*) **6**:pii:E18.
5. Drall KM, Tun HM, Kozyrskyj AL (2018) Commentary: The influence of proton pump inhibitors on the fecal microbiome of infants with gastroesophageal reflux-a prospective longitudinal interventional study. *Front Cell Infect Microbiol* **8**:430.
6. Fan Y, Sanyal S, Bruzzone R (2018) Breaking bad: How viruses subvert the cell cycle. *Front Cell Infect Microbiol* **8**:396.
7. Guan W, Wu NC, Lee HHY, Li Y, Jiang W, Shen L, Wu DC, Chen R, Zhong N, Wilson IA, Peiris M, Yang Z, Mok CK (2018) Clinical correlations of transcriptional profile in patients infected with avian influenza H7N9 Virus. *J Infect Dis* **218**:1238-1248.
8. Herfst S, Mok CK, van den Brand JMA, van der Vliet S, Rosu ME, Spronken MI, Yang Z, de Meulder D, Lexmond P, Bestebroer TM, Peiris JSM, Fouchier RAM, Richard M (2018) Human clade 2.3.4.4 A/H5N6 influenza virus lacks mammalian adaptation markers and does not transmit via the airborne route between ferrets. *mSphere* **3**. pii: e00405-17.
9. Ho NT, Li F, Lee-Sarwar KA, Tun HM, Brown BP, Pannaraj PS, Bender JM, Azad MB, Thompon AL, Weiss ST, Azcarate-Peril MA, Litonjua AA, Kozyrskyj AL, Jaspan HB, Aldrovandi GM, Kuhn L (2018) Meta-analysis of effects of exclusive breastfeeding on infant gut microbiota across populations. *Nat Commun* **9**:4169.
10. Huang J, Liang W, Chen S, Zhu Y, Chen H, Mok CK, Zhou Y (2018) Serum cytokine profiles in patients with dengue fever at the acute infection phase. *Dis Markers* **2018**:8403937.
11. Lai JC, Karunarathna HM, Wong HH, Peiris JS, Nicholls JN (2019) Neuraminidase activity and specificity of influenza A virus are influenced by haemagglutinin-receptor binding. *Emerg Microbes Infect* **8**:327-338.
12. Lee SM, Yip TF, Yan S, Jin DY, Wei HL, Guo RT, Peiris JS (2018) Recognition of double-stranded RNA and regulation of interferon pathway by Toll-Like Receptor 10. *Front Immunol* **9**:516.

13. Li R, Yuan B, Xia X, Zhang S, Du Q, Yang C, Li N, Zhao J, Zhang Y, Zhang R, Feng Y, Jiao J, Peiris M, Zhong N, Mok CK, Yang Z (2018) Tree shrew as a new animal model to study the pathogenesis of avian influenza (H9N2) virus infection. *Emerg Microbes Infect* **7**:166. (*Co-corresponding authors)

14. Mak GCK, Kwan MY, Mok CK, Lo JYC, Peiris M, Leung CW (2018) Influenza A(H5N1) virus infection in a child with encephalitis complicated by obstructive hydrocephalus. *Clin Infect Dis* **66**:136-139.

15. Mayr J, Lau K, Lai JC, Gagarinov I, Chan RW, von Itzstein M, Nicholls JN, Haselhorst T (2018) Unraveling the role of O-glycans in influenza A virus infection. *Sci Rep* **8**:1-12.

16. Ng YP, Yip TF, Peiris JS, Ip NY, Lee SM (2018) Avian influenza A H7N9 virus infects human astrocytes and neuronal cells and induces inflammatory immune responses. *J Neurovirol* **24**:752-760.

17. Nguyen THO, Sant S, Bird NL, Grant EJ, Clemens EB, Koutsakos M, Valkenburg SA**,** Gras S, Lappas M, Jaworowski A, Crowe J, Loh L, Kedzierska K (2018) Perturbed $CD8^+$ T cell immunity across universal influenza epitopes in the elderly. *J Leukoc Biol* **103**:321-339.

18. Obiakor VC, Tun HM, Bridgman SL, Arrieta M, Kozyrskyj AL (2018) The association between early life antibiotic use and allergic disease in young children: recent insights and their implications. *Expert Rev Clin Immunol* **14**:841-855.

19. Pombo JP, Sanyal S (2018) Perturbation of cholesterol and fatty acid homeostasis during flavivirus infections. *Front Immunol* **9**:1276.

20. So RT, Perera RA, Oladipo JO, Chu DK, Kuranga SA, Chan KH, Lau EH, Cheng SM, Poon LL, Webby RJ, Peiris M (2018) Lack of serological evidence of Middle East respiratory syndrome coronavirus infection in virus exposed camel abattoir workers in Nigeria, 2016. *Euro Surveill* **23**:32.

21. Tam YH, Valkenburg SA, Perera RAPM, Wong JHF, Fang VJ, Ng TWY, Kwong ASK, Tsui WWS, Ip DKM, Poon LLM, Chau CKV, Barr IG, Peiris JSM, Cowling BJ (2018) Immune Responses to Twice-Annual Influenza Vaccination in Older Adults in Hong Kong. *Clin Infect Dis* **66**:904-912.

22. Tun MH, Tun HM, Mahoney JJ, Konya TB, Guttman DS, Becker AB, Mandhane PJ, Turvey SE, Subbarao P, Sears MR, Brook JR, Lou W, Takaro TK, Scott JA, Kozyrskyj AL, CHILD Study Investigators (2018) Postnatal exposure to household disinfectants, infant gut microbiota and subsequent risk of overweight in children. *CMAJ* **190**:E1097-E1107.

23. Valkenburg SA, Leung NHL, Bull MB, Yan LM, Li APY, Poon LLM, Cowling BJ (2018) The Hurdles From Bench to Bedside in the Realization and Implementation of a Universal Influenza Vaccine. *Front Immunol* **9**:1479.

24. Valkenburg SA, Li OTW, Li A, Bull M, Waldmann TA, Perera LP, Peiris M, Poon LLM (2018) Protection by universal influenza vaccine is mediated by memory CD4 T cells. *Vaccine* **36**:4198-4206.

25. Yip TF, Selim A, Ida Lian, Lee SMY (2018) Advancements in host-based interventions for influenza treatment. *Front Immunol* **9**:1547.

26. Zhang J, Lan Y, Li MY, Lamers MM, Fusade-Boyer M, Klemm E, Thiele C, Ashour J, Sanyal S (2018) Flaviviruses exploit the lipid droplet protein AUP1 to trigger lipophagy and drive virus production. *Cell Host Microbe* **23**:819-831.

27. Zhang N, Bao YJ, Tong AH, Zuyderduyn S, Bader GD, Peiris JS, Lok S, Lee SM (2018) Whole transcriptome analysis reveals differential gene expression profile reflecting macrophage polarization in response to influenza A H5N1 virus infection. *BMC Med Genomics* **11**:20.

28. Zhang J, Su R, Jian X, An H, Jiang R, Mok CK (2018) The D253N Mutation in the polymerase basic 2 gene in avian influenza (H9N2) virus contributes to the pathogenesis of the virus in mammalian hosts. *Virol Sin* **33**:531-537.

29. Zhang T, Xiao M, Wong CK, Mok KC, Zhao X, Ti H, Shaw PC (2018) Sheng Jiang San, a traditional multi-herb formulation, exerts anti-influenza effects in vitro and in vivo via neuraminidase inhibition and immune regulation. *BMC Complement Altern Med* **18**:150.

30. Zhao X, Li R, Zhou Y, Xiao M, Ma C, Yang Z, Zeng S, Du Q, Yang C, Jiang H, Hu Y, Wang K, Mok CK, Sun P, Dong J, Cui W, Wang J, Tu Y, Yang Z, Hu W (2018) Discovery of highly potent pinanamine-based inhibitors against amantadine- and oseltamivir-resistant influenza A viruses. *J Med Chem* **61**:5187-5198.

31. Jahan AS, Biquand E, Munoz R, Le Quang A, Mok CK, Wong HH, Teo Q, Doak S, Chin AWH, Poon LLM, te Velthuis A, García-Sastre A, Demeret C, Sanyal S (2019) OTUB1 functions as a ubiquitin sensor for RIG-I activation and is targeted for proteasomal degradation by Influenza A virus NS1. *Immunity* (under review).

32. Lai JC, Karunarathna HM, Wong HH, Peiris JS, Nicholls JN (2019) Neuraminidase activity and specificity of influenza A virus are influenced by haemagglutinin-receptor binding. *Emerg Microbes Infect* **8**:327-338.

33. Tang YS, Lo CY, Mok CK, Chan PK, Shaw PC (2019) The extended C-terminal region of influenza C nucleoprotein is important for nuclear import and RNP activity. *J Virol*, in press.

34. Wong HH, Sanyal S (2019) Viral strategies of manipulating autophagy to benefit infection. *Semin Cell Dev Biol (invited review).*

35. Wu NC, Lv H, Thompson AJ, Wu DC, Ng WWS, Kadam RU, Lin CW, Nycholat CM, McBride R, Liang W, Paulson JC, Mok CK, Wilson IA (2-19) Preventing an antigenically disruptive mutation in egg-based H3N2 seasonal influenza vaccines by mutational incompatibility. *Cell Host Microbe*, in press.

## 4.2 Presentations at Meetings

1. Guan W, Wu NC, Liang W, Peiris M, Yang Z, Mok CK (2018) Clinical correlated transcriptional signatures in severe patients with the infection of avian influenza (H7N9) virus. *The 2nd International Meeting on Respiratory Pathogens, The International Society for Influenza and Other Respiratory Virus Diseases*, Singapore (**Poster**).
2. Jahan A, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Oral**).
3. Kang LJ, Tun HM, Oberlander TF, Becker AB, Azad MB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL (2018) Maternal prenatal depressive symptoms, serotonergic antidepressant use and alterations to infant gut microbiota. *7th International Human Microbiome Congress* (IHMC 2018), Killarney, Ireland (**Poster**).
4. Lan Y, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Poster**).
5. Li MY, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Oral**).
6. Pombo J, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Poster**).
7. Poonsuk K, On H, Chan CL, Tun HM (2018) Antimicrobial resistant *E. coli* recovered from aero- and hydro- environments. Regional Symposium on AMR, Fighting AMR – Partnerships in Action, Hong Kong, Hong Kong SAR (**Poster**).
8. Teo Q, Sanyal S (2018) *Keystone Conference: Framing the response to emerging infectious diseases.* Hong Kong, Hong Kong SAR (**Poster**).
9. Sanyal S (2018) *Keystone Conference: Ubiquitin Signaling.* Tahoe City, USA (**Oral**).
10. Tun HM, Konya T, Chari R, Field CJ, Guttman DS, Becker AB, Azad MB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL (2018) Delayed gut microbiota maturation during infancy is associated with food sensitization in children. *7th International Human Microbiome Congress* (IHMC 2018), Killarney, Ireland (**Poster**).
11. Tun HM, Tamana S, Chari R, Field CJ, Guttman DS, Becker AB, Azad MB, Mandhane PJ, Moraes TJ, Sears MR, Turvey SE, Subbarao P, Scott JA, Kozyrskyj AL (2018) Association between the infant gut microbiome and cognitive development in a general population. *7th International Human Microbiome Congress* (IHMC 2018), Killarney, Ireland (**Poster**).
12. Tun HM, Shum MHH, Lam TTY, Kozyrskyj AL (2018) Early life antibiotic exposure and infant gut resistome. *Institut Pasteur International Network Symposium*, Paris, France (**Oral**).
13. Valkenburg SA, Kavian NT, Li APY i, Leung NHL, Poon LLM, Cowling BJ (2018) ADCC antibodies correlate with reduced infection in a household model of influenza transmission. *Keystone Symposia: Framing the response to emerging Infectious Diseases,* Hong Kong SAR (**Oral**).

14. Valkenburg SA, Wang Y, Li APY, Fang VJ, Leung NHL, Ip DKM, Chu D, Perera RAPM, Peiris JSM, Poon LLM, Cowling BJ (2018) Determining baseline CMI and ADCC immune correlates in a household model of influenza transmission. *CEIRS Annual meeting*, NYC, USA (**Oral**).
15. Valkenburg SA, Kavian NT, Li APY i, Leung NHL, Poon LLM, Cowling BJ (2018) ADCC antibodies correlate with reduced infection in a household model of influenza transmission. 5th European Congress of Immunology, Amsterdam, The Netherlands (**Poster**).

## 4.3 Seminars, Invited Lectures and Other Oral Presentations

1. Chris Mok (2018) 14th International Congress of Parasitology (ICOPA 2018), Daegu, South Korea.
2. Chris Mok (2018) Global Meeting on Avian Influenza East Asia Influenza Centre, Jeju, South Korea.
3. Chris Mok (2018) The Virus Research Symposium of Korea Research Institute of Bioscience and Biotechnology, Daejeon, South Korea.
4. Sumana Sanyal (Jan 2018) California Institute of Technology, Pasadena, USA.
5. Sumana Sanyal (Jan 2018) Whitehead Institute for Biomedical Research/Massachusetts Institute of Technology, USA.
6. Sumana Sanyal (May 2018) Karolinska Institutet, Stockholm, Sweden.
7. Sumana Sanyal (Sept-Nov 2018) Doris Zimmern HKU-Cambridge Visiting Fellowship, University of Cambridge, UK.
8. Sumana Sanyal (Sept 2018) Cambridge Institute of Medical Research, University of Cambridge, UK.
9. Sumana Sanyal (Oct 2018) Department of Pathology, University of Cambridge, UK.
10. Sumana Sanyal (Nov 2018) Sir William Dunn School of Pathology, University of Oxford, UK.
11. Sumana Sanyal (Dec 2018) Keynote speaker at the Annual Influenza Update Meeting, Emmanuel College, University of Cambridge, UK.
12. Hein Min Tun (2018) School of Public Health, Nanjing Medical University, Nanjing, PR China.
13. Hein Min Tun (2018) BGI-Research, Shenzhen, PR China.
14. Hein Min Tun (2018) Guangzhou Medical University, Guangzhou, PR China.
15. Hein Min Tun (2018) Institute Pasteur of Ho Chi Minh City, Ho Chi Minh City, Vietnam.
16. Hein Min Tun (2018) Gut Health Congress: Asia, Hong Kong, Hong Kong SAR.
17. Hein Min Tun (2018) University of Alberta, Edmonton, Canada.
18. Sophie Valkenburg (2018) St Jude Children's Research Hospital, Memphis, TN, USA.
19. Sophie Valkenburg (2018) CDC Atlanta, GA, USA.
20. Sophie Valkenburg (2018) Chinese Vaccinology Course, University of Chinese Academy of Sciences, Gates Foundation.

# 4.4 Active Grants in 2018

### *Calmette & Yersin Intra-Network Grant*

| | |
|---|---|
| Principal Investigator: | Dr Hein Min Tun |
| Amount: | €825 |
| Period: | 01/Nov/2018 to 31/Oct/2019 |

### *CEIRS NIH*

| | |
|---|---|
| Co-Investigator: | Dr Sophie Valkenburg |
| Amount: | USD273,234 |
| Period: | ending 08/2019 |

### *CEIRS NIH*

| | |
|---|---|
| Co-Investigator: | Dr Sophie Valkenburg |
| Amount: | USD250,000 |
| Period: | ending 08/2020 |

### *Center for Disease Control*

| | |
|---|---|
| Principal Investigator: | Prof Ben Cowling |
| Co-Investigator: | Dr Sophie Valkenburg |
| Amount: | HK$38,982,801 |
| Period: | ending Jul/2021 |

### *Health and Medical Research Fund (HMRF)*

| | |
|---|---|
| Principal Investigator: | Prof Leo Poon |
| Co-Investigator: | Dr Sophie Valkenburg |
| Amount: | HK$1,199,608 |
| Period: | 01/May/2016 to 30/Apr/2018 **(Closed)** |

### *Health and Medical Research Fund (HMRF)*

| | |
|---|---|
| Principal Investigator: | Dr Sumana Sanyal |
| Amount: | HK$1,200,000.00 |
| Period: | 01/Jul/2017 to 30/Jun/2019 |

### *Health and Medical Research Fund (HMRF)*

| | |
|---|---|
| Principal Investigator: | Dr Roberto Bruzzone/Dr Mingyuan Li |
| Amount: | HK$1,130,112.00 |
| Period: | 01/Sep/2017 to 31/Aug/2019 |

### *Health and Medical Research Fund (HMRF)*

| | |
|---|---|
| Principal Investigator: | Dr Roberto Bruzzone/Dr Yun Lan |
| Amount: | HK$1,184,712.00 |
| Period: | 01/Jul/2018 to 30/Jun/2020 |

*Health and Medical Research Fund (HMRF)*

Principal Investigator: Dr Chris Mok
Amount: HK$996,376.00
Period: 01/May/2018 to 30/Apr/2020

*Health and Medical Research Fund (HMRF)*

Principal Investigator: Dr Sumana Sanyal
Amount: HK$1,199,424.00
Period: 01/Sept/2018 to 31/Aug/2020

*Health and Medical Research Fund (HMRF)*

Principal Investigator: Dr Sophie Valkenburg
Amount: HK$1,187,554.00
Period: 21/Aug/2018 to 20/Aug/2020

*Health and Medical Research Fund (HMRF)*

Principal Investigator: Dr Tami Zhang/Dr Iolanthe Lan
Amount: HK$1,179,424.00
Period: 01/May/2018 to 30/Apr/2020

*HKU-UCL Strategic Partnership fund*

Principal Investigator: Prof Malik Peris
Co-Investigator: Dr Hein Min Tun
Amount: GBP20,000
Period: 07/Jan/2019 to

*Korea Research Institute of Bioscience and Biotechnology (KRIBB) Korea*

Collaborator: Dr Chris Mok
Amount: KRW 50,000,000.00
Period: 01/Aug/2018 to 31/Dec/2019

*National Natural Science Foundation of China*

Principal Investigator: Dr Zi Feng Yang
Co-Investigator: Dr Chris Mok
Amount: RMB1,500,000.00
Period: 01/Jan/2015 to 30/Apr/2018 **(Closed)**

*Research Grants Council*

Principal Investigator: Dr Sophie Valkenburg
Amount: HK$1,200,839.00
Period: 01/Jan/2018 to 31/Dec/2020

*Research Grants Council*

Principal Investigator: Dr Sumana Sanyal
Amount: HK$829,393.00
Period: 01/Jan/2018 to 31/Dec/2019

### *Research Grants Council*

Principal Investigator: Dr Sophie Valkenburg
Amount: HK$980,969.00
Period: 01/Jan/2019 to 31/Dec/2021

### *Research Grants Council (2018/19)*

Principal Investigator: Dr Suki Lee **(PI contract ended 31-Dec-2018)**
Amount: HK$953,377.00
Period: 01/Jul/2018 to 30/Jun/2020

### *Research Grants Council/Consulate General of France – PROCORE – France/Hong Kong Joint Research Scheme*

Principal Investigator: Dr Suki Lee
Amount: HK$30,600.00
Period: 01/Jan/2017 to 31/Dec/2018 **(Closed)**

### *Research Impact Fund (RIF)/RGC*

Principal Investigator: Prof Keiji Fukuda
Co-Principal Investigator: Dr Hein Min Tun
Amount: HK$14,000,000.00
Period: 30/June/2019 to 29/June/2022

### *RGC Seed Funding for Basic research*

Principal Investigator: Dr Suki Lee
Amount: HK$55,400.00
Period: 01/May/2017 to 30/Apr/2018 **(Closed)**

### *RGC Seed Funding for Basic research*

Principal Investigator: Dr Chris Mok
Amount: HK$44,320.00
Period: 01/May/2017 to 30/Apr/2019

### *RGC Seed Funding for Basic research*

Principal Investigator: Dr Sumana Sanyal
Amount: HK$80,470.00
Period: 01/Jun/2016 to 31/May/2018 **(Closed)**

### *Science Research Project of the Guangdong Province*

Principal Investigator: Dr Zi Feng Yang
Co-Investigator: Dr Chris Mok
Amount: RMB1,000,000.00
Period: 01/Jul/2016 to 30/Jun/2018 **(Closed)**

*Seed Funding for Basic research*

Principal Investigator: Dr Hein Min Tun
Amount: HK$148,000.00
Period: 01/Nov/2018 to 30/Apr/2020

*Seed Funding for Basic research*

Principal Investigator: Prof Keiji Fukuda
Co-Investigator: Dr Hein Min Tun
Amount: HK$66,570.00
Period: 30/June/2019 to 29/June/2021

*Seed Funding for Basic research*

Principal Investigator: Dr Sophie Valkenburg
Amount: HK$150,000.00
Period: 14/Oct/2016 to 13/Oct/2018 **(Closed)**

*Seed Funding for Basic research*

Principal Investigator: Dr Peng Wu
Co-Investigator: Dr Hein Min Tun
Amount: HK$66,570.00
Period: 07/Jan/2019 to 06/Jan/2021

*Viral, Host and Environmental Determinants of Influenza Virus Transmission and Pathogenesis*

Principal Investigator: Dr Suki Lee **(PI contract ended 31-Dec-2018)**
Amount: HK$1,100,000.00
Period: 01/Jan/2015 to 31/Dec/2019

*Viral, Host and Environmental Determinants of Influenza Virus Transmission and Pathogenesis*

Principal Investigator: Dr Chris Mok
Amount: HK$1,774,581.00
Period: 01/Jan/2015 to 31/Dec/2019

*Viral, Host and Environmental Determinants of Influenza Virus Transmission and Pathogenesis*

Principal Investigator: Dr Sumana Sanyal
Amount: HK$1,924,581.00
Period: 01/Jan/2015 to 31/Dec/2019

*Wonkwang University acting through Zoonosis Research Centre, Korea*

Collaborator: Dr Chris Mok
Amount: KRW 50,000,000.00
Period: 01/Sept/2018 to 31/Dec/2019

## 4.5 Pending Grant Applications

*Research Grants Council (2018/19)*

Principal Investigator: Dr Chris Mok
Amount: HK$1,188,520.00

*Research Grants Council (2018/19)*

Principal Investigator: Dr Sumana Sanyal
Amount: HK$1,200,000.00

*Research Grants Council (2018/19)*

Principal Investigator: Dr Hein Min Tun
Amount: HK$1,198,914.00

*Health and Medical Research Fund (HMRF) – Fellowship*

Principal Investigator: Dr Hein Min Tun
Amount: HK$1,090,000.00

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Chris Mok
Amount: HK$1,488,520.00

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Kan Poonsuk
Co-Investigator: Dr Hein Min Tun
Amount: HK$942,800.00

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Sumana Sanyal
Amount: HK$1,300,000.00

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Iolanthe Lan
Amount: HK$1,080,400.00

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Hein Min Tun
Amount: HK$1,127,144.00

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Sophie Valkenburg
Amount: HK$1,500,000

*Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Niloufar Kavian-Tessler
Amount: HK$1,500,000

### *Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Min Tun Hein
Amount: HK$1,090,000.00

### *Health and Medical Research Fund (HMRF) (2019/20)*

Principal Investigator: Dr Kanchana Poonsuk
Co-Investigator: Dr Hein Min Tun
Amount: HK$942,800.00

### *Health and Medical Research Fund (HMRF) Commissioned Research*

Principal Investigator: Dr Michael Ni
Co-Investigator: Dr Hein Min Tun
Amount: HK$9,000,000.00
Period: Pending

### *Horizon 2020 Call: H2020 – SC1-BHC-2018-2020*

Co- Investigator: Dr Hein Min Tun
Amount: €11,999,741.25

### *NIH R21 (2018/19)*

Principal Investigator: Dr Sophie Valkenburg
Amount: USD250,000 (resubmission 2019)

### *NSFC Excellent Yong Scientists Fund (Hong Kong and Macau)*

Principal Investigator: Dr Hein Min Tun
Amount: RMB1,300,000.00

### *Programmes Transversaux de Recherche Institut Pasteur – PTR 2019*

Co- Investigator: Dr Hein Min Tun
Amount: €32,000.00

# 5. Annexes

## 5.1 List of Staff

| *Name* | *Position* |
|---|---|
| BRUZZONE, Roberto | Co-Director |
| PEIRIS, Malik | Co-Director |
| DI-SANTO, James | Visiting Research Professor |
| TORDO, Noel | Honorary Professor |
| ZHAO, Jincu | Honorary Professor |
| SANYAL, Sumana | Assistant Professor (non-Clinical) |
| LEE, Man Yan Suki | Research Assistant Professor (Contract ended: 31-Dec-2018) |
| MOK, Ka Pun Chris | Research Assistant Professor |
| HEIN, Min Tun | Research Assistant Professor |
| VALKENBURG, Sophie | Research Assistant Professor |
| KAVIAN-TESSLER, Niloufar | Post-Doctoral Fellow |
| ZHANG, Jingshu Tami | Post-Doctoral Fellow (Contract ended: 31-Dec-2018) |
| LI, Mingyuan | Post-Doctoral Fellow |
| LAN, Yun | Post-Doctoral Fellow |
| POONSUK, Kanchana | Post-Doctoral Fellow |
| GAYRAUD-MOREL, Barbara | Honorary Research Associate |
| LI, Wai Sum Iris | Honorary Research Associate |
| LI, Ping Hung | Research Technician (Secondment ended: 31-Dec-2018) |
| SIU, Yu Lam Lewis | Research Technician |
| CHAN, Chak Lun Darren | Research Assistant |
| CHAN, Jodi | Research Assistant |
| CHEN, Lin Lynn | Research Assistant |
| COHEN, Carolyn | Research Assistant |
| HACHIM, Asmaa | Research Assistant |
| LYU, Tomas | Research Assistant |
| MA, Nok Lam Fionn | MPhil Student (Graduated: 31-Aug-2018)<br>Research Assistant (Starts: 01-Sept-2018) |
| NG, Wilson | Research Assistant |
| TRUPTI, Naik | Research Assistant |
| YIP, Tsz Fung | Research Assistant (Contract ends: 31-Dec-2019) |

| | |
|---|---|
| LI, Pui Yee Athena | PhD Student |
| AKHEE, Sabiha Jahan | PhD Student (Graduated: 31-Jul-2018)<br>Research Assistant (Starts: 01-Sept-2018) |
| BULL, Máiréid | PhD Student |
| WONG, Ho Him | Research Assistant<br>PhD Student (Starts: 01-Sept-2018) |
| HO, Julian | MPhil Student |
| POMBO, Joao | MPhil Student (Graduated: 30-Nov-2018) |
| SELIM Aisha | MPhil Student (Graduated: 31-Dec-2018) |
| TEO, Qi Wen | MPhil Student |
| YIP, Garrick | MPhil Student |
| CHUNG, Jordan | Student Intern (Brunel University London) |
| GHO, Sylvian | Student Intern (Erasmus MC Rotterdam) |
| VAN LEUR, Sophie | Student Intern (Erasmus MC Rotterdam) |
| KAMPMANN, Martin | Student Intern (University of Heidelberg) |
| SAUTEDE, Oscar | Student Intern (French International School) |
| KHONG, Kawa Matthew | Student Intern (HKU) |
| DAI, Zi Xi | Student Intern (HKUST) |
| CHAN, Chun Kit | Student Intern (IVE) |
| CHAN, Hiu Wah | Student Intern (IVE) |
| MAK, Chung Lam | Student Intern (IVE) |
| ON, Heilda | Student Intern (IVE) |
| LIAN, Lexin Ida | Student Intern (Ngee Ann Polytechnic) |
| LACLIDE, Marie | Student Intern (University of Bordeaux) |
| FERNANDES GONCALVES Pedro | Visiting Post-Doctoral Fellow (Institut Pasteur, Paris) |
| LI, Suk Yin Anne | Administration Manager |
| MULLER, Simon | Communication Officer<br>(International Volunteer of the French Ministry of Foreiogn Affairs) |
| LAI, Chun Cheong Jimmy | Post-Doctoral Fellow (Joint Appointment with Depart of Pathology)<br>Laboratory Manager (Starts: 01-10-2018) |
| CHAN, Wai Sze Karen | Executive Assistant |
| CHEUNG, Wai Sze | Laboratory Attendant |

## 5.2 Income & Expenses for the year ending 30 June 2018

### INCOME (HK$)

| | | | |
|---|---|---|---|
| Central Fund | c/f | 798,569.18 | |
| | | 3,736,082.50 | 4,534,651.68 |
| Faculty Matching Fund | c/f | 1,000,000.00 | |
| | | 625,000.00 | 1,625,000.00 |
| Institut Pasteur | c/f | 1,366,436.00 | |
| | | 3,483,043.43 | 4,849,479.43 |
| Private Donation | c/f | 0.00 | |
| | | 52,900.00 | 52,900.00 |
| **External Grants*** | c/f | 717,879.95 | |
| | | 4,255,006.13 | 4,972,886.08 |
| Teaching/Training | c/f | -(28,904.33) | |
| | | 381,719.95 | 352,815.62 |
| **TOTAL INCOME** | | | **HK$16,387,732.81** |

### EXPENSES (HK$)

| | | |
|---|---|---|
| Staff Cost | | |
| Central/IPP | 42% | 5,447,509.03 |
| External Grants | 15% | 1,920,953.52 |
| Research | 39% | 5,052,600.52 |
| Administration | 1% | 149,479.16 |
| Teaching/Training | 4% | 539,543.37 |
| **TOTAL EXPENSES** | | **HK$13,110,085.60** |

**Balance carry forward to 2018/2019 HK$3,277,647.21**

# External Grants 2017-2018 (HK$)

| | c/f | |
|---|---|---|
| **Suki Lee Team** | | |
| *PROCORE* France/HK Joint Research Grant | 12,240.00 | 24,480.00 |
| HKU-Internal Research Grant | 9,000.00 | 46,400.00 |
| Theme-based Research Scheme | 34,862.07 | 350,000.00 |
| **Chris Mok Team** | | |
| HKU-Internal Research Grant | 2,920.00 | 22,160.00 |
| HKU-Internal Research Grant | 0.00 | 23,000.00 |
| Donation | 11,088.79 | 31,000.00 |
| Theme-based Research Scheme | 62,796.31 | 447,700.00 |
| HMRF | 0.00 | 83,031.33 |
| **Sumana Sanyal Team** | | |
| HKU-Internal Research Grant | 37,204.10 | 36,920.00 |
| HKU-Internal Research Grant | 0.00 | 27,762.50 |
| Theme-based Research Scheme | 5,262.68 | 478,348.00 |
| GRF/RGC | 9,295.38 | 128,503.33 |
| GRF/RGC | 0.00 | 207,348.25 |
| Enchanced New Staff Funds | 0.00 | 54,285.71 |
| HMRF | 0.00 | 600,000.00 |
| HMRF | 0.00 | 470,915.00 |
| Croucher Start Up Funds | 48,611.11 | 116,666.67 |
| HMRF | 0.00 | 95,785.33 |
| BNP | 208,150.63 | 0.00 |
| Institut Pasteur – PTR | 28,799.89 | 155,524.66 |
| **Sophie Valkenburg Team** | | |
| HKU-Internal Research Grant | -(25,111.41) | 75,000.00 |
| HMRF | 135,085.68 | 199,965.60 |
| GRF/RGC | 0.00 | 300,209.75 |
| **Visiting Research Professor Scheme 2015-2016** | 137,674.72 | 250,000.00 |
| | **717,879.95** | **4,255,006.13** |

**TOTAL GRANTS INCOME** **HK$4,972,886.08**

## 5.3 Forecast for Income for the year ending 30 June 2019

## INCOME (HK$)

| | | | |
|---|---|---|---|
| Central Fund | c/f | 1,193,727.28 | |
| | | 3,595,698.25 | 4,789,425.53 |
| Faculty Matching Fund | c/f | 1,625,000.00 | |
| | | 1,375,000.00 | 3,000,000.00 |
| Institut Pasteur | c/f | 1,731,345.3. | |
| | | 366,892.48 | |
| Adjustment | | -(57,006.25) | 2,041,231.53 |
| Private Donation | c/f | 0.00 | |
| | | 450,000.00 | 450,000.00 |
| **External Grants*** | c/f | 1,492,799.71 | |
| | | 7,675,932.86 | 9,168,732.57 |
| Teaching/Training | c/f | 17,755.66 | |
| | | 821,729.27 | 839,484.93 |
| **TOTAL INCOME** | | | **HK$20,288,874.56** |

# External Grants (On-going)

| | c/f | |
|---|---|---|
| **Chris Mok Team** | | |
| HKU Internal Research Grant | -(15,580.00) | 18,460.00 |
| HKU Internal Research Grant | 23,000.00 | 0.00 |
| TRS | 145,031.18 | 793,700.00 |
| Donation | 42,088.79 | 0.00 |
| HMRF (2017) | 33,889.33 | 498,188.00 |
| Wonkwang University (Korea) | 0.00 | 343,499.19 |
| KRIBB (Korea) | 0.00 | 343,836.39 |
| **Sumana Sanyal Team** | | |
| HKU Internal Research Grant | -(11,940.70) | 55,525.00 |
| Seeding Fund | 0.00 | 56,000.00 |
| TRS | 262,675.48 | 596,641.00 |
| RGC (2017) | -(31,135.85) | 414,696.50 |
| Enchanced New Staff Funds | 54,285.71 | 108,571.43 |
| HMRF | 257,411.83 | 600,000.00 |
| HMRF | 3,475.40 | 565,056.00 |
| HMRF | 45,889.30 | 589,712.00 |
| HMRF | 0.00 | 483,093.30 |
| HMRF | 0.00 | 577,356.00 |
| Croucher Start up funds | 263,313.65 | 252,150.54 |
| **Sophie Valkenburg Team** | | |
| RGC(2017) | 126,734.53 | 400,279.66 |
| RGC(2018) | 0.00 | 163,494.83 |
| HMRF(2017) | 0.00 | 494,814.17 |
| **Hein Mun Tun Team** | | |
| HKU Internal Research Grant | 0.00 | 66,000.00 |
| Calmette & Yersin Intranetwork Travel Grant | 0.00 | 4,858.85 |
| **Visiting Research Professor Scheme** | 293,661.06 | 250,000.00 |
| | 1,492,799.71 | 7,675,932.86 |

**TOTAL GRANT INCOME** **HK$9,168,732.57**

## 5.5 8th HKU-Pasteur Cell Biology Course 2018

# 8th HKU- PASTEUR CELL BIOLOGY COURSE

## 14 - 23 March 2018

## HKU-Pasteur Research Pole, Hong Kong

## PUBLIC LECTURES

**19-Mar-2018**

09:00 - 11:00 "Contribution of the stroma secretome to tumour invasion"
by Dr Sara Zanivan, Cancer Research UK Beatson Institute, UK

11:30 - 12:30 "Proteomic methods to study the extracellular matrix composition of normal tissues and tumors"
by Dr Alexandra Naba, University of Illinois at Chicago, USA

13:30 - 14:30 "Application of "matrisomics" to human cancer"
by Dr Alexandra Naba, University of Illinois at Chicago, USA

**20-Mar-2018**

09:00 - 11:00 "Interrogating the Cell Biology of Infection and Immunity with Alpaca Nanobodies"
by Dr Florian Schmidt, University of Bonn, Germany

11:30 - 12:30 (Part 1)
13:30 - 14:30 (Part 2) "Proteomic and genetic approaches to viral evasion"
by Prof Paul Lehner, Cambridge Institute for Medical Research, UK

**21-Mar-2018**

09:00 - 11:00 "Quantitative multiplexed proteomics to investigate host-pathogen interactions"
by Prof Michael Weekes, Cambridge Institute for Research, UK

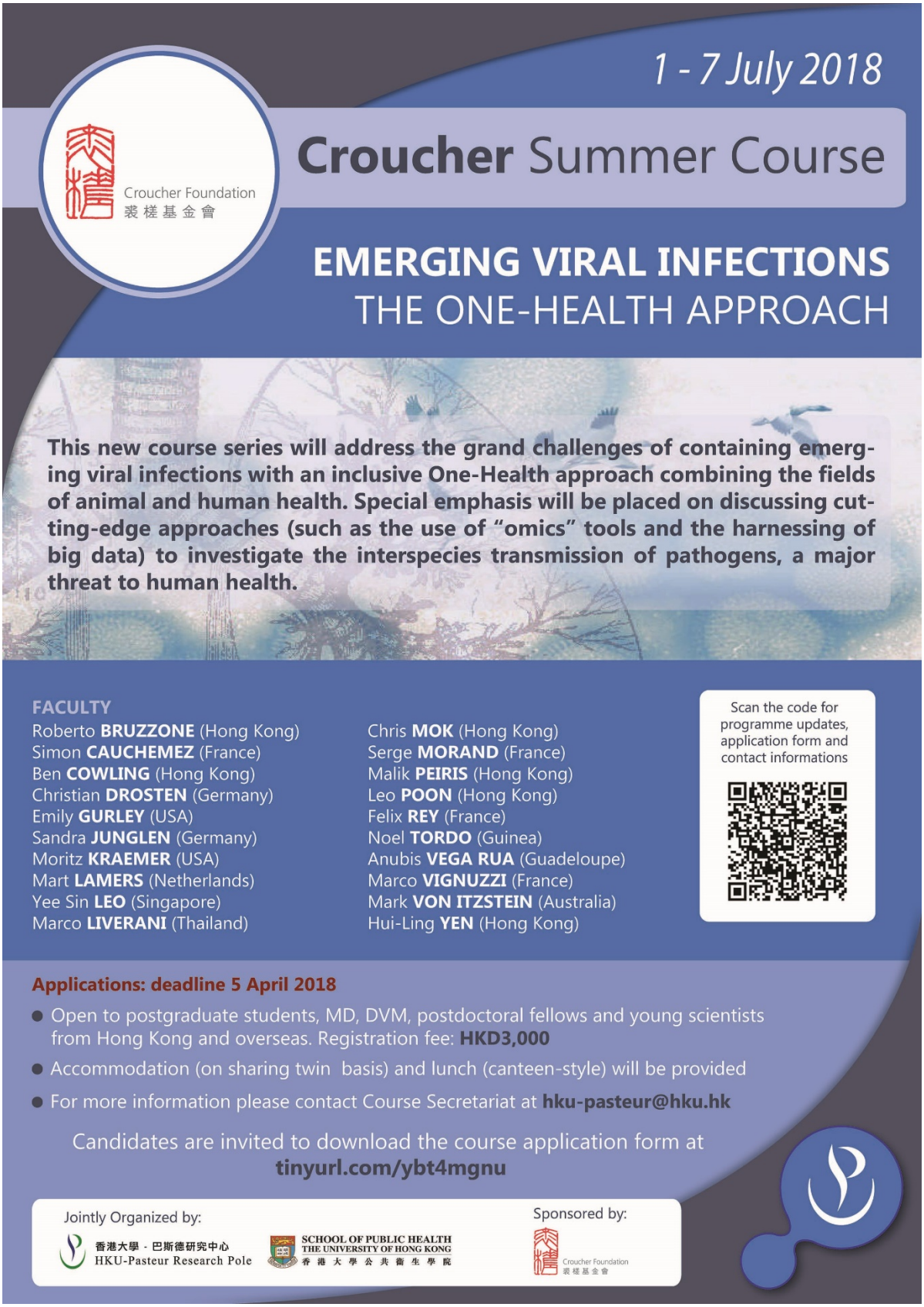
11:30 - 12:30 (Part 1)
13:30 - 14:30 (Part 2) "Chemical proteomic approaches to studying protien lipidation"
by Dr Remigiusz Serwa, Imperial College London, UK

Venue:
Rm 7-03, 7th Floor
HKJC Building for IR
5 Sassoon Road, Pokfulam

## ALL ARE WELCOME

International network Institut Pasteur
THE UNIVERSITY OF HONG KONG LI KA SHING FACULTY OF MEDICINE
香港大學李嘉誠醫學院
香港大學 · 巴斯德研究中心 HKU-Pasteur Research Pole
Institut Pasteur

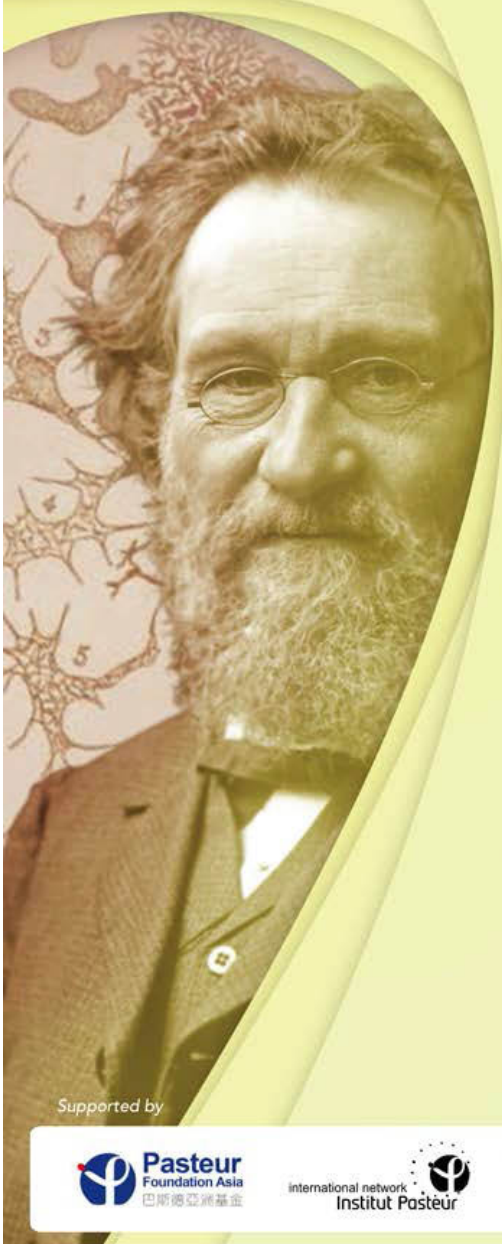
## 5.6 1st Croucher Summer Course
## Emerging Viral Infections: The One-Health Approach



## 5.7 10th HKU-Pasteur Immunology Course 2018

# 10th HKU Pasteur Immunology Course

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



## Quantitative Immunology

December 3-14, 2018

### Open Lectures

*December 3, 14:00-16:30 - HRI-S2*
Defining the determinants of a healthy immune response for a better understanding of disease - **Darragh Duffy, France**

*December 4, 09:00-12:00 - HRI-S2*
Modelling virus infections in vitro and in vivo - **Catherine Beauchemin, Canada**

*December 6, 09:00-12:00 - HRI-S2*
Dendritic Cell and Macrophage Biology: From Development to Functions - **Florent Ginhoux, Singapore**

*December 10, 09:00-12:00 - HRI-S2*
Developmental Options and Functional Plasticity of Innate Lymphoid Cells - **James Di Santo, France**

*December 11, 09:00-12:00 - HRI-S2*
Decoding Human B-Cell Responses to Pathogens with Monoclonal Antibodies - **Hugo Mouquet, France**

*December 12, 09:00-12:00 - HRI-S2*
High-dimensional cellular immune profiling in health and disease - **Evan Newell, Singapore**

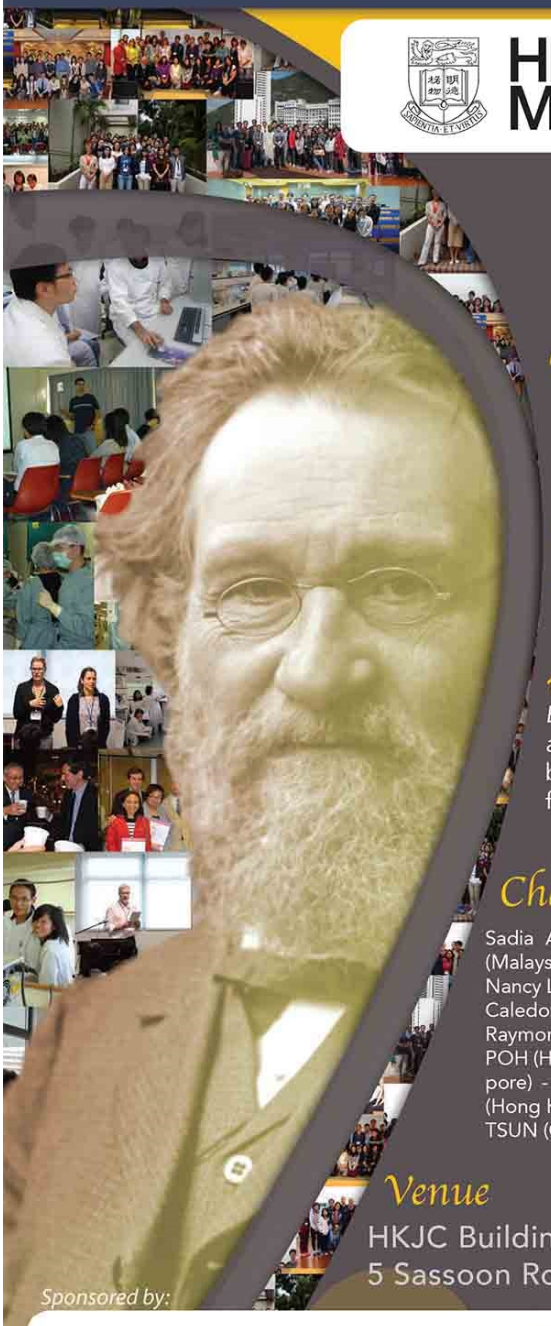
***December 14, 08:00-18:30- HRI-S3***
10th Anniversary Symposium

HKJC Building for Interdisciplinary Research
5 Sassoon Road, Pokfulam, Hong Kong

Supported by

Pasteur Foundation Asia 巴斯德亞洲基金
international network Institut Pasteur
DAKEWE
BioLegend®

# 10th HKU Pasteur Immunology Course



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

## Anniversary Symposium

### December 14, 2018

To celebrate the **10th Anniversary** of the **HKU-Pasteur Immunology Course**, we are delighted to welcome back our alumni for a world class symposium.

### Keynote Lectures

**9:20 - 10:00**
*Elie Metchnikoff and the birth of immunology*
by **Dr Jean-Marc Cavaillon,** Institut Pasteur, France

**16:40 - 17-20**
*Broad protection against influenza viruses by active and passive immunization*
by **Dr Kanta Subbarao**, The Peter Doherty Institute for Infection and Immunity, Australia

### Chairs and Speakers

Sadia AFRIN (USA) - Francisca ALMEIDA (Australia) - Ling Ling CHUA (Malaysia) - Claudio COUNOUPAS (Australia) - Regina HE (Hong Kong) - Nancy LEUNG (Hong Kong) - Sherene LIM (Malaysia) - Mariko MATSUI (New Caledonia) - Isabelle MEUNIER (Canada) - Diana MUMBAIWA (Australia) - Raymond NING (Hong Kong) - Mahen PERERA (Hong Kong) - Chek Meng POH (Hong Kong) - Gavin POON (Hong Kong) - Jaya SENIRAVATNE (Singapore) - Fernando SOUZA-FONSECA-GUIMARES (Australia) - Edwin TAM (Hong Kong) - Hyon-Xhi TAN (Australia) - Ooiean TENG (Singapore) - Andy TSUN (China) - Vincent VAGENENDE (Singapore) - Rachel YIU (Hong Kong)

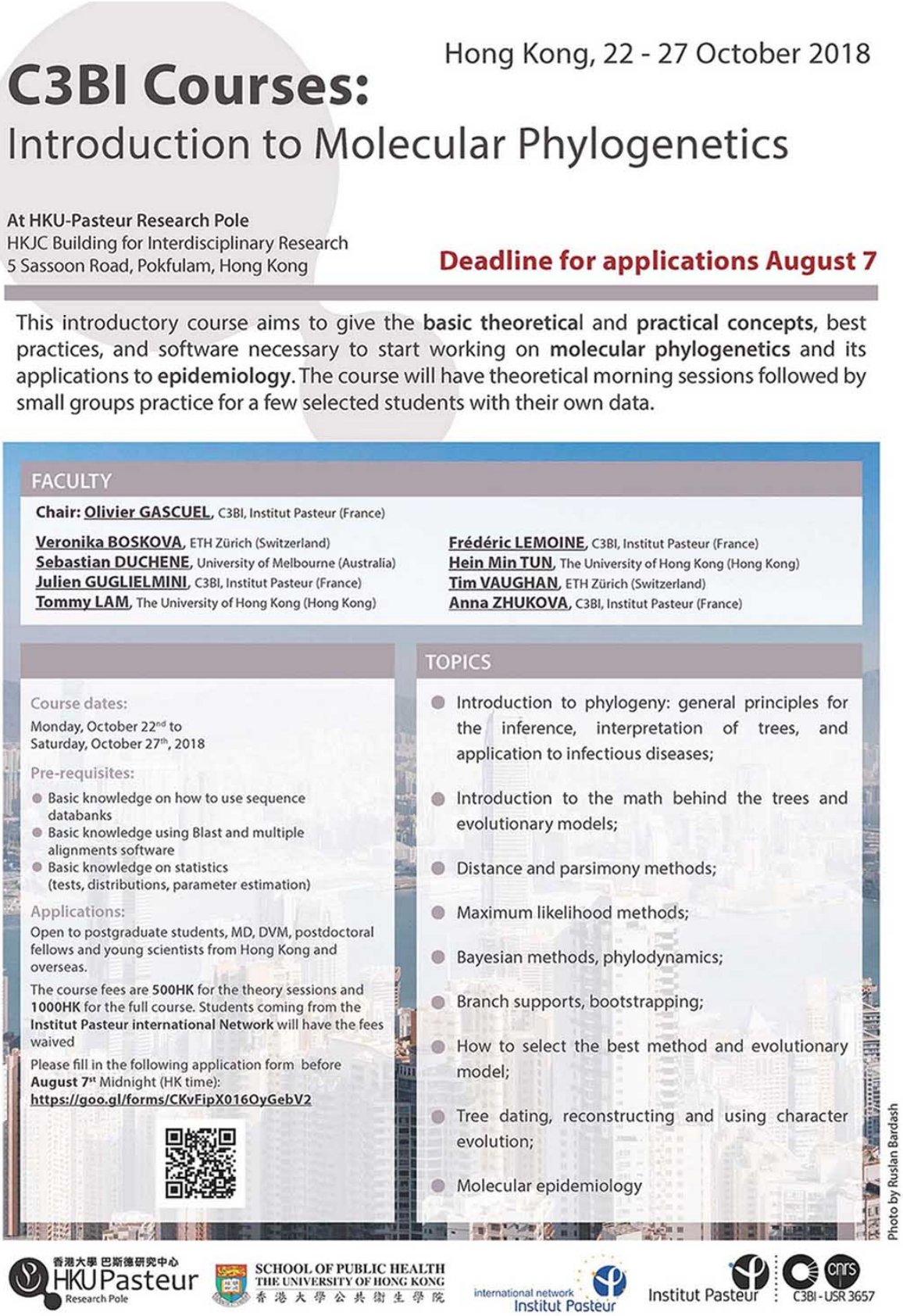
### Venue

HKJC Building for Interdisciplinary Research
5 Sassoon Road, Pokfulam, Hong Kong

Sponsored by:

international network Institut Pasteur
Pasteur Foundation Asia 巴斯德亞洲基金
DAKEWE
BioLegend®

## 5.8 C3BI Cfourse: Introduction to Molecular Phylogenetics



## 5.9 International Workshop: Epidemiology, Surveillance, and Elimination of Viral Hepatitis

INTERNATIONAL WORKSHOP

### Epidemiology, Surveillance, and Elimination of Viral Hepatitis

October 29 - November 2, 2018
Ho Chi Minh City, Vietnam

**NEW DEADLINE FOR APPLICATIONS: September 7, 2018**

No registration fees
Accommodation will be provided

#### Topics

- Epidemiology of viral hepatitis;
- Diagnostic tests and ethical considerations;
- Surveillance: purpose and methods, optimizing screening strategies, risk reduction;
- Prevalence and burden of disease of chronic hepatitis, cirrhosis, HCC;
- Surveillance: management, data analysis for communication and assessment of surveillance;
- Prevention and treatment: vaccines and antivirals;
- Access to treatment, infrastructure to monitor delivery and compliance;
- Role of government, NGOs, patients, industry.

#### Confirmed Faculty

**Roberto Bruzzone** (Hong Kong);
**Benjamin Cowie** (Australia);
**Hoang Quoc Cuong** (Vietnam);
**Jennifer MacLachlan** (Australia);
**Nguyen Thi Na** (Vietnam);
**Yusuke Shimakawa** (France);

#### Participants' Profile

The course is specifically designed for health personnel, mainly but not exclusively from countries in South East Asia, including medical and health professionals, policy makers, disease researchers interested in expanding their critical understanding of the complex issues to combat viral hepatitis in the context of the global WHO strategy towards its elimination as a public health threat.

#### Applications

Candidates are invited to download application forms at tinyurl.com/y85nbee8. Please return the completed form, including 1-2 letters of recommendation, to hku-pasteur@hku.hk. Selected applicants will be notified by **September 13, 2018.**

HKU Pasteur · Pasteur Institute Ho Chi Minh City Training Center · Pasteur Foundation Asia · SANOFI PASTEUR · international network Institut Pasteur

## 5.10 List of Public Lectures organized by HKU-PRP

14/12/2018
**Jean-Marc Cavaillon**, Department of Infection & Epidemiology, Institut Pasteur, France
**Elie Metchnikoff and the birth of immunology**

**Kanta Subbarao**, WHO Collaborating Centre for Reference and Research on influenza, The Peter Doherty Institute for Infection and Immunity, Melbourne, Australia
**Broad protection against influenza viruses by active and passive immunization**

12/12/2018
**Evan Newell**, Singapore Immunology Network, Singapore
**High-dimensional cellular immune profiling in health and disease**

11/12/2018
**Hugo Mouquet**, Department of Immunology, Institut Pasteur, France
**Decoding Human B-Cell Responses to Pathogens with Monoclonal Antibodies**

10/12/2018
**James Di Santo**, Department of Immunology, Institut Pasteur Paris, France
**Developmental Options and Functional Plasticity of Innate Lymphoid Cells**

06/12/2018
**Florent Ginhoux**, Singapore Immunology Network, Singapore
**Dendritic Cell and Macrophage Biology: From Development to Functions**

04/12/2018
**Catherine Beauchemin**, Ryerson University, Toronto, Canada
**Modelling virus infections in vitro and in vivo**

03/12/2018
**Darragh Duffy**, Department of Immunology, Institut Pasteur, Paris, France
**Defining the determinants of a healthy immune response for a better understanding of disease**

28/11/2018
**Jerome Nigou**, IPBS, CNRS, Toulouse, France
**Rational design of immunomodulatory molecules targeting C-type lectins**

27/11/2018
**Jason Mercer**, University College London, United Kingdom
**Seeing is believeing: Super-resolving poxvirus protein architecture**

05/11/2018
**Ka Yee Fung**, Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia
**Understanding the role of Interleukin-11 in Th17 cells-linked diseases**

29/06/2018
**Marcel Bokelmann**, Centre for Biological Threats and Special pathogens, Robert Koch Institute, Berlin, Germany
**Studying Factors for Ebola Virus Entry in a Potential Reservoir Host**

29/06/2018
**Mart Lamers**, Erasmus Medical Center, Rotterdam, The Netherlands
**MERS coronavirus host interactions at the subcellular level**

08/06/2018
**Karsten Kristiansen,** Department of Biology, University of Copenhagen, Denmark
**The Gut Microbiome in Health and Diseases- Moving from Mice and Pigs to Humans**

17/04/2018
**Yan Li**, Department of Immunology, Institut Pasteur Paris, France
**Evaluation and development of immunotherapies with humanized mouse models**

21/03/2018
**Michael Weekes**, Cambridge Institute for Medical Research, Cambridge, United Kingdom
**Quantitative multiplexed proteomics to investigate host-pathogen interactions**

21/03/2018
**Remigiusz Serwa**, Imperial College London, United Kingdom
**Chemical proteomic approaches to studying protein lipidation**

20/03/2018
**Florian Schmidt**, University of Bonn, Germany
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