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# "Chance favors invention only for minds prepared for discoveries by patient study and persevering efforts."

Every day, scientists at the Institut Pasteur and in the International Network continue their ongoing battle to improve the prevention and treatment of disease. From the very first "lieutenants", Émile Duclaux, Émile Roux, Élie Metchnikoff, Alexandre Yersin, Albert Calmette and Camille Guérin, to the scientists of today and tomorrow, all these pioneers were and continue to be committed to nurturing a powerful spirit of creativity, and a rigorous and dynamic approach to life sciences.

What drives them on? Perseverance. Perseverance guides them in their work, day in, day out. Perseverance has been their inheritance and their legacy for high on 130 years. Perseverance is a core value in the Pasteurian identity.

view 2017

Œuvres de Pasteur, Vol. VII. p. 215



Louis Pasteur

# **Interview** with Christian Vigouroux, Chairman of the **Board of Directors**

**66** The Institut Pasteur is where we expect it to be today. This is confirmed by its high levels of success and recognition in 2017.

## You chaired the Board of Directors through 2017, a year of transition for the Institut Pasteur. How did the institute approach this important turning point?

It was clearly the start of a new phase for the Institut Pasteur, with major changes to the leadership team, but all institutions are constantly faced with turning points as they grow and develop. So in 2017, the Institut Pasteur continued its activities, full of confidence and firmly convinced of the importance of its work and its longterm role. And that long-term perspective gives rise to ambition, enabling it to look beyond the recent transitions and focus on its core activity, science. I would add that during this period, the Institut Pasteur was particularly attentive to the advice and guidance So 2017 was a successful year. Is that partly because provided by the Pasteur Scientific Advisory Board (PSAB), the Institut Pasteur Scientific Council and the Search Committee that was tasked with proposing a new President for the institute. Stewart Cole, with whom we have been working for some months now, embodies our ambition. And we can be very proud, because the Institut Pasteur is where we expect it to be today. This is confirmed by the new units set up in 2017, the long list of national and international honors and awards bestowed on Institut Pasteur scientists, the Institut Pasteur's leading role in addressing national and international health crises – including recently with the plague outbreak in Madagascar and the Salmonella outbreak in France-, its engagement in topical issues such as the debate over vaccination, technology transfer to industry. And finally, we would like to thank and its dynamic, ambitious International Network. Maintaining and our industry partners. Our economic model is one that is open to improving the Institut Pasteur's scientific performance is the primary goal of all our endeavors, and the very key to our existence.



# of the stability of the Institut Pasteur's economic model?

It is true that our economic model enables us to uphold our scientific commitments. It is a constant focus of attention for the Board of Directors, and it is up to us to use all the tools at our disposal to maintain this model. We are extremely grateful to our donors for their generosity, since a third of our income comes from public gifts and donations. We must thank the public authorities for their ongoing endorsement, since the support of our supervisory bodies represents a significant share of our income. We also owe a great deal to the Institut Pasteur staff, whose outstanding research leads to funding and research contracts, and paves the way for society, much like our missions in the areas of research, public health and education.

# What areas does the Institut Pasteur need to focus on to remain on course?

the Board of Directors will support the First, we have the challenge, with the new President, of developing a new scientific strategy for the next five years. This means having new senior management team in its the vision to develop new ambitions while continuing our day-toambition to continue to advance science day activities. We are also particularly attentive to issues that are central to our work, such as biosafety, an area in which we must and serve the general public. give a strong lead. On this topic, it is worth recalling that the Institut Pasteur receives, analyzes and stores a huge number of samples. particularly because of the activities of the National Reference Centers (CNRs). It is not mentioned enough that the Institut Pasteur holds nearly half of the permits for the use of microorganisms and toxins in France, because of the nature of its activities. We are therefore fully committed to ensuring absolute safety in this area, in What is your own ambition for the Institut Pasteur? close cooperation with the General Secretariat for Defense and I sincerely hope that it will continue to bring young scientists on National Security (SGDSN) and the French National Agency for the board and make new discoveries. Its focus on young scientists has Safety of Medicines and Health Products (ANSM). already given rise to real results through its G5s – research groups Another area of focus is to ensure the continued effective operation geared towards promising young scientists for a five-year period. of the Institut Pasteur International Network, which can be achieved They represent one of the tools that the Institut Pasteur has introby promoting links with the Institut Pasteur in Paris and also via duced to revitalize its approach and persevere in its research. interregional exchanges, which have already been set up between With continuity and confidence, the Board of Directors will support institutes in various countries and are a real source of progress. the new senior management in its ambition to continue to advance Finally, we need to work closely and effectively with our partners. science and serve the general public. whether at the institutional level in France – government ministries, In my New Year message to Institut Pasteur staff in January, I quoted Raymond Poincaré, who at Louis Pasteur's funeral said: "Duty only the CNRS, Inserm, the Institut Curie, etc. - or with our partners abroad, such as in Brazil. I would use the simple but effective ceases when there is no longer power to do more (...) Reducing the metaphor that we are part of an ecosystem: the Institut Pasteur is scope of his own power every day. Louis Pasteur discovered more stronger when it works with others. duties every day, and his sole ambition and joy was to fulfill them.' We can rest assured that in 2018, neither duty nor power – not in a As the Institut Pasteur prepares to celebrate its 130th Machiavellian sense but in a Pasteurian sense - will be lacking.

# anniversary, what historical strengths can it draw on?

The Institut Pasteur is a place that is steeped in history, but it also looks boldly to the future. Since the time of its founder, the role of the Institut Pasteur has been about disproving evidence, daring to tread the risky path of hypothesis and exploration rather than relying on received knowledge, exchanging ideas with experts all over the world and, against all the odds, pursuing its core missions of research, education and public health. It goes without saying that the future strategic plan will draw on these historical strengths as a means of inspiring and empowering our scientists. Perseverance has always been a core value for the Institut Pasteur; it understands the importance of giving scientists time - a vital commodity for research - but also resources, teams, contacts and a strategy to guide them.

With continuity and confidence,

# Interview with Stewart Cole, President

**66** The Institut Pasteur must make humans and human health the focus of its work.

## You have been President of the Institut Pasteur for a few months, how do you currently view this institution that you know so well?

I do indeed know the Institut Pasteur well as I worked here for 24 years. I arrived in the 1980s, at that historic moment when HIV had just been isolated by Francoise Barré-Sinoussi, Luc Montagnier and Jean-Claude Chermann. At the time, I joined a very dynamic team and was able to make my contribution to the fight against AIDS by sequencing the genome of the virus, before later focusing on other public health scourges, such as tuberculosis and leprosy. I've now returned\* to the Institut Pasteur, at another important moment in its history, as its teams have been rejuvenated - following the recruitment of many outstanding researchers – and major innovative programs have been launched, for example, the Integrated Biology of Infectious Diseases (IBEID) Laboratory of Excellence and the "Milieu Intérieur" project. I have been struck by the quality and potential of the 5-year groups recruited over the past few vears. I am optimistic about the future because these young researchers are working on very promising topics. In fact, this ability for constant renewal has existed at the Institut Pasteur for the past 130 years. Dedication is essential for research and is in keeping with Pasteurian tradition.

# Which Institut Pasteur undertakings do you also consider promising?

The Institut Pasteur is moving ahead with innovation and medical progress by investing in major research projects. There are two projects that particularly stand out for me. The installation of a cryo-electron microscopy platform on campus and the construction of the new OMICS buildings, which will house most of the teams working on integrative biology - big data in life



Dedication is essential for research and is in keeping with Pasteurian tradition.

sciences – as well as the new disciplines arising from the latest major developments in the field of sequencing. These two key facilities, to be opened this year, are currently essential "tools" for conducting out creative and cutting-edge research in a competitive international environment.

# Creativity for excellence, is this the planned direction for the scientific policy that will be put in place?

We need to be creative to open up new fields of research and respond to key public health issues in the world today. In keeping with the initiatives introduced over the last few years, the Institut Pasteur must always make humans and human health the focus of its work, while focusing on biology, microbiology and infectious diseases. I can see three major scientific challenges that need to be met - fighting against emerging infectious disproud we are to work at the Institut Pasteur. eases, such as Ebola and Zika, identifying solutions to respond \* From 2007, Stewart Cole was Professor and Director of the Global Health Institute at the Swiss Federal Institute of Technology (EPFL) – a world-leading education to the development of resistance to antimicrobial agents, and and research center. \*\* Inaugurated November 14, 1888. combating neurodegenerative conditions to finally offer effective avenues for treatment. For me, the Institut Pasteur must be involved in meeting these three scientific and health challenges of the 21st century and we will include them in our new five-year strategic plan.

Our scientific creativity is the key to success in addressing these challenges. For example, with the development of new models – such as the zebrafish which has gained unexpected importance – to study certain diseases. The Institut Pasteur has followed some of these innovative paths to develop its research, and they will perhaps lead to great opportunities for future scientific discoveries. The academic sector must take an innovative and dedicated stance towards research, as must the Institut Pasteur.

# What strengths can the Institut Pasteur draw on to succeed?

In January, when I took up my post and we entered the 130th year of the Institut Pasteur's existence\*\*, I addressed our scientists and said: "When we look back at the career of Louis Pasteur, our mentor, it is not only his creativity and determination that stand out but his unequaled versatility." Our greatest strengths are therefore not only our creative ability and tenacity, but also our multidisciplinary and interdisciplinary approaches, which are key to success. For example, our expertise in systems biology and microbiota opens up new avenues for research into neurodegenerative conditions. If we combine these attributes with a more pragmatic approach to develop diagnostic or therapeutic solutions, we will be firmly rooted in our values for the benefit of life sciences and human health. And these strengths have a global reach because our expertise is also based on the Institut Pasteur International Network, whose scope is an asset for meeting the public health challenges emerging in the field. The appointment of a new Scientific Director, dedicated to this international presence, will inject energy into these activities and further promote our strengths.

## The Institut Pasteur is therefore on track to celebrate its 130th anniversary.

The 130th anniversary of the Institut Pasteur is a historic moment in the life of this center of excellence for research, public health and education. It provides the perfect opportunity for reflecting on the way in which the Institut Pasteur considers tomorrow's research and medicine, while we are drawing up our next strategic plan. In this respect, the senior management team is here to make sure the Institut Pasteur runs smoothly by establishing this ambitious but attainable scientific policy, and to provide the scientific teams with the best possible working conditions by giving them access to high-tech facilities and making full use of the buildings and economic resources available. I therefore hope that this anniversary will also remind us how happy and

The Institut Pasteur must make a contribution in its fields of excellence to meet the scientific and health challenges of the 21st century.

# Review of the year 2017

# WHY BRONCHIOLITIS ONLY AFFECTS INFANTS

Scientists from the Institut Pasteur in Paris and Shanghai, together with Bicêtre Hospital, Paris-Sud University and the CNRS, discovered a new group of immune cells (B lymphocytes) which are only present in infants and are the preferred target of the virus responsible for bronchiolitis. Their finding shows why this infection mainly affects newborns, often severely because of their young age.

# 14

The number of new research entities (10 units and 4 five-year groups) set up at the Institut Pasteur in Paris in 2017.



# How nicotine acts on the brains of schizophrenic patients

Several studies have indicated that schizophrenic patients are likely to show a high level of nicotine dependence. Scientists from the Institut Pasteur, the CNRS, Inserm and the ENS visualized the direct impact of nicotine on the restoration of normal activity in nerve cells involved in psychiatric disorders such as schizophrenia.

![](_page_4_Picture_8.jpeg)

# The migratory history of the Bantu peoples

Scientists from the Institut Pasteur, the CNRS and a large international consortium analyzed the genomes of more than 2,000 samples from individuals in 57 populations in Sub-Saharan Africa. They traced the migratory route of the Bantu peoples, previously a source of debate, and revealed that the admixture that resulted from successive encounters with local populations conferred advantageous genetic mutations on them. The study also shed light on the narrative of slavery, via a vast comparative analysis of the genomes of 5,000 African-Americans and those of African populations.

# The expert view

Lluis Quintana-Murci, a scientist at the Institut Pasteur and coordinator of the study

Our research shows that the admixture of the Bantu peoples with local populations was beneficial for their adaptation to their environment, especially in terms of immunity.

# COMMUNICATING THE RESULTS OF CLINICAL TRIALS MORE CLEARLY

The Institut Pasteur demonstrated its commitment to enforcing compliance with clinical trial procedures by becoming one of the first co-signatories of the joint statement on public disclosure of results from clinical trials, initiated by the World Health Organization (WHO), together with other academic institutions involved in global health.

06

# A NEW APPROACH FOR IMPROVING BCG

Scientists at the Institut Pasteur and their partners in the international TBVAC2020 consortium developed a tuberculosis vaccine candidate derived from conventional BCG but with higher efficacy. Tuberculosis ranks among the ten leading causes of death globally.

> **1.8** Tuberculosis is responsible for 1.8 million deaths every year (source: WHO figures).

# LAUNCH OF THE INFRAVEC2 PROJECT

In February 2017, the European Commission gave its go-ahead to Infravec2, the research infrastructures project for the control of insect vectorborne diseases. The aim of this project is to improve European infrastructures for research on mosquitoes and other insects that transmit diseases to humans or animals. The international consortium is composed of 24 partner institutions coordinated by the Institut Pasteur.

# ORIGINAL HERVÉ DI ROSA EXHIBITION AT THE INSTITUT PASTEUR

In December 2017, the Institut Pasteur officially unveiled the redesigned collection in its Salle des Actes, a place steeped in history. The founder and director of the International Museum of Modest Arts in Sète, Hervé Di Rosa, was commissioned by the Institut Pasteur to use his artistic talents to redesign this display area. His painted ceramics, illustrating some of the pioneering men and women that have shaped the Institut Pasteur over the years, are accompanied by artifacts and objects from the collections and archives of the Pasteur Museum.

![](_page_4_Picture_25.jpeg)

# Review of the year 2017

![](_page_5_Picture_1.jpeg)

# RESTORING HEARING AND BALANCE IN A GENETIC CONDITION

A team of French researchers, including Institut Pasteur scientists, restored hearing and balance in a mouse model of Usher syndrome, a rare genetic disorder, for the first time. How? Using gene therapy. By locally injecting the USH1G gene, they successfully restored the function of the sensory cells in the inner ear. This breakthrough paves the way for the development of treatments for some forms of hereditary hearing loss.

# 38

The number of Pasteurdon media partners in 2017: 24 TV channels and 14 radio stations.

![](_page_5_Picture_6.jpeg)

# A concerted effort in support of vaccination

In 2017, the Institut Pasteur showed its support for the French government's policy for the prevention of infectious diseases: it signed a manifesto alongside scientific, medical and paramedical companies and medical unions; Pasteurian scientists Philippe Sansonetti and Frédéric Tangy published two books about vaccines; it hosted the 2017 Annual Congress of the International Society for Vaccines (ISV), the biggest international scientific conference on vaccine issues; and it held a press conference in December 2017, under the auspices of Paris Descartes University and in partnership with Inserm and AP-HP, at which the main questions currently under debate were discussed.

# Colon cancer: APC protein prevents pre-cancerous inflammation

Adenomatous polyposis coli (APC) is a gene whose mutations are associated with a rare, hereditary form of colorectal cancer known as familial adenomatous polyposis. Scientists demonstrated that mutations to this gene do not only lead to the emergence of colon polyps; they also harm the immune system, leaving it unable to tackle inflammation of the colonic mucosa. This dual impact encourages the development of cancer.

![](_page_5_Picture_11.jpeg)

# Institut Pasteur actively engaged in Madagascar

Madagascar faced a particularly severe outbreak of pneumonic plague in the major urban centers of Antananarivo and Toamasina. The Institut Pasteur in Madagascar was on the front line in diagnosing the disease, with support from the Institut Pasteur in Paris. The Laboratory for Urgent Response to Biological Threats (CIBU) sent two technicians to assist the teams with the huge number of cases that needed to be confirmed. The Mathematical Modeling of Infectious Diseases Unit also seconded two staff members to monitor the development of the outbreak.

# AIDS: discovery of a new function of NK cells

Scientists from the Institut Pasteur proved that NK cells ("natural killer" cells in the immune system) migrate to lymphoid follicles, an area known to be the primary anatomical reservoir for HIV, where they control replication of simian immunodeficiency virus (SIV). This discovery raises the prospect of one day being able to control HIV in humans that have stopped treatment, a phenomenon that is currently only seen very rarely in a handful of patients known as post-treatment controllers.

# The expert view Michaela Müller-Trutwin, a scientist at the Institut Pasteur and author of the paper

![](_page_5_Picture_17.jpeg)

# We have demonstrated a new

function of NK cells: their ability to migrate to lymphoid follicles and differentiate there to control viral replication.

# THE INSTITUT PASTEUR ENTERS ITS 130TH YEAR

On November 14, 2017, the Institut Pasteur celebrated its 129th anniversary and embarked on its 130th year. In November 2017, a book went on sale in bookshops: Institut Pasteur: Todav's Research, Tomorrow's Medicine, published by Abrams. This volume outlines the major challenges and medical issues facing the Institut Pasteur and its International Network. Shortly after. on December 14, 2017, the exhibition Louis Pasteur, the experimenter, produced by Universcience in collaboration with the Institut Pasteur, opened at the Palais de la découverte in Paris. It will run until August 19, 2018.

![](_page_5_Picture_23.jpeg)

# CHOLERA: FROM MAJOR GLOBAL OUTBREAKS TO A BETTER CONTROL STRATEGY

![](_page_5_Picture_25.jpeg)

**Researchers at the Institut Pasteur and the Wellcome Trust** Sanger Institute, in collaboration with several other international institutions, traced the history of cholera outbreaks in Africa, Latin America and the Caribbean over the last 60 years. They carried out a vast genomic analysis of Vibrio cholerae strains collected since 1961, revealing that the most recent cholera pandemic originated in Asia and that the majority of antibiotic-resistant strains come from this continent.

Salmonella outbreak: the Institut Pasteur issues the alert

In late November 2017, after observing an excessive number of salmonellosis cases in

![](_page_5_Picture_29.jpeg)

infants, the CNR for *Escherichia coli*, *Shigella* and *Salmonella* alerted the health authorities, which launched epidemiological investigations with the parents of the infected infants. A powdered baby milk was soon identified as the source of the contamination. Each year, the CNR receives between 8,000 and 10,000 salmonella samples for analysis, 400 to 600 of which are from infants under the age of one (see also pp. 48-49).

# **Kecognition** Awards and appointments in 2017

# **PEOPLE APPOINTED TO THE RANK OF PROFESSOR**

![](_page_6_Picture_2.jpeg)

Hervé Bourhy Head of the Lyssavirus Dynamics and Host Adaptation Unit

# **APPOINTMENTS**

![](_page_6_Picture_5.jpeg)

**Patrick Forterre** Elected member of Academia Europaea

![](_page_6_Picture_7.jpeg)

Claude Leclerc Member of the US National Academy of Inventors, Associated Member of the French Academy of Pharmacy

![](_page_6_Picture_9.jpeg)

Jean-Marc Ghigo Elected member of the European Academy of Microbiology

![](_page_6_Picture_11.jpeg)

Marc Lecuit Elected member of the European Molecular Biology Organization (EMBO)

# HONORS **AND PRIZES**

![](_page_6_Picture_14.jpeg)

Laure Bally-Cuif Head of the Zebrafish Neurogenetics Unit 2017 CNRS Silver Medal

![](_page_6_Picture_16.jpeg)

David Bikard Head of the Synthetic Biology Unit Pasteur Vallery-Radot Prize

![](_page_6_Picture_18.jpeg)

Philippe Bousso Head of the Dynamics of Immune Responses Unit Jean Valade Prize. Grand Prix Robert Debré for Fundamental Research. Maurice Girard Award from the French Academy of Pharmacy

![](_page_6_Picture_20.jpeg)

Anne Chevallereau PhD student PhD research prize from the French Society of Microbiology (SFM)

![](_page_6_Picture_22.jpeg)

**Pascale Cossart** Head of the Bacteria-Cell Interactions Unit 2017 Ernst Jung Gold Medal for Medicine

![](_page_6_Picture_24.jpeg)

Ludovic Deriano Head of the Genome Integrity, Immunity and Cancer Unit Cancer Research Award from the Simone and Cino Del Duca Foundation

![](_page_6_Picture_26.jpeg)

Mélodie Duval Post-doctoral fellow in the Bacteria-Cell Interactions Unit 2017 Madeleine Lecoq Award (Academy of Sciences)

![](_page_6_Picture_28.jpeg)

**Olivier Gascuel** Director of the Center of Bioinformatics, Biostatistics and Integrative Biology (C3BI) and head of the Evolutionary Bioinformatics Unit Inria–French Academy of Sciences Grand Prize

![](_page_6_Picture_30.jpeg)

Romain Koszul Head of the Spatial Regulation of Genomes Unit Pasteur Vallery-Radot Prize

![](_page_6_Picture_32.jpeg)

Fani Koukouli Post-doctoral fellow in the Integrative Neurobiology of Cholinergic Systems Unit **UNAFAM Biomedical Science Research Award** 

![](_page_6_Picture_34.jpeg)

Marc Lecuit Head of the Biology of Infection Unit René & Andrée Duquesne Award

![](_page_6_Picture_36.jpeg)

Pierre Legrain Vice-President Development and Grants Office HUPO Award 2017 (Human Proteome Organization)

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![](_page_6_Picture_39.jpeg)

![](_page_6_Picture_42.jpeg)

![](_page_6_Picture_44.jpeg)

![](_page_6_Picture_46.jpeg)

![](_page_6_Picture_49.jpeg)

Javier Pizarro-Cerda Head of the Yersinia Unit Georges, Jacques and Elias Canetti Prize

![](_page_6_Picture_51.jpeg)

Hilde de Reuse Director of the Microbiology Department and head of the Helicobacter Pathogenesis Unit **Christoffel Plantin Prize** 

![](_page_6_Picture_53.jpeg)

**Brice Rotureau** Head of the Trypanosome Transmission Group **Deschiens Prize (French Academy** of Medicine)

![](_page_6_Picture_55.jpeg)

Fabrizia Stavru Bacteria-Cell Interactions Unit Sanofi–Institut Pasteur Award Human Frontier Science Program Young Investigator Grant

![](_page_6_Picture_57.jpeg)

# **INVENTOR AWARDS**

The Institut Pasteur recognized the efforts of 14 scientists whose research gave rise to US patents, licensing, and new start-ups, etc. These inventors were elected as members of the US National Academy of Inventors.

![](_page_7_Picture_2.jpeg)

In alphabetical order: Françoise Barré-Sinoussi, Luc Montagnier and Simon Wain-Hobson (HIV1) Pierre Charneau (lentiviruses) André Choulika and Bernard Dujon ("molecular scissors") Marie Flamand (dengue) Claude Leclerc and Christine Petit (deafness) Catherine Rougeot (opiorphin) Pierre Sonigo (HIV2) Frédéric Tangy (Measles Platform) **Pierre Tiollais and Marie-Louise Michel** (hepatitis B)

# **5 "WOMEN IN SCIENCE" LAUREATES**

L'Oréal-UNESCO For Women in Science French Fellowships

![](_page_7_Picture_6.jpeg)

Juliette Fédry PhD student in the Structural Virology Unit

Fani Koukouli Post-doctoral fellow in the Integrative Neurobiology of Cholinergic Systems Unit

![](_page_7_Picture_9.jpeg)

Ai Ing Lim PhD student in the Innate Immunity Unit

**Blandine Monel** 

Post-doctoral fellow in the Virus and Immunity Unit

![](_page_7_Picture_13.jpeg)

Pascale Vonäsch Researcher in the Molecular Microbial Pathogenesis Unit

# IN THE INTERNATIONAL NETWORK

![](_page_7_Picture_16.jpeg)

**Richard Njouom** Head of the Virology Department at the Pasteur Center in Cameroon Laureate of the 2017 Dedonder Clayton Award

![](_page_7_Picture_18.jpeg)

![](_page_7_Picture_19.jpeg)

![](_page_7_Picture_20.jpeg)

Sylvain Brisse Biodiversity and Epidemiology Image Analysis Hub of Bacterial Pathogens

Jean-Yves Tinevez

![](_page_7_Picture_23.jpeg)

**Thomas Wollert** Membrane Biochemistry and Transport

# **ERC GRANTS**

![](_page_7_Picture_26.jpeg)

**Romain Levayer** 

Head of the Cell Death

and Epithelial Homeostasis

Romain Koszul Head of the Spatial Regulation of Genomes Unit SynarchiC project

![](_page_7_Picture_29.jpeg)

Pablo Navarro-Gil Head of the Epigenetics of Stem Cells Unit Bin D project

![](_page_7_Picture_31.jpeg)

Nicolas Reyes Head of the Molecular Mechanisms of Membrane Transport Unit **T** Receptors project

![](_page_7_Picture_33.jpeg)

# **INTERNATIONAL JOINT UNITS (UMI) SET UP IN 2017**

UMI on viral evolution

![](_page_7_Picture_36.jpeg)

Benjamin R. tenOever

Director of the Virus Engineering Center for Therapeutics and Research at the Icahn School of Medicine at Mount Sinai (New York)

![](_page_7_Picture_39.jpeg)

Marco Vignuzzi Head of the Viral Populations and Pathogenesis Unit at the Institut Pasteur in Paris

# **NEW FIVE-YEAR GROUPS** (G5s)

![](_page_7_Picture_42.jpeg)

**Grégory Batt** InBio - Experimental and Computational Methods for Modeling Cellular Processes

![](_page_7_Picture_44.jpeg)

Mathilde Gendrin Microbiota of Insect Vectors (at the Institut Pasteur in French Guiana)

![](_page_7_Picture_46.jpeg)

**Romain Levayer** Cell Death and Epithelial Homeostasis

![](_page_7_Picture_48.jpeg)

**Eugène Gladyshev** Fungal Epigenomics

![](_page_7_Picture_50.jpeg)

Jean-Baptiste Masson Decision and Bayesian Computation

![](_page_7_Picture_52.jpeg)

14

# search

Observe, question, hypothesize, design, test, collaborate, experiment, analyze, discuss. Then repeat the cycle. Search. Research. The Institut Pasteur is committed to conducting outstanding research to improve global health. Its scientists never give up and persevere continually. In the wake of each discovery, they challenge themselves to begin the search again.

![](_page_8_Picture_4.jpeg)

# RESEARCH

# Department of Cell Biology and Infection

![](_page_9_Picture_1.jpeg)

The Cell Biology and Infection Department explores the fundamental workings of cells in a healthy and pathogenic state, *in vivo* and *in vitro*. Gaining a thorough understanding of the structure and function of individual cells can help shed light on the mechanisms of pathological conditions and pave the way for the development of tools and approaches to tackle disease.

Some of the department's teams examine host-pathogen interactions at the cellular and the tissue level, while others focus on specific diseases, such as cancer and neurodegenerative conditions, at the molecular level. A number of teams make use of quantitative tools and innovative techniques to improve understanding of the molecular mechanisms at work in cells. To achieve its aims, the department draws on a wide range of different disciplines:

high-throughput approaches, new modeling systems and highly sensitive techniques to analyze cells in vitro. New cellular, tissue and animal models that are of particular interest for studying infections and other diseases are currently being developed. They raise new questions and provide scientists with a better vantage point from which to examine diseases and perform clinical research. The department is directed by Chiara Zurzolo.

![](_page_9_Picture_5.jpeg)

# A first link between redox and cell division

Cytokinesis is the final stage in cell division, leading to the physical separation of a parent cell into two daughter cells. Cytokinesis begins when a parent cell contracts at its center, leaving the two daughter cells connected by an "intercellular bridge" for several hours. The final cleavage (known as "abscission") is complex and requires local disassembly of the actin cytoskeleton (a network of protein polymers located under the plasma membrane in cells). The Membrane Traffic and Cell Division Unit, directed by Arnaud Echard, has discovered that redox plays an unexpected role in abscission. The team identified an enzyme, MICAL1, which oxidizes actin filaments at the abscission site and induces their local depolymerization. This stage is crucial in recruiting the ESCRT machinery responsible for abscission. This machinery is also involved in the scission of the HIV virus from infected cells. a process that in many ways is similar to cytokinesis.

Source: Frémont et al., Nature Communications, February 2017.

![](_page_9_Picture_9.jpeg)

# Double-strand breaks in DNA make the chromatin more rigid and more mobile.

# How DNA damage disrupts chromosomes

One of the greatest imperatives for a living organism such as yeast is to keep its genome intact to ensure faithful replication. Cells have developed various processes to repair DNA damage - including the most severe type of damage, namely breaks to both strands of the double helix. Cell repair processes modify the chromatin fiber, the complex of proteins and DNA that structures the genome, leading to an increase in chromatin mobility in yeast nuclei. The Imaging and Modeling Unit, directed by Christophe Zimmer, used live cell microscopy to carry out a quantitative analysis of

by DNA breaks. and function.

![](_page_9_Picture_15.jpeg)

chromatin structure and movements. With computer simulations, the scientists examined the mechanisms underpinning chromatin movement caused

They provided evidence that the chromatin fiber becomes more rigid as a result of this damage and the repair processes used by cells. They believe that this stiffening is responsible for enhanced chromatin mobility. The scientists' research highlights the key role played by changes to chromatin structure in the cell response to DNA damage and improves our understanding of the links between chromatin organization

Source: Herbert et al., EMBO J., September 2017.

![](_page_9_Picture_21.jpeg)

mmunofluorescence and segmentation analysis of cells infected with *Listeria monocytogenes*.

# How Listeria activates a program of resistance to stress and its virulence

Listeria monocytogenes is responsible for severe foodborne infections that can prove fatal. The Bacteria-Cell Interactions Unit directed by Pascale Cossart is studying the different aspects of infection with this bacterium.

The scientists used a cutting-edge technique known as N-terminomics to identify all the translation initiation sites for the Listeria monocytogenes genome. This technique, which involves mass spectrometry-based sequencing of N-terminal peptides, demonstrated that alternative translation initiation sites in bacterial genes are more common than is generally believed, and that the genome codes for a series of very small proteins whose function remains unknown. A closer examination of one of these proteins, pRli42. which can be found in many Firmicutes including Bacillus subtilis, revealed that it is anchored in the membrane and acts as the link that scientists have long been trying to find between external stress and the stressosome, an intracellular nanomachine that activates genes regulated by the sigma B factor, especially virulence genes.

Source: Impens et al., Nature Microbiology, February 2017.

# Awards

**Pascale Cossart** 2017 Ernst Jung Gold Medal for Medicine

Mélodie Duval 2017 Madeleine Lecog Award, Paris Academy of Sciences

Arnaud Echard 2017 Georges Zermati Prize from the Fondation de France

Marc Lecuit elected as a member of EMBO and an ESCMID Fellow

Philippe Sansonetti Chief Editor of EMBO Molecular Medicine

Fabrizia Stavru 2017 Sanofi-Institut Pasteur Award for microbiology and infection

![](_page_10_Picture_0.jpeg)

![](_page_10_Picture_1.jpeg)

imulation: gradient information (in green) is converted into regular strips (in orange) en into rows of regularly spaced cells (in pink)

t=5

t=2

# Department of Developmental and Stem Cell Biology

How does a cell acquire its identity? How does an organ begin to form? We still know relatively little about the mechanisms involved in the "building" of animals and humans. This research department is committed to improving our understanding of these mechanisms, which are responsible for the healthy development of the embryo and also play a part in maintaining adult tissues.

As embryos develop, the fertilized egg gives rise to multiple cells that form our organs. Research into embryonic cells, organ formation and the regeneration of these organs in adults can help shed light on the rules, often common to all living beings, that underpin development in embryos and adults. Understanding how tissues are formed also means understanding how they regenerate and repair themselves, which can pave the way for innovative therapeutic approaches. Recent research

in the department has focused on the distribution of sensory organs in flies, the topology of the genome and its role in gene expression during development. and torsion of the heart tube in mice. The department is directed by François Schweisauth.

# A simple rule for the spatial distribution of cells

How do cells organize themselves spatially to produce complex structures at regular intervals? Are there simple rules that are applicable to all superior animals? Scientists in the Drosophila Developmental Genetics Group (Institut Pasteur/CNRS), in collaboration with the Statistical Physics Laboratory (École normale supérieure/CNRS), set out to improve their understanding of how sensory organs are distributed at regular intervals in around ten rows on the backs of flies. Using real-time imaging to monitor the expression profile of genes that play a critical role in this process, and drawing on a mathematical model inspired by the Turing model, these scientists proposed a simple construction rule involving a self-organization mechanism. It remains to be determined whether changing the initial conditions in which this basic mechanism is implemented results in different distribution profiles, which would help explain the evolutionary variations in these profiles.

Source: Corson et al., Science, May 2017.

# The organization of the genome in areas of regulation

The 2m-long human genome has to be folded to fit into a 10µm-diameter nucleus in an orderly manner so that sequences that are linearly distant can interact efficiently and specifically. Such long-distance interactions are particularly important for embryonic development and organ formation. Researchers from the 'Genomics and Epigenomics of Animal Development' group (Institut Pasteur/CNRS) showed in collaboration with groups at EMBL and MIT that a molecular

![](_page_10_Picture_14.jpeg)

is blocked

# of the heart

The heart is partitioned into a right and a left side, supporting the double blood circulatory system. This left-right asymmetric morphogenesis is established as the heart develops inside the embryo, when the initial cardiac tube is transformed into an anti-clockwise helix shape (loop), similar to the shell of a snail. Researchers from the 'Heart Morphogenesis' group (Institut Pasteur/Institut Imagine/INSERM) have investigated the process of heart looping in mice and quantified the shape changes

machine, known as the cohesin complex, is essential for the formation of distinct "topological domains" along the chromosomes. Erasing those domains leads to changes in gene expression, demonstrating their importance. Strikingly, in absence of cohesin. new, smaller structures appear that segregate active and inactive genomic intervals into different compartments. This work shows that the packaging of the chromatin is driven by two distinct, sometimes antagonistic, processes. These findings have important implications for understanding the etiology of the numerous human diseases that are caused by abnormal interactions between distant genomic regions.

Source: Le Garrec et al., eLife, November 2017.

![](_page_10_Picture_21.jpeg)

The folding of a chromosomal region in three compact structures (on the left) is impaired (on the right) when cohesin loading on chromatin

# Formation of the left and right sides

using 3D reconstructions of high-resolution episcopic microscopy images. In combination with cell labeling and live-imaging of the developing heart, they identified sequential left-right asymmetries. A computer model was developed, which can predict not only the direction of the heart loop, but also its shape - from initial asymmetries and from the mechanical constraints at the sites of attachment of the heart to the body.

Source: Schwarzer et al., Nature, November 2017,

![](_page_10_Picture_26.jpeg)

Reconstruction of the shape of a normal embryonic heart (on the left) and a mutant hbryonic heart (on the right).

# **Awards**

# Laure Bally-Cuif

CNRS Silver Medal for her pioneering work on the role of stem cells in brain development and homeostasis in vertebrates

# **Romain Levayer**

European Research Council (ERC) Starting Grant to carry out research on cell competition, cell death and tissue homeostasis

# Pablo Navarro-Gil

ERC Consolidator Grant for his research on stem cells and pluripotency

The Institut Pasteur thanks the donors who contributed to the acquisition of the Titan Krios™ microscope and the construction of this building.

![](_page_11_Picture_1.jpeg)

![](_page_11_Picture_2.jpeg)

# Department of Structural Biology and Chemistry

Structure and function of a biological macromolecule are intimately related. The Structural Biology and Chemistry Department studies the three-dimensional structure of these molecules and their interactions in order to gain detailed understanding of their functions, especially those that play a role in human pathologies. The department also uses chemical synthesis to develop new therapeutic and vaccinal strategies.

Deciphering the molecular mechanisms involved in the assembly of protein complexes associated with pathological or infectious processes makes it possible to design chemical tools capable of modulating them. The study of these interactions at the molecular level is based on several advanced technologies which allow the determination of the 3D structures of molecules, their dynamics and interactions, in isolation and in large complexes or in the cellular context. These cutting-edge techniques and special skills include: crystallography; nuclear magnetic resonance, or NMR; electron cryo microscopy; molecular modeling; mass

spectrometry; chemical and/or chemoenzymatic synthesis for therapeutic, vaccinal and diagnostic purposes; the design of molecular tools to dissect molecular/cellular interactions and host-pathogen recognition. The department has been highly successful in obtaining competitive funding to contribute to the purchase of state-of-the-art equipment for the Institut Pasteur, in particular a Titan Krios™ 300 kV electron microscope, which was delivered in December 2017, and an 800 MHz NMR spectrometer, which was inaugurated in February 2017. The department is directed by Michael Nilges.

# Human excitatory neurotransmitter transporter gets in the picture

Glutamate is the main excitatory neurotransmitter in the brain. and its extracellular concentration has to be tightly regulated to allow for neurotransmission, and to avoid the cytotoxicity observed in some neurodegenerative disorders. Membrane glutamate transporters (EAATs) are kev players in this regulatory function. Recently, the G5 Molecular Mechanisms of Membrane Transport (headed by Nicolas Reyes) has determined the first 3D structures of a thermostable human EAAT The structures reveal novel architectural features, and atomic insights that explain a wealth of functional data. as well as human mutations. Moreover, in collaboration with the Unit of Mass Spectrometry for Biology (headed by Julia Chamot-Rooke), they unravelled the first allosteric inhibition mechanism of glutamate transporters, setting the basis for rational design of novel compounds targeting these proteins.

Source: Juan C. Canul-Tec et al., Nature, April 2017.

![](_page_11_Picture_10.jpeg)

Crystal structure of the human EAAT1 transporter.

# Structure of the calcium-dependent type 2 secretion pseudopilus

20

Bacteria use complex nanomachines to secrete proteins essential for nutrient acquisition, adaptation and virulence. In the type II secretion system polymerization of a fiber called pseudopilus is essential for transport of enzymes and toxins. The molecular assembly and function of this dynamic fiber can only be studied by using an integrative approach. Three teams from our department, led by O. Francetic,

N. Izadi-Prunevre and M. Nilges. combined their complementary expertise in type 2 secretion biology, NMR and molecular modeling to elucidate the subunit structure and fiber biogenesis. The fiber structure was solved with the Titan Krios cryo-electron microscope in collaboration with E. Egelman. University of Virginia. This structure, with the highest resolution obtained so far for this type of polymer (5 A), highlights unexpected atomic details and conformational changes. Interestingly, our combined approaches reveal a key regulatory role of calcium fiber dynamics in this bacterial secretion pathway.

Source: Lopez-Castilla et al., Nature Microbiology, September 2017.

# **Creation of the Unit** "Structural studies of macromolecular machines in cellulo"

This new unit will be headed by Dorit Hanein, whose research encompasses a critical question in cell biology: how do cells employ large, macromolecular

machines in cellular processes? For this. Hanein will continue to push the envelope in developing and employing a unique set of powerful tools, merging state-of-the-art light and electron microscopy imaging with micromechanical engineering, computational methods, cell biology, and protein biochemistry. The new electron crvo-microscopy equipment, in particular the Titan Krios<sup>™</sup> delivered to the Institut Pasteur in 2017, will allow her and other researchers at the Institut Pasteur to extend microscopic methods to perform quantitative analysis of molecular machines in unperturbed, intact mammalian cells, at nanometer resolution. Key examples are the resolution of single actin filaments and macromolecular complexes. This will be supplemented with atomic resolution studies of reconstituted systems. The resulting quantitative integration of scales between macroscopic cellular behavior and high-resolution structural changes will position these efforts at the forefront of science, with high impact in both medicine and basic biological research.

# Awards

# Laurence Mulard

(Chemistry of Biomolecules Unit) Thérèse Lebrasseur Prize. Fondation de France

# **Nicolas Reyes**

(Molecular mechanisms of membrane transport G5) ERC Consolidator Grant

# Michael Nilges

(Structural Bioinformatics Unit) Institut Pasteur Chair of Excellence

![](_page_12_Picture_0.jpeg)

# Department of Genomes and Genetics

Decoding the architecture and content of genomes sheds light on new biological functions and offers a vast array of research possibilities for scientists in the Genomes and Genetics Department.

The department explores the genetic information of microorganisms such as yeast and bacteria, as well as that of humans. It also investigates the evolution of infectious agents and the selective pressures they have exerted on both human and

insect vector genes over time. The progress of these research programs is largely based on new sequencing and genotyping techniques. The department is directed by Didier Mazel.

![](_page_12_Picture_5.jpeg)

# A better vaccine strain for tuberculosis

Bacillus Calmette-Guérin (BCG), an attenuated vaccine strain. is lacking the ESX-1 secretion system which, in some other mycobacteria, leads to phagosomal rupture and induces a series of innate immune responses in the host. To improve the immunogenic and vaccine efficacy of BCG, the team in the Integrated Mycobacterial Pathogenomics Unit, directed by Roland Brosch, introduced the ESX-1 system of a low-virulence aquatic mycobacterium (M. marinum) in a recombinant BCG strain. In mouse models, this significantly improved the innate and adaptive immune responses induced by this strain and offered better protection against subsequent infection with M. tuberculosis.

Source: Matthias I. Gröschel et al., Cell Reports, March 2017.

# Reconstructing the migratory and adaptive history of the Bantu peoples

Using data from a vast genomic analysis of more than 2,000 samples taken from individuals in 57 populations throughout Sub-Saharan Africa, the Human Evolutionary Genetics Unit has traced the migratory route of the Bantu peoples, previously a source of debate. The study revealed that the admixture which occurred as a result of successive encounters with local populations enabled the Bantu to acquire alleles that helped them adapt to their new environments. From the genetic admixture with pygmies, for example, the Bantu peoples acquired a form of the HLA system, which helps trigger immune response to infection. Another compelling example indicates that when the Bantu arrived in eastern Sub-Saharan Africa, the local populations passed on a mutation that enabled them to continue digesting milk in adulthood.

Source: Étienne Patin et al., Science, May 2017.

# The genetics of quiescence

Life alternates between periods of growth and periods of quiescence. The vast majority of genetics research focuses on mutations and their impact on evolution during periods of growth; few studies actually look at what happens during periods of cell quiescence. The Dynamics of the Genome Unit demonstrated that, unlike growing cells, which accumulate mutations as they divide, quiescent cells accumulate mutations in a linear fashion over time. This alternation between two types of mutation optimizes genome potential, which is vital for the evolution of species. These findings directly introduce the

notion of time as a factor in the process of mutation (the molecular clock theory) and support the model of sexual dimorphism (anisogamy).

Source: Serge Gangloff et al., elife, December 2017.

# A new microfluidics unit

The Physical Microfluidics and Bioengineering Unit, directed by Charles Baroud, is developing quantitative biology tools for single-cell analysis based on an original microfluidics approach. The unit's research will be applied to the manipulation of microorganisms and to 3D mammalian cell culture. Cooperation with the other teams in the department has already resulted in the development of an original approach to antibiotic resistance by combining microbiological methods, quantitative experiments and mathematical modeling.

![](_page_12_Picture_23.jpeg)

![](_page_13_Picture_0.jpeg)

# Department of Immunology

The Immunology Department's research focuses on the development of the immune system, protective and pathological immune responses, and its medical applications.

To understand how the immune system works, and use our knowledge to develop preventive and therapeutic immunotherapies, the department is studying its development, its innate and adaptive reactions, and its pathological deregulations. This research reveals the properties of the cells and molecules involved in immune responses to infectious agents and tumors, those that ensure

our well-being, and that of the billions of microbes inside our bodies, and also those that trigger autoimmunity and allergies. The aim is to strengthen our immune balance and defenses, generate new cell- or molecule-based vaccines and treatments, and tackle inflammatory diseases. The department is directed by Gérard Eberl.

![](_page_13_Picture_5.jpeg)

Scientists of the Innate Immunity Unit.

# **Creating human** innate lymphoid cells "on demand"

The immune defenses comprise an early "innate" stage, involving a unique family of innate lymphoid cells (ILCs), and a late "adaptive" phase, with antibody-producing B lymphocytes and T cells. The ILCs maintain tissue homeostasis and help to form a barrier in the mucosal sites, guaranteeing protection against infection and inflammation. Until now, tissue-based ILC analysis was a lengthy process, and research into human ILCs was rare given the limited access to tissue samples. Scientists from the Innate Immunity Unit identified human ILC precursors (ILCPs) in blood and tissue. They examined circulating ILCPs to develop laboratory techniques capable of generating large quantities of specific mature ILCs. This ability to generate ILCs "on demand" may open up avenues for new applications, particularly cell therapy for fighting infection, cancer, metabolic diseases (obesity, diabetes) and allergies.

Source: Ai Ing Lim et al., Cell, March 2017.

# A link between microbiota and tuberculosis severity

Latent infection by *Mycobacterium* tuberculosis affects 30% of the global population. In most cases, people who are infected with the bacterium do not develop the active disease. In mice, *M. tuberculosis* infection is generally kept under control. Researchers from the Immune Regulation and Vaccinology Unit showed that colonization of mouse intestines by Helicobacter hepaticus brings about major changes in gut microbiota, uncontrolled inflammation and, as a consequence, increased proliferation of mycobacteria leading to the destruction of lung tissue. These findings suggest that chronic microbial colonization by Helicobacter species, such as H. pylori, which affects over half the world's population, could strongly influence the development of active tuberculosis in infected individuals.

Source: Majlessi L. et al., Mucosal Immunology, February 2017.

![](_page_13_Picture_13.jpeg)

Mycobacterium tuberculosis.

# **Repairing the** intestine using stromal cells

Intestinal stem cells are found in "cavities", from where they renew the entire intestinal epithelium every five days and repair this essential barrier following

inflammation or injury. Together with the Molecular Microbial Pathogenesis Unit, scientists in the Stroma, Inflammation and Tissue Repair Unit identified stromal cells - or fibroblasts - that are partly responsible for the maintenance and activity of intestinal stem cells, which at the same time organize inflammation. This discovery improves understanding of how stem cells react to inflammation and injury, and how they prevent the development of cancer. This research paves the way for new therapeutic approaches, targeting stromal cells in the fight against inflammatory intestinal diseases and colon cancer.

Source: Stzepourginski I. et al., PNAS, January 2017.

# Awards

# Philippe Bousso

Advanced Grant from the European Research Council (ERC) for his Enlighten project, which explores propagation and integration of immunological signals in cancer or an infection. and Grand Prix Robert Debré from the Robert Debré Association for medical research

# Ludovic Deriano

Cancer Research Award from the Simone and Cino Del Duca Foundation, Institut de France

# Claude Leclerc

member of the American National Academy of Inventors and associate member of the French Academy of Pharmacy

# Department of Infection and Epidemiology

![](_page_14_Picture_1.jpeg)

The Infection and Epidemiology Department conducts research in the field of emerging and re-emerging infectious diseases, and is also deeply committed to public health issues.

The department studies all aspects of infectious diseases – pathogen reservoirs and transmission mechanisms, virulence factors, host immune response, pathophysiological processes, therapeutic strategies, and the impact of vaccination. These challenges are addressed using transversal approaches and tools from a range of disciplines. In addition, the department plays a key role in public health issues, particularly via six National Reference Centers (CNRs), two WHO Collaborating Centers (WHOCCs), and the Laboratory for Urgent Response to Biological Threats (CIBU). These activities call for close collaboration with the Institut Pasteur International Network. The department is directed by Prof. Marie-Lise Gougeon.

![](_page_14_Picture_5.jpeg)

# A bacterial mutant responsible for an unusual outbreak

In November 2015, an outbreak caused by the Elizabethkingia anophelis bacterium - first described in 2011 - was reported in Wisconsin (USA) and affected 66 people. Despite the introduction of an antibiotic treatment protocol, 21 patients died. To shed light on this unusual outbreak, full genomic and evolutionary characterization of the bacterial strain was carried out by researchers at the Institut Pasteur and CNRS and was coordinated by Sylvain Brisse in collaboration with American and Australian teams. The study revealed that this was a highly mutant strain of the bacterium as it had undergone nearly 300 mutations in just one year – ten times more than "traditional" bacteria. This high mutation rate might therefore have given the bacterium a selective advantage - facilitating its survival in the environmental reservoir or increased its pathogenicity in humans. This study also dated the emergence of their common ancestral strain back to one year before the first confirmed case of infection. In addition, it gave the scientists the opportunity to highlight the importance of real-time data exchange during outbreaks - in line with the ideals of the Open Data movement – as a means of providing the best possible response to public health emergencies.

Source: Perrin A. et al., Nature Communications, May 2017.

# Visceral leishmaniasis – when a parasite infects the brain

Leishmaniasis is caused by Leishmania parasites, which are spread by insect bites. It causes highly debilitating cutaneous or visceral lesions which can prove fatal if left untreated. Through experimental infection of mice with Leishmania donovani. which causes a visceral infection affecting the lymphoid organs, scientists from the Trypanosoma Infectious Processes Laboratory. directed by Paola Minoprio, investigated the causes of neurological lesions associated with the infection. Thanks to this dynamic model of infection in vivo, and the use of a bioluminescent parasite, they showed that *L. donovani* infects the brain, and induces inflammation with monocytic infiltration and the release of proinflammatory mediators. The inflammatory process comprises an early phase, triggered by infection of the brain, followed by a late stage, several months after, when the parasitemia reappears in the bone marrow. This pioneering research reveals the cerebral tropism of L. donovani and sheds light on the mechanisms responsible for neurological lesions associated with leishmaniasis.

Source: Melo GD et al., Scientific Reports, August 2017.

![](_page_14_Picture_12.jpeg)

Picture of an organ parasitized by Leishmania donovani.

of pandemics Cholera is an acute infection of the small intestine caused by the bacterium Vibrio cholerae. Though considered an ancient disease, cases were reported in 38 countries in 2016. To trace the history of cholera outbreaks in Africa, Latin America and the Caribbean over the past 60 years, scientists from the Enteric Bacterial Pathogens Unit directed by François-Xavier Weill, together with the Institut Pasteur International Network and the Wellcome Trust Sanger Institute (Cambridge, UK), analyzed the genomes of more than 1,200 strains of V. cholerae collected from across the globe during the current pandemic, which began in 1961. Their research shows that the cholera bacterium has been regularly introduced into Africa from an Asian source (at least 11 times in 44 years) and that humans are the main vectors for disease dispersal. Thanks to the genomic tools developed, we now understand how cholera is moving across the globe and we can predict the risk of outbreak according to the V. cholerae populations identified and therefore adapt the public

26

![](_page_14_Picture_16.jpeg)

*Cholera vibrio,* responsible for cholera, discovered by Koch in 1883. Colorized image.

# Cholera – a step towards a better understanding of pandemics

## Source: Weill FX et al., Science, November 2017.

health response.

# Joining forces against the plague in Madagascar

From September to November 2017, Madagascar faced the most severe outbreak of pneumonic plague in the world since the advent of antibiotics. The Institut Pasteur in Madagascar played a key role in responding to the outbreak by providing diagnostic testing for all suspected cases. Several units from our department – those led by Jean-Claude Manuguerra (CIBU), Arnaud Fontanet and Simon Cauchemez – assisted with diagnostic and epidemiological aspects.

![](_page_14_Picture_22.jpeg)

Rapid diagnostic kit for plague produced at the Pasteur Institute of Madagascar.

![](_page_15_Picture_0.jpeg)

# Escherichia coli strain

# Department of Microbiology

Besides their major role in infectious diseases, bacteria also serve as models to understand fundamental biological mechanisms. The research performed in the Department of Microbiology focuses on the molecular characterization of functions that enable bacteria to interact with their environment and, in some cases, to cause diseases.

The scientists of the Department of Microbiology study, at the cellular and molecular levels, fundamental biological processes of bacteria and archaea (and their viruses) using genomics, genetics, metabolism, etc. They also focus on the mechanisms that render some of these microorganisms virulent and enable them to evade the host immune system or to develop resistance to antibiotics. These studies not only

improve our understanding of the life cycle of these microorganisms, but also constitute a prerequisite for the development of new therapies or new diagnostic tools that can be used to treat or prevent bacterial infections. The Department of Microbiology is directed by Hilde De Reuse.

![](_page_15_Picture_6.jpeg)

Schematic representation of the assembly of Bcs proteins from *E. coli* and their interaction within a macro-complex producing extracellular

# **Biofilm-promoting** cellulose is secreted by a new type of bacterial nanomachine

Bacterial biofilms are microbial communities whose cohesion often results from the production of extracellular polysaccharides such as cellulose, a glucose-rich polymer determinant for bacterial survival and virulence. Although the structure and function of the c-di-GMP-responsive catalytic duo formed by the inner membrane synthase BcsA and the membrane-anchored BcsB has been studied in great detail, its interplay with additional Bcs structural and regulatory subunits remained enigmatic until recently. Using electron microscopy, structure-function and protein interaction analyses, the team of Jean-Marc Ghigo (Genetics of Biofilms), Petya Krasteva (CNRS) and Rémi Fronzes (CNRS) revealed that Escherichia coli biofilm-promoting cellulose is secreted by a megadalton-sized multicomponent secretion system composed of BcsA, B, Q, R, E, F and G, displaying a previously undescribed asymmetric architecture. This study adds a sophisticated secretory nanomachine to the arsenal involved in bacterial adaptation to their environment.

Source: Krasteva PV, Bernal-Bayard J. et al., Nature Communications, December 2017.

DNA replication is a fundamental molecular process ensuring the continuity of life on Earth. The key enzymes in this process are DNA polymerases. All previously known replicative DNA polymerases can only add new nucleotides to a strand of DNA or RNA if they have a primer. However, this 60-year-old belief was recently overturned by the discovery of a novel group of DNA polymerases by Mart Krupovic (in the Molecular Biology of Gene in Extremophiles laboratory headed by Patrick Forterre) and Modesto Redreio-Rodríguez from the Autonomous University of Madrid. The newly discovered DNA polymerases can add a first nucleotide directly opposite its complementary nucleotide to kick-start the synthesis process and are encoded within a novel group of mobile genetic elements. called "pipolins", found in bacteria and eukaryotic mitochondria. The possibility of copying DNA without the need for a primer may be useful for DNA amplification in a number of biotechnological applications.

polymerase

![](_page_15_Picture_14.jpeg)

# **Synthesizing DNA** without a primer

Source: Redrejo-Rodriguez M. et al., Cell Reports, November 2017.

# Destroying Helicobacter pylori by disrupting synthesis of its cell wall!

How do bacteria produce their cell walls? The Biology and Genetics of the Bacterial Cell Wall Unit, headed by Ivo Gomperts Boneca, tackles this question using Helicobacter pylori as a model organism. This bacterium infects the gastric mucosa of half the human population worldwide and causes ulcers and cancer. The scientific community knew that bacterial cell wall synthesis requires an entire protein machinery. The team identified a complex made up of two proteins, PBP2 and MreC, whose assembly is vital to the bacterium. Using crystallographic techniques, the team was able to determine the structure of the PBP2:MreC complex and to define what happens when the association of the two proteins is disrupted. Under these conditions, H. pylori fails to elongate and ends up dying. These results open interesting perspectives in the search for anti-H. pylori molecules that target this complex.

Source: Contreras-Martel C. et al., Nature Communications, October 2017.

E. coli bacteria expressing a new group of DNA

# Awards

# **Hilde De Reuse**

Awarded the 2017 Christoffel Plantin Prize This prize is granted to a Belgian citizen residing abroad whose scientific work contributes to the prestige of Belgium.

**Patrick Forterre** Elected as member of the Academia Europaea

Jean-Marc Ghigo Elected as member of the European Academy of Microbiology

## Anne Chevallereau Thesis prize from the Société Française de Microbiologie (SFM)

![](_page_16_Picture_0.jpeg)

![](_page_16_Picture_1.jpeg)

# Department of Mycology

Fungal infections have been a major and growing public health concern since the early 1980s. The Mycology Department conducts research on the biology of human pathogenic fungi and their virulence mechanisms, with the aim of developing new diagnostic, prevention and treatment strategies for fungal infections.

The Mycology Department's work is focused on the three main fungi responsible for invasive fungal infections in humans: Aspergillus fumigatus, Candida albicans and Cryptococcus neoformans, as well as model fungi such as Neurospora crassa. The research teams in the department are investigating the genetic diversity of these species, and its link with virulence and resistance to antifungal molecules. Functional genomics approaches are used to identify the virulence factors employed by these fungi in different contexts - formation of biofilms, infection - and to understand how these mechanisms are regulated. The study of host-pathogen interactions, at the

level of both individual cells and the organism as a whole, reveals how pathogenic fungi bypass host defenses or how a protective immune response is initiated in the host. The department also provides expertise to partner institutions and hospitals via the National Reference Center for Invasive Mycoses and Antifungals. The department is directed by Christophe d'Enfert.

![](_page_16_Picture_6.jpeg)

# **Regulation of** morphogenesis, a process central to Candida albicans virulence

Candida albicans is characterized by its ability to switch between different morphotypes among which the filamentous form plays critical roles in virulence, allowing the fungus to invade host tissues. Scientists in the Fungal Biology and Pathogenicity Unit have studied the mechanisms by which the transcription factor Skn7 controls the switch between the yeast form and the filamentous form. Their work has revealed that Skn7 is a component of a network of transcription factors that concertedly regulate this switch. Surprisingly, they have also observed that Skn7 is necessary to limit the accumulation of reactive oxygen species that accumulate during the yeast-to-filament switch. This suggests that C. albicans uses this transcription regulator for self-defense against its own production of these toxic molecules.

Source: Basso et al., Molecular Microbiology, August 2017.

# Impaired

During infection with the fungal pathogen Candida albicans. recognition of the carbohydrate  $\beta$ -glucan by the host receptor Dectin-1 is essential for engulfing and killing the pathogen. Remarkably, whether phagocytosis of fungal  $\beta$ -glucan leads to an inflammatory response in human monocytes was previously unknown. The scientists in the Group Immunology of Fungal infections have now shown that phagocytosis of particulate  $\beta$ -glucan does not activate monocytes. However, inhibition of actin-dependent phagocytosis of β-glucan triggers a strong inflammatory signature. Their results highlight the mechanism by which phagocytosis tightly controls the activation of phagocytes by fungal pathogens and strongly suggest that actin cytoskeleton dynamics is an essential determinant of the host's susceptibility or resistance to invasive fungal infections.

# **Fungal cell wall** remodeling: ramification of β-glucan is essential for fungal survival

Fungal cells are protected by a cell wall made up of different polysaccharides. Disruption of the cell wall leads to fungal death due to the exposure of the fungal cell membrane to osmotic imbalance. The core cell wall structure is made up of a branched  $\beta$ -(1,3)-glucan;

# phagocytosis directs human monocyte activation in response to fungal derived **B**-glucan particles

Source: Camilli et al., European Journal of Immunology, January 2018.

branching leads to β-glucan ramification, facilitating its interaction with other cell wall components. to form a mature cell wall structure. The scientists in the Aspergillus Unit have identified the enzymes, belonging to the GAS/GEL-family of alvcosvlhvdrolases, responsible for  $\beta$ -(1,3)-glucan branching in the fungal cell wall as well as the mechanism of branching. Further. deletion of the branching enzyme genes resulted either in a sick phenotype or inviability, confirming the essentiality of  $\beta$ -(1,3)-glucan ramification for fundal survival and suggesting that such activity could be exploited as an antifungal target.

Source: Aimanianda., MBio, June 2017.

# Department of Neuroscience

![](_page_17_Figure_1.jpeg)

The Neuroscience Department aims to improve understanding of how the human brain works, in both its normal and pathological states. Communication between neurons and brain plasticity is the common thread running through the research carried out by its teams. The Department's scientists combine molecular, cellular and behavioral approaches, drawing on expertise in a wide variety of fields including genetics, mathematics, neuronal biology and functional imaging using animal models.

The Neuroscience Department comprises nine research units. It seeks to elucidate the genetic. molecular and cellular mechanisms underpinning the development, plasticity and pathogenesis of sensory circuits in the brain and cognitive functions. The various strands of its work come together to shed light on conditions such as autism, schizophrenia and depression. It has adopted a multiscale approach, ranging from the structure and function of synaptic proteins to intraand interneuronal information processing and the identification of genetic and epigenetic factors that influence cognitive functions (such as learning, memory and sensory perception) and defects in these functions (neurological and

psychiatric disorders). The department's scientists aim to develop new pharmacological and genetic tools for the prevention, attenuation and treatment of brain dysfunction in children and adults. Computational neuroscience is used to analyze information from a mathematical perspective, in conjunction with experimental research. The department also focuses on improving understanding of the rules governing the complex interactions between the microbiota. the immune system and the functioning of the nervous system. It is committed to the development of clinical trials and also organizes academic training programs. The department is directed by Prof. Pierre-Marie Lledo.

# How nicotine acts on the brains of schizophrenic patients

The prefrontal cortex (PFC) is a brain region associated with cognitive processes such as decision-making and memory. It is largely modulated by nicotinic acetylcholine receptors and is characterized by spontaneous neuronal activity, which is modified in psychiatric disorders such as schizophrenia. The fact that between 80 and 95% of schizophrenic patients are heavy smokers suggests a link between nicotine dependence and schizophrenia. Scientists introduced the human CHRNA5 gene ( $\alpha$ 5 SNP), which increases the risks of nicotine dependence and schizophrenia, into mice with the aim of reproducing the behavioral problems that characterize schizophrenia. In the mice carrying the CHRNA5 mutation, they observed reduced activity in PFC cells and identified the neuron type with impaired function. The repeated administration of nicotine restored normal activity in the PFC, thereby pinpointing a new therapeutic target for schizophrenia treatment.

Source: Fani Koukouli et al., Nature Medicine, January 2017.

![](_page_17_Picture_8.jpeg)

Genetic mutation regulating nicotine addiction.

![](_page_17_Picture_10.jpeg)

Aosquito larval breeding in Martinique

# **Clinical research on** Zika virus infection

Following the Zika virus outbreak that affected half of all those living in the French West Indies in the spring and summer of 2016, the Perception and Memory Unit began to conduct clinical research\* on the neurological, neurosensory and neurocognitive aspects of Zika virus infection, in collaboration with hospitals in Guadeloupe and Martinique. Zika is an arbovirus from the Flaviviridae family which is transmitted by mosquitoes of the Aedes genus. It recently emerged in Central and South America and in the Caribbean. Zika infection is usually harmless and lasts for up to a week. But in rare cases, it can lead to long-term neurological, psychomotor and neurosensory symptoms. Thus it is important to carry out clinical monitoring to observe the development of the infection and make an accurate prognosis. Using recent results for which a patent application was filed in November 2017, the Perception and Memory Unit is now working with teams of neurologists and infectious disease specialists

bv Zika.

and biomedicine.

from hospitals in Pointe-à-Pitre and Fort-de-France, and Bichat Hospital in Paris, as well as epidemiologists from the Institut Pasteur, to assess early olfactory and psychometric deficits in individuals infected

The teams are performing simple, painles's olfactory tests in a bid to provide an early diagnosis for people at risk of neurological complications after Zika virus infection. This early diagnosis means that patients can be given appropriate treatment with the aim of preventing the irreversible deterioration of their neurological condition.

\* Approval given by the Ethical Research Committee on June 12, 2017.

# New software for microscopy and biomedicine

The objective of the DIVA project is to create a generalized software platform that generates useful and automatic representations of scientific images using new visualization modalities including virtual reality (VR), mixed reality (MR) and augmented reality (AR). We are developing application solutions for both microscopy

The biomedicine application focuses on the needs of the surgeon. Our software platform generates automatic stereoscopic representations of patient imaging data (i.e. MRI and CT) using AR and MR for headsets (Microsoft HoloLens) and tablet computers. Our first application is a tool to facilitate decision-making in breast cancer surgery. Our microscopy solution generates detailed automatic representations of all types of microscopy images (e.g. widefield, confocal, light-sheet, electronic) using VR technology. We are creating novel and innovative ways of visualization that notably allow easy

# exploration, quantification and spatiotemporal comprehension of users' imaging data.

![](_page_17_Picture_26.jpeg)

vo examples of prototypes of the DIVA project At the top, our application of RV microscopy elow, our biomedical application RA

![](_page_17_Picture_28.jpeg)

# Awards

# Aziz El Amraoui

Charles Nicolle Chair of Excellence. Institut Pasteur (2017-2019)

# **Thomas Bourgeron**

Chair of Excellence from the Bettencourt Schueller Foundation for research on autism and the "social brain", (2018-2022)

# Jean-Pierre Corringer

Louis Pasteur Chair of Excellence, Institut Pasteur (2018-2021)

# David Digregorio

Elie Metchnikoff Chair of Excellence. Institut Pasteur (2018-2021)

# Pierre-Marie Lledo

Flie Metchnikoff Chair of Excellence. Institut Pasteur (2018-2021)

# **Department of Parasites** and Insect Vectors

![](_page_18_Picture_1.jpeg)

The Department of Parasites and Insect Vectors investigates the biology of parasites and their vectors. Its research program addresses global public health concerns in terms of disease prevention, control and antiparasitic treatment.

With seven research units and the Center for the Production and Infection of Anopheles (CEPIA), the department focuses its research on three key eukaryotic parasites responsible for severe diseases that have significant health and economic implications and affect most of the world's population: Plasmodium - the causative agent of malaria, Leishmania – the agent of leishmaniasis, and Trypanosoma brucei – responsible for sleeping sickness. The Anopheles mosquito, which is the vector of *Plasmodium* and a number of arboviruses. is being studied along with the tsetse fly, the vector of African trypanosomiasis. The work of

the department combines academic research programs on in vitro and in vivo models - including field work in Africa and Asia - with applied programs on resistance to antimalarial drugs and on the discovery of new antiparasitic drugs. Original models and new experimental tools are being developed to help understand the dynamic interactions between these microorganisms and their hosts, to identify the fundamental nature of parasitism and transmission by vectors, to clarify host invasion mechanisms, and to determine the virulence factors, pathology, and survival strategies of these organisms. The department is directed by Gérald Spaeth.

# "The Future of **Parasitology**' **Symposium**

The department organized the international symposium "The Future of Parasitology" on the Institut Pasteur campus on October 2nd and 3rd 2017. The organizing committee established a new format by inviting a mix of well-established scientists and young researchers (doctoral students, post-docs, junior staff). This led to exciting exchanges between three generations of scientists and showed the striking evolution of parasitology over the last decades. It also highlighted the complex challenges of translating discoveries to the field. Debates were lively among the frontiers of different disciplines at the heart of parasitology, with particular emphasis on the crossfertilization between fundamental and applied sciences. This was illustrated by outstanding keynote presentations on vaccine and drug discovery.

![](_page_18_Picture_7.jpeg)

![](_page_18_Picture_8.jpeg)

# Study of naturallyacquired anti-*P. vivax* immunity indicates path to multicomponent vaccine

A vaccine would greatly assist in the elimination of *Plasmodium* vivax malaria. However, to-date there are very few well-characterized candidate antigens. In order to identify and prioritize antigens for further functional characterization, we conducted the largest ever study of antigenic targets of naturally-acquired anti-P. vivax immunity. IgG antibodies to 38 P. vivax antigens were measured in a cohort of Papua New Guinean children, ages one to three years old; their relationships with prospective risk of malaria were also investigated. In addition, the potential protective efficacy of antibodies to multiple antigen-combinations, and the antibody thresholds associated with protection, were investigated for the first time.

P. vivax vaccine.

Source: França C.T. et al., eLife, September, 2017.

# The genome of *Leishmania* reveals how this parasite adapts to environmental changes

High antibody levels to multiple known and newly identified proteins were strongly associated with 26-56% protection. Among five-antigen combinations with the strongest protective effect (>90%), EBP. DBPII, RBP1a, CvRPA, and PVX 081550 were most frequently identified. Some of these required very low antibody levels to show a protective association. These antigens should be prioritized for further functional testing to establish a clear path for developing a multicomponent

Leishmaniasis is an important human and veterinary disease. caused by Leishmania parasites, that affects 12 million people in over 98 endemic countries. The disease is now emerging in Europe due to climate change and massive population displacement. The parasite is known to rapidly adapt to new environments and this quality has important consequences for disease outcome. A team in our department has demonstrated that Leishmania adaptation results from frequent and reversible chromosomal amplifications. Such variations, named aneuploidies, are similar to those occurring in many types of cancer. These findings represent an important step towards a better understanding of human Leishmania infection. with relevance to parasite drug resistance, pathogenicity, and tissue tropism. As part of the recently funded H2020 LeiSHield-MATI project

(www.leishield.org), this novel insight into Leishmania genomic instability will pave the way for the discovery of parasite biomarkers with diagnostic and prognostic value.

Source: Prieto and Pescher et al, Nature Ecology and Evolution. September 2017.

![](_page_18_Picture_20.jpeg)

sect-stage Leishmania promastigote parasites

# Award

Brice Rotureau (head of the Trypanosome Transmission Group) received the 2017 Deschiens Prize from the French National Academy of Medicine for his work on skin-dwelling trypanosomes and their importance in the context of sleeping sickness elimination. Sleeping sickness is caused by African trypanosomes that are transmitted by tsetse fly bites. These unicellular parasites were previously thought to proliferate only in patient blood. However, the skin has recently been identified as an overlooked anatomical trypanosome reservoir that may significantly contribute to their transmission.

# Department of Virology

![](_page_19_Figure_1.jpeg)

Viruses that are pathogenic for humans are vast in number and they cause chronic or acute infections that often prove fatal. The Virology Department studies all aspects of viruses to improve our defenses against them.

Researchers in the 17 units of this department investigate the mechanisms used by viruses to hijack cells and multiply. They study how viruses spread, pass from one individual or species to another, and how they outsmart host defense mechanisms. Research topics also include identifying the mechanisms involved in the evolution of viruses and the molecular bases of their pathogenicity. The viruses studied include respiratory viruses (influenza, etc.), enteric viruses (polio, Coxsackie, etc.), cancer-causing viruses (papillomaviruses and hepatitis B and C viruses). retroviruses (HIV or HTLV). insect-borne viruses that are responsible for severe diseases (dengue, chikungunya, Zika,

yellow fever and Rift Valley fever), and viruses causing hemorrhagic fevers (Lassa fever virus). The researchers work closely with others on the Paris campus and with members of the Institut Pasteur International Network. The Virology Department is also involved in translational research projects to design vaccine candidates, screen new therapeutic targets and develop diagnostic tools. As it houses several National Reference Centers and WHO Collaborating Centers, it plays a crucial role in the epidemiological monitoring of viral infectious diseases. The department is directed by Monique Lafon.

![](_page_19_Picture_5.jpeg)

# A new method for producing live attenuated vaccines

Vaccines obtained from attenuated virus strains are very effective and induce high immune responses. Until now, attenuated strains were selected according to long and empirical protocols, for instance multiplying a viral strain on different cell types until it lost its virulence. A new strategy was developed to attenuate RNA viruses by modifying their evolutionary potential. By using the Coxsackie B3 and Influenza A virus infections as models. scientists introduced errors into the viral genome and this resulted in reduced viral proliferation and lower virulence. The protective power of viral strains obtained by this method has been established in vivo.

Source: Moratorio G. et al., Nature Microbiology, June 2017.

# Natural Killer cells – overlooked components in the fight against HIV infection

The role of Natural Killer cells, part of the first line of host defense in the fight against tumors or infection. has been well documented for certain viral infections. However, the role played by NK cells in controlling infections caused by HIV had yet to be established. Studies conducted on a model of non-lethal infection by the simian immunodeficiency virus (SIVagm) have established that NK cells are indeed stimulated during SIVagm infection, and that they migrate to the lymph nodes - one of the reservoirs of the human and simian (SIVmac) immunodeficiency virus – where they play a crucial role in protection. This research, carried out on a simian immunodeficiency virus model, could lead to the development of therapies to activate NK cell responses to

Source: Huot N. et al, Nature Medicine, 2017.

destroy HIV infection reservoirs.

![](_page_19_Picture_12.jpeg)

Natural killer cells (NK).

![](_page_19_Picture_15.jpeg)

# A MOOC focused on medical entomology

The online medical entomology course (Insect Vectors and Pathogenic Agents) is run by Anna-Bella Failloux from the Arboviruses and Insect Vectors Unit (Institut Pasteur) and Vincent Robert from the Research Institute for Development (IRD), in partnership with the CNAM. It covers the biology of arthropod vectors (mosquitoes and other hematophagous insects, or ticks) which transmit diseases like dengue, malaria. or the Zika or chikungunya viral infections, and presents the methods available for limiting the spread of outbreaks.

# Awards

Blandine Monel. L'Oréal-UNESCO For Women in Science French Fellowship for her PhD research on the proliferation of the Zika virus in human cells, and on the ability of IFITM3, a cell protein with antiviral activity, to limit infection and the destruction of infected

cells. *EMBO* J, 2017

![](_page_19_Picture_21.jpeg)

Juliette Fédry. L'Oréal-UNESCO For Women in Science French Fellowship for her PhD research on the structural and functional analysis of a protein expressed on the cell surface, used for both gamete fusion, and virus or parasite entry into cells. This research could lead to the development of new therapeutic tools to fight infections caused by these pathogens. *Cell*, 2017

![](_page_19_Picture_23.jpeg)

# **Center for** Bioinformatics, Biostatistics and Integrative Biology

The C3BI was launched in 2015 with significant support from the Institut Pasteur. In 2017 it went from strength to strength, with the development of interdisciplinary research within the INCEPTION project and the recruitment of several new staff members, making it one of France's largest bioinformatics centers.

![](_page_20_Picture_2.jpeg)

vice and research unit with the CNRS (USR 3756), affiliated with structures for biology and information science. Its activities are multidisciplinary and cross-sectoral: fundamental research; the provision of services for experimental units and for platforms; and offering training designed to improve the skills of the Institut Pasteur - and especially its junior scientists - in these fields. Its ambition is to become a leading national and international center in bioinformatics, related disciplines and their applications in biology and health. In 2017, a new modeling unit was set up in partnership with the French National Institute for Computer Science and Applied Mathematics (Inria).

# The two major activities of the C3BI

→ The research area is an umbrella structure for affiliated research units (9 units and 2 G5s\*) – both units that existed before the C3BI was set up, which are still primarily affiliated to their scientific department, and new units that are generally affiliated to the C3BI. The skills of scientists in these units range from mathematical modeling to algorithms, statistics and machine learning.

- Structural Bioinformatics;
- Mathematical Modeling of Infectious Diseases;
- Imaging and Modeling;
- Human Evolutionary Genetics;

![](_page_20_Picture_10.jpeg)

# LAUNCH OF THE INCEPTION PROJECT

INCEPTION (a project selected under the "Convergence" Institute" call for proposals, part of the Investing in the Future program) is designed to study the emergence of diseases in populations and individuals using integrative and multidisciplinary approaches. The C3BI teams are closely involved in the initial stages of this project, which has a budget of €12 million over ten years and will involve all the Institut Pasteur units in synergy with its partners\*. In 2017, progress was made on the project in several areas:

• recruitment of multidisciplinary PhD students in epidemiology and human genetics; integrative projects on zoonoses in Africa and the resurgence of whooping cough in Europe;
training on biological data analysis (for PhD students);
a rapid response unit to intervene as quickly as possible in the event of a major pandemic outbreak (such as plague in Madagascar).

![](_page_20_Picture_15.jpeg)

- Human Genetics and Cognitive Functions;
- Microbial Evolutionary Genomics:
- Spatial Regulation of Genomes;
- Evolutionary Bioinformatics;
- InBio: Experimental and Computational Methods for Modeling
- Cellular Processes (set up in March 2017);
- G5 Statistical Genetics:
- G5 Decision and Bayesian Computation (set up in January 2017).

## 

sible for providing services to scientific units and platforms, for performing analyses, developing applications and data processing pipelines, and providing training. These services are aimed at all the units on the Paris campus and also the Institut Pasteur International Network.

# C3BI achievements in 2017

This year, the C3BI recruited 11 advanced research engineers (from a total of 190 applicants). Since 2015, it has recruited 40 new research engineers. The target set in the 2014-2018 strategic plan has therefore been reached, in a field where recruitment is notoriously difficult. These engineers are affiliated to the HUB and work for the Institut Pasteur's units and platforms on projects submitted on a regular basis.

A new unit was set up with Inria: InBio: Experimental and Computational Methods for Modeling Cellular Processes. With four new units or G5s set up over a period of three years, the C3BI has become one of France's leading bioinformatics centers. The C3BI's units are recognized for their expertise and regularly publish papers in top international scientific journals. In 2017, papers were published in Science, PNAS, Genetics, Nature Communications, Nature Genetics, Nucleic Acids Research, EMBO Journal, eLife, Genome Research, Genome Biology, Molecular Biology and Evolution, Structure, PLOS Computational Biology

![](_page_20_Picture_30.jpeg)

research engineers in bioinformatics and biostatistics were recruited to the C3BI in 2017

J projects were dealt with by the HUB in 2017, which participated in more than 50 publications

and Bioinformatics. This research covers epidemiology, the phylodvnamics of infectious diseases (HIV. dengue, Zika, etc.), human genetics, real-time control of cellular processes, and the development of sophisticated, novel methods and software for data analysis in several fields.

In 2017, the HUB worked on more than 90 new projects (250 over three years). It was involved in 12 long-term projects approved by the C3BI steering committee, including the PIBnet project which provides the tools required for the analysis of microbial genomes with a view to monitoring diseases and disease emergence: the discovery of new pathogens or new pathogen combinations in animal reservoirs and in outbreaks of unknown etiology; and the overhaul of the ARIAweb interface, a project supported by the French Institute of Bioinformatics (IFB) aimed at determining protein structures using NMR data.

The C3BI is also actively involved in scientific training and activities, both on campus and at the international level. A bimonthly seminar

regularly attracts around 40 participants from the Institut Pasteur and beyond. The C3BI ran courses with the International Network in Hong Kong, Hanoi, Montevideo, Bogota, Copenhagen and Paris. Other courses were run on campus, representing nearly 300 hours of training in 2017. Examples include Python programming, machine learning, introduction to data analysis, metagenomics, NGS data processing, analysis of connections between genes and functions, protein-protein interactions, and molecular phylogenics.

\* G5 or five-year group: a research team geared towards promising young scientists.

# **Center for Global Health**

The aim of the Center for Global Health (CGH) is to consolidate the global health activities carried out by Institut Pasteur teams worldwide. Its work is based around three strategic priorities: outbreak investigation, research to improve human health, and training for tomorrow's scientists. It was set up in September 2014 and is directed by Prof. Arnaud Fontanet.

# **Deployment of the Outbreak Investigation** Task Force (OITF)

More than 50 scientists from 10 institutes in the Institut Pasteur International Network (IPIN), specializing in a wide variety of disciplines including epidemiology, microbiology, entomology, social science and veterinary medicine, have joined the Outbreak Invesin tackling several outbreaks worldwide. The most severe threat was an outbreak of pneumonic plague in Madagascar from September to November 2017 (see inset). OITF was also deployed in other situations:

- an epidemiologist and anthropologist were seconded to support the teams at the National Institute of Hygiene and Epidemiology in Hanoi (a member of the International Network) dealing with outbreaks of pediatric encephalopathy in northern Vietnam caused by toxins (hypoglycin A) in lychees;

- a clinician specializing in infectious diseases was deployed to offer support during an outbreak of necrotizing fasciitis in São Tomé and tigation Task Force (OITF). In 2017, OITF members were involved Principe, alongside the microbiologists at the Pasteur Center in Cameroon (a member of the International Network), based in Yaoundé; - surveillance of microcephaly cases was introduced in Sub-Saharan Africa and Asia to estimate the impact of the circulation of the Zika virus on pregnancies in these regions.

![](_page_21_Picture_6.jpeg)

![](_page_21_Picture_7.jpeg)

# PNEUMONIC PLAGUE OUTBREAK **IN MADAGASCAR**

Pneumonic plague, which is spread from person to person through the inhalation of respiratory droplets, is a formidable disease that is systematically fatal in less than three days if not treated by antibiotics. Over a three-month period, more than 2,000 suspected cases were reported in Madagascar, raising fears that this may signal the start of a global pandemic. The Institut Pasteur in Madagascar was a key partner in responding to this outbreak, providing diagnostic tests to hospitals treating patients and confirming all the results in its laboratories. Nine scientists from the Institut Pasteur in Paris provided support to their colleagues in Madagascar, offering expertise in microbiology (National Reference Center for Plague and Laboratory for Urgent Response to Biological Threats (CIBU) and epidemiology (mathematical modeling and analytical epidemiology).

The outbreak was ultimately brought under control through a strategy of isolation and early antibiotic prophylaxis to anyone who had come into contact with patients. Our teams are now working alongside colleagues at the Institut Pasteur in Madagascar on research projects designed to improve diagnostic tests for the pneumonic forms of plague, and to analyze the immune response in recovered patients with a view to developing a vaccine. These research projects have received €450,000 in funding from the international community.

# A scientific strategy for global health led by the IPIN

Working in conjunction with the Institut Pasteur International Affairs Department and the International Network for Data Analysis (INDA), the CGH carried out an online survey with scientists in the Institut Pasteur International Network (including the Institut Pasteur in Paris) to identify global health research priorities. The most frequently cited research topic was antimicrobial resistance, reflecting the growing urgency of this issue at the international level. In consultation with scientists in the International Network, two research protocols were developed on this topic:

- a first on the circulation of the Escherichia coli bacterium, which carries several resistance plasmids, between humans, animals and the environment:

- a second on mortality attributable to antibiotic resistance in sepsis patients.

The survey also revealed the growing need for skills and resources in bioinformatics and statistical analysis of big data among the institutes in the International Network.

# **Disease outbreaks seminar run by the Open** Medical Institute and the Institut Pasteur

In partnership with the Open Medical Institute, the CGH organized a week-long seminar on disease outbreaks in Salzburg. Austria, in August 2017. The seminar was attended by 30 physicians and public health professionals from Eastern Europe, Africa and Latin America. Teaching was provided by experts from the Institut Pasteur, Weill Cornell Medicine, Geneva University Hospital and the World Health Organization.

# Pan-African Coalition for Training in Research and Public Health (PACT)

In close collaboration with the International Affairs Department, the Education Department, and the MAASC, the CGH provided support for the development of the Pan-African Coalition for Training in Research and Public Health (PACT). The emphasis is on strengthening relations between English- and French-speaking African research groups.

- African colleagues in the International Network were invited to the meetings organized to discuss the DELTAS Africa Program (Wellcome Trust) and the H3Africa Initiative (Wellcome Trust and NIH).

- The Science, Language and Culture Initiative, which aims to boost researcher mobility in Africa, was launched with the participation of the Wellcome Trust. AESA. the DELTAS Africa Program. the British Council, the Francophone University Agency (AUF), the Paris Chamber of Commerce and Industry, the Institut Français and the Calouste Gulbenkian Foundation.

# **Global Health e-Academy**

In an effort to guarantee access to training for as many people as possible, the CGH is supporting the PACT program by offering its network and its experience in designing and leading massive online open courses (MOOCs) to improve the availability of advanced teaching in the field of public health. In 2017, in cooperation with the Virchow-Villermé Center, the CGH laid the foundations for a Global Health e-Academy, a consortium of several universities from Africa, Europe and America committed to strengthening higher education in Africa via MOOCs.

# **Innovation** and Technological Research (Citech)

The Citech's mission is to advance innovation and technological research by rapidly addressing the needs and requirements of Institut Pasteur biology projects. The Citech fosters the development of technological research projects involving teams, Departments and/or external (academic or industrial) partners, and helps to share research findings via the platforms.

![](_page_22_Picture_2.jpeg)

researchers quantitatively interpret microscopy images.

# New methods and technologies

The following new methods and technologies have been adopted within UTechS and platforms:

- high-resolution photonic imaging systems: light sheet fluorescence microscope (PBI UTechS) and StellarVision microscope (Chemogenomic and Biological Screening platform);

- a robust protocol based on cryomicroscopy and cryotomography, including image processing (UBI UTechS);

- a microfluidic chip manufacturing facility (Biomaterials and Microfluidics platform);

- a pipetting robot for automation and high throughput screening of cell culture processes (Recombinant Proteins platform);

and Chromium and Polaris systems for research on single cells (CB UTechS):

- embryo vitrification and intracerebral *in vivo* imaging (two-photon microscopy), and an innovative housing system for axenic mice and those with controlled microbiota, at the Central Animal Facility; via targeted transgenesis (Mouse Genetics Engineering Center);

- a facility required to continually mass-produce Anopheles mosquitoes and infect them with *P. falciparum* (Center for the Production and Infection of Anopheles);

he Citech houses the technological platforms - 3D printers and manufacturing tools at the FabLab (approxi-

mately 150 people). It manages four tech- In addition, concerted action by the CB UTechS, Biomics Pole nology and service units (UTechS) set up and Genomics and Epigenomics of Vertebrate Development Unit in 2017 - Photonic Biolmaging (PBI), has enabled the importation of the innovative MARS-seq pipeline Ultrastructural Biolmaging (UBI), Mass (single cell sequencing) developed at the Weizmann Institute.

# with the Center for Translational Science At the center of European Core Facility networks

The Citech has been made an associate member of the Core for Life technological platform association, a network of excellence featuring the equivalent structures of seven European institutions. The teams take part in different Working Groups to share expertise on cutting-edge topics. The Citech also supports the Core Technologies for Life Sciences (CTLS) association, co-founded by Institut Pasteur scientists Spencer Shorte and Patrick England, which brings together the life science platform community in Europe.

# Teaching and training in new technologies

The Citech runs several classes and courses in France and abroad, particularly within the Institut Pasteur International Network. As part of the courses held at the Paris campus, teams from the Citech teach protein characterization, fluorescence microscopy, and cytometry - Simoa technologies for highly sensitive detection of biomolecules methods. Within the Institut Pasteur International Network, a transgenesis course was jointly organized by the three International Network transgenesis platforms in Athens, and a cytometry course was held in Hong Kong. A workshop on biomolecular screening was organized in partnership with the University of Cape Town. Regulatory animal testing training for campus scientists is run by teams from - electroporation of zygotes to integrate new CRISPR/Cas9 systems the Central Animal Facility, and has included continuing education sessions since 2017 (biostatistics, pain and drug management). The Citech also innovates in terms of training methods, with the introduction of a SPOC (Small Private Training Online Course) on Bioanalyzer technology for DNA/RNA quality control.

![](_page_22_Picture_19.jpeg)

# **Promoting technological research within** and outside the Institut Pasteur

The Citech supports the development of new technologies, enabling novel biological results to be generated. This includes supporting and sharing the innovations achieved by its teams and within the Departments, and entering into strategic agreements with academic and industrial partners. After an internal call for proposals, the first projects were launched in 2017 at the Tech Lab, a dedicated space on campus.

The framework agreement signed in 2015 with ESPCI ParisTech is starting to produce results. A method based on microfluidics, which can be used to rapidly analyze tens of thousands of single immune cells, was developed and published in Nature Biotechnology\*. This research, the result of cooperation between the Chemistry, Biology and Innovation laboratory (ESPCI ParisTech/ CNRS), Antibodies in Therapy and Pathology Unit (Institut Pasteur/ Inserm) and the Citech, could be applied to improve vaccines or identify therapeutic antibodies.

Jean-Christophe Olivo-Marin and Elodie Brient-Litzler (Citech). and Patrick Tabeling (Pierre-Gilles-de-Gennes Institute for Microfluidics) have co-coordinated an ELICIT DIM (Empowering Life Sciences with Innovative Technologies) network since 2016, which is funded by the Paris Region (€2 to 3m/year) and dedicated to developing innovative technologies for life sciences. In 2017, the ELICIT DIM launched its first call for proposals and five teams from the Institut Pasteur were selected. Finally, partnerships have been set up with Lumicks and Emulate to develop new applications for acoustic force spectroscopy and organs-on-chips. As part of a project funded by BPI France and its Japanese counterpart NEDO, the Photonic Biolmaging UTechS developed, alongside the Japanese company Konica Minolta, new nanoparticles for cell and in vivo imaging, which can be used for medical diagnosis.

\*Nature Biotechnology, volume 35, pages 977-982 (2017) doi:10.1038/nbt.3964

![](_page_22_Picture_30.jpeg)

# **FIRST CORE FACILITIES OPEN HOUSE**

On October 19, the Citech had its first open house day to introduce its work to new arrivals to campus. Around 70 people met the teams and visited the Citech premises to get information about the services and expertise available.

# MEDICINE, PUBLIC HEALTH AND CLINICAL RESEARCH

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OLYMPUS CKX41

The Institut Pasteur reacts to the medical issues most relevant today and anticipates those of tomorrow. Agile and always vigilant, our scientists respond to evolving public health challenges. They apply their expertise and research findings to the needs of populations as well as of the individual. The link between the lab and the clinic, between the scientist, the medical practitioner, and the patient, has never been stronger.

100

# **Center for** Translational Science

The mission of the Center for Translational Science (CRT) is to promote the transfer of knowledge from academic research to the clinical field, and vice versa. The center is a place where clinicians can develop new research hypotheses, with the aim of improving our understanding of disease and enhancing patient care.

# Strengthening cooperation between clinicians and scientists

The CRT plays an active role in attracting new clinical staff to the Institut Pasteur by funding partnership contracts, quest researcher posts, joint units and second-year Master's internships. In 2017, the CRT supported cross-disciplinary research projects on a variety of broad themes including bacteriology, hematology, hepatology, rheumatology, psychiatry, mycology, hereditary diseases, deafness, spondylitis, bipolar disorder, depression, transplants and cryptococcosis.

The CRT also develops partnerships with healthcare establishments such as Necker-Enfants Malades University Hospital; International Network; in 2017, both the Institut Pasteur and Necker Hospital reiterated

their commitment to formalizing and strengthening their working relationship.

# Providing integrated support by means of a panel of complementary expertise

The CRT is strongly committed to its policy of listening to scientists' needs and improving its services. In 2017, this policy led to:

- the award of ISO 9001: 2015 quality certification, improving the CRT's visibility with industry and within the Institut Pasteur

- the introduction of "Open Desk" sessions (see inset).

![](_page_24_Picture_10.jpeg)

# "OPEN DESK": ANTICIPATING THE NEEDS OF **CROSS-DISCIPLINARY RESEARCH PROJECTS INVOLVING HUMAN SUBJECTS**

The aim of the CRT's Open Desk scheme is to provide guidance for scientists embarking on research projects involving human subjects by anticipating the ethical, regulatory and administrative procedures required. It does this with the help of its committee of experts, composed of specialists in ethics, law, technology, bioresources, and methodological and regulatory questions. After providing a brief presentation of their project, scientists are given an overview of the procedures involved and the people they will need to liaise with as well as the departments that can help them with the preparation, launch and implementation of their project. In 2017, the CRT met with 37 project leaders and provided them with ongoing guidance and support. The administrative and regulatory procedures recommended by the Open Desk experts have already been launched for 55% of the projects dealt with from January to December 2017.

The CRT was also very keen to receive feedback on its Open Desk sessions; it improved its tools and follow-up methods based on the results of two satisfaction surveys and systematic monitoring of short-term projects.

With a wide range of complementary expertise among its The ICAReB platform coordinates an extensive biobank members, the CRT promotes medical research by providing and also manages two permanent open prospective cohorts various forms of support for scientists and clinicians. of healthy volunteers and patients. In 2017, the platform was involved in the launch of the OHTicks project, set up to iden-→ **The Technical Core** is affiliated both to the CRT and to tify pathogens transmitted by ticks.

the Center for Innovation and Technological Research (the Cytometry and Biomarkers UTechS, set up in 2017). It offers a → Scientific events unique array of sophisticated technologies that can be used Each year, the CRT also organizes and funds several scientific in translational research. These technologies are constantly events and activities based on the theme of biomedical research. being improved and updated, to make sure the 270 users In 2017, it organized the first edition of the Patients/Scientists have access to the latest techniques available. The CRT has Day, which provided an overview of the innovative initiatives received new funding and acquired a number of new tools. It under way in France to address the question of patient particiis also involved in teaching, setting up a lab work module in pation in research. The CRT also plays a key role in developing flow cytometry for continuing education students and a lab interdisciplinary relations; it leads several working groups on work module at the Institut Pasteur in Hong Kong. topics such as aging, vaccination and liver cancer.

-> The Clinical Core provides support for cross-disciplinary research projects in France and abroad to make sure they can be carried out within the shortest possible time frame and in accordance with applicable regulations. In 2017, the CRT was involved in research projects on the human microbiome, arboviruses, emerging and neglected diseases, medical devices and new technologies. It was also closely involved in a phase I clinical trial for the first administration in humans of a vaccine candidate for bacillary dysentery, based on research conducted at the Institut Pasteur.

-> The INCREASE initiative for the active promotion of - to facilitate the finalization of funding for projects presented clinical research in the Institut Pasteur International Network in Open Desk sessions by proposing the option of micro-fundlaunched its collaborative website www.together.pasteur.fr/ ing to project leaders via the CRT's partnership with the *increase* in 2017. It is exploring new themes such as research crowdfunding platform Thellie; - to implement an Ambassador Physicians strategy for the into venoms and vaccine-preventable diseases. For several of these projects, the CRT has also secured funding from public recruitment of volunteers in the prospective cohorts for bioresources at the Institut Pasteur. and private organizations. It is involved in a flagship European project for clinical research in the International Network via the EDCTP, with approximately €2 million earmarked for International Network institutes.

# What scientists think of Open Desk:

The Open Desk session went very well and the people I spoke to were able to provide answers to virtually all my questions. The subsequent guidance offered was very effective.

Martial Marbouty, who presented his project in January 2017

*Responsive and* multidisciplinary – those are the two words I would use to describe the support offered by the CRT.

Marie Flamand, who presented her project in September 2017

# Aims and priorities

Building on its achievements in 2017, the CRT has set itself four broad aims for 2018:

- to contribute to the development of the new strategic plan, strengthening the dynamic of reflection and action in partnership with the Paris Public Hospital Network (AP-HP);

- to pursue the development of Open Desk, placing the emphasis on providing training for scientists and monitoring projects;

# **National Research** Centers

In 2017, the French national health agency, Santé publique France (SpF), officially selected the Institut Pasteur to host 14 National Research Centers (CNRs) in mainland France (12 in Paris and two in Lyon) and four associated CNR laboratories in French Gujana. The new five-vear CNR term began on April 1, 2017.

> NRs provide support for health authorities and work in association with their host research units to fulfill four key public health missions: microbiological expertise, consultancy services for health professionals and authorities, epidemiological surveillance and health alerts. The shared microbiology platform (P2M), used by the CNRs to sequence pathogens (bacteria, viruses and fungi) and characterize their

genomes, is a valuable asset that allows scientists to identify causative pathogenic agents quickly and precisely and to detect clustered cases. The use of sequencing to enhance scientific expertise led to the rapid identification of the pathogen responsible for the contaminated powdered milk, a high-profile news story in late 2017. In 2017, a total of 18,000 strains were sequenced by the P2M platform, for both CNRs and World Health Organization Collaborating Centers (WHOCCs).

# Listeriosis: improving understanding and treatment

Listeria monocytogenes, the causative agent of listeriosis, is thought to be responsible for 400 cases every year in France. The Listeria CNR receives strains isolated from patients and foodborne strains isolated by hygiene and food safety laboratories. Since 1998, 98% of reported cases in France have the Caribbean over the last 60 years. Based on the whole-genome been submitted to the CNR for analysis. This led the CNR to sequencing of V. cholerae strains for cholera surveillance, prevenset up the MONALISA (Multicentric Observational National Analysis on Listeriosis and Listeria) cohort, headed by Caroline Charlier, a member of the team run by Marc Lecuit (Institut the WHO Collaborating Center during outbreak investigations. The Pasteur/Necker-Enfants-Malades University Hospital). The results, published in January 2017 in Lancet Infectious Dis-

eases, revealed several crucial factors concerning the disease. Only 5% of pregnant women infected did not experience pregnancy complications. In elderly people (over the in septicemia or a neurological form known as neurolisteriosis. The study revealed that two-thirds of these patients died or experienced sequelae, but also that there are clear therapeutic advantages associated with the use of a specific class of antibiotics, aminoglycosides, whereas the use of corticosteroids had a harmful effect. Another key prospect raised by the study was the identification of a genetic predisposition to the disease.

![](_page_25_Picture_7.jpeg)

# **Cholera: understanding the link between** maior outbreaks worldwide

Researchers from the Institut Pasteur and the UK-based Wellcome Sanger Institute, in collaboration with several other international institutions, published two studies in the journal *Science* in November 2017 tracing the history of cholera outbreaks in Africa, Latin America and tion and control, these studies illustrated the benefits of combining epidemiological data with laboratory data collected by the CNR and scientists analyzed the genomes of more than 1,200 current and past strains of V. cholerae collected from across the globe since 1961. The findings revealed that the cholera bacterium had been introduced into Africa at least 11 times over a period of 44 years, always from Asia, and that human populations were the main vecage of 65) and/or those with comorbidity, infection may result tors for disease dispersal throughout Africa. They also showed that in the vast majority of cases, the multidrug resistance that the bacteria had developed over time was acquired in South Asia before the bacteria were introduced into Africa. In Latin America, where epidemic cholera reemerged in 1991, the researchers proved that the risk of a large-scale epidemic varied depending on the strain of V. cholerae. These two studies shed new light on how the cholera bacterium circulates, improving our ability to anticipate the risk of new outbreaks and adapt our control strategies accordingly.

![](_page_25_Picture_10.jpeg)

In 2017, the Institut Pasteur also signaled its support for the Global Task Force on Cholera Control by signing the Declaration to Ending Cholera.

# Salmonella outbreak: the Institut Pasteur issued the alert

Each year, the National Reference Center for Escherichia coli, Shigella In October 2017, the Institut Pasteur in Madagascar was given a and Salmonella receives between 8.000 and 10.000 Salmonella major boost in its efforts to tackle the pneumonic plaque outbreak strains for analysis, 400 to 600 of which are from infants under the affecting urban areas. Working in close collaboration with the age of one. In late November 2017, after observing a significant National Reference Center for Plague and Other Yersinia Infections number of cases of salmonellosis in infants, the CNR alerted the and several other structures at the Institut Pasteur in Paris (the Epidemiology of Emerging Diseases and Mathematical Modeling health authorities. This enabled Santé publique France to launch epidemiological investigations on December 1 with the parents of of Infectious Diseases Units, the Laboratory for Urgent Response the infected infants, which soon led to the identification of powto Biological Threats (CIBU) and other CNRs that freed up staff to dered baby milk as the source of the contamination. Identifying work on the outbreak, with the involvement of the CNR Coordination an outbreak as soon as it begins (clustered cases in a short Department), the Institut Pasteur in Madagascar was able to play a space of time caused by the same type of bacteria) enables key role in the response to the outbreak, performing a laboratory analysis of all reported cases (more than 2,300) and communiepidemiologists - who take over the investigative process to determine the origins of the outbreak – to get to work quickly, and cating key epidemiological information to help the local health signals to authorities that the contaminated product should be authorities and WHO develop a coordinated strategy. removed from the shelves as soon as possible. The alert mecha-This collaborative effort once again demonstrated the close links in nism relies on a network of public and private laboratories sendthe field of public health between the Institut Pasteur in Paris and ing the Salmonella strains they have identified to the CNR for the institutes in the Institut Pasteur International Network. in-depth analysis. The scientists used new techniques that have been available at the Institut Pasteur since 2016 - the PIBnet-P2M platform for complete DNA sequencing and a series of bioinformatics tools developed by the CNR - to analyze the results. This enabled them to sequence the 2005 strain to see how similar it is to the Salmonella Agona strain responsible for the 2017 outbreak.

Confirming this hypothesis provided key information for the government inquiry launched to determine where, when and how the baby milk may have been contaminated.

# Plague: the CNR supports Madagascar in tackling the pneumonic plague outbreak

# **Medical Center**

The Institut Pasteur Medical Center (CMIP) is the Paris-based entity in direct contact with patients, providing a range of services including a vaccination center; consultations for infectious and tropical diseases, travel medicine, allergies; and the Anti-Rabies Center.

> he Institut Pasteur International Vaccination Center (CVI) is a leading center for people traveling to countries where the environment and health and hygiene conditions are not the same as those usually encountered in France. Given its outstanding reputation, it attracts high numbers of people seeking vaccinations and specific information relating to their planned trips abroad.

# Vaccinations and travel medicine

Two categories of travelers make use of the CMIP's expertise in travel medicine and the services offered by the International Vaccination Center: those who attend the center privately prior to family holidays or leisure trips, and those who come in connection with their business trips. In this second category, it is worth noting that several public institutions, companies and especially NGOs, which are also concerned by this field, send their employees to the CMIP on the basis of contracts concluded with the Institut Pasteur.

These travelers are examined before they set off and can also return for a further examination once they are back in France. Travel medicine activities are often closely linked with recent outbreaks of emerging infectious diseases at the international level, an area in which the expertise of the Medical Center is widely recognized.

# Medical consultations

As well as providing vaccinations and advice for adult and child travelers, vulnerable patients (i.e. those with HIV, organ transplants or other immune deficiencies) and humanitarian travelers, much of the Medical Center's work involves treating diseases imported by returning travelers (malaria, arboviruses such as dengue, rickettsial infections, intestinal parasitic infections, leishmaniasis, cutaneous larva migrans, etc.), HIV infection, and widespread infectious diseases such as I vme disease.

Some of these pathologies are monitored in collaboration with Necker-Enfants Malades University Hospital, via the Neck- monitor a considerable number of patients infected with HIV Necker Hospital hold clinics at the CMIP, alongside physicians tion with the French Agency for Research on AIDS and Viral from the Institut Pasteur. Together these medical specialists Hepatitis (ANRS).

![](_page_26_Picture_9.jpeg)

# THE MEDICAL CENTER ON THE PASTEUR.FR WEBSITE

The Medical Center pages are the most frequently visited section on the pasteur.fr website. They represent a valuable source of information for the general public, containing health recommendations for travelers, vaccination schedules and disease fact sheets.

er-Pasteur Infectiology Center (CINP). Most of the physicians or viral hepatitis. These consultations also serve as the basis from the Infectious and Tropical Diseases Department at for a significant amount of clinical research, mainly in conjunc-

![](_page_26_Picture_13.jpeg)

The Medical Center also offers dermatology consultations, particularly to treat patients with hidradenitis suppurativa. The CMIP monitors a large caseload of patients and is consulted

on a regular basis to provide advice to organizations in France and abroad.

The Anti-Rabies Center provides care and vaccines treatment for patients who have been administered exposed to rabies via a bite, a scratch, (excluding the or a lick to a wound or mucous membrane. Anti-Rabies Although there have been no cases of infection reported in mainland France for a great many years, there are still occasional

visits to the International Vaccine Center (CVI)

Center)

consultations for infectious and tropical diseases

and travel medicine

The multidisciplinary specialists on the allergy clinic team provide treatment for allergies of all types, including rhinitis, asthma, conjunctivitis and allergic dermatitis.

![](_page_26_Picture_22.jpeg)

deaths in people who have been infected abroad. There are two types of risk: exposure during foreign travel, or being bitten by an animal imported from abroad. Antirabies treatment should be started as soon as possible following exposure. Treatment consists of several vaccine doses generally combined with serotherapy. Current vaccines are highly effective and well tolerated.

# **Clinical research**

The CMIP is also involved in clinical research in its specialist medical areas, with cohorts in fields such as HIV infection, the pathophysiology of hidradenitis suppurativa (genetics and immunology, in collaboration with the ICAReB platform, units on the Institut Pasteur campus and Necker Hospital), vaccinology (interaction of the yellow fever and measles vaccines in children, immunogenicity of the yellow fever vaccine in patients with bone marrow allografts), sociology (the study of traveler perceptions and practices relating to vaccination to improve understanding of their reasoning and concerns), and allergology (research into immune phenotypes of patients with wasp venom or penicillin allergies, in cooperation with a unit on the Institut Pasteur campus).

consultations at the Anti-Rabies Center

consultations for allergies

In 2017 the Chronovac study was published. This vaccine study in infants under the age of 2 confirmed that it is possible to administer two live attenuated vaccines (measles followed by yellow fever) less than a month apart, without a major impact on the immune response to either vaccine, even though a longer gap between vaccines appears to improve the immune response further.

The new insights offered by these projects fully justify the Medical Center's place in the Center for Translational Science.

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Innovation and technology transfer involve continual inventing and reinventing. The multidisciplinary approach at the Institut Pasteur means seeing scientific discoveries from the standpoint of the medical progress they could generate, whether it be a vaccine or a diagnostic test. With each new development, as with each new scientific collaboration or industrial partnership, the Institut Pasteur returns to the task of invention, never letting what has already been done eclipse what might become.

# INNOVATION

# Fostering research on campus and supporting funding applications

In 2017, the Department of Development – Grants Office (DD-GO) provided the Institut Pasteur's scientists with new tools to help them secure funding for their research. The DD-GO also continued its work to develop new strategic and scientific partnerships for the Institut Pasteur.

![](_page_28_Picture_2.jpeg)

he results achieved by the DD-GO reflect a combined effort involving the administrative and technical support work on specific projects. Key institutional partners are:

for the medical and clinical dimensions of projects;

Industrial Relations Department (DARRI) for industrial partnerships:

→ the International Affairs Department for programs involving teams from the Institut Pasteur International Network.

# An integrated vision within the global scientific community

The DD-GO monitored the activities of some 150 research entities to build up a comprehensive overview of the Institut Pasteur's scientific research in the short and medium term. In connection with its work to document the International Network's scientific activities, which began in 2016, the DD-GO organized a further series of visits to institutes in the organized a One Health Day with the French Association for network (Cambodia, Italy and Tunisia). This scientific mapping the Animal Health Industry (SIMV); and it identified a Japanese was developed in close collaboration with the Department of Scientific Affairs, the Department of Communications and Fundraising and DARRI, with the aim of securing new scientific and strategic partners, especially to fund ambitious new ship program. research programs.

# Incentive programs and the search for strategic partners

departments and the entire scientific In 2017, the DD-GO stepped up its work to help secure longcommunity, which join forces with it to term funding for the Institut Pasteur's research. The various incentive programs were continued, especially with a view to supporting cooperation within the International Network → the Center for Translational Science (Transversal Research Projects (PTRs) and Inter-Pasteurian Concerted Actions (ACIPs)), and a new Major Federating Program (GPF) was launched to explore the links between infec-→ the Research Applications and tions, nutrition, metabolism and cancer. The Institut Pasteur also joined forces with the Bill & Melinda Gates Foundation and the African Academy of Sciences to launch a new program entitled Grand Challenges Africa, which saw the selection of eight proposals, including three from African institutes in the International Network, from a total of nearly 400. In preparation for this scheme, the DD-GO and the International Affairs Department organized a "Grant Writing Bootcamp" at the Institut Pasteur in Dakar.

> The DD-GO continued its efforts to find new key partners with the aim of guaranteeing the sustainability of existing research programs. With the help of the support departments, it launched a partnership with the Coalition for Epidemic Preparedness Innovations (CEPI, a WHO initiative) on vaccine projects; it partner (TRI Kobe) to promote clinical trials in Japan. Advanced discussions are under way with the US Juvenile Diabetes Research Foundation (JDRF) with a view to a research partner-

The DD-GO has played an active role in securing and promoting the Institut Pasteur's place in the European Research Area. As well as the outstanding achievements of its scientists in EU funding programs, the Institut Pasteur is one of the top five

![](_page_28_Picture_13.jpeg)

European institutions to receive funding from the European Research Council (ERC). An ongoing dialog has been launched with leading European research organizations to identify research topics with a strong societal impact, with the aim of developing the next framework program (FP9) that will govern EU research funding for the period up to 2030. The first discussions emphasized joint participation in European research programs and researcher mobility.

# Supporting scientists as they apply for competitive funding

As part of its commitment to offering the Institut Pasteur's researchers the best possible support to achieve their scientific goals, the DD-GO has set up a monitoring scheme for potential research funding bodies. A targeted weekly list of funding possibilities is sent out to scientists who may be interested in the topics for which funding is available. In 2017, the DD-GO also developed a new IT tool known as Grant Manager (GM), which can be used by scientists to inform the support departments that they are intending to submit a proposal in response to a call issued by an external funding body. This web application covers all the stages in managing project proposals, from the submission of the initial application to the establishment and monitoring of contracts. Grant Manager, launched in early 2018, reduces the time spent preparing proposals and improves the quality of applications and their chances of success in highly competitive calls. It also provides scientists with a "one-stop shop" and a single contact person for each funding application they submit. Support of the DD-GO covers, for example, Python programming, machine learning, data analysis initiation, metagenomics, NGS data processing, gene-function linkage analysis, protein-protein interactions and molecular phylogeny.

![](_page_28_Picture_18.jpeg)

# THE LEISHIELD-MATI EUROPEAN PROJECT

An Institut Pasteur team working for the past few years as part of the Institut Pasteur Leishmania Network has been selected to coordinate a consortium in the MSCA-RISE program, designed to promote mobility for scientists. This consortium supports research on leishmaniasis in several member institutes in the International Network. It is currently composed of 9 institutes and 16 laboratories.

# Research applications and technology transfer

The Research Applications and Industrial Relations Department (DARRI) works with industry partners in France and abroad to detect, promote, support, protect, and transfer inventions arising from Institut Pasteur research.

![](_page_29_Picture_2.jpeg)

y developing, maturing and transferring innovations, the Institut Pasteur can help to meet global public health challenges and partly fund its scientific research. In this era of theranostics and precision medicine, powerful tools and breakthrough technologies need to be developed (challenge of multidrug resistance, new vaccine and therapeutic approaches, etc.). With its high-caliber research teams, strategic industrial

partnerships, and new start-ups, the Institut Pasteur is a major stakeholder.

The DARRI continues to optimize its strategy and operations to face these challenges. It strives to professionalize the teams that oversee the entire innovation process, from invention discovery and maturation to the marketing of medical products and solutions.

# Intellectual property constantly evolving

In 2017, the rate of innovation remained high with 63 invention disclosures registered, a figure which is stable in relation to the average of the previous three years, resulting in 21 new priority patents being filed and 20 provisional applications (software, expertise, biological material). Examples include a patent on a super-resolution microscopy image processing method using artificial intelligence, new lentiviral vector applications as tools for screening and selecting the best epitopes (with the development of a new malaria vaccine candidate, etc.), and a patent on aptamers which can be incorporated into DNA molecules to mimic polyhistidine tagging used for proteins.

The selectiveness and quality of patent applications and their content remains central to the Institut Pasteur's industrial property strategy.

![](_page_29_Picture_9.jpeg)

# **THE CARNOT INSTITUTE -PASTEUR "MICROBES & HEALTH"** (MICROBES & SANTÉ, MS)

In 2017, in collaboration with the DARRI, Pasteur MS issued a call for proposals aimed at supporting new start-ups and entrepreneurship, backed Carnot maturation programs, and provided two coordinators. An Inter-Carnot call for proposals was issued with France Futur Elevage. Knowledge application, technology transfer and links with industry partners are the focus of the Pasteur MS strategy, and research themes include microbiota and non-communicable diseases, development of early, rapid and sensitive diagnosis, emerging and re-emerging diseases, nosocomial infections and antibiotic resistance, therapeutic strategies targeting the host and personalized medicine.

![](_page_29_Picture_12.jpeg)

# New partnerships under development

Thanks to the Business Development center's contribution to national and international business agreements, new companies have been contacted, 50% of which assessed and selected to build potential synergies with our researchers on topics of mutual interest. In addition to

**b**.5 invention disclosures

# new priority patents and 20 provisional

applications

industrial contracts signed in 2017 (+30% R&D & expert

assessments. +100% licenses)

industria contracts in place

R&D cooperation contracts with our long-standing partners (Sanofi, Sanofi Pasteur, bioMérieux and Bio-Rad), 2017 was marked by the signing of these major agreements.

• A framework agreement with the Hoffman-Laroche group to facilitate deal-(Genentech, Roche Pharma, Institut Roche). A partnership agreement was signed with a Genentech team, and others are under discussion with companies in the group.

• As part of a framework agreement with Moderna, a pioneer in the use of RNA messengers as a vaccine tool, an initial partnership produced very encouraging results and a second one began recently. They focus on finding vaccine solutions to tackle infectious diseases affecting disadvantaged populations in developing countries.

 Sublicenses granted to Novartis, Celgene and GSK in the field of gene therapy by strategic Institut Pasteur partner Blue-Birdbio. These sublicenses give access to tools arising from Pasteurian research to develop innovative drugs in oncology. Short- and medium-term revenue can be generated for the Institut Pasteur at

# FORWARD STRIDES FOR BIOASTER

Bioaster is a technology research institute specializing in technological innovations in microbiology, and has the support of high-profile academic and industrial partners. Since it was set up in 2012 (by the Institut Pasteur and Lyonbiopôle competitiveness health cluster on the initiative of the French government), it has coordinated over 53 research projects with 25 academic partners and 26 industry partners (source: Bioaster). Two examples of projects in 2017: • Evaluating the performance of a diagnostic test prototype using human samples infected with the Ebola virus in the BSL-4 laboratory in Lyon, in collaboration with the Institut Pasteur Biology of Emerging Viral Infections Unit, as part of a project with Fujifilm; • Monitoring the impact of anticoagulants and time on phenotypic markers in mass cytometry, and on NMR-based metabolomic analysis, in association with the Institut Pasteur ICAReB platform.

each successful development stage, alongside long-term operating revenues from marketed drugs. Novartis, a sublicensee of BlueBirdbio, has for instance marketed a gene therapy drug.

• A license signed with Kurma Diagnostic to market and CE mark an innovative pneumocystis pneumonia diagnostic kit used to distinguish between a healthy carrier and active infection.

 Co-ownership and license agreement signed with Humabs to develop and characterize antibodies that target the rabies virus, in association with the Rabies CNR in France.

# **Consolidating maturation of inventions**

ings with companies in the group. In addition to filing patents, the maturation of inventions to industrial standards is a prerequisite for signing agreements with partners. The Institut Pasteur benefits from the Pasteur Innov and ValoExpress programs, which are designed to accelerate project maturity for transfer to industry.

Financial investments will be needed in 2018 to fast track and consolidate the maturation of high-potential innovations on campus. In the short term, the aim is to develop innovative projects fostering R&D cooperation agreements. In the medium term, patent portfolios need to be renewed and, in the long term, public health solutions need to be provided by exploiting our patents through license agreements.

By educating the scientists of tomorrow, the Institut Pasteur regenerates itself. Transmission of knowledge and an ongoing exchange with learners – with their fresh perspective and curiosity – rejuvenate the field. This creates a positive future for science and medicine. Educating and partnering with the next generation in this way means extending the institute's benefit to society.

# cenerate

# EDUCATION

# Transferring and sharing knowledge

Education and training are at the center of the Institut Pasteur's activities, continuing the legacy of its founder, Louis Pasteur. For almost 130 years, and since the first microbiology course taught by Émile Roux in 1889, the Institut Pasteur has played a key role in science teaching.

![](_page_31_Picture_2.jpeg)

and healthcare professionals from around 70 countries attend one of the 60 courses and workshops run at the Institut Pasteur in Institut Pasteur International Network. Over 600 young scientists are also hosted by ate. Master's and PhD research projects.

# A unique setting for science and research training

Renowned for its outstanding research, the Institut Pasteur provides young scientists from France and abroad with a unique laboratories, they can complete internships for their undergraduate to PhD level studies. The Institut Pasteur also runs high-level Master's and PhD courses, as well as vocational science courses leading to recognized university diplomas. Courses in Paris are run by scientists on campus, with valuable input from lecturers based at partner institutions in France (such as Paris Descartes, Sorbonne, Paris Diderot, Paris-Saclay and Paris Sciences et Lettres universities, the Institut Curie, the CNRS and Inserm) and abroad. The fact that renowned scientists are involved in Institut Pasteur courses on a daily basis is pivotal to the success of our teaching, providing students with ongoing access to the latest developments in research. The focus on experimentation and practical work is a key strength and one of the distinctive characteristics of edu-MOOCs and 20% of health MOOCs available on the French cation at the Institut Pasteur. Teaching has also been consider- FUN platform. ably influenced by the development of the Institut Pasteur International Network, in terms of both the scientific subjects taught and the countries of origin of the students.

To maintain its leading position, the Institut Pasteur is extending its teaching activities by increasing the emphasis on online courses

ach vear. over 1.200 students. PhD students encouraging multidisciplinarity and links with medicine, and promoting entrepreneurship and business development.

# Paris, or at one of the 33 institutes in the The Institut Pasteur and online courses in life sciences and health

laboratories on the Paris campus to train as The Institut Pasteur is continuing to develop its online teachscientists and complete their undergradu- ing activities, with the aim of making the courses taught at the Education Center or at institutes in the Institut Pasteur International Network available to as many people as possible. In 2017, just two years after the launch of the first MOOCs, the Institut Pasteur held 12 online courses in the fields of life sciences and/or health, which were a huge success in terms of numbers (1.500 to 4.500 students enrolled per session) and international visibility (95 to 124 countries). To make it easier to distribute Institut Pasteur MOOCs in China, an setting for training through experience. By joining its various agreement has been reached with the Chinese XuetangX MOOC platform via the French equivalent France Université numérique (FUN). MOOCs produced on the Institut Pasteur campus now take precedence over courses held at the CNAM, which was until now the main means of enrollment.

Four new MOOCs, developed in 2017, will be made available in 2018 – "Tuberculosis" (over 4.000 students enrolled). "Malaria" (enrollment underway), "Resistance to Antibacterial Agents" (enrollment began late February 2018), and "Advances in Stem Cell Biology". Two of these MOOCs were launched in partnership with the Shenzen Nanshan Center for Chronic Disease Control (Tuberculosis) and Paris Diderot University (Resistance to Antibacterial Agents).

The Institut Pasteur currently represents 24% of life science

# **Programs for undergraduate and** Master's students from around the world

The Institut Pasteur is keen to step up its training for students (MOOCs and SPOCs), opening up courses to younger students, at earlier stages in their academic career. Several predoctoral

![](_page_31_Picture_14.jpeg)

![](_page_31_Picture_15.jpeg)

# **NEW DOCTORAL STUDENTS' OFFICE**

A new Doctoral Students' Office was set up for PhD students at the Institut Pasteur in 2017. The aim is to create a tightknit student community, raise awareness of the Institut Pasteur's academic and social commitments to PhD students, and offer these students one-on-one support during their research. It is open weekly for PhD students on campus, can be contacted at any time regarding any issue, and has already introduced numerous initiatives, such as the first Welcome Day specifically for PhD students in their first year in 2017-2018. It publishes a weekly newsletter for all PhD students on the Paris campus, keeping them informed of main events on their academic and social calendar. Together with the Institut Pasteur Alumni Association (AAEIP), the Francophone University Agency (AUF) and the Institut Pasteur International Network, the Doctoral Office runs a series of video conferences led by renowned scientists. These video conferences are followed by international debates which have proved to be very popular.

programs have therefore been developed at undergraduate and Master's level for students from all over the world. The Amgen Scholars Program, for example, enables around 20 students from European universities and higher education institutions to come and work on a research topic for eight weeks in one of the Institut Pasteur's laboratories. This international program is run entirely in English and culminates in a conference in Cambridge, UK. The Institut Pasteur also hosts students under the EU Erasmus+ program, thanks to its partnerships with several European universities. Similarly, a program run by the Pasteur Foundation provides for five or six undergraduate students from the US to complete training through research at the Institut Pasteur.

In an effort to vary its predoctoral courses and consolidate its position at the forefront of innovation in synthetic biology. the Institut Pasteur set up its own International Genetically Engineered Machine (iGEM) team in 2015. Since MIT launched the iGEM competition in 2004, teams from all over the world have competed to develop the most innovative

![](_page_31_Picture_21.jpeg)

![](_page_31_Picture_22.jpeg)

synthetic biology project. The 2017 Institut Pasteur team was composed of around 20 undergraduate and Master's students from a variety of disciplines (biology, physics, chemistry, mathematics, political science, law and industrial design). As well as partnerships with the Sorbonne and Paris Diderot universities, the program has been boosted by new partnerships with ESPCI Paris-Tech engineering school, ENSCI-Les Ateliers design school, the Faculty of Law at Paris-Sud University and Central Supélec, the French institute of research and higher education in engineering and science.

# Training through research for PhD students

With 130 research units in Paris and a network of 33 institutes worldwide, the Institut Pasteur is truly a higher-education hotspot for many young scientists. Each year, around 80 PhD students complete their studies in laboratories on the Paris campus. The students may be eligible for various types of funding – from their university, via the laboratories' own resources obtained through regional, national or European themed programs, from non-governmental organizations or through the Institut Pasteur's international doctoral program (*see below*). In addition, the Institut Pasteur provides scientific monitoring of the doctoral program with thesis committees, and also personal support through a post-doc tutoring and career development program.

The Institut Pasteur in Paris runs specialized PhD programs, like the Pasteur-Paris University (PPU) international doctoral program, open to students with a Master's degree (or equivalent) from a foreign university who wish to carry out their PhD research in an Institut Pasteur laboratory. This high-level program, launched in 2008, is run in close partnership with Paris-Descartes, Sorbonne and Paris-Diderot universities, and, since 2015, the University of Paris-Saclay. Led by Susanna Celli since November 2015, this three-year program leads to a PhD from a French university.

To improve mobility for health and environment researchers between Latin American and Caribbean countries and Europe, the Institut Pasteur pursued the PPU-Enhancing Mobility in Health and Environment (EMHE) doctoral program in 2017. This program is run in partnership with research funding bodies in Argentina, Mexico, Costa Rica, Peru and Uruguay. In 2017, two PhD students on the PPU-EMHE program joined the "Charles Nicolle" PPU year group.

Each year, the Institut Pasteur Department of International Affairs also awards doctoral grants for the completion of PhDs at one of the institutes in the International Network (outside mainland France). The research topic can be related to any subject under study in the International Network, ranging from infectious diseases (infectious pathophysiology, immunology, microbiology, epidemiology, virology and parasitology) to public health activities (diagnosis, surveillance, resistance, etc.). Applicants must hold a Master's or equivalent degree and be enrolled at a doctoral school based at a French or foreign university.

To keep up with the major changes in medical practice and biomedical research brought about by scientific breakthroughs and recent technological advances, the Institut Pasteur, Institut Curie and École Normale Supérieure (ENS) are continuing their "Médecine-Sciences" program. This program was set up in 2015 and offers high-level joint medical and scientific training. It includes an early introduction to research, to train up a body of professionals with both scientific and medical expertise. Students are recruited through a competitive examination at the end of their second year of medicine or pharmacy studies. The program offers comprehensive interdisciplinary training and provides students with an outstanding range of top quality teaching, lectures and internship possibilities. The many advantages include guaranteed funding for the first three years, effective scientific and medical tutoring, a prestigious ENS qualification and a PhD in Science. Graduates of the "Médecine-Sciences" program can enjoy excellent career prospects in either academia or the healthcare industry, in France or abroad.

![](_page_32_Picture_6.jpeg)

![](_page_32_Picture_7.jpeg)

# "CHARLES NICOLLE" PPU YEAR GROUP

The Pasteur-Paris University (PPU) 2017 year group, named "Charles Nicolle", welcomed 19 students from Europe (Germany, Spain, France, Italy, Portugal, Russia, UK and Switzerland), the Americas (Brazil, Canada, Colombia, USA, Peru and Uruguay) and Asia (China). It is worth noting that in 2017 a higher number of European PhD students were selected compared with previous years. Each year, students specializing in a wide variety of fields are given the chance to work together during joint activities run by the PPU organizing committee, during literature seminars or the international doctoral program annual retreat. In May 2017, this retreat was held in Pornichet. All current PhD students attended a conference where they discussed the progress of their research in a focused but informal setting with the aim of providing constructive suggestions to improve their projects.

![](_page_32_Picture_10.jpeg)

# Courses in business development and entrepreneurship for science

Out of conviction and in keeping with its calling, the Institut Pasteur has made a deliberate effort to develop business based on its research, and this is reflected in its teaching. Throughout 2017, several initiatives were developed and pursued in this field, especially the "Creating your own company" series – informal monthly events for Institut Pasteur scientists interested in business development, featuring guest speakers who have enjoyed entrepreneurial success in biotechnology – and the summer school held in July 2017 in partnership with Medicen.

To conclude, the Institut Pasteur has developed well-structured, effectively organized teaching activities at the local, national and international levels, boosted by the involvement of leading experts and professionals. The courses and initial and continuing training on offer at the Institut Pasteur have earned an outstanding international reputation, attracting promising young scientists from across the world and helping to build an international network of researchers.

The Institut Pasteur reaffirms its place through its connections to scientists all around the world. The complex systems that affect human health do not stop at country borders, and neither do successful scientific collaborations and medical developments. Every cooperative project within the Institut Pasteur International Network reaffirms the validity, if not the urgency, of this idea, linking the local with the global.

![](_page_33_Picture_3.jpeg)

Institu

# International highlights

# 

A mobile insectarium to fight malaria

The parasites most resistant to the latest generation of antimalarial drugs are very widespread in Cambodia **①**. Thanks to the backing of the Rotary Club, the Institut Pasteur in Cambodia is now equipped with a mobile insectarium to carry out research and provide entomological training for local populations.

# MAY

# DISCOVERY

Resistance to insecticides identified in mosquitoes that carry malaria in Bangui

Research carried out in the Central African Republic (2) by scientists from the four-year group at the Institut Pasteur in Bangui, the University of Denver in the US and the University of Abomey-Calavi in Benin shows that malaria-carrying *Anopheles gambiae* mosquitoes are resistant to DDT and pyrethroids. This resistance jeopardizes vector control efforts.

# MARCH

# INSTITUTIONAL

Health and the environment: launch of the ECOMORE 2 project

With €4 million in funding from the French Development Agency over a three-year period, this project will study the impact of ecosystem changes on the health of populations under the effect of human activity and climate change in five countries in South-East Asia (Cambodia, Laos, Vietnam, Myanmar and the Philippines).

![](_page_34_Picture_12.jpeg)

# INSTITUTIONAL

The Hong Kong University-Pasteur Research Pole renewed for 10 years

Set up in 1999, this research and training center, affiliated to the School of Public Health, Li Ka Shing Faculty of Medicine at Hong Kong University 2, focuses on host-pathogen interactions, particularly in respiratory tract viruses.

![](_page_34_Picture_16.jpeg)

8

# JUNE PUBLIC HEALTH

MosKeyTool: a free interactive tool for identifying mosquitoes

Mosquito identification is crucial for monitoring and controlling the diseases they carry. As part of the MediLabSecure project, free software was developed to identify the 128 species of mosquito present in Europe and the Mediterranean Basin. With funding from the European Commission, the purpose of MediLabSecure is to strengthen capabilities within a network of 55 laboratories working on emerging viruses in 19 countries in the Mediterranean () and Black Sea () regions.

![](_page_34_Picture_21.jpeg)

# AUGUST

DISCOVERY

Dengue: understanding the mechanisms that prevent symptoms developing following infection

Scientists from the Institut Pasteur in Paris and the Institut Pasteur in Cambodia (), in collaboration with teams from the CNRS and Inria, demonstrated that asymptomatic dengue infection in children is associated with activation of the immune system via control mechanisms, resulting in the elimination of viral infection without excessive immune activation. This study is important for shedding light on the role of immunity in dengue viral infection and developing new vaccine strategies.

# PUBLIC HEALTH

Joining forces against the plague in Madagascar

An exceptional plague outbreak raged on the island from August to late November 2017 and claimed over 200 lives. Alongside the health authorities and the World Health Organization, the Institut Pasteur in Madagascar , supported by the Institut Pasteur in Paris, was on the front line of the response.

# **SEPTEMBER**

# INSTITUTIONAL

# The 49th Institut Pasteur International Network Directors' Council in Abidjan

The annual Council of the Directors of the Institut Pasteur International Network took place from September 20 to 22, 2017 in Abidjan (). Over three days, representatives from the 33 member institutes reviewed the main areas of development for the International Network. Priorities included career management and development for network researchers and the need to strengthen scientific cooperation between the institutes.

![](_page_35_Picture_4.jpeg)

# <mark>SCIENTIFIC EVENT</mark> The Institut Pasteur II

# The Institut Pasteur International Network adopts a scientific strategy

Based on collaborative work, this strategy aims to promote the international visibility of the Network through federative transversal research programs addressing global health challenges. It focuses on four main areas – implementing a One Health approach to explore the main endemic or emerging zoonoses, investigating vector-borne infectious diseases, studying mother and child health and other health challenges in children, and looking into the impact of aging/ longevity on health, including chronic diseases.

# AWARD/APPOINTMENT

# Pasteur International Talent awards

Dr. Anubis Vega Rua (entomology) from the Institut Pasteur in Guadeloupe 2 and Felipe Trajtenberg from the Institut Pasteur in Montevideo 3 (molecular and structural microbiology) were the first winners of this award, which recognizes and supports career development for promising scientists in the International Network.

![](_page_35_Figure_11.jpeg)

# **OCTOBER**

SCIENTIFIC EVENT

# Three projects selected for funding from AESA's Grand Challenge Africa

Two teams from the Institut Pasteur in Dakar () and one from the Institut Pasteur in Madagascar () are involved in eight innovative projects, selected by the African Academy of Sciences and the Alliance for Accelerating Excellence in Science in Africa (AESA). The aim is to improve maternal, neonatal and infant health on the African continent.

# SCIENTIFIC EVENT

# A Pasteur joint international research unit to study viral evolution

Co-led by Prof. Marco Vignuzzi, Head of the Viral Populations and Pathogenesis Unit at the Institut Pasteur and Prof. Ben tenOever, Director of the Virus Engineering Center for Therapeutics and Research at the Icahn School of Medicine at Mount Sinai () (New York), this Pasteur joint international research unit will develop a program combining research into the natural evolution of viruses with synthetic biology to fight emerging infections.

![](_page_35_Picture_19.jpeg)

# **NOVEMBER**

# DISCOVERY

The "virome" of two bat species elucidated

In collaboration with the Institut Pasteur and INRA, scientists from the Institut Pasteur in French Guiana revealed a substantial presence of viruses in two bat species in close contact with humans in French Guiana. This data is valuable as bats harbor many viruses, particularly those responsible for severe diseases (rabies, SARS, Ebola, etc.).

![](_page_35_Figure_25.jpeg)

![](_page_35_Picture_26.jpeg)

Mobility and exchange programs between Institut Pasteur International Network (IPIN) scientists (2017 figures)

57 network scientists received training through the Calmette & Yersin program.

**6** network researchers took advantage of the "IPIN-Affiliate" program, which enables them to develop a joint scientific project with an Institut Pasteur unit over two years.

**6** internships for young French researchers in the International Network funded by the Pierre Ledoux–Jeunesse Internationale Foundation.

**5** three-month missions in the Network for newly recruited Institut Pasteur researchers.

ne

The Foundation renews itself constantly by keeping its leadership team current and by seeking new ways to give its scientists the means to achieve their missions. The Institut Pasteur also continually creates new approaches to engage the public in supporting Pasteurian research. It steadfastly renews its efforts at excellent financial stewardship to ensure its missions will be carried forward into the future.

# OUR RESOURCES

11

Cn

Am

71

# Financial review of 2017

The Institut Pasteur's economic model is characterized by its multi-sourced funding, from public and private realms, which supports its resolutely long-term aim – to prevent and treat diseases, particularly infectious ones, through research, education and public health initiatives.

## MISSIONS AND FUNDING

As indicated in the Institut Pasteur 2017 *Use of resources* statement, set out in the financial report, €231.2 million was earmarked for its mission areas, distributed and funded as follows.

![](_page_37_Figure_4.jpeg)

## Government contributions and research contracts

Government contributions are made up of a grant from the French Ministry of Higher Education, Research and Innovation, as well as funding for the 14 National Reference Centers managed by the Institut Pasteur, which is provided by Santé Publique France. Research contracts include all funding granted to Institut Pasteur scientists within calls for proposals. Public, French or international contracts make up 74% of the total funding.

## Breakdown of public gifts and donations

Within the range of different funding sources relied upon by the Institut Pasteur, the proportion of gifts and donations is on the rise. €81.8 M was raised in 2017 (see *adjacent chart and Institut Pasteur 2017 Use of resources statement in the financial report*). In addition to its mission areas, the public gifts and donations received in 2017 covered the Institut Pasteur's fundraising expenses and operating expenditure. For each €100 raised, the Institut Pasteur earmarked €78 for its missions, €11 for its fundraising expenses and €11 for its operating expenditure.

![](_page_37_Figure_9.jpeg)

€46,7 M

Legacies

# THE INSTITUT PASTEUR'S ASSETS

Having been a foundation officially recognized for its charitable status since its inception in 1887, the Institut Pasteur must also hold assets, built up over time, and make them grow. The aim of these assets is to sustain the work of the foundation by annually generating income so that it can continue its missions of public interest; efficient asset management guarantees its ability to fulfill these missions over the long term.

The Institut Pasteur has four main types of productive asset – property to let, long-term financial investments, cash and equity securities.

	2017	
	€M	%
Total	857	100%
Property	166	19%
Securities	649	76%
Private equity	0.3	0%
Cash	42	5%

Productive assets account for the equivalent of 2.6 times the Institut Pasteur's annual operating costs (ratio set out in late 2017).

These assets generated  $\in$  37.2 M during the 2017 fiscal year, reported in the profit-and-loss account, representing a rise of + $\in$ 1 M in relation to 2016.

# **EARNINGS FROM ASSETS**

	2017
	€M
Total	37.2
Property	6.4
Securities	27.6
Cash	3.2

As well as the income generated, the Institut Pasteur has statutory provisions and a reserve policy to ensure that its assets are regularly built up when the fiscal year ends with a surplus.

In addition to its productive assets, the Institut Pasteur owns all its buildings in rue du Docteur Roux in Paris and its scientific equipment, reported on its balance sheet as tangible capital assets. It also owns its brand name and a portfolio of patents, which are not reported on the balance sheet but in the profit-and-loss account for their revenue from license agreements.

# **INCOME STATEMENT**

The financial statements presented in the financial report concern the Institut Pasteur foundation in Paris, the Institut Pasteur in Guadeloupe and the Institut Pasteur in French Guiana.

	2017
data in €M	Realized
Institut Pasteur operating revenue	290.2
Institut Pasteur operating expenses	327.2
Contribution to IP Guadeloupe and IP French Guiana	- 1.4
Operating income	- 38.3
Institut Pasteur financial result	29.5
Contribution to IP Guadeloupe and IP French Guiana	- 0.0
Financial income	29.5
Recurring operating income	- 8.8
Institut Pasteur non-recurring income	8.9
Contribution to IP Guadeloupe and IP French Guiana	0.1
Non-recurring income	8.9
Employee profit sharing	0.0
NET INCOME	0.1

Recurring operating income, which broke even in 2016, showed a deficit of  $\in$ 8.8 million in 2017.  $\in$ 1.4 M of this deficit is due to the institutes outside mainland France, and  $\in$ 7.4 M to the Institut Pasteur Paris campus. This current account deficit is a result of a decorrelation between increased costs due to the implementation of the 2014-2018 strategic plan, which neither operating revenue nor financial revenue from short and long-term investments were able to cover over the fiscal year. But income from public donations reported as non-recurring income, in accordance with the provisions of article 19 of the articles of association, balanced the Institut Pasteur's net income at year-end.

# Promoting sustainable development

The Institut Pasteur stepped up discussions on current topics and projects related to sustainable development with Institut Pasteur staff and its external networks.

# Host of the Annual Responsible Campuses day

Since 2016, the Institut Pasteur has been a member of "Responsible Campuses", the first French network of universities and higher education institutions committed to sustainable development. In June 2017, the Institut Pasteur hosted the annual members' day. This event aims to:

- take stock of network activities over the past year;
- present projects and prospects for the year to come;
- set out international initiatives in terms of sustainable development;

- run a constructive workshop on 17 sustainable development targets.

These highlights were interspersed with discussions to enable participants to share their daily routines, and tours of the Institut Pasteur waste storage facilities.

# **Promoting material recovery**

In December 2017, and in line with events held during the European Week for Waste Reduction, the Quality, Environment and Sustainable Development Department worked with Terracycle and Bic<sup>®</sup> to launch a voluntary recycling program for writing materials. Ballpoint pens, felt tip pens, highlighter pens, marker pens, correction fluid, ink cartridges and fountain pens were recycled and converted into new equipment. Several containers were installed on site to collect writing materials, including one located near a picnic table made from recycled pens! This voluntary recycling program aims to promote material recovery (or upcycling) as opposed to energy recovery through incineration.

# Accreditation of events for the European Week for Waste Reduction

On Thursday November 23 and Friday November 24, 2017, the Quality, Environment and Sustainable Development Department organized events as part of the European Week for Waste Reduction. These events were accredited, for the first time, by the French Environment and Energy Management Agency (ADEME).

For the 2017 edition, the focus was on reuse and recycling. • Reuse involves reusing material for the same purpose it was designed for. To implement this concept, a recovery point was set up to drop off and take away unwanted scientific and administrative equipment.

• Recycling involves making use of existing products in a different way. To give Institut Pasteur staff ideas, a workshop showed how wood from storage pallets can be turned into garden or indoor furniture.

![](_page_38_Picture_15.jpeg)

![](_page_38_Picture_16.jpeg)

![](_page_38_Picture_17.jpeg)

![](_page_38_Picture_18.jpeg)

![](_page_38_Picture_19.jpeg)

![](_page_38_Picture_21.jpeg)

![](_page_38_Picture_22.jpeg)

![](_page_38_Picture_23.jpeg)

![](_page_38_Picture_24.jpeg)

\* Tip boxes are part of a pilot scheme involving around forty units that will be extended to the entire campus if successful.

![](_page_38_Picture_26.jpeg)

# In touch with campus needs:

# accompany, modernize and simplify

The Human Resources Department is committed to supporting Institut Pasteur staff and their career development. In 2017, it pursued and consolidated its initiatives to change, modernize and simplify its practices.

In terms of human resources, supporting the Institut Pasteur's strategy means implementing an HR policy that is relevant for an institute of outstanding research and – this goes without saying - modernizing its HR practices. The year 2017 was marked by the launch of new services for the Institut Pasteur In 2017, the MAASCC welcome, support and career developcommunity, in line with work to optimize and computerize procedures undertaken in recent years.

# **Progress to benefit the campus**

The main HR procedures, including requests for promotion, monitoring of training plans and identification of recruitment requirements (not forgetting annual appraisals since 2016), have been possible online since 2017. With the rollout of these modules on the Career Portal – an online Talentsoft solution – Institut Pasteur staff (managers, employees and assistants) can access new services and receive tracked answers tailored to their needs.

In addition, since June 2017, a web space has enabled candidates and future employees to consult job offers and apply online. They can also access helpful information, documents and links via this personalized platform to prepare for their arrival on campus, further strengthening the employer brand and integration initiatives at the Institut Pasteur.

# **Commitment to people and careers**

With support for talent at the heart of its HR policy, the Institut Pasteur is focusing efforts on training by supporting transversal, interdisciplinary and innovative science, and by developing training programs for specific professions. 2017 also witnessed the introduction of a brand new training course for research unit support staff and assistants. The "Biology for non-biologists" sessions are designed to improve understanding of the

working environment of scientists. The program includes an introduction to the basics of biology, the main research topics at the Institut Pasteur and the workings of laboratories.

ment structure for scientists extended its service - 279 staff members had personalized career reviews. 130 researchers and engineers met with the Careers Committee, and over 30 events or workshops were organized on campus. The Institut Pasteur is also mindful of the international dimension of careers as 21 scientists from the International Network received support from the MAASCC this year.

With its 1,250 members, the Alumni & Pasteurian Community continues to build and develop its network. The new Pasteurians & Alumni Cafés, for instance, enabled members to share their thoughts during informal debates on various topics (e.g. dare to dream about your career, the Pasteurian spirit).

Lastly, the Institut Pasteur reiterated its commitment to health in the workplace in 2017 with a day for the prevention of musculoskeletal disorders (MSDs), run by a physiotherapist and the Occupational Health Department. The aim was to explore the question of ergonomics and working with display screen equipment.

![](_page_39_Picture_13.jpeg)

![](_page_39_Picture_14.jpeg)

STAFF MEMBERS as at 12/31/2017

500

58.3%

employees from external

and health officers

2,139 IP employees 71.7% with permanent

Of the

2.639

employees

(excluding interns)

interns

research organizations (OREX) contracts

29.4% senior scientists

staff

# FOCUS ON RECRUITMENT 399

people hired in 2017

# CATEGORIES AT THE **INSTITUT PASTEUR**

65.6%

Research

2.6%

Health

PROFESSIONAL

Of the 2,139 Institut Pasteur employees, percentage per category (as set out in the Jobs and Skills Guide)

![](_page_39_Picture_23.jpeg)

**58.9%** women hired

47.4% researchers hired

(excluding engineers)

16.5% employees under 25 hired

31.8% Administrative and Technical

![](_page_39_Picture_31.jpeg)

non-managerial

12.3% administrative and technical managers

# DIVERSITY **ON CAMPUS**

the average age of IP employees

![](_page_39_Picture_36.jpeg)

**59**% of IP staff members

![](_page_39_Picture_38.jpeg)

66 nationalities on campus

# **DEVELOPMENT OF SKILLS (TRAINING)**

4,200

courses, including 900 for employees of external research organization or interns

# **€3,468**

invested in professional training (costs including time spent on training and compulsory contributions)

training hours (including 5.500 for members of external organizations and interns)

# **CAREER SUPPORT** FOR SCIENTISTS

![](_page_39_Picture_48.jpeg)

state-employed researchers and engineers met with the Careers Committee

![](_page_39_Picture_51.jpeg)

scientists followed the career quidance program at the MAASCC welcome, support and career development structure for scientists, including 69 post-doctoral fellows, 34 PhD students and 23 engineers

career events (round tables, sessions, etc.) held and 24 skills workshops organized

# Donations, sponsorship and legacies Your continued support

In 2017, nearly a third of the Institut Pasteur's resources came directly from individual and corporate donations and legacies. This support is essential for our institution!

> 2017, the Institut Pasteur received financial support from almost 230,000 individual donors. The funds raised through the generosity of these individuals, as well as our partner companies and foundations, will enable the Institut Pasteur's scientists to continue their vital work and explore new avenues for research. In 2017, we received €32.7 million.

More than 60,000 new donors joined the loyal supporters of the Institut Pasteur. And of the latter, close to 25,000 chose to set up a direct debit, which enables them to spread their donations over the entire year.

For the 11th year in a row, our donors showed extraordinary generosity in supporting the Institut Pasteur's research during Pasteurdon, which was held from October 12 to 15, 2017. Loval Pasteurdon patron Alexandra Lamy, a tireless supporter of the cause, met with scientists to find out about their work. For the first time this year, the Institut Pasteur was honored to welcome on board the famous film director Claude Lelouch, who agreed to use his creative talents to advance science by producing a promotional video for Pasteurdon.

# **Donations from companies** and foundations

2017 saw the sixth edition of the Sanofi-Institut Pasteur Awards, which are presented to scientists in recognition of their innovative work in life science and biomedical research. The Sanofi Group also renewed its support for the INCEPTION\* integrative biology program, which focuses on disease emergence for both populations and individuals.

Like last year, the "Vivons Vélo" cycling event in aid of the Institut Pasteur ended with a mass cycle ride that finished at the Institut Pasteur. This event, organized throughout the year by AG2R La Mondiale, raised close to €90,000 for the Institut Pasteur.

\* Convergence Institute for the emergence of pathologies through individuals and populations

![](_page_40_Picture_9.jpeg)

# **Testimonial**

66 Reflecting the values of performance and solidarity that have always guided AG2R La Mondiale, the "Vivons Vélo" cvcling event in aid of the Institut Pasteur invites the public to get pedaling to raise funds for research into neurodegenerative conditions. We are delighted to be associated with Pasteurdon, which promotes our charity sports event.

Yvon Breton, advisor to senior management at AG2R LA MONDIALE

![](_page_40_Picture_13.jpeg)

The Roch-Les Mousquetaires Foundation remains a loyal part-Legacies increasingly shared ner, and stood by its firm commitment to Institut Pasteur scientists. It gave generous funding to two research programs on 2017 saw 107 new legacies and gifts submitted to the Board of food safety and, as part of Pasteurdon, organized the sale of Directors, representing €32.9 million. The Institut Pasteur shares a range of charity-linked products in two store chains in the most of its bequeathed legacies with many other institutions. Les Mousquetaires group, Intermarché and Bricomarché. New sponsors joined the ranks of Institut Pasteur supporters Life insurance policies continued to represent a leading source of in 2017 – the Bettencourt Schueller Foundation decided to recurring income, and remained stable in 2017, raising €9.2 million. contribute to research into autism, and the insurance com-These policies, like legacies and gifts, offer favorable tax arrangepany MTRL is supporting developments in neuroscience. ments in that they are exempt from transfer duties.

In addition, Odyssey Reinsurance Company, Mutuelle Air France, and the CRPCEN pension fund renewed their support.

In total, donations from companies and foundations raised over €9 million.

Finally, despite challenging circumstances in 2017, support remained strong abroad and €2 million was raised in Europe and the US.

The Institut Pasteur would like to express its heartfelt thanks to its sponsors and donors for their generosity and continued support. These contributions are its greatest asset as it strives to advance knowledge and make significant progress in biomedical research.

# **Quality procedures: renewal of** certification that is one of a kind

The Institut Pasteur's Legacies and Real Estate Assets Management Office is the only department of its kind in France to have applied quality procedures to all its activities. Following its annual audit, AFNOR Certification renewed the Institut Pasteur's ISO 9001 certification for 2017.

# **Communications activities**

In 2017, for the third year in a row, the major annual promotional campaign for legacies and gifts was launched on radio stations and TV channels, and in the mainstream and legal press, to raise awareness of these important funding methods for the Institut Pasteur. The number of people asking for information about legacies, life insurance and donations, as well as gift notifications, has continued to rise. Questions concerning more innovative schemes, such as the temporary transfer of usufruct rights and posthumous gifts, have also grown in number. In order to process all these new contracts, the Legacies and Real Estate Assets Management Office employs two dedicated staff members in charge of legator relations. Benefactors can contact these staff members for advice and guidance or speak to one of the office's three legal experts. The six-monthly "Legacies and gifts newsletter" is our key means of communicating with legators, and the sixth edition was sent out at the end of 2017. This newsletter covers a specific aspect of gifts, legacies, and life insurance policies in each issue, and generates substantial feedback and a large number of personal testimonials.

The "Think Tank de la philanthropie" (philanthropic trusts group), which was set up by the Institut Pasteur following the **FM.** donor success of its first Conference on Philanthropic Trusts in 2009, developed its activities and issued a series of opinions. The experts in this think tank include notaries, lawyers, and bankers. To date, it is the only platform where experts from a variety of disciplines can share their thoughts and ideas on questions relating to generosity and philanthropy.

# Testimonials

Human life is at the heart of the Fondation Le Roch-Les Mousquetaires' priorities. Supporting research teams, in particular those teams ensuring progress in food safety, is our way of backing actions that contribute to the well-being of each and every one of us.

Marie-Thérèse Le Roch. President of Fondation Le Roch-Les Mousquetaires

# I was lucky enough to attend one of your lectures on aging. It was both informative and reassuring about the future. Your scientists are fascinating. And I will continue to give while I can.

![](_page_41_Picture_9.jpeg)

# **MAJOR SPONSORS**

![](_page_41_Picture_11.jpeg)

![](_page_41_Picture_12.jpeg)

# **SPONSORS**

AG2R LA MONDIALE ASSU 2000 CONNY-MAEVA CHARITABLE FOUNDATION CRPCFN DENNIS AND MIREILLE GILLINGS FOUND FLORENCE GOULD FOUNDATION FONDATION AIR LIQUIDE FONDATION BETTENCOURT SCHUELLER FONDATION BNP PARIBAS FONDATION COGNACQ-JAY FONDATION D'ENTREPRISE BRISTOL-MY SQUIBB FONDATION D'ENTREPRISE MICHELIN FONDATION LE ROCH-LES MOUSQUETA

# **PARTNERS**

AXA ATOUT CŒUR BANQUE PRIVÉE EUROPÉENNE **BNP PARIBAS** L'ORÉAL PRODUITS PROFESSIONNELS SOCIÉTÉ GÉNÉRALE

![](_page_41_Picture_18.jpeg)

![](_page_41_Picture_19.jpeg)

![](_page_41_Picture_20.jpeg)

	FONDATION ORANGE
	FONDATION RAOUL FOLLEREAU
ON	FONDS AXA POUR LA RECHERCHE
	LHW STIFTUNG
DATION	MGEN
	MUTUELLE AIR FRANCE
	MUTUELLE MTRL
R	NOUVELLE CASSIUS FONDATION
	ODYSSEY REINSURANCE COMPANY
	ONET
/ERS	PASTEUR FOUNDATION US
	SANOFI PASTEUR
	TARIFOLD
AIRES	VON DUHN STIFTUNG

# Board of Directors

# April 2018

The Board of Directors makes decisions on all Institut Pasteur matters. It gives its opinion on the strategic policies proposed by the President, votes on budgets, and approves the accounts.

# **BOARD OF DIRECTORS BUREAU**

Chairman CHRISTIAN VIGOUROUX French Council of State Department Head

Vice-Chairman

HUBERT DU MESNIL Ponts et Chaussées engineer and Chairman of Tunnel Euralpin Lyon-Turin

# Vice-Chairman

**ARTUR SCHERF** Head of the Biology of Host-Parasite Interactions Unit

# Secretary

**FABRICE CHRÉTIEN** Head of the Human Histopathology and Animal Models Unit at the Institut Pasteur, and Head of the Neuropathology Department at Sainte-Anne Hospital

# Treasurer

AMÉLIE VERDIER Director of the Budget, French Ministry of the Economy and Finance

# Permanent guest of the Bureau

ANTOINE TRILLER Head of Research at Inserm and Director of the École Normale Supérieure Institute of Biology

# **OTHER MEMBERS**

GENEVIÈVE ALMOUZNI Director of the Research Center at the Institut Curie, Paris

**ALAIN BERETZ** Director-General of Research and Innovation. French Ministry of Education, Higher Education and Research

**GÉRARD BERRY** Professor at the Collège de France, Chair of Algorithms, Machines and Languages

MICHÈLE BOCCOZ Assistant Director-General for External Relations, World Health Organization (WHO)

PIERRE-MARIE GIRARD Head of the Infectious and Tropical Diseases Department, Saint-Antoine Hospital, Paris

**MURIEL HILAIRE-SOULE** Curator of the Pasteur Museum

**ISABELLE LAMOTHE** CEO of ManpowerGroup Solutions

YVES LÉVY Chairman and Chief Executive Officer of Inserm (French National Institute for Health and Medical Research)

SUSAN LIAUTAUD Independent Director (Susan Liautaud & Associates Limited)

JEAN-CLAUDE MANUGUERRA Head of the Environment and Infectious Risks Research and Expertise Unit

INÈS-CLAIRE MERCEREAU Chief Advisor to the French Government's Accounting Office

**ANTOINE PETIT** President of the CNRS (French National Center for Scientific Research)

FÉLIX REY Head of the Structural Virology Unit, Institut Pasteur

**JÉRÔME SALOMON** Director-General for Health, French Ministry of Social Affairs and Health

MARIE-NOËLLE UNGEHEUER Head of the Clinical Investigation and Access to BioResources Platform (ICAReB)

# Scientific Council

The Scientific Council advises on all issues relating to scientific policy, organization, and research and teaching programs. The Council is consulted on all research and teaching unit creation, closure and merger decisions.

# ELECTED PASTEURIAN MEMBERS

ANDRÉS ALCOVER Head of the Lymphocyte Cell Biology Unit

**AZIZ EL AMRAOUI** Head of Laboratory in the Genetics and Physiology of Hearing Unit

**Secretary JEAN-MARC GHIGO** Head of the Genetics of Biofilms Unit

Vice-Chair MICHAELA MÜLLER-TRUTWIN Head of the Aspergillus Unit

# **APPOINTED PASTEURIAN MEMBERS**

# **CARMEN BUCHRIESER**

Chair Head of the Biology of Intracellular Bacteria Unit

PHILIPPE BASTIN Head of the Trypanosome Cell Biology Unit

**JAMES DI SANTO** Head of the Innate Immunity Unit

CARLA SALEH Head of the Viruses and RNA Interference Unit

April 2018

# **EXTERNAL MEMBERS**

# AMOS BAIROCH

Prof. Department of Human Protein Science, Computer and Laboratory Investigation of Proteins of Human Origin (CALIPHO), University of Geneva Medical School, Switzerland

# **ARTURO CASADEVALL**

Prof. Microbiology and Immunology Department, Albert Einstein College of Medicine, New York, USA

# ANGELA GRONENBORN

Prof. Department of Structural Biology, University of Pittsburgh School of Medicine, Pittsburgh, USA

# **EVA HARRIS**

Prof. Division of Infectious Diseases and Vaccinology, Director, Center for Global Public Health, UC Berkeley School of Public Health, USA

# NICHOLAS HASTIE

Prof. MRC Human Genetics Unit, MRC Institute of Genetics and Molecular Medicine at the University of Edinburgh, Edinburgh, UK

# JULIAN PARKHILL

Prof. Genomics of Bacterial Pathogens, Sanger Institute, Cambridge, UK

# **CLAUDIO D. STERN**

Prof. Department of Cell & Developmental Biology, University College of London, UK

# Governing bodies

![](_page_43_Figure_1.jpeg)

# Management of the Institut Pasteur April 2018

The President, a figure from the world of science, prepares and implements strategic planning. He is supported by a management team comprising an Executive Board and a Senior Management Board.

**ISABELLE BUCKLE** Vice-President Researc Applications and Industrial Relation

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![](_page_43_Picture_6.jpeg)

NATHALIE DENOYÉS

ALAIN ISRAËL

Assessment

Vice-President Technical

Resources and Environment

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CHRISTOPHE D'ENFERT Vice-President Technology and Scientific Programs

![](_page_43_Picture_9.jpeg)

Vice-President Legal Affairs

Vice-President Scientific

![](_page_43_Picture_11.jpeg)

![](_page_43_Picture_12.jpeg)

MONICA SALA

MICHAËL PRESSIGOUT Vice-President Information Systems

Executive Board

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JEAN-FRANCOIS CHAMBON Vice-President

Communications and Fundraising

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![](_page_43_Picture_22.jpeg)

![](_page_43_Picture_23.jpeg)

CORINNE FORTIN Vice-President Financial Affairs

![](_page_43_Picture_25.jpeg)

NATHALIE DE PARSEVAL Scientific Secretary General

![](_page_43_Picture_27.jpeg)

PATRICK TRIEU-CUOT Vice-President Scientific Careers

STEWART COLE President

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**OLIVIER SCHWARTZ** Scientific Director

MARC JOUAN Vice-President International Affairs and Internationa Network

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![](_page_43_Picture_34.jpeg)

**ODILE GELPI** Vice-President Medical Affairs and Public Health

![](_page_43_Picture_36.jpeg)

**ODILE HERMABESSIERE** Vice-President Human Resources

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# perpetual stability in carefully considered resolutions

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**Institut Pasteur Ambassador** Erik Orsenna

f all the definitions of perseverance, one might well opt for this one proposed by Jean-Francois Marmontel, an author, philosopher, essayist and active contributor to Diderot's Encyclopedia, elected in 1763 to occupy seat number 17 at the Académie française - the same seat that would subsequently be held by none other than Louis Pasteur. Perseverance: perpetual stability in carefully considered resolutions. The construction of the word itself is also interesting: the prefix per suggests the notion of thoroughness (pernicious, perversity), while severus means serious or severe. People known for their perseverance are hardly likely to be elected class clown... So with this two-pronged approach – etymological and academic –, we can begin to piece together the profile of any researcher, any

scientist - starting with one of the very first.

# Here's an example.

On June 5, 1865, when Louis Pasteur took a train to the south of France, he did not vet know much about all those little creatures that he was meant to be curing. On arriving in the glorious city of Avignon, he knocked on the door of the greatest entomologist of the time, Jean-Henri Fabre. His host welcomed him by handing him a cocoon. Pasteur held it up to his ear and shook it.

- "It rattles! Is there something inside?" - "Well of course, there's a chrysalis!"

We can only imagine the look of stupefaction on Fabre's face at such a level of ignorance. But he had not reckoned with Pasteur's sheer determination. Not long afterwards, following numerous short trips and some longer stays, the scientist would know all there was to know about silkworms: how they lived, how they were bred and the diseases that were destroying them. This inquiry, worthy of the most meticulous detective, took three whole years of his life. He would not embark on another battle until he had saved the troubled French silk industry.

Perseverance cannot be encapsulated within an idea or isolated in the certainty of being right. Perseverance endures, but with doubt. And the best way of overcoming doubt is to investigate.

Pasteur's entire existence is a succession of similar stories of perseverance. Once he identified an enigma, he would mobilize all efforts - his own (and those of his entire family, including his children), but also those of his team, a carefully selected blend of the requisite expertise and skills. For we should not forget that this chemist was not a doctor, nor was he a veterinarian. One can accomplish creative work alone (by drawing on the legacy of others). But trying to understand the diversity of the ever-changing, infinite world on our own is a pipe dream.

And that's where the other dimension of perseverance comes in, the collective element. How can we bind together a group of top researchers – who by their very nature are inevitably stubborn and demanding - for long enough? One might liken the process to driving a team of wild horses. How can we make these fiery animals put up with each other and, if possible, work together to move forward, as quickly as possible, in the chosen direction? How can we inspire the same levels of energy day after day? How can we move on from failure, overcome doubt, rekindle ambition after a victory? How can we harness jealousy and use it to fuel the next adventure?

Perseverance is the very opposite of the attitude expressed in the French as après moi, le déluge ("Who cares what happens after I'm gone?"). It is the determined battle of all those who know that the struggle for knowledge is endless. Perseverance means making a pact with Time - which, when it comes to sheer cunning, is easily the devil's equal. It also means respecting those that laid and continue to lay the foundations. They know that nothing is more fleeting than a lifetime - even the most noteworthy. So they lay the foundations with an eye to the future.

What would remain of Pasteur without the institute he set out to create? A man at the very zenith of Science. Countless streets bearing his name. And two or three dates, milestones of major breakthroughs. But Pasteur's perseverance did not stop on September 27, 1895. I have always found his last words bewildering: "I cannot." He was wrong. He still could. His perseverance continued to bear fruit, even after his death. For his institute is still there, and its achievements are astounding. Fourteen new research units were set up in Paris in 2017, and there are teams from the 33 institutes that make up the Institut Pasteur International Network in 26 countries on every continent.

Finally, it is important to point out that perseverance is not the same as stubbornness. Perseverance cannot be encapsulated within an idea or isolated in the certainty of being right. Perseverance endures, but with doubt. And the best way of overcoming doubt is to investigate; in other words, to check in with reality. When an ignoramus like me learns about Pasteur's life, there is an inevitable fascination with the number of objects the scientist invented to test his theories, including the wonderful swan neck flask, with which he finally put to rest the idea of spontaneous generation.

In July 2018, our institute will officially inaugurate the Titan Krios™, one of the most powerful microscopes in the world. The aim is to see with ever greater clarity so that we might improve our understanding; to improve our understanding so that we might better care for those in need. Now that's perseverance.

By using Cocoon Silk rather than non-recycled paper, the environmental impact was reduced by:

![](_page_45_Picture_1.jpeg)

Sources: Carbon footprint data evaluated by Labelia Conseil. Virgin fiber paper data from latest European BREF data.

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![](_page_46_Picture_0.jpeg)

![](_page_46_Picture_1.jpeg)

![](_page_46_Picture_2.jpeg)

# Gilberte Clodion

Assistant, Deputy Directorate General for Administration and Finance

![](_page_46_Picture_5.jpeg)

# Virginie Ponsin \_

Academic Material Transfer Agreement (MTA) Coordinator, Office of Technology Transfer & Entrepreneurship

# Nhân Pham Thi \_

Medical Doctor specializing in allergies, and researcher, Institut Pasteur Medical Center (CMIP)

# Armelle Phalipon Researcher, Director of research within the Molecular Microbial Pathogenesis Unit

# Fabien Taieb \_

Medical Doctor specializing in Infectious Disease and Epidemiology, Center for Translational Science, Epidemiology of Emerging Diseases Unit

# Eliza

Jones Project Manager, Editorial Service, Department of Communications and Fundraising

# Arnaud <u>Fo</u>ntanet

Researcher, Director of the Center for Global Health and Head of the Epidemiology of Emerging Diseases Unit Elodie Brient-Litzler\_ Deputy Director, Center for Innovation & Technological Research

![](_page_46_Picture_18.jpeg)

on diseases at www.pasteur.fr

![](_page_46_Picture_20.jpeg)