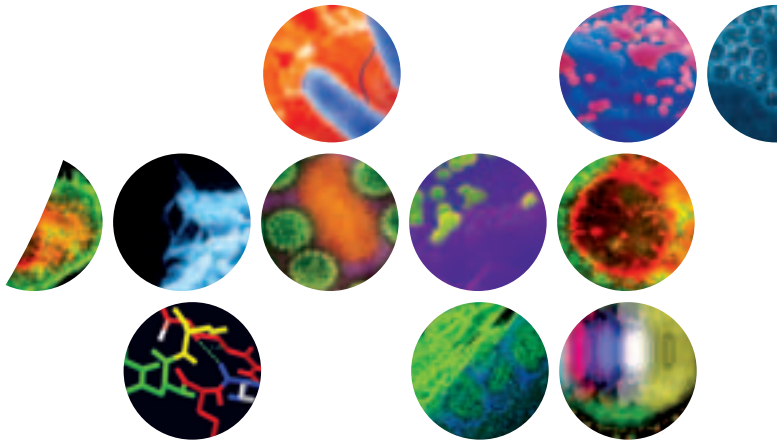
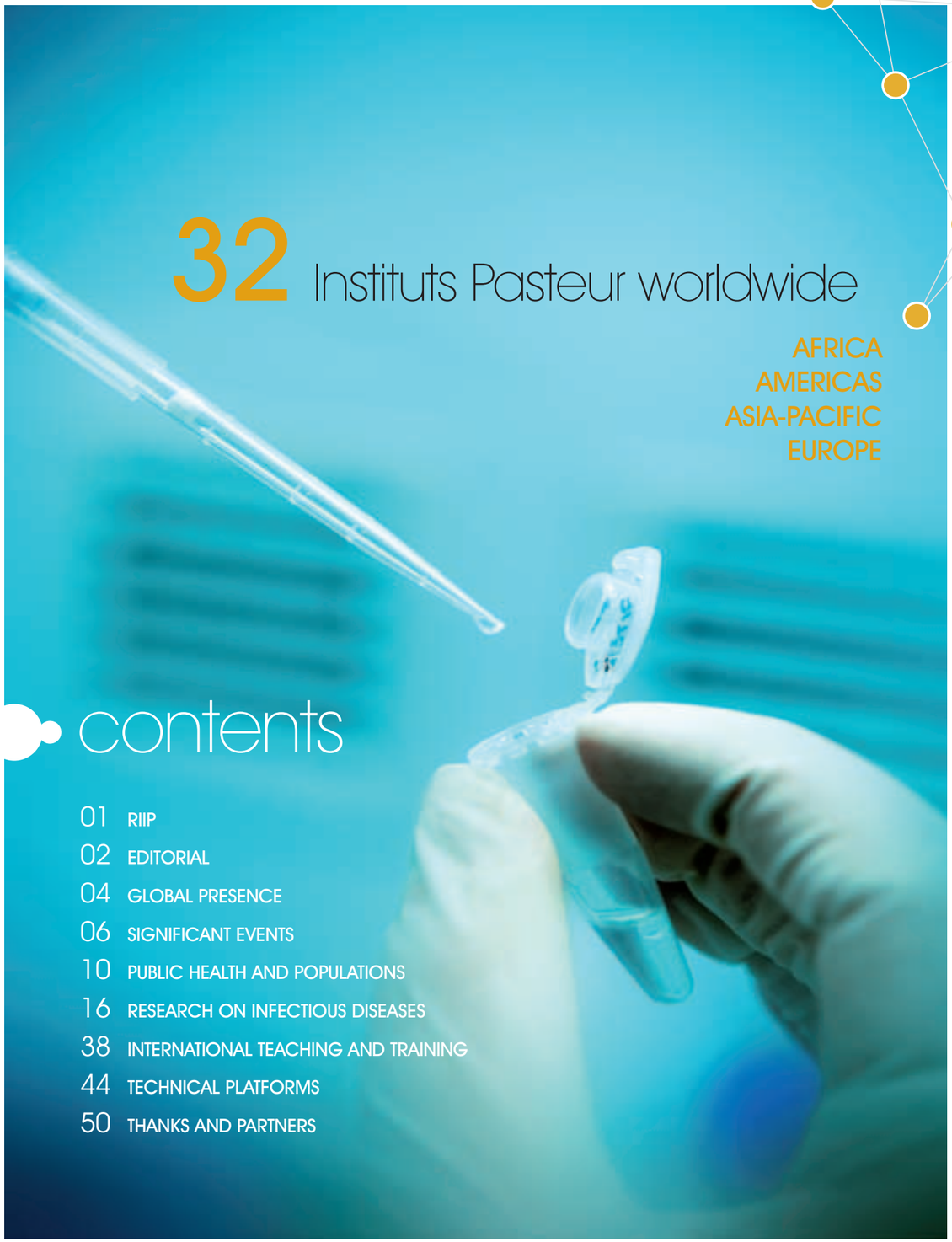
international network
Institut Pasteur



# Institut Pasteur International Network

REPORT 2010



# 32 Instituts Pasteur worldwide

AFRICA
AMERICAS
ASIA-PACIFIC
EUROPE

## contents



# RIIP

MARC JOUAN

SECRETARY-GENERAL OF THE INSTITUT PASTEUR INTERNATIONAL NETWORK

**"In 2010, 32 Institutes signed the new Institut Pasteur International Network partnership agreement.** This agreement confirms their commitment to international scientific cooperation, first and the fight against infectious diseases. Preoccupied with respect for ethical values and the commitment to the most vulnerable populations, the network rallies in this fight different institutes very much involved in public health research and monitoring and a new generation of institutes boasting innovative research facilities. Grounded in a close partnership with local health authorities, the network relies integrated sustainable institutions, benefiting from statuses adapted to their tasks: certain public institutions under the supervision of Ministries of Health, such as the new Institut Pasteur in Laos, others benefiting from a private status under local law like the Institut Pasteur in Dakar, which became a private foundation under Senegalese law in 2010. Very keen to meet the expectations of these countries and the international community in the prevention of infectious diseases, the network faces new healthcare, demographic and environmental challenges in light of financial constraints and political developments. In order to meet these challenges, the network has devised ambitious international programs in liaison with the different countries' Ministries of health and the WHO: monitoring of bacterial meningitis in Africa, creation of a network to monitor influenza in Africa and Asia, prevention of respiratory and diarrhea-related infections, surveillance of resistance to anti-infectives, hepatitis, and neglected diseases such as Buruli ulcer, etc. The network's WHO Collaborating Centers is currently key actor in the international monitoring networks, in support of the International Health Regulations. As national bodies for intervention, these institutes now constitute with their ability to mobilize expertise beyond borders a single regional and international force of intervention, ready to take action in areas where epidemics strike (Africa, Asia, South America, etc.). Major efforts have been made recently to increase the network's intervention abilities by creating high security BSL3 laboratories and new clinical research facilities, but also by strengthening new areas of expertise, particularly in entomology and epidemiology. The network now constitutes a unique and original international scientific cooperation model that draws upon the development of local skills to guarantee the sustainability of its actions. The ambitious international training program supported by all the institutes confirms this commitment. It is based on new partnerships with universities and Ministries of health. It is one of the priority areas for the network's development. This report describes some of the recent achievements of the International Network. It does not claim to be exhaustive but outlines the milestones and major achievements in the fields of public health and research."

# editorial

## ALICE DAUTRY

PRESIDENT OF INSTITUT PASTEUR

I hope that we will continue to move forward, together, on the road to biomedical knowledge, communication and collaboration, for the benefit of as many people as possible."

**"This year we celebrate the 120th anniversary** of the first Institut Pasteur overseas, located in Saigon. Many other institutes followed in the same international spirit characterizing Institut Pasteur since it was founded in 1887. Louis Pasteur's desire was for progress in healthcare to be shared by all, as rapidly as possible, and to benefit those affected by the disease, in the field. Driven by a sense of ethics and the respect for pasteurian values, each of the institutions belonging to the Institut Pasteur International Network works in the name of disease research and monitoring, particularly in infectious diseases, public health, prevention, the fight against epidemics and pandemics, and the training of technicians, engineers and doctoral students in countries where these institutions are located and are perceived as benefaction centers, heirs to Alexandre Yersin and Charles Nicolle. This said, the institutes' work benefits the entire world's population. Diseases are unhindered by borders, hence it is essential that disease research and monitoring are too. In this respect, the Institut Pasteur International Network is a unique collaboration tool that is particularly useful and effective for monitoring and raising the alert in the event of an emerging disease as was the case with the potential influenza pandemic. I would like to salute the friendship binding the different institutes and their members, which adds extraordinary wealth to the network and its partnerships. We have formed close ties with major international partners, as demonstrated by the presence of senior representatives from the Wellcome Trust, NIH or the Riken at the network's scientific meetings in Hong Kong in November 2010. Aware that disease prevention requires mutual action, we have developed the network's scientific meetings, facilitated regional meetings and decided to create a network association. The main objective of this Pasteur International Network Association, will be to facilitate the development of scientific projects involving several members of the international network and other partners. It is expected to increase the available means, broaden the network institutes' project opportunities, and provide them with even greater international visibility, for everyone's benefit. Finally, I want to thank the staff of institutes from the international network who have worked this year in local conditions may be extremely difficult and painful, as in Niger, Cote d'Ivoire and Tunisia."

## FRANÇOISE BARRÉ-SINOUSSI

HONORARY PRESIDENT OF THE INSTITUT PASTEUR INTERNATIONAL NETWORK

The Institut Pasteur International Network is unique in its global geographic presence but also in the diversity of its activities, varying from fundamental research to diagnosis and routine vaccination."

**"More precisely, I have been pleased to note,** over the years, a growing interest from RIIP members for thematic multicenter programs combining clinical research and more fundamental research. This involvement in clinical research enhances the ties with national health structures, particularly hospitals, which are essential to the creation of efficient networks integrating research and care in a translational spirit of multidisciplinarity. Through these close ties, the RIIP member institutes are able to contribute fully to the training of researchers and health workers. Furthermore, the high quality technological facilities present there can facilitate international partnerships with the public and private sectors. National data collected unearths scientific evidence meeting the expectations of health authorities and helping them to make decisions adapted to national context. Very much rooted in the local reality, these RIIP institutes are a veritable means of improvement in public health in the countries where they are present; their reason for existing."

## JÉRÔME SALOMON

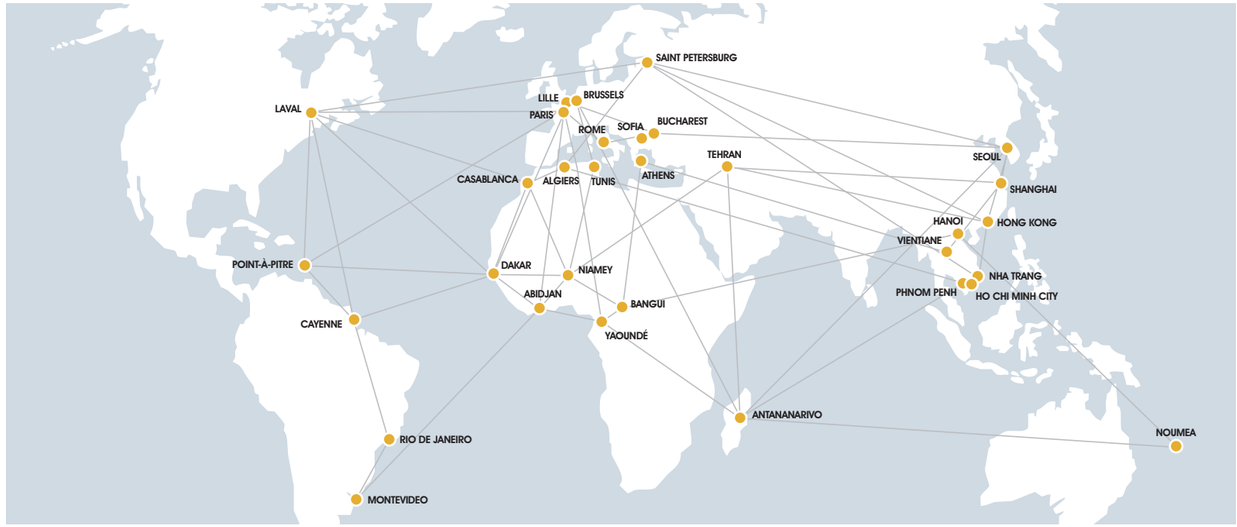
HEAD OF THE INTERNATIONAL DIVISION

For over 120 years the Institut Pasteur has accomplished its triple mission of public health, teaching and research, defending its ethics and value of sharing and drawing on a network of 32 institutions on the 5 continents."

**"In the George Institute's G-Finder study,** the Institut Pasteur has pride of place, particularly in the prevention of Buruli ulcer. It is among the top 12 for malaria, leishmaniasis, trypanosomiases and dengue. Globally, Institut Pasteur is ranked 11th and even 5th among self-financed institutions. The work accomplished is impressive but we must face new challenges. The increasing number of exchanges and the circulation of infectious agents and resistance mechanisms require partnerships to be strengthened on a global level. The endemics or epidemics in the southern hemisphere can affect countries in the northern hemisphere. The examples of the chikungunya virus or dengue are very much relevant today. A multidisciplinary synergic approach is now essential with a number of field partners. Current developments are putting the competitivity of our research system to the test, and its ability to contribute to major international projects. In order to develop innovative diagnostic tools and new therapeutic methods, the boundaries of research must be broken. We have to step up certain lines of research and enhance communication. Scientific priorities must take into account public health problems, niches of expertise and the benefits of a multidisciplinary synergic network. New funding mechanisms are emerging, requiring monitoring and the use of experts in financing and specific administrators. The international network is a major contributor to infectious disease research. It is expanding, and shares its pasteurian values and ethics. It thrives on the wonderful breeding ground of ideas and skills of the Pasteur scientists in infectious disease research. It is unable and unwilling to work alone and is ready to welcome teams from Europe, the US or elsewhere while fostering pasteurian values and ethics. It thrives on the wonderful breeding ground of ideas and skills of Pasteur scientists the world over."

# RIIP global presence

The Institut Pasteur International Network (RIIP) is a partnership of 32 research and public health institutes on five continents. The Network was born from the will of Louis Pasteur to contribute, through high quality research activity, to the fight against infectious diseases directly in countries where they emerge.




**1887**
Institut Pasteur
PARIS – **FRANCE**

**1891**
Institut Pasteur in
Ho Chi Minh City
**VIETNAM**

**1893**
Institut Pasteur in Tunis
**TUNISIA**

**1894**
Institut Pasteur in Algeria
**ALGERIA**

**1894**
Institut Pasteur in Lille
**FRANCE**

**1895**
Institut Pasteur
in Nha Trang
**VIETNAM**

**1898**
Institut Pasteur
in Madagascar
**MADAGASCAR**

**1900**
Fondation Oswaldo Cruz
FIOCRUZ – **BRAZIL**

**1919**
Hellenic Institut Pasteur
ATHENS – **GREECE**

**1920**
Institut Pasteur in Iran
**IRAN**

**1921**
Scientific Institute
of Public Health
BRUSSELS – **BELGIUM**

**1921**
Cantacuzino Institute
**ROMANIA**

**1923**
Institut Pasteur
in Saint Petersburg
**RUSSIA**

**1923**
Institut Pasteur in Dakar
**SENEGAL**

**1925**
National Institute of
Hygiene and Epidemiology
HANOI – **VIETNAM**

**1929**
Institut Pasteur in Morocco
CASABLANCA, TANGER – **MOROCCO**

**1938**
Institut Armand Frappier
LAVAL – **CANADA**

**1940**
Institut Pasteur
in French Guiana
**GUIANA**

**1947**
Stephan Angeloff Institute
**BULGARIA**

**1948**
Institut Pasteur
in Guadeloupe
**GUADELOUPE**

**1953**
Institut Pasteur
in Cambodia
**CAMBODIA**

**1955**
Institut Pasteur
in New Caledonia
**NEW CALEDONIA**

**1959**
Pasteur Centre
in Cameroon
**CAMEROON**

**1961**
Institut Pasteur in Bangui
**CENTRAL
AFRICAN REPUBLIC**

**1972**
Institut Pasteur
in Cote d'Ivoire
**COTE D'IVOIRE**

**1976**
Institut Pasteur – Cenci
Bolognetti Foundation
ROME – **ITALY**

**1978**
CERMES
NIAMEY – **NIGER**

**1999**
Hong Kong University-Pasteur
Research Centre
**HONG KONG**

**2003**
Institut Pasteur in Korea
**KOREA**

**2004**
Institut Pasteur
of Shanghai – Chinese
Academy of Sciences
**CHINA**

**2004**
Institut Pasteur
in Montevideo
**URUGUAY**

**2011**
Institut Pasteur
in Laos
**LAOS**

# 2009 2010 significant events

Numerous events marked out these two years 2009-2010: international agreements, major building works, regional meetings....

## MAJOR BUILDING WORKS

**A BSL-3 laboratory was inaugurated at the Institut Pasteur in Madagascar** in early February 2009.

**Inauguration of the new building of the Institut Pasteur Korea.** The new building of the Institut Pasteur Korea in Pangyo, south of Seoul, was officially opened on May 8, 2009.

**Construction work on the Institut Pasteur in Laos** will be finalized in September 2011.

**Construction work** is under way on phase II of **the Institut Pasteur of Shanghai.**

## STATUS

**The status of the Institut Pasteur in Dakar** has changed; it has become a private foundation under Senegalese law.

## INTERNATIONAL AGREEMENTS

MAY 2009

**Signing of an agreement between DNDi** (the Drugs for Neglected Diseases initiative) and **the Institut Pasteur Korea** during the official inauguration of the Institut Pasteur Korea's new building. The agreement concerns therapeutic development in the area of neglected diseases.

The Institut Pasteur and **the Centers for Disease Control and Prevention (CDC)** sign a declaration of intention in the public health domain.

OCTOBER 2009

**Fiocruz–Pasteur Agreement**
Signing of a new bilateral cooperation agreement between the Oswaldo Cruz Foundation (Fiocruz) and the Institut Pasteur for

cooperation in the fields of biomedical and biotechnological research. This cooperation, which will also involve the RIIP institutes, will take the form of exchanges of experience and personnel, joint research programs, the organization of bilateral seminars and the setting up of joint teaching and training programs.

APRIL 2010

**Signing of a partnership agreement between the Institut de Recherche pour le Développement (Development Research Institute – IRD) and the Institut Pasteur** to develop joint research projects in France's overseas regions and collectivities and in countries in Africa, the Mediterranean, Southeast Asia, Latin America and the Indian Ocean. The IRD and the Institut Pasteur hope to strengthen cooperation between their local teams in these countries and to pool their infrastructures and funding instruments. Sara Eyangoh's laboratory at the Pasteur Centre in Cameroon named as a "Young Team Associated with the IRD" for its research on Buruli ulcer, becomes the first joint Institut Pasteur–IRD research team.

APRIL 2010

Adoption of a **new RIIP cooperation agreement** that confirms the institutes' membership to the International Network.

JUNE 2010

Renewal of **the Institut Pasteur–Total Foundation corporate funding agreement,** demonstrating the determination of both parties to strengthen the partnership begun in 2005. The new funding will be used to create a Françoise Barré-Sinoussi Chair for HIV/AIDS training and research, for the development of research programs to combat infectious diseases and for public health initiatives, notably against emerging and re-emerging diseases.

**The Institut Pasteur of Shanghai** signed two new partnership agreements to fight against infectious diseases

on June 23, 2010, with the Institute for Glycomics at Griffith University, Australia, to strengthen cooperation in the research and **development of new therapies** and to consolidate the institutes' expertise in research into anti-infective and antiviral agents.

on August 13, 2010, with the **Children's Hospital of Fudan University,** for clinical research into **hand, foot and mouth disease,** the second most deadly disease in China in 2010.

DECEMBER 2010
Partnership between the **Principality of Monaco** and the Institut Pasteur.

# 2009 2010 significant events

## MEETINGS / EVENTS

2009

Celebration of the **50th anniversary of the Pasteur Centre in Cameroon.**

**Regional Meetings – North Africa and Iran** in Tunis in January and the **Americas** in Guadeloupe in September.

OCTOBER 20-22, 2009

**Franco-Brazilian scientific conference,** Rio de Janeiro, in connection with the Year of France in Brazil, a Franco-Brazilian scientific conference on 'The challenges facing biomedical science at the beginning of the 21st century', organized by Fiocruz and **the Institut Pasteur, was held on October 20-22, 2009, in Rio de Janeiro.** On October 19-20, 2009, to coincide with this conference, the Council of the Directors of the RIIP was held.


MAY 18-20, 2010

To mark the Year of France in Russia and the **Year of Russia in France in 2010, the international conference on 'Scientific research and monitoring of infectious diseases',** was organized by **the Institut Pasteur in Saint Petersburg** with the support of the Ministry of Public Health and the Russian Academy of Medical Sciences. This important event was attended by 300 scientists, doctors and leading public health figures, as well as health monitoring organizations from Russia and other countries.

NOVEMBER 22-25, 2010

**Hong Kong – Scientific Meeting and Council of the Directors of the RIIP.**

The RIIP annual meeting was organized by **the HKU–Pasteur Research Centre** at the campus of the University of Hong Kong's Faculty of Medicine. This annual meeting, a major scientific event for the RIIP, was opened with a lecture by Françoise Barré-Sinoussi. It was attended by international scientists including representatives from the NIH, RIKEN and the Wellcome Trust, who reflected on four themes (Vaccine Preventable Diseases, Neglected Diseases, Networking to Improve Health, and The Nature of Altruism). The Council of the Directors of the RIIP was held on November 24-25.

DECEMBER 4, 2010

**French Guiana.** To mark its 70th anniversary, **the Institut Pasteur in French Guiana** opened its doors to the public on Saturday December 4. Research stands – Lectures for the general public – Meetings with researchers – Laboratory tours.

DECEMBER 7-10, 2010

**Madagascar. The Institut Pasteur in Madagascar** hosted the closing meeting of the project aimed at "Support, Training and Capacity Building for Infectious Disease Surveillance Networks", led jointly by the Institut Pasteur, the Institut Pasteur International Network and the United States Department of Health and Human Services (HHS), with representatives from the Centers for Disease Control and Prevention (CDC) in Kenya and the United States Department of Defense.

## VISITS

APRIL 2010

**Yves Jégo,** French State Secretary for Overseas Affairs, held a meeting for the Directors and representatives of research bodies at **the Institut Pasteur in French Guiana.**

ON MAY 11, 2010

**Roselyne Bachelot,** French Minister for Health and Sports, visited **the Institut Pasteur of Shanghai.**

ON JULY 6, 2010

**Valérie Pécresse,** French Minister for Higher Education and Research, visited **the Institut Pasteur of Shanghai** on July 7. She expressed her wish to see the institute contributing to the development of new diagnostic tools, new medicines and new vaccines in the humanist spirit of Louis Pasteur.

## HONORS

IN SEPTEMBER 2010

**Dr Imen Rabhi,** from the Immunopathology, Vaccinology and Molecular Genetics Laboratory at **the Institut Pasteur in Tunis,** was awarded the **L'Oréal–UNESCO Fellowship 'For Women in Science'** for her work on the biological validation of the effect of *Leishmania* parasitic infection on macrophage metabolic pathways.

## COMMUNICATIONS

**New website**
www.pasteur-international.org

## HAL-RIIP

**The scientific publications of the RIIP are listed on the online open bibliographc archive HAL-RIIP: http://hal-riip.archives-ouvertes.fr/, operational since July 2009. The platform HAL-RIIP allows the on-line submission of scientific publications from the RIIP and their consultation by institute, author, year or thematic. All works mentioned in this report can be found by consulting the online open bibliographic archive HAL-RIIP.**

# Public health and populations

One of the primary vocations of the Institut Pasteur International Network (RIIP) is to protect the health of populations in the countries where it works. RIIP member institutes perform a wide range of public health and service activities including vaccination, voluntary counseling and testing for HIV and other infections, and also including support for national health programs. RIIP institutes are linked into an international network that can be mobilized to respond to outbreaks and contain epidemics using the latest techniques and in partnership with worldwide bodies such as the World Health Organization (WHO).

**18**
WHO collaborating centers (WHOCCs)

**16**
vaccination centers

# Surveillance and outbreak intervention

With its global presence and the top-level expertise of its scientists, the RIIP is well-positioned to perform infectious disease surveillance and participate in the global response to major epidemics. The Network hosts several Reference Centers and WHO Collaborating Centers, which carry out constant surveillance for diseases with epidemic potential such as influenza, cholera, dengue, yellow fever and emerging infectious diseases. As such, RIIP member institutes provide technical advice at the national and international level. The RIIP interacts with local and international public health authorities and works closely with health ministries, the WHO's Global Outbreak Alert and Response Network (GOARN) and the Institut Pasteur's Laboratory for Urgent Response to Biological Threats (CIBU).

## SURVEILLANCE

### HUMAN AND AVIAN INFLUENZA IN AFRICA

The sentinel network for human influenza in Africa operates via a multi-center study grouping together the six RIIP member institutes in sub-Saharan Africa: Central African Republic, Cote d'Ivoire, Madagascar, Niger, Senegal and Cameroon. Since the emergence of influenza A(H1N1), its detection is a priority for this network with the opening of sentinel sites.. This network demonstrated the circulation of the influenza virus in Niger and Central African Republic (CAR) for the first time. The first cases of influenza associated with the A(H1N1) virus were detected in Niger by the CERMES in February 2010 and in CAR at the Institut Pasteur in Bangui in September 2010.

The RIIP's initiative is all the more important given that very few African countries monitor influenza viruses, which makes any efforts made to counter this disease on the African continent particularly complicated.

### DENGUE

The Institut Pasteur in Cambodia is working with the National Anti-Dengue Program in Cambodia and carries out laboratory surveillance of the clinical syndromes of severe dengue in patients in public hospitals on five sentinel sites. Various techniques (serological, molecular and viral isolation) are used to search for infection by the dengue virus or by other medically important arboviruses in Southeast Asia (the Japanese encephalitis, Langat, Sindbis and Chikungunya viruses).

In 2009, even though surveillance of endemic dengue in Cambodia demonstrated normal circulation of the four serotypes, a system to monitor the emergence of new viral genotypes was set up.

A prospective and descriptive study on the prevalence of dengue during febrile episodes is being carried out by the Institut Pasteur in Cote d'Ivoire.

### YELLOW FEVER

In connection with the surveillance activities for yellow fever being carried out in Central African Republic, the Institut Pasteur in Bangui has diagnosed several fatal cases of this arbovirus infection, confirmed by the WHO Regional Center for Arbovirus Research at the Institut Pasteur in Dakar. A total of 29 cases, including 9 deaths, were recorded in 2009. Entomological research conducted jointly by the Institut Pasteur in Bangui, the Ministry of Health and WHO into these positive cases has shown a strong presence of mosquito vectors, including *Aedes africanus* and *Aedes aegypti*. Vaccination campaigns have been organized in response.

### ENTEROVIRUS AND POLIOVIRUS

The Instituts Pasteur in Tunis, Saint Petersburg and Bangui are strongly involved in monitoring some diseases that are targets for vaccination. Enterovirus surveillance activities carried out in the framework of the global program for the eradication of poliomyelitis have enabled researchers to establish a profile of the circulation of these viruses in North Africa and in Europe. Investigations are often conducted to provide more detailed characterization of the viral strains in circulation and to assess the impact of poliomyelitis vaccination on the population.

### LEISHMANIASIS

In Tunisia, data relating to morbidity due to leishmaniasis at a national level over the past twenty years have been gathered from local surveys at health services in the endemic area. Environmental information and clinical parameters are being analyzed at the Institut Pasteur in Tunis, which is also developing a spatio-temporal model to predict the emergence of epidemics.

Vaccination Center, Institut Pasteur in Bangui.

## RESPONSE TO EPIDEMICS

### YELLOW FEVER AND DENGUE OUTBREAKS IN COTE D'IVOIRE

In 2010, Cote d'Ivoire suffered a joint epidemic of yellow fever and dengue. The Ministry of Health and Public Hygiene set up a technical committee, including the Institut Pasteur in Cote d'Ivoire, to assess the epidemics. The various cases of yellow fever and dengue were confirmed by the Institut Pasteur in Cote d'Ivoire and the Institut Pasteur in Dakar. The Ministry of Health and Public Hygiene in Cote d'Ivoire implemented a number of initiatives to curb this epidemic. A vaccine strategy was also applied in Grand-Bassam and Bouaké and around the city of Abidjan; this strategy consisted of a targeted vaccination campaign around the confirmed cases. A mosquito eradication program (elimination of larvae breeding grounds) was also carried out with the support of the local authorities.

### THE INSTITUT PASTEUR IN DAKAR DIAGNOSES THE FIRST DENGUE EPIDEMIC IN CAPE VERDE

Scientists from the Institut Pasteur in Dakar, in cooperation with WHO and the Cape Verdean Ministry of Health, have confirmed that an epidemic of dengue-3, a highly virulent strain that is rare in Africa, has emerged for the first time in West Africa, in Senegal and in Cape Verde in particular. The initial investigation was followed up with support from laboratories, diagnosis efforts and entomological and epidemiological studies. The response also involves vector control and recording and analyzing trends. Maintaining vector control efforts in the long term will help contain the emergence of other arbovirus infections such as chikungunya.

The Instituts Pasteur in French Guiana and New Caledonia also intervened during dengue epidemics in their respective regions.

### PLAGUE IN PERU: MISSION CARRIED OUT BY THE INSTITUT PASTEUR IN MADAGASCAR IN AUGUST 2010

In a coastal region of Peru, intense circulation of *Yersinia pestis* led to the death of three people out of a total of 27 recorded cases. The first confirmations of cases were made using antigen detection tests supplied by the Institut Pasteur in Madagascar. The only way that plague can be brought under control is by improving understanding of the region's natural cycle, agricultural practices and poverty.

### CHOLERA IN HAITI

The National Reference Center (CNR) for Vibrios and Cholera at the Institut Pasteur in Paris, in cooperation with the Institut Pasteur in Guadeloupe and the Institut Pasteur in French Guiana, were actively involved in the response to the cholera epidemic in Haiti.

This CNR also intervened during the cholera epidemic in Vietnam, working together with the National Institute of Hygiene and Epidemiology (NIHE) in Hanoi.

### LEPTOSPIROSIS

The RIIP is mobilizing its efforts to fight against leptospirosis, an emerging disease recognized by WHO, in particular in the Asia–Pacific region. The Institut Pasteur in New Caledonia was responsible for the biological diagnosis of leptospirosis in Futuna during the recent outbreaks of cases.

# National and international technical expertise

The RIIP includes a large number of national and international reference centers for infectious diseases and resistance to antimicrobial agents. National Reference Centers act as microbiological observatories for communicable diseases in the countries where they are located. WHO Collaborating Centers perform a similar function for the WHO network. National and regional reference laboratories are recognized by national health ministries as competent to diagnose certain diseases.

## IN THE RIIP

| INSTITUTE | WHO COLLABORATING CENTERS | NATIONAL REFERENCE CENTERS RECOGNIZED BY WHO | REGIONAL REFERENCE LABORATORIES |
|---|---|---|---|
| **Pasteur Centre in Cameroon** | | Influenza. Yellow fever. Poliomyelitis. Measles | Bacteriology (WHO). Avian influenza (WHO) – Food-borne infections (WHO). Poliomyelitis (WHO) |
| **Institut Pasteur in Bangui** | Arboviruses, hemorrhagic fevers. Influenza. Rabies. HIV/AIDS | Measles. Rubella | Poliomyelitis (WHO) |
| **Institut Pasteur in Cote d'Ivoire** | | | Avian influenza (WHO) |
| **Institut Pasteur in Dakar** | Arboviruses, hemorrhagic fevers | Influenza and respiratory viruses. Poliomyelitis. Measles. Rotaviruses | Avian influenza (WHO) |
| **Institut Pasteur in Madagascar** | Plague | Influenza. Avian influenza. Poliomyelitis. Measles | Avian influenza (WHO) |
| **Institut Pasteur in Cambodia** | | Influenza. Avian influenza | Rapid diagnostic test for malaria (WHO) Evaluation of the diagnostic test for dengue (WHO) |
| **NIHE (Vietnam)** | Health in the workplace | Influenza. Poliomyelitis | |
| **Institut Pasteur in Guadeloupe** | | Supranational Reference Laboratory for Tuberculosis | |
| **Institut Pasteur in French Guiana** | | Arboviruses and *Influenzae* viruses*. Malaria chemoresistance* | |
| **Cantacuzino Institute (Romania)**** | Influenza | Influenza. Poliomyelitis. Measles/ rubella | Influenza (WHO) |
| **Hellenic Institut Pasteur** | | Influenza. Poliomyelitis. Measles/ rubella. Avian influenza | Leishmaniasis. *Neisseria gonorrhoeae* |
| **Institut Pasteur in Saint Petersburg** | | Poliomyelitis | Avian influenza. SARS. Poliovirus. Rabies. Papillomavirus. Viral hepatitis. Measles. Rubella |
| **Scientific Institute of Public Health (Belgium)** | | Influenza. Measles. Rubella. Rabies. Viral hepatitis | |
| **Institut Pasteur in Algeria** | | Influenza. Poliomyelitis. Rabies prevention. Measles. Tuberculosis | |
| **Institut Pasteur in Iran** | Rabies | Arboviruses and hemorrhagic fevers. Rabies | |
| **Institut Pasteur in Tunis** | Leishmaniasis | Poliovirus. Salmonellosis. *Shigella*. Vibrios–Cholera | Poliovirus (WHO). Measles (WHO). |

** In the Antilles–French Guiana region.*
*** Accredited as a competent body for surveillance, response to epidemics and scientific expertise by the ECDC (European Centre for Disease Prevention and Control).*

## VACCINATION AND OTHER HEALTHCARE SERVICES

**Vaccines are the most effective weapon to fight infectious diseases in individuals and populations. Given their prerogative to protect public health, many RIIP institutes provide vaccination services or otherwise support in-country vaccination campaigns.**

### INTERNATIONAL VACCINATION CENTERS

The Instituts Pasteur in Algeria, Bangui, Cambodia, Dakar, Guadeloupe, Ho Chi Minh City, Iran, Lille, New Caledonia, Madagascar, Morocco and Saint Petersburg and the Pasteur Centre in Cameroon have a vaccination center that provides several essential vaccines.

The rabies vaccination is available at the Pasteur Centre in Cameroon and at the Instituts Pasteur in Algeria, Bangui, Cambodia, Dakar, French Guiana, Ho Chi Minh City, Iran, Madagascar, Morocco and Tunis. A total of 200,000 rabies vaccinations are performed each year. As we celebrate the 125th anniversary of the first rabies vaccination, this disease continues to cause devastation in many areas across the world.

In Paris, the Institut Pasteur carries out routine infant vaccination and performs the vaccinations required for international travel, including the rabies vaccine.

### PRODUCTION OR SUPERVISION OF THE PRODUCTION OF SERUMS AND VACCINES IN SOME INSTITUTES IN THE NETWORK

Some of the RIIP member institutes are also involved in the production of vaccines. The Institut Pasteur in Dakar runs the only yellow fever vaccine production unit in Africa. The Institut Pasteur in Ho Chi Minh City and the Institut Pasteur in Iran produce the BCG and the rabies vaccine. The Institut Pasteur in Algeria produces vaccines for rabies and typhoid, and is responsible for importing and distributing several vaccines to the Algerian population. The Cantacuzino Institute supervises the production of vaccines for measles, influenza and tuberculosis and the DTP. The Institut Pasteur in Tunis produces vaccines and serums to meet the needs of the country (intradermal BCG vaccine, therapeutic serums).

The RIIP institutes are also responsible for providing several healthcare services for local populations, including:

- counseling and testing for HIV and hepatitis C
- a variety of medical tests carried out by medical biology centers and laboratories (anatomical pathology and cytology, hematology, biochemistry, immunoserology, mycobacteriology, microbiology, parasitology, virology)
- diagnostic tests for dengue, salmonella, bacterial meningitis, etc.
- food and environmental safety tests
- microbiological and physicochemical analyses of water, food and agricultural products, as well as toxicological assessments
- support for national and international health programs focused on several diseases (HIV+/AIDS, tuberculosis, dengue, malaria, etc.) through epidemiological surveys, monitoring of vaccination programs, genotyping, clinical trials, etc.)
- occupational and school health
- vector control
- health education

## SOME ACTIVITIES CARRIED OUT BY THE PASTEUR CENTRE IN CAMEROON, YAOUNDÉ (2009)

- **Activities conducted by medical analysis laboratories:** 320,000 tests 450 people each day (average over 200 working days), 90,000 people and 107,939 samples
- **Anatomical Pathology and Cytology Service:** 2,080 histological analyses (66% biopsies and 34% operative specimens), 5,240 cytopathological analyses
- **The International Vaccination Center:** 29,700 vaccinations performed, including 8,300 yellow fever vaccinations
- **The Anti-Rabies Center:** 1,380 post-bite consultations and 760 rabies vaccinations
- **Intradermal reactions to tuberculin:** 2,130 performed

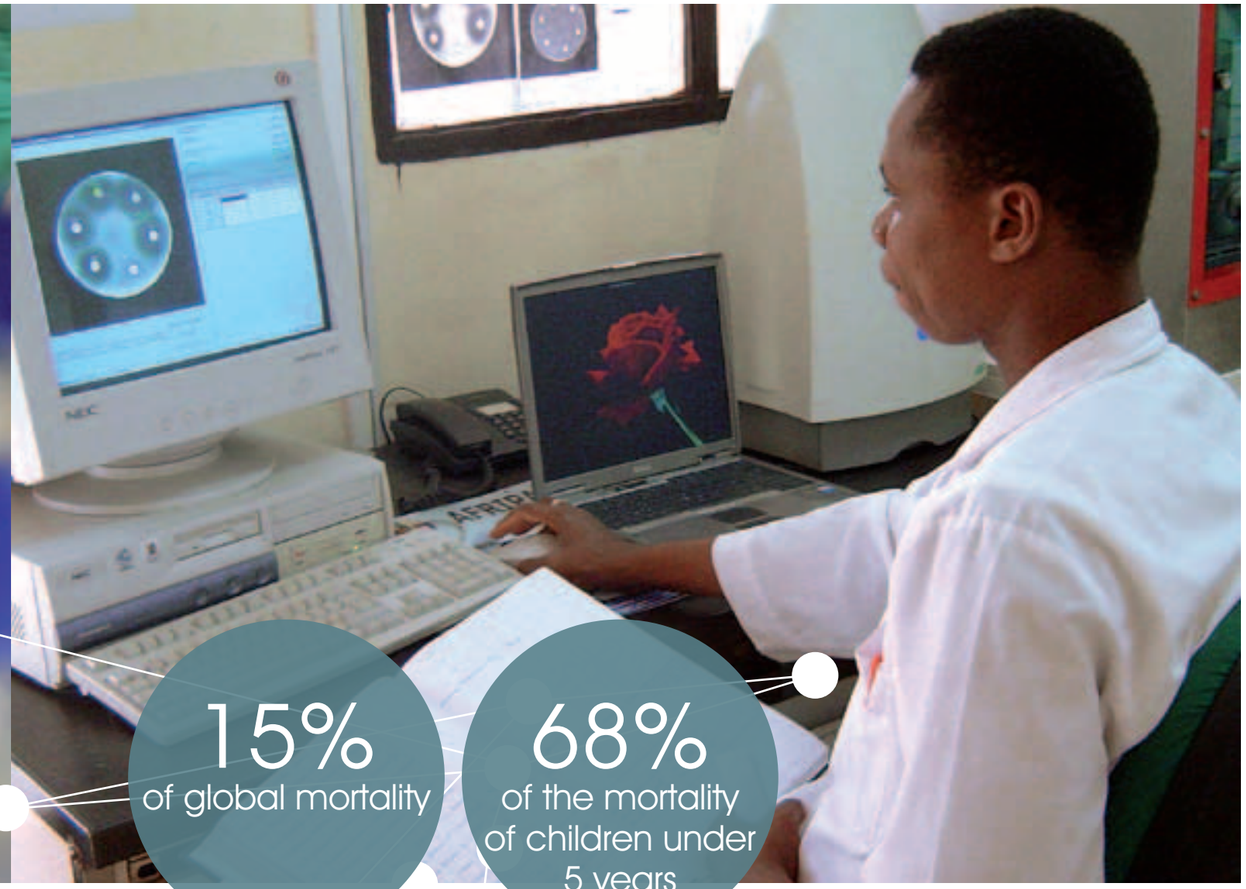
## CNRS AND WHOCCS UNDER THE RESPONSIBILITY OF THE INSTITUT PASTEUR (PARIS)

### FIELD OF INTERVENTION

- Arboviruses and Viral Hemorrhagic Fevers (CNR–WHOCC)
- Arboviruses and *Influenzae* Viruses (Antilles–French Guiana region) (CNR)
- Anaerobic Bacteria and Botulism (CNR)
- *Borrelia* (CNR)
- Anthrax (CNR)
- Malaria Chemoresistance (Antilles–French Guiana region) (CNR)
- Pertussis and other Bordetella (CNR)
- Toxicogenomic Corynebacteria (CNR)
- Enteroviruses (viral vaccines – poliovirus) (WHOCC)
- *Escherichia coli* and *Shigella* (CNR)
- Viral Hemorrhagic Fevers (Lyon) (CNR)
- Influenza – *Influenzae* Viruses (France-North) (CNR)
- Viral Hepatitis B, C and Delta (laboratory associated with CNRs)
- Leptospirosis (CNR–WHOCC–FAO)
- *Listeria* (CNR–WHOCC)
- Meningococcus (CNR–WHOCC)
- Mycology and Antifungals (CNR)
- Human Papillomavirus (CNR)
- Plague and other Yersinia Infections (CNR–WHOCC)
- Rabies (CNR–WHOCC)
- Resistance to antibiotics (CNR)
- Salmonella (CNR–WHOCC)
- Streptococcus (laboratory associated with CNRs)
- Vibrios and Cholera (CNR)

# Research on infectious diseases

Infectious diseases are the leading cause of mortality in countries with limited resources, particularly in Africa. Beyond the few health consequences, their economic and social impact is a considerable brake for development, leader to greater poverty and inequality.

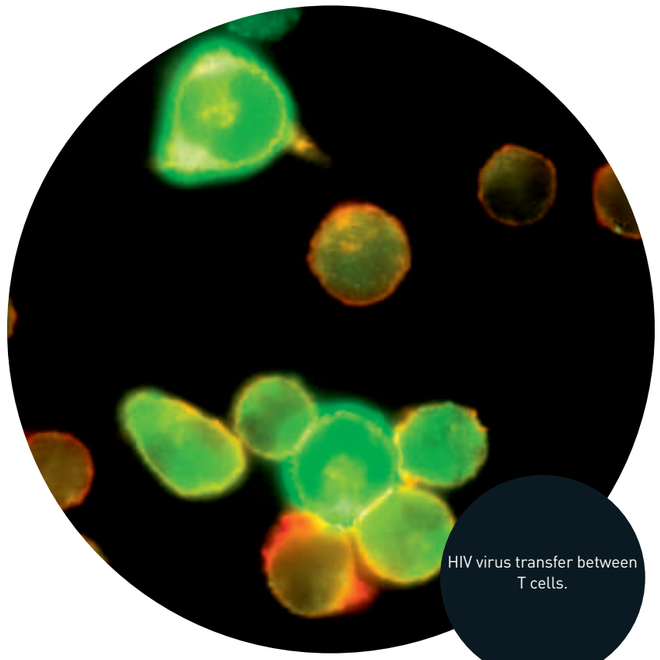


**15%**
of global mortality

**68%**
of the mortality of children under 5 years

# HIV/AIDS

Human immunodeficiency virus (HIV) is a retrovirus which causes chronic immune deficiency leading to the development of acquired immunodeficiency syndrome (AIDS). Thanks to research efforts, there are currently six classes of effective antiretroviral drugs (ARVs), reducing treated patient mortality by over 85%. Today, 5.4 million patients from low-income countries have access to ARVs, compared with under 500,000 in 2002[1]. However, this progress is still not enough. In resource-limited countries, only 36% of patients are treated, and AIDS still kills 1.8 million people in the world each year.



HIV virus transfer between T cells.

## INTRODUCING IMMUNOVIROLOGICAL MONITORING TOOLS FOR PATIENTS UNDERGOING TREATMENT

Since 2001, the international political commitment to universal access to prevention, care and treatment[2] has led to considerable progress in the global response to the HIV/AIDS epidemic. Eight countries with limited resources, including Cambodia, have now achieved the aim of providing treatment to 80% of patients in need. *"In 2003, a few hundred patients in Cambodia were treated by NGOs. By the end of 2010, patients receiving treatment numbered 40,000, most of whom were being treated through the national program. This rapid development must be accompanied by the introduction of financially accessible immunovirological tools that allow treated patients to be monitored. These include CD4+ T-lymphocyte and viral load counts and ARV resistance tests. In Cambodia, the analysis of these virological markers is currently only available at the Institut Pasteur,"* explains Dr Eric Nerrienet, Virologist at the Institut Pasteur in Cambodia. Thanks to these tools, the effectiveness of ARVs used as first-line treatment was confirmed in the medium and long term in follow-up patients treated by NGOs[3]. *"Second-line treatments are also very effective, offering a 93% virological success rate after a 4-year monitoring period. We are currently looking to move to third-line therapy by examining the profile of patients that develop resistance to these treatments,"* continued Dr Nerrienet. However, given that this research is usually carried out on cohorts of patients monitored in optimal conditions, it is essential to confirm these results in patients treated through national structures.

## FROM CLINICAL TO FUNDAMENTAL... AND VICE VERSA

As well as serving public health, these assessment and surveillance tools can also support the development of operational research projects, such as the Camelia study. This clinical trial, supported by the Agence Nationale de Recherche sur le Sida et les Hépatites Virales (French National Agency for Research on AIDS and Viral Hepatitis – ANRS) and the National Institutes of Health (NIH) in association with the Instituts Pasteur in Cambodia and Paris[4], was performed on patients co-infected with HIV and tuberculosis presenting a very low CD4+ lymphocyte count. It was demonstrated that early initiation of ARVs, 15 days after beginning treatment with antituberculosis drugs, reduced the risk of death in patients at an advanced stage of HIV infection by 34%. This paves the way for optimal management of the most widespread and deadly co-infection in developing countries[5].

Other more fundamental research projects (CAPRI-NK and CAPRI-T) are associated with this trial; these focus on the immunopathogenesis of immune reconstitution inflammatory syndromes (IRIS). These IRIS phenomena, sometimes associated with a worsening of tuberculosis (paradoxical reaction), occur in 20 to 30% of co-infected patients treated with antituberculosis drugs and ARVs. *"We have demonstrated that the level of NK cell activation before the initiation of ARVs was a predictive marker for the occurrence of a paradoxical reaction: the higher the level, the higher the risk of occurrence of a paradoxical syndrome,"* explained Dr Pean Polidy, immunologist in charge of projects at the Institut Pasteur in Cambodia.

This approach combining operational and fundamental research for HIV is also implemented at the Pasteur Centre in Cameroon through the ANRS 12140-PEDIACAM project. The aim of this project is to assess, in a Cameroonian context, the feasibility, tolerance and efficacy of early antiretroviral multitherapy in infants infected with HIV. *"This study will enable us to support the national program in implementing the WHO recommendations for early ARV treatment of HIV-infected infants,"* explained Mathurin Tejiokem, a researcher at the Pasteur Centre in Cameroon. *"Since the study began in November 2007, we have demonstrated that the application of the WHO recommendations for preventing mother-to-child transmission of HIV in the operational context of a country with limited resources is feasible and effective[6]. The preliminary results for ARV initiation in infected infants were presented in Casablanca, at the Francophone Conference on HIV/AIDS[7]."* The support provided by the Total Foundation for the PEDIACAM project has led to an improvement in conditions for the medical and psychosocial management of HIV-infected children at the sites where the study is being conducted.

## ASSESSING THE RESPONSE TO VACCINATION IN HIV-INFECTED INFANTS

A further aim of the PEDIACAM project is to assess the immune response in HIV-infected infants to vaccines from the Expanded Program on Immunization (EPI), which follows and extends the study previously conducted as part of an RIIP project in the framework of the Inter-Pasteurian Concerted Actions. This study, conducted from 2004 to 2006 in cooperation with the Instituts Pasteur in Bangui and Paris, showed that children infected by HIV had a lower persistence of antibodies induced in response to EPI vaccines than non-infected children born to seropositive mothers. Furthermore, non-infected children born to seropositive mothers responded less than children born to HIV-seronegative mothers, suggesting that in utero exposure to HIV has an influence on immune response. The ANRS 12207-PRIVAR study, associated with PEDIACAM, focuses specifically on the response to the measles vaccine in HIV-infected children. The goal is to determine whether HIV-infected newborns are capable of developing and maintaining a specific CD4 and CD8 cellular response to measles, and which NK cell populations are activated in these children when vaccinated. This project will help to identify potential indicators of vaccine failure in these children and to suggest an adaptation of the vaccination schedule if necessary.

Institut Pasteur in Cambodia.

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(7) Tejiokem MC *et al., Faisabilité des multithérapies anti-rétrovirales précoces systématiques chez les nourrissons âgés de moins de 7 mois infectés par le VIH dans un pays à ressources limitées:* ANRS 12140 – PEDIACAM – 5th Francophone Conference on HIV/AIDS, Casablanca, March 2010.

# TUBERCULOSIS

Tuberculosis (TB) is an infectious disease caused by the *Mycobacterium tuberculosis* bacterium, also known as "Koch's bacillus", transmitted through the air. There are close to 10 million cases in the world each year, and between 1.6 and 2.3 million patients die from the disease. A large number of these are not diagnosed or are not sufficiently monitored. 25% of deaths in HIV-seropositive patients are due to tuberculosis. The concomitant circulation of strains exhibiting multiple resistance to treatment is particularly worrying. The epidemiological predictions are also a cause for concern: the WHO estimates that by 2020 almost a billion more people will be infected and 35 million patients will die.

Tuberculosis Laboratory, Institut Pasteur in Bangui.

## SURVEILLANCE AND PUBLIC HEALTH

The Instituts Pasteur in Bangui, Cote d'Ivoire, Madagascar, Guadeloupe, New Caledonia, Cambodia, Ho Chi Minh City, Saint Petersburg, Algeria, Morocco and Tunisia, as well as the Pasteur Centre in Cameroon and the Scientific Institute of Public Health in Brussels, are involved in surveillance and diagnosis activities, and most of them are involved in national programs to fight tuberculosis. The institutes in Cote d'Ivoire and Madagascar host regional reference laboratories.

## EPIDEMIOLOGY

The Stephan Angeloff Institute, the Institut Pasteur in Saint Petersburg and the Institut Pasteur in Lille are working on the diversity and global distribution of strains of *M. tuberculosis*[1-3]. The Institut Pasteur in Guadeloupe is recording the results of molecular typing studies in a database accessible on the Internet (genetic map constructed with 75,000 isolates from 160 countries). For many years now, this expertise has led to involvement in epidemiological and molecular phylogenetic studies, on all continents and particularly in the Caribbean and South America[4] (more than 14 publications in 2009-2010).

## GENETIC AND MOLECULAR STUDIES

The Institut Pasteur in Saint Petersburg has demonstrated that the virulence of some strains is acquired because of the high circulation of the bacteria in certain regions such as Russia. By unraveling the evolutionary path of strains with multidrug-resistance (MDR), researchers from the Institut Pasteur in Tunis[5] have been able to identify the pre-epidemic susceptible parent strain. This research could improve understanding of the sequential molecular events that caused the emergence of these resistant strains. The Institut Pasteur in Madagascar has studied the diversity of clinical strains of *M. tuberculosis* and their impact on infection[6]. Research carried out at the Institut Pasteur in Guadeloupe has helped identify the existence in Trinidad of an emerging *M. tuberculosis* clone. These approaches have also enabled a rare Beijing strain that was responsible for a deadly tuberculosis outbreak in Colombia to be genotyped for the first time.

These genetic and molecular approaches are being pursued and developed in several institutes, particularly comparative genetics studies based on MDR strains in Cambodia, Central African Republic and Cote d'Ivoire.

## IMPROVING THE DIAGNOSIS AND TREATMENT

Although a suitable antibiotic treatment should be introduced as quickly as possible, confirmed diagnosis of *M. tuberculosis* infection can take up to two months. Research into methods for the rapid diagnosis of tuberculosis is therefore vitally important if the management of patients is to be improved.

To differentiate *M. tuberculosis* from other members of the mycobacterium family, the Institut Pasteur in Guadeloupe has developed a simple method based on the detection of an enzyme (nitrate reductase) directly from pathological samples. At the Institut Pasteur in Lille, the heparin-binding protein has proved to be a precious tool in helping diagnose latent infection. This method could also be used to diagnose active tuberculosis, particularly extra-pulmonary tuberculosis, in less than 24 hours.
Teams at the Institut Pasteur Korea[7] have developed a new technique for large-scale automated screening to select highly virulent mutants and analyze their biochemical determinants.
As part of their efforts to improve treatments, scientists at the Institut Pasteur in Lille have validated the "ETH-boost" concept. This involves developing molecules which, when associated with ethionamide (an antibiotic), would increase its efficacy.

## OTHER MYCOBACTERIA

Diagnosis of leprosy caused by *Mycobacterium leprae* is carried out in connection with the surveillance and monitoring of this disease at the Instituts Pasteur in Guadeloupe and New Caledonia.


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(7) Brodin P *et al., PLoS Pathogens.* 2010, 6 (9):e1001100.


### Discovery of new genes involved in the parasitism of cells by the tubercle bacillus

A European–Asian group of scientists, particularly involving the CNRS, the Institut Pasteur in Paris, the Institut Pasteur Korea and the University of Toulouse in the framework of the European Union–funded TB-VIR Project, has recently identified ten virulence genes of the tubercle bacillus. The inactivation of these genes reduces the pathogenic effect of the bacillus. This discovery, published in the journal *PLoS Pathogens,* will be particularly useful in proposing new therapeutic strategies and testing new tuberculosis vaccine candidates.

### The International Network hosts two WHO supranational reference laboratories (SRLs) in Algeria and Guadeloupe

The aims of the SRLs are to assess the level of pharmacoresistance in the world, to anticipate trends, to supply data useful for policy decision-making, to evaluate progress made in anti-tuberculosis programs, and finally to strengthen laboratory networks. Since 2009, the Institut Pasteur in Guadeloupe has hosted the 6th SRL in the Americas region (North and South).

### REGPOT 2 Project

A European Union–funded project involving the Instituts Pasteur in Algeria, Paris, Guadeloupe and Tunis and the Stephan Angeloff Institute in Sofia. The aim is to build a sustainable Euro–Mediterranean network to combat tuberculosis.

# MALARIA

Malaria is an infectious disease caused by parasites belonging to the genus *Plasmodium,* transmitted to humans by a mosquito of the genus Anopheles. There are almost 300 million cases of this infectious disease each year, leading to one million deaths, mainly in children under five. It threatens some 3.3 billion people in over 100 countries, but 90% of cases are concentrated in the 19 most populous countries in sub-Saharan Africa.

Gut of *Anopheles gambiae* parasitized by *Plasmodium falciparum.*

Given the major problem of the emergence of strains of *Plasmodium* showing resistance to antimalarial therapy, the RIIP's work is focused on diagnostic capability with the assessment of new diagnostic tools, on resistance to treatment, and on immunovaccinology.

## RESISTANCE TO ANTIMALARIAL THERAPY

The analysis of markers of treatment resistance has been the subject of several publications by the Instituts Pasteur in Cambodia and Madagascar, the CERMES in Niger and the Institut Pasteur in French Guiana. The aim of this research is to quantify and contain the risk of dissemination of treatment-resistant strains.

Several studies reviewing the current situation or looking at new progress concerning the emergence and dissemination mechanisms of resistance to antimalarial drugs were published in 2009-2010. The emergence of resistance to artemisinin in Cambodia and Thailand was analyzed and reported in the *New England Journal of Medicine,* and other publications have assessed the development of resistance in Cambodia and Madagascar. Comparative *in vivo* and *in vitro* studies in Madagascar have improved understanding of the dynamics and distribution of chloroquine-resistant mutants. In Cote d'Ivoire, a study has confirmed the effectiveness of a new combination therapy using artemisinin and naphthoquine as a treatment for malaria.

Understanding the molecular basis of resistance, particularly resistance to artemisinin, as well as its associated genotypes and phenotypes, is a field of research that is being actively explored.

### The parasite *P. vivax* infects resistant human populations

A multidisciplinary study conducted by the Institut Pasteur in Madagascar, in cooperation with the Malagasy Ministry of Health and the Institut Pasteur in Paris, focused locally on the comparison of Duffy blood group-positive populations of Indonesian or Asian origin with Duffy-negative populations of African origin. The researchers showed that some individuals develop malaria despite their Duffy-negative blood group, believed to protect them from infection by *P. vivax*. These results signal the possibility of a spread of *P. vivax* to regions of the world where it is currently absent.

Menard D *et al. 2010. Plasmodium vivax clinical malaria is commonly observed in Duffy-negative Malagasy people. PNAS,* 107, 13.

## ASSESSING NEW MALARIA DIAGNOSTIC TOOLS

In Cambodia, Senegal, Madagascar, Niger and French Guiana, an assessment of rapid diagnostic tests showed that detection capabilities were limited when the tests were used in field conditions. In Cambodia, a DNA microarray (FlexiChip) with high-throughput analysis capability comparable to sequencing methods was assessed. New innovative and effective detection techniques such as pyrosequencing have been developed in Cambodia and Madagascar; these enable the detection of rare parasite variants.

## IMMUNOVACCINOLOGY OF MALARIA

Research in the field of immunovaccinology has been developed in Dakar, based on the longitudinal monitoring survey being carried out in the villages of Dielmo and Ndiop and the recruitment of patients suffering from urban and hospital-based malaria (see inset). Immune responses to a vaccine candidate have been confirmed, enabling the identification of a protective epitope. In Ndiop, an effective prospective approach is being used to assess the impact of different intervention methods aiming to reduce exposure and infection at an early stage based on reduced cohorts.

Search for mosquito larvae, French Guiana.

### A new functional test to assess the degree of protection against *P. falciparum*

Researchers at the Institut Pasteur in Dakar, the IRD and the Institut Pasteur in Paris have developed a new test for the *in vitro* analysis of the efficacy of antibodies induced naturally or after vaccination against merozoite surface antigens, important vaccine targets. This functional assay correlates with prospective immunity.

Joos C *et al.* 2010. *Clinical protection from falciparum malaria correlates with neutrophil respiratory bursts induced by merozoites opsonized with human serum antibodies. PLoS ONE,* 5, e9871.

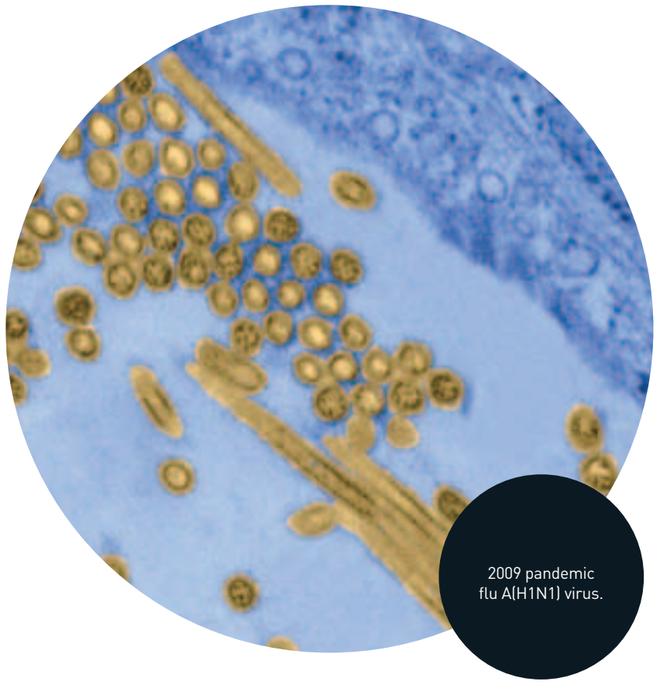
### Severe urban malaria: low transmission and high parasite polymorphism

Severe malaria in Dakar mainly affects adults. It is associated with infection by a pool of *P. falciparum* isolates with a high degree of variability, unlike benign cases of malaria. The treatments used favor the selection of a group of parasites; this raises the problem of inappropriate self-medication leading to longer delays in treating patients and a worsening of the outcome of the disease.

Bob NS *et al.* 2010. *Parasite polymorphism and severe malaria in Dakar (Senegal): a west african urban area. PLoS ONE,* 5, e9817.

# INFLUENZA

Influenza is an acute viral infection caused by three types of influenza virus (A, B and C) that circulate in all regions of the world[1]. These viruses are capable of infecting birds and some mammals, including pigs and humans. Influenza generally occurs in seasonal epidemics, but influenza pandemics can occur several times per century when new viral strains emerge. This was the case with "Spanish" influenza, the most deadly outbreak known to date, which hit in 1918 and 1919, and more recently the influenza epidemic caused by the A(H1N1)pdm virus, which emerged in Mexico during spring 2009.



2009 pandemic flu A(H1N1) virus.

## A LARGE-SCALE PROBLEM

Influenza is recognized as a health problem faced by both developed and developing countries. Each year it causes hospital admissions and a high number of deaths among populations at risk (children, the elderly and the chronically ill). According to the latest estimates published by the World Health Organization (WHO), influenza viruses are responsible for about 3 to 5 million severe cases leading to almost 500,000 deaths each year[1].

The year 2009 was marked by the A(H1N1)pdm influenza pandemic, caused by a virus presenting a genetic recombination that had never previously been described. Several RIIP member institutes designated as WHO National Reference Laboratories for influenza were directly involved in diagnosing this new virus. The various programs set up for the sentinel surveillance of respiratory viruses represented a precious tool for the epidemiological monitoring of this pandemic.

## MAJOR INTERNATIONAL PROJECTS LED BY THE RIIP FOR INFLUENZA VIRUSES

Research on influenza covers various aspects of infection by influenza viruses and is carried out within the framework of innovative multidisciplinary projects that establish links between biologists, clinicians, epidemiologists and fundamental research scientists from the RIIP.

• The SISEA *(Surveillance and Investigation of Epidemic Situations in Southeast Asia)* Project[2] (2006-2011) aims to develop surveillance and response capabilities to tackle the emergence of new pathogenic agents with epidemic potential in Southeast Asia, focusing particularly on respiratory infections and acute encephalitis[3]. It is funded by the Agence Française de Développement (French Development Agency – AFD) and involves the Instituts Pasteur in Cambodia, Shanghai, Ho Chi Minh City and Nha Trang, as well as the National Institute of Hygiene and Epidemiology (NIHE) in Hanoi and the National Center for Laboratory and Epidemiology (NCLE) in Laos.

• The *Support, Training and Capacity Building* Program (2006-2011) aims to strengthen the surveillance networks for influenza viruses in Africa and Southeast Asia, particularly for avian influenza, and to perform epidemiological studies on these diseases. To achieve these objectives, the program is setting up surveillance networks and providing suitable training so that effective support can be offered for investigations conducted during epidemics. It is funded by the US Department of Health and Human Services (HHS)/ASPR and involves the Instituts Pasteur in Cambodia, Ho Chi Minh City, Nha Trang, Laos, Bangui, Cote d'Ivoire, Dakar and Madagascar, the NIHE in Hanoi and the Pasteur Centre in Cameroon.

• The *Reinforcement of a Surveillance Network for Flu in Africa* Program (2006-2012) involves the detection and characterization of influenza viruses and the strengthening of corresponding laboratories. This is achieved by harmonizing and standardizing existing systems to improve the integration and processing of data collected through networks, and also by consolidating the research dimension through improved diagnosis of influenza and other respiratory viruses. It is funded by the French Ministry of Health (EPRUS) and involves the Instituts Pasteur in Bangui, Cote d'Ivoire, Dakar and Madagascar, as well as the Pasteur Centre in Cameroon and the CERMES in Niger. This program complements the project funded by the US Department of Health and Human Services (HHS)/ASPR. The project is also subsidizing the setting up of a cross-disciplinary study (SURGIRA) for typing and sequencing influenza strains circulating in sub-Saharan Africa with the aim of improving understanding of transmission pathways and the emergence of resistance on this continent.

• A multi-center case-control study (2010-2012) will enable the characterization of factors associated with severe forms of influenza in developing countries, where there is a heavy burden of viral, bacterial and parasitic co-infections. Co-funded by the Institute of Microbiology and Infectious Diseases (IMMI) and the Institut Pasteur, it is conducted in Asia and Africa on patients infected by influenza virus. It is the result of interdisciplinary cooperation between the Instituts Pasteur in Cambodia, Dakar, Madagascar and Paris, and the Pasteur Centre in Cameroon.

• The RIVERS *(Resistance of Influenza Viruses in Environmental Reservoirs and Systems)* Project[3] (2006-2010) aims to study the role played by the environment in the survival of the highly pathogenic A(H5N1) avian influenza virus and in the re-emergence of the disease. It is co-funded by the European Commission and involves Instituts Pasteur in Europe and Asia (Cambodia, Shanghai, Lille and Paris), along with the Cantacuzino Institute in Romania, the Stephan Angeloff Institute in Bulgaria, the Centre de Coopération Internationale en Recherche Agronomique pour le Développement (International Cooperation Center of Agricultural Research for Development – CIRAD), the Interdisciplinary Centre for Mathematical and Computational Modelling (Warsaw, Poland) and the Wuhan Institute of Virology (China).

• The RESPARI *(Research-driven rESPonse to Acute Respiratory Infection)* site contains information on all the RIIP's activities in the area of respiratory infections[4].

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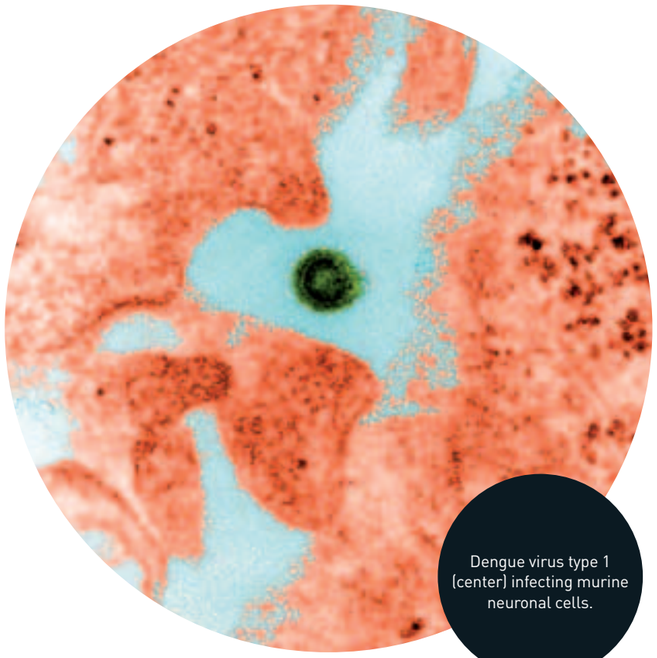
### Progress on influenza diagnosis

The A(H5N1) avian influenza virus is a highly virulent pathogen than can be transmitted to humans by aerosols (≃ 60% mortality rate). This means that it has to be manipulated in a Biosafety Level 3 laboratory (BSL-3 on a scale of 1 to 4), subject to very strict procedures. The Hong Kong University–Pasteur Research Centre has developed a new diagnostic test. It is as sensitive as the current reference test known as "microneutralization" and offers the significant advantage of not using the A(H5N1) virus. It therefore allows avian influenza to be diagnosed in a Biosafety Level 2 laboratory[5].
During the A(H1N1)pdm pandemic in 2009, the RIIP helped in the distribution of diagnostic tools for the rapid identification of this new virus that were developed at the Institut Pasteur in Paris (Molecular Genetics of RNA Viruses Laboratory / Influenza CNR (France-North).

# DENGUE

Dengue is a viral disease transmitted by the bite of mosquitoes, mainly *Aedes aegypti,* infected by one of the four dengue viruses (DENV-1 to DENV-4) of the Flavivirus genus. The tiger mosquito, *Aedes albopictus,* an aggressive species undergoing rapid expansion across the world, and even in non-tropical areas, can also transmit the dengue virus. In most cases, the disease's symptoms are similar to those of influenza. At the global level, 50 million people are infected each year, and 500,000 of them, mostly children, suffer from the hemorrhagic form of the disease. At least 2.5% of these severe cases lead to death[1]. There are currently no commercially available vaccines or specific antiviral treatments for dengue.



Dengue virus type 1 (center) infecting murine neuronal cells.

## THE INSTITUT PASTEUR INTERNATIONAL NETWORK: A UNIQUE INSTRUMENT FOR DENGUE SURVEILLANCE ON SEVERAL CONTINENTS

The global expansion of dengue observed in recent decades is a major cause for concern. While in 1970 only 9 countries had experienced hemorrhagic dengue outbreaks, by 1995 this figure had more than quadrupled[1], mainly affecting Southeast Asia and the South American continent. Dengue is now endemic in more than a hundred countries, and it is believed that two fifths of the world's population is exposed to it. This inexorable propagation of dengue is thought to be caused by an extension of the geographical distribution area of the four virus types and of their vector mosquito, together with the growing urbanization of tropical areas favorable to the proliferation of these insects.

In the light of this increasingly urgent health threat, the Institut Pasteur International Network is playing an active role in health and epidemiological surveillance. In late 2009, the health authorities in Cape Verde reported more than 17,000 cases although the country had never previously suffered an epidemic outbreak of dengue. The team from the Institut Pasteur in Dakar, in its capacity as a regional reference center, analyzed initial samples and confirmed the presence of dengue serotype 3, identified for the first time in West Africa (Cote d'Ivoire) one year earlier. A joint mission with the WHO Regional Office also enabled rapid assistance to be provided in terms of diagnosis, entomology, epidemiology and the implementation of vector control activities[2].

In 2009, a team from the Institut Pasteur in French Guiana published an article on a dengue epidemic that had occurred three years earlier in Maripasoula, an inland town in French Guiana along the Maroni River[3]. According to Philippe Dussart, Head of the CNR for Arboviruses and Influenza Viruses for the Antilles-French Guiana region, *"This study explores uncharted territory because dengue outbreaks are usually observed on the coast and result from people traveling to and from the Antilles. An epidemiological study has now demonstrated the presence of indigenous cases on the Maroni for the very first time. By analyzing the viral strains circulating in Maripasoula, we were subsequently able to clearly demonstrate that this dengue was introduced from neighboring Surinam."*

Treated bed net.

### *"WORKING TOGETHER TO TRY TO UNDERSTAND WHAT DETERMINES THE SEVERITY OF THE DISEASE"*

The Institut Pasteur International Network is a unique instrument for dengue observation and research on all continents and has the potential to make a major contribution to progress in treatment and prevention of the disease. This idea was the basis for the creation of the GLOBEN network (Global Network for Dengue Research), which should coordinate 12 research teams working on dengue from seven of the Network's institutes. Anavaj Sakuntabhai, from the Viral Pathogenesis Unit at the Institut Pasteur in Paris, explains that *"the frequency of severe cases of dengue is higher in Southeast Asia. Is this due to factors relating to the host, the virus, the vector or the environment? By working together, we will be able to compare these parameters between continents to try to understand what determines the severity of the disease."*

The European project DENFRAME[4], involving the Instituts Pasteur in French Guiana, Cambodia, Ho Chi Minh City and Paris, enabled research to be carried out on asymptomatic patients. By taking blood samples from the members of a single household in which there is a confirmed case of dengue[4], researchers have for the first time been able to obtain samples from people infected asymptomatically. They hope to compare immunological and genetic criteria of the host, and also to analyze the mutations of the virus observed in each person with the aim of identifying which interactions are involved in the progression to a severe or non-severe form of the disease. *"No one has done this before,"* continues Anavaj Sakuntabhai. *"Researching asymptomatic patients and also those exposed to the virus but not infected can throw up valuable information on the protection mechanisms that an effective vaccine should induce."*

Alongside these efforts, it is vital to improve diagnostic techniques for the infection. A team from the Hong Kong University–Pasteur Research Centre was the first to develop a stable production system for non-infectious viral particles known as VLPs (virus-like particles) for the four dengue serotypes[5]. On the basis of these VLPs, a research project involving teams from the RIIP institutes in Hong Kong, New Caledonia and Paris is under way with the aim of developing a diagnostic test for dengue specific to each serotype and assessing the potential of VLPs in the development of seroneutralization tests for the dengue viruses. These applications – more rapid, less restrictive and less costly than current techniques – will help to improve the serodiagnosis of patients and also epidemiological studies carried out on the circulation of dengue.

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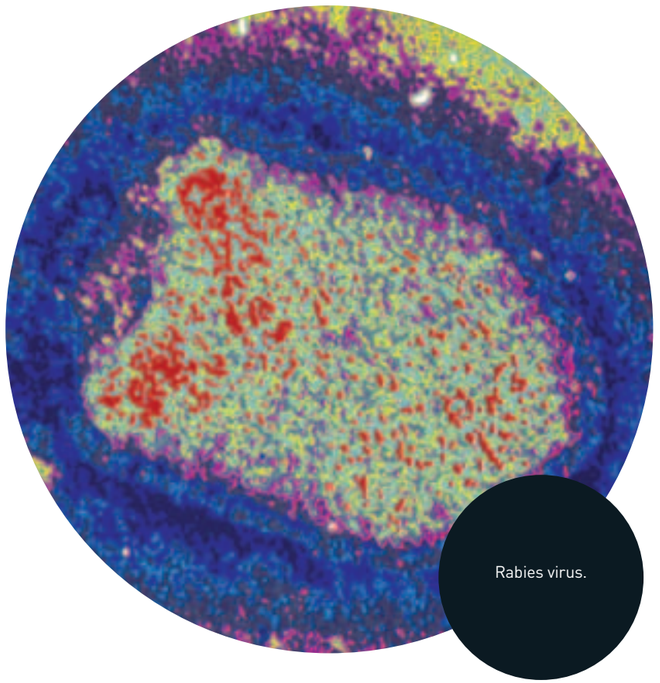
*Aedes aegypti.*

# RABIES

Rabies is a fatal viral infection of the nervous system. Accountable for 99% of fatal cases in humans, dogs are the primary vector of the disease, which is also carried by wildlife (e.g. bats, wolves, foxes, etc.). Although an effective preventive vaccine was discovered by Louis Pasteur more than 125 years ago, every year around the world 55,000 people, who did not receive any post-exposure treatment, die from rabies. 95% of them are of Asian or African descent. Moreover, each year 14 million people receive post-exposure treatment following contact with an animal that may have been carrying the virus[1].



Rabies virus.

## THE INCIDENCE OF RABIES IS LARGELY UNDER-ESTIMATED

Whereas effective control strategies have succeeded in almost eradicating the native animal reservoir of rabies in industrialized countries such as France[2], in low-income countries, this infection is still very widespread and ranks among the "neglected" diseases. Due to the Institut Pasteur's historical involvement and the presence of institutes in countries with a high endemic status, the Institut Pasteur International Network continues to play a major global role in the monitoring and control of rabies. Each year within the Network, over 200,000 post-bite vaccinations are performed on patients who are at risk[3]. Additionally, several teams are involved in development work and in implementing control programs specifically targeted at canine rabies.

The reason that rabies is not considered a public health priority in many countries stems from the fact that its incidence is largely under-estimated, due to an absence of reliable epidemiological data. The teams of Philippe Buchy in Cambodia and Hervé Bourhy in Paris have implemented a mathematical model that uses a collection of epidemiological data in a given region to calculate the incidence at a national level. This model has shown an incidence in Cambodia of 5.8 cases for every 100,000 inhabitants (15 times higher than the official figures), positioning rabies ahead of dengue fever and malaria in terms of mortality[4].

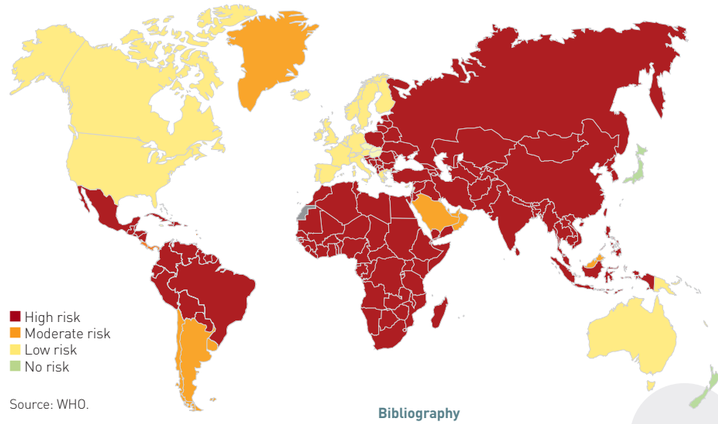
## IMPROVING DIAGNOSTIC AND CONTROL TECHNIQUES

Epidemiological monitoring can also be improved by using reliable, field-specific diagnostic tools. A research project that brings together the Institut Pasteur in Cambodia, Madagascar and Paris has enabled the development and validation at various sites of a highly sensitive diagnostic technique using a biopsy from the skin at the base of the neck or samples of saliva[5]. In addition, a detection technique that is heavily based on DNA microarrays has been developed with the Institut Pasteur in Dakar[6]. This technique not only facilitates diagnosis of rabies, but also the identification of new viruses belonging to the same family of rhabdoviruses.

Intervention strategies to fight canine rabies cannot succeed without an exact understanding of the ways in which the virus is disseminated and maintained in a given environment. A study carried out in North Africa with the Institut Pasteur in Morocco and Algeria, as part of the European project RABMEDCONTROL (see inset), has managed to highlight the low transmission rate of the rabies virus across administrative borders between countries, but on the other hand its high national spread along the main highways[7]. Human intervention, through the transportation of infected dogs, is thus a predominant factor in the propagation of rabies in North Africa that must be considered when developing policies to fight rabies.

Rabies seems to be a disease that is often overlooked, but the associated human and financial cost is far from insignificant. The increased number of fatal cases of rabies in certain African and Asian countries, problems with access and the cost of post-exposure treatment all call for the programs in the fight against rabies to be stepped up.

## DISTRIBUTION OF RABIES RISK WORLDWIDE




Source: WHO.

### Chokri Bahloul, coordinator of the RABMEDCONTROL project, Laboratory of Immunopathology, Vaccinology and Molecular Genetics, Institut Pasteur in Tunis

"The aim of this European project that came to a close in 2009 was to identify in Algeria, Egypt, Morocco and Tunisia, all countries where the rabies virus is highly endemic, the key ecological and epidemiological factors that influence the dynamics of the disease. We adopted a multi-disciplinary approach that simultaneously involved descriptive epidemiological studies of rabies within the Mediterranean perimeter, analysis of the circulation of the virus among bats, molecular study of strains in circulation and also the impact of humans on the propagation of the virus and the fight against the disease. In Tunisia, our work succeeded in highlighting differences between the North of the country, where the vaccine is widely administered, and the South. At the time of our study, only 31% of dogs in this region had been vaccinated, thus leaving a sufficient reservoir to maintain the virus(8). Since the publication of our work, the authorities have increased efforts to reduce the number of rabies cases. We are currently analyzing epidemiological data collected during the project in order to be able to recommend ways to raise the population's awareness of the transmission factors and of dog vaccination."

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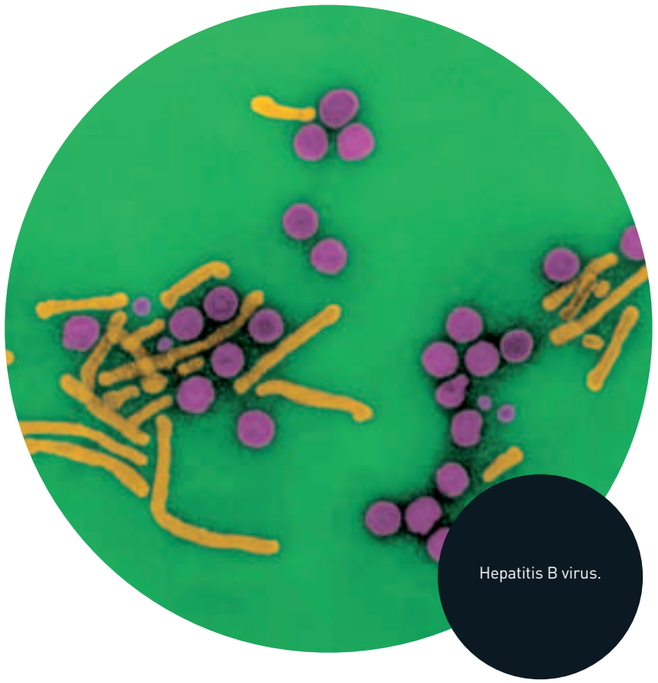
# VIRAL HEPATITIS

Hepatitis viruses that cause acute and/or chronic infections and inflammations of the liver are one of the greatest global public health concerns, particularly the hepatitis B and C viruses. WHO estimates that about two billion people have been infected with the hepatitis B virus – over 350 million with the chronic form – and that 130 to 170 million people are chronic carriers of hepatitis C. These two viruses, both very different in nature, are responsible for 57% of cirrhosis and 78% of primary liver cancer cases, and kill a million people every year. According to experts, the already high global mortality burden due to acute hepatitis B and C, as well as to cancer and cirrhosis (around 2.7% of all deaths) is set to rise over the next two decades[1].



Hepatitis B virus.

## LOCATING HIGH-RISK PATIENTS AND IMPROVING THEIR CARE

In the light of this major threat to public health, several Network teams are working together to specifically research the markers of liver cancer (hepatocellular carcinoma) in patients infected with a hepatitis virus. In China, which has the world's highest population of people infected with the hepatitis B virus, the Institut Pasteur of Shanghai is working with the Institut Pasteur in Paris to identify these markers in patients who are infected with the hepatitis B virus and have developed liver cancer. The project that began in 2009 and is funded by the Total Foundation also focuses on comparing viral quasispecies found in tumor or healthy cells of these patients. *"The presence of a signature of viral quasispecies in cancerous cells has never really been looked for. Yet, it seems to be increasingly evident that, despite their viral etiology, the development of liver cancers is highly influenced by numerous viral as well as host factors. By linking all these data to patient virological monitoring parameters, we can hope to locate those who are at high risk and improve their care"*, explains Ke Lan, a virologist at the Institut Pasteur of Shanghai.

## CHARACTERIZING NEW PREDICTIVE MARKERS OF EVOLUTION TOWARDS CANCER IN PATIENTS

Similarly, a project is underway to assess the role of hepatitis viruses in the development of hepatocellular carcinoma in Eastern Europe, involving the Cantacuzino Institute and the Institut Pasteur in Saint Petersburg and in Paris. The aim is to correlate viral variability with the specific genetics of tumors in an attempt to explain the clinical differences observed at population level. For the first time in Europe, this project has succeeded in highlighting a specific mutation of the tumor suppressor protein p53, which had thus far only been observed in Africa and Asia. In North Africa, a transversal research program between the Institut Pasteur in Algeria, Morocco, Tunisia and Paris is concerned with the molecular epidemiology of hepatocellular carcinoma. The results of this collaboration have highlighted risk factors linked to gender, specific mutations of certain genes or to heredity[2, 3].

Finally, in Equatorial Africa, there are plans to set up a program involving the Pasteur Centre in Cameroon and the Institut Pasteur in Bangui and in Paris. Its aim is to characterize the biomarkers of hepatic cancers in African patients. *"We want to detect straight from the blood of patients, not a protein, but raw DNA or microRNA released by the tumor. By analyzing these markers, we should be able to highlight mutations that are characteristic of liver cancers, but also chromosome defects. We thus hope to be able to detect the occurrence of liver cancer very early on in patients that are chronically infected with a hepatitis virus and monitor them more closely"* says Richard Njouom, medical virologist at the Pasteur Centre in Cameroon. To date, alpha-fetoprotein is the only known tumor marker of liver cancer. Although this protein is highly specific, it has low sensitivity since it is not secreted by all tumors. There is therefore a need to discover new markers that will allow for intervention at the earliest possible stage. This should be possible through the molecular techniques used in these research projects.

## RESEARCH ON THE MECHANISMS OF INFECTION BY THE HEPATITIS C VIRUS

Researchers at the Institut Pasteur in Saint Petersburg and Iran have been working with the Hepacivirus Unit of the Institut Pasteur in Paris in efforts to understand the entry and transport mechanisms of the hepatitis C virus in hepatocytes. This work has shown that an enzyme, lipoprotein lipase, was involved in binding the virus to target cells and was capable of inhibiting infection[4]. It also highlighted the significance of microtubules in initiating the infection and transporting the virus inside the cell, notably through an original mechanism of interaction with the capsid proteins[5].

Work resulting from a Transversal Research Program funded by the Institut Pasteur and involving the Hellenic Institut Pasteur, the Institut Pasteur in Cambodia, Dakar, Saint Petersburg and in Paris has shown that specific mutations in the gene encoding the capsid protein of the hepatitis C virus produced an unusual serological profile in infected patients[6]. The article published in *PloS ONE* shows, in three Cambodian patients, the absence of anti-capsid antibodies commonly seen in individuals infected with the hepatitis C virus. In comparison, these patients have a high level of antibodies directed against the protein encoded by a frameshift mutation in the capsid gene. This specific protein had so far never been detected in cases of human infection. In addition, researchers have shown that synonymous mutations found in these patients at RNA level lead to changes in the structure of the viral genome that could promote production of the alternative protein. The study of pathologies in this type of patient would provide fresh information regarding the respective roles of the capsid protein and the protein encoded by an alternate reading frame and new elements for diagnosing the infection.

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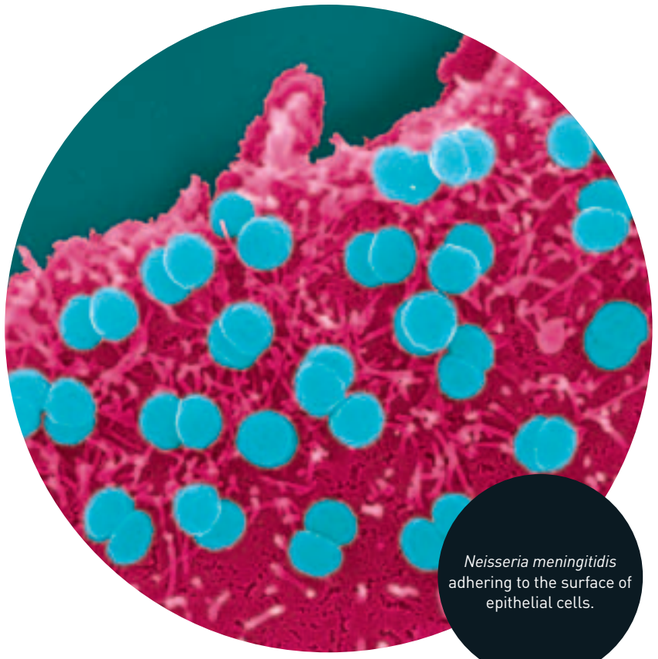
# BACTERIAL MENINGITIS

Aside from outbreaks of the disease, an average 1.2 million cases of bacterial meningitis are reported worldwide each year, 135,000 of which prove to be fatal[1]. Although bacterial meningitis is diagnosed in all continents, it poses a particular threat in the region known as "the African meningitis belt", which extends from Ethiopia to Gambia. In these countries, the disease is endemic all year round, with seasonal epidemic peaks, varying in intensity from year to year. Meningococcus, Pneumococcus and *Haemophilus* are the three main pathogenic agents that cause acute bacterial meningitis and each one has several "sub-types".



*Neisseria meningitidis* adhering to the surface of epithelial cells.

## IMPROVING THE FIGHT AGAINST MENINGITIS IN SUB-SAHARAN AFRICA

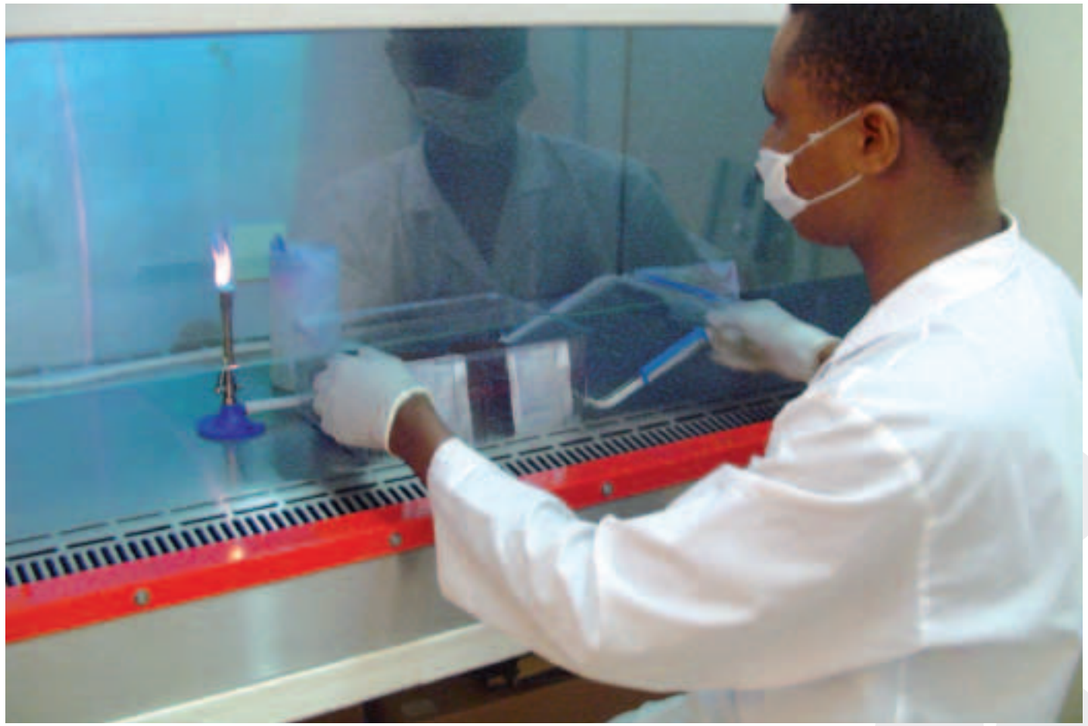
A program was started in 2007 to improve the diagnostic capability of meningitis given the findings observed in the laboratories of the African belt countries in the last decade. Funded by the French Ministry of Foreign and European Affairs as part of the Priority Solidarity Fund (FSP), this program is coordinated by the Institut Pasteur on a partnership between the following countries: Niger, Mali, Burkina Faso, Cameroon, Cote d'Ivoire and Central Africa. The project has improved epidemiological monitoring of meningitis and capacity for research in molecular biology by transferring the required techniques to reference laboratories in countries that are partners for the majority of the RIIP member institutes.

Victims of bacterial meningitis are mainly children under the age of five. Infants between 4 and 18 months are particularly vulnerable. Between 15 and 35% of children who survive *Haemophilus* meningitis are left with permanent hearing deficiencies, speech problems, visual impairment or motor defects[2]. There is a lack of sufficient documentation in Africa and knowledge in this area needs to be updated to facilitate more effective management of these disabilities. The CERMES is currently carrying out a study to improve identification of the nature and frequency of the long-term effects of meningitis in Niger.

## THE IMPACT OF VACCINATION

Up until now, the solution for meningitis outbreaks in Africa has been anti-meningococcal polyosidic vaccines but these have shown their limits. The introduction of the new conjugate vaccine MenAfriVac is therefore a significant step in this fight, since it specifically targets meningococcal serogroup A, which is the primary cause of the major outbreaks observed.

Alongside the major vaccination campaigns that began in 2010 in Burkina Faso, Mali and Niger, the project coordinated by the London School of Hygiene and Tropical Medicine and funded by the Wellcome Trust and the Bill and Melinda Gates Foundation involves seven countries from within the meningitis belt. The aim of the project is to study the spread of meningococcal meningitis in Africa and to document the impact of the MenAfriVac vaccine on transmission of the infection. The CERMES plays a significant role, being responsible for carriage studies in this field for a three-year period.



CERMES, Niger.

## FAST-CHANGING BACTERIAL STRAINS

The major fear now however is that there will be a rapid change in the bacterial strains circulating in these countries if the proportion of type A strains is reduced as these are the only strains targeted by MenAfriVac. Other hitherto minor "sub-types" may then become increasingly prevalent.

## RAPID DIAGNOSTIC TESTS

In view of this, monitoring based on rapid diagnostic tests (RDT) jointly developed by the CERMES and the Institut Pasteur to detect the main types of meningococcal meningitis, represents a particularly effective field tool[3,4]. This simple and inexpensive test uses dipsticks and can be administered at the patient's bedside. By enabling rapid identification of the etiological agent in remote areas with little access to molecular diagnostic techniques, it would improve monitoring capabilities and save precious time in terms of patient care. Funding is currently being sought to support the development and field evaluation of the required tests as part of a multi-site post-vaccination study to obtain a complete and effective rapid diagnostic kit capable of detecting the majority of bacterial meningitis strains in circulation around the world.

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# ANTIBIOTIC RESISTANCE

Infections caused by antibiotic resistant bacteria are steadily increasing worldwide, both in the community and in healthcare institutions. Their consequences are often more serious than those caused by "sensitive" bacteria, resulting in the need for second-line treatment that is generally more expensive, and a more intensive and costly follow-up. In 2007, the estimated cost of infections caused by antibiotic resistant bacteria amounted to about euro 1.5 billion in Europe (including direct extra charges and charges associated with additional days of hospitalization, ambulatory care and loss of productivity due to sick leave, death, etc.)[1].

Due to its worldwide propagation and the speed at which it is developing, antibiotic resistance is currently one of the greatest public health concerns. As there is no new class of antibiotic expected in the next few years, antibiotic resistance is threatening the effectiveness of many drugs in use today, thus challenging significant progress made in the fight against infectious agents.

## LOW-INCOME COUNTRIES OPEN TO THREAT

In low-income countries, the use of antibiotics is often anarchic, and this has a significant impact on the emergence and development of bacterial resistance. The use of drugs in these countries is poorly regulated and a medical prescription is not required to obtain antibiotics. The quality of antibiotics is inconsistent due to the high volume of counterfeit drugs available. Moreover, patients often do not complete their treatment regimen correctly. Also, a lack of hygiene, vulnerability and an increase in immunosuppression due to HIV infection, encourage the dynamics for resistance transmission, by placing the populations of these countries in constant contact with germs, some of which are resistant.

A prospective study carried out in Africa on the strains of methicillin-resistant *Staphylococcus aureus* (MRSA) has shown the alarming ability of this particularly virulent bacterium to spread over a large geographic area, as well as the potential role of Africa as the initial reservoir, responsible for sporadic spread to other continents[2].
*Institut Pasteur in Madagascar, Dakar and Morocco, Pasteur Centre in Cameroon and the CERMES*

Another international study has confirmed the important role played by enterobacteria in the dissemination of antibiotic resistance, due in particular to their presence in the intestinal lumen, a preferred place for exchange of genetic information between different types of bacteria.
*Pasteur Centre in Cameroon, Institut Pasteur in Dakar, Morocco, Algeria, Cote d'Ivoire, Madagascar, Cambodia, Ho Chi Minh City and National Institute of Hygiene and Epidemiology in Hanoi*

Contamination with salmonella, the main cause of food poisoning in humans, has also been evaluated on domestic consumption of chickens in Senegal and Madagascar. An analysis of the flora present on the skin of the neck of thousands of chickens at the time of slaughter has shown that resistant salmonella bacteria could have been spread, by cross-contamination, into the domestic environments where they were then ingested.
*Institut Pasteur in Dakar and Madagascar, Pasteur Centre in Cameroon, AFSSA (French Food Safety Agency) and LERQAP (Laboratory for Study & Research on Food Quality & Processes)*

Finally, an international study coordinated by the Institut Pasteur has recently detected a type of salmonella that has become multi-resistant in the space of ten years and that is spread by contaminated poultry in Africa and the Middle East[3]. The emergence of these bacteria, detected by the surveillance systems of Northern countries in travelers and migrants, emphasizes both the need to establish such networks in the Southern countries and the fundamental role played by the RIIP institutes as sentinels for these emerging phenomena.

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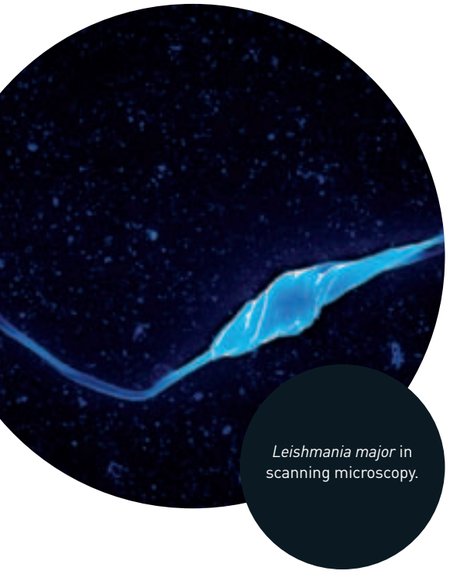
### Study program for antibiotic resistance in different parts of the world: Children's Antibiotic Resistant infections in Low Income countries: an international cohort study (ChARLI)

Currently, surveillance networks for bacterial resistance focus mainly on industrialized countries. However, monitoring in low-income countries, the main environments for the origin and dissemination of resistant infections, is essential to stem their development. In December 2010, the Principality of Monaco and the Institut Pasteur signed a partnership agreement to combat infant antibiotic resistant infections in low-income countries. The main objective of the ChARLI project is to assess the incidence and medical and economic effects of antibiotic resistant bacteria in severe infant and neo-natal infections, acquired in a healthcare environment or the community. An international pediatric cohort will be set up and monitored within the RIIP, with the benefit of the Network's expertise in the field, its ideal geographical presence and its effective partnerships established at local level.
**www.charliproject.org**

# LEISHMANIASIS

Leishmaniasis is a chronic disease which may be cutaneous and/or visceral, caused by protozoan parasites belonging to the genus *Leishmania*. The parasites are transmitted by the bite of an insect vector, the phlebotomine sandfly.



*Leishmania major* in scanning microscopy.

## THE EXTENT OF THE PROBLEM

Leishmaniasis occurs in many tropical and subtropical countries, as well as in areas around the Mediterranean Basin. It is considered endemic in 88 countries, 72 of which are developing countries. Leishmaniasis is a poverty-related disease. Leishmaniasis threatens about 350 million men, women and children around the world. As many as 12 million people are believed to be currently infected, with around 1 to 2 million estimated new cases occurring every year.

## RIIP'S STUDY OF LEISHMANIASIS

Among the institutes of the RIIP, at least 9 are located in endemic countries, namely Morocco, Algeria, Tunisia, Italy, Greece, Iran, Brazil, French Guiana and France.

The European project Leishdrug, funded by the European Union's Seventh Framework Programme, is an example of a collaborative Network project on leishmaniasis. It involves 13 teams, including four RIIP institutes (Institut Pasteur in Paris, Korea, Tunis and Montevideo). Its main objective is to exploit parasite-specific pathways for anti-leishmanial drug development and overcome current limitations in anti-leishmanial therapy.
The main strength of the consortium lies in the complementary expertise in imaging and cell biology, peptide biochemistry, genomics and proteomics, drug development and structural biology, and finally *in vivo* assessment of leishmanicidal activity and pharmacokinetics of lead compounds. (www.leishdrug.org).

Other topics of research on leishmaniasis within the RIIP include:
• Study of key determinants of the natural history of *L. major* infection
• Study of animal reservoirs, particularly wild rodents
• Study of transmission and of virulence factors in host-pathogen interaction

Sandfly.

• Epidemiology of leishmaniasis, including diagnosis, population genetics and risk assessment
• Study of climate change's effect and its impact on infection in the Mediterranean Basin
• Study of new anti-parasitic strategies involving testing of natural products and study of resistance to treatments using preclinical and clinical therapeutic trials
• Vaccine development.

Recently a network working on leishmaniasis has been set up (LeishRIIP Network) to improve interaction between the various RIIP groups working on this pathology. (http://www.pasteur.fr/infosci/conf/leishriip-TMP/index.html).

## LEISHMANIASIS/HIV CO-INFECTION

Visceral leishmaniasis is a serious opportunistic infection sometimes associated with HIV. A concomitant HIV infection increases the risk of developing active visceral leishmaniasis by between 100 and 2,320 times. In Southern Europe, an increase of 70% in the number of cases of visceral leishmaniasis in adults is associated with HIV infection.

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# DIARRHEAL DISEASES

In low-income countries, diarrhea is the third main cause of death in children under the age of 5 (18%). This percentage is slightly lower than for respiratory infections (19%), but higher than the one for malaria (8%). According to the World Health Organization (WHO), gastrointestinal infections that cause diarrhea still kill approximately 2.2 million people each year, mainly due to contaminated food or water, or transmission between humans resulting from poor hygiene.

## FIGHTING INFANT DIARRHEAL DISEASES IN BANGUI

At the Pediatric Complex in Bangui, severe diarrhea is responsible for 13% of hospitalizations and causes 5.4% of infant deaths. The Institut Pasteur in Bangui, the Pediatric Complex in Bangui and the Saint Joseph Health Center in Ouango are working with the Institut Pasteur on a research program focusing on severe infant diarrhea in developing countries with the aim of:
• improving management of cases of severe child diarrhea by diagnosing them earlier on and adapting medical care to local working conditions.
• developing and improving epidemiological knowledge.
• answering fundamental questions regarding physiopathology, immunity, the infected host's response and prevention through vaccination in endemo-epidemic regions.

The first phase of the project in Bangui will involve improving infrastructures, equipment and knowledge at the operational level. Plans for a second phase involve launching a case-control epidemiological study necessary for developing, establishing and supporting an epidemiological and operational-style program as a basis for fundamental research.
This project in the Central African Republic is funded by the Total Foundation which has worked with the Institut Pasteur for several years to fight infant diarrheal diseases through a similar project in Madagascar.

## FIGHTING INFANT DIARRHEAL DISEASES IN MADAGASCAR

This field project involving the Institut Pasteur in Madagascar and Paris concerns a new integrated treatment and research facility in Moramanga. The center provides diagnosis, treatment and prevention programs, but also conducts advanced research on the acute and chronic complications of severe diarrhea.

**Bibliography**


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**Total Foundation**

Following an initial corporate funding agreement signed in 2005, the Total Foundation renews its continued commitment to the Institut Pasteur in the fight against infectious diseases.
This new agreement, signed on June 15, 2010, highlights the common desire of the Total Foundation and the Institut Pasteur to pursue a quality partnership in the fight against infectious diseases. The Total Foundation will help to fund research programs, in particular transversal programs involving several Institut Pasteur teams, as well as the group research of young researchers.

# International Teaching and Training

The Institut Pasteur International Network (RIIP) strives to improve scientific capabilities and human resources around the world. To achieve this, the RIIP develops training programs in partnership with universities and local stakeholders. Although primarily aimed at staff from member institutes, the programs are also open to external researchers, technicians and students. Over 100 RIIP trainees come every year to complete their training by taking courses or serving traineeships in Paris. The Institut Pasteur and the Institut Pasteur International Network provide international grants for traineeships and courses taken in Paris.

**31**
international courses
in 2009 and 2010

**165**
fellowships
in 2009 and 2010

# Teaching – a priority for the RIIP

Training activities are not just intended for staff from member institutes but also for external personnel, technicians and students, who may then use their experience in other national, regional or international bodies.

**In 2009 and 2010, 31 courses in French and English** were run in various RIIP institutes in proteomics, genomics, bioinformatics, biostatistics, epidemiology, genetics, molecular biology, new vaccine strategies, etc.

## INTERNATIONAL RIIP COURSES

- A Call for Proposals is issued every year
- The courses are run every year or every two years
- Each course is awarded funding of between 10,000 and 30,000 euros (including grants for RIIP members) provided from the combined budget of the Institut Pasteur International Network and the Institut Pasteur.

**TOPICS**
- Malaria, cell imaging, immunology, biosafety, virology, epidemiology, monitoring, etc.

**EXAMPLES**
- The Malaria workshop - Institut Pasteur in Madagascar
- HKU-Pasteur Cell Biology Course, Virology Course and Immunology Course – Hong Kong University-Pasteur Research Centre
- Global Foodborne Infectious Network (GFN) Courses on salmonellosis monitoring - Pasteur Centre in Cameroon, Institut Pasteur in Saint Petersburg, Institut Pasteur in Madagascar and Institut Pasteur in Tunis in partnership with the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) in the US.
- Bioinformatics and comparative Genome Analyses - North Africa, Asia and Latin America

## REGIONAL COURSES

**AFRICA**
West-African anti-biology program - Institut Pasteur in Cote d'Ivoire

**THE AMERICAS**
Macromolecular Crystallography: Introduction and Applications – Institut Pasteur in Montevideo.

**ASIA-PACIFIC**
Pasteur Immunology Course – Hong Kong University-Pasteur Research Centre
Pasteur-Areva Anti-Viral Immunity Course – Institut Pasteur of Shanghai

**NORTH AFRICA - IRAN**
Analysis of data using STATA software - Institut Pasteur in Tunis
Course on immunophysiology of infections - Institut Pasteur in Algeria

### Regional courses are also held on various subjects

**Infectious diseases (research and public health)**
- Pertussis and Diagnostic Techniques (molecular and classical) - Institut Pasteur in Iran
- Avian Flu Training - Institut Pasteur in Cambodia
- New Development in Rabies Epidemiology, Diagnosis and Control – Institut Pasteur in Ho Chi Minh City
- Virological monitoring within the framework of the Polio Eradication Program - Institut Pasteur in Saint Petersburg in partnership with WHO

**Biosafety, hygiene, quality assurance**
- Biosafety and BSL-3 level pathogenic agents - Institut Pasteur of Shanghai
- Regional workshop on BSL-2/BSL-3 biosafety - Institut Pasteur in Cambodia

**Bioinformatics**
- Advanced course on Bioinformatics and Comparative Genome Analysis – Fiocruz, Brazil
- Bioinformatics and Comparative Genome Analysis – Institut Pasteur in Tunis



**ADDITIONAL TRAINING COURSES**

### Amsud-Pasteur courses in Latin America

The Amsud-Pasteur partnership organizes regional courses in Argentina, Brazil, Chile, Paraguay and Uruguay. Eight Amsud-Pasteur courses were run in 2009 and 2010.

### Training funded as part of projects

- Training for local personnel: quality approach, laboratory techniques, good clinical research practice (CAMELIA clinical trial: Cambodian Early vs. Late Introduction of Antiretroviral drugs) and SISEA (Surveillance and Investigation of Endemic Situations in Southeast Asia) project
- Theoretical and practical workshop: "Setting up an intervention unit", (diagnostics, warning plan, communication) with the CIBU, designed for RIIP researchers working on influenza
- Regional workshop on virology in Cambodia

### Initial and Continuous professional development: strengthening of capabilities

Several RIIP institutes are laboratories that welcome university students, both national and international, particularly for Licence (Bachelor's degree), Masters and PhD. In addition, they provide supervision for national and foreign trainees as part of the continuing training of specialist doctors and laboratory technicians. Researchers of the RIIP institutes are involved in training specialists through courses and seminars in postgraduate teaching.

**Examples include:**
Training school for health and medical technicians, medical analyses option at the Pasteur Centre in Cameroon
- Construction of an Education Center and a Hall of Residence for trainees, funded by sponsors, the Institut Pasteur and CERMES in Niger.
- In 2010, the Institut Pasteur in Bangui organized its first workshop on writing and editing scientific publications for its researchers.
- The Institut Pasteur in Montevideo organizes a program of courses for the Latin-American scientific community that includes theoretical and practical courses on new technologies.

## DISTANCE TEACHING

**PARTNERSHIP WITH AUF (FRANCOPHONE UNIVERSITY AGENCY)**
The CCSTVN (Committee for Scientific and Technical Cooperation with Vietnam), the Asia-Pacific bureau of the Francophone University Agency (AUF) and the Institut Pasteur in Paris signed an agreement on October 7, 2008 to define the terms of their cooperation on a series of video conferences.

### Topics include

- Resistance of bacteria to antibiotics
- Cholera: epidemiological aspects
- Rabies: clinical and epidemiological aspects

>> http://cstvn.free.fr/html/visioconferences.html

### Continuous professional development in Medical Biology

This interactive continuous professional development course by internet covers hematology (e-HEMATimage), parasitology, mycology and pathological cytology with a multilingual program, e-MEDICINimage. Funding is provided as part of the Institut Pasteur's continuous professional development for expatriates and potential funding is available from the institutes for local researchers.

>> www.e-hematimage.eu

## STUDENTS FROM AROUND THE WORLD WELCOMED AT THE INSTITUT PASTEUR IN PARIS

**Each year, the Teaching Center at the Institut Pasteur in Paris** organizes 29 advanced theoretical and practical courses rooted in scientific research that are taken by students and researchers from around the world (500 students each year from more than 48 nationalities).
Funded by the Institut Pasteur's Calmette and Yersin program of study grants, the 2010-2011 session brought together 31 RIIP students and seven Amsud-Pasteur students.

>> www.pasteur.fr/enseignement

**The specialized Master's program of School Pasteur-Cnam of Public Health**
Certain forms of training provide students who are interested in doing so with the opportunity to obtain a Master's in public health, specializing in "risk of infection" at the School Pasteur-Cnam of Public Health.

>> http://school-pasteur.cnam.fr/

**Pasteur-Paris University International Doctoral Program**
An international program welcoming PhD students at the Institut Pasteur in life sciences and biomedicine.

>> http://www.pasteur.fr/ip/easysite/pasteur/en/teaching/overview-teaching

# Support for scientists

**The Pierre Ledoux - Jeunesse Internationale Foundation** and the Institut Pasteur (International Division) jointly provided 10 grants per year.

## GRANTS FROM THE PIERRE LEDOUX - JEUNESSE INTERNATIONALE FOUNDATION

Biomedical research grants for traineeships in the laboratories of the Institut Pasteur International Network for students of French nationality from Universities and Schools (biologists, doctors, pharmacists, veterinary surgeons or young researchers) (under the age of 35). The traineeships last from 3 to 12 months. There are two calls for applications per year.

## CALMETTE AND YERSIN PROGRAM OF THE INSTITUT PASTEUR

### Study grants

Grants funded by the International Division of the Institut Pasteur, to promote and facilitate the participation of scientific personnel (students, researchers, engineers and licensed technicians) from the RIIP:

- in courses run by the Institut Pasteur in Paris,
- in training workshops organized at an RIIP member institute,
- in any other course recognized by the International Division.

The training must be closely related to the applicant's research subject and must supplement their initial training and strengthen their skills in their research fields.

### Traineeship grants

Aimed at the employees of the RIIP institutes (researchers, technicians or students) to complete an internship in a laboratory of the Network or at another research institution.

Each year, the International Division launches two calls for applications for traineeship grants.

### Doctoral grants

A three-year doctoral grant funded by the Institut Pasteur allowing a student to carry out their PhD traineeship in an RIIP institute (outside of Paris).

**Objective:** to encourage and enable French and foreign researchers to carry out a PhD internship in an RIIP laboratory.

The traineeship can be conducted in any topic developed in the laboratories of the RIIP member institutes, whether in infectious diseases (physiopathology of infections, immunology, microbiology, epidemiology, virology, parasitology) or public health activities (monitoring, resistance).

**Calmette and Yersin program - Study and Traineeship grants**
In 2009 and 2010, the International Division awarded 64 study grants for training and 44 grants for internships, carried out in France and within the RIIP.

Within the framework of the RIIP Doctoral Program that was created in 2010, the first doctoral grant funded by the International Division of the Institut Pasteur has been awarded by the selection committee to a French student, who complete a three-year PhD at the Institut Pasteur of Shanghai and in partnership with the Institute for Glycomics at Griffith University in Australia, on the subject of "Drug Discovery: Virology, Systems Biology, Biochemistry".

## GRANTS FROM THE INSTITUT PASTEUR INTERNATIONAL NETWORK

### Traineeship grant as part of a PhD

These RIIP-funded grants aim to encourage and enable students to carry out traineeships, as part of their PhD, at an RIIP institute or at another research institution. These can be co-supervised PhDs (North/South) or PhDs without co-supervision.

### Conference grant

These RIIP-funded grants aim to make it possible for the RIIP's young scientists to take part in international conferences.

## AMSUD-PASTEUR GRANTS

Amsud-Pasteur is a network of 62 research institutes in Latin America.

### For courses at the Institut Pasteur in Paris

10 grants per year
2 calls for proposals per year
2 students per country (Argentina, Brazil, Chile, Uruguay and Paraguay)

### For regional exchange programs

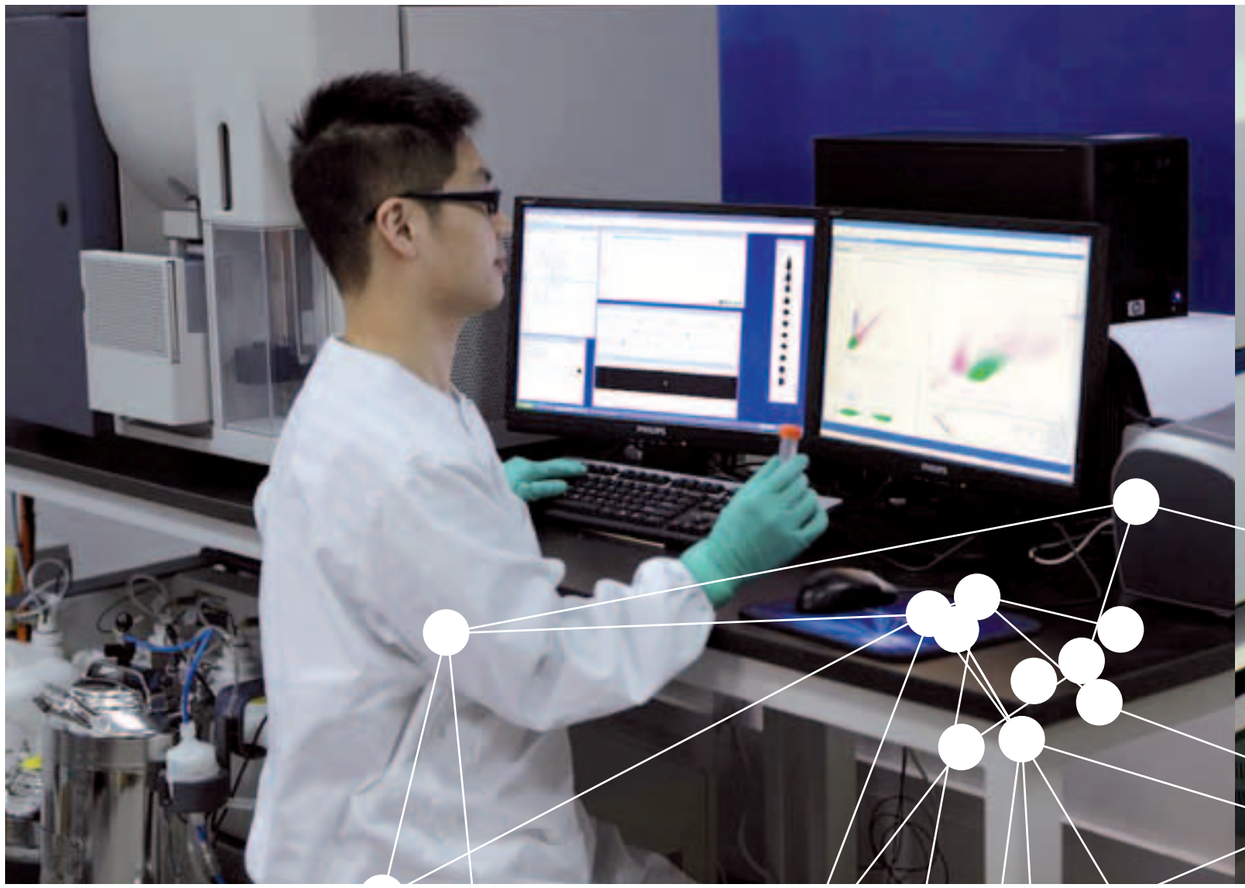
12 Amsud-Pasteur grants between 2009 and 2010 for regional exchange programs.

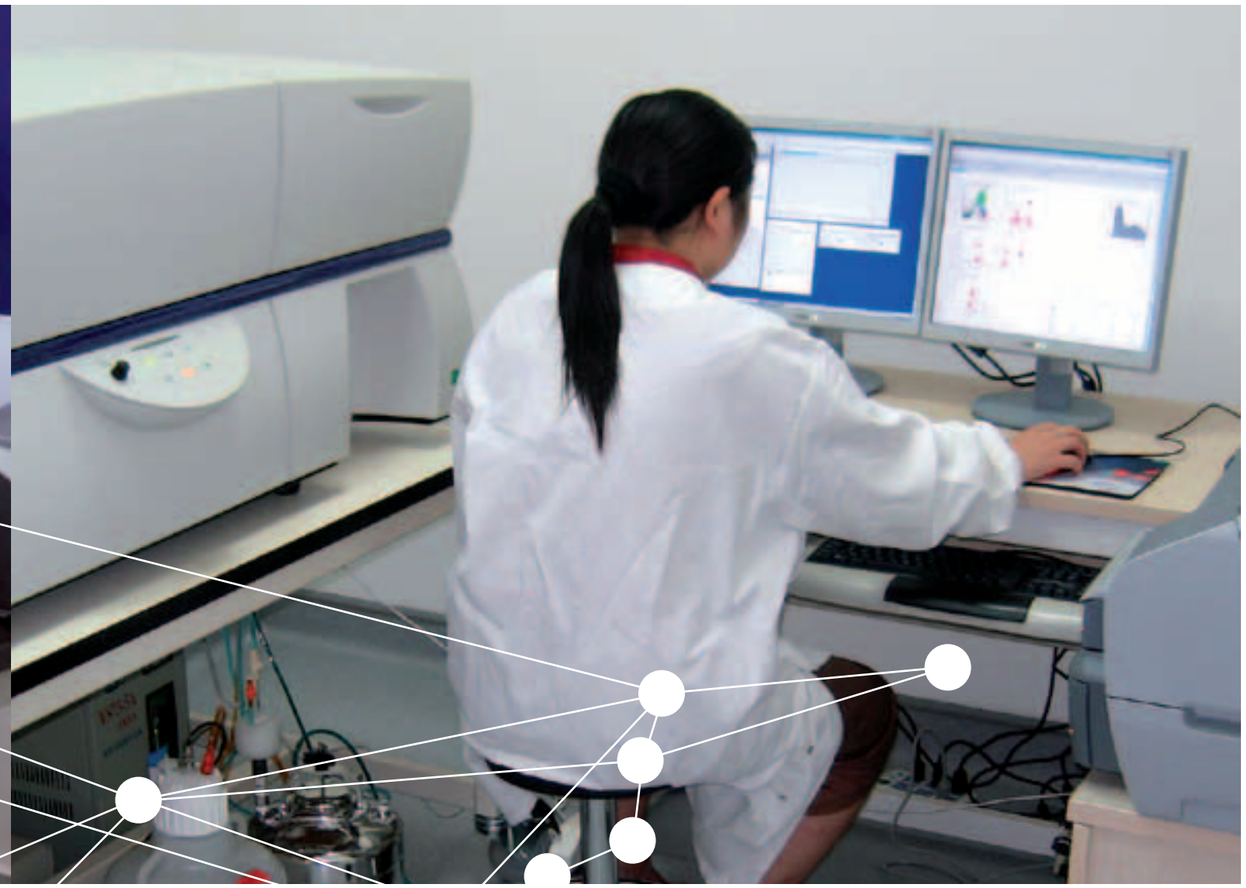
**2009**
8 grants (5 PhDs and 3 conferences).

**2010**
13 grants (9 PhDs and 4 conferences).

# Technical platforms

These platforms are a set of equipment and technology techniques required to carry out research projects, particularly in the area of infectious diseases.





# Biosafety level 3 (BSL3) facilities in the RIIP


Several BSL-3 facilities are equipped with modules for mosquito infection (Dakar, French Guiana, Madagascar and Paris).

## Construction of BSL-3 and BSL-2 laboratories at the Institut Pasteur in Bangui

"The Institut Pasteur in Bangui* in the Central African Republic, located at the heart of Central Africa and characterized by a distinctive equatorial and intertropical ecosystem, is a preferred facility for microbiological monitoring. The recent concept of emerging diseases and the arrival of new resistant strains have led this institute to dedicate a significant part of its research to microbiological monitoring. With the support of the French Ministry of Health and the Institut Pasteur in Paris, the Institut Pasteur in Bangui is therefore building two new safety level 2 (bacteriology) and level 3 (virology) laboratories to strengthen diagnostic capabilities and allow for on-site development of research projects on microbiological monitoring in this region of the world, in collaboration with other teams from the Institut Pasteur and the RIIP."
(Interview with Mirdad Kazanji, Head of the Institut Pasteur in Bangui).

* In 2011 the Institut Pasteur in Bangui will celebrate its fiftieth anniversary in the Central African Republic. This BSL-3 laboratory will be opened in June 2011.

## OTHER TECHNICAL PLATFORMS IN THE RIIP

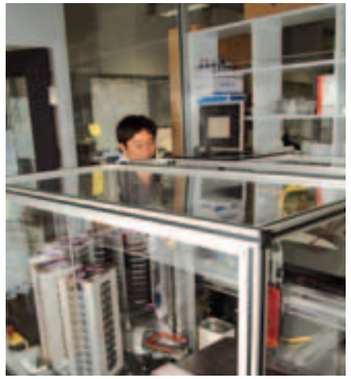
Several institutes have equipment for implementing cellular and molecular biology techniques:

- **Flow cytometry** (Algeria, Bulgaria, Cameroon, Canada, Hong Kong, French Guiana, Montevideo, Shanghai, Tunis)
- **Traditional and real-time PCR** (Bangui, Bulgaria, Cameroon, CERMES, Greece, Guadeloupe, French Guiana, Madagascar, Montevideo, New Caledonia)
- **Recombinant protein purification** (Algeria, Montevideo)

In addition, several institutes have biobanks (cell banks, collections of viruses, microorganisms and cell cultures) and epidemiological tools (cohorts, sentinel sites, hospital partnerships).

## OTHER TECHNICAL PLATFORMS AVAILABLE

- **Pasteur Centre in Cameroon:** Liquid chromatography, ion chromatography
- **CERMES:** Immunochromatography, cell cultures
- **Institut Pasteur in Madagascar:** anatomopathology, production of reagent strips for rapid diagnosis
- **Institut Armand Frappier:** Confocal microscopy, digital imaging and electron microscopy, Center of experimental biology; mass spectrometry; proteome analysis; biostatistics consultation; robotic platform for high-throughput screening; histocompatibility laboratory
- **Institut Pasteur in Guadeloupe:** Pesticide and heavy metal analyses
- **Institut Pasteur in French Guiana:** Equipment enabling implementation of molecular biology techniques of immunology, identification and chemical dosage of substances; sequencer ; liquid chromatography; gas chromatography, mass spectrometry
- **Institut Pasteur in Montevideo:** bioinformatics, protein crystallography, biophysics and production, analytical biochemistry, proteomics, genomics, mass spectrometry, DNA microarrays, confocal microscopy, epifluorescence microscopy
- **Institut Pasteur in Cambodia:** Automated mycobacteria culture system, Gen-Probe system for identification of mycobacteria
- **Institut Pasteur Korea:** Cell biophysics; diagnoses using microfluidics; dynamic imaging with ultrafast Multi-D imaging and imaging processing; screening and pharmacology through automated confocal microscopy; robotics, drug development and chemical genomics, high-throughput visual screening programs
- **Institut Pasteur in New Caledonia:** Technical platform for dengue fever (automated system)
- **Institut Pasteur of Shanghai:** Scientific and virological imaging (proteomics and genomics); microinjection into the oocytes of frogs; radioisotope, ion exchange
- **Institut Pasteur - Cenci Bolognetti Foundation:** transcriptomics, bioinformatics
- **Hellenic Institut Pasteur:** Imaging, DNA microarrays and molecular epidemiology microarrays, recombinant protein production, molecular diagnosis
- **Institut Pasteur in Lille:** Transcriptomics, genomics, bioinformatics, DNA microarrays
- **Scientific Institute of Public Health - Brussels:** Mass spectrometry and chromatography platform
- **Stephan Angeloff Institute - Bulgaria:** Electron, confocal laser scanning and fluorescence microscopy; liquid chromatography
- **Institut Pasteur in Tunis:** Protein analyses, sequencers, electron microscopy, liquid chromatography, irradiator, metrology, bio-fermentation and genetic sequencing units



# Hygiene, quality, environment and sustainable development

Studying the dynamics of transmission of infectious agents from the environment involves field monitoring of populations of pathogenic agents, vectors and potential reservoirs (e.g. animals, foods, soil, water, sediments, etc.). In addition, understanding these dynamics is essential for developing effective alert and counter strategies in the fight against infectious diseases. Within the RIIP, these studies are carried out thanks to the existence of specialized hygiene and environment laboratories.

## HYGIENE, QUALITY AND ENVIRONMENT: A SHARED CONCERN

The Hygiene and Environment department at the Pasteur Centre in Cameroon conducts more than 10,000 tests each year in microbiology (water, food, cosmetic products) and physicochemistry (water, food, toxicological assessments). Several projects on the monitoring of legionellosis; pathogenic flora present on table chickens at the time of slaughter in 11 towns located across 4 continents, in Cayenne and in New Caledonia; the FRAT (Fortification Rapid Assessment Tool) study as part of the National Food-Fortification Program; evaluation of the exposure of Yaoundé's food chain to heavy metals and training workshop on the "Regional Total Diet Study for Sub-Saharan Africa" are linked to this department.

**The Institut Pasteur in Cambodia** is involved in monitoring legionellosis in water supplies and cooling towers in tropical areas in order to establish the current situation and to study the feasibility of setting up a monitoring strategy at the national level. Another study focuses on the sociocultural aspects of hygiene in healthcare in Cambodia given that hospital employees are frequently becoming infected with diseases through blood pathogens in the Southeast regions of Asia. This study has prompted reconsideration of the importance of hygiene, with precautions taken to improve practices to control infections in Cambodian medical environments.

**The Institut Pasteur in Cote d'Ivoire** gives priority to research and initiatives associated with controlling and improving the environment, with a particular focus on food safety and the various ecosystems, especially the lagoon ecosystem. The main issues are still the conditions for persistence and emergence of pathogenic infectious agents for humans in the environment, microbial population biology and microbial ecology. The ecological approach and the microbial biodiversity approach are those used. Two programs are run by the Institut Pasteur in Cote d'Ivoire and focus on the pathogens responsible for diseases associated with food and the environment.

**The Institut Pasteur in Dakar** is equipped with a food safety and environmental hygiene laboratory (LSAHE), accredited by the French Committee for Accreditation (COFRAC) since 2009, according to ISO 17025. This laboratory is affiliated with Senegal's Food Safety Authority and is considered by the Department of Fish Processing Industries as the reference laboratory for the detection of marine toxins. The LSAHE is still a laboratory for bacteriology, but water analysis work has given way to food analyses. The LSAHE is associated with two projects within the framework of Inter-Pasteurian Concerted Actions (ACIP), the first of these focusing on quantitative evaluation of the risks associated with salmonella and with *Campylobacter* through domestic consumption of chickens at two pilot sites, namely Dakar (Senegal) and Antananarivo (Madagascar), and the second focusing on legionellosis that in turn associates Cameroon and Cambodia. The Institut Pasteur in Dakar is also working to characterize the isolated strains of *Vibrio parahaemolyticus* in fishing products and in the marine environment in Senegal.

**The Institut Pasteur in Guadeloupe** is equipped with an environmental hygiene and agri-food laboratory that develops tests for pesticides and metals. The institute therefore helps to control environmental quality by ensuring that drinking and bathing water is analyzed (bacteriological quality and physicochemical quality, microbiological risk) and that industrial matter and effluent from treatment plants are monitored (organic load and pathogenic agents).

The Hygiene and Environment Laboratory (LHE) at the **Institut Pasteur in French Guiana** provides public health services and expert assessments, involving microbiological and chemical tests on water and microbiological tests on foods. The laboratory's main activity involves sanitary control of water; additional activities include food hygiene in the agri-food and catering industries, hospital hygiene and also tests on residual water. Finally, the LHE carries out unprecedented work for the RIIP, known as "space" microbiology, performed for the company Arianespace.
Since 2008, the LHE has been accredited by the French Committee for Accreditation (COFRAC) within the field of water microbiology and physicochemistry of water. This accreditation has led to the laboratory being approved by the French General Directorate of Health for sanitary control of water. The LHE's employees are on duty around the clock and can intervene in cases of water pollution or to handle any suspicious letters or parcels, in collaboration with the other units of the Institut Pasteur in French Guiana.

**The Institut Pasteur in Tunis** has a water and food-control laboratory that is a WHO national reference center for salmonellosis, shigella and the bacterium *Vibrio cholerae*.


Institut Pasteur in Madagascar.

## SUSTAINABLE DEVELOPMENT: A VOLUNTARY APPROACH TO SOCIAL RESPONSIBILITY

Sustainable development satisfies current needs without compromising the ability of future generations to satisfy theirs. It incorporates the necessity to combine the fulfillment of needs, particularly the basic needs of the most impoverished to whom the greatest priority should be given, with the preservation of the environment. The Institut Pasteur, whether as part of its work in Paris or in its international connections, aims to integrate the principles of sustainable development in a number of ways:

- at its Paris site via the "Green Campus" approach that specifically aims to step up measures to reduce the impact of its work on the environment.

- internationally, via collaborations initiated within the RIIP to optimize local management of harmful waste. **A guide called "For sustainable and responsible management of waste from healthcare and laboratory activities"** has been published, with the aim of providing the RIIP institutes and their partners with assistance in defining and implementing a sustainable management strategy for waste produced during healthcare and laboratory activities which is adapted to local policies and conditions. The guide is a simple and practical tool, offering information and decision-making criteria required for implementing a strategy that is realistic and respectful to both humans and the environment.
A mission that is in keeping with the RIIP institutes' support for the management of their waste was conducted in May 2010 at the Institut Pasteur in Cambodia; this country being the pilot site. At the moment, there are no regulations in Cambodia, but they are currently being drafted by the Ministries for Environment and Health. Waste management at the **Institut Pasteur in Cambodia** will be carried out according to the same principles as those in force in Paris.

**Since 2010, the Institut Pasteur has adhered to the United Nations Global Compact** and to its ten principles relating to human rights, labor rights, environmental protection and the fight against corruption. Finally, as part of a voluntary measure based on the evaluation method AFAQ 26000 (AFNOR Certification), the Institut Pasteur has also undergone a social responsibility audit which served to highlight its strengths and weaknesses in this area.

# Thanks…

We would like to offer special thanks to a large number of collaborators for their help in writing, editing and producing this Report 2010 of the International Network.

## INSTITUT PASTEUR INTERNATIONAL NETWORK

All the Directors of institutes as well as the communication 's correspondents, Benoit Garin (Institut Pasteur in Madagascar), Chokry Bahloul (Institut Pasteur in Tunis), Philippe Dussart (Institut Pasteur in French Guiana), Mathurin Tejiokem (Pasteur Centre in Cameroon), Eric Nerrienet (Institut Pasteur in Cambodia), Ke Lan (Institut Pasteur of Shanghai), Richard Njouom (Pasteur Centre in Cameroon).
All collaborators and the populations of the RIIP.

## INSTITUT PASTEUR

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- All collaborators at the Institut Pasteur.

## AND ALSO

The Agency of translation id2m and the Agency Avantgarde.

# …and partners

## FRENCH AND INTERNATIONAL MINISTRIES AND AGENCIES

- French Agency for Development (AFD)
- American Centers for Disease Control (CDC)
- Department of Health and Social Services (DHSS)/ASPR
- U.S. Agency for International Development (USAID)
- French Ministry of Foreign and European Affairs (MAEE)
- French Ministry of Higher Education and Research (MESR)
- Ministries from the countries of RIIP
- French Ministry of Health
- Union for the Mediterranean (UPM)
- Mexican National Council for Science and Technology (CONACYT)
- Friends of the Global Fund
- RIKEN (Japanese research institution for science and technology)

Numerous French national research institutions - CEA, CIRAD, CNES, CNRS, IFREMER, INRA, INRIA, INSERM, InVS, IRD, IRES, IMMI - and agencies - ANR, ANRS, AIRD

## INTERNATIONAL ORGANIZATIONS

- World Health Organization (WHO)
- European Union (EU)
- National Health Institutes (NIH)
- European & Developing Countries Clinical Trials Partnership (EDCTP)
- Global Alliance for Vaccines and Immunization (GAVI)

## FOUNDATIONS, ASSOCIATIONS, AND NON-GOVERNMENTAL ORGANIZATIONS

- Bill and Melinda Gates Foundation
- Doctors without Borders (MSF)
- Drugs for Neglected Diseases Initiative (DNDi)
- French Association for Preventive Medicine (AMP)
- Fondation de France
- Fondation Pierre Ledoux Jeunesse Internationale
- Fondation BNP Paribas
- Fondation EDF
- Fondation Mérieux
- Fondation Sanofi Espoir
- Fondation Total
- Francophone University Agency (AUF)
- Medical Research Council
- Multilateral Initiative on Malaria (MIM)
- Rockefeller Foundation
- Wellcome Trust

## PRIVATE SECTOR

- Air France
- Areva
- AXA
- EDF
- Institut Mérieux
- Sanofi-Pasteur
- Veolia



# Abbreviations

| | |
|---|---|
| **AFD** | Agence française de développement (French development agency) |
| **ANRS** | Agence nationale de recherche sur le sida et les hépatites virales (French National Agency for Resesarch on AIDS and Viral Hepatitis ) |
| **BCG** | Bacille Calmette-Guérin (vaccine against tuberculosis) |
| **BSL-3** | Biosafety Level 3 laboratory |
| **CERMES** | Centre de recherche médicale et sanitaire (Niamey, Niger) (Medical and health research center) |
| **CDC** | American Centers for Disease Control and Prevention |
| **ChARLI** | Children's Antibiotic Resistant infections in Low Income countries: an international cohort study |
| **CIBU** | Laboratory for Urgent Response to Biological Threats (Institut Pasteur) |
| **CIRAD** | Centre de coopération internationale en recherche agronomique pour le développement (International Cooperation Center of Agricultural Research for Development) |
| **CNR** | National reference center |
| **DHHS** | Department of Health and Human Services/ASPR – Département américain de la Santé |
| **DNA** | Deoxyribonucleic Acid |
| **EPI** | United Nations Expanded Program on Immunizations |
| **FACS** | Fluorescence Activated Cell Sorting |
| **FAO** | Food and Agriculture Organization of the United Nations |
| **FIOCRUZ** | Oswaldo Cruz Foundation (Rio de Janeiro, Brazil) |
| **FSP** | Priority Solidarity Fund |
| **GLODEN** | Global Network for Dengue Research |
| **HPLC** | High-performance liquid chromatography system |
| **IMMI** | Institut de microbiologie et des maladies infectieuses (Institute of Microbiology and Infectious Diseases) |
| **INSERM** | Institut national de la santé et de la recherche médicale (French National Institute of Health and Medical Research) |
| **NCLE** | National Center for Laboratory and Epidemiology (Vientiane, Laos) |
| **NGO** | Non Governmental Organizations |
| **NIH** | National Institutes of Health (Bethesda, United States) |
| **NIHE** | National Institute of Health and Epidemiology (Hanoi, Vietnam) |
| **OIE** | World Organisation for Animal Health |
| **PCR-(RT)** | (Real-time) Polymerase Chain Reaction |
| **PDVI** | Pediatric Dengue Vaccine Initiative |
| **PTR** | Transversal research program |
| **RIIP** | Institut Pasteur International Network |
| **RIKEN** | Japanese Research Institution for Science and Technology |
| **SRL** | Supranational reference laboratories |
| **TDR** | Rapid diagnostic test |
| **TDR** | Special United Nations tropical disease research and training program |
| **WHO** | World Health Organization |

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