Pasteur Institute of Cambodia

- The activities towards biomedical research and surveillance of infectious diseases.
- Research developed based on the diagnosis, biological characterization and molecular epidemiology of viruses’ bacteria and malaria with emphasis on the study mechanisms of resistance of these microorganisms to treatment.
- Provides a platform for comprehensive medical and biological analyses.
  - QA process, equipped with modern equipment, highly qualified staff and provides service delivery in biology, blood biochemistry and microbiology.
  - Also provides services for the control of food hygiene and the chemical and microbiological analysis of water.

Biomedical Analysis & Vaccinations

Laboratory profile

- Its panel of over 150 tests in various fields.
- Rigorous quality control at the pre-analytical level, at the analytical level and at the post-analytical level.
- A training center: student’s medical doctor, student’s pharmacist, student’s technician and engineer.
- Technology transfer from research units of Institute Pasteur.

The International Vaccination Center

- Japanese Encephalitis Vaccine
- HPV vaccine
- Meningococcique A+C vaccine
- MMR vaccine
- Rotavirus vaccine

Food and water testing

Rabies Prevention Center

- National Reference Center for confirmatory testing and an Epidemiology & Public Health unit in an enzootic setting also provides a unique opportunity for research to combat this fatal disease.
Public Health

Especially through the epidemiological and lab-based investigation, expertise and confirmation by National Reference Centers (NRC) in case of epidemics.

- Since 2011 confirmed human cases of A (H5N1) influenza and has documented the emergence of Chikungunya or enterovirus Ev71 viruses in Cambodia.
- Review of epidemiological and microbiological data on the pathogens involved in community-acquired pneumonia (CAP) and their antimicrobial resistance profiles.

1-EPI support

- Essential role in confirmatory testing and national reference center activities, its epidemiology team has contributed to investigating human A (H5N1) cases, documenting the emergence in 2012 of Chikungunya or EV71 enterovirus.
- The Epidemiology & Public Health unit also mentors students in the national Applied Epidemiology Training (AET) program.

2-National Surveillance Program for Dengue and Other Arboviruses

- Various techniques are used to detect dengue virus (DENV) infections and other arboviruses infections (Japanese encephalitis virus, Langat, Sindbis and Chikungunya virus).
- For the first time since the establishment of virological surveillance of arbovirus infections, Chikungunya virus was detected.

3-Seasonal and Avian Influenza Surveillance in Human

- Virology Unit was recognized by the WHO as an H5 Reference Laboratory of the WHO Global Influenza Surveillance and Response System (GISRS).

4-Surveillance and Diagnostics for Rabies Infections

5-Voluntary Counselling and Testing Centre (VCTC)

6-Enteroviruses

- Human enterovirus 71 (EV71) outbreak occurred between April and June 2012, and was characterized by severe encephalitis with pulmonary oedema (SEP). EV71 serotype C4 was identified as the causative organism.
- Since this outbreak, the Virology Unit diagnosis and surveillance of encephalitis among children.
Research

1-Epidemiology

Projects:

Endemic ID (Dengue, influenza, CAP…), Epidemiology Projects:

- CHARLI Project on Antibioresistance situation in Cambodia
- Respiratory diseases (influenza, CAP)
- Dengue

2 HIV / hepatitis

- Co-infections associated with HIV / AIDS, especially those involved in mother-to-child transmission
- Viral hepatitis
- Tools for the diagnosis and characterization of the virus and resistance to anti-viral
- The host response to infection
Research projects:

**Hepatitis B, HBV**

- Prevention of mother-to-child transmission (PMTCT) of hepatitis B virus in context of late access to care in Cambodia.
  - To evaluate analytical performance (sensitivity, specificity) of rapid tests for the detection of HBsAg and HBe Ag.
- Validation of an automated, low-cost real-time PCR test for diagnosing and monitoring of hepatitis B infection in African and Asian resource-limited settings.
  - **FRANCE:**
    - Edouard TUAUILLON, INSERM U 1058, Montpellier
    - Pr Jean-Christophe PLANTIER, Virology laboratory, CHU of Rouen, Rouen
  - **CAMBODIA:**
    - Dr Alexandra KERLEGUER, Clinical laboratory, Pasteur Institute, Phnom Penh, Cambodia.
  - **OTHER ASIAN COUNTRIES:**
    - Dr Nicole NGO-GIANG-HUONG, IRD UMI 174, Chiang Mai, Thailand
    - Dr Duy Hoang Chuong LE, Institute Pasteur in Vietnam, Ho Chi Minh Ville, Vietnam
  - **AFRICAN COUNTRIES:**
    - Dr Dramane KANIA, Centre Muraz, Bobo-Dioulasso, Burkina Faso.
    - Dr Richard NJOUOM, Institute Pasteur in Cameroon, Yaoundé, Cameroon.
    - Dr Thomas d’Aquin TONI, CeDRes, Abidjan, Ivory Coast.
    - Dr Almoustapha Issiaka MAIGA, SEREFO, Bamako, Mali.
    - Pr Ndèye Coumba TOURE-KANE, Virology laboratory, CHU Le Dantec, Dakar, Senegal.
    - Pr Anoumou DAGNRA, BIOLIM, Lome, Togo.

**Hepatitis C**

- The many faces of Hepatitis C virus: Impact of defective genomes on pathogenesis of liver disease by assessment of exosomes secretion.
  - **Collaborations:**
    - Dr Urania GEORGOPOULOU, Hellenic Pasteur Institute (HPI), Athena, Greece.
    - Dr Soumaya BENJELLOUN, Pasteur Institute in Morocco, Casablanca, Morocco.
    - Dr Pascal PINEAU, Pasteur Institute in Paris, Paris, France.
  - **Main goals:**
    - To search for HCV natural mutants, containing large in-frame deletions affecting the envelope region, in plasma/serum and tissue biopsies of HCV-infected individuals.
    - To characterize exosomes isolated from serum/plasma of HCV-infected individuals at different disease stages in the presence or absence of IFDMs.

**Hepatitis E**

- Hepatitis E virus (HEV) infection among specific groups from Cambodia: individuals with unexplained ALT elevation, immunocompromised HIV-1-infected adult patients, blood donors and HIV-1-infected men having sex with men.
  - **Collaboration:**
Acute hepatitis E virus infection in developing countries: Molecular viral characterization and seroprevalence rates in Cambodia, Vietnam and Brazil.

- **Main goals:**
  - To determine the seroprevalence of HEV antibodies (IgG and IgM) among specific groups of Cambodian.
  - To assess HEV RNA viremia among patients presenting positive HEV serology.

Role of innate immunity in acute hepatitis E among Cambodian and Senegalese patients.

- **Main goals:**
  - To study innate immune response in HEV-infected asymptomatic and symptomatic patients.

**HIV projects**

- **National evaluation of PI-based 2nd line efficacy in Cambodia.**

  - **Collaboration:**
    - Vonthanak Saphonn (NCHADS, Phnom Penh, Cambodia),
    - Eric Nerrienet (Regulation of Retroviral Infection Unit, Institute Pasteur Paris),
    - Bruno Spire (Observatoire régional de la santé – UMR912 SE4S, Marseille, France)

The specific objective are

i) identify risk factors associated to treatment failure on PI-based 2nd line,

ii) to identify individual risk factors and structural factors associated with non-adherence in patients treated with PI-2nd line based regimens,

iii) to describe the ARV resistance profiles of patients experiencing virological failure on PI-based 2nd line,

iv) To design alternative salvage ARV regimens.
3-Malaria

Scientific projects developed in the Malaria Molecular Epidemiology Unit are built around the concept of elimination of malaria in South East Asia.

- Supporting and evaluating the impact of strategies against malaria implemented by National Malaria Control Programs
- Conduct researches focused on P. falciparum artemisinin resistant parasites.
- Conduct researches on vivax malaria & other emerging Plasmodium sp.

Malaria Projects:

1. Malaria Cohort Study to Assess Disease Burden in Northeast Cambodia

2. A Multi-application Barcode for Plasmodium vivax

   Collaborators:
   - R. Price, L. von Seidlein, S. Auburn (Menzies School of Health Research, Darwin, Australia),
   - D. Kwiatkowski (Wellcome Trust Sanger Institute, Cambridge, UK),
   - Q. Cheng (Australian Army Malaria Institute, Enoggera, Australia),
   - JY. Kim (NIH, Korea Center for Disease Control and Prevention, Republic of Korea),
   - D. Menard (IP Cambodia, Phnom Penh, Cambodia),
   - O. Miotto (Mahidol-Oxford Research Unit, Bangkok, Thailand),
   - F. Nosten (Shoklo Malaria Research Unit, Tak, Thailand),
   - B. Petros, S. Alemu (Addis Ababa University, Addis Ababa, Ethiopia),
   - G. Qi (Global Health Division Jiangsu Institute of Parasitic Diseases, Jiangsu, P.R. of China),
   - J. Reeder (Burnet Institute, Melbourne, Australia),
   - H. Trimarsanto, R. Noviyanti (Eijkman Institute for Molecular Biology, Jakarta, Indonesia)

3. Genomic Analyses of Plasmodium vivax Responses to Antimalarial Drugs in Cambodia

   Collaborators:
   - D. Serre, E. Chan (Genomic Medicine Institute, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, USA & D. Ménard, C. Benedet (IP Cambodia).

4. Madagascar P. vivax Invasion of Duffy-negative Red Cells

   Collaborators:
   - P. Zimmerman, B. Grimberg (Center for Global Health and Diseases, Case Western Reserve University, Cleveland, Ohio, USA), D. Serre (Genomic Medicine Institute, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, USA), A. Ratsimbhasoa (NMCP, Antananarivo, Madagascar) & D. Ménard (IP Cambodia).

5. Public Interventions and Health Inequalities in Recomposed Natural and Social Ecosystems of the Mekong Sub-Region

6. Etude de la dormance induite par les artémisinines

   Collaborations:

7. Multi-site assessment of the reduced susceptibility to artemisinin of Plasmodium falciparum ring stage parasites using a new in vitro assay

   Collaborators:
8. Long-term culture adaptation of Plasmodium falciparum isolates with different genetic backgrounds: Useful tools for studying artemisinin derivatives resistance and screening new anti-malaria compounds

   Collaborations.

9. Efficacy of Dihydroartemisinin-piperaquine and Atovaquone-Proguanil Therapy for Uncomplicated Plasmodium falciparum and Dihydroartemisinin-piperaquine for Plasmodium vivax malaria in Cambodia


4- Virology

Research projects:

- Respiratory Viruses
- **Seasonal influenza & other respiratory viruses**: virus evolution, drug resistance, co-infections, molecular characterization
- **Avian influenza**: molecular characterization of HPAI A (H5N1) virus, virus evolution, drug resistance, Animal-Human-Environment interface survey for HPAI in Live Birds Markets

**Arboviral Diseases**

- **Dengue**: markers of disease severity
  - dengue diagnostic field and provide new prognostic markers for predicting a progression evolution towards severe dengue hemorrhagic fever and dengue shock syndrome
  - evaluate the usefulness of saliva and urine for dengue diagnosis
- **Dengue**: role of asymptomatic infections in dengue epidemiology
  - Compare immune response, viral genetic characteristics human genetic background, epidemiological characteristics, transmissibility by vectors that distinguish the asymptomatic carriers from the patients who develop mild to severe disease.
- **Chikungunya**
  - To characterize the Chikungunya virus strains detected. The ability to follow host-specific evolutionary trajectories of viruses is essential to predict, prepare for, and ultimately prevent epidemic emergence events.

**Zoonosis**

- **Zoonotic viruses transmitted by bats, rodents and primates/Pathogen discovery**
  - Prevent, detect, and rapidly respond to the spillover of novel infectious pathogens from wildlife to humans.

**Neurotropic Infections**

- **South East Asia Encephalitis Project (SEAe)**
  - To reduce the morbidity and mortality associated with infectious encephalitis in Southeast Asia by improving diagnosis and medical care for patients.
  - To describe the etiologies of acute encephalitis in Cambodia, Laos, Vietnam and Myanmar, with the prospect to extend the study to Thailand, Indonesia, Malaysia and Philippines.
  - To improve laboratory diagnosis of encephalitis caused by known pathogens through developing new diagnostic capacities at hospitals in Cambodia, Laos, Vietnam and Myanmar.
  - To implement a quality assurance program and bio banking facility, to detect non-traditional or unusual pathogens in samples that test negative to current diagnostic procedures, to improve diagnostic tools and to discover novel pathogens.

- **Seroprevalence survey for Hand, Foot and Mouth disease in Cambodia**
  - To undertake a seroprevalence study in 2015 to measure and describe the extent of a Hand Foot and Mouth Disease (HFMD) outbreak in Cambodia (Apr-Sep 2012) ascribed to Enterovirus 71 (EV71), persistence in 2015 and to test risk associations of susceptibility.
  - conduct field and laboratory investigations to elucidate the risk factors associated with severe cases of EV71.
describe clinical presentation and associated risk factors for severe HFMD cases compared with non-cases or mild cases

Elaborate the pattern of EV71 circulation during outbreaks and assess point prevalence in communities to compute future vaccine needs.

5. **Immunology research**

Research interests are:

1. Mechanisms of host-pathogen interaction (on a cellular and molecular level)
2. The contribution of the immune response to disease severity
3. Immune correlations of disease severity (biomarker discovery)

**1-Immunology platform**

- Research programs on the innate response to microbial infections.
- It conducts its own research, in particular on the inflammatory responses which occur in some patients co-infected with HIV and tuberculosis.

**2- Immunology Group (G4)**

- The aim is to investigate the role of protective versus detrimental adaptive immune responses in dengue viral infection.

**Research projects:**

- HIV infection and HIV/Tuberculosis Co-infection, Immunology Projects
  - Improving diagnosis of tuberculosis in HIV infected children in Asia: Cambodia, Vietnam
    - Dr Olivier Marcy (France), Dr Ung Vibol (Cambodia), Dr NGUYEN Huy Dung (Vietnam), Dr Arnaud Tarantola (Epi. Unit IPC), Dr Laurence Borand (Epi. Unit IPC), Dr Pean Polidy (Platform of Immuno IPC), Dr Guislaine Carcelin (France)

- **Characterization of Innate Immunity and Biomarkers in HIV/TB Co-infected Patients.**
  - Labortatoire of AIDS & Molecular Immunologie, Fiocruz Foundation, Brazil + Institut Pasteur, Paris, France,
  - Aims to determine innate immune response and associated biomarkers in the onset of inflammatory reaction linked to immune reconstitution inflammatory syndrome in HIV/tuberculosis co-infected patients receiving combined antiretroviral therapy (cART) and the evolution of both infections in the context of diagnosis and ARV treatment of HIV/ tuberculosis co-infection.

- **T cell activation and Immune reconstitution in Patients with TB-IRIS**
• Institute Pasteur du Cambodia, Program in Cellular and Molecular Medicine, Children’s Hospital Boston, Institute Pasteur Paris, Bicêtre Hospital Assistance Publique of Paris,

• Natural Killer cell degranulation predicts early development of TB-IRIS

• Institute Pasteur, France; Institute Pasteur in Cambodia, Cambodian Health Committee, Phnom Penh, Cambodia; Agency National de Recherché sur le Side, Ho Chi Minh City, Vietnam; Harvard Medical School AIDS Initiative in Vietnam, Innate immune correlation of the Dengue Severity

• to quantify the blood circulating dendritic cells subset (BDC) in dengue infected children in all the disease forms and at three time points after onset of fever
• Adaptive immune response to dengue virus infection

Main Research Projects

PRR-Asia

The creation of a regional platform of research in Cambodia offers to research teams from the North and the South laboratories to develop “in situ” researches on infectious diseases in relation with institutions in the region. This platform will:

• Strengthen the capacity of regional research in South-East Asia;
• Respond to the needs to direct research and scientific and technical monitoring of priority communicable infectious diseases in Asia, integrating new issues of human and animal health by the concept of “One World, One Health”

PRR-Asia aims to provide a platform for laboratories and integrated epidemiology at the Institute Pasteur in Cambodia to strengthen high-level research in the field of HIV / AIDS and communicable infectious diseases, particularly zoonotic diseases.

International Call for Proposal (2015) within the Regional Research Platform – Asia implemented in the campus of Institute Pasteur in Cambodia

Research:

• DRUG SUSCEPTIBILITY TESTING OF MALARIA PARASITES
• ROLE OF VECTORIAL TRANSMISSION ON THE EVOLUTION OF PLASMODIUM FALCIPARUM ARTEMISININ RESISTANCE

Training-information

• 4-6 month Internship at Institute Pasteur in Cambodia, 2015-2016 - 29 Jul 2015
  • The internship is for a 4-6 month period.
  • Research Subjects for Master 2 Students at Institute Pasteur in Cambodia 2015-2016

Subject/ Title

• Description and risk factors associated with bites from confirmed rabies or non-rabies dogs
• Characterization of low pathogenic avian influenza viruses in Cambodia
• Diagnostic, évolution moléculaire et compétence vectorielle des Aedes pour le virus Zika au Cambodge
- Development of molecular barcoding for genotyping of Plasmodium falciparum antimalarial drug resistance in Cambodia
- Determination of Plasmodium vivax Duffy-Binding Protein gene copy number in Cambodian and Malagasy isolates
- Phenotyping of B-cell subsets in patients with dengue virus infection
- Iron contents in dry beans (black bean, green bean, red bean, and soy bean) and peanut vended in Phnom Penh markets
- HEV infection in Cambodia: HEV IgG Seroprevalence, and associated epidemiological and pork consumption related risk factors.
- Biodiversity and population dynamics of mosquito vectors of Japanese encephalitis
- Study of immunity against 1960s Chikungunya strains among Cambodian people with immunity acquired in 2012

**Workshop on Surveillance and Control of Rabies from October 27th to November 7th 2015 at Institute Pasteur in Cambodia – 25 May 2015**

- Institute Pasteur with partners will organize a Workshop on Surveillance and Control of Rabies from October 27th to November 7th 2015 at Institute Pasteur in Cambodia.