香港大學－巴斯德研究中心
HKU-Pasteur Research Centre

Annual Report 2009

HKU-Pasteur Research Center

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8, Sassoon Road

Hong Kong SAR, China

Roberto Bruzzone, CEO

Malik Peiris, Scientific Director

Hong Kong, April 22, 2010

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1. Executive Summary

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. The key aspect of our research approach is to bring together the cutting edge developments in the cell-biology of infectious disease, which is the strength of Institut Pasteur, with the expertise in the clinical virology and immunology of infectious disease, which is the strength of HKU. **This concept allows maximizing synergies between the founding partners with the objective to maintain a vigorous, top quality research and teaching programs, while taking advantage of the exceptional and complementary network of collaborators**. The results obtained in 2009 are clearly in line with these targets, which were presented by the new directorate team to the Board of Management and to the Scientific Advisory Board. These achievements are reflected in the pivotal role of HKU-PRC in **leading local and regional network projects**.

We have solidified our research focus on respiratory infections and on the mosquito borne disease of dengue by securing several independent extramural grants, which have allowed strengthening several research teams and also attest to the quality of the Group Leaders. These programs are developed through several key collaborations with Institut Pasteur, HKU, the International Network of Pasteur Institutes and many leading laboratories worldwide. **The scientific output of the Center has remained very strong, with 25 manuscripts published in 2009** (up from 10 in 2008) and several publications having already appeared in 2010 or being in the final stages before submission. The Center is an **integral part of the Area of Excellence** on Influenza and has a number of research programs related to this program. **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** programs of the International Network of Pasteur Institutes. Finally, **HKU-PRC is directly involved in the organization of several international scientific meetings (including a Keystone Conference)** that will take place in the second half of 2010 and in 2011.

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**. As a first step toward a more complete integration with the Li Ka Shing Faculty of Medicine of HKU, **Dr Beatrice Nal-Rogier has been appointed Research Assistant Professor in the Department of Anatomy to** be seconded to the Center. We have strengthened our team with **the addition of another group led by Dr Hui-Ling Yen, who holds an appointment as Research Assistant Professor in the Department of Microbiology**. Dr Yen leads the Molecular Virology team that uses reverse genetics to study the pathogenesis of influenza in by combining cellular (in vitro) and animal (in vivo) models. The Yen lab moved to the Center in August, and has already established solid contacts with the other Group Leaders. Dr Yen's expertise in applying animal models and plasmid-based reverse genetics technique to study the biology of influenza virus will be a great asset to achieve our goals in research and teaching, having already resulted in new collaborative projects and her involvement in the organization of the HKU-Pasteur Immunology Course. This **strategy of joint appointments**, which we have **discussed with Professor Sum-Ping Lee**,

the Dean of the Li Ka Shing Faculty of Medicine**, will be pursued to facilitate the interactions of the Center with the Faculty**, the career development of Junior Group Leaders and the gradual involvement of the Center in undergraduate teaching.

The Teaching and Training Center of Excellence in Biomedical Research has become operational and we have achieved our goal to offer an annual program of courses for postgraduate students and young scientists that is extremely competitive and comparable in quality to other international programs (EMBO, Cold Spring Harbor). HKU-Pasteur courses in Cell Biology, Virology and Immunology are gaining a strong reputation in Hong Kong and the Asia-Pacific region. **The Teaching Center of HKU-PRC has provided the necessary bench space for the practical sessions of the 1st International Course on Stem Cell Biology and Regenerative Medicine** (August 23 - August 29, 2009), which was co-organized by the University of Toronto, The Hospital for Sick Children Research Institute, Mount Sinai Hospital (Canada), and the Strategic Themes of Development and Reproduction, Cancer and Healthy Ageing (HKU).

The research programs of **HKU-PRC have received** in 2009 **important endorsements through private donations**. **The French Chamber of Commerce and Industry in Hong Kong** chose again our Center as the charitable organization to which **proceeds of the Annual Gala Dinner have been donated**. This allowed a brief presentation of the mission and activities of the Centre in front of a strong audience of executives and businessmen. In addition, **BNP Paribas Corporate & Investment Banking** (CIB) has decided to renew its **partnership with Institut Pasteur** and to help again this year in the global fight against infectious diseases. **BNP Paribas CIB offers financial aid** across 26 countries **to research teams of the International Network of Pasteur Institutes**, as well as to laboratories working in collaboration with the Institut Pasteur in Paris. **The donation to HKU-PRC will be used to fund our studies to fight dengue virus**, with a focus on achieving a complete understanding of the molecular mechanisms of regulating assembly, budding, trafficking and egress of the virus.

HKU-PRC has joined the Department of Cell Biology and Infection of Institut Pasteur as an "Associated Unit" with the support of the Board of Management and the Scientific Direction of Institut Pasteur. This association will strengthen the already existing ties (viz., in teaching and imaging) and favor scientific exchanges between Paris and Hong Kong. HKU-PRC has participated to the annual retreat of the Department (next one coming up on October 12-14) with several presentations and will continue hosting several investigators from the Department of Cell Biology and Infection during the annual courses and **Croucher-Pasteur seminar series**.

The continuous improvement of our performance validates the overall strategy developed over the past three years and, in turn, constitutes a solid foundation to ensure the long-term sustainability, as well as the full participation of HKU-PRC in the academic life of HKU and Hong Kong. We envisage that the Center will be able to expand its scope and output by targeting an interdisciplinary approach and recruiting talented Group Leaders who will contribute to forge strategic partnerships with other departments, as well as with the Area of Excellence on influenza.

2. General Overview of the Programs

Research

HKU-PRC has currently 37 staff members: 22 scientific (13 students), 11 technical and 4 administrative. The scientific activity is broadly subdivided into four main areas (Virus-Host Interaction; Viral Infection & Immunity; Molecular Virology; Translational Research) that complement each other in both scientific goals and technical aspects. All groups are actively engaged in the Teaching and Training program.

The Virus-Host Interactions team led by Dr Beatrice Nal-Rogier has expanded its studies on the identification of novel cellular targets that interact with viral components during different phases of the viral life cycle. The main objective of the group is **to identify the cellular pathways** used or modified by enveloped viruses and **to decipher what are the molecular mechanisms** involved. Three enveloped viruses of different families are used as models: influenza A (orthomixoviridae), SARS coronavirus (SARS-CoV; coronaviridae) and dengue (flaviviridae). More specifically, the group focuses on the **role of viral structural proteins**, their interactions with cellular machineries and implications for viral pathogenesis. We have pursued our studies on the cellular interactome of SARS-CoV, focusing on proteins identified in a yeast-two-hybrid screen in which the carboxy-termina tails of all structural proteins were used as baits. By a combination of biochemical experiments *in vitro* and in mammalian epithelial cells we have demonstrated a specific interaction between a coronavirus protein and PALS1, a component of tight junctions, which compromises the integrity of epithelial cells. We speculate that hijacking of PALS1 by E protein of SARS-CoV during infection plays a determinant role in disrupting lung epithelium and in the pathogenesis of the disease. **The PhD student involved in this project has successfully defended his thesis at the beginning of 2010** and has now moved to Singapore for a postdoctoral position in the laboratory of Dr Lai Guan Ng (Singapore Immunology Network). **Another PhD student working on the cellular interactome of human coronaviruses has submitted his work to the Faculty Office at the end of March 2010** and his Viva has been tentatively scheduled at the beginning of June 2010. We have uncovered the minimal sets of viral structural proteins driving assembly and budding of the SARS-CoV, dengue and H5N1 influenza A viruses in human epithelial cells by developing virus-like particles (VLPs). These VLPs formed in host cells are free of viral genome and can be used as a safe model to study viral and cellular requirements for particle assembly and budding. **We are developing strong international collaborations** with leading laboratories to exploit VLPs both in basic (ultrastructure, genomic screens) and applied research programs (diagnosis, vaccine development). **A library of small interfering RNA (siRNA) targeting human genes involved in membrane trafficking** has been screened using a human cell line that stably secretes dengue virus VLPs. So far, **five cellular factors** have been selected for their **interaction with a viral structural protein** or for their interference with a step of the viral life cycle. Specific studies are being implemented to decipher the molecular mechanisms regulating these virus-host interactions. **A declaration of invention has been filed in March 2009 to patent our system for generation of dengue VLPs of the four serotypes as a means to produce native antigens for several applications: antibody production, diagnosis, vaccination**. Further validation of this tool requires an extensive ultrastructural characterization of

purified dengue prME VLPs by cryo-electron microscopy and tomography, which will be carried out in collaboration with Professor Michael G. Rossmann at Purdue University. **The successful continuation of these projects has been secured by several external grants** received from the Research Fund for the Control of Infectious Diseases, the Research Grants Council and the Area of Excellence on the "Control of Pandemic and Inter-pandemic Influenza".

The Viral Infection & Immunity team led by Dr Martial Jaume focuses on the investigation of specific mechanisms underlying the interplay between viral infection and the immune response, innate and acquired by implementing research projects that are at the interface of fundamental and applied research. Our previous studies had established that **Natural Killer** (NK) **cells can bind to hemagglutinin** (HA) **of highly pathogenic avian influenza** (H5N1) via the natural cytotoxicity receptor (NCR) NKp44. **During the continuations of this project, supported by a grant** from the Research Fund for the Control of Infectious Diseases, **we have found that this interaction occurs with a fairly low affinity** and, further, that human **NKp44 binding to recombinant H5 proteins (rH5) is not affected by their N-linked glycosylation profile**. These results point to differences in the ability of envelope proteins to activate NK cells, as shown by the functional interactions observed with West Nile and dengue viruses. **These results have formed the basis of an MPhil thesis that has been submitted to the University Committee at the beginning of 2010**. Following the departure of the student, this project will not be developed further. Our previous work has strongly suggested a major role for immune receptors, particularly Fc receptors, in triggering infection of immune cells by SARS-CoV. We want to extend these observations and define the **molecular basis of the antibody-mediated infection pathway**. Our data show unambiguously that **FcγR-dependent viral entry is a novel, ACE2** (angiotensin-converting enzyme-2; the natural receptor for SARS-CoV)**-independent mechanism by which SARS-CoV can infect immune cells.** The relevance of this phenomenon is now being further tested with human primary immune cell populations. **We are now exploring whether anti-influenza antibodies may perversely facilitate infection of humans by viruses from avian origin**. Our initial results have suggested a possible role of human heterosubtypic anti-influenza antibodies (*i.e.* anti-H1N1 and anti-H3N2) in triggering infection by avian H5 influenza virus. Briefly, we have observed that several human sera display the unexpected ability to enhance infectivity of a macrophage-like cell line (*i.e.* P388D1) by H5pp. **We are, therefore, pursuing our investigations with live virus, which requires the infection to be conducted in a BLS3 facility**. These experiments are carried out in collaboration with Dr Hui-Ling Yen, who has received special training in the State Key Laboratory of Emerging Infectious Diseases thanks to her joint appointment with the Department of Microbiology at HKU. **Our findings with live virus 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 help establishment of the virus into the host**. Indeed, considering that pre-immunity against seasonal flu (*i.e.* H1N1 and H3N2) is common among the human population, it will be of interest to unravel mechanisms of antibody-mediated infection of influenza viruses. Further investigations on the role of vaccination in the exacerbation of influenza symptoms are needed. **These projects have been supported by two external grants** received from the Research Fund for the Control of Infectious Diseases.

The Molecular Virology lab has been established in 2009 with the recruitment of Dr Hui-Ling Yen (see Annex 2), a Research Assistant Professor who holds a joint appointment with the Department of Microbiology at HKU and HKU-PRC. The Yen lab uses reverse genetics to study the pathogenesis of influenza in by combining cellular (in vitro) and animal (in vivo) models. **A major effort is devoted to elucidate viral factors that determine differences in pathogenicity** between the highly pathogenic H5N1 viruses and seasonal human influenza virus. As hyper-induction of pro-inflammatory cytokines correlates with severity of disease following H5N1 influenza infection, it is crucial to identify molecular determinants of H5N1 virus that trigger the host innate immune response. **The current focus is on viral surface glycoprotein hemagglutinin** and its potential interaction with dendritic cells. Parallel studies are carried put to **map molecular determinants that enable transmission and replication of avian or swine influenza viruses in human.** The **host range of influenza A virus is determined by multiple viral and host factors**. As a result, inter-species transmission usually leads to unapparent or mild clinical symptoms without further transmission in the new host species. However, the **gene constellations that enable transmission and replication of avian-origin H5N1/ H9N2 or swine-origin H1N1 influenza viruses in human are not known**. We **aim to address this question by generating recombinant viruses with different gene constellations** and applying in vitro and in vivo models to assess viral replication and transmissibility. **These projects have been supported by external grants** received from the Research Fund for the Control of Infectious Diseases and the Area of Excellence on the "Control of Pandemic and Inter-pandemic Influenza". An application has been submitted for review to the Research Grants Council.

The activity of the Translational Research group, led by Dr Jean-Michel Garcia, has followed three main axes of research, with a focus on **molecular biology/tool development, diagnostics and drug discovery**. This diversity of applications exploits the adaptability of a very flexible tool, pseudotyped viral particles. The rationale for this option has been to create a strong interface between fundamental research and possible clinical applications, as illustrated by the following examples. One important achievement of 2009 has been the complete optimization and evaluation of the diagnostic **performance of the H5pp assay using well-characterized sera from humans with confirmed H5N1 disease**. Furthermore, in collaboration with Sanofi-Pasteur, we found evidence of H5N1 neutralizing antibodies (titer ≥20) in a minority of post-seasonal vaccine sera, which indicates that these **healthy volunteers unexposed to H5N1 possess heterosubtype antibodies that cross-react with H5 haemagglutinin**. In another work, in **collaboration with Institut Pasteur-Cambodia and the Hospital for Tropical Diseases in Ho Chi Minh City** (Oxford University Clinical Research Unit/Wellcome Trust), we have investigated and **compared the kinetics of anti-H5 avian influenza antibodies in naturally infected**, hospitalized patients and asymptomatic individuals living in villages with recorded H5N1 outbreak. **We found that the time course of antibody production is different from that reported for seasonal influenza**, in which antibody titers fall significantly few months post infection, although the slopes of the decay of titers were not significantly different between the two groups by linear regression analysis. Patients with clinically severe manifestation of H5N1 infection usually develop higher neutralizing antibody titers, which last longer than those of individuals with asymptomatic or mild infection. **This study provides new data on the kinetics of the humoral immune response to influenza H5N1 infection**. Our findings, therefore, may have significant

implications in the clinical management of the disease, because they define a useful time frame to apply and interpret serological data for H5N1 infection. These developments have led to **establish collaborations with other partners** based in the region, such as **AFRIMS** (Armed Forces Research Institute of Medical Sciences, whose regional centre is based in Bangkok, Thailand) and **CIRAD** (Agricultural Research for Development, France). In the area of **Molecular biology/Tool development, we have** previously shown that virus like particles (VLPs) can be conveniently produced **to investigate the interactions of the viral glycoprotein with** its sialylated ligands **at atomic level with** a physical technique called **Nuclear Magnetic Resonance** (NMR). We are continuing the collaboration with Prof Mark von Itzstein's group (Institute of Glycomics, Griffith University, Australia), and **have obtained initial data showing that this technology can also be used to investigate NA-ligands interactions**. We have already observed that some parameters, such as pH, appear to shift the activity towards either enzymatic activity (at acidic pH) or binding (at neutral pH). Furthermore, in the course of experiments aimed at generating a robust source of VLPs containing neuraminidase (NA), we have demonstrated that NA has a key role in virus budding and morphogenesis, a finding that has led us to propose that NA-VLPs represent a useful tool in influenza research. These studies have defined the minimal viral genetic requirement for the generation of influenza virus like particle (VLP) assembly and budding. **These projects have been supported by external grants** received from the Area of Excellence on the "Control of Pandemic and Inter-pandemic Influenza" and the Research Grants Council.

The activity of HKU-PRC has naturally been influenced by **the outbreak of swine flu that has caused a great deal of alarm worldwide**. Pandemic influenza remains the pre-eminent emerging infectious disease threat to global health and Hong Kong is located at the epicenter of a possible pandemic emergence. **Being within Hong Kong but also being linked to the Pasteur Network of laboratories worldwide, and in Asia-Pacific in particular, we are well placed to be at the forefront of an early warning and response to emerging disease threats**. In close collaboration with the department of Microbiology, **HKU-PRC has contributed to the development of a novel, specific and sensitive test to detect the novel human H1N1 influenza virus**. This test allows a rapid detection of the virus, can be performed with conventional PCR methods that are available in most laboratories in a BSL-2 containment and uses Asian swine H1N1 virus (A/SW/HK/PHK1578/03), which is not adapted to human transmission, and represents a much safer option as a positive control. These reagents and methodology have already been supplied to a number of countries in the region.

Teaching and Education

We have achieved our goal to offer an annual program of courses for postgraduate students and young scientists that is extremely competitive, comparable in quality to other international programs (EMBO, Cold Spring Harbor), and is becoming a reference for Hong Kong and the Asia-Pacific region. **Two other milestones have marked 2009**. First, the **organization of a World EMBO Course** (supported by the International Network of Pasteur Institutes) **on Bioinformatics**, that was an overwhelming success. The huge number of applications has prompted plans to run a second edition in 2011. Second, together with Dr Frederick Keck, social anthropologist at the CNRS in Paris, who joined us as a Visiting Fellow of the Fyssen Foundation, we have **organized a conference on "Avian**

Flu: Social and Anthropological Perspectives" to discuss the social aspects of networks of surveillance and measures of control, and to open perspectives for the future at an international level. **The Center is taking an active role in training undergraduate students who are part of the "BIOC3614 Biochemistry Project".** In addition, we **collaborate with the** Victor Segalen **French International School in the implementation of targeted educational programs in science.** We have begun to be involved with the **International Thai-French Master Program on "Infectious, Vector-Borne and Food-Borne Diseases",** which has been launched by the University of Montpellier 2 with Kasetsart University in Bangkok, and is supported by CIRAD, Institut Pasteur and the International Network of Pasteur Institutes. Finally, the **Teaching Center of HKU-PRC has provided the necessary bench space for the practical sessions of the 1st International Course on Stem Cell Biology and Regenerative Medicine** (August 23 - August 29, 2009), which was co-organized by the University of Toronto, The Hospital for Sick Children Research Institute, Mount Sinai Hospital (Canada), and the Strategic Themes of Development and Reproduction, Cancer and Healthy Ageing (HKU).

Network projects

HKU-PRC exerts a leadership role in a number of network projects. Dr Roberto Bruzzone is the Scientific Coordinator of the RESPARI ((www.hku.hk.respari/) **and SISEA** (www.hku.hk/respari/research_07.htm) programs that federate the Institutes of the Pasteur-Asia network in a multi-center project. The RESPARI network emphasizes fundamental and translational research; it has established itself as one of the flagship research programs of the network having acquired international reputation, and has been instrumental in promoting active collaboration between the Pasteur network in Asia, HKU-PRC and HKU. **The aim of the Surveillance and Investigation of Endemic Situations in Southeast Asia (SISEA) program,** a key initiative financed by the French Development Agency (AFD), **is to contribute to the improvement of the detection and handling of epidemic situations in the region**. As the Scientific Coordinator of this major Public Health project, Dr Bruzzone has played a major role in the implementation and output of surveillance programs, as well as in the conception and organization of regional scientific meetings and training sessions. One of the main achievements of 2009 has been **the organization of an International Scientific week** hosted by the Pasteur Institute of Ho Chi Minh City (VietNam), which included an **International Scientific Forum**, followed by a **Technical Workshop on Encephalitis**. **The forum was also attended by SISEA's Scientific Advisory Board (SAB)**, which **praised the results obtained with respect to wealth of information that was being generated, harmonization of procedures and building of a strong team that represents a solid foundation for the long-term impact of SISEA**.

The past year has seen the birth of GLODEN (GLObal network for DENgue research). This is a **new initiative launched by Institut Pasteur and the International Network of Pasteur Institutes** with the goal to investigate the complex interplay between viral, mosquito, human genetics and environmental factors underlying differential outcomes of dengue infection. **HKU-PRC is committed to the establishment of a global network for dengue study and has elaborated a project encompassing basic research, serology and immunology.**

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 in 2008and 2009 to successfully implement specific research areas and strengthen our scientific collaborations with many groups at HKU and other universities in Hong Kong. It is worth mentioning that **Area of Excellence team members responded rapidly to the emergent H1N1 pandemic by developing molecular diagnostic tests for the pandemic virus within 4 days of the WHO announcement** on the 24th April of a novel H1N1 virus of swine origin spreading in Mexico and USA. This work was **signed by HKU-Pasteur Research Centre** (see reference #8 of the scientific output: Poon et al, Clin Chem 2009). **Professor Peiris also continues to serve on a number of WHO working groups in relation to both avian influenza H5N1 and, more recently, the swine origin influenza virus H1N1.**

Finally, several major international events will be organized and/or chaired by the directorship of HKU-PRC, including: **Options for the Control of Influenza VII** (Hong Kong, 3-7 September 2010); **Annual Scientific Meeting of the International Network of Pasteur Institutes** (Hong Kong, 22-25 November 2010); **IBRO/UNESCO School of Neuroscience** on "**Neurobiology of Infectious Diseases: a view for Global Neuroscience**" (Reunion Island, 27November-2 December 2010); **2nd International Neuroinfection Meeting** (Reunion Island, 2-6 December 2010); **Keystone Conference** on "**Pathogenesis of Influenza: Virus-Host Interactions**" (Hong Kong, 23-28 May 2011).

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 intramural funds have been made available from Institut Pasteur, including a special donation that has been increased by HKU through a matching scheme (2:1 ratio). Annual contributions from the University of Hong Kong and Institut Pasteur account for about 50% of current income. The remaining income is obtained through the competition for project-based external grants and donations. HKU-PRC has posted a very good success rate in obtaining extramural grants from RGC (Research Grants Committee) and RFCID (Research Fund for the Control of Infectious Diseases) to support its core research activities. It is worth mentioning that in 2007 the Centre had only 1 approved RFCID grant, whereas our Group Leaders currently hold 1 RGC, 7 RFCID and 3 Area of Excellence contracts, with 1 RGC and 3 RFCID proposals currently under review.

In summary, the financial position of the Centre is considered as healthy with a total net asset of HK$3.13M and a balance of cash and cash equivalent of HK$7.15M stood at June 30, 2009.

3. Progress Report

3.1 PROGRAM 1: VIRUS-HOST INTERACTIONS

The Virus-Host Interactions (VHI) group investigates host-pathogens interactions using as models enveloped viruses that are of great concern to Public Health in the region.

Main Objectives and Strategy

The main objective of the group is **to identify the cellular pathways** used or modified by enveloped viruses and **to decipher what are the molecular mechanisms** involved. Three enveloped viruses of different families are used as models: influenza A (orthomixoviridae), SARS coronavirus (SARS-CoV; coronaviridae) and dengue (flaviviridae). More specifically, the group focuses on the **role of viral structural proteins**, their interactions with cellular machineries and implications for viral pathogenesis. The research projects of the group can be broadly divided into two major areas of investigation:

1. Viral structural proteins: expression, maturation, intracellular transport, assembly and budding into viral particles

A detailed **understanding of the expression, subcellular localization at steady state, dynamic transport and maturation of viral structural proteins** is a prerequisite for the **study** of their functions in the **viral replication cycle and their involvement in pathogenesis**. Assembly and budding of progeny virions in host cells is the last stage of enveloped virus life cycle. Formation of viral particles depends on expression of viral structural proteins and replication of viral genome, transport of viral components to the assembly site, assembly, budding and pitching off from cellular membranes. By co-expressing different combinations of viral structural proteins in human cells, **we can address key questions on the identification of essential components for particle formation**.

Over the past years, we have been investigating the properties of viral structural proteins when expressed in human mammalian cells. We have characterized the biochemical and cellular properties of the SARS-CoV spike (S), membrane (M), small envelope (E) proteins (Nal et al., 2005). We have found that the H5 hemmaglutinin from different clades of H5N1 HPAI present differential maturation and intracellular trafficking profiles and are not incorporated with similar efficacies onto the envelope of lentiviral pseudotyped particles (see below: **Influenza virus-host interactions**). We have uncovered the minimal sets of viral structural proteins driving assembly and budding of the SARS-CoV, dengue and H5N1 influenza A viruses in human epithelial cells by developing virus-like particles (VLPs) (Siu et al., 2008; Wang et al., 2009). These VLPs formed in host cells are free of viral genome and can be used as a safe model to study viral and cellular requirements for particle assembly and budding. **We are developing strong international collaborations** with leading laboratories to exploit VLPs both in basic (ultrastructure, genomic screens) and applied research programs (diagnosis, vaccine development) (see below: **Study of the late stages of dengue virus replication cycle** and **Influenza virus-host interactions**).

2. Interactions between viral structural proteins and cellular pathways

We have designed **genomic library screens to decipher host machineries** that play critical role in the viral life cycle. Yeast-two-hybrid screens have been conducted for the viral structural proteins of the five human coronaviruses and H5N1 influenza A virus. **A library of small interfering RNA (siRNA) targeting human genes involved in membrane trafficking** has been screened using a

human cell line that stably secretes dengue virus VLPs. So far, **five cellular factors** have been selected for their **interaction with a viral structural protein** or for their interference with a step of the viral life cycle. Specific studies are being implemented to decipher the molecular mechanisms regulating these virus-host interactions. A particular interest is given to cellular pathways that may lead to cytopathogenicity through their disregulation during viral infection (See below: **Molecular mechanisms of coronavirus-host interactions** and **Influenza virus-host interactions**).

Collaborations (local and international)

- Pr Ben Margolis (Howard Hughes Medical Institute and University of Michigan, Ann Arbor, USA), to investigate the impact of SARS-E protein on Pals-1-mediated cellular polarity in a MDCK cell model (PhD student exchange program for 3 months).
- Dr Volker Thiel (Institute of Pathology, St. Gallen, Switzerland), to produce of SARS-CoV recombinant viruses lacking the capability to bind Pals1, a tight junction associate protein that interacts with SARS-E.
- Dr Leo Poon (Department of Microbiology at HKU) for the co-supervision of a PhD student working on the interactome of avian influenza, to produce of SARS-CoV recombinant viruses lacking the capability to bind the pals1 cellular factor with Dr Volker Thiel.
- Professor Michael Rossmann (Purdue University, USA) for the ultrastructural analysis of dengue prM-E VLPs by cryo-electron microscopy and tomography 3D reconstruction.
- Dr Martin Sachse and Marie-Christine Prevost (Platform of electron microscopy at Institut Pasteur), to analyze late stages of dengue life cycle by electron microscopy (MPhil student exchange program).
- Dr Marc Grandadam (National Reference Centre for Arboviruses, Institut Pasteur), To test and adapt dengue VLPs producer cells to serodiagnosis of dengue virus.
- Suzanne Chanteau (Insitut Pasteur-New Caledonia), to develop a diagnostic assay for the optimal monitoring of dengue infections in the Asia-Pacific region.
- Dr Philippe Despres (Flavivirus-Host Interaction Unit, Institut Pasteur), to study the role of cellular GTPases in dengue virus secretion with replicative viruses.
- Dr. F. Tangy and P.O. Vidalain (Institut Pasteur), to delineate the differential cellular interactome of the five human coronaviruses (PhD student exchange program).
- Pr. George Tsao (Department of Anatomy at HKU), to further develop the HKU Core Imaging Facility in a BSL2/3 environment.
- Dr Michael Chan (Department of Microbiology at HKU), to develop cellular models of polarized lung epithelium to study infection by SARS-CoV.
- Dr John Nicholls (Department of Pathology at HKU), for imaging of infected tissues and visualization of viral particles by electron microscopy.
- Dr. Ulf Nehrbass (Institut Pasteur Korea), with the aim to design of a genome-wide siRNA screenings with live influenza viruses in a BSL-3 environment and revisit the pathways used by influenza virus during infection.
- Prof Xiaowei Zhuang (Harvard University, USA), for the characterization of H5N1 virus using fluorescently labeled H5-pseudotyped particles.

- Professor Stephen Moss (University College London, UK), to assess influenza infection in knockout mice lacking annexin A6.

Funding

These projects have been supported through grants awarded in 2008 and 2009. We have 6 active grants and 4 proposals are under review.

1. Regulation of early steps of coronavirus infection by the ezrin ERM protein (**Research Grants Council**, end September 2010).
2. Recruitment of the tight junction factor PALS1 by the SARS-CoV E envelope protein: consequences for integrity of the infected airway epithelium (**Research Fund for the Control of Infectious Diseases**, ends October 2010).
3. Mechanistic study on the assembly and release of lentiviral particles pseudotyped with hemagglutinin of avian influenza H5N1 viruses: implication for strain-specific H5 pseudotype development (**Research Fund for the Control of Infectious Diseases**, ends January 2011).
4. Identification of cellular enhancing and restricting factors of dengue virus egress (**Research Fund for the Control of Infectious Diseases**, ends September 2010).
5. Definition of the cellular interactome of the highly pathogenic avian influenza H5N1 virus: identification of human cellular regulators of viral entry, assembly and egress (**Research Fund for the Control of Infectious Diseases**, ends October 2011).
6. The cellular interactome of the H5N1 influenza virus (**Area of Excellence**, ends December 2009).
7. **HKU Student Exchange fellowship** for Jean Millet
8. **HKU Student Exchange fellowship** for Kim Tat Teoh
9. **Pasteur Network traineeship** for Mateusz Kudelko
10. **Alexandre Yersin fellowship** for Joanne Lo
11. **Pasteur Network traineeship** for Joanne Lo
12. Molecular dissection of dengue virus egress: involvement of the class II ARF small GTPase (submitted to the **Research Fund for the Control of Infectious Diseases**, *under review*).
13. Characterization of cellular pathways hijacked by influenza A virus in human lung alveolar epithelial cells (submitted to the **Research Fund for the Control of Infectious Diseases**, *under review*).
14. Role of Cyclin D3-influenza A Virus M2 Ion Channel Interaction in Influenza Virus Infection and Pathogenesis (submitted to the **Research Grant Council**, *under review*).
15. Dengue virus-like particles: applications for immunological diagnostic and sero-neutralization (**Actions Concertees InterPasteuriennes-ACIP**, Pasteur Network, *under review*).

Personnel

Name	Position	End of contract (renewable)
Beatrice Nal-Rogier	Research Assistant Professor Department of Anatomy	31 July 2011
Francois Kien	PDF	30 June 2011
Dong Jiang Tang	PDF	30 June 2011
Pei Gang Wang	PDF	31 March 2011
Kim Tat Teoh	PhD student	28 February 2010
Jean Millet	PhD student	31 March 2010
Mateusz Kudelko	PhD student	30 June 2012
Jason Ma	PhD student	31 August 2012
Lewis Siu	Research Technician	31 December 2011
Jane Tse	Research Technician	Permanent Staff
Patrick Lam	Laboratory Technician	31 March 2010
Kevin Kwok	Laboratory Technician	30 October 2010
Wallace Chan	MPhil student	30 August 2011
Gladys Lam	MPhil student	30 August 2011
Joey Zhang	MPhil student	30 August 2011
Joanne Lo	MPhil student	17 July 2009

3.2 PROGRAM 2: VIRAL INFECTION & IMMUNITY

The Viral Infection & Immunity team studies specific mechanisms underlying the interplay between viral infection and the immune response, innate and acquired, by implementing research projects that are at the interface of fundamental and applied research.

Main Objectives and Strategy

The host responds to infecting viruses by activating its innate immune system and mounting pathogen-specific humoral and cellular immune responses to control viral replication and eliminate the virus from the host. **The objective of the Viral Infection & Immunity lab is to gain insights into host reactions to viral infections.** More specifically, we focus on two related research areas.

1. **Understanding innate immunity during viral infection**. This project focuses on cells of the innate immunity system such as Natural Killer, macrophages, and dendritic cells, which are the frontline players in the event of a viral attack. **We are investigating the activation mechanism of Natural Killer cells by viral envelope proteins of the highly pathogenic avian influenza virus.**

2. **Determining whether immune-mediated mechanisms are involved in infection of the human host by SARS-CoV and influenza viruses**. In addition to their interaction with specific receptors, viruses may also rely on anti-viral antibodies to infect cells, a phenomenon known as Antibody Dependent Enhancement (ADE) of infection. **Following our previous findings with SARS-CoV, we are now exploring whether anti-influenza antibodies may perversely facilitate infection of cells of the immune system.**

Collaborations (local and international)

- Professor Angel Porgador (Ben-Gurion University of the Negev, Israel), to further develop the ongoing projects on NK cells and molecular immunology.
- Professor Eric Vivier (Centre d'Immunologie de Marseille-Luminy, France), to investigate functional interactions of NK's NCR with avian influenza A HA.
- Dr Chung Cheung (Department of Microbiology at HKU), to investigate the occurrence of ADE of live SARS-CoV in human hematopoietic cells.
- Professor Marc Daëron (Institut Pasteur, France), with the goal to investigate the signaling cascade triggered through FcγR during ADE.

Funding

These projects have been supported by extramural grants. One new proposal has been approved for funding in 2009.

1. Interaction of NK activating receptors and hemagglutinin from avian flu – Potential implication of NKp44 in anti-flu therapy (**Research Fund for the Control of Infectious Diseases**, ends September 2009).
2. Analysis of interactions of NK inhibitory and activatory receptors and viral envelope proteins (Small Project Funding from the **Research Grants Council,** ends September 2009).

3. Investigation of Antibody-Dependent Enhancement (ADE) of SARS coronavirus infection and its role in pathogenesis of SARS (**Research Fund for the Control of Infectious Diseases,** ends September 2011).

Personnel

Name	**Position**	**End of contract (renewable)**
Martial Jaume	PDF	31 December 2010
Simon Yip	PhD student	30 April 2011
Cherry Xia	MPhil student	31 December 2009
Isabelle Dutry	MPhil student	31 August 2010
Nancy Leung	MPhil student	31 August 2011
Ping Hung Li	Research technician	31 May 2011
Horace Lee	Research Assistant	1 October 2010

3.3 PROGRAM 3: MOLECULAR VIROLOGY

The Molecular Virology lab has been established in 2009 with the recruitment of Dr Hui-Ling Yen, a Research Assistant Professor who holds a joint appointment with the Department of Microbiology at HKU and HKU-PRC. The Yen lab uses reverse genetics to study the pathogenesis of influenza in by combining cellular (in vitro) and animal (in vivo) models.

Main Objectives and Strategy

Influenza viruses are constant threats for human and animal health. Influenza A virus, with its segmented RNA genome that allows genetic reassortment and the existence of multiple natural reservoirs, is a non-eradicable zoonosis. **The objectives of the Molecular Virology team focus on applying animal models and the plasmid-based reverse genetics technique to study the biology of influenza virus**, with specific interests in two related areas of viral pathogenesis.

1. **Identification of molecular determinants of H5N1 influenza virus pathogenesis**

This project aims to elucidate viral factors that determine differences in pathogenicity between the highly pathogenic H5N1 viruses and seasonal human influenza virus. As hyper-induction of pro-inflammatory cytokines correlates with severity of disease following H5N1 influenza infection, it is crucial to identify molecular determinants of H5N1 virus that trigger the host innate immune response. The current focus is on viral surface glycoprotein hemagglutinin and its potential interaction with dendritic cells (See below: **Role of hemagglutinin receptor binding domain of H5N1 viruses in infection of dendritic cells and induction of innate immune response**).

2. **Mapping molecular determinants that enable transmission and replication of avian or swine influenza viruses in human**

The host range of influenza A virus is determined by multiple viral and host factors. As a result, inter-species transmission usually leads to unapparent or mild clinical symptoms without further transmission in the new host species. However, **the gene constellations that enable transmission and replication of avian-origin H5N1/ H9N2 or swine-origin H1N1 influenza viruses in human are not known**. We aim to **address this question by generating recombinant viruses with different gene constellations and applying in vitro and in vivo models** to assess viral replication and transmissibility. The ability of neuraminidase (NA) inhibitor-resistant variants to transmit among human will affect the application of this class of drugs in antiviral therapy. We will study the role of balanced hemagglutinin-neuraminidase activity on the genesis of transmissible NA inhibitor-resistant variants in seasonal and novel pandemic influenza A H1N1 viruses (see below: **Molecular determinants that enable swine-like H1N1 influenza virus infection and transmission in humans** and **The role of balanced hemagglutinin-neuraminidase activity on the genesis of transmissible NA inhibitor-resistant variants in seasonal and novel pandemic influenza A H1N1 viruses (Objective #2; Grant support: RFCID)**.

Collaborations (local and international)

- Dr Wen-Wei Tu (Department of Pediatrics and Adolescent Medicine at HKU), on the "Role of hemagglutinin receptor binding domain of H5N1 viruses in infection of dendritic cells and induction of innate immune response".
- Dr Leo Poon (Department of Microbiology at HKU), Dr Gavin Smith (National University Singapore) as well as Drs Robert Webster and Richard Webby (St. Jude Children's Research Hospital, Memphis, TN, USA), on the "Molecular determinants that enable swine-like H1N1

influenza virus infection and transmission in humans".

- Dr John Nicholls (Department of Pathology at HKU), on the "Identification of influenza neuraminidase sialyl substrates using glycan arrays".
- Prof Bryan Cullen (Duke University, Durham, NC, USA) and Prof Daniel Kolakofsky (University of Geneva, Switzerland), on the "Role of short 5'-vRNA detected in influenza infected cells".
- Dr Mustapha Si-Tahar (Institut Pasteur, Paris, France), on the "Role of LGP2 in H5N1 influenza infection".

Funding

These projects are supported in part by several extramural grants obtained in 2009-2010. Four grants were received from January 2009 to February 2010, and two proposals are currently under review.

1. Role of hemagglutinin receptor binding domain of H5N1 viruses in infection of dendritic cells and induction of innate immune response (**Area of Excellence**, ends December 2009).
2. Identification of influenza neuraminidase sialyl substrates using glycan arrays (**HKU Seed Fund**, ends June 2010).
3. Molecular determinants that enable swine-like H1N1 influenza virus infection and transmission in humans (**Research Fund for the Control of Infectious Diseases**, *Commissioned Study on Swine Influenza*, ends May 2011).
4. The role of balanced hemagglutinin-neuraminidase activity on the genesis of transmissible NA inhibitor-resistant variants in seasonal and novel pandemic influenza A H1N1 viruses (**Research Fund for the Control of Infectious Diseases**, ends Dec 2011).
5. Role of influenza hemagglutinin glycoprotein in activation of dendritic cells and induction of effective immune response through C-type lectin receptors (submitted to the **Research Grants Council**, *under review*).
6. Understanding the role of short 5'-vRNA detected in influenza infected cells in interacting with the members of the RIG-I-like receptors (submitted to the **Area of Excellence**, *under review*).

Personnel

Name	**Position**	**End of contract (renewable)**
Hui-Ling Yen	Research Assistant Professor Department of Microbiology	4 January, 2012
Peter Cheung	PhD student	31 August, 2012
Terry Choy	Research Assistant I	31 July, 2010
Diana Wong	Research Assistant II	30 April, 2010

3.4 PROGRAM 4: TRANSLATIONAL RESEARCH

The activity of the group focuses on the development of high throughput methodologies to create a strong interface between the fundamental research and possible clinical applications.

Main Objectives and Strategy

Three main axes of research have been followed, with a focus on **molecular biology/tool development, diagnostics and drug discovery**. This diversity of applications exploits the adaptability of a very flexible tool, pseudotyped viral particles, which we have reviewed in an invited chapter for a book on "Advanced Techniques in Viral Detection" (Garcia, *in press*).

1. Molecular biology/Tool development

This project aims at determining how influenza virus binds to its receptor(s) by utilizing saturation transfer difference (STD) NMR, which represents a powerful technique to investigate receptor-ligand interactions at the atomic level. **The current focus is to develop new tools** to explore how changes in hemagglutinin (HA) sequence can affect binding, thus enabling to predict receptor binding preferences in emerging influenza viruses for which the HA sequence is known.

2. Diagnostic

Serological methods are important for investigating the health threat posed by highly pathogenic avian influenza (HPAI) H5N1, providing an alternative option for sero-diagnosis, sero-epidemiology and gaining evidence of either naturally acquired or vaccine induced immunity. **We are extending our studies using pseudotyped particles in collaboration with several partners in the region**.

3. Drug discovery

We are extending our analysis of the **influenza entry inhibitors, whose activity was** confirmed as single molecules and showed no cytotoxicity, using live H5N1 virus. We are also keen on **validating an alternative approach to identify broad spectrum drugs by testing candidate molecules against a wide range of pathogens.**

Collaborations (local and international)

- Hugo Naya (Institut Pasteur-Montevideo), Amadou Sall (Institut Pasteur-Dakar) and Pierre-Olivier Vidalain (Institut Pasteur), to establish a multi-application technical platform based on high-content/high-throughput flow cytometry.
- Olivier Schwartz, Noel Tordo, Philippe Despres (Institut Pasteur), Eleanor Fish (University Health Network-UHN, Canada), L.P. Kotra (UHN and University of North Carolina at Greensboro), Vincent Deubel (Institut Pasteur-Shanghai), and Michael Chan (Department of Microbiology at HKU), to develop a testing platform for broad spectrum anti-infectious agents.
- Philippe Buchy (Institut Pasteur-Cambodia) and Menno de Jong (University of Amsterdam), to study the sero-epidemiology of avian influenza.

- Francois Roger and Carlène Trévennec (CIRAD-Agricultural Research for Development, France/Thailand) and Dr Zhong (National Institute for Veterinary Research, Vietnam) for animal surveillance of influenza in Vietnam.
- Sathit Pichyangkul (AFRIMS-Armed Forces Research Institute of Medical Sciences, Thailand) for the study of cross-reactive antibodies against avian and swine influenza viruses in humans.
- Mark von Itzstein (Griffith University, Australia), John Nicholls (Department of Pathology at HKU) and Dr Zhu (Department of Biochemistry at HKUST), with the goal of dissecting the molecular requirements of receptor preference of haemagglutinins from avian and human influenza viruses.
- Paul Vanhoutte (Department of Pharmacology at HKU) to monitor drug development of the hits identified from our screening campaigns (lead selection, preliminary toxicity).
- Jiang Ping Zuo (Shanghai Institute of Materia Medica) and Michael Jacobs (University College London) to complete the drug discovery projects on avian influenza and dengue.

Funding

1. High content-high throughput flow cytometry: Development of a multi-application technical platform (**Actions Concertees InterPasteuriennes-ACIP**, ends October 2009).

2. Broad spectrum antiviral agent testing (**Actions Concertees InterPasteuriennes-ACIP**, ends June 2009).

3. Pseudotyped influenza viruses for serodiagnosis and sero-epidemiology **Area of Excellence**, ends December 2009).

4. A Noval approach to exploring the interactions between influenza and sialic acid linked glycans using virus like pseudoparticles (VLP) – Supplementary funding (**Area of Excellence**, ends December 2009).

5. H1 Pseudotyped influenza viruses for sero-diagnosis (**Area of Excellence** ends December 2010).

6. Virus receptor binding of highly pathogenic H5N1, seasonal H1N1 and H3N2, pandemic H1N1 pdm and avian H9N2 subtype viruses using STD NMR techniques and correlation with biological methods. (**Area of Excellence Year**, ends April 2010).

7. Influenza and sialic acid linked glycan interactions using virus like pseudoparticles (VLP) and STD-NMR (**Research Grants Council**, ends October 2012).

Personnel

Name	Position	End of contract (renewable)
Jean-Michel Garcia	PDF	2 November 2011
Jimmy Lai	PhD student	31 December 2011
Agnes Dumont	Research Technician (Fellow of the French Ministry of Foreign Affairs)	30 September 2009
Eugenie Baudon	Research Technician (Fellow of the French Ministry of Foreign Affairs)	30 November 2010
Nadege Lagarde	Research Technician	30 June 2011
Camille Shek	Research Assistant	31 August 2009

3.5 Program 5: Teaching and education

We have achieved our goal to offer an annual program of courses for postgraduate students and young scientists that is extremely competitive, comparable in quality to other international programs (EMBO, Cold Spring Harbor) and is becoming a reference for Hong Kong and the Asia-Pacific region. We would like, however, to draw the attention of the Board to the fact that Cold Spring Harbor Laboratories is now offering Asia Conferences in Mainland China, at the Shuzhou Dushu Lake Conference Center (for more information, see: http://meetings.cshl.edu/CSHAsia/index.html). Only one Summer School Course has been scheduled in 2010 by CSH, but this may soon change. We need, therefore, the full backing of HKU, , Institut Pasteur and their Communication Teams to be able to develop an even stronger program that will ensure the long-term success of our courses.

Achievements

Three major milestones have marked 2009. First, **the completion of our annual Teaching and Training Program, with the successful organization of three Master Classes** on Cell Biology, Virology and Immunology. **All courses have been approved by HKU as part of the coursework curriculum for Research Postgraduate studies**. Of note, the number of applications to attend the 2nd Immunology course has more than doubled from the previous year. Second, **the organization of a World EMBO Course (supported by the International Network of Pasteur Institutes) on Bioinformatics**, that was an overwhelming success. The huge number of applications has prompted plans to run a second edition in 2011. Third, **together with Dr Frederick Keck, social anthropologist at the CNRS in Paris**, who joined us as a Visiting Fellow of the Fyssen Foundation, we have **organized a conference** on "**Avian Flu: Social and Anthropological Perspectives**" to discuss the social aspects of networks of surveillance and measures of control, and to open perspectives for the future at an international level.

Students

We have currently 6 PhD students and 6 MPhil students working at the center. Two students (1 PhD and 1 MPhil) have successfully defended their thesis. Three PhD students have been awarded exchange program fellowships to complete their training abroad, at Institut Pasteur and the University of Michigan at Ann Arbor. **Several students have been interviewed and three of them have been selected together with the Group Leaders. All candidates have been admitted into the HKU postgraduate program and will join the center for a PhD or MPhil degree in the course of 2010**. In addition, we are hosting **one International Volunteer**, Eugenie Baudon, who will be **supported by the French Consulate** for a traineeship period of 1-2 years. Eugenie Baudon graduated from the National Veterinary College of Toulouse (France) where she obtained a Master 2 degree in *Animal Health and Epidemiological surveillance in Tropical Countries* with the French Institute of Agricultural Research for Developing Countries (CIRAD) and the University of Montpellier (France).

The Center is taking an active role in training undergraduate students who are part of the "BIOC3614 Biochemistry Project". This course, which is one of the requirements in the Sciences majors and minors offered by the Department of Biochemistry at HKU, enables students to acquire the basic skills in scientific research by actively participating in a research project in molecular life sciences. **Two students, Wallace Chan and Nancy Leung**, have been trained under the supervision of Drs Martial Jaume and Francois Kien for their BSc in the 2008-2009 Academic Year. They have elected to stay at HKU-PRC for their MPhil thesis and one of them (WC) has already co-authored a submitted manuscript (Lai *et al*, *J Gen Virol*).

We have welcomed **one rotating student**, Sandy Favini, from the Ecole Polytechnique of Paris, who worked for 4 months under the supervision of Dr Beatrice Nal. She presented the results of her projects at the end of their lab rotation, which focused on the "***Study of Severe Acute Respiratory Syndrome Coronavirus virus-like particles trafficking***".

The Centre is a regular contributor of educational programs in science sponsored by the Victor Segalen **French International School**. We have teamed up with the School to organize a scientific workshop for grade 11th students. This project has been initiated by the Agency for French Teaching abroad, under the administration of the French Ministry of Foreign Affairs. The workshop consisted of two visits of the Centre for 2 groups of 17 students, during which they discovered various aspects of scientific research and work in an academic laboratory. **We also welcomed two students from the French International School for a one-week traineeship** (March 2-6, 2009) during which he had the opportunity to follow different activities and be confronted with work in a research centre. Finally, for the second consecutive year **Nadège Lagarde**, a Research Technician, has presented to French students the molecular biology of the Human Immunodeficiency Virus **on the occasion of the AIDS World Day 2009**.

We have begun to be involved with the **International Thai-French Master Program on "Infectious, Vector-Borne and Food-Borne Diseases", which has been launched by the University of Montpellier 2 with Kasetsart University in Bangkok, and is supported by CIRAD, Institut Pasteur and the International Network of Pasteur Institutes.** The curriculum has a regional dimension and offers real opportunities of international mobility and training for French students and students from South-East Asia. The curriculum will address the field of human or animal health and both established and emerging diseases, food-safety and public sanitary and health security. These cutting edge scientific topics are deeply rooted in today societal, economic and sanitary issues of high social impact and are addressed in a comprehensive and multidisciplinary way. HKU-PRC has been selected as one of the labs to host students during their research work. The first student has completed his initial rotation in January-February 2010 and is expected to come back for a 6-month period at the beginning of November 2010.

Courses

The Faculty Higher Degrees Committee (FHDC) and the Board of Graduate Studies (BoGS) of HKU have formally approved that all three regular HKU-Pasteur Master Classes to be included in the coursework curriculum for Research Postgraduate Studies. The three courses have attained a very strong reputation, attracting a significant number of applications from other countries (see Annexes). The number of local applications has significantly increased, and we are now training 30-40 HKU students every year. **In addition, several lectures delivered by leading scientists (viz., several EMBO members, Professors at College de France, members of the National Academy of Sciences USA) are open to the public** and attract a wide audience including faculty members, postdocs and students who attended previous courses. A comprehensive mid-term plan has been approved by the Research Sub-committee of HKU, which has granted an annual contribution to help in the organization of the courses. It is important to emphasize that each course includes a full-time senior faculty member of HKU, as well as of Institut Pasteur in the organizing committee, thereby strengthening the ties between the two institutions. **The establishment of the Teaching Center will further increase the quality of the courses and their impact in the region**. Moreover, we will pursue the organization of EMBO Global Exchange Lecture Courses or Lecture Series.

The Teaching Center of HKU-PRC has provided the necessary bench space for the practical sessions of the 1st International Course on Stem Cell Biology and Regenerative Medicine (August 23 - August 29, 2009), which was co-organized by the University of Toronto, The Hospital for Sick Children Research Institute, Mount Sinai Hospital (Canada), and the Strategic Themes of Development and Reproduction, Cancer and Healthy Ageing (HKU). The aim of the course was to

introduce current theoretical knowledge through in-depth lectures and focused hands-on experience in stem cell biology and regenerative medicine.

Croucher-Pasteur Exchange Program

This **program has been established** with the aim **to encourage** highly motivated **students and post-doctoral fellows resident in Hong Kong to perform research work at Institut Pasteur**. **One student, Ken YC CHOW, defended his thesis at Institut Pasteur in 2009** and is now doing postdoctoral training in the Division of Medicinal Chemistry, Department of Chemistry and Pharmaceutical Sciences, Vrije Universiteit Amsterdam, The Netherlands. **We are in regular contact with him** and he has visited HKU-PRC during the last Chinese New Year. There are currently two Hong Kong students who went to Institut Pasteur thanks to the Seminar Series of the Exchange Program.

The Croucher-Pasteur Lecture Series has been organized for the fourth consecutive year. Of note, one of the Croucher Speakers in 2009, **Dr Spencer Shorte, had a meeting with Professor SP Lee, the Dean of the Li Ka Shing Faculty of Medicine and Professor George SW Tsao, Head of the Imaging Core Facility, to discuss the strategic plans of HKU with respect to developing an imaging platform**. This is a concrete example of how HKU-PRC can catalyze the synergistic interactions of the two parent institutions. It also represents a logical follow-up of the Imaging and Cell Biology workshops ("Fluorescence Lifetime Imaging Microscopy" and "Seminar Series in Cell Biology: Subcellular structures and Cellular Dynamics") that had been organized in 2008 together with Professor Tsao. **We have organized again an information session at HKUST** together with the three invited speakers and **with the support of the French Consulate, which provides "Yersin fellowships" to MPhil candidates** who want to obtain their degree in a French laboratory, in order **to present other opportunities for studies in France.** It has to be acknowledged that the response from HKUST was not very encouraging and may not be continued in its present form. We have also advertised the **new International PhD program launched at Institut Pasteur** to further increase these exchanges. **One student has been shortlisted and interviewed in March 2010**, but did not make the final selection. We realize that most local students are concerned about language barrier, but believe that combining the scientific quality of the host laboratories with the increased international dimension of the doctoral program, we should be able to attract more top candidates who will compete for Croucher fellowships to join IP. Ultimately, **we want to promote a significant collaboration agreement that will set a framework allowing research students to work jointly in the laboratories of HKU and IP**. We realize that this plan may take time to be implemented but are persuaded that we should have long-term objectives.

Other Events
Avian Flu: Social and Anthropological Perspectives (February23-24, 2009)

Highly Pathogenic Avian Influenza is an emerging infectious disease currently active in the animal reservoir and causing hundreds of human deaths in many countries, bringing along fears of a worldwide pandemic. Since 1997, **networks of surveillance and measures of control have been set up to prevent the spread of this disease**, profoundly transforming the economy and public health infrastructures of these countries. **Dr Frederick Keck, social anthropologist at the CNRS in Paris**, who joined us as a Visiting Fellow of the Fyssen Foundation **has organized a conference to discuss the social aspects of these networks and measures**, and to open perspectives for the future at an international level. This conference will gather microbiologists, social anthropologists and public health officials to study the impacts of Avian Flu surveillance in different parts of the world (Asia, Europe, Africa, America) and at different stages of the spread of the virus (from the animals to the humans). Hong Kong being at the door of the epicentre of the disease in 1997 and a sentinel for watching its evolution since then, it is the adequate place to

gather experts in animal health, human health and social issues in order to assess the signification of ten years of mobilization against Avian Flu. **This conference has opened the way for an anthropological analysis of Avian Flu, integrating all the aspects of this global phenomenon: environmental, biological, social and psychological**. Videos of this conference are available online on our website.

Unveiling ceremony of a Tribute to Alexandre Yersin

Last year, **HKU-Pasteur Research Centre co-organized an exhibition** entitled "**From the Plague to New Emerging Diseases: A Chronicle of Pasteurian Research in Hong Kong" hosted** first **by** the **University Museum and Art Gallery** and subsequently by the **Hong Kong Museum of Medical Sciences** to celebrate the 120th anniversary of the Institut Pasteur through the life and work of Alexandre Yersin. On July 15, 2009 **a bronze portrait statue of Alexandre Yersin** (1863-1943), physician trained at Institut Pasteur, **was unveiled in the garden of the Hong Kong Museum of Medical Sciences** on the occasion of the 160th anniversary of the establishment of France–Hong Kong consular relations, as **a tribute to his role in identification and isolation of the bacillus *Yersinia pestis* that caused the bubonic plague in Hong Kong in 1894**. The ceremony was held in the presence of the Honorable Dr York YN Chow, GSBS, JP, Secretary for Food and Health, Mr. Jean-Pierre Thébault, Consul general of France in Hong-Kong and Macau, Dr. Laurence LT Hou, Director, Hong Kong Museum of Medical Sciences Society, Dr. Roberto Bruzzone, Chief Executive Officer of HKU-Pasteur Research Centre, and Dr Faith CS Ho, Chairman, Education and Research Committee, Hong Kong Museum of Medical Sciences Society.

Funding

The Teaching and Educational program is **supported** by targeted funds from **Institut Pasteur**, **HKU** and the **Croucher Foundation**. Additional support for new initiatives has been obtained from **EMBO**, the **French Consulate** and through **private sponsorship**. **The French Chamber of Commerce and Industry in Hong Kong** chose again our Center as the charitable organization to which **proceeds of the Annual Gala Dinner have been donated**. We want to work in close relationship with the Public Relation team of HKU to explore the possibility of securing a major donation for the implementation of this initiative that offers a unique combination of two major brand names, together with exceptional quality of the programs and an indisputable international dimension.

3.6 NETWORK PROJECTS

HKU-PRC exerts a leadership role in a number of network projects.

RESPARI/SISEA

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 2007 Annual Report). The **RESPARI network** emphasizes fundamental and translational research; it has established itself as **one of the flagship research programs of the network** having acquired international reputation, and has been instrumental in promoting active collaboration between the Pasteur network in Asia, HKU-PRC and HKU. More details are available on the RESPARI website (www.hku.hk.respari/). Several achievements have been already presented in previous reports and a full account of the results obtained by **HKU-PRC in the framework of RESPARI was included as Annex 7 of the 2008 Report**.

The aim of the **Surveillance and Investigation of Endemic Situations in Southeast Asia (SISEA) program is to contribute to the improvement of the detection and handling of epidemic situations in the region. The SISEA project is a key initiative financed by the French Development Agency (AFD) (www.hku.hk/respari/research_07.htm).** The specific goal of SISEA is to set up a surveillance and investigation program in four of the region's countries (China, Laos, Vietnam, and Cambodia). As the Scientific Coordinator of this major Public Health project, Dr Bruzzone has played a major role in the implementation and output of surveillance programs, which have put more emphasis on the expected patients' benefit component, as well as in the conception and organization of regional scientific meetings and training sessions. Below is a summary of the key results obtained in 2009.

During 2009 all partners have implemented surveillance of respiratory infections in the designated sentinel hospitals and monthly reports have allowed monitoring of pathogen prevalence. In addition, surveillance of acute encephalitis has begun in Vietnam and has immediately produced a significant impact in Public Health awareness and policies to control disease spread. For example, thanks to SISEA activities, new cases of Japanese Encephalitis have been detected in Ben Tre province. This has led to entomology and field investigations and further to the implementation of a comprehensive plan of immunization with JE vaccine.

We have organized an International Scientific week hosted by the Pasteur Institute of Ho Chi Minh City (VietNam), which included an **International Scientific Forum** (8-9 June), followed by a **Technical Workshop on Encephalitis** (10-11 June). The Scientific Forum served as platform to share the results of SISEA activities with several regional partners (viz., Asian Development Bank, Mekong Basin Disease Surveillance, US-CDC, Wellcome Trust, Chinese-CDC, CIRAD, Regional Emerging Diseases Intervention Center at Singapore). **A total of 38 abstracts were submitted for presentation as oral communications or posters**. The Technical Workshop on acute encephalitis syndrome (AES) was organized to review the situation in South East Asia and outline the best strategy to confront the challenge posed by this group of diseases in the long term. Besides the presentations of SISEA partners, there were several invited speakers from Asia and Europe who gave their expert opinion on the clinic biology, pathogenesis and epidemiology of AES. In addition, two sessions gave an overview of the latest information on encephalitic virus circulation in Asia and on the current laboratory tests available.

The forum was also attended by SISEA's Scientific Advisory Board (SAB), which evaluated the progress of the project and prepared an independent report that included and evaluation of the implementation of SISEA activities and a series of recommendations regarding the preparation of future activities. **The SAB particularly praised the results obtained with respect to wealth of**

information that is being generated, harmonization of procedures and building of a strong team that represents a solid foundation for the long-term impact of SISEA. The SAB stressed that SISEA has resulted in a clear success in organizing a true local capacity and has established an excellent molecular diagnostic platform, which will be very useful not only for present, but also future activities (for instance response to the threat posed by the outbreak of the new H1N1). The SAB recognized the enormous progress achieved in terms of commitment to the project at the individual and institutional level and is very pleased to note that the actual commitment of the team is impressive. In addition, the SAB expressed strong support for the maintenance of the current partnership structure, which should be extended to interfacing with other regional initiatives (with clearly defined objectives), in order to build a solid and sustainable network thanks to SISEA program.

Funding

This program has been supported by grants from French Ministry of Health (3.9M HK$) and from the Li Ka Shing Foundation (1.7M HK$). Although both grants have been completed by HKU-PRC in 2008, RESPARI and SISEA are the flagship projects of the International Network of Pasteur Institutes in the Asia-Pacific region and their coordination significantly contributes to the recognition and visibility of HKU-PRC. The scientific reports of SISEA for the years 2007-2009 are available upon request.

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

Professor Malik Peiris is the Coordinator of the 8-year research program "Control of Pandemic and Inter-pandemic Influenza", which has been funded through the Areas of Excellence (AoE) scheme implemented by the University Grants Committee. The program represents **a multi-disciplinary and multi-institutional approach with strong links to international networks and collaborators to address a single disease of global relevance.** It is based on a highly integrated research program of basic AND applied research, encompassing laboratory, clinical and epidemiological expertise and spanning the animal-human interface. Few among the other research centers of global pre-eminence in one or the other of these areas truly encompass all these aspects. The main objectives of the project are:

1. Defining the ecology and molecular evolution of animal influenza viruses in southern China and other parts of Asia so as to identify animal viruses of potential risk to humans;
2. Identify the viral and host determinants of pathogenesis, antiviral immunity and interspecies transmission;
3. Develop novel diagnostics, clinical studies, vaccines and therapeutics;
4. Identify evidence-based options for control of influenza in humans and animals by defining the transmission dynamics of influenza.

HKU-PRC takes an active part in this program and is involved in Objectives #2 and #3. We have secured several grants in 2008and 2009 to successfully implement these specific research areas and strengthen our scientific collaborations with many groups at HKU and other universities in Hong Kong. **To give an idea of the impact of the program, in 2009 there were 50 peer reviewed research papers published or accepted for publications supported by the Area of Excellence**, compared to 12 in the first year of the program (2008). It is worth mentioning that **Area of Excellence team members responded rapidly to the emergent H1N1 pandemic by developing molecular diagnostic tests for the pandemic virus within 4 days of the WHO announcement** on the 24th April of a novel H1N1 virus of swine origin spreading in Mexico and USA. **This work was signed by HKU-Pasteur Research Centre** (see reference #8 of the scientific output: Poon et al, Clin Chem 2009). The protocol was shared with WHO laboratories and is one of the WHO approved

diagnostic protocols for pandemic H1N1. Detailed protocols and reagents have been sent to local and overseas laboratories, including Taiwan, Singapore, China, India, Malaysia, Senegal, Sri Lanka, Italy, USA and France. **Professor Peiris also continues to serve on a number of WHO working groups in relation to both avian influenza H5N1 and, more recently, the swine origin influenza virus H1N1.**

Funding

The program is distributing funds on a competitive basis. **We currently hold one grant as PI and one as Co-PI for 2010 with the following goals:**

- Development and validation of novel assays for serodiagnosis and sero-epidemiology of avian and human influenza viruses;
- A novel approach to exploring interactions between influenza and sialic acid linked glycans using virus-like particles.

GLObal network for DENgue research (GLODEN)

This is a **new initiative launched by Institut Pasteur and the International Network of Pasteur Institutes** with the goal to investigate the complex interplay between viral, mosquito, human genetics and environmental factors underlying differential outcomes of dengue infection.

Almost all **dengue studies have concentrated on only one site or region and have mostly investigated only one component** (virus or human) at a time. This approach is unlikely to reveal the complex interplay among several elements on the outcome of infection that include not only viral or human factors but also vector, environmental and social ones. **It is, therefore, important to create a global network for dengue study and bring in experts from different domains and different regions in the world to take a multidisciplinary approach** to unraveling the contribution of each factor and interactions among them for the outcome of dengue infection.

The Institut Pasteur and the International Network of Pasteur Institutes have access to patients/populations, viruses and mosquitoes in different environmental, social and population genetic backgrounds, and can rely on a panel of **experts in virology, entomology, epidemiology, immunology, human genetics, biostatistics and bioinformatics**. **The ambition of GLODEN is**, therefore, to extend the work established in DENFRAME to other countries and to include other aspects of dengue research, notably entomology and climatology, with the aim of **understanding the complex interplay of viral/human/vector/environmental factors in the differential outcome of dengue infection in different regions of the world.**

The GLODEN initiative was officially launched with a 2-day workshop organized at Institut Pasteur (December 2009) by Dr Anavaj Sakuntabhai, who is the Scientific Coordinator of the network. HKU-PRC was represented by Mateusz Kudelko, a PhD student, who gave a summary of our current research projects and future interests in dengue research. More specifically, **HKU-PRC has elaborated a project encompassing basic research, serology and immunology**, which will focus on:

- Identification of new involved in DENV egress through genome-wide siRNA screen;
- Development of a VLP-based highly sensitive assay for serological tests;
- Testing immune response against DENV VLPs of the 4 serotypes.

Funding

Several sources of funds will be pursued by preparing targeted proposals.

Other major international events organized by HKU-PRC

Several major international events (listed below) will be 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). This meeting has grown into the largest international conference devoted exclusively to influenza, covering every imaginable topic from basic science to health care policy.

Annual Scientific Meeting of the International Network of Pasteur Institutes (Hong Kong, 22-25 November 2010), co-organized by Dr Roberto Bruzzone and Professor Malik Peiris. The meeting will be opened by a **keynote lecture delivered by Professor Francoise Barre-Sinoussi, the 2008 Nobel Laureate in Physiology and Medicine** for the discovery of the HIV virus.

IBRO/UNESCO School of Neuroscience on "**Neurobiology of Infectious Diseases: a view for Global Neuroscience**" (Reunion Island, 27November-2 December 2010), co-organized by Dr Roberto Bruzzone. This school is the first Africa-Western Europe inter-regional collaboration and will train 30-35 students from Africa, Western Europe and Asia.

2nd International Neuroinfection Meeting (Reunion Island, 2-6 December 2010), co-organized by Dr Roberto Bruzzone. The meeting will bring together specialists working in neurobiology, microbiology, immunology, virology, parasitology and clinical neurology. The conference is a continuation of the first International Conference on Infections Diseases of the Nervous System, held at Institute Pasteur in September 2008, which led to the publication of an article in PLoS Pathogens and a special issue of Progress in Neurobiology with a series of reviews contributed by some of the invited speakers.

Keystone Conference on "**Pathogenesis of Influenza: Virus-Host Interactions**" (Hong Kong, 23-28 May 2011), co-organized by Professor Malik Peiris. The current symposium brings together researchers working on the virus, viral receptors and tissue tropism, innate and adaptive immunity, systems biology and clinical aspects of lung injury and host defense, to address questions on the pathogenesis of influenza. The aim will be to integrate data from animal and ex vivo / in vitro human experimental models as well as human disease to understand pathogenesis of influenza and how this may lead to effective interventions. As this symposium will take place in the aftermath of the first pandemic in 40 years, there will be a wealth of new knowledge as well as intense scientific interest in the subject.

4. Scientific Output

Publications cited in PubMed (#9-11 refers to work completed by Dr Yen in her previous lab)

1. Bruzzone R, Dubois-Dalcq M, Grau GE, Griffin DE, Kristensson K (2009) Infectious diseases of the nervous system and their impact in developing countries. *PLoS Pathog* **5**:e1000199.
2. Garcia JM, Gao A, He PL, Choi J, Tang W, Bruzzone R, Schwartz O, Naya H, Nan FJ, Li J, Altmeyer R, Zuo JP (2009) High-throughput screening using pseudeotyped lentiviral particles: A strategy for the identification of HIV-1 inbibitors in a cell-based assay. *Antiviral Res* **81**:239-247.
3. Smith GJ, Vijaykrishna D, Ellis TM, Dyrting KC, Leung YH, Bahl J, Wong CW, Kai H, Chow MK, Duan L, Chan AS, Zhang LJ, Chen H, Luk GS, Peiris JS, Guan Y (2009) Characterization of avian influenza viruses A (H5N1) from wild birds, Hong Kong, 2004-2008. *Emerg Infect Dis* **15**:402-407.
4. Hui KP, Lee SM, Cheung CY, Ng IH, Poon LL, Guan Y, Ip NY, Lau AS, Peiris JS (2009) Induction of proinflammatory cytokines in primary human macrophages by influenza A virus (H5N1) is selectively regulated by IFN regulatory factor 3 and p38 MAPK. *J Immunol* **182**:1088-1098.
5. Peiris M (2009) Avian influenza viruses in humans. *Rev Sci Tech* **28**:161-173.
6. Yen HL, Peiris JS (2009) Mapping antibody epitopes of the avian H5N1 influenza virus. *PLoS Med* **6**:e1000064.
7. Chan KH, Lai ST, Poon LL, Guan Y, Yuen KY, Peiris JS (2009) Analytical sensitivity of rapid influenza antigen detection tests for swine-origin influenza virus (H1N1). *J Clin Virol* **45**:205-207.
8. Poon LL, Chan KH, Smith GJ, Leung CS, Guan Y, Yuen KY, Peiris JS (2009) Molecular detection of a novel human influenza (H1N1) of pandemic potential by conventional and real-time quantitative RT-PCR assays. *Clin Chem* **55**:1555-1558.
9. Reed ML, Bridges OA, Seiler P, Kim JK, Yen HL, Salomon R, Govorkova ., Webster RG, Russell CJ (2009) The pH of activation of the hemagglutinin protein regulates H5N1 influenza virus pathogenicity and transmissibility in Ducks. *J Virol* **84**:1527-1535.
10. Yen HL, Webster RG (2009) Pandemic influenza as a current threat. *Curr Top Microbiol Immunol* **333**:3-24.
11. Reed ML, Yen HL, Dubois RM, Bridges OA, Salomon R, Webster RG, Russell CJ (2009) Amino acid residues in the fusion peptide pocket regulate the pH of activation of the H5N1 influenza virus hemagglutinin protein. *J Virol* **83**:3568-3580.
12. Peiris JS, Poon LL, Guan Y (2009) Emergence of a novel swine-origin influenza A virus (S-OIV) H1N1 virus in humans. *J Clin Virol* **45**:169-173.
13. Chiu SS, Chan KH, Tu W, Lau YL, Peiris JS (2009) Immunogenicity and safety of intradermal versus intramuscular route of influenza immunization in infants less than 6 months of age: A randomized controlled trial. *Vaccine* **27**:4834-4839.
14. Smith GJ, Bahl J, Vijaykrishna D, Zhang J, Poon LL, Chen H, Webster RG, Peiris JS, Guan Y (2009) Dating the emergence of pandemic influenza viruses. *Proc Natl Acad Sci USA* **106**:11709-11712.

15. Cheung PP, Leung YH, Chow CK, Ng CF, Tsang CL, Wu YO, Ma SK, Sia SF, Guan Y, Peiris JS (2009) Identifying the species-origin of faecal droppings used for avian influenza virus surveillance in wild-birds. *J Clin Virol* **46**:90-93.

16. Hershkovitz O, Rosental B, Rosenberg LA, Navarro-Sanchez ME, Jivov S, Zilka A, Gershoni-Yahalom O, Brient-Litzler E, Bedouelle H, Ho JW, Campbell KS, Rager-Zisman B, Despres P, Porgador A (2009) NKp44 receptor mediates Interaction of the envelope glycoproteins from the West Nile and dengue viruses with NK cells. *J Immunol* **183**:2610-2621.

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18. Peiris JS, Tu WW, Yen HL (2009) A novel H1N1 virus causes the first pandemic of the 21(st) century. *Eur J Immunol* **39**:2946-2954.

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23. Schultsz C, Van Dung N, Hai le T, Quang Ha D, Peiris JS, Lim W, Garcia JM, Dac Tho N, Thi Hoang Lan N, Huu Tho H, Xuan Thao P, van Doorn HR, Vinh Chau NV, Farrar J, de Jong MD (2009) Prevalence of antibodies against avian influenza A (H5N1) virus among cullers and poultry workers in Ho Chi Minh City, 2005. *PLoS One* **4**:e7948.

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25. Wang P, Kudelko M, Lo J, Sachse M, Nicholls J, Peiris JS, Bruzzone R, Altmeyer R, Nal B (2009) Production of recombinant subviral particles for the four serotypes of dengue virus by expression of native prM and E proteins in human cells *PLoS One* **4**:e8325.

26. Garcia JM, Lagarde N, Ma ES, de Jong MD, Peiris JS (2010) Optimization and evaluation of an influenza A (H5) pseudotyped lentiviral particle-based serological assay. *J Clin Virol* **47**:29-33.

27. Bruzzone R, Dubois-Dalcq M, Kristensson K (2010) Neurobiology of Infectious Diseases: Bringing them out of neglect. *Prog Neurobiol*, in press.

28. Cavailler P, Chu S, Ly S, Garcia JM, Ha DQ, Bergeri I, Som L, Ly S, Sok T, Vong S, Buchy P. (2010) Seroprevalence of anti-H5 antibodies in rural Cambodia, 2007. *J Clin Virol*, in press.

29. Garcia JM (2010) Pseudotyped viruses: a new tool for sero-diagnostic. *In*: Advanced Techniques in Viral Detection (Marks RS, Lobel L, Sall A, eds), Neobionics Ltd, Omer, in press.

30. Chan MC, Chan RW, Yu WC, Ho CC, Yuen KM, Fong JH, Tang LL, Lai WW, Lo AC, Chui WH, Sihoe AD, Kwong DL, Wong DS, Tsao GS, Poon LL, Guan Y, Nicholls JM, Peiris JS (2010) Tropism and Innate Host Responses of the 2009 Pandemic H1N1 Influenza Virus in ex Vivo and in Vitro Cultures of Human Conjunctiva and Respiratory Tract. *Am J Pathol* **176**:1828-1840.

31. Chan RW, Yuen KM, Yu WC, Ho CC, Nicholls JM, Peiris JS, Chan MC (2010) Influenza H5N1 and H1N1 virus replication and innate immune responses in bronchial epithelial cells are influenced by the state of differentiation. *PLoS One* **5**:e8713.

32. Mao H, Tu W, Liu Y, Qin G, Zheng J, Chan PL, Lam KT, Peiris JS, Lau YL (2010) Inhibition of human natural killer cell activity by influenza virion and hemagglutinin. *J Virol*, in press.

33. Cheung TK, Chin AW, Chan KH, Schumaker M, Mak PW, Leung HS, Wong A, Peiris JS, Petrauskene OV, Poon LL (2010) Evaluation of novel H1N1-specific primer-probe sets using commercial RT-PCR mixtures and a premixed reaction stored in a lyophilized format. *J Virol Methods*, in press.

34. Buchy P, Vong S, Garcia JM, Chu S, Hien TT, Hien VM, Katz JM, Ha DQ, Simons C, Farrar JJ, Peiris JSM, de Jong MD (2010) Kinetics of neutralizing antibodies in patients naturally infected by H5N1 virus. *PLoS ONE*, in press.

Manuscripts submitted or in preparation

1. Lai JCC, Chan WWL, Kien F, Nicholls JM, Peiris JSM, Garcia JM (2010) Formation of virus-like particles from human cell lines exclusively expressing Influenza neuraminidase. *Submitted*.

2. Helbig I, Eliava M, Sammler E, Rozov A, Bruzzone R, Monyer H, Hormuzdi S (2010) A carboxy-terminal domain necessary for incorporating connexin 36 into electrical synapses. *Submitted*.

3. Teoh KT, Siu YL, Chan WL, Schlüter MA, Liu CJ, Peiris JS, Bruzzone R, Margolis B, Nal B (2010) The SARS coronavirus E protein interacts with the PALS1 tight junction protein and alters polarity of epithelial cells. *Submitted*.

4. Millet J, Cheung C, Kien F, Chan WL, Siu YL, Altmeyer R, Peiris M, Vidalain PO, Nal B (2010) The ezrin protein actin linker interacts with the SARS coronavirus S protein and restricts viral infection. *In preparation.*

5. Millet J, Mesel-Lemoine M, Nal B, Tangy F, Vidalain PO (2010) Human monocyte differentiation into dendritic cells increases susceptibility to HCoV-229E infection and cell death. *In preparation.*

6. Jaume M, Yip MS, Cheung CY, Li PH, Kien F, Dutry I, Escriou N, Daëron M, Altmeyer R, Bruzzone R, Nal B, and Peiris JSM. Anti-SARS-CoV Spike Antibodies Trigger Infection of Human Immune Cell via a pH- and Cathepsin L-Independent FcγR Pathway. *In preparation.*

Seminars, Invited Lectures and Oral Presentations at Meetings

1. Peiris JSM (2009) **Pre-clinical papers literature review – SARS & Influenza.** XI International Symposium on Respiratory Viral Infections, 19-22 February 2009, Bangkok.

2. Peiris JSM (2009) **Chair session on "Public Health: How to build expert networks with a division of labour?"** Avian Flu – Social and Anthropological Perspectives, 23-24 February 2009, HKU, Hong Kong.

3. Wang P (2009) **Assembly and Secretion of Recombinant Subviral Particles of the Four Dengue Serotypes: A model to study involvement of cellular machineries in late stage of flavivirus life cycle**. 8th Asia-Pacific Medical Virology Congress, 26-28 February 2009, Hong Kong.

4. Garcia JM (2009) **Pseudotyped lentiviral particles: multi-potent tool for the investigation of influenza**. 8th Asia-Pacific Medical Virology Congress, 26-28 February 2009, Hong Kong.

5. Peiris JSM (2009) **Congress Chairman of the 8th Asia-Pacific Medical Virology Congress**, 26-28 February 2009, Hong Kong.

6. Peiris JSM (2009) **Pathogenesis of Influenza**. 8th Asia-Pacific Medical Virology Congress, 26-28 February 2009, Hong Kong.

7. Bruzzone R (2009) **Confronting Infectious Diseases: HKU-Pasteur Research Centre and Pasteur International Network**. REDI (Regional Emerging Diseases Intervention) Center, Singapore.

8. Peiris JSM (2009) A**vian flu H5N1: Molecular epidemiology, transmission and pathogenesis**. Nature Symposium on Genetics and Genomics of Infectious Diseases, 22-24 March 2009, Singapore.

9. Peiris JSM (2009) **Avian influenza in humans: impact, surveillance and research**. International Symposium on Viral Respiratory Disease Surveillance, 25-28 March 2009, Seville, Spain.

10. Bruzzone R (2009) **Of Viruses and Cells: A Network of Dynamic Interactions**. Department of Pathology, HKU, Hong Kong.

11. Peiris JSM (2009) **Current Global H5N1 situation**. 3rd Annual NIAID Centers of Excellence for Influenza Research and Surveillance Network Meeting, 23-25 June 2009, Minneapolis, MN, USA.

12. Peiris JSM (2009) **Comparing host responses to H5N1 and seasonal influenza viruses in-vitro**. 3rd Annual NIAID Centers of Excellence for Influenza Research and Surveillance Network Meeting, 23-25 June 2009, Minneapolis, MN, USA.

13. Garcia JM (2009) **Pseudoviral particles: The "Swiss army knife" of the virologist**. Area of Excellence on Control of Pandemic and Inter-pandemic Influenza, HKU, Hong Kong.

14. Jaume M (2009) **Antibody-dependent enhancement of SARS-CoV infection of human immune cells**. Scientific Conference of the International Network of Pasteur Institutes, June 2009, Ho Chi Minh City, VietNam.

15. Lai JC (2009) **Revisiting influenza virus interaction with its receptor by STD NMR spectroscopy**. Scientific Conference of the International Network of Pasteur Institutes, June 2009, Ho Chi Minh City, VietNam.

16. Nal B (2009) **Deciphering the Cellular Interactome of Influenza A Viruses**. Scientific Conference of the International Network of Pasteur Institutes, June 2009, Ho Chi Minh City, VietNam.

17. Bruzzone R (2009) **A network approach to vector-borne diseases: the impact of DENFRAME and the International Network of Pasteur Institutes**. EU-SEA Expert Meeting on Vector Borne Diseases, Singapore Immunology Network, Singapore.

18. Peiris JSM (2009) **Scientific Organizing Committee and Chair of 4 Symposia** on Emerging Virus Diseases; Viruses at the Edge; Which Virus for which Disease; Novel H1N1 influenza: Late Breakers. Interscience Conference on Antimicrobial Agents and Chemotherapy, 12-15 September 2009, San Francisco, CA, USA

19. Peiris JSM (2009) **We are faced with an H1N1influenza pandemic, now what?** GSK Satellite Symposium on "Emergence of the new influenza A/H1N1 2009 pandemic", 3-5 October 2009, Singapore.
20. Nal B (2009) **Interaction between the pals1 cellular tight junction factor and the SARS-CoV E envelope protein: consequences for infected epithelia**. Retreat of the Department of Cell Biology and Infection, Institut Pasteur, 12-14October 2009, France.
21. Bruzzone r (2009) **Virus-host cell interactions: From cell biology to diagnostic**. Fiocruz, Fundacao Oswaldo Cruz, Rio de Janeiro, Brazil.
22. **Lagarde N. (2009) AIDS-HIV: life cycle, molecular biology, vaccination and treatment. "**Victor Segalen " French International School.
23. Peiris JSM (2009) **Confronting emerging infections: A view from Hong Kong**. Imperial College, London, UK
24. Peiris JSM (2009) P**rogram Planning Committee and Plenary Speaker**. WHO Global Consultation on Public Health Research Agenda for Influenza, 17-20November 2009, Geneva, Switzerland.
25. Kudelko M (2009) **Dengue VLPs: an efficient system to study dengue egress**. GLObal network for DENgue research (GLODEN), Institut Pasteur, France.
26. Millet J (2009) **Interactome of the C-terminal domains of Human Coronavirus Spike (S), Envelope (E) and Membrane (M) glycoproteins**. 14th Research Postgraduate Symposium, Li Ka Shing Faculty of Medicine, HKU, 2-3 December 2009, Hong Kong.
27. Kien F (2010) **Identification and Characterization of Cellular Interactants of Influenza M2 Ion Channel Protein**. Area of Excellence on Control of Pandemic and Inter-pandemic Influenza, HKU, 26Feburary 2010, Hong Kong.

List of Posters

1. Kien F, Tang DJ, Millet J, Teoh KT, Bruzzone R, Peiris M, Nal B (2009) Definition of the cellular interactomes of SARS-CoV and the highly pathogenic avian influenza H5N1 virus: identification of human cellular regulators of viral entry, assembly and egress. 8th Asia-Pacific Medical Virology Congress, 26-28 February 2009, Hong Kong.
2. Yen HL, Aldridge JR, Boon AC, Ilyushina NA, Salomon R, Hulse-Post DJ, Marjuki H, Franks J, Boltz DA, Bush D, Lipatov AS, Webby RJ, Rehg JE, Webster RG (2009) Changes in H5N1 influenza virus hemagglutinin receptor binding domain affect systemic spread. Keystone Symposium on "Pattern Recognition Molecules and Immune Sensors of Pathogens", March 29-April 3 2009, Fairmont Banff Springs, Alberta, Canada.
3. Garcia JM, Lagarde N, Ma ESK, de Jong MD, Buchy P, Peiris JSM (2009) Optimization and evaluation of an influenza A (H5) pseudotyped lentiviral particle – based serological assay. Scientific Conference of the International Network of Pasteur Institutes, June 2009, Ho Chi Minh City, VietNam.
4. Dutry I, Li PH, Bruzzone R, Peiris JSM, Jaume M (2009) Investigation of Antibody-Dependent Enhancement (ADE) of influenza infection and its role in pathogenesis of avian flu. Scientific Conference of the International Network of Pasteur Institutes, June 2009, Ho Chi Minh City, VietNam.

5. Tang DJ, Lam PCH, Chu KSL, Lam YM, Bruzzone R, Nal B (2009) Mutational analysis of H5N1 hemagglutinins: identification of molecular determinants for efficient packaging into pseudotyped lentiviral particles. Retreat of the Department of Cell Biology and Infection, Institut Pasteur, 12-14October 2009, France.

6. Wang PG, Kudelko M, Lo J, Kwok K, Sachse M, Bruzzone R, Nal B (2009) Assembly and Secretion of Recombinant Subviral Particles of the Four Dengue Serotypes: A model to study involvement of cellular machineries in late stage of flavivirus life cycle. Retreat of the Department of Cell Biology and Infection, Institut Pasteur, 12-14October 2009, France.

7. Wang PG, Kudelko M, Lo J, Kwok K, Bruzzone R, Nal B (2009) Identification of Cellular Factors Involved in Egress of Dengue Virus Using a Cell Line that Stably Expresses Dengue Recombinant Subviral Particles. International Conference on "Emerging Infectious Diseases", Duke-NUS, December 2009, Singapore.

8. Lo J, Sachse M, Prevost MC, Despres P, Peiris JS, Bruzzone R, Kudelko M, Wang PG, Nal B, Nicholls JM (2009) Development of Dengue Recombinant Subviral Particles as a Tool to Study Dengue Virus Egress. International Conference on "Emerging Infectious Diseases", Duke-NUS, December 2009, Singapore.

9. Yip MS, Li PH, Buzzone R, Jaume M (2009) Antibody-dependent Enhancement of Severe Acute Respiratory Syndrome Coronavirus. 14th Research Postgraduate Symposium, Li Ka Shing Faculty of Medicine, The Univerity of Hong Kong, December 2009, Hong Kong

10. Xia Z, Lee HY, Dutry I, Ho W, Bruzzone R, Peiris JSM, Jaume M (2009) Interactions of Human Natural Killer Cells with the Hemagglutinin from an H5N1 Influenza Virus. 14th Research Postgraduate Symposium, Li Ka Shing Faculty of Medicine, The University of Hong Kong, December 2009, Hong Kong.

11. Ma HL, Kien F, Zhang Y, Poon LLM, Bruzzone R, Peiris JSM, Nal B (2009) Interaction between influenza A virus M2 and annexin A6 protein: implication for the viral life cycle. 14th Research Postgraduate Symposium, Li Ka Shing Faculty of Medicine, The University of Hong Kong, December 2009, Hong Kong.

12. Lai JCC, Garcia JM, Haselhorst T, Nicholls J, von Itzstein M, Peiris JSM (2009) Revisiting influenza virus interaction with its receptor by STD-NMR spectroscopy. 14th Research Postgraduate Symposium, Li Ka Shing Faculty of Medicine, The University of Hong Kong, December 2009, Hong Kong (**Award of the best poster presentation** in the category of *Infectious diseases*).

13. Chu S, Channa M, Bun Thin Y, Garcia JM, Buchy P (2009) H5 pseudotyped lentiviral particles: a new tool for H5N1 infection sero-diagnosis. XI International Symposium on Respiratory Viral Infections, Bangkok, Thailand.

14. Teoh KT, Siu YL, Chan WL, Peiris M, Bruzzone R, Margolis B, Nal B (2009) 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", 16-21 February 2010, Taos, New Mexico, USA.

15. 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 (2009) Host Cell Susceptibility to Human Coronavirus Infections. Keystone Symposium on "Cell Biology of Viral Entry, Replication and Pathogenesis", 16-21 February 2010, Taos, New Mexico, USA.

Current Grants

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 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 Grants Council

Principal Investigator:	Dr Roberto Bruzzone
Amount:	HK$908,545.00
Period:	01/Nov/2008 to 30/Dec/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 Huiling 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

Pending Grant Applications

Research Grants Council

Principal Investigator: Dr Beatrice Nal-Rogier
Amount: HK$1,642,102.00
Period: 24 months

Research Fund for the Control of Infectious Diseases

Principal Investigator: Dr Beatrice Nal-Rogier
Amount: HK$909,000.00
Duration: 24 months

Research Fund for the Control of Infectious Diseases

Principal Investigator: Dr Peigang Wang
Amount: HK$970,000.00
Duration; 24 months

European Commission (FP7)

Principal Investigator: Dr Malik Peiris/Dr John Nicholls
Amount: Euro 375,150.00
Duration; 36 months

Grants Completed in 2009

Research Fund for the Control of Infectious Diseases

Principal Investigator: Dr Joanna W Y Ho
Amount: HK$800,000.00
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 Huiling Yen
Amount: HK$498,417.00
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

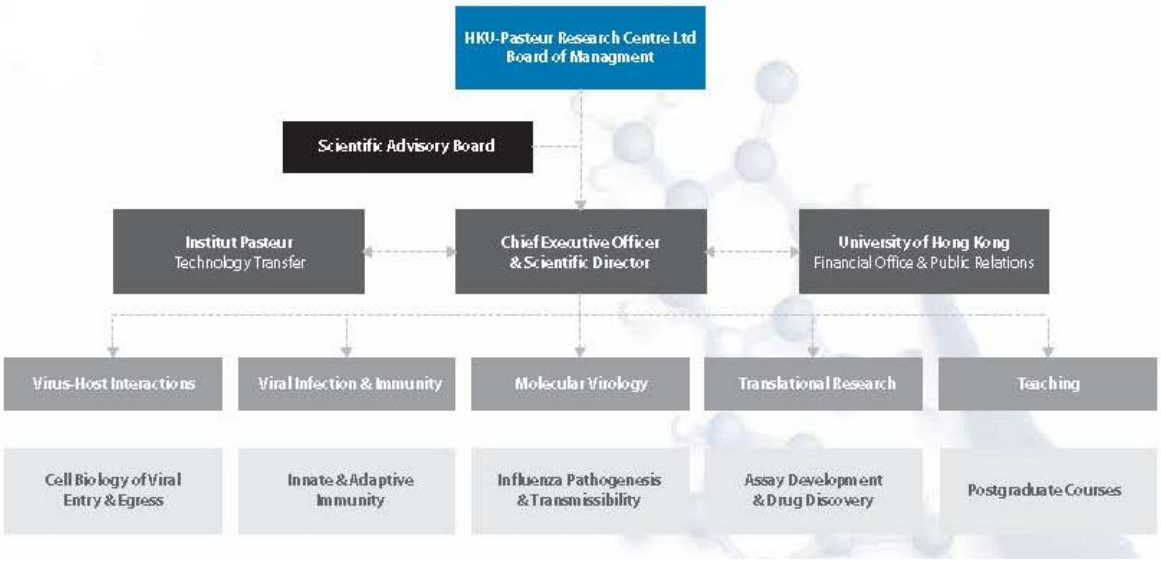
Area of Excellence, Control of Pandemic and Inter-pandemic Influenza
Principal Investigator: Dr John Nicholls/Dr Jean-Michel Garcia
Amount: HK$ 413,832.00
Period: 01/Jan/2009 to 31/Dec/2009

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

Organization Chart



List of Staff as of 31 December 2009

Administration:-

Chief Executive Officer	BRUZZONE, Bruzzone
Scientific Director	PEIRIS, Malik
Administrative Assistant	LI, Anne
Secretary	TSENG, Bella
System Engineer	WONG, Eric
Office Assistant	KWONG, Annie

Scientist:

Research Assistant Professor	NAL-ROGIER, Beatrice
Research Assistant Professor	YEN, Huiling
Post Doctoral Fellow	GARCIA, Jean-Michel
Post Doctoral Fellow	JAUME, Martial DA
Post Doctoral Fellow	KIEN, Francois
Post Doctoral Fellow	TANG, Dong Jiang
Post Doctoral Fellow	WANG, Pei Gang

Technician:

Research Technician	LAGARDE, Nadege
Research Technician	LI, Ping Hung
Research Technician	SIU, Lewis
Research Technician	TSE, Jane
Research Assistant	LEE, Horace
Research Assistant	KWOK, Kevin
Research Assistant	BAUDON Eugenie
Research Assistant	MOK, Chris
Research Assistant	WONG, Diana
Research Assistant	CHOY, Terry
Laboratory Attendant	LAM, Simon

Student:-

PhD Student	CHEUNG, Peter
PhD Student	KUDELKO, Mateusz
PhD Student	LAI, Jimmy
PhD Student	MA, Huai Liang
PhD Student	MILLET, Jean
PhD Student	TEOH, Michael
PhD Student	YIP, Simon
Mphil Student	CHAN, Wallace
Mphil Student	DUTRY, Isabelle
Mphil Student	LAM, Gladys
Mphil Student	LEUNG, Nancy

Mphil Student	XIA, Cherry
Mphil Student	ZHANG, Joey

Budget for the year ending June 2010

BUDGET AND FINANCIAL FORECAST	2008/2009 Actual	2008/2009 Budget	2009/2010 Forecast	2010/2011 Forecast
Opening Cash Balance (A)	**2,842**	**2,842**	**6,573**	**6,400**
1. Income				
HKU Central Fund	6,470	6,470	6,470	6,470
Salary for seconded staff	642	642	636	670
Teaching Programme		100	300	300
Faculty in-kind contribution	3,356	3,137	2,850	2,845
PDF & RAP funds	431			
Other		15	9	
HKU	**10,899**	**10,364**	**10,265**	**10,285**
Institut Pasteur				
Central Fund** **(Re. matching fund managed by Physiology)**	725	1,628 *	103 *	*
Virology course	338	619	300	300
Cell biology course	259	259	271	250
Immunology course	234	493	259	250
ACIP	114	130	16	
Contribution toward Central Expenses			15	
Trf (to)/from Deferred Income				
Institut Pasteur	**1,670**	**3,129** *	**964** *	**800** *
Grants				
HKSAR - RFCID	1,601	1,496	1,658	1,628
HKSAR - Area of Excellence (AOE)	1,027	1,030	585	300
European Grant - Denframe	358		348	
European Grant - Foundation de France	12	12		
New Grants (HK)			761	800
New Grants (EC)				980
LKSF	318	318		
Trf (to)/from Deferred Income				
Grants	**3,316**	**2,856**	**3,352**	**3,708**
Croucher Foundation				
Virology course	68	68	68	68
Cell biology course	70	52		52
Immunology course	52	52	52	
Pasteur-Croucher Exch Progm	62	62	105	62
Croucher Foundation	**252**	**234**	**225**	**182**
Special Projects/Gifts/Sponsoring (One-off)				
Mahathir Science Awards (MP)		40	12	
New Croucher Seminar Series				96
Croucher Cell Biology Seminar Series	78	96		
Consulate General de France	43	43	20	20
Italian Chamber of Commerce	28	28		
French Chamber of Commerce HK (BSL3)			137	
Sanofi Pasteur		20	22	20
O/H income fm LKS	116			
O/H income fm Denframe	161			
Others (BNP)			400	
Trf (to)/from Deferred Income				
Special Projects/Gifts/Sponsoring (One-off)	**426**	**227**	**591**	**136**
Others				
Industrial contracts	435	435		
Bank Deposit Interest Income	10	8	2	2
Others	**445**	**443**	**2**	**2**
Total Income (B)	**17,008**	**17,252**	**15,399**	**15,113**
2. Expenditure				
Staff Costs				
Central	5,879	6,162	5,728	5,488
University secondment	644	642	636	668
Courses and Projects	1,694	1,687	1,273	1,755
Staff Costs	**8,217**	**8,491**	**7,637**	**7,911**
General expenses				
Central	2,226	1,313	2,043	1,366
Courses and Projects	3,081	2,856	2,241	3,360
HKU Mgt Services and Rental	3,356	3,137	2,850	2,845
General expenses	**8,663**	**7,305**	**7,134**	**7,571**
Total Expenditure (C)	**16,880**	**15,796**	**14,771**	**15,482**

Cash Generated from Operation (D = B - C)	**128**	**1,457**	**628**	**(369)**
3. Cashflows with Captial nature				
Drs Richard Charles & Esther Yewpick Lee Charitable Foundation	999	999		
Loan for building the Teaching Centre	3,200	3,200		
- Equipment for the Teaching Centre	(2,236)	(1,786)		
- Renovation for the Teaching Centre	(475)	(7)		
Loan Repayment				
General Equipments	(86)	(132)		
Total Cashflows with Capital nature (E1)	**1,402**	**2,274**		
4. Net changes in current assets and liabilities (E2)				
Total Cash Surplus / (Deficit) (F = D + E)	**1,530**	**3,731**	**628**	**(369)**
Closing Cash Balance (A + F)	**4,372**	**6,573**	**7,201**	**6,031**

Operating Profits and Loss

Cash Generated from Operation (D)	**128**	**1,457**	**(173)**	**(25)**
Deferred capital fund	**200**	**200**	**200**	**200**
Depreciation	**(1,631)**	**(1,655)**	**(1,596)**	**(1,023)**
Operating Profits and Loss	**(1,303)**	**1**	**(1,569)**	**(848)**

Headcount	**29**	**29**		

PM	*Fund for Seconded Staff*	*642*	*642*	*657*	*670*
	Faculty's in-kind Contribution				
	- HKU Management Services	*2,407*	*2,188*	*1,901*	*1,896*
	*-HKU Office rental **	*949*	*949*	*949*	*949*
		3,356	*3,137*	*2,850*	*2,845*
	Total	*3,998*	*3,779*	*3,507*	*3,515*

Fundings managed by other Departments (not shown on Budget & Forecast):-

** Contribution from Institut Pasteur for 2008/2009, 2009/2010 and 2010/2011 are covered under Matching Funds (HK$2,367K) now managed by Department of Physiology.
Remarks:

EUR150K (equv. HKD1,708K) grant from Institut Pasteur on 21 Dec 07 was matched with government funding of HKD643K. Money was released to Department of Physiology on 8 Jan 2010 for the Center's research expenses.

RGC Grant (HK$909K)
Managed by: Faculty of Medicine
Grant Period: 1 Nov 08 to 30 Oct 10

1st HKU-PASTEUR CELL BIOLOGY COURSE

FOR RESEARCH POSTGRADUATE STUDENTS

30 March - 10 April 2009

HKU-Pasteur Research Centre, Hong Kong

INSTITUT PASTEUR

香港大學 - 巴斯德研究中心
HKU-Pasteur Research Centre

THE UNIVERSITY OF HONG KONG
LI KA SHING FACULTY OF MEDICINE
香港大學李嘉誠醫學院

SPEAKERS:

David BANFIELD	Hong Kong
Michel BORNENS	France
Roberto BRUZZONE	Hong Kong
Arnaud ECHARD	France
Auguste GENOVESIO	Korea
Walter HUNZIKER	Singapore
Dong-yin JIN	Hong Kong
Yun-wah LAM	Hong Kong
Andrew MILLER	Hong Kong
Béatrice NAL-ROGIER	Hong Kong
Ulf NEHRBASS	Korea
Javier PIZARRO-CERDA	France
Anthony PUGSLEY	France
Philippe SANSONETTI	France
Nathalie SAUVONNET	France
George TSAO	Hong Kong
Chiara ZURZOLO	France

ORGANISERS:

Roberto BRUZZONE, HKU-Pasteur Research Centre
Béatrice NAL-ROGIER, HKU-Pasteur Research Centre
Chiara ZURZOLO, Institut Pasteur
George TSAO, University of Hong Kong

TUTORS:

Dong-jiang TANG, HKU-Pasteur Research Centre
François KIEN, HKU-Pasteur Research Centre
Wilson YP CHING, University of Hong Kong

Contact: hku-pasteur@hku.hk
or Anne Li at +852 2816 8403

Jacques Monod (1910-1976) co-recipient of the 1965 Nobel Prize in Medicine for "discoveries concerning genetic control of enzyme and virus synthesis"

SUPPORTED BY:

THE CROUCHER FOUNDATION

THE FRENCH CHAMBER

AIR FRANCE

6th HKU-PASTEUR VIROLOGY COURSE

FOR RESEARCH POSTGRADUATE STUDENTS

7 - 24 July 2009

HKU-Pasteur Research Centre, Hong Kong

INSTITUT PASTEUR

香港大學 - 巴斯德研究中心
HKU-Pasteur Research Centre

THE UNIVERSITY OF HONG KONG
LI KA SHING FACULTY OF MEDICINE
香港大學李嘉誠醫學院

FOCUS ON NEUROTROPIC VIRUSES

ORGANISERS

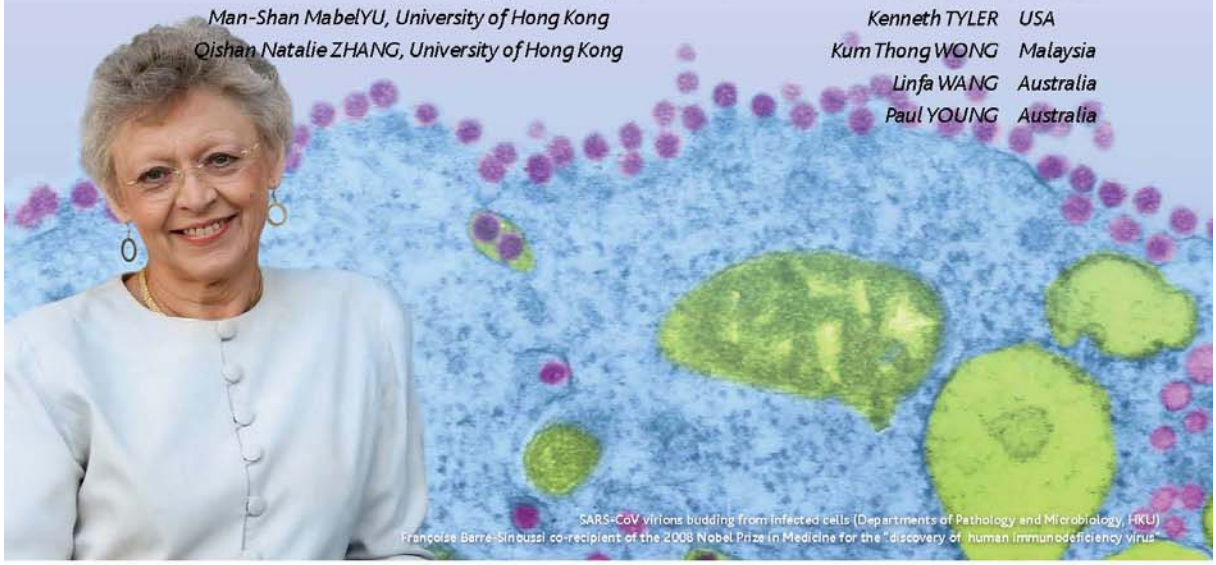
Roberto BRUZZONE, HKU-Pasteur Research Centre
Malik PEIRIS, HKU-Pasteur Research Centre & University of Hong Kong
Noël TORDO, Institut Pasteur

TUTORS

Guillaume CASTEL, Institut Pasteur
Jean-Michel GARCIA, HKU-Pasteur Research Centre
Nadège LAGARDE, HKU-Pasteur Research Centre
Camille SHEK, HKU-Pasteur Research Centre
Justin BAHL, University of Hong Kong
Gavin SMITH, University of Hong Kong
Dhanasekaran VIJAYKRISHNA, University of Hong Kong
Raymond CHANG, University of Hong Kong
Jian-fei Faye CHAO, University of Hong Kong
Yuen-Ting Katie CHEUNG, University of Hong Kong
Hiu-ling Clara HUNG, University of Hong Kong
Suthicha WUWONGSE, University of Hong Kong
Man-Shan MabelYU, University of Hong Kong
Qishan Natalie ZHANG, University of Hong Kong

SPEAKERS

Roberto BRUZZONE	*Hong Kong*
Mary Jane CARDOSA	*Malaysia*
Raymond CHANG	*Hong Kong*
Zhi-wei CHEN	*Hong Kong*
Roberto CHIESA	*Italy*
Thérèse COUDERC	*France*
Philippe DESPRES	*France*
Vincent DEUBEL	*China*
Lynn ENQUIST	*USA*
Philippe GASQUE	*La Réunion*
Antoine GESSAIN	*France*
Pascale GIRAUDON	*France*
Daniel GONZALEZ-DUNIA	*France*
Vu Thi Que HUONG	*Vietnam*
Ching-Chuan LIU	*Taiwan*
Mohamed NEJMEDDINE	*UK*
Malik PEIRIS	*Hong Kong*
Benjamin PENG	*Hong Kong*
Noël TORDO	*France*
Kenneth TYLER	*USA*
Kum Thong WONG	*Malaysia*
Linfa WANG	*Australia*
Paul YOUNG	*Australia*



SARS-CoV virions budding from infected cells (Departments of Pathology and Microbiology, HKU)
Françoise Barré-Sinoussi co-recipient of the 2008 Nobel Prize in Medicine for the "discovery of human immunodeficiency virus"

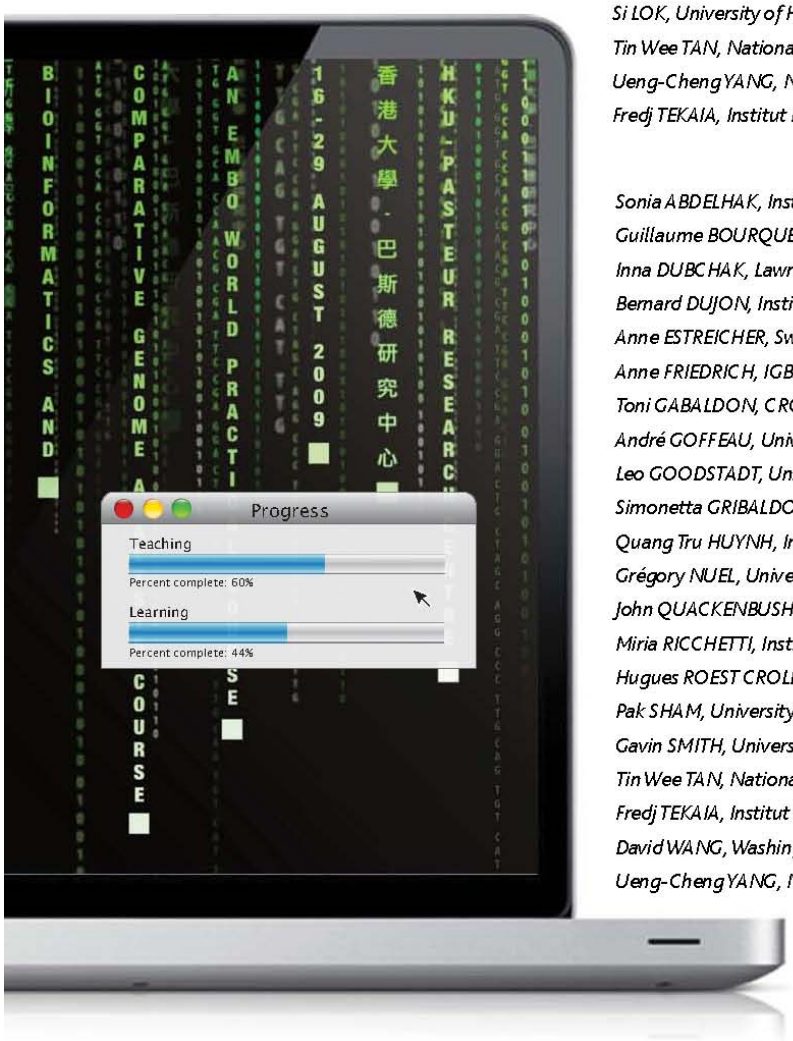
SPONSORS: THE CROUCHER FOUNDATION · international network Institut Pasteur · sanofi pasteur · THE FRENCH CHAMBER · AIR FRANCE

16- 29 August 2009
Li Ka Shing Faculty of Medicine
The University of Hong Kong

An EMBO World Practical Course

Bioinformatics & Comparative Genome Analysis

For PhD and post-doctoral students, and junior scientitsts



ORGANISERS

Roberto BRUZZONE, HKU-Pasteur Research Centre
Si LOK, University of Hong Kong
Tin Wee TAN, National University of Singapore
Ueng-Cheng YANG, National Yang-Ming University, Tapei
Fredj TEKAIA, Institut Pasteur Paris

SPEAKERS

Sonia ABDELHAK, Institut Pasteur Tunis
Guillaume BOURQUE, Genome Institute of Singapore
Inna DUBCHAK, Lawrence Berkeley National Laboratory, Berkeley
Bernard DUJON, Institut Pasteur Paris
Anne ESTREICHER, Swiss Institute of Bioinformatics Geneva
Anne FRIEDRICH, IGBMC – Strasbourg
Toni GABALDON, CRG-Centre for Genomic Regulation, Barcelona
André GOFFEAU, Université Catholique de Louvain
Leo GOODSTADT, University of Oxford
Simonetta GRIBALDO, Institut Pasteur Paris
Quang Tru HUYNH, Institut Pasteur Paris
Grégory NUEL, Université Paris-Descartes
John QUACKENBUSH, Harvard School of Public Health, Boston
Miria RICCHETTI, Institut Pasteur Paris
Hugues ROEST CROLLIUS, Ecole Normale Supérieure Paris
Pak SHAM, University of Hong Kong
Gavin SMITH, University of Hong Kong
Tin Wee TAN, National University of Singapore
Fredj TEKAIA, Institut Pasteur Paris
David WANG, Washington University, St Louis
Ueng-Cheng YANG, National Yang-Ming University, Tapei

For more information please visit the course web page: http://www.pasteur.fr/~tekaia/BCGA2009.html

Supported by: EMBO INSTITUT PASTEUR

2nd HKU-PASTEUR IMMUNOLOGY COURSE

FOR RESEARCH POSTGRADUATE STUDENTS

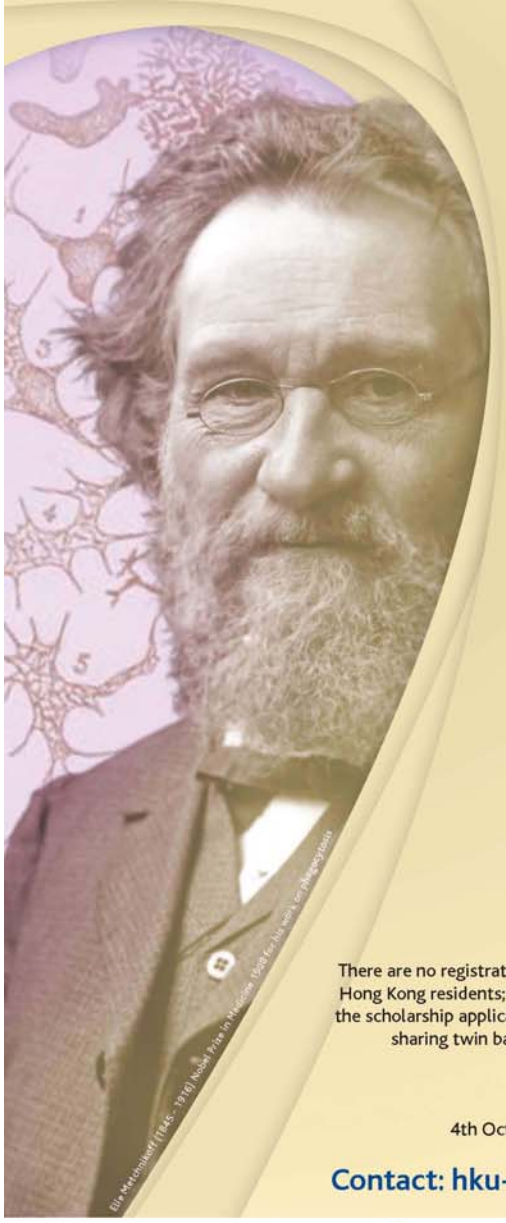
19 November - 2 December 2009

HKU-Pasteur Research Centre, Hong Kong

INSTITUT PASTEUR

香港大學 - 巴斯德研究中心
HKU-Pasteur Research Centre

THE UNIVERSITY OF HONG KONG
LI KA SHING FACULTY OF MEDICINE
香港大學李嘉誠醫學院



ORGANISERS:

Roberto BRUZZONE, HKU-Pasteur Research Centre
Allan LAU, University of Hong Kong
Jean-Marc CAVAILLON, Institut Pasteur
Armelle PHALIPON, Institut Pasteur
Daniel SCOTT-ALGARA, Institut Pasteur

SPEAKERS:

Paola CASTAGNOLI	*Singapore*
Jean-Marc CAVAILLON	*France*
Keh Chuang CHIN	*Singapore*
Katja FINK	*Singapore*
Takashi FUJITA	*Japan*
Allan LAU	*Hong Kong*
Jay A LEVY	*USA*
Stephan LUDWIG	*Germany*
Kensuke MIYAKE	*Japan*
Lisa NG	*Singapore*
Malik PEIRIS	*Hong Kong*
Armelle PHALIPON	*France*
Lluis QUINTANA-MURCI	*France*
Laurent RENIA	*Singapore*
Daniel SCOTT-ALGARA	*France*
Wen Wei TU	*Hong Kong*

TUTORS:

Martial JAUME	*Hong Kong*
James LI	*Hong Kong*

There are no registration fees for the course. Travel fellowships (up to 5) will be awarded to the best non Hong Kong residents; non-Hong Kong residents who need scholarship for travel are advised to complete the scholarship application and return all completed forms to HKU-pasteur@hku.hk. Accommodation (on sharing twin basis) and food (canteen-style) will be provided for non-Hong Kong residents.

Deadline for application:
20th September 2009 for Non-Hong Kong residents
4th October 2009 for students from HKU and other Hong Kong universities

Contact: hku-pasteur@hku.hk or Anne Li at +852 2816 8403

SPONSORS:

international network Institut Pasteur

THE CROUCHER FOUNDATION

THE FRENCH CHAMBER

AIR FRANCE

Seminar Room 7, LG1/F, Laboratory Block
Li Ka Shing Faculty of Medicine,
The University of Hong Kong,
21 Sassoon Road, Hong Kong

February 23-24, 2009

Avian Flu: Social & Anthropological Perspectives

With the support of the Fyssen Foundation for anthropological research

February 23

9.00 a.m.: Opening
Roberto Bruzzone (HKU-Pasteur Research Centre) and Jean-François Huchet (French Centre for Research on Contemporary China).

9.15 a.m.: Presentation of the conference
Frédéric Keck (National Centre for Scientific Research, Paris).

9.30 a.m.-12.30 p.m.
Animal Surveillance: How to control birds while protecting the environment?
Chairman:
Mike Kilburn (Civic Exchange, Hong Kong).
Speakers:
- Yi Guan (Microbiology Dpt, Hong Kong University): Evolutionary Dynamics and Emergence of Panzootic H5N1 Influenza Viruses in Southern China.
- Vincent Martin (Food and Agriculture Organization, Beijing): The Influence of Farming and Cultural Practices in the Emergence of Avian Flu in Asia.
- Vanessa Manceron (National Centre for Scientific Research, Paris): Problems of Confinement after the Bird Flu Outbreak in France.
- Captain Wong (Kadoorie Farm, Hong Kong): Avian Flu and Wild Bird Release in Hong Kong.

2.30 p.m.-5.30 p.m.
Public Health: How to build expert networks with a division of labor?
Chairman:
Malik Peiris (HKU-Pasteur Research Centre & Hong Kong University).
Speakers:
- Nyoman Kandun (Health Dpt, Djakarta): Clusters of Avian Influenza and Public Health Policy in Indonesia.
- Sirenda Vong (Pasteur Institute, Phnom Penh): Surveillance of Emerging Infectious Diseases in the Context of Cambodia.
- François Moutou (French Food Safety Agency, Paris): Animal Health and Public Health in the French Food Safety Agency.
- Carlo Caduff (Anthropology Dpt, UC Berkeley): The Publics of Public Health: Pandemic Vaccine Prioritization in the United States.

February 24

9.30 a.m.-12.30 p.m.
Food and Hygiene : How to change habits in a free market society?
Chairman:
Kwok-Yung Yuen (Microbiology Dpt, Hong Kong University).
Speakers:
- Richard Fielding (School of Public Health, Hong Kong University): Avian Influenza Risk Perception and Live Poultry Purchase in China and Southeast Asia.
- Constance Chan (Centre for Food Safety, Hong Kong): Avian Influenza Control Measures on Poultry Trade in Hong Kong.
- Tik-Sang Liu (Anthropology Dpt, HK University of Science and Technology): Local Culture and Chicken Consumption in Hong Kong.
- Noelie Vialles (Collège de France, Paris): Food Safety in France, from Mad Cow Disease to Avian Flu.

2.30 p.m.-5.30 p.m.
Media and Communication : How to prepare for a possible pandemic?
Chairman:
David Palmer (Sociology Dpt, Hong Kong University).
Speakers:
- Thomas Tsang (Centre for Health Protection, Hong Kong): Risk Communication at the Centre for Health Protection.
- Mary Ann Benitez (South China Morning Post, Hong Kong): The Media and Bird Flu Fatigue: What's Next?
- Matthieu Fintz (French Environmental Safety Agency, Paris): Media Framing and the Web of Causation in Avian Flu Crisis in Egypt.
- Annick Guenel (National Centre for Scientific Research, Paris): Avian Flu, Vietnamese Media and the "Renovated Chicken".

All are welcome.
For more information, contact Frédéric Keck (f.keck@cegetel.net).

香港大學 - 巴斯德研究中心
HKU-Pasteur Research Centre

cefc
Centre d'études français sur la Chine contemporaine
法国现代中国研究中心

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

September 17-18, 2009

5th Croucher-Pasteur Exchange Programme

Ph.D. / Post-doc at Institut Pasteur Paris
for Research Postgraduate Students (MPhil and PhD)

Croucher-Pasteur Exchange Programme

The HKU-Pasteur Research Centre, the International Affairs Department of Institut Pasteur and the Croucher Foundation are establishing a post-doc and student exchange programme in order to strengthen the scientific collaboration between Hong Kong and France. A 2 to 3 year scholarship will be available for students and post-doctoral fellows resident in Hong Kong wishing to perform research work at Institut Pasteur. The scholarship programme will be open to all scientific domains covered by Institut Pasteur.

Applications are normally open by early October and closed by mid-November.

More information at www.hkupasteur.hku.hk and at www.croucher.org.hk

Pasteur Lecture Series

A lecture series is organised to enable Hong Kong students to meet personally principal investigators from Institut Pasteur and discuss their scientific work with the aim to pursue training in their laboratories.

Thursday September 17, 2009

Venue:
Room 3301 (lift 17/18), Academic Building,
The Hong Kong University of Science and Technology
Clear Water Bay, Hong Kong

2:00 p.m. - 4:00 p.m.:
Information Session
Prof Yung-Hou Wong (HKUST)
Dr Béatrice Nal-Rogier (HKU-Pasteur Research Centre)
Mr Jean-Charles Briand (Consulate General of France in Hong Kong)
Mr P. Prashanth (Consulate General of France in Hong Kong)
Dr Mathieu Picardeau (Institut Pasteur)
Dr Spencer L. Shorte (Institut Pasteur)
Dr Mustapha Si-Tahar (Institut Pasteur)

Friday September 18, 2009

Venue:
HKU-Pasteur Research Centre
1st Floor, Room 104, Dexter H C Man Building
8 Sassoon Road, Pokfulam, Hong Kong

9:30 a.m. - 11:00 a.m.:
Antiviral innate immunity in the lung mucosa: the flu as an example
Dr Mustapha Si-Tahar
Department of Infection and Epidemiology

11:30 a.m. - 1:00 p.m.:
Leptospira: from genetics to pathogenesis
Dr Mathieu Picardeau
Department of Microbiology

2:30 p.m. - 4:00 p.m.:
Imaging infection
Dr Spencer L. Shorte
Department of Cell Biology and Infection

Remarks: Light refreshment will be provided.

Organised by 香港大學・巴斯德研究中心 HKU-Pasteur Research Centre

Supported by 思德基金會 THE CROUCHER FOUNDATION

HKU – Pasteur Research Centre 2010 Courses

Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong SAR, China

HKU-Pasteur Cell Biology: 18 March - 1 April 2010

Deadline for applications: 31 December 2009

Programme available: 30 October 2009

There is a growing interest in studying cell function through the magnifying lens of pathogen-host cell interactions as pathogens hijack cellular machineries to suit their needs. This intensive course, consisting of lectures and laboratories, provides a special interdisciplinary training ground spanning cellular and molecular biology, physiology and microbiology.

HKU-Pasteur Virology: 7 -23 July 2010

Deadline for applications: 30 April 2010

Programme available: 26 February 2010

This course presents every year a different focus to analyze the ecology, epidemiology and molecular biology of viruses that have been responsible of recent outbreaks. The program includes practical sessions and lectures covering complementary aspects of viral diseases, from molecular diagnosis to immune response, anti-viral therapy and prevention strategies.

HKU-Pasteur Immunology: 8 - 19 November 2010

Deadline for applications: 31 August 2010

Programme available: 30 June 2010

A lecture and practical course that provides a comprehensive overview of modern immunology with an introduction to the repertoire of effector cells. The course has a major focus on innate immunity and its signaling mechanisms in response to viral, parasitic and bacterial infections.

HKU-Pasteur courses provide students and young postdocs with an opportunity to interact with leading scientists and train in cutting edge techniques. HKU-Pasteur courses attract every year an international group of students who discuss with scientists from different fields the most recent developments across disciplines.
There are no registration fees. Accommodation and food will be provided for non-Hong Kong residents.
Limited to 24 students.

Supported by the University of Hong Kong, Institut Pasteur, the International Network of Pasteur Institutes and the Croucher Foundation.

Contact: hku-pasteur@hku.hk or Anne Li at +852 2816 8403 **Website:** http://www.hkupasteur.hku.hk

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