

Annual Report 2011

HKU-Pasteur Research Center Dexter HC Man Building 8, Sassoon Road Hong Kong SAR, China

Roberto Bruzzone, CEO Malik Peiris, Scientific Director

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1. Executive Summary

HKU-Pasteur Research Centre (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. 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. HKU-PRC fosters an interdisciplinary approach to generate information on fundamental processes of infectious diseases that may be translated into clinical applications.

<u>Research.</u> The scientific output of HKU-PRC has been of the highest quality, with more than 20 manuscripts, including several high-impact papers published in *Nature*, *Proceedings of the National Academy of Sciences USA*, etc. We have secured several independent extramural grants to continue our research focus on respiratory infections and the mosquito borne disease of dengue. With respect to influenza research, we have shown that an exquisite balance between hemagglutinin and neuraminidase, the two main structural proteins of the viral envelope, play a critical role in acquisition of efficient and sustained human-to-human transmissibility. With respect to dengue research, we have identified novel cellular factors that are necessary in assisting the release of progeny viruses from infected cells. In addition, HKU-PRC is an integral part of the Area of Excellence on Influenza, which is coordinated by Professor Peiris, and Professor Bruzzone has been the Scientific Coordinator of the RESPARI/SISEA projects of the International Network of Pasteur Institutes, which were completed in 2011.

Teaching. 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. Our educational programs have established a wide network of trainees across Asia and beyond, who seek our mentorship well after the course. Some of the best students of these courses have joined HKU-PRC or Institut Pasteur for their PhD studies.

Perspectives. HKU-PRC has developed a strong identity that is contributing to promote the presence and image of HKU, as well as of IP and its international network, in the region through research, teaching and public health activities. In order to ensure a long-term continuation of this successful partnership HKU-Pasteur Research Centre Limited will be transformed into the HKU-Pasteur Research Pole (HKU-PRP), a laboratory integrated into the new Center of Influenza Research (CIR) of the School of Public Health in the Li Ka Shing Faculty of Medicine. HKU-PRP will continue its focus on the Cell Biology of Infections and will expand its current strength on respiratory diseases by developing programs that will tackle neglected tropical diseases, such as arboviroses, as well as basic cell biology that is relevant to the advancement of our understanding of pathogenetic mechanism. HKU-PRP will strengthen its position as a regional reference for postgraduate training and will be firmly engaged also in undergraduate training to contribute to the development of the new Bachelor in Biomedical Sciences launched in 2012.

In summary, the results obtained in 2011 are clearly in line with our strategic objectives and represent a solid foundation to develop the new HKU-Pasteur Research Pole as a cluster of excellence based on Young Group Leaders, fostering research and teaching.

2. General Overview of the Programs

2.1 Research

The scientific activity of HKU-PRC is implemented 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 has continued studies to identify and characterize cellular pathways used or modified by enveloped viruses during their replicative cycle inside infected cells. One of the major achievements of this project was the discovery of a crucial role for ADP-Ribosylation Factors 4 and 5 (Arf4 and Arf5) during dengue viruses egress. These findings have been accepted for publication in the Journal of Biological Chemistry and have formed the core of the doctoral work of Mateusz Kudelko, who defended his thesis in June 2011. We have also pursued our studies with influenza by focusing on human cellular factors that we identified in two-hybrid screen for their ability to interact with the cytoplasmic domain of the M2 envelope viral protein of H5N1 influenza virus. In particular, we characterized the role of annexin A6, a calciumbinding protein that negatively regulates influenza infection as shown by detection of higher or lower progeny virus titers in human lung cells infected with different influenza virus strains when annexin A6 was depleted or overexpressed respectively. We have conducted a systematic dissection of the viral life cycle and concluded that AnxA6 is a novel cellular regulator that targets and impairs budding and release of influenza A virus. These findings have been accepted for publication in the Journal of Virology.

The objective of the Viral Infection & Immunity group is to gain insights into host reactions to viral infections with a focus on understanding the role of cells of the innate immunity system. We have recently reported in the Journal of Virology that antibodies elicited by a SARS-CoV vaccine candidate trigger infection of immune cell lines. These observations prompted an investigation into the molecular mechanisms and responses to antibody-mediated infection in human macrophages, which are innate immune cells with well-established roles in the primary response to pathogens. We have now found conclusive evidence that human macrophages can be infected by SARS-CoV as a result of IgG-mediated ADE and further demonstrated that this infection route requires signaling pathways activated downstream of binding to FcyRII receptors. Recently, the activation mode of macrophages has been revisited and in addition to the classical activation pathway induced by the pro-inflammatory cytokine IFN-Y new mechanisms, designated as alternative activation, have been proposed. We have successfully established in vitro model of classical and alternatively activated primary human macrophages and have initiated evaluation of their susceptibility to pandemic H1N1 and highly pathogenic H5N1 Influenza A virus.

The projects of the **Molecular Virology team** 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 re-assortment and the existence of multiple natural reservoirs, is a non-eradicable zoonosis. The host range of influenza A virus is determined by multiple viral and host factors. Human zoonotic infection with swine or avian influenza viruses did not lead to sustained

human-to-human transmission prior to 2009 when a novel pandemic H1N1 virus with genes derived from the swine influenza reservoir emerged. This illustrates the need of understanding the molecular determinants of influenza A viruses that confer to efficient transmission among humans. The team has obtained important results demonstrating that an exquisite balance between hemagglutinin and neuraminidase, the two main structural proteins of the viral envelope, plays a critical role in acquisition of efficient and sustained human-to-human transmissibility and have subsequently observed that inserting the neuraminidase gene from the H1N1 pandemic virus into a swine virus is sufficient to increase respiratory droplet transmission efficiency in ferrets. These results have appeared in the *Proceedings of the National Academy of Sciences USA*.

The activity of the **Translational Research** group has been re-focused on two axes of research: molecular biology/tool development, and diagnostics. Through the years, we have developed a considerable expertise on the use and applications of influenza lentiviral particles system. These particles mimic the surface of influenza virus allowing the investigation of viral properties that are dependent on the main surface glycoproteins (hemagglutinin and neuraminidase) of influenza viruses. With these constructs we applied Saturation Transfer Difference (STD)-NMR and could demonstrate for the first time the presence of a secondary binding site of neuraminidase to sialic acid. This approach of epitope mapping should lead to a real definition at atomic resolution of the interactions between the influenza surface proteins HA and NA and their cognate, sialylated receptors, as well as provide essential knowledge that may be utilized for the rational design of new influenza antivirals.

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. We have launched a HKU-Pasteur Courses Series Newsletter (http://www.hkupasteur.hku.hk/index.php/Teaching/hku_pasteur_courses_series_newsl etter) and also common interest groups in social media (LinkedIn and Facebook). All our educational programs are self-funded with *ad hoc* grants. We are actively engaged in postgraduate training in our lab with 2 PhD and 4 MPhil students having defended their thesis in 2011.

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 Croucher Foundation, the French Consulate and other private donations. Our funds cover advertising costs, travel and accommodation for all lecturers and students (except from industry). Selected students are expected to pay for their travel costs, but a small number of travel grants may be available at the discretion of the course directors (3-5 per course). These basic guidelines have been modeled after those set for years by EMBO Global Exchange Courses. The courses are, therefore, self-sustained and do not draw from other intramural funds.

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 (14-16 February 2011, London, UK) with the aim to establish an International Severe Acute Respiratory Infection Consortium (ISARIC) under the auspices of the Heads of International Research Organizations, which includes the Bill and Melinda Gates Foundation, CIHR, EC, Inserm, Institut Pasteur, MRC UK, NIH and Wellcome Trust. Professor Bruzzone has served as the Scientific Coordinator of the RESPARI and SISEA programs that were implemented in the Asia Pacific region of the Pasteur Network and completed in 2011 These programs have been a platform to promote active (www.hku.hk.respari/). 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\$76M by the University Grants Committee in the fourth round of its Areas of Excellence scheme. Professor Peiris continues to serve on a number of WHO working groups in relation to both avian and swine origin influenza virus. Moreover, HKU-PRC has entered into a collaborative project (Funding scheme: Largescale integrating project) supported through the 7th Framework Program of the European Union. Professor Peiris will coordinate the activity of HKU-PRC.

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 had 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 of more than HK\$1.7 million. 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. In summary, the financial position of the Centre is considered as stable with a total net asset of HK\$0.552M and a balance of cash and cash equivalent of HK\$1.776M stood at June 30, 2011.

3. Scientific Output 2011

3.1 Publications cited in PubMed

- Bahl J, Nelson MI, Chan KH, Chen R, Vijaykrishna D, Halpin RA, Stockwell TB, Lin X, Wentworth DE, Ghedin E, Guan Y, Malik Peiris JS, Riley S, Rambaut A, Holmes EC, Smith GJ (2011) Temporally structured metapopulation dynamics and persistence of influenza A H3N2 virus in humans. Proc Natl Acad Sci USA 108:19359-19364.
- 2. Brault JB, Kudelko M, Vidalain PO, Tangy F, Desprès P, Pardigon N (2011) The interaction of flavivirus M protein with light chain Tctex-1 of human dynein plays a role in late stages of virus replication. Virology 417:369-378.
- Chan LY, Kwok HH, Chan RW, Peiris MJ, Mak NK, Wong RN, Chan MC, Yue PY (2011) Dual functions of ginsenosides in protecting human endothelial cells against influenza H9N2-induced inflammation and apoptosis. J Ethnopharmacol 137:1542-6
- Chan RW, Kang SS, Yen HL, Li AC, Tang LL, Yu WC, Yuen KM, Chan IW, Wong DD, Lai WW, Kwong DL, Sihoe AD, Poon LL, Guan Y, Nicholls JM, Peiris JS, Chan MC (2011) Tissue tropism of swine influenza viruses and reassortants in ex vivo cultures of the human respiratory tract and conjunctiva. J Virol 85:11581-7
- Chiu SS, Chan KH, Wong WH, Chan EL, Peiris JS (2011) Age-Matched Comparison of Children Hospitalized for 2009 Pandemic H1N1 Influenza with Those Hospitalized for Seasonal H1N1 and H3N2. PLoS One 6:e21837.
- 6. Chu DK, Leung CY, Gilbert M, Joyner PH, Ng EM, Tse TM, Guan Y, Peiris JS, Poon LL (2011) Avian coronavirus in wild aquatic birds. J Virol 85:12815-12820.
- Desvaux S, Garcia JM, Nguyen TD, Reid SA, Bui NA, Roger F, Fenwick S, Peiris JS, Ellis T (2011) Evaluation of serological tests for H5N1 avian influenza on field samples from domestic poultry populations in Vietnam: Consequences for surveillance. Vet Microbiol 156:277-84
- Hui KP, Lee SM, Cheung CY, Mao H, Lai AK, Chan RW, Chan MC, Tu W, Guan Y, Lau YL, Peiris JS (2011) H5N1 Influenza Virus-Induced Mediators Upregulate RIG-I in Uninfected Cells by Paracrine Effects Contributing to Amplified Cytokine Cascades. J Infect Dis 204:1866-1878.
- 9. Jaume M, Yip MS, Cheung CY, Leung HL, Li PH, Kien F, Dutry I, Escriou N, Altmeyer R, Nal B, Daëron M, Bruzzone R, Peiris JS (2011) Anti-SARS-CoV Spike Antibodies Trigger Infection of Human Immune Cell via a pH- and Cysteine Protease-Independent Fc{gamma}R Pathway. J Virol 85:10582-10597.
- 10. Mak PW, Wong CK, Li OT, Chan KH, Cheung CL, Ma ES, Webby RJ, Guan Y, Malik Peiris JS, Poon LL (2011) Rapid genotyping of Swine influenza viruses. Emerg Infect Dis 17:691-694.
- II. Poon LL, Chan KH, Chu DK, Fung CC, Cheng CK, Ip DK, Leung GM, Peiris JS, Cowling BJ (2011) Viral genetic sequence variations in pandemic H1N1/2009 and seasonal H3N2 influenza viruses within an individual, a household and a community. J Clin Virol 52:146-50.

- Trevennec K, Chevalier V, Grosbois V, Garcia JM, Thu HH, Berthouly-Salazar C, Peiris JS, Roger F (2011) Looking for avian influenza in remote areas. A case study in Northern Vietnam. Acta Trop 120:160-166.
- 13. Trevennec K, Cowling BJ, Peyre M, Baudon E, Martineau GP, Roger F (2011) Swine influenza surveillance in East and Southeast Asia: a systematic review. Anim Health Res Rev 12:213-223.
- Vijaykrishna D, Smith GJ, Pybus OG, Zhu H, Bhatt S, Poon LL, Riley S, Bahl J, Ma SK, Cheung CL, Perera RA, Chen H, Shortridge KF, Webby RJ, Webster RG, Guan Y, Peiris JS (2011) Long-term evolution and transmission dynamics of swine influenza A virus. Nature 473:519-522.
- 15. Wu JT, Ho A, Ma ES, Lee CK, Chu DK, Ho PL, Hung IF, Ho LM, Lin CK, Tsang T, Lo SV, Lau YL, Leung GM, Cowling BJ, Peiris JS (2011) Estimating Infection Attack Rates and Severity in Real Time during an Influenza Pandemic: Analysis of Serial Cross-Sectional Serologic Surveillance Data. PLoS Med 8:e1001103.
- Yang L, Chiu SS, Chan KP, Chan KH, Wong WH, Peiris JS, Wong CM (2011) Validation of statistical models for estimating hospitalization associated with influenza and other respiratory viruses. PLoS One 6:e17882.
- Yang L, Ma S, Chen PY, He JF, Chan KP, Chow A, Ou CQ, Deng AP, Hedley AJ, Wong CM, Peiris JS (2011) Influenza associated mortality in the subtropics and tropics: Results from three Asian cities. Vaccine 29:8909-8914.
- 18. Yen HL, Liang CH, Wu CY, Forrest HL, Ferguson A, Choy KT, Jones J, Dik-Yan Wong D, Pak-Hang Cheung P, Hsu CH, Li OT, Yuen KM, Chan RW, Poon LL, Chan MC, Nicholls JM, Krauss S, Wong CH, Guan Y, Webster RG, Webby RJ, Peiris M (2011) Hemagglutinin-neuraminidase balance confers respiratory-droplet transmissibility of the pandemic H1N1 influenza virus in ferrets. Proc Natl Acad Sci U S A. 108:14264-9
- Yu WC, Chan RW, Wang J, Travanty EA, Nicholls JM, Peiris JS, Mason RJ, Chan MC (2011) Viral replication and innate host responses in primary human alveolar epithelial cells and alveolar macrophages infected with influenza H5N1 and H1N1 viruses. J Virol 85:6844-55
- 20. Zhou Y, Ng DM, Seto WH, Ip DK, Kwok HK, Ma ES, Ng S, Lau LL, Wu JT, Peiris JS, Cowling BJ (2011) Seroprevalence of antibody to pandemic influenza A (H1N1) 2009 among healthcare workers after the first wave in Hong Kong. J Hosp Infect. 78:308-11
- 21. Zhou Y, Ng DM, Seto WH, Ip DK, Kwok HK, Ma ES, Ng S, Lau LL, Peiris JS, Cowling BJ (2011) Seroprevalence of Pandemic H1N1 Antibody among Health Care Workers in Hong Kong Following Receipt of Monovalent 2009 H1N1 Influenza Vaccine. PLoS One 6:e27169.
- 22. Garcia JM and Lai JCC (2011) Production of influenza pseudotyped lentiviral particles and its use in flu research and diagnosis-an update. Expert Rev Anti Infect Ther. 9:443-55.
- 23. Keng CT, Akerström S, Leung CS, Poon LL, Peiris JS, Mirazimi A, Tan YJ (2011) SARS coronavirus 8b reduces viral replication by down-regulating E via an ubiquitinindependent proteasome pathway. Microbes Infect 13:179-188.
- 24. Lee SM, Gai WW, Cheung TK, Peiris JS (2011) Antiviral activity of a selective COX-2 inhibitor NS-398 on avian influenza H5N1 infection. Influenza Other Respi Viruses 5 Suppl 1:230-232.

- 25. Garcia JM (2011) Pseudotyped viruses: a new tool for sero-diagnostic. In: Advanced techniques in viral detection (Marks RS, Lobel L, Sall A, eds), Neobionics, in press.
- 26. Nicholls JM, Lai JCC and Garcia JM (2011) Investigating the interaction between influenza and sialic acid making and breaking the link. In: Milestones in Drug Therapy. BioSciences (von Itzstein M, ed), Birkhäuser, in press.

3.2 List of Posters presented at Meetings

- Ma H, Kien F, Manière M, Zhang Y, Tse K, Poon L, Nal B. Human annexin A6 interacts with the influenza A virus M2 protein and negatively modulates infection. 16th Research Postgraduate Symposium, Li Ka Shing Faculty of Medicine, The University of Hong Kong, December 8, 2011, Hong Kong (oral presentation).
- 2. Ma H, Kien F, Manière M, Zhang Y, Tse K, Poon L, Nal B. Human annexin A6 interacts with the influenza A virus M2 protein and negatively modulates infection. Scientific International Meeting of the Young Researchers from Institut Pasteur International Network, November 10, 2011, Paris (oral presentation).
- 3. Ma H, Kien F, Manière M, Zhang Y, Tse K, Poon L, Nal B. Human annexin A6 interacts with the influenza A virus M2 protein and negatively modulates the infection. 6th International Conference on Annexins, August 28-31, 2011, Barcelona (poster).
- 4. Ma H, Kien F, Manière M, Zhang Y, Tse K, Poon L, Nal B. Human annexin A6 interacts with the influenza A virus M2 protein and negatively modulates the infection. Keystone Symposia, Pathogenesis of Influenza: Virus-Host Interactions, May 23-28, 2011, Hong Kong (oral presentation).
- 5. Tang DJ, Lam YM, Lam CH, Chu SL, Bruzzone R, NaL B. Mutational analysis of H5N1 hemagglutinins: identification of molecular determinants for efficient packaging into pseudotyped lentiviral particles. ASBMB Special symposia: Recent Advances in Pathogenic Human Viruses, July 24-26, 2011, Guangzhou, China (Poster).
- 6. Tang DJ, Lam YM, Lam CH, Chu SL, Peiris MJS, NaL B, Bruzzone R. Mutational analysis of H5N1 hemagglutinins: identification of molecular determinants for efficient production of H5 pseudotyped lentiviral particles. Scientific International Meeting of the Young Researchers from Institut Pasteur International Network, November 10, 2011, Paris (Poster).
- 7. Tang DJ, Lam YM, Lam CH, Chu SL, Bruzzone R. Identification of molecular determinants for efficient production of H5 pseudotyped lentiviral particles. Surveillance and Discovery in Respiratory and Other Emerging Diseases, May 29-31, 2011, Phnom Penh, Cambodia (Poster).
- 8. Zhang Y, Kien F, Ma HL, Tse J, Poon LLM, Nal B. Identification of a novel interaction between the M2 proton channel of influenza A virus and cyclin D3: consequences for cell cycle progression. Keystone Symposia, Pathogenesis of Influenza: Virus-Host Interactions, May 23-28, 2011, Hong Kong (poster).

3.3 Seminars, Invited Lectures and Oral Presentations at Meetings

- 1. Roberto Bruzzone (2011) International Severe Acute Respiratory Infection Consortium (ISARIC) Workshop, Wellcome Trust, London, UK.
- 2. Roberto Bruzzone (2011) 2nd Regional Workshop on Infectious Encephalitis, Institut Pasteur du Cambodge, Kingdom of Cambodia.
- 3. Roberto Bruzzone (2011) Surveillance and Discovery in Respiratory and Other Emerging Infectious Diseases, Phnom Penh, Kingdom of Cambodia.
- 4. Roberto Bruzzone (2011) Roberto Bruzzone (2011) Workshop on "Microbiology, Pathogenesis and Therapies for Pandemic Threats and Emerging Diseases", Singapore.
- 5. Roberto Bruzzone (2011) Scientific Conference on "120 Years for Control and Prevention of Communicable diseases", Institut Pasteur of Saigon-Ho Chi Minh City, Vietnam.
- 6. Roberto Bruzzone (2011) International Symposium on "Non-traditional security and Global collaboration and Networking", Waseda University, Tokyo, Japan.
- 7. Huailiang Ma (2011) Human annexin A6 interacts with the influenza A virus M2 protein and negatively modulates infection. Scientific International Meeting of the Young Researchers from Institut Pasteur International Network, Paris, France.
- 8. Huailiang Ma (2011) Human annexin A6 interacts with the influenza A virus M2 protein and negatively modulates infection. Keystone Symposia, Pathogenesis of Influenza: Virus-Host Interactions, Hong Kong SAR.

3.4 Active Grants in 2011

Research Fund for the Control of Infectious Diseases

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

Research Fund for the Control of Infectious Diseases

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

Research Fund for the Control of Infectious Diseases

Principal Investigator:	Dr Huiling Yen
Amount:	HK\$819,442.00
Period:	01/Jan/2010 to 30/Jun/2012

Research Fund for the Control of Infectious Diseases (Special mission)

Principal Investigator: Amount: Period: Dr Huiling Yen HK\$138,000.00 31 May 2011

Research Fund for the Control of Infectious Diseases

Principal Investigator: Amount: Period: Dr Francois Kien HK\$955,648.00 01/Nov/2011 to 31/Oct/2013

Research Grants Council

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

European Commission (FP7)

Principal Investigator: Amount: Period: Dr Malik Peiris/Dr John Nicholls Euro 375,150.00 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 31/Aug/2012

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

Principal Investigator:	Dr Francois Kien
Amount:	HK\$482,340.00
Period:	01/Jan/2011 to 31/Dec/2011

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

Principal Investigator: Amount: Period: Dr Francois Kien HK\$511,320.00 01/Jan/2012 to 31/Dec/2012

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

Principal Investigator: Amount: Period: Dr Martial Jaume HK\$200,000.00 01/Jan/2012 to 31/Dec/2012

Research Fund for the Control of Infectious Diseases

Principal Investigator:	Dr Suki Lee
Amount:	HK\$996,576.00
Period:	01/Jan/2012 to 31/Dec/2013

BNP

Principal Investigator:	Dr Roberto Burzzone
Amount:	HK\$600,000.00
Period:	01/Jan/2011 to 31/Dec/2012

3.5 Pending Grant Applications

Research Fund for the Control of Infectious Diseases

Principal Investigator:	Dr Chris Mok
Amount:	HK\$696,067.00
Period:	01/Oct/2012 to 30/Sep/2014

Research Fund for the Control of Infectious Diseases

Principal Investigator:Dr Suki LeeAmount:HK\$998,544.00Period:01/Jan/2013 to 31/Dec/2014

Research Fund for the Control of Infectious Diseases

Principal Investigator:	Dr Peigang Wang
Amount:	HK\$960,000.00
Period:	24 months

4. Annexes

4.1 Organization Chart and List of Staff

4.2 Budget for the year ending June 2012

FUNDING:

Central Fund	2,484,762.42
LKS Faculty of Medicine	200,000.00
Institut Pasteur	400,000.00
Endowment Fund & Private Donation	1,603,976.67
External Grants	<u>2,279,022.00</u> 6,967,761.09

EXPENSES:

Executive	1,084,101.00
Research Team One	1,335,198.67
Research Team Two	2,903,840.00
Teaching & Training	840,000.00
Administration	<u>804,621.42</u> 6,967,761.09

4.3 International Meetings co-organized by HKUPRC

Institut Pasteur International Network

"Surveillance and Investigationof Respiratory Diseases" Phnom Penh, Cambodia May 29 – 31, 2011



International Workshop Surveillance and Discovery in Respiratory and Other Emerging Infectious Diseases

KEYNOTE SPEAKERS

Sylvie Briand Global Influenza Programme World Health Organization Geneva, Switzerland

Jeremy Farrar

Oxford University Clinical Research Unit The Hospital for Tropical Diseases Ho Chi Minh City, Vietnam

Raymond Lin

National Public Health Laboratory Ministry of Health Singapore

Yoshiko Okamoto

RIKEN Center of Research Network for Infectious Diseases (CRNID) Tokyo, Japan Ben Cowling The University of Hong Kong Pokfulam, Hong Kong SAR

Chin Kei Lee

World Health Organization, Regional Office for the Western Pacific Manila, Philippines

Paul N. Newton

Wellcome Trust – Mahosot Hospital – Oxford Tropical Medicine Research Collaboration Vientiane, Lao PDR

Raul Sotomayor

U.S. Department of Health and Human Services Washington DC, USA

Keystone Symposia Meeting

"Pathogenesis of Infulenza: Virus-Host Interactions" Hong Kong May 23 - 28,

2011

KEYSTONE SYMPOSIA on Molecular and Cellular Biology Pathogenesis of Influenza: Virus-Host Interactions (E3)

Fathogenesis of influenza. Virus-host interactions (ES)

May 23-28, 2011 • Sheraton Hong Kong Hotel & Towers • Kowloon, Hong Kong • China

Scientific Organizers: Siamon Gordon, Malik Peiris and Kanta Subbarao

Organized in Collaboration with The University of Hong Kong and part of its Centenary Celebration; also made possible by an Area of Excellence in Influenza grant funded by the University Grants Committee of Hong Kong

Abstract & Scholarship Deadline: January 21, 2011 / Late-Breaking Abstract Deadline: February 22, 2011 / Early Registration Deadline: March 22, 2011

MONDAY, MAY 23

Keynote Session

Sir John J. Skehel, MRC National Institute of Medical Research, UK Structure Function of HA Robert G. Webster, St. Jude Children's Research Hospital, USA

Ecology Peter C. Doherty, University of Melbourne, Australia

T Cells

TUESDAY, MAY 24

Virology

Ron A.M. Fouchier, Erasmus Medical Center Rotterdam, Netherlands Viral Virulence Yoshihiro Kawaoka, University of Wisconsin; University of Tokyo, USA Influenza Pathogenesis Yi Guan, Hong Kong University, China The Emergence and Development of H1N1/2009 Pandemic Influenza Virus Nadia Naffakh, Institut Pasteur, France Influenza Ribonucleoproteins - Host Cell Interactions

Virus Receptors/Glycans/Structure

John Nicholls, University of Hong Kong, China Receptors in the Human Respiratory Tract Ram Sasisekharan, Massachusetts Institute of Technology, USA *Glycans and HA* Gillian M. Air, University of Oklahoma Health Sciences Center, USA *Glycans:HA-NA Interaction*

WEDNESDAY, MAY 25

Human Disease, Lung Injury and Human-Cell Experimental Models

Sherif R. Zaki, Centers for Disease Control and Prevention, USA Talk Title to be Determined Arthur Slutsky, University of Toronto, Canada Lung Injury and ARDS Chi-Huey Wong, Academia Sinica, Taiwan Glycans: Receptor Binding and Immune Response Malik Peiris, University of Hong Kong, China Human ex vivo and in vitro Experimental Models

Workshop 1: Pathogen-Host Interaction Short Talks to be Chosen from Abstracts

Experimental Models

Andrew S. Pekosz, Johns Hopkins University, USA Influenza Infection of Primary, Differentiated Human Respiratory Epithelial Cell Cultures

Jacqueline M. Katz, Centers for Disease Control and Prevention, USA Ferrets/Mice Kanta Subbarao, NIAID, National Institutes of Health, USA Non-Human Primates

THURSDAY, MAY 26

Immunity (Myeloid Cells)

Caetano Reis e Sousa, Cancer Research UK, London Research Institute, UK Innate Recognition of Influenza Virus Siamon Gordon, University of Oxford, UK Macrophage Receptors and Activation Jenny P. Ting, University of North Carolina at Chapel Hill, USA Cytosolic Recognition Ken J. Ishii, Immunology Frontier Research Center, Osaka University, Japan Talk Title to be Determined

Immunity, Systems Biology, Gender and Susceptibility

Tao Dong, Oxford University, UK CD4 Cells Jack R. Bennink, NIAID, National Institutes of Health, USA Antigenic Drift: Mechanisms of Influenza A Virus Hemagglutinin Immune Escape Ronald N. Germain, NIAID, National Institutes of Health, USA Systems Biology Sabra Klein, Johns Hopkins University, USA Sex Differences in Susceptibility to Influenza A Viruses

FRIDAY, MAY 27

Pathogenesis/Lung Injury

Adolfo Garcia-Sastre, Mount Sinai School of Medicine, USA Induction and Inhibition of IFN Responses by Influenza Viruses Tracy Hussell, Imperial College London, UK Influenza-Induced Immunological Alterations in the Respiratory Tract Jeffrey A. Whitsett, Cincinnati Children's Hospital Medical Center, USA

Surfactant

Speaker to be Announced

Workshop 2: Modulation of Infection

Short Talks to be Chosen from Abstracts

Interventions

Aviv Regev, Massachusetts Institute of Technology, USA Host-Influenza Interactions Philip Dormitzer, Novartis Vaccines, USA Advances in Vaccines against Seasonal and Pandemic Influenza Stephan Ludwig, University of Münster, Germany Immunomodulation

Program current as of January 14, 2011. Program subject to change. For the most up-to-date details, visit www.keystonesymposia.org/11E3. * Session Chair † Invited but not yet accepted

4.4 List of Public Lectures organized by HKU-PRC

12 Apr 2011

13 Apr 2011

"Genetic and proteomic approaches to study cell cycle proteins in development and in cancer" by Dr Peter Sicinski

14 Apr 2011

"Automated live-cell microscopy for high content RNAi screening", "Overview on cell division " & "Bridging spatial and temporal resolution gaps in the study of cell division" by Dr Daniel Gerlich

18 Apr 2011

- "Nucleo-cytoplasmic trafficking and Viruses" & "Nucleo-cytoplasmic trafficking: from viral target to antivirals" by Dr Beatriz M Fontoura
- "Signalling and cytoskeletal dynamics during the cell to cell spread of vaccinia virus"by Dr Michael Way

19 Apr 2011

- "The mechanisms of prion intracellular replication and spreading: role of tunnelling nanotubes" by Dr Chiara Zurzolo
- "Cell biology of Malaria parasite motility" by Dr Freddy Frischknecht
- "Dynamic Imaging 1. Managing photons and phototoxicity in vitro and in vivo" by Dr Spencer Shorte

20 Apr 2011

- "Assembly of cilia and flagella: a 500-piece jigsaw" by Dr Philippe Bastin
- "How does RNAi control viral infections in insects?" by Dr Carla Saleh
- "Dynamic Imaging 2. Understanding Fluorescence versus Bioluminescence by Dr Spencer Shorte

26 Apr 2011

- "Physiological consequences of Annexin A6-induced alterations in cholesterol homeostasis: from membrane trafficking to signalling" by Dr Carlos Enrich

6-Jul-2011

"Dengue- pathogenesis, epidemiology and novel approaches to prevention" by Dr Cameron Simmons

7-Jul-2011

"Virus evolution and quasispecies" by Dr Esteban Domingo

8-Jul-2011

- "Epidemiology of Arboviral hemorrhagic fevers" by Dr Herve Zeller
- "Detecting new and emerging viruses (Part 1)" by Dr Christian Drosten
- "Detecting new and emerging viruses (Part 2)" by Dr Christian Drosten

11-Jul-2011

- "Introduction to Flavivirus" by Dr Felix Rey

[&]quot;Cells, images and numbers" by Dr JC Olivo-Marin

- "Class II enveloped viruses" by Dr Felix Rey

20-Jul-2011

- "Mouse model of disease: a focus on alphavirus infections" by Dr Suresh Mahalingam

7-Oct-2011

- "Novel human restriction enzymes for microbes – part of a much bigger picture" by Dr Simon Wain-Hobson

14 Nov 2011

- "Symbiotic bacteria and intestinal innate immunity" by Dr Gérard Eberl
- "Intestinal adaptive immunity" by Dr Gérard Eberl

15 Nov 2011

- "Protection against tuberculosis towards new TB vaccines" by Dr Hazel Dockrell
- "Immune defence of respiratory system" by Dr Wenwei Tu

23 Nov 2011

- "Vaccines for FMD and influenza virus" by Dr Shu Mei Liang
- "Future challenges: towards anti-cancer vaccines?" by Prof Claude Leclerc

05 Dec 2011

- "Targeting of host endomembrane compartments by invasive bacterial pathogens novel insights through automated fluorescence microscopic approaches" by Dr Enninga