2016

The Institut Pasteur International Network Report

NETWORK

international network
Institut Pasteur

international network
Institut Pasteur

A message from the President of the Institut Pasteur

Over the past two years, the Institut Pasteur International Network has been characterized by the unprecedented strength of the links between its different institutes, which continue to evolve from a group of excellent research, public health and teaching institutions into a true human community with shared values, objectives and missions. The way these institutes in the network united to face the Ebola virus showed the diversity of their expertise, from detecting the virus strain responsible for the epidemic to field deployment supporting local authorities, via remarkable research activities, leading to the publication of high-quality papers in one third of the network's institutes. In the same way, the coordinated response to the Zika virus has led to over 100 publications since 2014, bringing together 16 network institutes.

The organization of an annual Institut Pasteur International Network symposium, the creation of joint units, the systematic involvement of at least two network institutes in Institut Pasteur research incentive programs, the coordination of six research consortia, the creation of 4-year research groups and the promotion of mobility within the network are just some of the elements that are contributing to the gradual construction of a human community among the 23,000 people working for the network. Wherever possible, it is also crucial for the development of an effective, united research community that institutes facing technical difficulties (construction of buildings meeting strict safety standards, installation of high-performance IT tools, creation of biobanks) are provided with assistance. At an institutional level, the new International Network Cooperation Agreement, adopted in 2015, focuses on the sharing of Pasteurian values, and respect for human rights and for the environment.

These joint actions have enabled the Pasteur International Network, the association that represents the network, to establish an official relationship with the WHO and to have a seat at the World Health Assembly. Such a relationship servers as genuine recognition of the network's unique role in global health. In order to accomplish its historic mission to serve global public health, the institutes must continue to develop new research projects, strengthen inter-institutional mobility and establish new partnerships to maintain the unique cohesiveness of their activities within the Institut Pasteur International Network.

Christian Bréchot

"Over the past two years, the Institut Pasteur International Network has been characterized by the unprecedented strength of the links between its different institutes."

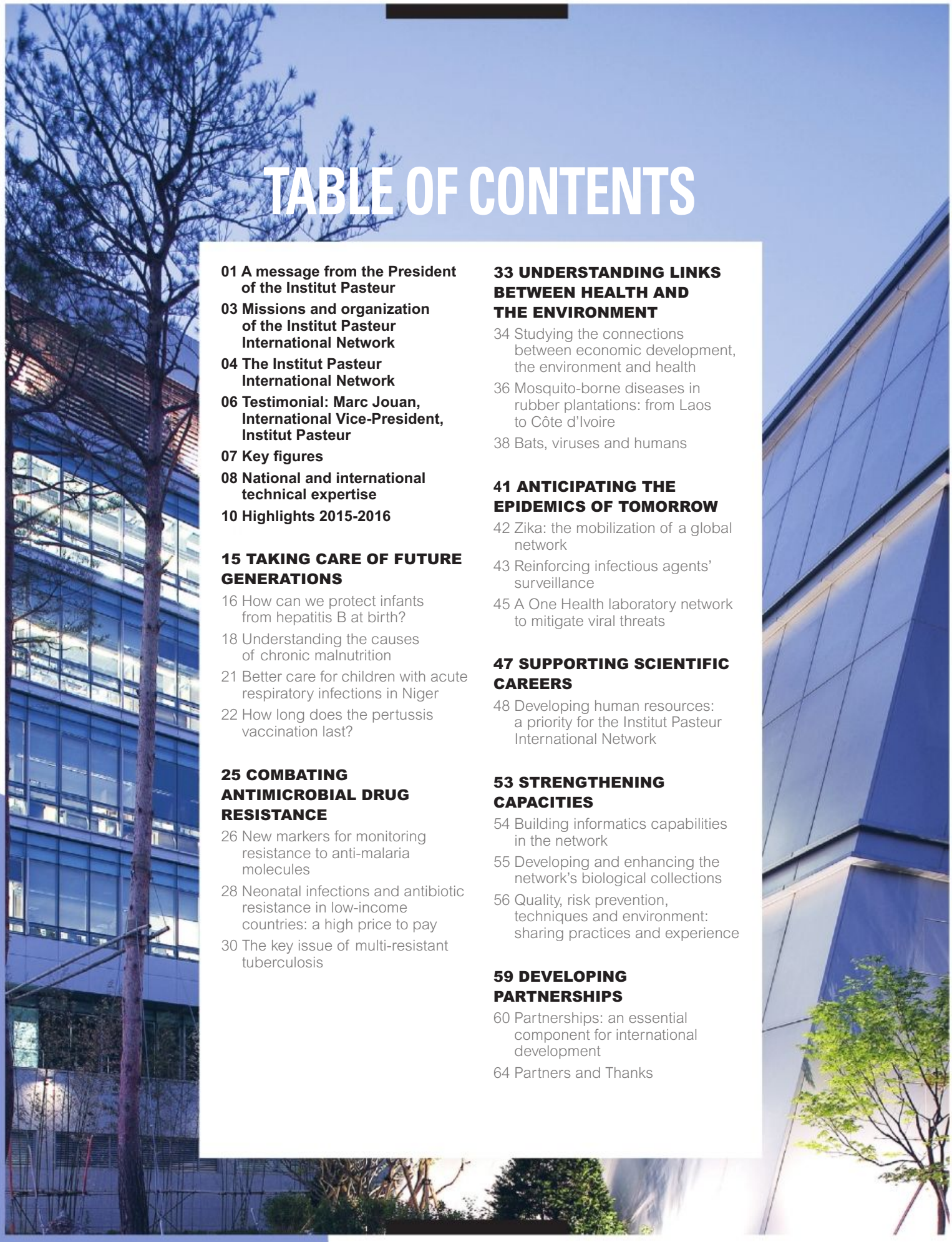


TABLE OF CONTENTS

Missions and organization of the Institut Pasteur International Network

Present in 26 countries across all continents continents, the Institut Pasteur International Network (IPIN) brings together 33 institutions united by shared missions and values for the benefit of local populations.

Beyond its individual structures, as a unique model of cooperation in healthcare, the IPIN brings together a human and scientific community working on both local and international priorities in the field of health. With a strong presence at the heart of several areas struck by endemic and epidemic disease, time and again the IPIN has demonstrated its key role as a sentinel against emerging infections.
The mission of the Institut Pasteur International Network is to contribute to the improvement of human health, in particular relating to infections, through:

- biomedical research;
- public health activities;
- training;
- innovation and technology transfer.

These activities are carried out with a view to promoting sustainable development, based on developing local capacities with respect for human rights and the environment.

The 33 member institutes of the Institut Pasteur International Network, partners and associates in scientific research, public health services and education alliances, have signed the Institut Pasteur International Network Cooperation Agreement, which includes a Charter of Pasteurian Values adopted by all members of the network.

The Council of Directors of the International Network is made up of the directors of each member institute. Chaired by the President of the Institut Pasteur in Paris, the Board meets once or twice per year and elects twelve representatives at the Institut Pasteur's General Meeting. When they meet, the Directors draw up and approve the main areas of development for the International Network and its procedures.

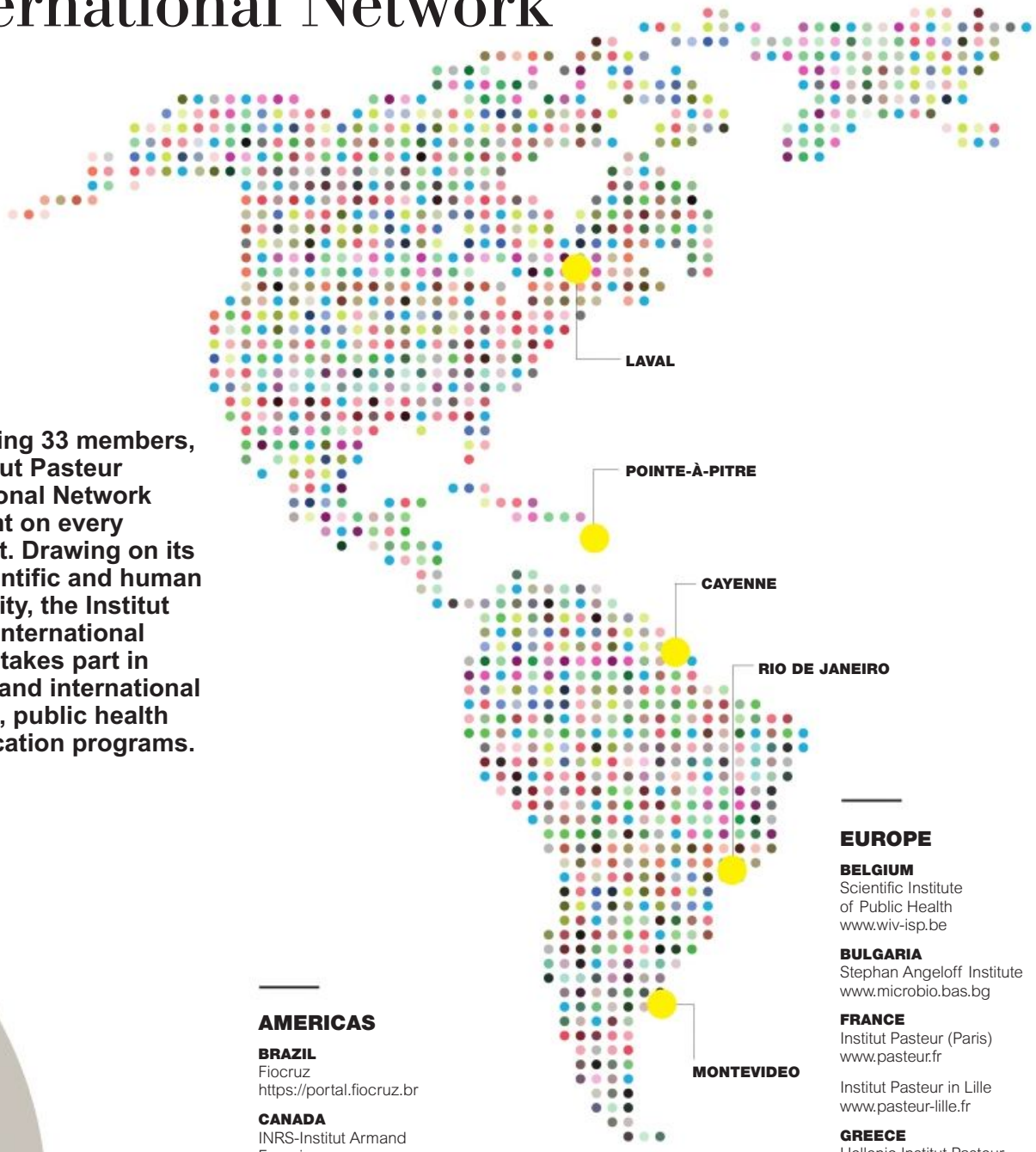
The Pasteur International Network Association, founded in 2011 under the 1901 French law, is the legal entity of the Institut Pasteur International Network. Its membership is made up of the International Network institutes. The Association, chaired by the Institut Pasteur via its President, has two governing bodies: a General Meeting, bringing together all member institutes, a Board of Directors, featuring member institute representatives, elected by region (Africa-Indian Ocean, the Americas, Asia-Pacific, Europe, North Africa-Iran), and representatives from the Institut Pasteur and external co-opted members.
On this basis, it manages the international courses and the organization of regional meetings. It was recognized as an organization in "Official Relations" with the World Health Organization in 2016.

The coordination of joint activities, and participation in the board of directors' and scientific council meetings of International Network member institutes are conducted in close collaboration with the **Department of International Affairs.** This Department also oversees funding and the secondment of personnel to certain institutes from the Institut Pasteur in Paris, with the backing of the French Ministry for Europe and Foreign Affairs and the Ministry for Higher Education and Research.

48th Council of Directors - June 2016.

The Institut Pasteur International Network

Comprising 33 members, the Institut Pasteur International Network is present on every continent. Drawing on its vast scientific and human community, the Institut Pasteur International Network takes part in national and international research, public health and education programs.



AMERICAS

BRAZIL
Fiocruz
https://portal.fiocruz.br

CANADA
INRS-Institut Armand Frappier
www.iaf.inrs.ca

FRANCE
Institut Pasteur in Guadeloupe
www.pasteur-guadeloupe.fr

Institut Pasteur in French Guiana
www.pasteur-cayenne.fr

URUGUAY
Institut Pasteur in Montevideo
www.pasteur.edu.uy

EUROPE

BELGIUM
Scientific Institute of Public Health
www.wiv-isp.be

BULGARIA
Stephan Angeloff Institute
www.microbio.bas.bg

FRANCE
Institut Pasteur (Paris)
www.pasteur.fr

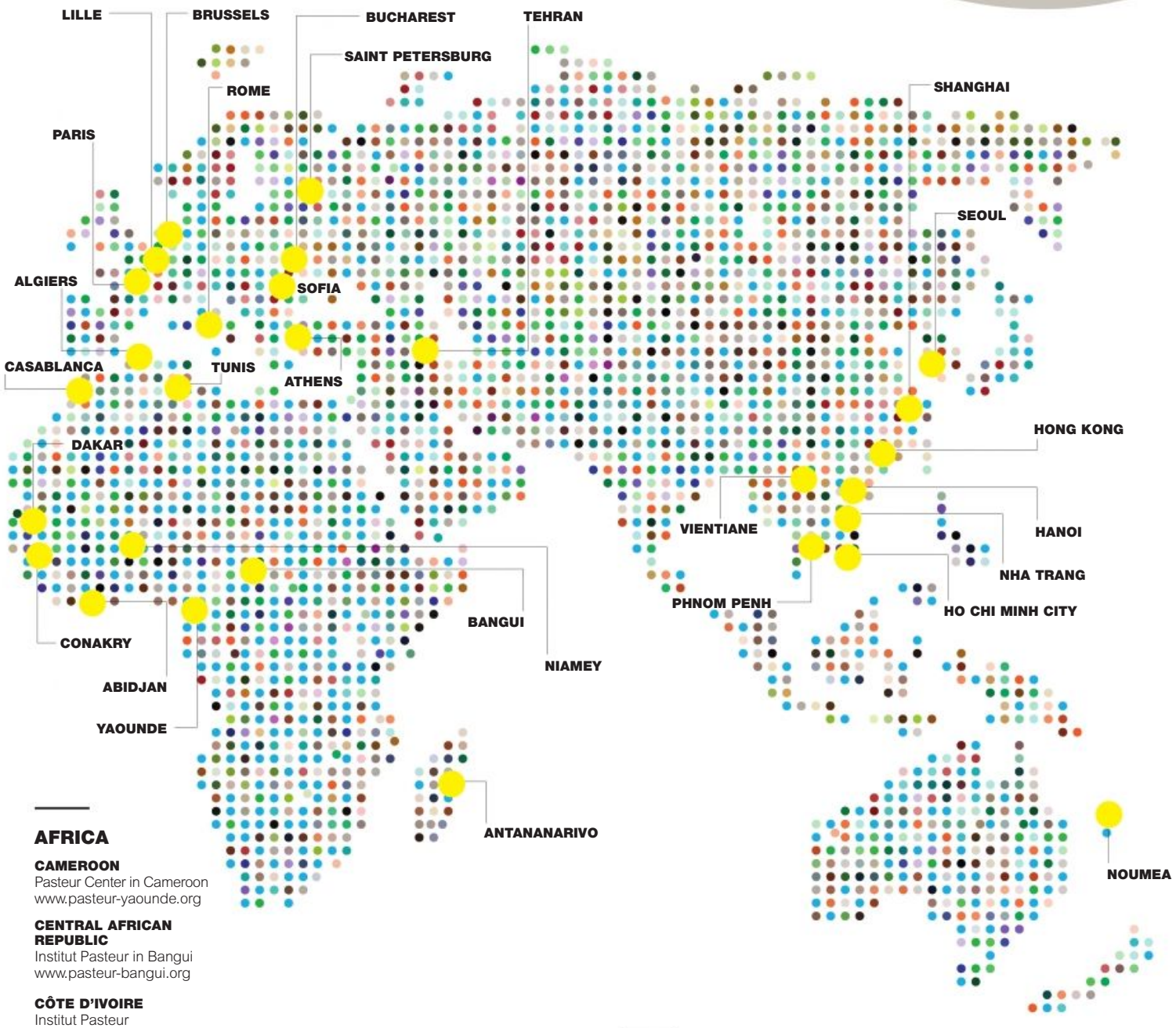
Institut Pasteur in Lille
www.pasteur-lille.fr

GREECE
Hellenic Institut Pasteur
www.pasteur.gr

ITALY
Institut Pasteur – Cenci Bolognetti Foundation
www.istitutopasteur.it

ROMANIA
Cantacuzene Institute
www.cantacuzino.ro

RUSSIA
Institut Pasteur in Saint Petersburg
www.pasteurorg.ru



AFRICA

CAMEROON
Pasteur Center in Cameroon
www.pasteur-yaounde.org

CENTRAL AFRICAN REPUBLIC
Institut Pasteur in Bangui
www.pasteur-bangui.org

CÔTE D'IVOIRE
Institut Pasteur
in Côte d'Ivoire
www.pasteur.ci

GUINEA
Institut Pasteur in Guinea
www.pasteur-guinee.org

MADAGASCAR
Institut Pasteur
in Madagascar
www.pasteur.mg

NIGER
Cermes (Niamey)
www.cermes.net

SENEGAL
Institut Pasteur in Dakar
www.pasteur.sn

MAGHREB-IRAN

ALGERIA
Institut Pasteur in Algeria
www.pasteur.dz

IRAN
Institut Pasteur in Iran
http://en.pasteur.ac.ir/

MOROCCO
Institut Pasteur in Morocco
www.pasteur.ma

TUNISIA
Institut Pasteur in Tunis
www.pasteur.tn

ASIA-PACIFIC

CAMBODIA
Institut Pasteur in Cambodia
www.pasteur-kh.org

CHINA
Hong Kong University –
Pasteur Research Pole
www.hkupasteur.hku.hk

Institut Pasteur in Shanghai
Chinese Academy of Sciences
www.shanghaipasteur.cas.cn

KOREA
Institut Pasteur Korea
www.ip-korea.org

FRANCE
Institut Pasteur in New Caledonia
www.institutpasteur.nc

LAOS
Institut Pasteur in Laos
www.pasteur.la

VIETNAM
National Institute of Hygiene
Epidemiology
www.nihe.org.vn

Institut Pasteur in Ho Chi Minh City
www.pasteurhcm.gov.vn

Institut Pasteur in Nha Trang
p:// asteur-nhatrang.org.vn/

Marc Jouan,
International Vice-President, Institut Pasteur

What makes this international network unique?

One of the unique assets of the Institut Pasteur International Network is its local roots. Despite the crises that some countries have faced, the institutes have always continued to exist. This level of adoption by local supervisory bodies explains the network's longevity. It explains the network's development and its attractiveness for some countries that approach us to create an institute. And this is no mere coincidence. Of course, there is the reputation of the Institut's founder, Louis Pasteur, but also the commitment, day in, day out, of all the people in each institute who produce high-quality diagnostics, respond to health crises, and carry out high-level research, including operational research. This factor sets our members apart from other local laboratories, and constantly leads them to modernize and anticipate future issues. A few years ago, some wondered if our network laboratories should integrate molecular biology. Today, this has become reality and the same question is being asked about new sequencing technologies, omics, and bioinformatics – tools that will support tomorrow's research and public health applications.

Finally, the network is a unit that works in synergy in the field and can mobilize in the event of health crises or sometimes neglected diseases that are a priority at the regional level, such as rabies.

How has the network developed over recent years?

There have been many developments. The mandates of some institutes have been modified so that they are better adapted to their environment, while other institutes have integrated new technologies, and the network has opened up to partnerships. Over the last few years, special attention has been paid to supporting scientific careers with programs such as the 4-year groups, mobilities, and bodies like the CESRI[1] or more recently the Careers Committee.
Our objective is to develop the career paths of the network's researchers and attract talented young scientists. Training is a Pasteurian mission, and it is essential to facilitate the emergence of the men and women who will be tomorrow's scientific leaders of the network. I am pleased that over the last few years we have seen researchers whom we have accompanied over the long-term move into leadership roles in the institutes. This movement, which plays a large part in the local footing of the institutes, should, in my opinion, be emphasized in the coming years.

What are the challenges facing the network today?

We need to anticipate developments in research and help the institutes with specific recruitments, but also modernize the infrastructures and platforms.
The challenges facing public health are also changing with the globalization of infectious diseases, the emergence of chronic diseases and environmental and demographic issues. The One Health approach is today at the heart of these challenges. The network has to take these changes into account, including in its partnerships, by developing ties with players in human and animal health as well as the environment.

(1) International Network scientific evaluation committee.

Key figures

33

members of the Institut Pasteur International Network in 26 countries

Over 23,000

employees

10 to 20

international courses organized every year by the member institutes

166

international scholarships in 2015 and 2016

4

four-year groups created within the RIIP

4

Pasteur international joint research units

National and international technical expertise

The IPIN is home to a large number of national and international reference centers for infectious diseases and antimicrobial resistance. National reference centers act as monitoring centers for transmissible diseases in the countries in which they are situated, while World Health Organization (WHO) collaborating centers carry out a similar role for the WHO network. National and regional reference laboratories are recognized by national health authorities for their expertise in the field of diagnostics.

	WHO Collaborating Centers	Regional reference laboratories
Pasteur Center in Cameroon		Bacteriology, avian influenza, food-borne infections, poliomyelitis
Institut Pasteur in Bangui	Arbovirus, hemorrhagic fevers, influenza, rabies, HIV/AIDS (in renewal)	Poliomyelitis
Institut Pasteur in Côte d'Ivoire		Avian influenza
Institut Pasteur in Dakar	Arbovirus, hemorrhagic fevers	Avian influenza
Institut Pasteur in Madagascar	Plague	Avian influenza
Institut Pasteur in Cambodia		Malaria rapid diagnostic tests program (WHO-FIND)
NIHE (Vietnam)	Occupational health	
Institut Pasteur in Guadeloupe		
Institut Pasteur in French Guiana	Monitoring of resistance to anti-malaria molecules[1]	
Cantacuzene Institute (Romania)[2]	Influenza	Influenza
Hellenic Pasteur Institute		*Leishmaniases, Neisseria gonorrhoeae*
Institut Pasteur in Saint-Petersburg		Poliovirus, yersiniosis, viral hepatitis, measles, rubella, rickettsiae
Scientific Institute of Public Health (Belgium)		Bacterial encephalitis, botulism, food-related microbiology and infections, listeriosis, medical mycology, salmonella, shigella, tuberculosis and myobacteria, toxoplasmosis, viral hepatitis, human papillomavirus, *Bordetella pertussis*, diphtheria, influenza, measles, rubella, mumps, rabies
Institut Pasteur in Algeria		
Institut Pasteur in Iran	Rabies	Arbovirus and hemorrhagic fevers, diphtheria, *Bordetella pertussis*, *Escherichia coli*, rabies, protein chemistry, prenatal diagnosis, national biochemistry, plague, Q fever, tularemia, malaria
Institut Pasteur in Tunis		Poliovirus, measles, human papillomavirus
Fundação Oswaldo Cruz (FioCruz)	Global health and South-South collaboration, public and environmental health, leptospirosis, pharmacological policies, Education of Health Technicians	Malaria, dengue, hantavirus, yellow fever, rotavirus, visceral leishmaniasis

(1) In the Antilles-French Guiana region.
(2) Designated as a competent body for surveillance, response to epidemics and scientific expertise by the European Center for Disease Prevention and Control (ECDC).

National reference laboratories
Influenza, yellow fever, measles, monitoring of antibiotic resistance of gonococci
Measles, rubella, hemorrhagic fevers, rabies, influenza
Arbovirus. Hemorrhagic fevers. Drug resistance of malaria, poliomyelitis, influenza and respiratory viruses, measles, yellow fever, rabies, sexually transmitted infections, viral hepatitis, cholera and shigellosis, bacterial meningitis, salmonella, tuberculosis, Buruli ulcer, diarrhea-causing viruses, molecular typing of infectious agents, evaluation of microbiological diagnostic tests, biological control of antimicrobial vaccines, resistance to anti-infection drugs, hospital-acquired infections
Influenza and respiratory viruses, poliomyelitis, measles, rotavirus
Influenza, poliomyelitis, measles, rubella, arbovirus, rabies, myobacteria, *Vibrio cholerae*, salmonella, shigella
Influenza
Influenza, poliomyelitis
Supranational reference laboratory for tuberculosis
Arbovirus and *virus influenzae*[1], malaria
Poliomyelitis, measles, rubella
Influenza, poliomyelitis, measles, rubella
Influenza, poliomyelitis, rabies prevention, measles, tuberculosis
Salmonellosis, shigella, Vibrio cholerae
Cutaneous leishmaniasis, schistosomiasis (bilharzia), Chagas disease, filariasis, viral hepatitis, rickettsiae, viral exanthema, anthrax, histopathological diagnosis of infectious diseases, enterobacterial infections, influenza, leptospirosis, systemic mycosis, plague, polio and other enteroviruses, surveillance of endemic diseases

NRC AND WHOCC UNDER THE RESPONSIBILITY OF THE INSTITUT PASTEUR (PARIS)

- Anaerobic bacteria and botulism (NRC)
- Whooping cough and other Bordetella (NRC)
- Corynebacterium diphteriae (NRC)
- *Escherichia coli, Shigella, Salmonella* (NRC, WHOCC for *Salmonella*)
- Viral hemorrhagic fevers (NRC, WHOCC)[1]
- Hantavirus (NRC)[1]
- Leptospirosis (NRC, WHOCC)
- *Listeria* (NRC, WHOCC)
- Invasive mycoses and antifungals (NRC)
- Meningococcal infections and *Haemophilus influenzae* (NRC, WHOCC for bacterial meningitis)
- Papillomavirus (NRC)
- Plague and other yersinia bacteria (NRC, WHOCC for *Yersinia*)
- Rabies (NRC, WHOCC)
- Vibrio and cholera (NRC)
- Viral respiratory infections, including influenza (NRC)
- Enterovirus and viral vaccines (WHOCC)

(1) The NRC is part of the Emerging Viral Infections Unit at the International Center for Infectiology Research (Lyon).

Highlights 2015-2016

2015

June

NATIVE CAPSID OF A RETROVIRUS OBSERVED FOR THE FIRST TIME AT THE INSTITUT PASTEUR IN MONTEVIDEO

These unique high-resolution images open up new avenues in developing antiretroviral treatments.

INSTITUT PASTEUR SIGNS A COOPERATION AGREEMENT WITH FIOCRUZ AND THE UNIVERSITY OF SÃO PAULO

Signed on June 8, 2015 in Rio de Janeiro, this tripartite agreement defines the main directions of scientific cooperation between these three major players in research and international public health, and lays the foundations for the project of creation of a future Institut Pasteur in Brazil.

July

TOWARDS A STRONGER PARTNERSHIP WITH MEXICO

On the occasion of the Franco-Mexican convention on Health, the Minister of Health of Mexico and Prof. Christian Bréchot, signed a memorandum of understanding to develop joint research programs.
A second agreement, signed with the Mexican National Council of Science and Technology (CONACYT) will give young Mexican post-doctorate researchers the opportunity to come to the Institut Pasteur laboratories.

September

MALARIA: A MUTATION OF *PLASMODIUM FALCIPARUM* COUNTERACTS CHLOROQUINE RESISTANCE

Described by the parasitology laboratory of the Institut Pasteur in French Guiana, this reversal of chloroquine resistance is made possible by the acquisition of a new mutation rather than the re-emergence of the original form of the parasite.

October

INSTITUT PASTEUR AND THE TOTAL FOUNDATION COMMIT TO CHILD HEALTH

The Institut Pasteur is launching four new international research programs on environmental pediatric enteropathy (malnutrition), hepatitis B, whooping cough, and hand, foot and mouth disease.
With €6 million in funding from the Total Foundation, these programs are mainly implemented within the Institut Pasteur International Network.

November

ALBERT II OF MONACO – INSTITUT PASTEUR AWARD

Presented to Samuel Myers, MD, an epidemiologist and researcher at the University of Harvard School of Public Health, this biennial prize rewards a researcher who has made an outstanding contribution to the study of the impact of environmental changes on human health.

INSTITUT PASTEUR IN HO CHI MINH CITY CELEBRATES 125 YEARS

Founded in 1891 by Albert Calmette in the city then known as Saigon, this Institut Pasteur was the first to be established outside of France.

Discovery | Institutional | Award/Appointment | Event | Scientific event | Birthday

DENGUE: ASYMPTOMATIC PEOPLE TRANSMIT THE VIRUS TO MOSQUITOES

Scientists at the Institut Pasteur in Cambodia, the Institut Pasteur in Paris and the CNRS have challenged a dogma in Dengue epidemiology, providing proof that people infected by dengue virus but showing no clinical symptoms play an essential role in the virus chain of transmission.

AGENCE UNIVERSITAIRE DE LA FRANCOPHONIE (AUF) AND INSTITUT PASTEUR SIGN A PARTNERSHIP AGREEMENT

This agreement will enable an international call for applications to be launched for candidates to head up two 4-year groups within the IPIN. These 4-year groups will propose research projects covering neglected or tropical infectious diseases, involving member universities of the AUF network.

December

DIDIER MÉNARD, WINNER OF THE ELOI COLLERY PRIZE FROM THE FRENCH ACADEMY OF MEDICINE

As Head of the Molecular Epidemiology of Malaria Unit at the Institut Pasteur in Cambodia, he is recognized for his works relating to "the understanding of the cellular and molecular mechanisms associated with the resistance of *Plasmodium falciparum* to derivatives of artemisinin."

IN 2015, THE INSTITUT PASTEUR IN FRENCH GUIANA CELEBRATED 75 YEARS OF RESEARCH AND SUPPORT TO PUBLIC HEALTH

2016

January

INSTITUT PASTEUR IN FRENCH GUIANA PUBLISHES THE FIRST COMPLETE GENETIC SEQUENCING OF THE ZIKA VIRUS CIRCULATING IN THE AMERICAS

Following the confirmation of the first cases of infection in Suriname and French Guiana in November 2015, the Institut Pasteur in French Guiana publishes in *The Lancet* the full sequence of the Zika virus genome, responsible for the unprecedented epidemic on the American continent. It shows the almost complete homology with the strains responsible for the 2013 and 2014 epidemic in the Pacific.

PASTEUR INTERNATIONAL NETWORK RECOGNIZED AS AN NGO IN OFFICIAL RELATIONS WITH THE WHO

This inclusion in the Official Relations of the WHO will strengthen the collaboration between the Institut Pasteur International Network and the United Nations public health institution.

Highlights 2015-2016

May

INSTITUT PASTEUR IN BANGUI WELCOMES FRENCH AND CENTRAL AFRICAN PRESIDENTS

Despite successive political crises and civil wars, the Institut Pasteur in Bangui has never interrupted its mission to serve the Central African population.

INSTITUT PASTEUR INTERNATIONAL NETWORK ASIA-PACIFIC REGIONAL MEETING AT THE INSTITUT PASTEUR IN SHANGHAI – CHINESE ACADEMY OF SCIENCES

70 participants were present at this meeting held from May 18-20. The attendance of representatives from the Myanmar National Health Laboratory and four Australian research institutions illustrated the strength of the partnerships that have been founded in the region.

INSTITUT PASTEUR AND CNES SIGN A FRAMEWORK COOPERATION AGREEMENT

This five-year agreement aims to promote the development of projects using space technologies in biomedical research, particularly in French Guiana.

INSTITUT PASTEUR IN KOREA DRUG DISCOVERY BOOSTER PROGRAM WINS DNDI PROJECT OF THE YEAR PRIZE

This project aims to reduce drug discovery costs, and strengthen and accelerate the emergence of new drugs for two of the most neglected diseases in the world – Chagas disease and leishmaniasis.

June

CREATION OF THE PASTEUR JAPAN FOUNDATION

The objective of the Foundation is to support research and researcher exchange programs to stimulate cooperation between the Japanese scientific community and the Institut Pasteur International Network.

July

INAUGURATION OF A NEW MALARIA RESEARCH LABORATORY AT THE PASTEUR CENTER IN CAMEROON

Directed by Dr Lawrence Ayong, head of a 4-year group since 2013, the creation of this laboratory is a major step forward for research in this field. Malaria remains a key concern for the country and the region.

August

INSTITUT PASTEUR IN BANGUI CONFIRMS CHOLERA EPIDEMIC IN BANGUI CITY

With the confirmation of the presence of the bacteria responsible for cholera in the feces of five patients living along the Oubangui river, the Institut Pasteur in Bangui alerted the Central African health authorities to a possible epidemic outbreak.

September

DISCOVERY OF A THIRD PLAGUE-CARRYING FLEA *(XENOPSYLLA BRASILIENSIS)* BY THE INSTITUT PASTEUR IN MADAGASCAR

Already known in other countries, this species was detected for the first time in Madagascar, highlighting the key role played by the Institut Pasteur in fighting this disease.

Discovery | Institutional | Award/Appointment | Event | Scientific event | Birthday

October

AVELIN FOBANG AGHOKENG: DEDONDER CLAYTON PRIZE 2015; OANH THI HAI KHUAT: DEDONDER CLAYTON PRIZE 2014

Avelin Fobang Aghokeng, a researcher at IRD (Cameroon), has been awarded for his work on the Test & Treat approach to HIV infections. He follows Ms Oanh Thi Hai Khuat, head of the NGO Center for Supporting Community Development Initiatives (Vietnam), who won the prize in 2014 for her project on marginalized adolescents.

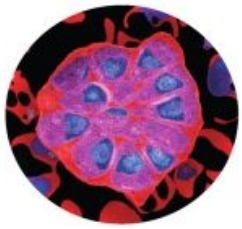
November

THE PRESIDENT OF THE REPUBLIC OF GUINEA LAYS THE FIRST STONE OF THE INSTITUT PASTEUR IN GUINEA

This event marks the official start of the construction works. The mission of the Institut Pasteur in Guinea, founded in October 2015, is to respond to epidemic emergencies and to participate in infectious disease surveillance and research.

MAGHREB AND IRAN INSTITUT PASTEUR REGIONAL MEETING

Organized at the Institut Pasteur in Iran on November 7-9, 2016, this meeting dealt with four main issues: vector-borne diseases, tuberculosis, leishmaniasis and snake/scorpion toxins and venoms.



MOLECULAR MARKER ASSOCIATED WITH RESISTANCE TO PIPERAQUINE TREATMENT DISCOVERED

A team of researchers, including scientists from the Institut Pasteur in Cambodia and Institut Pasteur in Paris, has identified a molecular marker for detecting the parasites responsible for piperaquine-resistant malaria. This discovery should pave the way for better monitoring of the emergence of resistance to this latest-generation treatment.

SIGNATURE OF AN AGREEMENT WITH THE UNIVERSITY OF KYOTO FOR THE CREATION OF AN INTERNATIONAL JOINT RESEARCH UNIT

The first international joint research unit has been established between Institut Pasteur and University of Kyoto. The scientists involved will work on immune responses to the influenza vaccine.

December

2016 INTERNATIONAL NETWORK SYMPOSIUM

Dedicated to biomarkers, the 3rd Institut Pasteur International Network Symposium took place from November 29 to December 2. In line with the previous event, this symposium brought together scientists from all of the member institutes of the Institut Pasteur International Network, highlighting the strength and quality of research being carried out.

AGREEMENT TO CREATE 3 INTERNATIONAL JOINT UNITS WITHIN THE IPIN

Three International Joint Research Units have been created to strengthen research collaboration within the network: with the Institut Pasteur in Cambodia on malaria, Montevideo on leptospirosis, and Shanghai on leishmaniasis.

10 YEARS OF THE INSTITUT PASTEUR IN MONTEVIDEO

This institute, with around 100 researchers, has become a regional reference point for research and technology.

PASTEURIAN

"Malnutrition is one of the major threats to child health in Madagascar."

In Madagascar, chronic malnutrition is a major health issue. For almost the last 25 years, the proportion of children under 5 years old presenting delayed development typical of this form of malnutrition has remained near 50%. In addition, 8% of Malagasy children suffer from acute malnutrition, associated with an increased risk of death, particularly for the severe form. Since 2013, the Institut Pasteur in Madagascar has taken part in research projects aiming to better understand the epidemiology of malnutrition in Malagasy children and improve the diagnosis of its causes and its care.

RINDRA RANDREMANANA
Epidemiologist, deputy-head of the epidemiology unit and leader of the nutrition thematic unit at the Institut Pasteur in Madagascar

Taking care of future generations

Between 1990 and 2015, international efforts have led to the reduction of child mortality by over 50%. Despite this remarkable progress, 6 million children die across the world each year before reaching the age of 5. The large majority of these deaths take place in sub-Saharan Africa and Southeast Asia.
Taking care of future generations therefore remains a priority for all global health players.

Wherever they are located, members of the Institut Pasteur International Network contribute to improving access to disease prevention, diagnosis and care for young children.
Several research programs are underway across the network to combat the main causes of childhood diseases such as whooping cough, hepatitis B, tuberculosis, bacterial infections, encephalitis and malnutrition, which we today know is linked to 45% of annual deaths of children under five. These multidisciplinary programs aim to define the origin of these diseases and develop effective interventions for the benefit of children.

How can we protect infants from hepatitis B at birth?

Infection with the hepatitis B virus (HBV) is a significant cause of adult deaths in sub-Saharan Africa. Every year, 61,000 people die from hepatocellular carcinoma (liver cancer) or cirrhosis associated with a chronic HBV infection. Yet the majority of chronic carriers of the hepatitis B virus affected by a liver disease are infected by their mother at birth. To prevent this transmission, since 2009, the WHO has recommended the immunization of newborns within 24 hours of birth using a monovalent anti-HBV vaccine. However, in sub-Saharan Africa, only 11% of newborns are currently vaccinated within this timeframe. This problem is particularly complex in a region of the world where a significant proportion of women still give birth at home and where availability of the monovalent vaccine remains limited.

What locally-adapted and sustainable strategies or practices would allow the trend in anti-hepatitis B vaccination at birth to be improved? To answer this question, in 2015 the Institut Pasteur, in partnership with the Institut Pasteur in Dakar and in Madagascar and the LAMIVAC consortium in Burkina Faso, the NeoVac research program[1]. In these three countries, the prevalence of chronic hepatitis B is high (8%), as is the neonatal mortality rate, although each country has its own specificities in relation to health care and the solidity of the health system.

Identifying the best strategy for increasing vaccination coverage at birth

A preliminary study, coordinated by Muriel Vray, Head of the Infectious Disease Epidemiology Unit at the

(1) Neonatal Vaccination against hepatitis B in Africa. (2) Systematic review with meta-analysis: the risk of mother-to-child transmission of hepatitis B virus infection in sub-Saharan Africa. Keane E, Funk AL, Shimakawa Y. Aliment Pharmacol Ther. 2016 Nov; 44(10):1005-1017.

Institut Pasteur in Dakar and Yusuke Shimakawa, from the Epidemiology of Emerging Diseases Unit at the Institut Pasteur, is currently underway in three partner countries. It will measure, on the epidemiological level, the proportion of home births, vaccinated newborns and their mortality rates. Health economists will examine the economic feasibility of the different potential options for delivering the HBV vaccine at birth as well as other postnatal care in medical units and at home in the three study countries. This data will be complemented by an anthropological analysis *(see page 20)* in order to obtain a precise cartography of the local contexts.

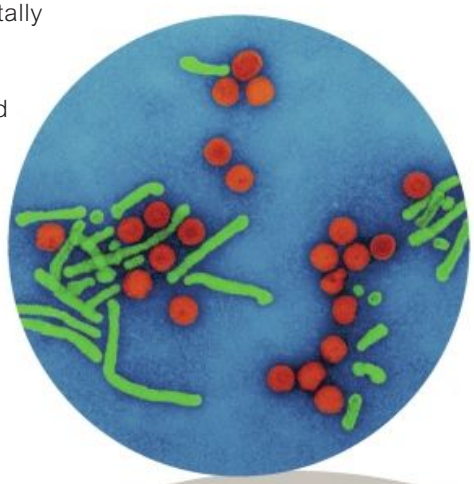
A large international study including almost 4,500 newborns

The data obtained during the preliminary study will serve as a basis to implement a major intervention in Senegal, Madagascar and Burkina Faso.
In each country, 12 communities of between 50,000 and 190,000 subjects (depending on the country) will be selected. Six of these communities will receive the intervention identified during the preliminary study, while the six others will act as control populations to assess the impact of the intervention on vaccination coverage at birth.
This research program will provide essential data for governments, international organizations and funding providers to implement a prevention and care strategy for hepatitis B in low- and middle-income countries

SUPPORT
NeoVac is supported by the Total Foundation.

THE NUMBER OF NEWBORNS INFECTED WITH HEPATITIS B MAY BE TWICE AS HIGH AS HIV IN SUB-SAHARAN AFRICA

While the risk of mother-to-child transmission of Hepatitis B is well documented in Asia, data regarding the situation in Africa are still scarce. In an article published in *Alimentary Pharmacology & Therapeutics*[2], epidemiologists from Institut Pasteur, Ecole Pasteur/ CNAM de Santé Publique (Paris) and *Mater Misericordiae* University Hospital (Dublin), estimate that more than 360,000 infants in sub-Saharan Africa are infected with the Hepatitis B virus (HBV) at birth each year. This figure is almost twice the annual number of newborns perinatally infected with HIV in this region (around 190,000 per year).
The scientists conducted a systematic review and meta-analysis to estimate the risk of mother-to-child transmission of HBV in sub-Saharan Africa. They identified fifteen studies from 11 African countries that enrolled infants born from HBV-infected women and that tested the infants aged between 3 and 12 months for Hepatitis B infection.
The results show that the risk of mother-to-child transmission of Hepatitis B is 5% when the mother is negative for HBe antigen (a marker of high viral replication), but it goes up to 38% when the mother carries this antigen.
"Mother-to-child transmission of Hepatitis B virus has so far been neglected in sub-Saharan Africa. Our result clearly highlights the need for implementing prevention strategies, in particular vaccination of all newborns," explains Dr Yusuke Shimakawa, from the Epidemiology of Emerging Diseases Unit at the Institut Pasteur.



Understanding the causes of chronic malnutrition

One in four children under the age of five globally suffers from malnutrition. It is involved in almost half of child deaths – over 3 million children under five every year. Malnutrition is also responsible for significant physical and mental developmental abnormalities. Undernourished children have diminished cognitive performance and severe learning difficulties. Malnutrition also feeds the vicious circle of poverty, having a serious impact on the opportunities for the socio-economic development of future generations.

The lack of food or inadequate nutrition practices are not, however, the only causes of undernutrition. Poor sanitary and hygiene conditions in resource-limited countries continously expose children to infectious agents. This permanently weakens their immune systems and provokes chronic intestinal inflammation, known as “pediatric environmental enteropathy (PEE)”. It is estimated that over 75% of children in developing countries suffer from this condition to varying degrees. This syndrome, which prevents the intestines from working properly, is today recognized as a major cause of malnutrition. However, scientific data on PEE is almost non-existent.
Carried out in partnership with the Institut Pasteur in Madagascar and in Bangui – located in two countries where the proportion of malnourished children is particularly high – the Afribiota project aims to identify markers for diagnosing pediatric environmental enteropathy, measuring the number of children suffering from this syndrome (prevalence) and better understand the biological mechanisms behind it. These results will form the basis for developing prevention and treatment strategies in order to improve the nutritional status, development and immunity of malnourished children.

An unprecedented multidisciplinary approach for understanding pediatric environmental enteropathy

Led by Prof. Philippe Sansonetti and Dr. Pascale Vonaesch, this research project proposes, for the first time, to address pediatric environmental enteropathy in all its complexity.
A diagnostic and epidemiological study will allow different biological markers for PEE to be compared in malnourished children (severely or moderately) and normally nourished children with the aim of developing a diagnostic test that is easy to use in the field. This study will also provide a first estimate of the number of children suffering from this intestinal inflammation in Madagascar and in the Central African Republic.

At the same time, **a medicoanthropological study** will analyze feeding, hygiene and childcare practices, the attitudes of parents to illness, and the economic and political context in order to understand why some children develop PEE and others do not. In Bangui, this aspect has already revealed certain beliefs and practices amongst parents of malnourished children.

A study of the intestinal flora (microbiota) and barrier is currently underway to better define the biological changes to the intestine as a result of PEE, including chronic inflammation, and potentially identify new markers of this syndrome.

An immunological study is also underway to understand why response to vaccines is lessened in malnourished children.

A psychomotor development study will be conducted for all children recruited to the study. Taking into account the cultural context of the two partner countries, a standardized test was developed to evaluate a number of criteria (language, motor skills, cognitive skills) and identify possible links between PEE, malnutrition and psychomotor issues.

Ultimately, a mathematical model will bring together all the data from each study to provide a holistic overview of PEE to be used as a basis for developing prevention and treatment strategies and improve the nutritional status, development and immunity of malnourished children.

SUPPORTS

Afribiota is supported by the Total Foundation and the Nutricia Research Foundation.

AFRIBIOTA – A PROJECT THAT SUPPORTS SKILLS TRANSFER

The project includes a significant component relating to the strengthening of local skills, focusing on training for pediatricians on malnutrition and gastroenterology. Jean-Louis Demarquez, a professor of pediatrics in Bordeaux, France, was involved as an expert in the training of 45 doctors and other healthcare professionals in Bangui and Antananarivo. This training will allow the needs of the project to be met, but also takes into account the expectations of local doctors, covering subjects which include perinatal asphyxia and nutrition for newborns.

Tamara Giles-Vernick leads the Medical Anthropology and Environment group in the Epidemiology of Emerging Diseases Unit at the Institut Pasteur.

Anthropology highlights the practices, concepts, priorities and politico-economic processes that are connected with diseases, transmission risks, or which will encourage or hinder the implementation of a health intervention. It is above all field work, thanks to which we can gather the viewpoints of those concerned, families, healthcare professionals, traditional healers etc. and observe their behavior. Sometimes there is a difference between what people say and what they actually do. With a project like Afribiota, parents describe best hygiene practices for their child perfectly. But we very quickly see that they may not apply them. There are various potential reasons for this difference, ranging from a lack of availability of soap to the consequences of political or economic crises in the countries concerned. Our role is to substantiate the logic that underpins these everyday practices and understand their impact on the children.

One of the main tools in our work is participant observation, which allows us to really immerse ourselves in the local population. We also use discussion groups and interviews. We define initial questions, but the fluidity of anthropology lies in the flexibility of our approach, which adapts to whatever the participants show or tell us. As part of the Afribiota program, we are looking at using the "photovoice" approach for the first time. Members of the community are asked to photograph places that, in their opinion, are a source of malnutrition, and explain their choices. This technique allows us to collect data and really involves the populations in the analysis stage so that we can develop interventions that meet the needs of parents of malnourished children.

"Anthropology is above all field work."

For the NeoVac project, which is evaluating the possibility of introducing a hepatitis B vaccine at birth with a package of other neonatal interventions, our approach is different. Our questions relate to births at home or on a maternity ward. Of course, the distance from home to hospital is a significant factor, but it is not the only one. Sometimes, the family-in-law influence the decision.

In some circumstances, it may also be linked to the idea that a "strong" woman should give birth at home. We have also observed that in some countries women are intimidated by healthcare professionals and prefer to stay home for that reason. Anthropology allows us to identify these issues and analyze them in order to define, together with the epidemiological and economic components of the project, the strategy that will be best suited to each country.

This approach is really unique. To my knowledge, there are very few clinical trials where anthropology is involved in the development of a health intervention to this degree. In my opinion, it is a model to be followed.

Better care for children with acute respiratory infections in Niger

In Niger, respiratory infections and pneumonia are the second cause of mortality in hospitalized children (10 to 20% of deaths according to information from health authorities). As in most African countries, little data on surveillance and etiology of these infections is available, although it is essential for guiding public health policies. Furthermore, in Niger, antibiotic treatment for acute respiratory infections is often given on the basis of clinical signs, with no biological analyses.

On July 21 2016, a ceremony at the Center for Medical and Health Research (CERMES) in Niamey marked the end of the Tonira project. Led by Dr. Jean-Paul Moulia-Pelat and started up in 2013, this project assessed the effectiveness of enhanced monitoring of children aged five years and under who have been hospitalized for respiratory infections.

In total, 791 children with respiratory infections were included in the project, and benefited from medical care. *"We set up an unprecedented organization in Niger. At each partner site, we used a test that detects the presence of pneumococcus in children in ten minutes, using a urine sample. These rapid results guide doctors in prescribing the right antibiotic,"* explains Dr. Moulia-Pelat. In fact, pneumococcus turned out to be the most frequently observed infectious agent, particularly during the first half of the year. This bacterium is also responsible for meningitis. The project also demonstrated the need to encourage the use of hemocultures in pediatrics units in Niamey National Hospital and Lamordé Hospital for better specific diagnosis.

In three years, Tonira has strengthened the technical skills and training of the staff of CERMES and the main hospitals in Niamey. It provided a starting point for genuine collaborative momentum between these structures thanks to which it is today possible to envisage future public health activities.

The final report, presented to the Ministry of Health of Niger and to partners, recommends introducing a health card enabling all healthcare professionals to better understand patients' medical histories and for better monitoring.

SUPPORT
Tonira is supported by the Total Foundation.

How long does the pertussis vaccination last?

Whooping cough is a highly contagious respiratory disease caused by the bacterium *Bordetella pertussis,* and which can be serious, or even fatal, for infants.
Most newborn deaths occur in Africa and Asia, where the percentage of children who are given primary vaccination (6-10-14 weeks) with the diphtheria, tetanus and pertussis (DTP) vaccine is very variable[1].

Studies conducted in developed countries have shown that this primary vaccination gives excellent protection from the disease, but that this protection only lasts a short length of time. Booster vaccinations were therefore introduced for children, adolescents and adults, so that they do not transmit the disease to unprotected 6-week-old babies. This vaccination strategy is not widely applied in low- and middle-income countries, where few studies have been carried out. Specifically, no studies have evaluated the period of protection given by the most commonly used whooping cough vaccine, the “whole cell” vaccine that is made from dead whole bacteria. These vaccines, often produced locally, have uncertain characteristics in terms of duration of protection. It is therefore difficult to know the age at which this vaccine booster should be given, particularly as studies conducted in industrialized countries with similar vaccines indicated the inconsistency of the vaccines used. What is the duration of protection for vaccines currently used in countries with limited resources?

A unique study into whooping cough in four regions of the world

The Institut Pasteur launched the Perilic[2] project in 2015 in an attempt to answer this question. Coordinated by Fabien Taieb – a doctor affiliated with the Institut Pasteur Translational Research Center responsible for coordinating clinical research across the Institut Pasteur International Network – and carried out in partnership with the Institut Pasteur in Cambodia, in Iran and in Madagascar as well as the Agency for Preventive Medicine in Togo, the Perilic project will provide an unprecedented data set on whooping cough.

A first study is currently underway in the four partner countries. This will enable the duration of protection provided by primary vaccination at 6-10-14 weeks with the whole-cell vaccines used in these four countries to be assessed. For this, in every country, the immunity induced by the vaccination of 800 children and adolescents aged between 3 and 15 with known vaccination status will be determined. The children will mainly be recruited from kindergartens and grade schools following parental consent. Vaccine-induced immunity will be detected from a small blood sample taken from a fingertip.
A second study, conducted in Cambodia, Iran and Madagascar, will document the clinical and microbiological characteristics

(1) Pertussis vaccines: WHO position paper, August 2015. (2) PERtussis In Low and middle Income Countries.

of infants under 6 months hospitalized for signs of whooping cough, and examine the source of contamination in the family environment of the infants with a positive lab-confirmed diagnosis of whooping cough.
Two hundred infants will be recruited from the hospitals participating in the study, as well as the persons in closest contact with the infected infants.

This data will be particularly important for **adapting the vaccination strategy in countries with limited resources and determining the characteristics of the vaccines used.**
The technology needed to detect and identify the bacterium responsible for whooping cough will be transferred to partner laboratories for the first time, and training provided for healthcare professionals.

The Perilic project will thus form a necessary foundation for implementing long-term monitoring of whooping cough in the partner countries.

SUPPORT

Perilic is supported by the Total Foundation.

IS THE WHOOPING COUGH VACCINE EFFECTIVE? YES… BUT NOT FOR LIFE

The *Bordetella pertussis* bacterium was identified in 1900 by Jules Bordet, microbiologist at the Institut Pasteur (Nobel prize 1919), then isolated in 1906 by Jules Bordet and Octave Gengou. Developed in the 1940s, the whole-cell vaccine reduced the incidence of the disease by 90% in industrialized countries. There are currently two types of vaccine for whooping cough. The “whole-cell” vaccine is made from completely inactivated (harmless) bacteria. The “acellular” vaccine only contains purified elements of the bacterium. The latter is much more expensive to produce but causes fewer side effects and is the most commonly used form in industrialized countries. Neither vaccine (nor the infection itself) provide immunity for life, and the protection decreases over time. This means it is possible to get the disease several times in your life. The resurgence in the global incidence of whooping cough led the WHO to list this disease as one of the major causes of child mortality in 2014.

PASTEURIAN

"Today we can track resistance to anti-malaria molecules virtually in real-time."

The Malaria Molecular Epidemiology Unit at the Institut Pasteur in Cambodia is examining the resistance of malaria agents to the drugs in use, and more specifically the molecular markers that enable us to track this resistance. Researchers from this unit contributed to the identification of a marker associated with resistance to artemisinin in the *Plasmodium falciparum* parasite in 2014. Based on this discovery, the same researchers participated in establishing the first global mapping of resistance to this molecule. In 2016, they also helped to reveal another marker associated with resistance to piperaquine in the same parasite.

NIMOL KIM
Researcher in the Malaria Epidemiology Unit at the Institut Pasteur in Cambodia

Combating antimicrobial drug resistance

The development of effective treatments for pathogens, particularly antibiotics, is one of the major advances of modern medicine. Today, the emergence of pathogens resistant to these treatments poses a threat to global public health.

It is estimated that 700,000 people die across the world every year due to the resistance to treatment of infections including bacterial infections, malaria, HIV/AIDS and tuberculosis. By 2050, antibiotic resistance alone could be responsible for 10 million additional deaths(1).
Strongly committed to resolving this global public health emergency, the members of the International Network are conducting several programs to evaluate, monitor and control resistant strains at the epidemiological level, as well as developing new diagnostic and treatment tools.

(1) Tackling drug-resistant infections globally: final report and recommendation – May 2016.

New markers for monitoring resistance to anti-malaria molecules

Since 2008, the emergence in Cambodia of strains of *Plasmodium falciparum* resistant to artemisinin derivatives, the latest generation of anti-malaria drugs, has seriously jeopardized global efforts to combat malaria. More recently, multi-resistant parasites have appeared in Cambodia and Thailand. The situation is even more worrying given that therapy failure rates of up to 60% are currently being observed in patients treated with artemisinin/piperaquine combination in certain regions of Cambodia, due to the ability of parasites to resist both molecules.

First global mapping of artemisinin resistance

In 2014, researchers from the Malaria Epidemiology Unit at the Institut Pasteur in Cambodia and the Institut Pasteur Parasite and Insect Vector Department were responsible for identifying certain mutations of the *P. falciparum* K13 gene associated with artemisinin resistance.
Building on the discovery of this molecular marker, Pasteurian researchers created the KARMA[1] consortium, bringing together 41 international partners including 13 members of the Institut Pasteur International Network in order to establish a global mapping of artemisinin resistance. Between May and December 2014, they analyzed 14,037 blood samples from patients infected by *P. falciparum,* coming from 59 different countries (72% in Africa, 19% in Asia, 8% in Latin America and 1% in Oceania).
All the samples analyzed were collected after 2012, to ensure the most possible up-to-date overview of the situation. Published in June 2016 in the *New England Journal of Medicine,* this study of unprecedented scale shows that, for the moment, the strains of *Plasmodium falciparum* resistant to artemisinin are confined to Southeast Asia, where the situation remains worrying[2]. In this region, two focal points for the emergence of artemisinin-resistant parasites were identified. However, these two areas (Cambodia-Vietnam-Laos

ALMOST HALF THE WORLD'S POPULATION IS EXPOSED TO MALARIA

Caused by *Plasmodium* parasites, every year malaria affects over 200 million people and is responsible for almost 429,000 deaths, mainly in sub-Saharan Africa where *Plasmodium falciparum* is the most common parasite. Currently, there is no effective vaccine and the treatment of simple *Plasmodium falciparum* malaria episodes is based on the use of a combined treatment with an artemisinin derivative (artesunate, artemether or dihydroartemisinin) and a drug with a long half-life, such as piperaquine, mefloquine, amodiaquine or lumefantrine.

(1) KARMA: K13 Artemisinin Resistance Multicenter Assessment Consortium. (2) A Worldwide Map of Plasmodium falciparum K13-Propeller Polymorphisms, D. Ménard, N. Khim, et al. N Engl J Med. 2016 Jun 23; 374(25):2453-64. (3) Witkowski B, Duru V, et al. A surrogate marker of piperaquine-resistant Plasmodium falciparum malaria: a phenotype-genotype association study. Lancet Infect Dis. 2017 Feb;17(2):174-183.

and Myanmar-western Thailand-southern China) are independent, suggesting that the international strategies have probably contained the dissemination of the resistance for the time being.
The KARMA study also revealed that the number of mutations to the K13 gene associated with resistance is limited and that the most commonly observed mutation in Africa (A578S) is not one of these.

Molecular marker associated with resistance to piperaquine

More recently, the same teams of Pasteurian researchers were involved in identifying another molecular marker of resistance, this time to piperaquine[3]. In resistant strains, scientists observed an increase in the number of copies of two genes, plasmepsin 2 and 3, which code for enzymes that contribute to breaking down hemoglobin in infected red blood cells. Furthermore, they also showed that when parasites have both this "molecular signature" and a K13 gene mutation providing resistance to artemisinin, the risk of failure for the first-line treatment recommended in Cambodia was over 20 times higher. At the same time, this study also showed that the amplification of these genes systematically coincides with a reduction in the number of copies of the MDR1 (multi drug resistance-1) gene associated with resistance to mefloquine. The authors therefore suspect that the emergence of piperaquine resistance coincides with regained efficacy of mefloquine. This discovery means that monitoring strategies can be proposed to ensure effective therapeutic combinations adapted to epidemiological evolutions are implemented.

Following the emergence of resistance in real time

"The KARMA project shows us that today it is possible to track resistance to anti-malarials at a global level virtually in real time," explains Didier Ménard, head of the Malaria Molecular Epidemiology Unit at the Institut Pasteur in Cambodia. In addition to the K13 marker, the identification of the piperaquine resistance marker should allow scientists to provide a global mapping of multi-drug resistant parasites, identify focal points for emerging outbreaks and take action by deploying effective treatment and appropriate control measures. *"It is imperative that we use these technologies to outpace the parasite and prevent history repeating itself in Africa – the tragic scenario we saw in the 1980s and 1990s with chloroquine,"* continues Didier Ménard. Parasites resistant to chloroquine, the first-generation molecule used to fight malaria, first emerged in Southeast Asia in the late 1960s. Sadly, the molecular markers used to detect this resistance were identified well after these parasites spread to Africa, causing millions of deaths.

SUPPORT
KARMA is supported by the WHO.

Neonatal infections and antibiotic resistance in low-income countries: a high price to pay

The risk of death from neonatal infection is ten times higher in low-income countries than in developed countries. Reducing this mortality is one of the United Nations' Sustainable Development Goals. The emergence of antibacterial-resistant bacteria poses an increasing threat to this goal.

By 2050, antibiotic resistance could cause up to 10 million additional deaths per year, with children under 5 being on the front line. Low-income countries combine a high rate of neonatal infections and an increased risk of emergence and dissemination of antibiotic resistance (overuse/misuse of antibiotics, over-the-counter [OTC] sale, counterfeits, promiscuity and precarious conditions). However, very few studies have actually examined their situation, particularly at the community level.

Documenting neonatal infections and assessing antibiotic resistance status in low-income countries. Implemented in Madagascar in 2012, then in Senegal and Cambodia in 2014, in partnership with the local Institut Pasteur facilities, the BIRDY[1]

(1) Bacterial Infections and antibiotic Resistant Diseases among Young children in low-income countries.

program examines the etiology of bacterial infections in children, estimates their incidence and defines their resistance to antibiotics.
This study, unique in its approach and scope, was conducted in rural and urban communities. Around 3,000 children were monitored from birth by local teams during the first months of their lives. Active monitoring of newborns (regular home visits) and the establishment of a network of pediatricians and community agents mean that each child can be cared for quickly if infection is suspected.

SUPPORTS

BIRDY is supported by the Monaco Department of International Cooperation in Madagascar, the Total Foundation in Senegal and by MSDAvenir in Cambodia.

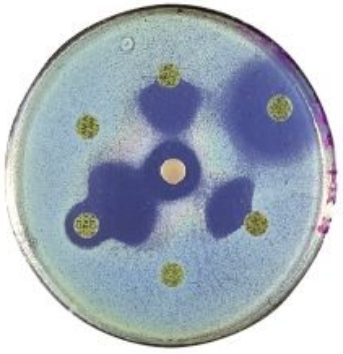
Biological samples, taken where necessary, are analyzed by the local Insitut Pasteur to identify the pathogen responsible for the infection and determine its sensitivity to antibiotics. These results are crucial for adapting antibiotic treatment and optimizing the care of each child. The success of this program lies in a multidisciplinary collaboration between Institut Pasteur International Network scientists and local partners (hospitals, health centers, traditional birth attendants, etc.). BIRDY also ensures the continued training of healthcare professionals and alerts mothers to the signs of infection in children. In the long-term, the data collected with this project should help inform national and international decision-makers of the issue of antibiotic resistance in low-income countries.

An alarming situation in Madagascar

In Madagascar, where 1,000 newborns were monitored during the pilot phase, initial results show an alarming rate of neonatal infections 17.7 per 1,000 live births. As a comparison, this incidence is 0.77 per 1,000 live births in the United States. Additionally, 85% of neonatal infections occur within the first week of life, which clearly reinforces the need to increase public health efforts for this crucial period. Another worrying observation: 70% of these infections do not respond to the treatments recommended by the WHO. It is urgent that decision-makers in public health are made aware of the situation and that recommendations for managing the issue are modified. The incidence of multi-resistant neonatal infections is estimated at 5.5 per 1,000 live births. This unprecedented figure at a community level in low-income countries must prompt decision-makers to rapidly implement measures for limiting the dissemination of multi-resistant strains.

WORRYING PREVALENCE OF ANTIBIOTIC-RESISTANT ENTEROBACTERIACEAE IN CENTRAL AFRICAN CHILDREN

A study conducted by researchers from the Bacteriology laboratory at the Institut Pasteur in Bangui shows that almost 59% of Central African children under 5 years are asymptomatic carriers of extended-spectrum beta-lactamase (ESBL) producing *Enterobacteriaceae,* bacteria which are resistant to all the antibiotics currently marketed in the country[(2)]. This is one of the highest prevalences ever described in the world. These works, published in August 2016, provide the first data ever collected on fecal carriage of these bacteria in communities in sub-Saharan Africa and increase the need to raise awareness of the appropriate prescription and use of antibiotics. Ranked 180 of 187 according to the Human Development Index, the Central African Republic is already in a situation of extreme poverty with very poor sanitary conditions. Almost one child in six dies before the age of 5.



(2) High rate of fecal carriage of extended-spectrum ß-lactamase-producing Enterobacteriaceae in healthy children in Bangui, Central African Republic. Farra A, Frank T, Tondeur L, Bata P, Gody JC, Onambele M, Rafaï C, Vray M, Breurec S. Clin Microbiol Infect. 2016 Oct;22(10):891.

The key issue of multi-resistant tuberculosis

Tuberculosis remains a major public health issue, with 1.8 million deaths and 10 million new cases per year across the world according to the WHO. The situation is all the more worrying given the emergence of multi-resistant tuberculosis (480,000 new cases per year), some cases of which are resistant to all treatments currently available.

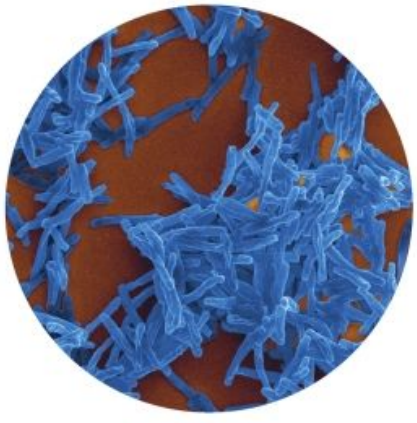
In China, again according to the WHO, 8% of new cases of tuberculosis are multi-resistant and this figure rises to 30% among patients who have already been treated. In Gabon, where the incidence of tuberculosis is very high (300 cases per 100,000 inhabitants), we estimate that 8% of new cases are carriers of a multi-resistant strain – a figure that is probably under-estimated.

The search for new treatments

Three years ago, the Institut Pasteur in Shanghai – Chinese Academy of Sciences established a new tuberculosis research unit. Coupled with the Mycobacterial Genetics Unit at the Institut Pasteur in Paris and in collaboration with the Gabonese Republic, the CDC in Shanghai and Fudan University, it is conducting a significant program aimed at studying the evolution of *M. tuberculosis* strains towards multi-resistance[1][2] on the one hand, and identifying new molecules that are effective in fighting multi-resistant forms of tuberculosis on the other. The acquisition of a screening platform has enabled two families of molecules that could improve the effectiveness of the antibodies currently used to treat resistant tuberculosis to be identified from the Chinese National Compounds Library. Another molecule found on screening the compound libraries of the Institut Pasteur in Paris' Chemistry and Biocatalysis Unit has been revealed as potentially effective. It is currently being studied as part of a European project[3], in association with nanoparticles, with the aim of improving its bioavailability. The effectiveness of these new molecules, associated with the antibiotics used to treat multi-resistant tuberculosis, will be tested on a wide range of clinical isolates, particularly at the National Public Health Laboratory in Gabon, a country in which the situation is worrying.

Stepping up the fight in Africa

Research conducted at the Institut Pasteur by Dr. Amel Kevin Alame Emane, from the National Public Health Laboratory in Gabon, as part of his thesis, revealed the existence of a multi-resistant tuberculosis epidemic in Libreville. Launched in 2013, a program supporting the fight against tuberculosis in Gabon in collaboration with the Gabanese Republic, the Institut Pasteur International Network, the Institut Pasteur and the Pasteur Center in Cameroon provided reinforcements for the teams and training for staff to supply the National Public Health Laboratory in Gabon with the resources needed to rapidly diagnose tuberculosis and detect antibiotic-resistant forms using new technologies (GenXpert and other molecular tools). This laboratory played a key role in the Gabanese authorities receiving funding from the Global Fund in 2016 to implement a program dedicated to fighting multi-resistant tuberculosis.
Other projects are being developed in sub-Saharan African countries (Cameroon, Central African Republic, Madagascar) to increase tuberculosis monitoring capabilities and improve management strategies, particularly for resistant forms.



(1) Prevalence and transmission of pyrazinamide resistant Mycobacterium tuberculosis in China. Xu P, Wu J, Yang C, Luo T, Shen X, Zhang Y, Nsofor CA, Zhu G, Gicquel B, Gao Q. Tuberculosis (Edinb). 2016 May; 98:56-61. (2) Pyrazinamide resistance in Mycobacterium tuberculosis arises after rifampicin and fluoroquinolone resistance. Alame-Emane AK, Xu P, Pierre-Audigier C, Cadet-Daniel V, Shen X, Sraouia M, Siawaya JF, Takiff H, Gao Q, Gicquel B. Int J Tuberc Lung Dis. 2015 Jun;19(6):679-84. (3) NAREB project: Nanotherapeutics against Antibiotic Resistant Emerging Bacterial pathogens.

Voahangy Rasolofo,

Scientific Director of the Institut Pasteur in Madagascar

"Avoiding the dissemination of multi-resistant tuberculosis in Madagascar."

The emergence of strains of *Mycobacterium* resistant to isoniazid and rifampicin, the main treatments for tuberculosis, is a major challenge in the fight against this disease. Many patients who have already been treated are at risk of developing multi-resistant tuberculosis in the event of therapeutic failure, chronic tuberculosis, relapse, premature termination of treatment or contact with a person already infected with a multi- resistant bacillus.

In Madagascar, the annual incidence of tuberculosis is 235 per 100,000 inhabitants according to the WHO. Currently situated at around 3%, the rate of multi-resistant tuberculosis in at-risk populations is low. The objective is to avoid the dissemination of these strains at all costs, through diagnosing and treating patients as early as possible. With this in mind, since 2012 we have been working with the Malagasy Ministry of Health's National Tuberculosis Control Program and reference centers for patient care. Currently, only two of these centers are able to conduct molecular testing to rapidly detect multi-resistance.

The Institut Pasteur in Madagascar is home to the National Reference Center for Mycobacteria, which conducts tests to definitively confirm the presence of a multi-resistant bacillus and takes on the bacteriological monitoring of patients under treatment. Data collected over the last five years provides essential information for adapting strategies to combat multi-resistant tuberculosis. Analyzing this data – in consultation with the Malagasy health authorities, the WHO and the International Union Against Tuberculosis and Lung Disease – has meant that the treatment duration has today been reduced from 18 to 9 months. By reducing this duration, we improve care for patients infected with these multi-resistant strains, while also reducing the risk of premature termination of treatment or lack of compliance. This also reduces the risk of these strains being disseminated!

PASTEURIANS

"Connecting entomological data with health data to quantify the risks of mosquito-borne diseases."

Founded in 2007, the Institut Pasteur in Côte d'Ivoire Entomology and Herpetology Unit is conducting various studies on mosquito-borne diseases. Since 2015, it has been involved in the Yersin project in partnership with the Institut Pasteur in Laos. The aim of this project is to better understand the dynamics of mosquitoes in rubber plantations in Côte d'Ivoire, identify the disease risk for workers and villagers living close by, and implement suitable preventive measures.

DR. BERNARD KOUADIO ALLALI
(right, head of unit)

DR. IBRAHIMA ZANAKOUNGO COULIBALLY
(left)
Entomology and Herpetology Unit,
at the Institut Pasteur in Côte d'Ivoire

Understanding links between health and the environment

Urbanization, growing populations, economic development, exploitation of natural resources...
Over the last fifty years, humans have changed ecosystems more rapidly and more profoundly than in any comparable period in the history of humanity[1].

The global climate change observed today is causing major changes that are likely to affect the epidemiology of diseases. According to the World Health Organization (WHO), it will be responsible for 250,000 additional deaths per year between 2030 and 2050[2]. Only multidisciplinary approaches can shed light on the complex links that connect human health, animal health and the environment. Present in five continents, the Institut Pasteur International Network is ideally positioned to play an important role in studying diseases, particularly vector-borne diseases, and address the challenge of controlling them in light of the upheaval facing global ecosystems.

(1) http://www.who.int/globalchange/ecosystems/mill_assess/fr/
(2) http://www.who.int/mediacentre/factsheets/fs266/fr/

Studying the connections between economic development, the environment and health

In recent years, Southeast Asia has undergone rapid demographic and economic development, leading to environmental transformations and significant consequences for health. Against this backdrop, the Institut Pasteur implemented the ECOMORE[1] project from 2013 to 2016. Conducted in collaboration with the Institut Pasteur in Cambodia, the Institut Pasteur in Laos, the National Institute of Hygiene and Epidemiology in Vietnam and the National Health Laboratory in Myanmar, the aim of the project was to better understand the environmental impact of human economic activities and their potential connection with the emergence of infectious diseases in Southeast Asia. It also looked at measuring the real health risks for local populations in order to provide public health recommendations to local authorities.

In each country, ECOMORE was built around a specific topic corresponding to a local priority, identified in consultation with health authorities: strengthening the monitoring of vector-borne diseases such as dengue and chikungunya in Cambodia; the consequences of deforestation and large-scale rubber plantations in Laos; the consequences of changing from traditional agriculture to more intensive agriculture in Vietnam; strengthening laboratory capabilities in terms of diagnostics and monitoring in Myanmar. *"We can only deal with such complex subjects in a multi-disciplinary way. ECOMORE followed the One Health approach, which consists of considering health holistically, involving animal health, human health and the environment,"* explains Yves Froehlich, regional coordinator of the project. With a view to strengthening exchanges between researchers and politicians, skills transfer was at the heart of the planning and implementation of this project.

Concrete results for preventing infection

In Cambodia, ECOMORE focused on improving the national dengue monitoring system in order to obtain the most reliable results possible. The existing network of sentinel hospitals was increased from five to eight, and an early warning tool allowing dengue epidemics to be forecast was validated, accompanied by a simple user manual. This will help the authorities to better anticipate the needs of hospitals in terms of consumables (drips, drugs, etc.) in the case of mass influx of patients during epidemic peaks.
In Laos, where the encouragement of rubber plantations has caused significant changes to ecosystems, the public health issue was to estimate the impact of this change on the dynamic of vector-borne diseases and the potential consequences for plantation workers and those living in neighboring villages. ECOMORE has shown that vector populations vary greatly in different environments (secondary forest, villages, immature plantations and mature plantations) and that the risk of contracting dengue is significantly higher for rubber plantation workers than for those living in the surrounding villages *(see page 36).*
Furthermore, a chapter on the health risks for plantation workers was added to the *Rubber Manual,* a technical reference book for Laos plantation owners. In Vietnam, epidemiological investigations in an area with traditional farming and in a zone with intensive farming, particularly pig farming, showed the significant circulation of hepatitis E (particularly in areas of more intensive farming) and leptospirosis, both water-borne zoonoses. These results should allow health authorities to be more aware of the potential risk of these neglected diseases and plan suitable preventive measures.
Finally, in Myanmar the project focused on access to diagnostics for severe respiratory infections, the main cause of child mortality in the country, against the background of the recent opening up of the borders making it necessary to reinforce capacities to diagnose and monitor the pathogens circulating in the region. ECOMORE thus assisted the National Health Laboratory (NHL)

(1) ECOsystem MOdification and emerging infectious diseases Risk Evaluation.

and two of the principal pediatric hospitals in Yangon by supplying the necessary materials and training. Today, these health structures are able to manage the monitoring of the circulation of major respiratory microbes.
All the ECOMORE results were presented at four symposiums at the end of 2016, bringing together the major players for the research topics in each country. The second phase of the project, ECOMORE 2, has been validated. This project will be even more ambitious, including a new partner country (the Philippines) and a transversal aspect on the role of climate change in the emergence of infectious diseases.

SUPPORT

ECOMORE is supported by the Agence Française de Développement (French Development Agency).

Mosquito-borne diseases in rubber plantations: from Laos to Côte d'Ivoire

What do Laos and Côte d'Ivoire have in common? Both countries are important producers of latex and home to huge areas covered by rubber plantations. These man-made forests provide the perfect habitat for mosquitoes and workers could be at higher risk of diseases such as dengue and malaria. In 2013, researchers at Institut Pasteur in Laos started a three year project to assess this risk and to identify possible preventive measures. Since 2015, they have helped their colleagues from Institut Pasteur in Côte d'Ivoire to implement a similar project. A good example of a south-south cooperation.

Understanding the dynamic of mosquito-borne diseases in Laos rubber plantations

In an attempt to fight poverty in the country, the Laos government has encouraged the establishment of rubber plantations, which in the past decade has resulted in their exponential growth. The latex naturally produced by the trees provides a good income for thousands of workers. However, these plantations are an ideal habitat for mosquitoes that transmit diseases and migrant plantation workers may introduce new pathogens to these areas. As part of the ECOMORE project *(see page 34),* researchers at Institut Pasteur in Laos studied the dynamic of mosquito-borne diseases in the country's rubber plantations and used this information to identify suitable preventive measures. Dr. Julie-Anne Tangena, a medical entomologist at Institut Pasteur in Laos, was the coordinator of this project: *"We looked at the risk of mosquito-borne disease infections for rubber workers compared with villagers living nearby. We found a higher risk for dengue, but not for malaria or Japanese encephalitis, for rubber workers in our study area."* The dengue vector *Aedes albopictus* is active during the day when workers are collecting the latex from the cups attached to the trees.

Scientists are now comparing different personal protection methods, such as insecticide-treated clothing, mosquito coils and topical repellents to assess which method is most effective, socially acceptable and cost-efficient for avoiding contact with mosquitoes.

Transferring the experience to Côte d'Ivoire

Interested in studying rubber plantations in a different context, the Laos team contacted the Entomology and Herpetology Unit at Institut Pasteur in Côte d'Ivoire. In 2015, the Yersin project began as a mirror study of the project in Laos. "*Although the rubber plantations are similar in Côte d'Ivoire, the way latex is collected and the mosquito dynamics are different. We are very happy our experience can benefit our colleagues in Côte d'Ivoire,"* explains Dr. Tangena. Indeed, Dr. Bernard Kouadio Allali (Head of Unit) and Dr. Ibrahima Zanakoungo Coulibally were trained in March 2015 in Côte d'Ivoire and in August 2015 in Laos by Dr. Tangena and Dr. Thammavong. The team is now working to implement the study in the district of Dabou, near Abidjan. The aim is to understand which mosquitoes bite, when and how they reproduce. This entomological data will be linked to local health data to quantify the risk of mosquito-borne disease infections arising in rubber plantations of Côte d'Ivoire and compare this with the villages.
This information will provide recommendations on how to decrease exposure to mosquito-borne diseases for rubber workers and their families.

SUPPORT
the Yersin Project is supported by the Michelin Corporate Foundation.

DUST AND HEAT CONTRIBUTE TO MORE CASES OF MENINGITIS IN SUB-SAHARAN AFRICA

A study conducted by CERMES (Niger) in collaboration with the Niger National Meteorological Service and the University of Liverpool revealed the association between meningitis and climate variations in sub-Saharan Africa[1]. On combining climate variables and epidemiological data on a daily time scale over a period of eight years (2003-2010), scientists observed that high temperatures (> 39.5°C/103.1°F) and a strong concentration of dust in the air are significant risk factors for an increased number of meningitis cases during epidemics. This link had already been suggested by general physician Léon Lapeyssonnie and reported as an endemic/sporadic cycle with a seasonal nature in a 1963 publication.
This study, published in July 2016, shows the importance of monitoring climate, epidemiological and microbiological data to predict or detect the emergence of invasive bacterial epidemics, but also the need to implement preventive measures to reduce their incidence. According to the latest report from the Intergovernmental Panel on Climate Change (IPCC), the global temperature could increase by 6°C (43°F) by the end of the century, raising fears of an increase in cases of meningitis in the Sahel, already the most affected region in the world.

(1) Airborne dust and high temperatures are risk factors for invasive bacterial disease. Jusot JF, Neill DR, Waters EM, Bangert M, Collins M, Bricio Moreno L, Lawan KG, Moussa MM, Dearing E, Everett DB, Collard JM, Kadioglu AJ, Allergy Clin Immunol. 2016 Jul 14. pii: S0091-6749(16)30616-9.

Bats, viruses and humans

Ebola, rabies, SARS, coronavirus... Bats are widely recognized as reservoirs for viruses that are highly pathogenic to humans. In French Guiana and Cambodia, the local Institut Pasteur facilities are taking a close interest in various endemic species of the flying mammal, and the viruses they transport, in order to assess the risks of transmission to humans.

Did you say vampire?

The Institut Pasteur in French Guiana is conducting research on the circulation of rabies in bat populations, 104 species of which are currently registered in the French overseas territory. Anne Lavergne, Vincent Lacoste and Benoît de Thoisy, researchers at the Virus-Host Interactions Laboratory, are focusing on the vampire bat with a blood-based diet in particular.

This species is responsible for 100 to 200 human bites per year and can give rise to rabies epidemics across Amazonia. Using transponders attached to the bats, the researchers have been following the dynamic of the rabies virus on almost 400 animals from two different colonies for almost ten years. Complementing this tracking data with molecular and serological analyses from almost 1,000 bats from 30 other species, scientists from the Institut Pasteur in French Guiana have recently been able to show that the prevalence of the rabies virus varies from 0 to 20% depending on species.

In reality, it is in colonies of bats living in the dense Amazonian forest, in particular vampire bats, that circulation of the virus is highest[1]. Researchers thus hypothesized that this habitat, where food is abundant, favors the survival of species and thus the circulation of the virus. Nevertheless, they warn against the adverse consequences that certain human activities could have on the modification of ecosystems, which would eventually force forest-based populations of bats to move closer to human populations.

More recently, the same team of scientists has looked at all viral populations found in vampire bats and also in an insectivore species, the free-tailed bat. This work, undertaken using a metagenomic approach, has enabled the identification of 48 families of viruses circulating in these species of bat.

The next step for the researchers will be to examine this data more closely in order to better define each viral entity, analyze its prevalence and understand how it circulates within a species or between species of bat. Finally, another research project conducted by the same laboratory consists of studying the innate immune system of bats to better understand how they can transfer highly pathogenic viruses without developing the disease. This is essential work for better understanding the dynamic of viral infections, the breaking of the species barrier and ultimately identifying potential risks for humans.

Tacking the Nipah virus at the Institut Pasteur in Cambodia

Transported by bats of the *Pteropus genus,* the Nipah virus is an infection that can cause encephalitis. Although no human transmission of the virus has yet been detected in Cambodia, the strong presence of host bats close to human habitation makes monitoring this situation indispensable for preventing or limiting a potential epidemic in the country.

As part of a vast program combating encephalitis viruses in Southeast Asia *(see box)*, researchers from the Institut Pasteur in Cambodia focused on *Pteropus lylei* bats[1].

The aim was to track the circulation of the Nipah virus between bats and study the factors, in particular seasonal factors, that influence this transmission. Once per month from 2013 to 2016, the researchers, led by Julien Cappelle, veterinary ecologist at the French agricultural research and international cooperation organization and hosted by the Institut Pasteur in Cambodia, visited Kom Poung Kor village Kandal province, 40 km south of Phnom Penh, which is home to a colony of approx. 5,000 *Pteropus lylei* bats – one of the largest colonies in the country. The analysis of blood,

(1) Bioecological Drivers of Rabies Virus Circulation in a Neotropical Bat Community. de Thoisy B, Bourhy H, Delaval M, Pontier D, Dacheux L, Darcissac E, Donato D, Guidez A, Larrous F, Lavenir R, Salmier A, Lacoste V, Lavergne A. PLoS Negl Trop Dis. 2016 Jan 25; 10(1):e0004378.

saliva, urine and fecal samples from bats revealed the presence of the Nipah virus, but also showed that the virus was more present in May, probably in connection with the species' reproduction cycle. During this time of year, females could have reduced immunity due to the energy used on feeding their young. This would mean that the Nipah virus is excreted more easily.

As a second stage, the researchers examined the bats' behavior and circulation at night. GPS trackers were placed on the bats before they were released, meaning the scientists could follow the zones in which they come into contact with humans and with pets very precisely.

Surprisingly, they observed that bats feed more often in the gardens of the villages around the colony than in the large fruit-tree plantations. Indirect contact between bats and humans could therefore be frequent.

Blood samples taken in September 2016 from people living in zones visited by bats revealed potential past contaminations. All this research aims to provide precise data for assessing the risk of the Nipah virus emerging in Cambodia, and for proposing measures to prevent or limit the risk of an outbreak as much as possible.

SUPPORT

SEAe is an inter-institutional initiative from AVIESAN cofunded by the Total Foundation.

ENCEPHALITIS – A SERIOUS DISEASE OF UNCLEAR ETIOLOGIES…

Encephalitis – an acute inflammation of the brain associated with neurological disorders – is essentially caused by infection. In Asia, it is one of the most common and serious causes of pediatric hospitalization. However, the pathogen responsible remains unknown in almost 60% of patients. Since 2013, the Institut Pasteur International Network has been involved in the international SEAe – Southeast Asia encephalitis – program, which aims to improve the prevention, diagnosis and treatment of this potentially fatal neurological inflammation, particularly in children. It covers six Southeast Asian countries (Cambodia, Indonesia, Laos, Myanmar, Vietnam, Thailand).

PASTEURIAN

"Responsiveness in the face of infectious disease outbreaks is our strength."

In May 2015, a Zika virus epidemic broke out in Brazil, rapidly spreading throughout the American continent's tropical zone. The Institut Pasteur in French Guiana, home to the National Reference Center for Arboviruses in the Antilles-Guiana region, confirmed the first cases in Suriname and French Guiana in late 2015. In January 2016, the same team published the complete sequence of the Zika virus genome responsible for this epidemic, showing its similarity to the strains responsible for the prior epidemic in the Pacific.

DOMINIQUE ROUSSET

Head of the Virology Laboratory and National Reference Center for Arboviruses at the Institut Pasteur in French Guiana

Anticipating the epidemics of tomorrow

Severe acute respiratory syndrome (SARS) in 2003-2004, H1N1 influenza in 2009, and the recent outbreaks of MERS-CoV, Ebola and Zika – there is no shortage of examples of infections that have caused international health crises in the past few decades.

According to the World Tourism Organization, there were 25 million travelers in 1950. Today, 1.2 billion people travel each year. Globalization thus creates the ideal conditions for the propagation of infections.
Over recent years, the Institut Pasteur International Network has shown its responsiveness and capacity for mobilization in the face of international infectious disease outbreaks. It also plays an active role in strengthening surveillance, laboratory capacities and implementation of early warning systems to rapidly detect emerging pathogens.

Zika: the mobilization of a global network

2015 – In just a few months, the Zika virus spread to the entire tropical zone of Latin America, leading to the largest ever reported outbreak.
The Institut Pasteur International Network once again demonstrated its remarkable ability to mobilize a multidisciplinary response to the threat posed by this infectious disease.

Back in October 2013, Zika – a mosquito-borne virus previously considered benign – reached French Polynesia. Four weeks later, adults arrived at the main hospital with severe neurological symptoms, including Guillain-Barré syndrome. Collaboration between experts in Tahiti and from the Institut Pasteur enabled the first link between these neurological conditions and infection with Zika virus (ZIKV) to be documented[1]. Following the introduction of the virus in Latin America in 2015 and the increase in reports of babies born with microcephaly in Brazil, a retrospective analysis of pregnancies in French Polynesia estimated the risk of microcephaly in babies born to women "infected" with ZIKV during pregnancy[2].

In January 2016, the Institut Pasteur in French Guiana published the whole genome sequence of the virus responsible for the Latin American outbreak, highlighting the similarity between this strain and the one responsible for the epidemic in French Polynesia[3]. The Institut Pasteur in Dakar, which had been studying ZIKV in mosquitoes and primates for years[4], shared its experience in viral isolate culture techniques, field testing using its mobile laboratory and in molecular and biological approaches to developing specific ZIKV diagnostic tests with the University of São Paulo. Teams from the Institut Pasteur in New Caledonia demonstrated that it is possible to detect the virus in urine for longer than in blood, enabling diagnosis of an infection up to two weeks after initial symptoms[5].
Several entomologists from the Institut Pasteur International Network demonstrated the higher capacity of *Aedes aegypti* in transmitting ZIKV, allowing more specific mosquito control measures[6]. Finally, researchers at Institut Pasteur Paris determined the three-dimensional structure of the virus, identifying potential targets for drugs and/or vaccine-induced antibodies[7].

Altogether, more than 100 scientific papers have been published on ZIKV by teams located across 16 institutes in the Institut Pasteur International Network since 2014.

(1) Cauchemez S., Besnard M., Bompard P., Dub T., Guillemette-Artur P., Eyrolle-Guignot D., Salje H., Van Kerkhove MD., Abadie V., Garel C., Fontanet A., Mallet HP. Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study. Lancet. 2016; 387(10033): 2125-32.
(2) Cao-Lormeau VM., Blake A., Mons S., Lastère S., Roche C., Vanhomwegen J., Dub T., Baudouin L., Teissier A., Larre P., Vial AL., Decam C., Choumet V., Halstead SK., Willison HJ., Musset L., Manuguerra JC., Despres P., Fournier E., Mallet HP., Musso D., Fontanet A., Neil J., Ghawché F. Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet. 2016; 387(10027):1531-9.
(3) Enfissi A, Codrington J, Roosblad J, Kazanji M, Rousset D. Zika virus genome from the Americas. Lancet. 2016 Jan 16; 387(10015):227-8.
(4) Faye O., Freire CC., Iamarino A., Faye O., de Oliveira JV., Diallo M., Zanotto PM., Sall AA. Molecular evolution of Zika virus during its emergence in the 20(th) century. PLoS Negl TropDis. 2014; 8(1):e2636.
(5) Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine. Emerg Infect Dis. 2015 Jan; 21(1):84-6.
(6) Chouin-Carneiro T., Vega-Rua A., Vazeille M., Yebakima A., Girod R., Goindin D., Dupont-Rouzeyrol M., Lourenço-de-Oliveira R., Failloux AB. Differential Susceptibilities of Aedes aegypti and Aedes albopictus from the Americas to Zika Virus. PLoS Negl Trop Dis. 2016; 10(3):e0004543.
(7) Barba-Spaeth G, Dejnirattisai W, Rouvinski A, Vaney MC, Medits I, Sharma A, Simon-Lorière E, Sakuntabhai A, Cao-Lormeau VM, Haouz A, England P, Stiasny K, Mongkolsapaya J, Heinz FX, Screaton GR, Rey FA. Structural basis of potent Zika-dengue virus antibody cross-neutralization. Nature. 2016 Aug 4; 536(7614):48-53.

Reinforcing infectious agents surveillance

In recent years, there have been many examples of infectious disease outbreaks and epidemics, highlighting the need to strengthen global health security through high-performance surveillance, warning and response networks. Launched in 2014, ASIDE[1] is the latest installment in a vast program of reinforcements for epidemic preparation and response capacities, in place since 2006 across the Institut Pasteur International Network.

Sentinel syndromic fever surveillance networks

In partnership with local health authorities, the institutes participating in the project[2] identify sentinel health sites. Health profesionals are trained to diagnose fever cases and collect epidemiological data and biological samples. When a case is detected, samples are analyzed to identify the pathogen responsible. This step also allows any mutations or new strains, including resistant ones, to be revealed, and any increase in the risk of an epidemic to be monitored. The results are then communicated to the health authorities and the WHO in order to decide on the appropriate public health response.

In order to reinforce preparation and response capabilities in the target countries, training is organized as part of ASIDE on the International Health Regulations (IHR, 2015), biological and epidemiological monitoring, investigating epidemics, crisis communication and laboratory-level epidemic management. Regular field missions allow partner's needs to be met effectively.

In Cambodia, ASIDE has focused on monitoring the circulation of avian influenza in poultry markets. This One Health approach will soon be adopted in Cameroon, Senegal and the Central African Republic.

SUPPORT

ASIDE is supported by the United States Department of Health and Human Services (DHHS).

SMARTPHONES FOR TRACKING INFECTIOUS DISEASE OUTBREAKS

In our increasingly connected world, ASIDE has drawn on new technologies to create an innovative early risk warning system for the Institut Pasteur International Network using a smartphone app. Distributed in the health centers participating in the project, these smartphones allow doctors to declare suspect cases in real-time and enter the clinical data directly into the Institut Pasteur database for the country. The team of ASIDE biostatisticians and epidemiologists immediately receive this information and can then decide on a response strategy.

Already in place in Madagascar, Cameroon and Senegal, this app will soon be available in Côte d'Ivoire.

(1) Alerting and Surveillance for Infectious Disease Epidemics. (2) The ASIDE is implemented in partnership with the Institut Pasteur in Bangui, in Cambodia, in Côte d'Ivoire, in Dakar, in Madagascar and the Pasteur Center in Cameroon.

Bertrand Cochery,

French Ambassador to Congo. In office in Conakry from February 2012 to July 2016, he supported French activities, including those carried out by the Institut Pasteur, in the fight against the Ebola epidemic.

Confronted with a health crisis of unknown duration and scope, the ambassador, like researchers, is faced with four challenges: precisely identifying the phenomenon, recommending security measures, constructing and coordinating an effective response, strengthening the local health system and preventing potential later crises. Step by step, I moved forward hand in hand with the Institut Pasteur teams in Guinea, nurturing this specific chemistry without which there could not be an effective joint response. From the outset, drawing on Sylvain Baize and Jean-Claude Manuguerra's first mission in Conakry, in April 2014, we addressed the French community together to put forward a credible, logical discourse in the face of fears and fantasies, and to help maintain the Air France line according to the principle "isolate the virus, not Guinea". This complicity continued throughout the duration of the fight against the epidemic, leading to the creation of the Institut Pasteur in Guinea, the 33rd in the international network.

The internationalization of health crises, the multiplication of players on the ground, the multilateralization of aid deployed and the increased responsibility of the state in the face of epidemics is leading to the improved integration of diplomatic activities and scientific approaches. Ebola was an important step in this regard: a mutual acculturation between researchers and diplomats is essential for developing the synergies needed, in an interdisciplinary dialog that brings together the strength of the Institut Pasteur International Network and that of our diplomatic network. Marc Jouan, Sylvain Baize, Noël Tordo, Jean-Claude Manuguerra, to name just a few, should be thanked for allowing me to experience this page of Pasteurian history with them.

"Ebola brought diplomats and scientists together on the same field."

A One Health laboratory network to mitigate viral threats

In August 2016, a man died after contracting Crimean-Congo Hemorrhagic fever virus (CCHFV) from a tick bite during a walk in Castilla-León region (Spain).
This was the first human case in Western Europe of this fever with a high mortality rate (from 10 to 40%). However, in some neighboring countries in the European Union, the disease is not new. Outbreaks have already occurred in the Balkans, Turkey, and Black Sea countries, constituting a threat to public health because of the epidemic potential and the difficulties related to the treatment and prevention of this disease.
Laboratory tests are available for the diagnosis of infections with this highly pathogenic virus, and their appropriate use can optimize containment measures and support public health decisions.
In order to harmonize diagnostic techniques, and ultimately enhance the integrated surveillance of diseases, a European project called MediLabSecure was launched in 2014. It aims to increase capacities in a network of laboratories working on emerging viruses around the Mediterranean and Black Sea.

SUPPORT
Medilabsecure is supported by the European Commission.

In response to the situation regarding Crimean-Congo Hemorrhagic fever, the MediLabSecure project has prompted a regional meeting on CCHFV. The conference was held in Belgrade in late 2016, where representatives from eleven countries of the MediLabSecure network in the region where CCHFV or the *Hyalomma marginatum* tick, its principal vector, were present. During this meeting, several aspects of the virus life cycle were tackled in a multidisciplinary way, including via medical entomology, animal and human virology, biorisk management and epidemiology. Moreover, a collaborative CCHF multisectoral risk assessment exercise was conducted to specifically examine national and regional contexts, fostering intersectoral collaboration, expertise and sharing of information. The “One Health” approach adopted by the MediLabSecure project, bringing together human health, animal health as well as veterinary and medical entomology provides an original framework for an integrated multidisciplinary collaboration of laboratory and public health professionals. Under the MediLabSecure project, such cross-discipline, cross-country encounters, coupled with dedicated research on intersectoral collaboration, are providing new paths and tools for public health professionals to face emerging viral threats in the Euro-Mediterranean region.
The MediLabSecure network encompasses 55 laboratories specialized in animal virology, human virology and medical entomology, as well as public health institutions in 19 beneficiary countries of the Balkans, North Africa (including Institut Pasteur in Algeria, Morocco and Tunis), the Middle East and South Caucasus regions. The project is collectively conducted by teams in France, Italy and Spain, and coordinated by the Department of International Affairs of the Institut Pasteur.

Since the beginning of the project in 2014, eight workshops and four international meetings have been conducted, involving more than 250 health professionals and relevant stakeholders. Through these activities, the project plays an active role in monitoring arbozoonotic infections and better preparing for their emergence via a harmonized collective approach designed to limit the risks associated with emerging viral diseases.

PASTEURIAN

“The G4 gave us considerable visibility at the national level.”

“Our research project aims to develop statistical methods for leveraging genomic data and identifying the factors involved in various infectious diseases. We are also supporting the research units at the Institut Pasteur in Dakar in exploiting their data. The establishment of a 4-year group in 2015 accelerated the development of bioinformatics within our institute and for our partners in universities and hospitals. Today, several research collaborations are in place, and request are made for defining training programs and teaching in faculties.”

CHEIKH LOUCOUBAR

Mathematician, head of Biostatistics, bioinformatics and modeling 4-year group, Institut Pasteur in Dakar

Supporting scientific careers

The development of human resources in public health and research remains a priority for many countries, particularly those with limited resources. The shortage of qualified personnel has been made clear during major health crises, and an increase in the number of medical professionals and scientists is an absolute prerequisite for sustainable development.

Considerable efforts are being made to train a critical mass of young scientists, technicians, biologists and doctors. The international network has played a role in these efforts for many years, through scholarships, exchanges and the hosting of young researchers. More recently, particular attention has been paid to the development of professional career paths for scientists in the network, with the implementation of programs designed to attract talented young scientists and reveal scientific leaders.

Developing human resources: a priority for the Institut Pasteur International Network

The Institut Pasteur International Network deploys – in collaboration with governments, national and international institutions, and other partners – continued training programs and international programs for doctoral and post-doctoral students in order to train, attract and keep scientists in their countries.

Each year, the Department of International Affairs of the Institut Pasteur offers funding (Calmette & Yersin program) and mobility aids to promote and facilitate the completion of theses, post-doctorates, internships and training within an IPIN institute, for scientists (students, researchers and technicians). The Pasteur International Network association also finances between 10 and 20 courses per year, organized by member institutes.

IPIN training: enhancing cutting-edge research capacities

True to the Pasteurian mission of education, the IPIN institutes contribute to enhancing scientific capacities and human resources across the world. For this, training programs are provided in the institutes in partnership with national universities and local players in scientific research. They are open to researchers, technicians and students from other institutions. Many IPIN institutes are host laboratories for university students at the bachelor, master and doctoral level. IPIN institute researchers also participate in training specialists with postgraduate level courses and seminars. There are several centers dedicated to training and welcoming interns in the IPIN (Cameroon, Madagascar, Niger, Côte d'Ivoire, Bangui, Cambodia, Korea, Vietnam, Montevideo, etc.).

RIIP DATABASE

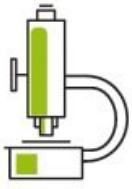
A single reference database accessible by institute, scientist, topic, project or key word: http:// databaseRiip.pasteur.fr

166
international scholarships
In 2015-2016

146 scholarships
funded by the Department of International Affairs of the Institut Pasteur, Calmette and Yersin programs

20 scholarships
cofunded by the Department of International Affairs of the Institut Pasteur and partners

78
study scholarships
to follow courses



62
traineeship scholarships
including 11 doctoral scholarships for 3 years and 6 post-doctoral scholarships for 2 years

6
congress scholarships

Fondation Pierre Ledoux Jeunesse Internationale
Sous l'égide de la Fondation de France

20
scholarships
from the Fondation Pierre-Ledoux – Jeunesse Internationale (Fondation Pierre-Ledoux – Jeunesse Internationale)

Coopération Internationale Principauté de Monaco

5
scholarships
from the Coopération internationale de la principauté de Monaco (Monaco Department of International Cooperation)

Fondation d'entreprise Total

1
doctoral scholarship
for 3 years from the Fondation Total (Total Foundation)

9 3-month long missions
for new recruits

4 4-year
groups created within the RIIP since 2013

Policy of attractiveness and diversity for young researchers

In order to strengthen basic research and improve the response to new emerging infectious agents, the Institut Pasteur has launched the **"4-year group"** initiative to support talented young scientists who want to develop international research groups within the IPIN. The aim is to allow young researchers to lead innovative research programs on infectious diseases in a network institute. Since 2013, the Institut Pasteur has selected four candidates who have established research groups in Cameroon, Madagascar, Dakar and Cambodia.

To encourage mobility within the IPIN, scientists recruited by the Institut Pasteur since 2014 carry out research missions lasting at least three months in an IPIN institute during the first two years of their career with us. In 2015 and 2016, nine new recruits completed three-month missions within the RIIP.

The Calmette & Yersin doctoral and post-doctoral program offers qualified, highly motivated French and foreign researchers the opportunity to complete their theses or post-doctoral internships in an IPIN institute, in countries with endemic diseases and/or limited resources outside of mainland France.

The Pierre-Ledoux Foundation – Youth international, under the auspices of the Foundation of France, has contributed to the training of young researchers for over 16 years, providing them with a better awareness of international realities. A product of the partnership between the Foundation of France and Institut Pasteur, the scholarships attributed fund biomedical research internships for French students in a country with limited resources within the IPIN.

Françoise Barré-Sinoussi,

Honorary President of the Institut Pasteur International Network

Reinforcing human resources is essential for the Institut Pasteur International Network. Some institutes, particularly those in countries with limited resources, are still sorely lacking scientists with the appropriate training to manage laboratories, obtain international funding and train young scientists independently. Supporting scientific careers is today a major issue that must be dealt with by the international network. The implementation of programs such as the 4-year groups is an excellent initiative, for example, but we need to look further. We must be able to support scientists beyond this, in conjunction with national authorities, and find locally-adapted solutions to sustain and develop their teams. The training of young scientists is a major part of this process. The net-work's institutes allow many young scientists to complete masters and theses, which is already a very good thing. Sadly, many of them do not continue their training to post-doctoral level, as is the case in the vast majority of industrialized countries. Yet for them, this is a critical step in acquiring the autonomy and maturity needed to establish, lead and develop their research. Young researchers should be encouraged to open themselves up to new scientific environments, including outside of the network, where approaches are different and the climate may be more competitive. This is they only way they can become true scientific leaders.

"Young researchers should be encouraged to open themselves up to new scientific environments."

PASTEURIAN

"Developing technical and human capacities in the field of genomics in Uruguay would significantly advance research and medicine in our country."

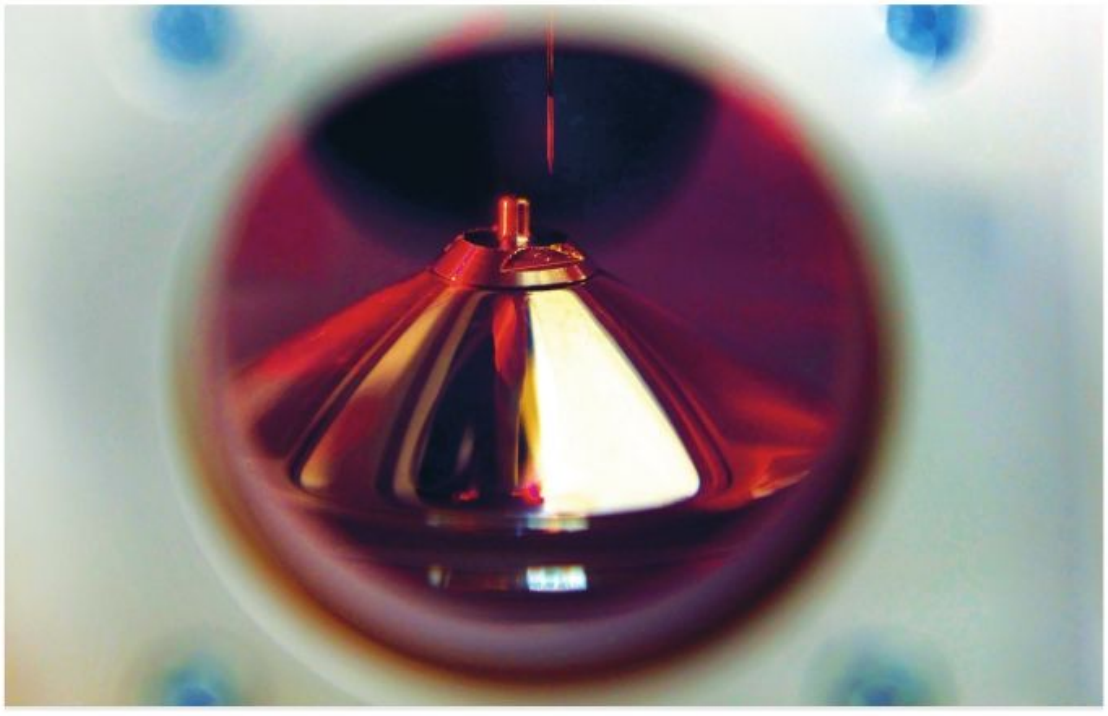
In September 2014, the Institut Pasteur in Montevideo launched the Urugenomes project in collaboration with Seoul National University. The overall objective of the project is to develop local capacities to analyze human genome sequences, both for research and to support genomic medicine and the scientific development of new products and technologies. While the first two phases of this project aim to increase our knowledge of the genetic context of the very mixed Uruguayan population, the third phase (currently ongoing) enables the creation of a national effort in applied medical genomics for rare and undiagnosed diseases.

HUGO NAYA
Head of the Bioinformatics unit, Institut Paster in Montevideo

Strengthening capacities

In an ever more competitive international environment, the members of the Institut Pasteur International Network must continuously evolve in order to modernize their tools, infrastructures and skills to best meet the increasingly complex requirements of research and public health.

In recent years, this need to constantly improve performance and keep up with changing means has led to the implementation of major programs, particularly in the area of biological data collection and bioinformatics support. Furthermore, several institutes in the network have benefited from assistance with quality and risk prevention.



Building informatics capabilities in the network

The International Network for Data Analysis (INDA) was established to federate and support research and education in Bioinformatics in the Institut Pasteur International Network. The core team, based in Paris, and working closely with the Center for Bioinformatics, Biostatistics and Integrative Biology (C3BI), manages ongoing projects in education and/or research, and communicates directly with the appointed bioinformatics representatives in each Institut Pasteur.

A fundamental part of INDA's mission is to promote training in bioinformatics. The network's practical courses promote a personalized education through research, based on using each student or participant's learning needs. As a result, the training is of immediate use to the students/participants that apply the lessons learned to their own research. Since 2015, five INDA hands-on courses have been organized gathering more than 125 people in four different locations in the International network (Senegal, Brazil, Montevideo and Paris). INDA also promotes more advanced and tailored courses relating to international research projects. Such projects include two training events as part of the Leishield Consortium[1] in 2015 and 2016. The Research Camp[2] is another such initiative, during which an international multidisciplinary community of experts were submitted with different challenges to crowdsource solutions. As part of this Research Camp, we organized an open meeting on "The Precision Medicine Revolution[3]", during which we invited eight experts to present the state-of-the-art in their field of expertise.

Building capacities thanks to the Institut Pasteur community is a priority. As part of this effort to make education accessible for all, two distance-learning platforms were developed with the Institut Pasteur Department of Information Systems: the Institut Pasteur MOOC platform[4] and the INDA collaborative website. Open to all, the Institut Pasteur MOOC platform is offering courses of interest for the Pasteurian community such as the one already accessible on how to use the Institut Pasteur IT services and the "Principles and Trends in Genomics and Computational Biology" MOOC. The INDA collaborative website[5] centralizes news and training sessions offered across the network. The website lets students and teachers stay connected and even reach out to past participants. This online forum enhances community learning and provides for continuous feedback. In this way, it offers fertile ground for new scientific collaborations and educational efforts to grow as a community.

The INDA commitment to offering high-quality bioinformatics and biostatistics courses will continue in 2017 and beyond with more courses being offered each year.

(1) https://c3bi.pasteur.fr/leishield-training-course-on-next-generation-sequencing (2) http://www.mispcamp.org (3) http://www.mispcamp.org/precisionmedicine
(4) https://moocs.pasteur.fr/courses (5) https://together.pasteur.fr/inda

Developing and enhancing the network's biological collections

Managing biological resources is a major international challenge, particularly in the context of the Nagoya protocol. The institutes in the network have exceptional biological collections. The development and enhancing of these collections is a strategic priority for the network, and is completed in close collaboration with national health authorities.

The PIBnet[1] project aims to harmonize, optimize and enhance network institutes' biological collections – micro-organisms and samples of human, animal, plant and environmental origin – as well as the analysis methods used in the network's expert laboratories. With the quality assurance and traceability of biological collections being guaranteed, academic and industrial partnerships can be developed according to strict rules, respecting ethics, intellectual property, national laws and regulations, and international agreements. The success of the One Health initiative, the epidemiological monitoring and the value of the data obtained with high-speed technologies depend on the quality of biological samples and their annotations. In addition to the Institut Pasteur network Biological Resource Centers (CRB and biobanks), the project involves NRCs and WHO Collaborating Centers, the Biological Resource Center of Institut Pasteur in Paris (CRBIP), the Laboratory for urgent response to biological threats and the European EVAg consortium (European Virus Archive goes global).

The key activities take two forms:
Coordination of the networks' biobanks: a pilot group has been established with 8 IPIN institutes[2]. This group is intended to be rolled out to other IPIN institutes. The objectives are to identify the existing biological collections and available resources, review the experience of those involved, improve the visibility of the collections to promote exchanges of biological materials as part of joint scientific projects, train personnel and improve communication.
Three working meetings have taken place to pool biobank experiences within the IPIN, train biobank managers – the deployment of an e-learning system adapted to the specific needs of the network is currently underway –, harmonize practices, coordinate activities and scientific projects, and create a catalog for accessing the collections.

The deployment of a pooled microbiology platform (P2M) at the Institut Pasteur in Paris, dedicated to innovative technologies in public health, open to members of the IPIN for routine use for high-speed multipathogenic sequencing. Almost 16,000 pathogen sequences were conducted in 2016.
The organization adopted shows that it is possible to routinely apply innovative techniques to public health, allowing decision-makers to benefit from more precise information: detection of grouped cases, quicker demonstration of their existence, demonstration of a absence of links (avoiding inquiries).
The technical facilities also include other equipment, in particular an automatic DNA extractor and a mass spectrometer (MALDI-TOF).
The platform follows the Institut Pasteur quality approach and is part of the scope of activities of the Multisite Expertise and Reference Laboratory (LREMS).

SUPPORT

PIBnet is supported by MSDAvenir.

(1) Pasteur International Bioresources Network. (2) With Institut Pasteur facilities in Côte d'Ivoire, Guinea, Madagascar, Tunis, Dakar, Cameroon, Cambodia and French Guiana.

Quality, risk prevention, techniques and environment: sharing practices and experience

Over the last two years, the Institut Pasteur's Technical Resources and Environment Department (DRTE) has created, together with scientists and non-scientists from the IPIN, a network for exchanging best practice and experiences relating to its key functions. This network is established by means of visits to the Paris premises, exchanges via videoconferences and missions across the IPIN.

The topic of laboratory accreditation under ISO 15189[1] was the subject of much communication between the Quality, Environment and Sustainable Development (QEDD) department and Institut Pasteur in French Guiana, Algeria, Côte d'Ivoire, Morocco and CERMES in Niger, in conjunction with the Laboratory for urgent response to biological threats and the 14 Institut Pasteur national reference centers that are accredited or in the process of becoming accredited. The Institut Pasteur in French Guiana benefits from enhanced support, in the form of assistance from Paris and several on-site quality engineering missions. Specifically, these missions have enabled internal quality audits to be conducted for various sections of ISO 15189 and ISO 17025[2]. **Metrology,** a key element in NRC accreditation, has also been addressed. Personnel from the Institut Pasteur in Cambodia and Dakar and from Fiocruz were thus welcomed to the Institut Pasteur metrology laboratory to discuss the methodology and tools used.

(1) This standard specifies requirements for quality and competence in medical laboratories. (2) This standard specifies the general requirements for the competence to conduct tests and/or calibrations, including sampling. It covers testing and calibration performed using standard methods, non-standard methods, and laboratory-developed methods.

In collaboration with the Department of International Affairs and the Purchasing Department, a specification was drafted for selecting an **incinerator** that is compliant with European standards, particularly with regard to airborne emissions, which will enable the elimination of most waste from the future Institut Pasteur in Guinea. This reliable, sustainable equipment addresses the local environmental, sanitary and economic challenges associated with waste processing. Several engineers from the QEDD department participating in collecting the necessary information. They mainly based their work on French and European regulations, feedback from the head of the technical department at the Institut Pasteur in Dakar, where they have been using an incinerator for several years, and interviews with the service providers who manage Institut Pasteur waste. All these elements were summarized in a call for tender, in line with the best practice of the French Development Agency, which is funding the project.

The Risk Prevention (PR) department is regularly called upon by IPIN institutes. For example, discussions took place regarding site decontamination services and the technical characteristics of personal protective equipment. The PR department team has also worked to support the Institut Pasteur in French Guiana in preparing regulatory visits relating to radioactivity and in establishing regulatory files for the biological agents they use. In close collaboration with the technical department, the PR department is regularly involved in issues relating to biological safety laboratories. This support takes the form of communicating on best practice, advice provided remotely or directly on site, as for the Institut Pasteur in New Caledonia. Additional assistance was provided, particularly in French Guiana, for monitoring projects and qualifications until the lifting of reservations. Thanks to the workshop division and the logistics department, equipment such as lab benches were sent to certain Institut Pasteur facilities. Furthermore, the Institut Pasteur in Guadeloupe benefited from on-site training associated with the qualification of biological safety laboratories and best practice to be complied with in this type of facility.

A NEW COLLABORATION AGREEMENT INTEGRATING THE PRINCIPLES OF THE UNITED NATIONS GLOBAL COMPACT

Faced with 21st century health challenges, the directors of all IPIN institutes reaffirmed, in March 2015, their determination to continue the work started over a hundred years ago, and signed the new IPIN Cooperation Agreement. They make a commitment to developing their activities in the fields of biomedical research, public health, training and technology transfer, taking into account the national and local contexts of their activities but regardless of ethnic, political or religious considerations that could divert them from their main objective of developing knowledge to improve human health. Through the inclusion of the ten principles of the United Nations Global Compact in this new agreement, all of the IPIN institute directors confirm that their activities are carried out with the aim of promoting sustainable development, based on the strengthening of local capacities with respect for human rights, international labor and environmental standards, and the fight against corruption.

PASTEURIAN

"Our commitment to the Pasteurian community aims to fight inequalities in healthcare."

Since 2005, the Total Foundation has chosen to take long-term action by partnering with the Institut Pasteur and the Institut Pasteur International Network to improve access to prevention, diagnosis and care in countries with limited resources. The programs implemented address the major global issue of child health. They help to advance research, while sustainably strengthening local capacities to combat infectious pathologies through the renovation and equipment of laboratories and hospitals, and the training of researchers, doctors and other local health workers.

NATHALIE BOU
Manager of the Health/Solidarity programs,
Total Foundation

Developing partnerships

Today, the challenges facing biomedical research and public health play out at the international level. The scope of the Institut Pasteur International Network has grown over recent years, particularly with regard to research, the surveillance of pathogens and mobilization in the face of epidemic emergencies.

The implementation of ambitious, sustainable partnerships is an essential prerequisite for developing the network. These partnerships mean infrastructures can be modernized, access to diagnostics facilitated, and new fields of research and technologies integrated. They offer researchers an opportunity to grow in competitive environments, giving them the means to address the challenges currently facing global health.

Partnerships: an essential component for international development

The development of the international network is based on long-term partnerships, most notably in France with government ministries[1], technical and funding agencies[2] and research institutions, in particular AVIESAN[3].
Recently, new international partnerships have been established, meeting member institutes' need for additional expertise, and the expectations expressed by third-party countries or institutions, such as the Philippines, which recently joined the ECOMORE project, or Myanmar where the collaboration continues with the strengthening of the National Health Laboratory, with the support of the French Development Agency. This policy of openness is materialized with the signing of agreements and new forms of partnerships, such as the creation of International Joint Research Units that perpetuate institutional commitments and are adapted to the current realities of international research. The first such unit was created with the University of Kyoto in 2016. More generally, the cooperation with Japan has been strengthened with the renewal of the partnership with RIKEN, a new collaboration program with the University of Tokyo and the determination to develop forms of cooperation between Japanese institutions and the Institut Pasteur in Dakar, Madagascar and the Pasteur Center in Cameroon – on the basis of the existing cooperation with the Institut Pasteur in Laos. The Institut Pasteur has also signed four agreements with Australian research institutions[4], serving as a new platform on which to develop collaborations with members of the network situated in the Asia-Pacific region.
A project studying Plasmodium vivax in Papua New Guinea and Cambodia thus obtained funding from the National Institute of Health (United States).
On the American continent, the Institut Pasteur has signed agreements with the Scripps Research Institute and the University of Miami. The latter will participate in programs connected with the Institut Pasteur facilities in the region. A project to create an International Joint Research Unit with Mount Sinai School of Medicine is being prepared. Finally, in Brazil, the signing of a tripartite agreement with the University of São Paulo in 2015 complements the historic cooperation that exists with the Oswaldo Cruz Foundation, and will work on the challenges to health associated with the modification of ecosystems and biodiversity.

Multilateral and international organizations

The 2016 recognition of the Pasteur International Network association as an organization in Official Relations with the World Health Organization strengthened our partnership with the United Nations institution. It currently holds a seat at the World Health Assembly as a non-State actor. In particular, it was involved in discussions and activities taking place under the R&D Blueprint for potential emerging and several member institutes of the IPIN worked together to propose vaccine and diagnostics development platforms.
In 2015, the Institut Pasteur signed a collaboration agreement with the World Organization for Animal Health (OIE), which aims to adopt a One health approach for its activities, through projects involving network institutes, particularly with regard to the monitoring of zoonoses and training for local personnel.
Our relationships with philanthropic organizations, such as the Bill Melinda Gates Foundation and the Wellcome Trust, have also been strengthened around programs to support young talents in low-income countries.

(1) Ministry for Europe and Foreign Affairs, Ministry of Higher Education, Research and Innovation, and Ministry for Solidarity and Health. (2) Expertise France and French Development Agency. (3) French National Alliance for Life Sciences and Health. (4) The Peter Doherty institute for infection and immunity, Monash university, Griffith university and Walter & Eliza Hall institute of medical research. (5) then Benoît Witkowski from September 1, 2017.

INTERNATIONAL JOINT RESEARCH UNITS: A NEW TOOL FOR STRONGER PARTNERSHIPS

As a new tool for establishing and reinforcing international scientific partnerships, Pasteur International Joint Research Units act as true conduits for communication. Bringing together a team from the Institut Pasteur in Paris with a team from an international institution, either within or outside of the IPIN, a Pasteur International Joint Research Unit is created for a period of five years and coordinated jointly by a scientist from each institution. Built around scientific projects selected for their quality, these research units facilitate scientific interactions and mobility (particularly for young researchers), enable better responses to international calls for tender and give greater visibility to the research teams involved.

In 2016, four International Joint Research Units were formed, three of which within the Institut Pasteur International Network, addressing:
• **leishmaniasis,** co-coordinated by Gérald Spaeth, head of the Institut Pasteur Laboratory of Molecular Parasitology and Signaling, and Guangxun Meng, head of research in the innate immunity unit at the **Institut Pasteur in Shanghai** – Chinese Academy of Sciences;
• **malaria,** co-coordinated by Jean-Christophe Barale, leader of the Biology of malaria Targets and Antimalarials Group within the Structural microbiology unit at the Institut Pasteur, and Didier Ménard, head of the Malaria Molecular Epidemiology Unit at the **Institut Pasteur in Cambodia**[5];
• **leptospirosis,** co-coordinated by Mathieu Picardeau, head of the Biology of Spirochetes unit at the Institut Pasteur, and Alejandro Buschiazzo, head of the Protein Crystallography unit at the **Institut Pasteur in Montevideo;**
• **"vaccinomics",** co-coordinated by Fumihiko Matsuda, director of the Genomic Medicine Center at the University of Kyoto, and Anavaj Sakuntabhai, head of the Functional Genetics of Infectious Diseases unit at the Institut Pasteur.

Professeur Htay Htay Tin,

Deputy Director General of the Myanmar National Health Laboratory (NHL)

In the past few years, cooperation between the Institut Pasteur international network and Myanmar health authorities has become much stronger. The objective is to help Myanmar health professionals reinforce their capacities to diagnose and treat major pediatric diseases such as encephalitis or severe acute respiratory infections. We have been collaborating with the Institut Pasteur in Cambodia for almost four years as part of the SEAe and ECOMORE projects. Over this very short period of time, we have been able to introduce new diagnostic techniques and strengthen laboratory services at the NHL but also consolidate the training of health professionals, best clinical practice and equipment in the Yangon Children's Hospital & Yankin Children's Hospital. Thanks to this collaboration, today we have a trained data manager who ensures the meticulous collection, processing and recording of data. The project is extremely useful for epidemiological surveillance but also for the identification of resistant strains and choosing the correct antibiotic for respiratory infection, for example. The majority of clinicians working in the two pediatric hospitals gave very positive feedback on this collaboration.

At the start of the collaboration, I was worried, as Myanmar was not as advanced as the other partners on this project. The constructive discussions and positive support from the Pasteurian collaborators were very encouraging and we were able to finish on time. Now we are eager to write a new chapter in our collaboration with the second part of the ECOMORE project that will be focused on Leptospirosis surveillance. This infection is common in our country but under-diagnosed, and improving our surveillance system will not be easy. But I am sure we can succeed thanks to the help of our Pasteurian partners.

For me, the Institut Pasteur International Network is a true symbol of French academic cooperation. Our relationship is genuine and based on equality. We have worked with other international organizations to enhance our medical care services and health system but I feel, perhaps because of our history, that we have a special bond with the Institut Pasteur International Network. It is not only a development partner but a member of our family.

"Our relationship is genuine and based on equality."

Christophe Paquet,

Head of the Health & social protection division, French Development Agency (AFD)

"There are similarities between the development values of the AFD and the founding principles of the Institut Pasteur."

Our collaboration with the Institut Pasteur is significant, in terms of both the volume of projects concerned and the variety of financial instruments and regions involved. We have supported emergency activities during the Ebola crisis with the establishing of the Institut Pasteur in Guinea, upgrading the production of the yellow fever vaccine at the Institut Pasteur in Dakar, and for over ten years we have supported research and public health programs in Southeast Asia with the assistance of local Institut Pasteur facilities.

The Institut Pasteur is renowned for its quality, not only in its fields of activity but also in its capacity to implement and manage major projects thanks to the support of the Institut Pasteur International Network. The local footing of the members of this network is a tremendous asset, making them legitimate actors and thus facilitating dialog with national authorities in the countries in which they intervene. The French Development Agency thus benefits from this reputation of excellence and contributes to reinforcing it via the projects it enables the Institut Pasteur to carry out. I think that the longevity of our cooperation is also attributable to the many similarities between the development values of the AFD and the founding principles of the Institut Pasteur.

Over our many years of cooperation, we have gradually got to know each other better and take into account, on both sides, the specificities, expectations and working methods of the other party. ECOMORE 2 *(see page 35)*, which will be starting shortly, is the perfect illustration of this relationship. This is the fourth project we have implemented in over ten years on the subject of emerging infectious diseases in several Southeast Asian countries. These projects have all been developed through genuine dialog between our institutions, ultimately enabling us to bring together research, sustainable development for health systems, and strong national capacities in the countries in which we are active. ECOMORE 2 follows this tradition, which has allowed the Institut Pasteur to develop a strategic and sustainable partnership with Myanmar and, surely soon, to duplicate the same approach with the Philippines. It is obvious to us that each time we find these similarities between the objectives of the Institut Pasteur and the AFD relating to issues in research, public health and development, there will be new potential opportunities to collaborate.

Partners

Ministries and government agencies in France and around the world

Chinese Academy of Sciences (CAS) • French Development Agency (AFD) • Japanese International Cooperation Agency (JICA) • American Center for Disease Control (CDC) • Assistant Secretary for Preparedness and Response within the Department of Health and Human Services (ASPR/DHHS) • Expertise France • Mexican National Council for Science and Technology (Conacyt) • French Ministry for Europe and Foreign Affairs (MEAE) • French Ministry of Higher Education, Research and Innovation (MESR) • French Ministry for Solidarity and Health • Korean Ministry of Science, ICT and Future Planning (MSIP) • US Agency for International Development (Usaid) • Monaco Department of International Cooperation

Research institutions

ANR • ANRS • All member institutions of AVIESAN • Cnes • University of São Paulo (Brazil) • University of Tokyo and University of Kyoto (Japan) • Japanese Research Institution for Science and Technology (Riken) • National Center for Global Health and Medicine (Japan)• The Peter Doherty institute for infection and immunity (Australia) • Monash university (Australia) • Griffith university (Australia) • Walter & Eliza Hall institute of medical research

International Organizations

World Health Organization (WHO) • World Organization for Animal Health (OIE) • European Commission • The Global Fund • National Institutes of Health (NIH) • European & Developing Countries Clinical Trials Partnership (EDCTP) • Global Alliance for Vaccines & Immunization (Gavi) • Food and Agriculture Organization of the United Nations (FAO)

Foundations, associations and NGOs

Francophone University Association (AUF) • Agency of Preventive Medicine (AMP) • Bill & Melinda Gates Foundation • Scientific Center of Monaco (CSM) • Drugs for Neglected Diseases initiative (DNDi) • EDF Foundation • Fondation de France • Mérieux Foundation • Michelin Corporate Foundation • Pierre-Ledoux Foundation – Youth international • Prince Albert II of Monaco Foundation • Rotary International Foundation and District 1660 Rotary Clubs • Sanofi Espoir Foundation • Total Foundation • MSDAvenir • Nutricia Research Foundation • Wellcome Trust

Private sector

AXA Research Fund • Institut Mérieux • Sanofi Pasteur

Thanks

We would like to thank all the collaborators working in the Institut Pasteur International Network, particularly those who accepted to appear in this report.
Many thanks to all the members of the Institut Pasteur Department of International Affairs for their daily commitment, with special thanks to Eliane Coeffier for her contribution to the development of IPIN cooperation programs throughout her career.
And finally, we express our sincere gratitude to all the Institut Pasteur team in Paris for their assistance and cooperation, and all the partners and institutions whose constant support enables these programs to provide valuable benefits for public health.

Using Cocoon Silk rather than non-recycled paper means that the environmental impact of this report is reduced by:

959 kg
of landfill

128 kg
of co_2

1,288 km
travel in an average European car

36,267 l
of water

2,037 kWh
of energy

18,600 kg
of wood

Sources: Labelia Conseil data for the carbon footprint. European BREF data for virgin fiver paper

Institut Pasteur: Department of International Affairs - Institut Pasteur International Network – 25-28, rue du Docteur-Roux – 75724 Paris Cedex 15, France. **Editor in chief:** Olivier Rescaniere, International Communications Manager, Institut Pasteur. **Photo credits:** Institut Pasteur, Institut Pasteur de Bangui/Jean-Marc Zokoué, Institut Pasteur Corée, Institut Pasteur de la Guyane, Institut Pasteur de la Guyane /Ronan Liétar, Institut Pasteur de Madagascar, Institut Pasteur d'Iran/Alireza Pesyani, Institut Pasteur du Laos, Instituts Pasteur Cambodge, Instituts Pasteur Cambodge/Veasna Hak, Instituts Pasteur Dakar, AFD/Éric Thauvin, Alejandro Buschiazzo, Amel Ghouila, Arnaud Tarantola, Bruno Deméocq, Caroline Sebilleau, CERMES/Mamane A. Oumarou, Charles Dauguet/Jean-Marc Panaud, Clement Tardif, Dominique Tardy, Fotolia/Chodyra Mike, Fotolia/pressmaster, François Gardy, Gael Cornier, Istock/Graphic_photo, Jacques Do Kokou, Jean-François Charles, Krees Raharison, Magali Herrant, Manuel Mendoza, ministère de l'Europe et des Affaires étrangères, Nabil Zorkot, Olivier Rescanière, Pascal Gaborit, Patrice Courvalin, Présidence de la République/Laurent Blevennec, Pyay Kyaw Myint, Réseau international des instituts Pasteur, Stéphanie Guadagnini/Mary Jackson/Jean-Marc Panaud, Steven W. Lindsay, Victor Yene, DR. **Design and production:** PUBLICORP – 14648.

This document respects environmental standards, with 100% FSC® Recycled certified paper and printing using plant-based inks.

Department of International Affairs
Institut Pasteur Intenational Network
25-28, rue du Docteur-Roux
75724 Paris Cedex 15, France
www.pasteur.fr

international network
Institut Pasteur