



香港大學 - 巴斯德研究中心

HKU-Pasteur Research Centre

## Annual Report 2010

HKU-Pasteur Research Center

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# 1. Executive Summary

HKU-PRC is a joint partnership between The University of Hong Kong (HKU) and Institut Pasteur (IP), which has been established with the aim to develop a program of excellence in the study of infectious diseases. **Since 2006 HKU-PRC has been under a dual directorship, Professor Malik Peiris from HKU and Dr Roberto Bruzzone from IP, which has led to significant growth of the research output and international leadership.** HKU-PRC had 42 staff members at the end of 2010: 26 scientific (16 students), 12 technical and 4 administrative.

**The year 2010 was marked by the demise of Dr James Z. Kung, our Chairman of the Board of Management and the driving force behind the establishment of HKU-PRC.** His contribution to our Centre cannot be simply expressed in words. **The whole team is committed to honor his vision of a world-class research center** bringing together HKU and IP in the fight against infectious diseases. **The achievements of 2010 are in line with these targets,** as reflected by our scientific productivity and the pivotal role of HKU-PRC in leading local and regional network project.

**The Research Programs developed by HKU-PRC are dealing with infectious diseases that may have devastating effect on public health and the economy of the community.** More specifically, the mission of HKU-Pasteur Research Centre is to foster an interdisciplinary approach to generate information on fundamental processes of infectious diseases that may be translated into clinical applications. This overarching goal is being implemented through a three-pronged strategy.

## 1.1 **Create a regional center to study the interactions between pathogens and host cells, which are the battlefields of infections, by applying cutting edge technology**

**The scientific output of HKU-PRC has remained very strong, with 18 manuscripts published in 2010** and several publications having already appeared in 2011 or being under review. HKU-PRC is an **integral part of the Area of Excellence** on Influenza and **Professor Peiris serves as the Scientific Coordinator** of this multi-departmental and multi-institutional program. **Dr Bruzzone is the Scientific Coordinator of the RESPARI/SISEA** projects of the International Network of Pasteur Institutes. The achievements of these network projects have been presented in several international forums. **HKU-PRC has been directly involved in the organization of two major international scientific conferences: Options for the Control of Influenza VII** (Hong Kong, 3-7 September 2010), which attracted more than 1,400 people from around the globe, and the **Annual Scientific Meeting of the Institut Pasteur International Network** (Hong Kong, 22-25 November 2010), which was opened with a **keynote lecture delivered by Professor Françoise Barre-Sinoussi, the 2008 Nobel Laureate in Physiology and Medicine.** The final session of this meeting was co-organized with the Centre for the Humanities and Medicine of HKU on the theme of altruism. To further expand our activities **we are actively engaged in securing important endorsements through private donations. BNP Paribas Corporate & Investment Banking has decided to renew its partnership with HKU-PRC** and support our research projects on dengue virus.

## **1.2 Develop novel approaches to confront the challenges posed by infectious diseases to create basic knowledge that will be applied to human diseases**

We have solidified our research focus on respiratory infections and on the mosquito borne disease of dengue by securing several independent extramural grants (6 approved for funding in 2010). HKU-PRC will be a partner in the FLUPIG network of the European Union, a project that aims at a better understanding of the role of pigs in influenza pandemics. **The common denominator of our research programs is to emphasize interdisciplinary approaches** to confront the challenges posed by pathogens and we wish to pursue this orientation by linking the Center to several departments at HKU. The new group led by **Dr Hui-Ling Yen, who holds an appointment as Research Assistant Professor in the Department of Microbiology** has grown in size and has developed in a short time a vigorous research program. **Dr Beatrice Nal has left the Centre after 7 productive years in Hong Kong.** A Group Leader will be recruited after the signing of the new Consolidated Agreement. **Dr Chris Mok has joined HKU-PRC in the Molecular Virology Team, as a postdoctoral fellow of the Area of Excellence.** His research focus is on the molecular mechanisms of virulence of influenza virus; **he has already submitted a grant** to the Research Fund for the Control of Infectious Diseases.

## **1.3 Foster education through a Regional Center of Excellence for Teaching & Training in Biomedical Research that will nurture the next generation of leading scientists working on human diseases**

The Teaching and Training Center of Excellence in Biomedical Research continues to offer an annual program of three courses for postgraduate students and young scientists, which is extremely competitive and comparable in quality to other international programs. **We have pioneered advanced master classes** for MPhil, PhD and young postdoctoral fellows in the region, creating a network of trainees across Asia and beyond, who seek our mentorship well after the course. **The three courses** have attained a very strong reputation, **attracting a record number of applications from other countries.** The number of local applications has also significantly increased, and we are now training 30-40 HKU students every year. **In addition, several lectures delivered by leading scientists (viz., EMBO members, Professors at College de France, members of the National Academy of Sciences USA) are organized together with other Centers and or Departments of the Li Ka Shing Faculty of Medicine, or as part of the Croucher-Pasteur Seminar Series and are open to the public,** attracting a wide audience including faculty members, postdocs and students who attended previous courses. We have been able to increase the involvement of HKU staff, making it possible to offer a choice of 2-3 practical sessions for each course. Some of the best students of these courses have joined HKU-PRC for their PhD studies. Furthermore, **the Teaching Center of HKU-PRC has also forged a strong partnership with the Faculty Core Facility and co-organized two technical workshops in 2010.**

In summary, **the results obtained in 2010 are clearly in line with our strategic objectives and represent a solid foundation to consolidate a structure based on Young Group Leaders,** fostering synergies between independent scientists at an early stage in their career, giving them the freedom to explore and tackle important questions.

## 2. General Overview of the Programs

### 2.1 Research

**HKU-PRC had 42 staff members at the end of 2010: 26 scientific (16 students), 12 technical and 4 administrative.** The scientific backbone of HKU-PRC is represented by four groups: Virus-Host Interaction; Viral Infection & Immunity; Molecular Virology; Translational Research. All groups are actively engaged in the Teaching and Training program.

**The Virus-Host Interactions team led by Dr Beatrice Nal-Rogier** has continued studies to identify and characterize cellular pathways used or modified by enveloped viruses during their replicative cycle inside infected cells. **A major result of 2010 has been the discovery of a novel role for two cellular factors, the small GTPases Arf4 and Arf5, in dengue virus egress.** We have found that the simultaneous depletion of these two proteins, which belong to Ras superfamily, blocks dengue VLP release for all dengue serotypes. This project has been mainly carried out by **Mateusz Kudelko** who **will defend his PhD thesis on this on June 28, 2011.** **A new doctoral student has been recruited in 2010 to continue this RFCID-funded project.** Furthermore, **Joanne Lo**, who did part of the ultrastructural characterization of dengue VLPs during her training at Institut Pasteur, **has submitted her MPhil thesis in March 2011.** These data were also presented at The Fourth ASEAN Congress of Tropical Medicine and Parasitology (Singapore), and a 2010 Cold Spring Harbor Asia Meeting (PR China). In addition, **we have received a donation from BNP Paribas Corporate & Investment Banking, thanks to its partnership with Institut Pasteur, to increase support to these investigations.**

**Our projects on the cellular interactome of SARS-CoV have achieved significant milestones in 2010.** We have completed our investigations on two proteins, PALS1 and ezrin, identified in a yeast-two-hybrid screen. **We have published our work on the interaction between the SARS-E viral protein and PALS1, a component of tight junctions crucial for cellular polarity, and its consequences for integrity of the epithelium.** Our data provide new insight into the molecular mechanisms that contribute to SARS-CoV-induced pathogenesis. We have proposed a model which places E as a virulent factor that hijacks the tight junction-associated protein PALS1, causing severe damage to the epithelial barrier of the lung in SARS patients. Further studies on animal models using recombinant SARS-CoV are ongoing to investigate the role of the E-PALS1 interaction in virus-induced pathogenesis *in vivo*. **Kim-Tat Teoh has defended his PhD thesis on the project in January 2010 and is now Lecturer at Ngee Ann Polytechnic in Singapore.** These results have been presented at a Keystone Conference (USA), during a Scientific Symposium (HKU), and at a Current Opinion in Cell Biology Conference (The Netherlands). **We have also completed our work on the interaction between the cellular ezrin protein and the SARS-CoV Spike viral envelope glycoprotein.** We have found that expression of a dominant negative form of ezrin is associated with higher levels of viral genes at early time points post SARS-CoV infection. Moreover, we have observed that more cells are infected when ezrin function is altered. These data allow us to propose a model that places ezrin as a restricting factor of SARS-CoV Spike-mediated entry at the fusion stage. **Jean Millet, the student involved in this project, has defended his PhD thesis in June 2010 and is now post-doctoral fellow in the lab of Dr Gary Whittaker at Cornell University, USA.** These results have been presented at a Keystone Conference (USA).

**Dr Beatrice Nal has left HKU-PRC at the end of 2010 for personal reasons.** She had developed a very competitive research program supported by a number of extramural grants, as well as strong international collaborations with leading laboratories to exploit

the tools generated in the lab for basic and applied research programs. **Dr Nal is still following closely the progress of the students whom she was supervising.**

**The objective of the Viral Infection & Immunity group, led by Dr Martial Jaume, is to gain insights into host reactions to viral infections** with a focus on understanding the role of cells of the innate immunity system, such as macrophages and dendritic cells, in response to viral infection. Recently, the mode of activation of macrophages has been revisited and in addition to the classical activation pathway induced by the proinflammatory cytokine IFN- $\gamma$ , a new mechanism, designated as alternative activation, has been proposed. Because classical and alternatively activated macrophages display different phenotypes and properties, we have postulated that they could be differentially susceptible to virus infection. **We have successfully developed an *in vitro* model of classical and alternative activation of primary human macrophages and have embarked on a new project to evaluate their susceptibility to pandemic H1N1 Influenza A virus.** The initial results point to differences in susceptibility of the classic and alternative activated human macrophages to pandemic H1N1 - and possibly other Influenza A viruses - and prompt for further investigations on the cellular and molecular components responsible for the distinct susceptibility of the human activated macrophages to infection. **An MPhil student has been recruited in September 2010 to develop this project.**

**The Jaume lab previously reported that immune serum elicited by vaccination with a subunit SARS vaccine candidate triggered infection of human B cell lines by both SARS-CoV Spike pseudotyped particles (SARS-CoVpp) and replication-competent SARS-CoV.** These observations prompted us to extend our investigation of the **occurrence of antibody-dependent enhancement (ADE) of SARS-CoV infection to primary human macrophages.** We found that 2 out of 3 donors exhibited a markedly increased percentage of SARS-CoV-positive macrophages, from 7% or less to about 20%. Our work suggests that **SARS-CoV is able to enter human immune cells via an antibody-mediated pathway** and raises reasonable concerns regarding the use of SARS-CoV vaccine in humans. **These results have been submitted for publication and will form the backbone of the PhD thesis of Simon Yip, whose defense has been scheduled in June 2011.** Recently, serious concerns have been raised in Canada about a possible association between anti-influenza vaccination and an enhanced susceptibility to pandemic (pdm) H1N1. **The Jaume lab is collaborating with a group at the University of British Columbia (Canada) in order to investigate whether human subjects vaccinated against seasonal influenza could be more prone to pdmH1N1 infection.** To this end we have screened a cohort of patients' sera who had received different influenza vaccines using a mouse macrophagic cell line. Our initial data indicate that all sera from the Canadian cohort of vaccinated individuals triggered an enhanced infection of cells by pandemic H1N1. Taken together, our findings provide evidence for the occurrence of heterologous ADE of pandemic influenza virus and raise the possibility that cross-reactivity of antibody against Influenza A might worsen the risk of infection by the pandemic strain. **Further investigations on the role of vaccination in the exacerbation of influenza symptoms are ongoing as part of the PhD thesis of another student.**

**The projects of the Molecular Virology team, established in 2009 with the recruitment of Dr Hui-Ling Yen, focus on the biology of influenza virus** by applying reverse genetics to the study of cellular (*in vitro*) and animal (*in vivo*) models. Influenza A virus, with its segmented RNA genome that allows genetic reassortment and the existence of multiple natural reservoirs, is a non-eradicable zoonosis and a constant threat for human and animal health. The Yen lab had previously observed that **changes in the hemagglutinin (HA) receptor binding domain may modulate the virulence of H5N1 viruses by affecting viral infectivity to bone marrow-derived dendritic cells (BMDCs) or conventional dendritic**

cells (DCs) in mouse lungs. The working hypothesis is that: a) **the HA glycoprotein, specifically the receptor binding domain, plays an important role in interacting with pathogen recognition receptors (PRRs) as well as in infection of DCs**, and b) **such binding influences pathogenesis and virus dissemination**. We have first compared infection of different H5N1 and H1N1 viruses in murine BMDCs. **We observed that H5N1 exhibit higher infectivity in DC, and triggers significantly higher levels of pro-inflammatory cytokines**. The next step has been to generate recombinant viruses carrying identical internal genes but differing in HA and neuraminidase (NA) surface glycoproteins, which were derived from H5N1 strains selected from different phylogenetic clades and, therefore, are antigenically distinguishable. We have observed that recombinant H5N1 viruses with HA and NA derived from different clades replicate to similar titers in susceptible cells but differed in their infectivity in murine BMDC, as well as in mice. **These results have prompted us to investigate in detail the interaction of these recombinant H5N1 viruses with DCs and their ability to disseminate in vivo via infected DCs**. In addition, a recently funded RGC-RGF project will focus on the **potential interaction between influenza HA glycoprotein with C-type lectins**, a member of PRRs that mediate specific interactions with different pathogens by recognizing specific glycans. The current approach is to generate non-infectious virus-like particles that express HA to evaluate their interaction with a panel of human C-type lectins. **This project forms the backbone of the doctoral thesis of a student recruited in the second half of 2010**.

The second main area of interest aims at mapping **molecular determinants that enable transmission and replication of avian or swine influenza viruses in human**. The working hypothesis is that **the unique genetic composition of the pandemic H1N1 influenza virus allows it to transmit among humans**. To test this possibility, the Hyen lab has generated recombinant viruses between pandemic HK415742 (H1N1) and swine precursor swHK915 (H1N2) by plasmid-based reverse genetics. **Two important findings have been obtained**. **First**, we have found that **pandemic virus HK415742 was observed to possess higher replication/transcription activity than that of the swine precursor swHK915 virus**. Replacing polymerase genes of swHK915 with those of HK415742 can increase polymerase activity. **Second**, we have observed that **human and swine influenza viruses transmitted differently**. Thus, swine influenza viruses all possess the ability to transmit via direct contact; however, **only one swine influenza isolate swHK915 (H1N2) demonstrated moderate aerosol transmissibility** as infection can be detected in one out of three aerosol contact animals. Phylogenetic analysis has shown that swHK915 virus possess seven genes (except NA) closely related to pandemic H1N1 influenza virus. This study is performed in collaboration with Dr Gavin Smith (National University Singapore), Dr Leo Poon (Department of Microbiology at HKU) as well as Drs Robert Webster and Richard Webby (St. Jude Children's Research Hospital, Memphis, TN, USA). **The project has been supported by the Research Fund for the Control of Infectious Diseases (Commissioned Study on Swine Influenza) since June 2009**.

**The activity of the Translational Research group, led by Dr Jean-Michel Garcia**, has been re-focused on two axes of research: **molecular biology/tool development, and diagnostics**. We are continuing the collaboration with Professor Mark von Itzstein's group (Institute of Glycomics, Griffith University, Australia) **to investigate how influenza virus binds to its receptor(s)** by utilizing a physical technique called saturation transfer difference nuclear magnetic resonance (STD-NMR), which represents a powerful method to investigate receptor-ligand interactions at the atomic level. While we are exploring how changes in hemagglutinin (HA) sequence can affect binding, in 2010 we have achieved a major breakthrough **obtaining initial data that validate this technology to study neuraminidase (NA)-ligands interactions**. We have already observed that some parameters, such as pH, appear to shift the NA properties towards either enzymatic



**activity** (at acidic pH) **or binding** (at neutral pH). These observations are currently being confirmed using an alternative method, lectin staining of NA-transfected cells. A PhD student, Jimmy Lai, has spent three months in the Itzstein lab to perform these experiments. He will defend his thesis at the end of 2011. **Another significant finding** has been the observation that **expression of NA alone is sufficient to generate and release in the supernatant virus like particles (VLPs)** that are morphologically similar to influenza virions. Thus, NA oligomerization is comparable to that of the live virus, and the enzymatic activity, although not required for the release of NA-VLP, is preserved. Together, these findings indicate that NA plays a key role in virus budding and morphogenesis and further validate NA-VLPs as a useful tool in influenza research.

Over the years the Garcia lab has developed an **expertise in influenza lentiviral particle system and has validated their diagnostic potential in comparison with microneutralization, the current gold standard method.** We have now used this approach to look at two aspects of influenza immunology: **cross-subtype neutralization** and the **kinetic human neutralizing antibodies in vivo.** In one study we found detectable H5N1 neutralizing antibodies in a minority of pre-seasonal vaccine sera and evidence of a serological response to H5N1 in others after seasonal influenza vaccination. **These results demonstrate that antibodies directed to haemagglutinin can induce heterosubtypic response to influenza A.** Our findings also have implications for the interpretation of sero-epidemiological data, as some individuals clearly respond to seasonal influenza vaccine with substantially higher H5N1 neutralizing antibody titers. In a second study, we have analyzed the characteristics of the antibody response in individuals infected by clade 1 H5N1 virus in Vietnam and Cambodia, who experienced a spectrum of illness ranging from fatal or severe disease to moderate illness or asymptomatic infection. **Our results indicate that people with asymptomatic H5N1 infection have lower H5N1 antibody titers compared to those with severe illness and that in many asymptotically infected patients the antibody titer decreased to levels below the threshold of positivity within one year.** These data are essential for the design and interpretation of seroepidemiological studies.

## 2.2 Teaching and Education

Our program of courses for postgraduate students and young scientists has become a **reference beyond the Asia region**, drawing an increasing number of highly qualified applications from around the world. **We offer courses that are very competitive and of the highest quality**, comparable to established benchmarks such as EMBO and Cold Spring Harbor courses. **Several milestones have been achieved in 2010.** First, **we have received a record number of applications for our master classes in Cell Biology, Virology and Immunology** (total number: 156), with selected applicants coming from more than 25 countries, including Canada, UK, Australia, Singapore and South America. Second, **we have organized two successful workshops together with Professor George Tsao (Department of Anatomy at HKU) and the Faculty Core Facility** on “Live Cell Imaging & Confocal Microscopy - Advances & Applications” and on “Flow Cytometry”. **These events were sponsored by private companies and attracted a huge interest with over 150 registrations for the Flow Cytometry Workshop.** Third, we have co-organized an IBRO UNESCO **School of Neuroscience** on “**Neurobiology of Infectious Diseases: A view for Global Neuroscience**” in **St Denis, Reunion Island**, in which students from Africa, Asia, Europe and Indian Ocean region had the opportunity to learn about the pathogenesis and important gaps in knowledge of some of the most prevalent diseases of the nervous system, which are rarely addressed in neuroscience courses. Finally, **three students from the Centre (2 PhD and 1 MPhil) have successfully defended their theses.**



## 2.3 Network Projects

HKU-PRC exerts a leadership role in a number of network projects with a major focus on viral respiratory infections. This position has been recognized by the invitation to take part in a meeting organized by Wellcome Trust (February 14-16, London, UK) with the aim to establish an **International Severe Acute Respiratory Infection Consortium (ISARIC)**. **This priority area had been selected by the Heads of International Research Organizations (HIROS), which includes the Bill and Melinda Gates Foundation, CIHR, EC, Inserm, Institut Pasteur, MRC UK, NIH and Wellcome Trust. Dr Roberto Bruzzone is the Scientific Coordinator of the RESPARI and SISEA programs** that federate the Institutes of the Pasteur-Asia network in a multi-center project (see also the 2009 Annual Report). The **RESPARI network** ([www.hku.hk/respari/](http://www.hku.hk/respari/)) has served as the platform to promote active collaboration between the Pasteur and other networks in Asia and establish the regional influence of HKU-PRC. The achievements of these network projects have been presented in several international forums. **Professor Malik Peiris is the Coordinator of the 8-year research program “Control of Pandemic and Inter-pandemic Influenza”** that has been awarded a HK\$ 76 millions by the University Grants Committee in the fourth round of its Areas of Excellence (AoE) scheme. HKU-PRC takes an active part in this application and has secured several grants to successfully implement specific research areas and strengthen our scientific collaborations with many groups at HKU and other universities in Hong Kong. **Professor Peiris continues to serve on a number of WHO working groups in relation to both avian and swine origin influenza virus.** In this context, it is important to mention that **HKU-PRC has entered into a collaborative project** (Funding scheme: Large-scale integrating project) **supported through the 7<sup>th</sup> Framework Program of the European Union. Professor Malik Peiris will coordinate the activity of HKU-PRC.**

**Finally,** several major international events have been organized and/or chaired by the directorship of HKU-PRC: **Options for the Control of Influenza VII** (Hong Kong, 3-7 September 2010), co-organized by Professor Malik Peiris (Conference Chair), Professor Yi Guan (HKU, Conference Scientific Chair) and Dr Gavin Smith (NUS, Conference Communication Liaison), which attracted more than 1400 researchers worldwide (<http://www.controlinfluenza.com/>); the **Annual Scientific Meeting of the Institut Pasteur International Network** (Hong Kong, 22-25 November 2010), co-organized by Dr Roberto Bruzzone and Professor Malik Peiris, which is the most important scientific event of the Pasteur Network and was opened with a **keynote lecture delivered by Professor Françoise Barre-Sinoussi, the 2008 Nobel Laureate in Physiology and Medicine** for the discovery of the HIV virus (<http://www.pasteur-network-meeting.org/HK2011/>); the **2<sup>nd</sup> International Neuroinfection Meeting** (Reunion Island, 2-6 December 2010), co-organized by Dr Roberto Bruzzone, Professor Monique Dubois-Dalcq (Institut Pasteur and NIH), Professor Philippe Gasque (Université de La Reunion) and Professor Krister Kristensson (Karolinska Institutet, Stockholm) (<http://www.ianis2010.fr/training-and-scientific-program/>), which brought together specialists working in neurobiology, microbiology, immunology, virology, parasitology and clinical neurology following the success of the first International Conference on Infections Diseases of the Nervous System, held at Institut Pasteur in September 2008.

## 2.4 Financial situation

The financial situation has been defined under the Consolidated Agreement stipulating that the Centre will receive intramural funding from HKU up to the end of the revised term (November 2011). Following the 2008 Board Meeting, HKU has agreed to increase its annual support to HK\$6.47 million in cash, keeping the existing level of in kind contributions). Starting in 2005 more funds have been made available from Institut Pasteur, including a one-off donation. Intramural funds from HKU and Institut Pasteur account for about 50% of current income. The remaining 50% is obtained through external grants and donations. HKU-PRC has secured extramural grants from RGC (Research Grants Committee), RFCID (Research Fund for the Control of Infectious Diseases), Area of Excellence and, more recently, from the European Union to support its core research activities. **It is worth mentioning that our Group Leaders currently hold 1 EU, 3 RGC, 9 RFCID and 2 Area of Excellence contracts, with 1 RGC and 5 RFCID proposals currently under review.** In summary, the financial position of the Centre is considered as healthy with a total net asset of HK\$1.177M and a balance of cash and cash equivalent of HK\$2.87M stood at June 30, 2010.

## 3. Scientific Output (since January 2010)

### 3.1 Publications cited in PubMed

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1. Kudelko M, Brault JP, Kwok KT, Pardigon N, Peiris JS, Bruzzone R, Despres P, Nal B, Wang PG (2011) Class II ADP-ribosylation factors regulate the release of dengue and yellow fever viruses. Submitted.
2. Millet JK, Kien F, Cheung CY, Siu YL, Chan WL, Li H, Leung N, Jaume M, Bruzzone R, Peiris JS, Altmeyer RM, Nal B (2011) Ezrin interacts with the SARS coronavirus spike protein and negatively modulates host cell susceptibility to infection. Submitted.
3. Jaume M, Yip MS, Cheung CY, Li PH, Kien F, Dutry I, Leung N, Escriou N, Daëron M, Altmeyer R, Nal B, Bruzzone R, Peiris JS (2011) Anti-SARS-CoV spike antibodies trigger infection of human immune cells via a pH- and cysteine protease-independent FcγR pathway. Submitted.
4. Desvaux S, Garcia JM, Nguyen TD, Reid S, Ngoc AB, Roger F, Fenwick F, Peiris JSM, Ellis T (2011) Evaluation of serological tests for H5N1 avian influenza on partially immunized domestic poultry populations in Vietnam: what is the most appropriate tool for surveillance? Submitted.

### 3.3 Seminars, Invited Lectures and Oral Presentations at Meetings

1. Roberto Bruzzone (2010) Surveillance and Investigation of Epidemics in South East Asia (SISEA). Mekong Basin Disease Surveillance Regional Forum. Louang Prabang, Lao PDR.
2. Roberto Bruzzone (2010) Co-Chair of the “2nd International Conference on Neuroinfections and their worldwide impact”. University of La Reunion, St Denis, La Reunion.
3. Roberto Bruzzone (2010) Co-organizer of the IBRO/UNESCO School of Neuroscience “Neurobiology of Infectious Diseases: a view for Global Neuroscience”. University of La Reunion, St Denis, La Reunion.
4. Roberto Bruzzone (2010) How to improve your presentation skills. IBRO/UNESCO School of Neuroscience “Neurobiology of Infectious Diseases: a view for Global Neuroscience”. University of La Reunion, St Denis, La Reunion.
5. Roberto Bruzzone (2010) Institut Pasteur International Network in the Asia-Pacific region. Western Pacific Regional Office of WHO, Manila, Philippines.
6. Roberto Bruzzone (2011) Institut Pasteur International Network. International Severe Acute Respiratory Infection Consortium (ISARIC) Meeting. The Wellcome Trust, London, UK.
7. Roberto Bruzzone (2011) Co-Chair, International Workshop on “Surveillance and Discovery in Respiratory and Other Emerging Infectious Diseases”, Phnom Penh, Cambodia.
8. Roberto Bruzzone and Malik Peiris (2010) Co-Chairs of the Annual Scientific Meeting of the Institut Pasteur International Network. The Li Ka Shing Faculty of Medicine of the University of Hong Kong, Hong Kong SAR.
9. Jean-Michel Garcia (2010) Cell-based assay: application to drug discovery. International course on “Animal cell biotechnology: Products from cells – cells as products”. Institut Pasteur Montevideo, Uruguay.
10. Martial Jaume (2010) Introduction to Flow Cytometry. Flow Cytometry Workshop, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR.
11. Martial Jaume (2010) Antibody dependent enhancement of viral infections: Concerns in the pathogenesis of SARS-CoV and Influenza A viruses. Symposium “Should we target the Virus, the Cell or Both?”, organized by the Area of Excellence “Control of Pandemic and Inter-Pandemic Influenza”. Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR.
12. Francois Kien (2010) Single-Virus Tracking - A Journey into the Cell. Live Cell Imaging & Confocal Microscopy – Advances and Application, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR.

13. F Kien (2010) Identification and characterization of cellular interactants of influenza M2 ion channel protein. Area of Excellence “Control of Pandemic and Inter-Pandemic Influenza” Seminars. Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR.
14. Malik Peiris (2010) Pre-clinical papers literature review – SARS & Influenza. XII International Symposium on “Respiratory Viral Infections”. Taipei, Taiwan.
15. Malik Peiris (2010) Comparison of disease spectrum and mechanisms of pathogenesis in H5N1 and pandemic H1N1 influenza. Gordon Research Conference on the “Biology of Acute Respiratory Infection”. Ventura, CA, USA.
16. Malik Peiris (2010) H5N1 pathogenesis. Gordon Research Conference on the “Biology of Acute Respiratory Infection”. Ventura, CA, USA.
17. Malik Peiris (2010) Influenza: expecting the unexpected. SGM Spring Meeting on “Global challenges of virus infection”. Edinburgh, UK.
18. Malik Peiris (2010) From avian flu to swine flu: epidemiology and pathogenesis. Keynote speaker of the “First International Symposium on the infectomics of influenza A virus”. University of British Columbia, Vancouver, Canada.
19. Malik Peiris (2010) Epidemiology and pathogenesis of pandemic H1N1: a view from Hong Kong. Meeting of the Influenza Pathogenesis and Immunology Research Centre (IPIRC) on “Swine origin H1N1 virus: The first pandemic of the 21st century”. Emory University, Atlanta, USA.
20. Malik Peiris (2010) Discussing the current and future challenges for influenza. World Vaccine Congress Asia 2010. Singapore.
21. Malik Peiris (2010) Influenza: Emergence and pathogenesis. 16th Symposium on “Infections in the Immunocompromised Host”. Budapest, Hungary.
22. Malik Peiris (2010) Plagues past, present and future. 2010 David Todd Oration. The Hong Kong Academy of Medicine, Hong Kong SAR.
23. Malik Peiris (2010). Chairman of the conference “Options for the Control of Influenza VII”. Hong Kong SAR.
24. Malik Peiris (2010) XII International Symposium on Respiratory Viral Infections. Scientific Advisory Board. Singapore.
25. Malik Peiris (2010) Expert Advisor to WHO consultation on the composition of Influenza Vaccines for the Northern Hemisphere. Geneva, Switzerland.
26. Malik Peiris (2010). Expert Advisor to WHO Scientific Advisory Group of Experts (SAGE) meeting. Geneva, Switzerland.
27. Malik Peiris (2010) Scientific Advisory Board Meeting of the MRC Centre for Outbreak Analysis and Modelling. London, UK.



28. Malik Peiris (2010) Scientific Advisory Board Meeting of The Wellcome Trust – Influenza Scientific Advisory Group. London, UK.
29. Malik Peiris (2011) Co-Chair, Keystone Symposia Conference on “Pathogenesis of Influenza: Virus-Host Interactions”, Hong Kong SAR.
30. Peigang Wang (2010). A novel role for class II ADP-Ribosylation Factors (Arfs) in the secretion of Dengue and Yellow Fever Virus. CSH - Asia, Emerging Infectious Diseases meeting. Oct, 2010. Suzhou, China.
31. Ming S. Yip (2010) Antibody-dependent Enhancement of Severe Acute Respiratory Syndrome Coronavirus. 15th Research Postgraduate Symposium. Li Ka Shing Faculty of Medicine, HKU, Hong Kong

### 3.4 List of Posters presented at Meetings

1. Millet J, Kien F, Cheung C, Siu L, Chan W, Vidalain PO, Mesel-Lemoine M, Tangy F, Bruzzone R, Peiris M, Altmeyer R, Nal B (2010) Host Cell Susceptibility to Human Coronavirus Infections. Keystone Symposium on “Cell Biology of Viral Entry, Replication and Pathogenesis” (Taos, New Mexico, USA, 16-21 February 2010).
2. Teoh KT, Siu YL, Chan WL, Peiris M, Bruzzone R, Margolis B, Nal B (2010) The E protein of the SARS coronavirus interacts with the PALS1 tight junction protein: an insight to understand the mechanism of deterioration of infected epithelia. Keystone Symposium on “Cell Biology of Viral Entry, Replication and Pathogenesis” (Taos, New Mexico, USA, 16-21 February 2010).
3. Hui-Ling Yen, Heather Forrest, Peter Cheung, Diana Wong, Olive Li, Scott Krauss, Angela Ferguson, Jeri-Carol Crumpton, Jeremy Jones, Terry Choy, Edward Ma, Leo LM Poon, Gavin J Smith, John Nicholls, Yi Guan, Robert G Webster, Richard Webby, Malik Peiris (2010) Transmissibility of pandemic H1N1 and genetically related swine influenza viruses in ferrets. Options for the Control of Influenza VII (Hong Kong, 3 – 7 September 2010).
4. D Bethell, A Jongkaewwattana, J kramyu, A Thitithayanont, S Wiboon-ut, D Saunders, K Yongvanitchi, A Limsalakpetch, U Kum-Arb, N Uthaimongkol, JM Garcia, M Peiris, S Thomas, A Engering, R Jarman, D Mongkolsirichaikul, C Mason, N Khemnu, S Tyner, M Fukuda, and S Pichyangkul (2010) Evaluation of in vitro cross-reactivity with avian influenza H5N1 and swine flu H1N1 2009 viruses in healthy volunteers vaccinated with a prime boost regimen of seasonal influenza vaccine. Keystone Symposium on “Immunological Mechanisms of Vaccination” (Seattle, USA, 27 October – 1 November 2010).
5. Lai JCC, Chan WWL, Nicholls JM, Peiris JSM and Garcia JM (2010) Formation of virus-like particles from human cell lines exclusively expressing Influenza Neuraminidase. Annual Scientific Meeting of the Institut Pasteur International Network (Hong Kong, 22-23 November 2010).
6. Ming S. Yip, Chung Y. Cheung, Ping H. Li, Roberto Bruzzone, J.S. Malik Peiris and Martial Jaume (2010) Investigation of Antibody-Dependent Enhancement (ADE) of SARS Coronavirus Infection and Its Role in Pathogenesis of SARS (RFCID grant 09080872). Health Research Symposium 2010: “Improving health and recognising excellence”. Food and Health Bureau, the Government of the Hong Kong Special Administrative Region (11 September 2010, Hong Kong).
7. Isabelle Dutry, Hui-Ling Yen, Horace Lee, Malik Peiris, Martial Jaume (2010) Antibody-Dependent Enhancement (ADE) of influenza infection and its possible role in the pathogenesis of influenza. 15th Research Postgraduate Symposium (Hong Kong, 1-2 December 2010).
8. Ming S. Yip, Chung Y. Cheung, Ping H. Li, Roberto Bruzzone, J.S. Malik Peiris and Martial Jaume (2010) Investigation of Antibody-Dependent Enhancement (ADE) of SARS Coronavirus Infection and Its Role in Pathogenesis of SARS. Annual Scientific Meeting of the Institut Pasteur International Network (Hong Kong, 22-23 November 2010).

9. Isabelle Dutry, Hui-Ling Yen, Horace Lee, Malik Peiris, Martial Jaume (2010) Antibody-Dependent Enhancement (ADE) of influenza infection and its possible role in the pathogenesis of influenza. Annual Scientific Meeting of the Institut Pasteur International Network (Hong Kong, 22-23 November 2010).
10. Isabelle Dutry, Hui-Ling Yen, Horace Lee, Malik Peiris, Martial Jaume (2010) Antibody-Dependent Enhancement (ADE) of influenza infection and its possible role in the pathogenesis of influenza. Options for the Control of Influenza VII (Hong Kong, 3-7 September 2010).
11. Tang DJ, Lam YM, Lam CHP, Chu SLK, Nal B, Bruzzone R (2010) Mutational analysis of H5N1 hemagglutinins: identification of molecular determinants for efficient packaging into pseudotyped lentiviral particles. Options for the Control of Influenza VII (Hong Kong, 3-7 September 2010).
12. Peigang Wang, Mateusz Kudelko, Kevin Kwok, Joanne Lo, Martin Sachse, Beatrice Nal and Roberto Bruzzone (2010) Identification of cellular enhancing and restricting factors of dengue virus egress. Health Research Symposium 2010: "Improving health and recognising excellence". Food and Health Bureau, the Government of the Hong Kong Special Administrative Region (11 September 2010, Hong Kong).
13. Y Zhang, F Kien, HL Ma, J Tse, LLM Poon and B Nal (2010) Identification of a novel interaction between the M2 proton channel of influenza A virus and cyclin D3: consequences for cell cycle progression. Annual Scientific Meeting of the Institut Pasteur International Network (Hong Kong, 22-23 November 2010).
14. HL Ma, F Kien, Y Zhang, J Tse, LLM Poon and BTM Nal. Identification of human annexin A6 as a novel cellular interactant of influenza A M2 protein: implications for influenza life cycle. Annual Scientific Meeting of the Institut Pasteur International Network (Hong Kong, 22-23 November 2010).
15. HL Ma, F Kien, Y Zhang, J Tse, LLM Poon and B Nal (2010) Identification of human annexin A6 as a novel cellular interactant of influenza A M2 protein: implications for influenza life cycle. Options for the Control of Influenza VII (Hong Kong, 3-7 September 2010).

## 3.5 Active Grants in 2010

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Beatrice Nal-Rogier  
Amount: HK\$724,000.00  
Period: 01/Aug/2008 to 31/Jul/2010

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Pei Gang Wang  
Amount: HK\$798,400.00  
Period: 01/Aug/2008 to 31/Jul/2010

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Pei Gang Wang  
Amount: HK\$962,504.00  
Period: 01/Sept/2010 to 31/Aug/2012

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Dong Jiang Tang  
Amount: HK\$737,000.00  
Period: 01/Jan/2009 to 31/Dec/2010

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Martial Jaume  
Amount: HK\$799,998.00  
Period: 01/Oct/2009 to 30/Sept/2011

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Francois Kien  
Amount: HK\$776,998.00  
Period: 01/Oct/2009 to 30/Sept/2011

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Huiling Yen  
Amount: HK\$771,196.00  
Period: 01/Jun/2009 to 31/May/2011

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Huiling Yen  
Amount: HK\$819,442.00  
Period: 01/Jan/2010 to 31/Dec/2012

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Huiling Yen  
Amount: HK\$138,000.00  
Period:

### **Research Grants Council**

Principal Investigator: Dr Roberto Bruzzone  
Amount: HK\$908,545.00  
Period: 01/Nov/2008 to 31/Oct/2010

**Research Grants Council**

Principal Investigator: Dr John Nicholls/Dr Jean-Michel Garcia  
Amount: HK\$538,560.00  
Period: 01/Nov/2009 to 31/Oct/2012

**Merit Award for GRF Project (HKU760208M)**

Principal Investigator: Dr Roberto Bruzzone  
Amount: HK\$50,000.00  
Period: 18/Feb/2009 to 30/Oct/2010

**HKU Seed Fund**

Principal Investigator: Dr Hailing Yen  
Amount: HK\$120,000.00  
Period: 01/Jul/2009 to 30/Jun/2010

**Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr Roberto Bruzzone/Dr Jean-Michel Garcia  
Amount: HK\$312,000.00  
Period: 01/Jan/2010 to 31/Dec/2010

**Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr Hailing Yen  
Amount: HK\$498,417.00  
Period: 01/Jan/2009 to 31/Dec/2010

**European Commission (FP7)**

Principal Investigator: Dr Malik Peiris/Dr John Nicholls  
Amount: Euro 375,150.00  
Period: 01/Jul/2010 to 30/Jun/2015

**Actions Concertees InterPasteuriennes (ACIP-3)**

Principal Investigator: Dr Peigang Wang  
Amount: Euro 49,500.00  
Period: 01/Sep/2010 to

**Special Fund (Institut Pasteur)**

Principal Investigator: Dr Roberto Bruzzone  
Amount: HK\$1,741,210.00  
Period: 1 Jul 2008 to 30 Jun 2011

**Matching Fund (Government Matching Grant)**

Principal Investigator: Dr Roberto Bruzzone  
Amount: HK\$642,915.00  
Period: 1 Jul 2008 to 30 Jun 2011

## 3.6 Pending Grant Applications

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Martial Jaume  
Amount: HK\$992,840.00  
Duration: 24 months

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Francois Kien  
Amount: HK\$980,456.00  
Duration: 24 months

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Suki Lee  
Amount: HK\$996,576.00  
Duration: 24 months

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Chris Mok  
Amount: HK\$955,360.00  
Duration: 24 months

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Dongjiang Tang  
Amount: HK\$910,446.00  
Duration: 24 months

### **Research Grants Council**

Principal Investigator: Dr Huiling Yen  
Amount: HK\$786,500.00  
Duration: 24 months

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Huiling Yen  
Amount: HK\$800,000.00  
Duration: 24 months

## 3.7 Grants Completed in 2009

### **Research Fund for the Control of Infectious Diseases**

Principal Investigator: Dr Joanna WY Ho  
Amount: HK\$800,000.00  
Period: 01/Oct/2007 to 30/Sep/2009

### **HKU Seed Fund**

Principal Investigator: Dr Joanna WY Ho  
Amount: HK\$58,840.00  
Period: 01/Oct/2007 to 30/Sep/2009

### **Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr Beatrice Nal-Rogier  
Amount: HK\$268,000.00  
Period: 01/May/2008 to 30/Apr/2009

### **Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr Beatrice Nal-Rogier  
Amount: HK\$575,027.00  
Period: 01/Jan/2009 to 31/Dec/2009

### **Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr Roberto Bruzzone/Dr Jean-Michel Garcia  
Amount: HK\$270,000.00  
Period: 01/May/2008 to 30/Apr/2009

### **Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr Roberto Bruzzone/Dr Jean-Michel Garcia  
Amount: HK\$153,027.00  
Period: 01/Jan/2009 to 31/Dec/2009

### **Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr John Nicholls/Dr Jean-Michel Garcia  
Amount: HK\$189,810.68  
Period: 01/May/2008 to 30/Apr/2009

### **Area of Excellence, Control of Pandemic and Inter-pandemic Influenza**

Principal Investigator: Dr John Nicholls/Dr Jean-Michel Garcia  
Amount: HK\$ 413,832.00  
Period: 01/Jan/2009 to 31/Dec/2009

### **Actions Concertees InterPasteuriennes (ACIP-1)**

Principal Investigator: Dr Jean-Michel Garcia  
Amount: Euro 10,000.00  
Period: 01/Apr/2008 to 31/Oct/2009



**Actions Concertees InterPasteuriennes (ACIP-2)**

Principal Investigator: Dr Jean-Michel Garcia  
Amount: Euro 7,000.00  
Period: 01/Apr/2008 to 30/Jun/2009

**European Commission (FP6 – Denframe)**

Principal Investigator: Dr Beatrice Nal-Rogier  
Amount: Euro 117,000.00  
Period: 01/May/2007 to 30/Apr/2009