# Human health

## at the heart of our mission

2018 Annual Report

Institut Pasteur

# Contents



## Institut Pasteur researchers strive year on year to advance science and improve human health

### THE INSTITUT PASTEUR'S STAFF CURRENTLY INCLUDES:

#### NOBEL PRIZES

**1 Nobel Laureate**
(***10 laureates*** *since 1907*)

#### CNRS MEDALS

**2** CNRS Gold Medal recipients
**6** CNRS Silver Medal recipients
**6** CNRS Bronze Medal recipients

#### OTHER FRENCH AWARDS

**3** Inserm Grand Prix for Medical Research recipients
**5** Allianz/Institut de France Foundation Research Prize recipients
**1** Emile Jungfleisch Grand Prix recipient
**1** Inria Grand Prix recipient
**2** Cancer Research Awards from the Simone and Cino Del Duca Foundation-Institut de France recipients
**2** Mémain-Pelletier Award recipients
**11** Schlumberger Foundation for Education and Research Prize recipients

#### INTERNATIONAL AWARDS

**1** Gairdner Award recipient
**1** Kavli Prize for Neuroscience recipient
**1** Sjöberg Prize from the Royal Swedish Academy recipient
**1** Balzan Prize recipient
**1** Brain Prize recipient
**3** Robert Koch Prize recipients
**3** L'Oréal-UNESCO For Women in Science Award recipients
**4** Louis-Jeantet Prize recipients

#### EUROPEAN GRANTS

**EUROPEAN RESEARCH COUNCIL (ERC) GRANTS**
**23** ERC Starting Grant recipients
**19** ERC Advanced Grant recipients
**8** ERC Consolidator Grant recipients
**2** ERC Proof of Concept Grant recipients

#### APPOINTMENTS


**5** members of the US National Academy of Sciences, Washington (USA)
**4** members of the British Royal Society
**38** members of EMBO (European Molecular Biology Organization)
**20** members of the French Academy of Sciences

INTERVIEW WITH

# Christian Vigouroux

## Chairman of the Board of Directors

> Excellence means striving to be exemplary across the board – in finance, ethics, biosafety and IT. Trust needs to be earned.

### What were the highlights of 2018 in human and scientific terms?

2018 was a year of consolidation and ambition. It also marked the Institut Pasteur's 130th anniversary and saw the opening of new facilities such as the Titan Krios™ and the Omics buildings *(see pages 7 and 8)*. This reminds us that science is a competitive business and that it is important to have the best tools to achieve success. Just as Pasteur inspired Duclaux, who inspired Roux, who in turn supported Yersin, the Institut Pasteur is a place for training and passing on knowledge, for spotting and inspiring talented young scientists. That is why we set up 5-year units, which are specially designed to enable them to shine. In 2019, we will continue to develop our site, because if we want to achieve excellence, we need to remain one step ahead.

### In 2018, a new Strategic Plan was also completed to ensure that the Institut Pasteur stays competitive. What particularly stood out for you during the process?

The Board of Directors approached its work on the Strategic Plan with enthusiasm. We adopted the plan both for scientists – the fabric of our institute –, and for patients and populations – the reason we exist. I would add that developing a Strategic Plan encourages a forward-looking approach, and it brings people together. It made us think about what we want for the future – it will guide us for the next five years; but it also gave us a sense of common purpose, as we held several meetings and seminars during the process. The draft plan was presented to the Institut Pasteur General Meeting and to our partners. The Strategic Plan concerns all of us, now and in the future. I would thank our President, Professor Stewart Cole – and his team, especially François Romaneix and Olivier Schwartz –, who, a year into his term, kept on track and delivered our roadmap within the agreed timeframe by bringing people together.

### How will the Institut Pasteur achieve the priorities in the plan?

We will do so by focusing on the resources we have and the funds required. We know that our resources are not limitless, even though the limits set for us by our donors and sponsors are favorable and may well stay that way. I would like to emphasize two of the plan's objectives that are guiding our work.
Our motto, "increasing the impact of research on health", keeps us firmly rooted in the Pasteurian approach. And the objective of strengthening our existing national and international partnerships to boost the Institut Pasteur's scientific excellence reminds us that we are not working alone.

> We adopted the new Strategic Plan both for scientists – the fabric of our institute –, and for patients and populations – the reason we exist.

### Will the Strategic Plan be a driver for change and progress?

I am certain that it will. The hallmark of outstanding research is being bold, making changes that pave the way for the architects of the future – people like the famous Pasteurians Roux and Duclaux. We need to put our faith in new generations, new processes (bioinformatics, artificial intelligence, etc.) and new geographical centers (Latin America, East Africa, etc.).
The Institut Pasteur has the freedom and ambition to be bold. It has changed over time: it no longer produces drugs or vaccines and no longer has its own hospital, but it is developing its network, its recruitments and its future priorities. So we need to be bold, we need to invest – including in areas that we might not have thought of ourselves –, and we need to seize opportunities for progress, such as collaborating in the creation of a Hearing Institute *(Institut de l'Audition)*.

### Back in 2017, you pointed to the importance of biosafety and CNRs in the Institut Pasteur's approach. The plan gives new momentum to these areas.

Excellence means striving to be exemplary across the board – in finance, ethics, biosafety and IT. Trust needs to be earned. We must not only guarantee compliance with the principles of ethics, scientific integrity and professional conduct; we also need to think about how to improve the quality of working life, how to cultivate employees' interest in and esteem for their work and instill a sense of usefulness for human health. Public health has always been a priority at the Institut Pasteur, involving our 14 National Reference Centers (CNRs) and the Laboratory for Urgent Response to Biological Threats (CIBU) – which provided public health expertise for health authorities worldwide in 2018 and will continue to do so in the future. The Strategic Plan emphasizes the Institut Pasteur's determination to enhance its research potential in the areas covered by the CNRs.

### Human health is central to our work, as reiterated in the Strategic Plan.

Yes – that is the path we have chosen. We have decided to focus on tackling diseases that represent a threat from a global health perspective. This is very much in line with current health approaches, as reflected in the modernization of the French Act on the Prevention of Vector-Borne Diseases, such as diseases caused by the *Aedes albopictus* mosquito[1]. This is the Institut Pasteur's objective as it looks to consolidate its CNRs, encourage the involvement of its scientists in the development of research applications, and further its support for innovative translational projects in cooperation with LabEx laboratories. Public health is a long-standing mission at the Institut Pasteur.

### What are your wishes for the Institut Pasteur in 2019?

I would say that it is up to the Institut Pasteur to extend its wishes to all those who recognize and appreciate it, who admire, support, help and finance its work. In any case, 2019 is off to a busy start for the Board of Directors, which will strive to implement the resolutions in the Strategic Plan and to lay the ground for a united, enthusiastic working community.
The Institut Pasteur is one of those rare places which can offer solutions to the inherent anxiety that comes with the job of being a scientist. Indeed, the ambition and, dare I say, success of the Institut Pasteur is in firmly dispelling the words of Robert Walser in *The Tanners* (1907): "In this way, it seems to me, you will perhaps find far more satisfaction in life than even the scholar who (though he clearly recognizes the strings from which all lives and deeds depend) remains chained to the narrow confines of his study but nonetheless, as I can report from experience, is often not so terribly content."[2] At the Institut Pasteur, on the contrary, we aim to make sure that our scientists are both satisfied and proud to contribute to our scientific and health missions.

*1. In 2019 a draft decree is set to modernize efforts to combat mosquitoes in France, for the purposes of health rather than human comfort (1964 decree).*

*2. Translated from the French for this annual report.*

INTERVIEW WITH

# Stewart Cole
## President

### 2018 was your first year as Institut Pasteur President. How do you look back on it?

A year ago I told the staff at the Institut Pasteur that I felt I had come to "the right place at the right time". 2018 was a successful year, with more than 1,100 scientific publications and several major awards for our scientists. In public health, our 14 National Reference Centers (CNRs) and WHO Collaborating Centers continued to strive daily to tackle and control communicable diseases.
(I would especially like to commend the *Escherichia coli, Shigella* and *Salmonella* CNR for its work during the infant *Salmonella* outbreak.) Among the year's highlights are the inauguration of the nanoimaging building for ultra-high resolution electron microscopy – which houses the Titan Krios™ microscope – and the official opening of the Omics building for big data generation and analysis applications.
The latter building's wings were named after two famous people: the legendary Pasteurian Alexandre Yersin and the French stateswoman Simone Veil, who saved the Institut Pasteur from bankruptcy in 1975. This is the first time we have honored a woman's legacy in this way, and I will do my best to ensure that this trend continues during my time in office.

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> Our goal is to turn the scientific knowledge generated at the Institut Pasteur into applications for health.

### The opening of these two buildings also marked the Institut Pasteur's 130th anniversary. What stood out for you during the anniversary celebrations?

The French Minister for Higher Education, Research and Innovation, Frédérique Vidal gave an inspiring address at the world health symposium we held on November 13, 2018, 130 years after the Institut Pasteur's official opening. The Minister recognized the exemplary role played by the Institut Pasteur in the French research landscape and in tackling disease. She emphasized our expertise in basic research, in prophylactic and therapeutic applications and in public health. These are cornerstones of our history and they also form the building blocks for our 2019-2023 Strategic Plan.



### The Strategic Plan reminds us that human health is central to the Institut Pasteur's work. What areas does it focus on?

We will pursue our multidisciplinary basic research in life sciences, which is the core focus of our scientific activity. Our ambition is to give new impetus to this research and increase its impact on health. We have also identified three priority scientific areas, which reflect some of the most alarming health issues today: emerging infectious diseases, antimicrobial resistance, and brain connectivity and neurodegenerative diseases. We aim to consolidate our expertise and invest in these areas, while maintaining our other key activities.
We will be introducing a “concerted action for cancer” to underpin our wide-ranging research in this field.
We will also be launching a “concerted action for vaccinology” that will bring together our vaccine experts and will rely on work in tandem with the international vaccination center.
Lastly, our goal is to turn the scientific knowledge generated at the Institut Pasteur into applications for health. In terms of public health this will involve closer partnerships with clinicians to develop the biomedical dimension of our work.

### How will the Institut Pasteur achieve these ambitions?

First and foremost, we need to rally all our teams around these joint projects. I would particularly like to thank all those who contributed to the plan, especially our Scientific Director Olivier Schwartz, who led a working group that spearheaded a collaborative process involving the entire campus. I also extend my thanks to our Board of Directors and its Chairman for supporting us and approving the plan.
We will work together to achieve these objectives, pursue a proactive policy of international partnerships with the Institut Pasteur International Network, foster an open approach to society, develop the Institut Pasteur's financial resources, and promote an attractive, collaborative working environment. I am particularly committed to the quality of working life at the Institut Pasteur, which I consider a vital prerequisite for our future success.
Finally, the Institut Pasteur needs to continue to build a relationship of trust with its public and private scientific partners, both in France and worldwide. The International Network needs to take full advantage of potential synergies with international institutions, NGOs and other public health stakeholders.

### What decisions have already been taken to implement the plan?

In autumn 2018, we launched a call for expressions of interest for new five-year units exclusively for Institut Pasteur scientists, and applications will be examined by the Scientific Council in 2019. Our Gender Equality Index was also published on the Institut Pasteur website.
We will strive to promote equality, and especially to improve the representation of women in senior scientific positions. It is vital that every individual, regardless of gender, is able to fully express their talent. We also aim to encourage young talent.

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> Over the coming years, we will actively promote gender equality and develop young talent.

An annual award for the best publications by Institut Pasteur PhD students and post-doctoral fellows was instituted in 2018, to encourage junior scientists, promote their teams and boost our visibility. Finally, research applications, one of our historical missions and sources of income, need to be more effectively integrated into the Institut Pasteur's work. Shortly after taking office I reorganized and strengthened the department responsible for this area, and we are already seeing closer synergy with the Department of Scientific Affairs. We are also offering greater incentives for filing patents to encourage inventors, and we intend to overhaul our support processes for those who create business start-ups.

### What is your message for 2019?

The Institut Pasteur owes its achievements – past, present and future – to all those who, following in Louis Pasteur's footsteps, have laid the foundations for major discoveries.
Let's be proud that we belong to the Institut Pasteur and that we can contribute to its success, whatever our role.

# Review of the year 2018

## The Institut Pasteur celebrated its 130th anniversary

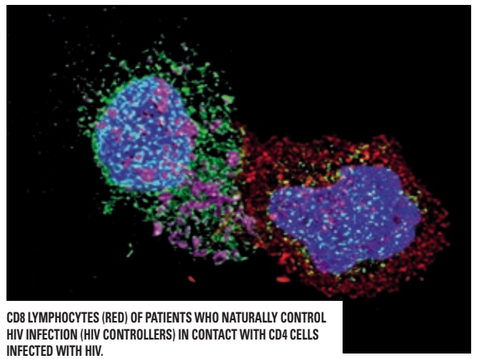
The Institut Pasteur commemorated the 130th anniversary of its inauguration (November 14, 1888) by organizing a high-level international conference on global health in November 2018 under the high patronage of Emmanuel Macron, the French President. The fight against emerging infectious diseases is incidentally one of the priorities of the Institut Pasteur's 2019-2023 Strategic Plan. The ceremony was attended by guests including Jérôme Salomon, French Director-General for Health, Elias Zerhouni, Professor Emeritus at Johns Hopkins University, Soumya Swaminathan, Deputy Director-General for Programs at WHO, and Trevor Mundel, President of Global Health at the Bill and Melinda Gates Foundation.

**79/100**

**An excellent popularity rating for the Institut Pasteur which continued to rise in 2019 (+2 points in relation to 2018 and +7 points in relation to 2016). This score is the highest of all similar studies carried out by TNS/Sofres.**

## AIDS – AN APPROACH FOR TARGETING HIV RESERVOIRS

Current HIV treatments need to be taken for life as antiretroviral therapy is unable to eliminate viral reservoirs lurking in immune cells. Thanks to metabolic activity inhibitors, scientists have managed to destroy these infected immune cells (CD4 T lymphocytes), or "reservoirs".



CD8 LYMPHOCYTES (RED) OF PATIENTS WHO NATURALLY CONTROL HIV INFECTION (HIV CONTROLLERS) IN CONTACT WITH CD4 CELLS INFECTED WITH HIV.

**Michèle Boccoz**
@MBoccoz – Nov. 13

**130th anniversary of the Institut Pasteur. Outstanding work for research, public health and education in Paris and the Institut Pasteur International Network. #institutpasteur #pasteurnetwork**

**Frédérique Vidal**
@VidalFrederique – Nov. 13

**Delighted to be part of the @institutpasteur 130th anniversary ceremony this evening. A visionary institute which has followed in the footsteps of its founder and stands at the forefront of technology, embracing experimental approaches and tackling the challenges facing public health. #Pasteur130Years**



## THE KAVLI PRIZE FOR CHRISTINE PETIT

Christine Petit, Professor at the Institut Pasteur and the Collège de France, won the 2018 Kavli Prize for Neuroscience from the Norwegian Academy of Science and Letters, for her pioneering work on the molecular and neural mechanisms of hearing. She was the first to decode the molecular physiology of the auditory system, based on the identification of genes responsible for early forms of deafness in humans.

## CANCER UNDER PRESSURE

Scientists from the Institut Pasteur and Inserm used *in vivo* video techniques and cell-specific staining to visualize the action of immune cells in response to the proliferation of cancer cells. These findings shed light on how the immune system acts when faced with tumor cells and how it exerts pressure on the genetic diversity of cancer cells.

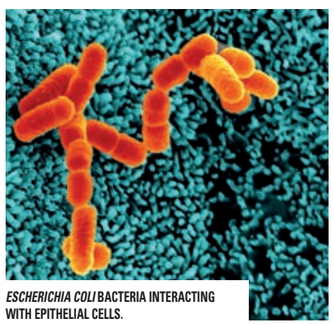

OMICS BUILDING.

## Omics – biology in the digital age at the Institut Pasteur

On September 13, 2018, the Institut Pasteur inaugurated its Omics buildings, designed to explore the myriad of possibilities offered by the development of computational biology. These buildings house scientists from a wide range of disciplines together with state-of-the-art technologies *(see page 46)*.

## DENGUE AND ZIKA – A BREAKTHROUGH IN UNDERSTANDING THEIR INNATE IMMUNE RESPONSES

We know that the innate immune response is based on recognition of viral genomes by protein receptors. By investigating protein receptors during infection by the dengue and Zika viruses, scientists from the Institut Pasteur discovered that a precise region of the viral genome was recognized by a receptor known as RIG-I. This discovery paves the way for the future development of vaccines for these diseases.



***ESCHERICHIA COLI* BACTERIA INTERACTING WITH EPITHELIAL CELLS.**

## Multiscale structure of the *Escherichia coli* genome

Using a genomic approach, scientists from the Institut Pasteur analyzed various *Escherichia coli* genome structure levels. This bacterium is a major focus of research in biology. The findings are important for understanding bacterial chromosome metabolism.

# Review of the year 2018

## Chronic malnutrition in children

Chronic malnutrition, which is usually associated with an inflammation of the small intestine, affects one in every four children under the age of five. It is the leading cause of child mortality in low-income countries. The Afribiota project aims to advance understanding of the mechanisms of chronic malnutrition and improve treatment. An initial study revealed the existence of a microbial signature in the gut, characterized by the widespread presence of bacteria that are normally found in the nose and mouth. Afribiota is led by institutes in the Institut Pasteur International Network (Paris, Madagascar and Bangui), in collaboration with the University of British Columbia (UBC), Inserm and the Collège de France.

## Titan Krios™ – the world's most powerful microscope at the Institut Pasteur

On July 12, 2018, the Institut Pasteur unveiled a new electron microscope with extraordinary capabilities – the Titan Krios™. It can visualize viruses, cell components and even protein complexes in their environments with an unprecedented level of detail.




**Philippe Goujon**
@Philippe_Goujon – July 12

**We pride ourselves on having such an extraordinarily powerful tool to observe cells and get a closer look at life, in our district of Paris. Well done to the @institutpasteur, at the forefront of innovation for health. #TitanPasteur #Paris15**

## Demographic history in Africa and deleterious mutations for health

How did demographic changes associated with the Neolithic transition also influence the effectiveness of natural selection? By comparing genome diversity in over 300 individuals, scientists discovered that the reason pygmies did not suffer from excessive deleterious mutations was because of their genetic diversity and their admixture with the Bantu peoples.



## Titan Krios™ WHAT IS SEEING?

## Erik Orsenna

Institut Pasteur Ambassador

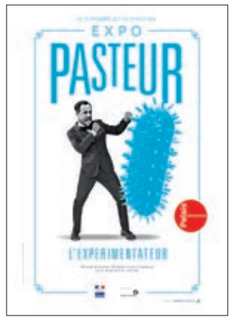
Now that Titan has brought fresh eyes to the Institut Pasteur – and what eyes, they are some of the most powerful in the world! – it is perhaps a good time to ask ourselves: "What is seeing?"
We can also turn the question around: do you see what I mean? You need to see to understand, as it is impossible to understand without seeing.
Saint Thomas once said "I only believe what I see", forgetting the mysteries without which there would be no faith.
Seeing with greater clarity to improve our understanding; improving our understanding to better care for those in need; showing with greater clarity to better teach and train – these are the three missions passed down to us by Louis Pasteur. And Titan's staggering capabilities will help us fulfill these missions. See, for example, the action of a drug through its eyes!
But what we see is just a small part as we only really see a speck of reality. This is why we need to multiply and cross check viewpoints. The first lesson from Pasteur is that life only reveals its secrets to a multidisciplinary team.
Seeing also fixes the image in time. All motion is lost and the picture is frozen. If we want to broaden our understanding, we need to move away from the comfort of visual evidence and venture into dizzying abstraction.
Remember the long journey to understand the night sky. Tycho Brahe learned to observe the sky like nobody before him and then Kepler came up with the first rules governing the movement of the planets. Based on all these observations, Newton came up with his law of universal gravitation.
But certain aberrant facts remain, aberrant because they do not fall within the scope of the laws. Think back to Le Verrier! He noticed that one planet – Uranus – followed an inexplicable path. There was only one explanation – the existence of another planet whose mass influenced Uranus's trajectory.
And not only did Le Verrier decide that this invisible planet existed but he also indicated where it could be found in the sky.
Shortly after, the astronomer Arago confirmed these two assumptions and came out with a wonderful sentence: "You found the new star (Neptune) at the end of your plume, that is to say at the end of your calculations."
In the same way, Pasteur rid us of rabies by fighting a virus that was invisible to him. Only electron microscopes would enable us to observe the virus thirty years after light was shed on its role in the terrible disease.
And take a look at art! It distances itself from the credible to reveal new aspects of the truth.
No being in this world, even amongst the most starved, is as thin as Giacometti's The Walking Man.
And yet this obvious "fake" portrays the human condition like nothing else.
Listen to the words of French writer Paul Valéry: "What should we be without the help of that which does not exist?" Reconsider Aragon and his definition of the novel "Le Mentir-Vrai", or true lying.
Seeing is an ongoing process – imagination needs to be everlasting and liberating!
And don't forget, the eye is not the only organ that allows us to see. Saint Exupery's "Little Prince" can see with his heart. Ask the scientists at the Natural History Museum. To find their way around the (often murky) waters, crocodiles see with... their skin. They have sensors all over their bodies.
Listen to Le Nôtre, gardener to Louis XIV of France: "The eye creates perspective, but walking makes it live."
But Rimbaud is without a doubt the greatest master of them all! At just 17 he showed us the way, how to become "a visionary through a long, boundless, and systematized disorganization of all the senses". And this is what I wish for you.

> Titan's staggering capabilities will help us fulfill the missions assigned to us by Louis Pasteur.

# Review of the year 2018

## 180,000

The number of people who visited the "Pasteur, the experimenter" exhibition at the Palais de la découverte. This high attendance rate shows the public's continuing interest in Louis Pasteur and the institute he founded.





**Emmanuel Macron**
@EmmanuelMacron – Dec. 13, 2017

**This exhibition tells the story of one of France's major figures; it showcases a series of scientific revolutions, a moment in time. The "Pasteur, the experimenter" exhibition is a wonderful example of how we can make science accessible.**

## 20

**The number of service and research units housing technological platforms on the Institut Pasteur Paris campus**

## SMOKING CESSATION – A GENETIC MUTATION INVOLVED IN RELAPSE

Nicotine dependence, a chronic condition with a high rate of relapse, is the leading preventable cause of death in developed countries. Seven million people die from tobacco use every year worldwide. A study conducted by Institut Pasteur scientists assessed the impact of this mutation on various stages of nicotine dependence with a greater degree of accuracy.

## Dengue – investigating antibodies to identify at-risk individuals

Using an original mathematical and statistical analysis method, a team of scientists from the Institut Pasteur partnered with researchers from the United States and Thailand to analyze a Thai cohort and obtain new information that should help identify individuals at risk of infection.

## INSECT VECTORS – A MOSQUITO CAPABLE OF LIMITING VIRAL INFECTION

There are over a hundred mosquito-borne diseases, including dengue – which affects over 50 million people each year – and chikungunya. Scientists at the Institut Pasteur have developed a mosquito that can recognize the dengue and chikungunya viruses and limit viral infection. This paves the way for an alternative arbovirus control strategy based on genetically modified mosquito vectors.



## ZIKA – THE NEUROLOGICAL RISKS IN UNBORN CHILDREN

Thanks to a study conducted on pregnant women and their unborn children during the Zika outbreak across the French territories in the Americas, scientists from Inserm, the Institut Pasteur and Guadeloupe University Hospital were able to accurately estimate the risk of serious neurological complications for babies.

## 68

**nationalities on the Institut Pasteur Paris campus**

## THE ALBERT EINSTEIN AWARD FOR JEAN-PIERRE CHANGEUX

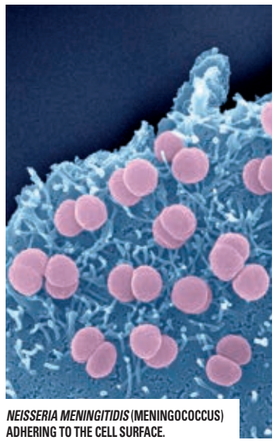
The 2018 Albert Einstein World Award of Science went to Professor Jean-Pierre Changeux, Emeritus Professor of Neuroscience at the Institut Pasteur. The prize was awarded in recognition of his outstanding work in the field of neuroscience and especially his pioneering contributions to science and the understanding of neuroreceptors over the past 50 years.

## LIVER CANCER – THE CELLULAR ENVIRONMENT PLAYS A ROLE IN TUMOR GROWTH

Liver cancer is the second leading cause of cancer death worldwide. A team of scientists from the Institut Pasteur, Inserm and the CNRS demonstrated that the cellular environment, with its dying liver cells, determines the path taken by tumor cells.

## Genes play a role in empathy

A new study led by scientists from the Institut Pasteur suggests that how empathic we are is not just a result of our upbringing and experience but is also partly influenced by genetic variations. This discovery helps us understand people such as those with autism who struggle to imagine another person's thoughts and feelings.



***NEISSERIA MENINGITIDIS*** **(MENINGOCOCCUS) ADHERING TO THE CELL SURFACE.**

## MENINGOCOCCAL MENINGITIS – STOMACH PAIN SHOULD BE SEEN AS A WARNING SIGN

Patients with meningococcal infection generally develop symptoms including a high temperature, vomiting and a stiff neck... but they might also just have a bad stomach ache. This can be so severe that they are sometimes wrongly operated for appendicitis. 10% of patients infected suffer from abdominal pain. This atypical form of the disease is becoming increasingly common and needs to be brought to the attention of physicians.

# Review of the year 2018

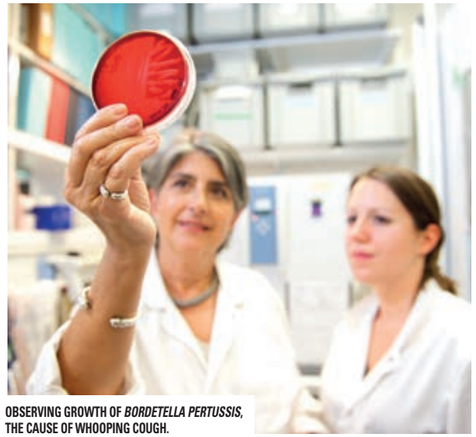
MODELING OF THE HEPATITS C VIRUS.

## HEPATITIS C – A NOVEL POINT-OF-CARE ASSAY

Scientists from the Institut Pasteur and Inserm, in collaboration with the company Genedrive, developed a rapid, reliable, point-of-care hepatitis C (HCV) assay.

## The resurgence of whooping cough

The resurgence of whooping cough is not due to recent changes in the epidemiology or biology of the bacterium but to several factors that have developed over time, according to an Institut Pasteur study.



OBSERVING GROWTH OF *BORDETELLA PERTUSSIS*, THE CAUSE OF WHOOPING COUGH.

## THE IMPACT OF GENETIC MUTATIONS ON NEURODEVELOPMENTAL DISORDERS

A recent study, co-led by Canadian and French scientists (including from the Institut Pasteur), presented a model that can predict the effect of a genetic variant on a person's cognitive traits and estimate the impact of genetic mutations on IQ.

## More than 6,000 antibiotic resistance genes discovered

Using a bioinformatics method for predicting gene function based on the 3D structure of the proteins encoded, European scientists analyzed a catalog of several million genes in the gut microbiota. This unique method enabled them to identify over 6,000 potential antibiotic resistance genes, with an average of more than 1,000 resistance genes per individual.



# 2019-2023 STRATEGIC PLAN
# THE INSTITUT PASTEUR'S AMBITION

On December 21, 2018 the Institut Pasteur adopted an ambitious yet realistic action plan for the next five years. The research activities carried out by the Institut Pasteur's 134 units stem from a wide range of interconnected fields including microbiology, immunology, genomics, structural and cell biology, developmental and stem cell biology, neuroscience, chemistry, the analysis of big biological data and clinical research. Research in these fields will be continued, since this forms the foundation of the Institut Pasteur's scientific work on molecules, cells and living organisms, microbes and their hosts, cancer, and its integrative vision of health and disease (individuals and populations).

The 2019-2023 Strategic Plan primarily focuses on **three priority scientific areas** that embody the Institut Pasteur's aim to increase its impact and assert its position of excellence in research for health worldwide:

- **emerging infectious diseases,**
- **antimicrobial resistance,**
- **brain connectivity and neurodegenerative diseases.**

In addition to these three priority areas, the Institut Pasteur will:

- launch a **concerted action for cancer,** a disease which the institute is actively engaged in combating through some 50 research projects,
- launch **a concerted action in vaccinology** to pool its strengths in this area *(see pages 53 and 57)*.

### EMERGING INFECTIOUS DISEASES

Infectious diseases claim 10 million lives each year. The Institut Pasteur aims to continue its longstanding tradition by investigating the disease mechanisms of pandemic and (re)emerging viruses, bacteria and parasites.
Research on insects and other vectors is also a priority area of study. Novel approaches, such as modeling and artificial intelligence, will be used to investigate and predict pathogen structure and function, establish diagnoses, identify therapeutic and immunological targets, and anticipate infection outcomes.

### ANTIMICROBIAL RESISTANCE

The fear of a post-antibiotic era, where common infections once again become life threatening, has raised concerns. The Institut Pasteur will intensify research programs on antimicrobial resistance, particularly by incorporating clinical and field data within molecular, genetic and physiological approaches. This will involve understanding the emergence of resistance, investigating the molecular mechanisms governing microbial growth, and identifying new drugs and therapeutic strategies in response to antimicrobial resistance.


### BRAIN CONNECTIVITY AND NEURODEGENERATIVE DISEASES

The complexity of brain function and the aging population are major challenges for 21st century biomedical research. The Institut Pasteur will use its basic research expertise in neuroscience, genetics, cell and developmental biology, immunology, microbiology and infection biology to address these challenges. Projects will focus on sensory deficits (deafness), neurodevelopmental disorders (autism) and psychiatric disorders (mood disorders and addiction), neurodegenerative diseases (Alzheimer's and Parkinson's diseases) and other neurological conditions (sepsis and neurovascular disorders).

# Awards and appointments in 2018

## PEOPLE APPOINTED TO THE RANK OF PROFESSOR

**1/ Anna-Bella Failloux-Manuellan**
Head of the Arboviruses and Insect Vectors Unit

## APPOINTMENTS

**2/ Laure Bally-Cuif**
Head of the Zebrafish Neurogenetics Unit
**Elected member of Academia Europaea**

**3/ Margaret Buckingham**
Honorary Professor at the Institut Pasteur
**Recipient of the French Legion of Honor (promoted to the rank of Commander)**

**4/ Arnaud Fontanet**
Head of the Epidemiology of Emerging Diseases Unit
**Collège de France annual Chair in Public Health**

**5/ Brigitte Gicquel**
Honorary Professor at the Institut Pasteur
**Elected member of Academia Europaea**

**6/ Isabelle Martin-Verstraete**
Pathogenesis of Bacterial Anaerobes Laboratory
**Elected member of the Institut universitaire de France**

**7/ Annick Perrot**
Honorary curator of the Pasteur Museum
**Recipient of the French Legion of Honor (promoted to the rank of Knight)**

**8/ David Prangishvili**
Molecular Biology of the Gene in Extremophiles Unit
**Elected member of Academia Europaea**

## HONORS AND PRIZES

**9/ Laure Bally-Cuif**
Head of the Zebrafish Neurogenetics Unit
**François Jacob Award**

**10/ Anu Bashamboo**
Human Developmental Genetics Unit
**Jayle Award**

**11/ David Bikard**
Synthetic Biology five-year group
**EMBO Young Investigator Award**

**12/ Carmen Buchrieser**
Head of the Biology of Intracellular Bacteria Unit
**Mémain-Pelletier Award**

**13/ Simon Cauchemez**
Head of the Mathematical Modeling of Infectious Diseases Unit
**Thérèse Lebrasseur Award**

**14/ Jean-Pierre Changeux**
Honorary Professor at the Collège de France and the Institut Pasteur
**Albert Einstein World Award of Science**
**Goldman-Rakic Prize**

**15/ Pierre-Jean Corringer**
Head of the Channel Receptors Unit
**CNRS Silver Medal**

**16/ Pascale Cossart**
Professor at the Institut Pasteur, Permanent Secretary of the French Academy of Sciences
**FEMS-Lwoff Award**
**Heinrich Wieland Prize**
**René & Andrée Duquesne Award**

**17/ Camille Danne**
Biology of Gram-Positive Pathogens Unit
**Jacques Monod Prize**

**18/ Anne Dejean**
Head of the Nuclear Organization and Oncogenesis Unit
**Sjöberg Prize**

**19/ Jost Enninga**
Head of the Dynamics of Host-Pathogen Interactions Unit
**Pasteur Vallery-Radot Prize**

**20/ Arnaud Échard**
Head of the Membrane Traffic and Cell Division Unit
**Gustave Roussy Award**

**21/ Pedro Escoll Guerrero**
Biology of Intracellular Bacteria Unit
**Jacques Monod Prize**

**22/ Louis Lambrechts**
Head of the Insect-Virus Interactions Unit
**CNRS Bronze Medal**

**23/ Jean-Paul Latgé**
Professor at the Institut Pasteur
**Georges Zermati Prize**

**24/ Romain Levayer**
Head of the Cell Death and Epithelial Homeostasis five-year group
**SBCF Young Researcher Award**

**25/ Sigolène Meilhac**
Head of the Heart Morphogenesis five-year group
**Pasteur Vallery-Radot Prize**

**26/ Nadia Naffakh**
Molecular Genetics of RNA Viruses Unit
**Georges, Jacques and Elias Canetti Prize**

**27/ Lucie Peduto**
Head of the Stroma, Inflammation and Tissue Repair Unit
**François Jacob Award**

**28/ Christine Petit**
Head of the Genetics and Physiology of Hearing Unit
**ARO (Association for Research in Otolaryngology) Award of Merit**
**Kavli Prize**

**29/ Hélène Quach**
Human Evolutionary Genetics Unit
**CNRS Crystal Medal**

**30/ Félix Rey**
Head of the Structural Virology Unit
**Lucien Tartois Prize from the French Foundation for Medical Research (FRM)**

**31/ Gerald Spaeth**
Head of the Molecular Parasitology and Signaling Unit
**Georges Zermati Prize**

**32/ Sven van Teeffelen**
Head of the Microbial Morphogenesis and Growth five-year group
**EMBO Young Investigator Award**

**33/ François-Xavier Weill**
Head of the Enteric Bacterial Pathogens Unit
**Eloi Collery Prize from the French National Academy of Medicine**

**34/ Chiara Zurzolo**
Head of the Membrane Traffic and Pathogenesis Unit
**Radcliffe Fellow, Harvard University**

## ERC GRANTS

**35/ Anne Dejean**
Head of the Nuclear Organization and Oncogenesis Unit
**ERC Advanced Grant: project SUMiDENTITY (Deconstructing the role of SUMO on chromatin in cell identity and tissue repair), led by Inserm**

**36/ Henrik Salje**
Mathematical Modeling of Infectious Diseases Unit
**ERC Starting Grant: project ARBODYNAMIC (Coupling dynamic population immunity profiles and host behaviours to arboviral spread)**

## IP 130TH ANNIVERSARY YOUNG SCIENTIST PRIZE

**37/ Claire Berthault**
Lymphopoiesis Unit

**38/ Gonzalo Moratorio**
Viral Populations and Pathogenesis Unit

## NEW UNITS

**39/ Paola Arimondo**
Epigenetic Chemical Biology (Structural Biology and Chemistry Department)

**40/ Frédéric Barras**
Stress Adaptation and Metabolism in Enterobacteria (Microbiology Department)

**41/ Simonetta Gribaldo**
Evolutionary Biology of the Microbial Cell (Microbiology Department)

## NEW FIVE-YEAR GROUPS (G5s)

**42/ Étienne Simon-Lorière**
Evolutionary genomics of RNA viruses (Virology Department)

**43/ Timothy Wai**
Mitochondrial Biology (Cell Biology and Infection Department)

## NEW TECHNOLOGICAL PLATFORMS

**44/ Iñaki Guijarro**
Biological NMR (C2RT, Structural Biology and Chemistry Department)

**45/ Matthijn Vos**
Nanoimaging (C2RT, Structural Biology and Chemistry Department)

# Research

**The Institut Pasteur is committed to conducting outstanding research to benefit human health the world over. Its ongoing ambition is to give fresh impetus to basic research and to increase the impact of this research on health issues.**

*"With its 130 years of history, ten Nobel Prize winners and world-renowned expertise, the Institut Pasteur perfectly exemplifies the excellence of French research. Its primary mission is to tackle diseases. This involves both research in its purest form and applications for public health and new therapies. Every aspect of the Institut Pasteur's work stands to gain from the state-of-the-art Titan cryo-electron microscope newly installed this year. Biology is undergoing a new revolution. It's by going back to the roots of knowledge, as the Institut Pasteur does so well, that major breakthroughs are made in human health. Drawing on its illustrious past, the Institut Pasteur will leverage all these developments to pave the way for tomorrow's medicine."*

**FRÉDÉRIQUE VIDAL,**
French Minister of Higher Education, Research and Innovation
**Inauguration of the Titan microscope at the Institut Pasteur on July 12, 2018**

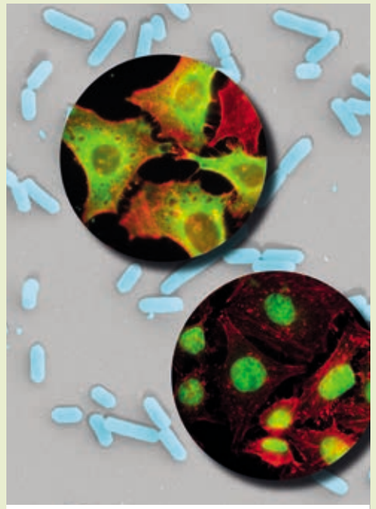
SEGMENTED FILAMENTOUS BACTERIA (SFB) VIEWED BY SCANNING ELECTRON MICROSCOPY.

# Department of **Cell Biology and Infection**

**The Cell Biology and Infection Department (BCI) develops an integrated understanding of the cell, the fundamental unit of life, in physiological conditions, during infection and in other cellular-based pathologies such as cancer and neurodegenerative diseases. Its research programs are highly interdisciplinary; they use and develop quantitative tools and innovative techniques to improve understanding of the molecular mechanisms at work in cells. The department fosters strong links with quantitative disciplines, such as mathematics and physics. BCI teams develop new cellular, tissue and animal models for studying infections and other diseases. The department is led by Chiara Zurzolo.**

## A MOLECULAR UNDERSTANDING OF HOST CHROMOSOME SUBVERSION BY *LISTERIA MONOCYTOGENES*

During infection, bacterial pathogens such as *Listeria monocytogenes* can hijack host signaling to promote their own growth and virulence. The Chromatin and Infection Unit, headed by Mélanie Hamon, studies how bacteria elicit long-lasting epigenetic modifications in the host to alter their response to the invading pathogens. Using proteomic and molecular biology methods, the group, in collaboration with Pascale Cossart, uncovered how *Listeria* hijacks an important host enzyme called SIRT2. They showed that infection modifies a residue of SIRT2, leading to its dephosphorylation. This modification alters the biology of SIRT2, enabling it to interact with host chromatin. There, it modifies histone H3 at lysine 18, leading to the repression of a specific host gene, and to the promotion of *Listeria* infection. By learning more about these takeover mechanisms we can uncover new cell signaling mechanisms and better understand how pathogens disrupt the biology of their host.



MONTAGE OF IMMUNOFLUORESCENT CELLS MARKED FOR SIRT2 AND SCANNING ELECTRON MICROSCOPY OF *L. MONOCYTOGENES*.

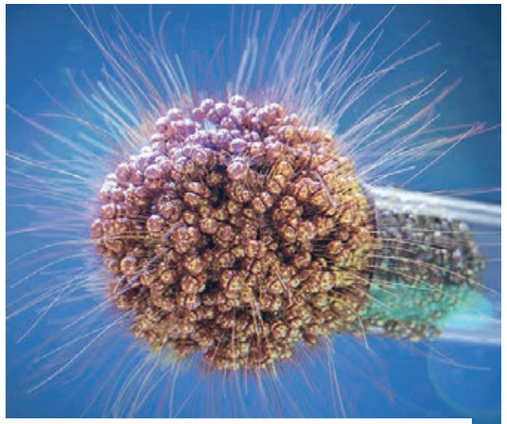
*Source: Pereira et al.,* Cell Rep. *2018 Apr 24;23(4):1124-1137.*



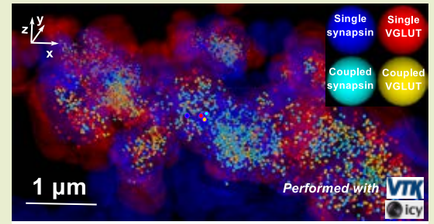
## BACTERIAL AGGREGATES OF *NEISSERIA MENINGITIDIS* FORM A THICK HONEY-LIKE LIQUID THAT FLOWS INSIDE BLOOD VESSELS

During human meningococcal infections, bacteria accumulate and finally fill up blood vessels, causing severe diseases such as septicemia and meningitis. However, the mechanisms governing formation of bacterial aggregates and their impact on infection have remained elusive. A multidisciplinary study by Daria Bonazzi, on Guillaume Dumenil's team, the Pathogenesis of Vascular Infections Unit, has unravelled that aggregates of *Neisseria meningitidis* behave like a viscous liquid similar to honey. This is due to type-IV pili, long adhesive filaments which are constantly extending and retracting at the bacterial surface. By these means, bacteria can find each other and come into contact transiently. Aggregation is therefore based on an intermittent process of attraction between bacteria, and gives rise to a new type of active material. Importantly, the unique physical properties of meningococcal aggregates allow them to gradually adapt to the complex geometry of the vascular network. As a consequence, these physical properties are essential for the progression of infection.

*Source: Bonazzi et al.,* Cell., *2018 Jun 28;174(1):143-155.e16.*



***NEISSERIA MENINGITIDIS*** WITH TYPE-IV PILI, LONG ADHESIVE FILAMENTS WHICH CONTINUALLY EXTEND AND RETRACT AT THE BACTERIAL SURFACE.




STATISTICAL MAPPING LOCALIZATION OF SINGLE (DARK BLUE) AND COUPLED (LIGHT BLUE) SYNAPSIN AS WELL AS SINGLE (RED) AND COUPLED (YELLOW) VGLUT.

## SODA, A NEW STATISTICAL ANALYSIS TOOL FOR FLUORESCENCE IMAGING

SODA (Statistical Object Distance Analysis) is a new method developed in the Biological Image Analysis Unit headed by Jean Christophe Olivo-Marin that allows statistical image analysis, identification of statistically coupled molecules and spatial mapping of coupled or isolated molecules. This program is applicable to all fluorescence images, and can be used either for conventional imaging or for super-resolution imaging (SIM, STED or STORM). Coupled with STORM 3D technology, SODA has provided unprecedented information on the organization of proteins at the synapse of hippocampal neurons and determined the relationships between thousands of locations of single molecules within synaptic buttons. In order to facilitate its dissemination within the scientific community and the reproducibility of the results, SODA is available free of charge on the Icy platform (www.bioimageanalysis.org).

Source: *Lagache et al.,* Nat Commun. 2018 Feb 15;9(1):698.

## AWARDS

**Pascale Cossart**
International FEMS Lwoff Award, Heinrich Wieland Prize, René & Andrée Duquesne Award

**Chiara Zurzolo**
Radcliffe Fellow, Harvard University

**Jost Enninga**
Pasteur Vallery-Radot Prize

**Arnaud Echard**
Gustave Roussy Award

ZEBRAFISH BREEDING IN THE DEPARTMENT.

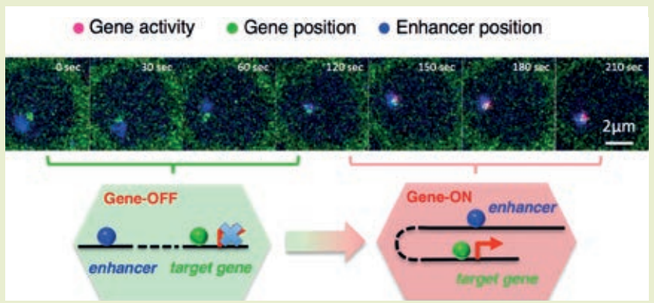
# Department of **Developmental and Stem Cell Biology**

**The Department of Developmental and Stem Cell Biology covers a broad spectrum of research, ranging from individual cells to whole organisms and from embryos to adults. How do cells acquire their identity, and how are organs formed? The department's work in the field of developmental biology has given rise to research on stem cells and their potential role in tissue regeneration. The department is led by François Schweisguth.**

## SEEING HOW TWO DISTANT DNA PIECES KISS TO ACTIVATE A GENE

A long-standing question in metazoan gene regulation is how remote enhancers communicate with their target promoters over long distances. Combining genome editing and quantitative live imaging, scientists in the Physics of Biological Function Unit (Institut Pasteur/CNRS) and the Physics Department at Princeton University (USA), have achieved the simultaneous visualization of physical enhancer-promoter communication and transcription in *Drosophila* embryos. They show that enhancers activate transcription of a reporter gene over a distance of 150 kb only after one of them (the activating enhancer) comes into close proximity with its regulatory target, and upon dissociation transcription ceases almost immediately. The team observed distinct topological architectures of the multi-enhancer gene locus, depending on the spatial identity of the activating enhancer, providing new insights into the folding and order of DNA inside the cell nucleus. Overall, the work demonstrated that sustained physical proximity and enhancer-promoter engagement is required for enhancer action; it provides a path to probe chromatin topology and the implications of long-range regulation on cellular fates in living embryos.

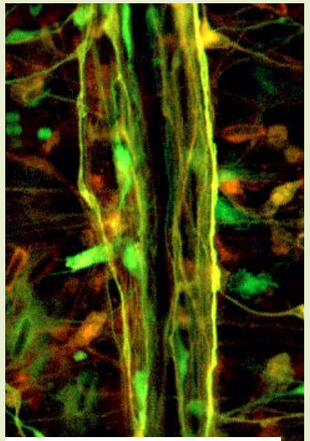
*Source: Chen et al.*, Nature Genetics, *August 2018.*




## THE FIRST SINGLE CELL TRANSCRIPTOMIC ATLAS FOR THE SEA ANEMONE

Development is the process by which an organism's full genomic potential becomes partitioned into the individual genetic programs which ultimately give rise to distinct cellular phenotypes and functions. Historically, our ability to catalogue cell types and construct the underlying genetic programs which define these cell types has been limited, particularly in non-model organisms, by a lack of resolution. Recently, an effort has been led by Heather Marlow in the unit of François Spitz (Genomics and Epigenomics of Animal Development) and the Technological Resources and Research Center of the Institut Pasteur, in collaboration with Amos Tanay's lab at the Weizmann Institute in Rehovot, Israel. They established a single-cell sequencing pipeline at the Institut Pasteur. Utilizing this technology, the researchers generated the first single cell transcriptomic atlas for the sea anemone *Nematostella vectensis*, an emerging systems biology model for gene regulation. This work identified more than one hundred distinct cell states in the sea anemone and tied these states to their defining genetic programs through the use of open chromatin analysis. In particular, the researchers uncovered an astounding diversity of neural cell types in the anemone, each with a highly-specific transcriptomic signature. The researchers were able to use this information to generate new transgenic reporter lines in an effort to rapidly advance the ability of the field to functionally characterize these newly described neural cell types. The approach employed in this study will rapidly improve phenotyping techniques in the sea anemone and other laboratory models and will also expand our ability to efficiently characterize environmental samples.

*Source: Sebé-Pedrós A. et al.*, Cell, *May 31, 2018.*

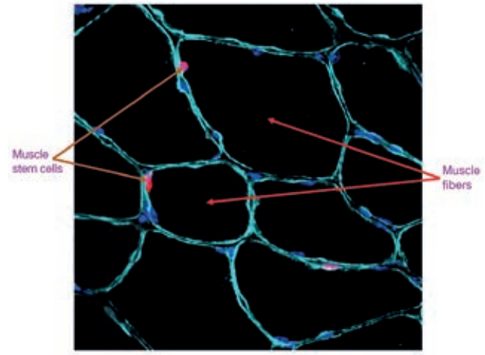


A PHOTO-CONVERTIBLE CELL-TYPE SPECIFIC DRIVER IN SEA ANEMONE NEURONS GENERATED FROM THIS STUDY.

## REGULATION OF SKELETAL MUSCLE STEM CELLS IN THEIR NICHE

Stem cells play critical roles during growth, regeneration and aging. Although they can self-renew and give rise to differentiating daughter cells, how this is achieved remains largely unexplored. The microenvironment (niche) is an essential regulator of stem cell behavior and it can be of cellular and non-cellular nature. Notch signaling acts as a potent regulator of muscle stem cell quiescence, where disruption of this pathway results in depletion of the stem cell pool. In a collaborative study, Shahragim Tajbakhsh's lab (the Stem Cells and Development Unit) showed that Notch signaling induces production of extracellular collagens in muscle stem cells (MuSCs). Notably, Notch-induced Collagen V was found to act as a surrogate ligand and bind the Calcitonin receptor (CALCR), which is a G-protein coupled receptor important for the maintenance of MuSCs. This work shows that an extracellular matrix protein secreted by the stem cells plays the unusual role of acting as a signaling molecule to prevent the depletion of the stem cell population.

*Source: Baghdadi MB et al.*, Nature, *May 23, 2018.*

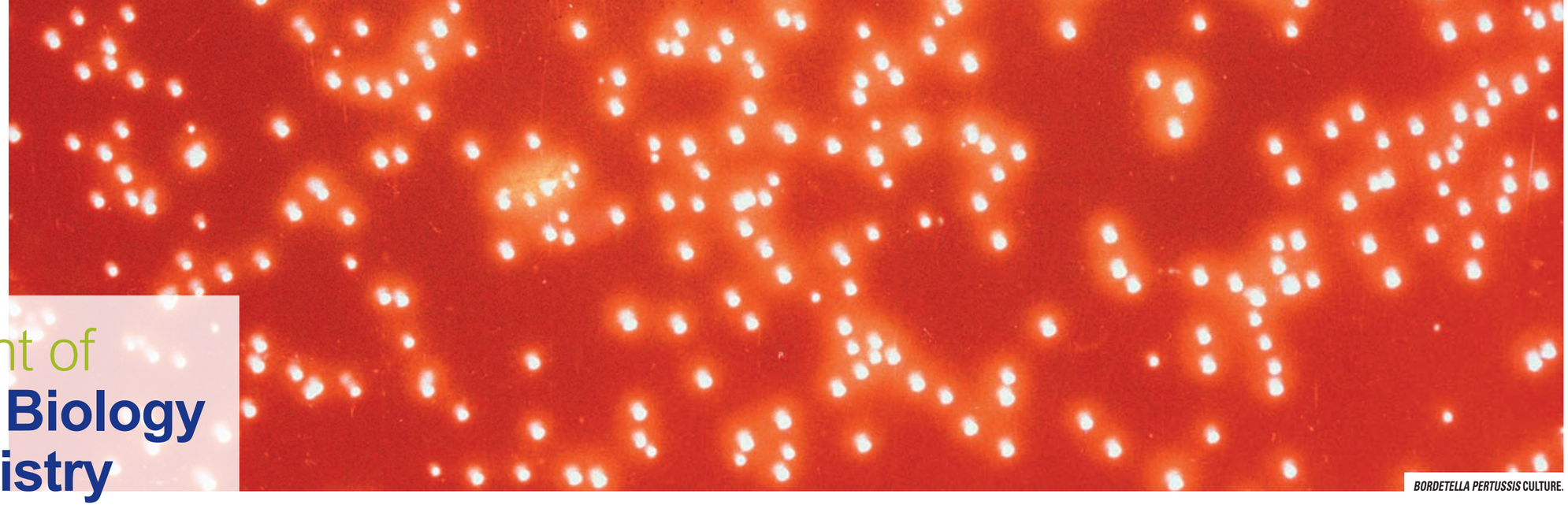



## AWARDS

**Laure Bally-Cuif**
2018 François Jacob Award and elected member of Academia Europaea

**Romain Levayer**
SBCF Young Researcher Award

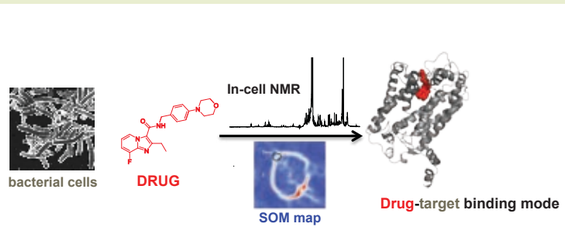
**Sigolène Meilhac**
Pasteur Vallery-Radot Prize



*BORDETELLA PERTUSSIS* CULTURE.

# Department of **Structural Biology and Chemistry**

**The structure of a molecule is intricately linked to its function. The units in the Department of Structural Biology and Chemistry focus their research on the three-dimensional organization, properties and synthesis of molecules of biological interest, especially those that play a role in human disease. This research reveals vital information for the development of new therapeutic, diagnostic and vaccine strategies. The department is led by Michael Nilges.**




## DETAILED INFORMATION OF DRUG-TARGET INTERACTIONS IN THE WHOLE CELL

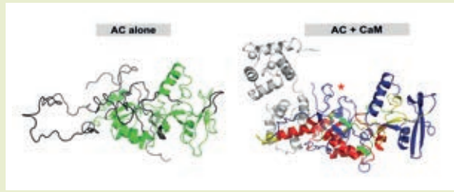
Detailed structural information on drug-target interactions is crucial for drug discovery and rational hit to lead optimization. We developed a new approach combining NMR in whole cells (*in-cell* NMR) and *in silico* docking to characterize these interactions at the atomic level. We used this method to decipher the binding mode of promising antituberculosis drugs with their target, cytochrome bc1. The drugs had been identified by phenotypic screening by the Institut Pasteur of Korea, and their most advanced molecule (Q203) is currently in clinical trials. By using in-cell NMR, we studied drug interactions with living bacterial cells, and identified the atoms involved in this interaction, basis for further development of the drug. This study is the first example worldwide of an application of in-cell NMR in the context of drug discovery. Our approach constitutes a pipeline to obtain atomic information on hit-target interactions in the cellular context.

*Source: Bouvier G, et al.,* Biochemistry, *2019 Feb 12;58(6):526-533.*

## MECHANISM OF ACTIVATION OF A MAJOR TOXIN INVOLVED IN WHOOPING COUGH

The CyaA toxin contributes to the early stages of bacterial colonization of the lungs in people infected by *B. pertussis,* the causative agent of whooping cough. This disease is particularly severe and potentially fatal for infants and vulnerable individuals. CyaA is activated by calmodulin binding in target cells and produces cAMP, which impairs the physiology of immune system cells, and give bacteria free rein to colonize the lung. Based on an integrative structural biology approach, a CyaA activation mechanism is proposed. A disordered region of 75 amino acids in the catalytic domain has been identified and serves as bait to capture calmodulin – a molecular piracy act. Calmodulin binding induces folding in this disordered region, a prerequisite for CyaA activation. This mechanism, which combines structural folding and enzyme activation of CyaA, is vital both to prevent its toxicity within the bacteria that produce it and also to activate CyaA once in the cytosol of target cells.

*Source: O'Brien DP, et al.,* PLOS Biology, *December 29, 2017.*




## A NEW STRUCTURE OF A BACTERIAL PENTAMERIC ION CHANNEL WITH SIMILARITIES TO THE HUMAN SEROTONIN RECEPTOR

Pentameric ligand-gated ion channels (pLGICs) constitute a widespread class of ion channels, present in archaea, bacteria, and eukaryotes, involved in cell-cell communications. Upon binding of their agonist in the extracellular domain, the transmembrane pore opens, allowing ions to go through via a gating mechanism that can be modulated by a number of drugs. Here we describe a gammaproteobacterial pLGIC from an endo-symbiont of *Tevnia jerichonana* (sTeLIC) and its crystal structure at 2.3 Å in an active conformation, where the pore is found to be open to a wider degree. In addition, two charged restriction rings are present in the vestibule. Functional characterization shows sTeLIC to be a cationic channel activated at alkaline pH. Additionally, we found that sTeLIC is allosterically potentiated by derivatives of aromatic amino acids such as Phe and Trp, as well as 4-bromo-cinnamate, whose cocrystal structure reveals a vestibular binding site. This site is equivalent to the one already described for benzodiazepines in *Erwinia chrysanthemi* pLGIC and is also present (and druggable) in the human 5HT3 (serotonin)-receptor.

*Source: Hu H, et al.,* Proc Natl Acad Sci, *USA, 2018 Apr 24;115(17):E3959-E3968.*

DNA SEQUENCING.

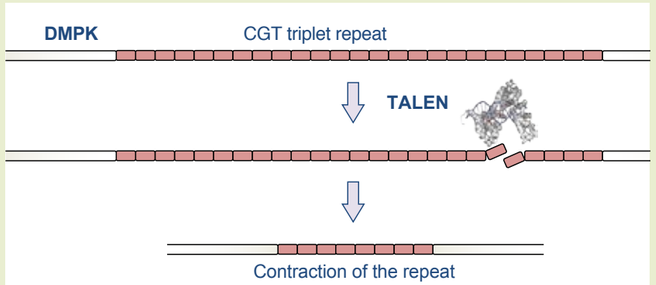
# Department of
# Genomes and Genetics

**Scientists in the Genomes and Genetics Department use experimental and informatics approaches to explore the nature of genetic information in organisms of increasing complexity, from bacteria and yeasts to humans. They also investigate the evolution of infectious microbes and the selective pressures they have exerted on human genes over time.**
**The department is led by Didier Mazel.**

## STEINERT DISEASE: TALEN USED TO SHORTEN CTG TRIPLET REPEAT

Myotonic dystrophy type 1 (or Steinert disease) is a neurodegenerative syndrome caused by the expansion of a sequence of three bases – C, T and G – which are repeated at the end of the *DMPK* gene. Patients have a higher number of CTG triplets in their DNA. There is no remedy and all medical treatments have so far proven unsuccessful. The team led by Guy-Franck Richard is trying to develop an original gene therapy approach that directly targets this repetition, shortening it enough so that it is no longer pathological in humans. The scientists used a pair of "DNA scissors" (known as a TALEN) to cut the CTG triplet repeat so that it could be shortened. The relevant sequence from a patient with Steinert disease was inserted into the genome of baker's yeast. Introducing a TALEN into this transgenic yeast effectively shortened the repeat. Guy-Franck Richard's team demonstrated that this contraction involves an iterative process during which the two ends of the repeat are joined, while being shortened. Similar experiments are now being performed in human cells.

*Source: Mosbach V, et al.,* Cell Rep., *2018 Feb 20;22(8):2146-2159.*

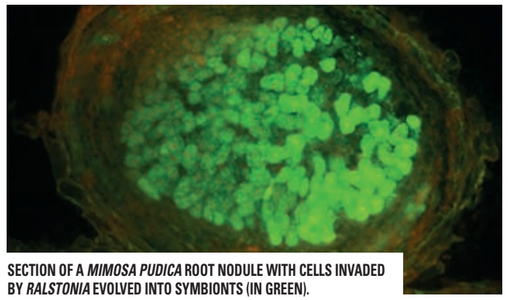



A TALEN IS USED TO INDUCE A DNA DOUBLE-STRAND BREAK WITHIN CTG TRIPLET REPEATS INVOLVED IN STEINERT DISEASE. BREAK REPAIR LEADS TO REPEAT SHORTENING.

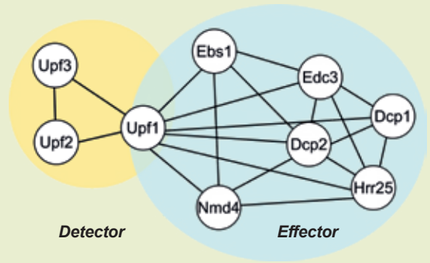
## UNDERSTANDING HOW BACTERIA EVOLVE IN THE LAB

In the natural world, it often takes millions of years for species to develop a successful symbiotic relationship in which they perform mutual services for each other. In collaboration with scientists from INRA, the Microbial Evolutionary Genomics Unit investigated rhizobia, bacteria that are capable of establishing nitrogen-fixing symbiosis with plants in the legume family. Rhizobia are responsible for a significant proportion of the nitrogen fixation which occurs on the planet, and they share this nitrogen with plant symbionts. In the laboratory, over a few years the scientists managed to evolve a bacterium in the soil so that it was capable of carrying out the first stages of symbiosis. They demonstrated the close parallels between this laboratory evolution and what occurred in nature millions of years ago, thereby highlighting the potential of experimental approaches to shed light on the natural evolutionary processes of complex functions. These approaches can now be used to produce symbionts for plant species naturally lacking in them, paving the way for improved agricultural productivity without the use of fertilizers and enhancing our understanding of bacteria-plant symbiosis.

*Source: Clerissi C, et al.,* Nat Commun., *2018 Jun 11;9(1):2264.*



SECTION OF A ***MIMOSA PUDICA*** ROOT NODULE WITH CELLS INVADED BY ***RALSTONIA*** EVOLVED INTO SYMBIONTS (IN GREEN).




LINKS IDENTIFIED BETWEEN YEAST PROTEINS INVOLVED IN RNA DEGRADATION.

## A MOLECULAR MECHANISM TO MONITOR RNA

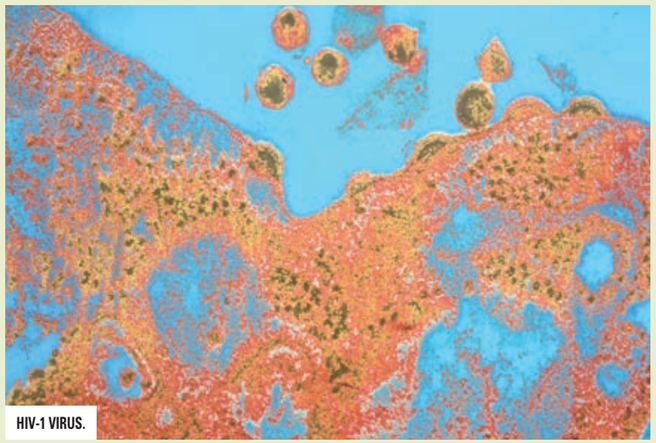
Baker's yeast, *Saccharomyces cerevisiae*, is a prime model organism for studying the molecular mechanisms acting on messenger RNA because it facilitates large-scale experimental strategies.
Given the considerable evolutionary distance between yeasts and humans, research on yeast can reveal vital aspects of some of the most conserved processes in living species. One of these processes is the translation of messenger RNA into proteins. RNA can only be translated if it is sufficiently stable over time – although its translation often leads, paradoxically, to its degradation.
To identify the molecular mechanisms involved in the stages from translation to degradation of messenger RNA, the Genetics of Macromolecular Interactions Unit combined mass spectrometry analysis of purified protein complexes with novel data analysis methods. The results obtained determined the basic building blocks of these mechanisms, giving rise to new theories about RNA degradation in yeast and humans.

*Source: Dehecq M, et al.,* EMBO J., *2018 Nov 2;37(21).*

ON THE RIGHT: F. JÖNSSON *(SEE BELOW)*.

# 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. Since the immune system was discovered, scientists at the Institut Pasteur have been captivated by its many facets. They share a determination to explore fundamental immunological processes with the aim of tracing the origins of disease, to inspire the development of new vaccines and to devise new therapeutic strategies. The department is led by Gérard Eberl.**



HIV-1 VIRUS.

## BLOCKING PATHOGENS WITH POLYREACTIVE ANTIBODIES

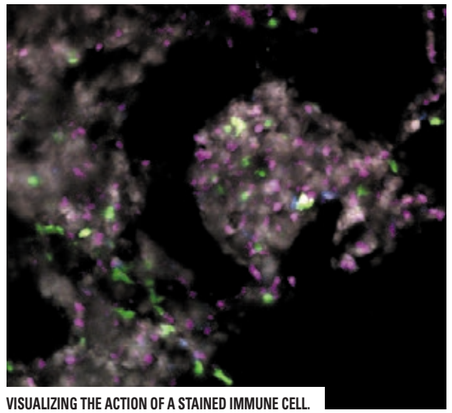
Human antibodies against pathogens often recognize molecules unrelated to the pathogens. The molecular origin and role of such promiscuous binding, termed polyreactivity, are unknown. In this study, the Humoral Immunity unit directed by Hugo Mouquet reports that broadly neutralizing antibodies (bNAbs) to the HIV-1 virus are frequently polyreactive, cross-reacting with non-HIV-1 molecules and self-antigens. In addition, compared to their non-polyreactive variants, polyreactive bNAbs exhibit an improved HIV-1 binding and neutralization capacity due to increased conformational flexibility. As a consequence, these bNAbs recognize a broader diversity of viral variants. These findings suggest that polyreactivity can be a trait of adaptable antibodies that display optimal pathogen recognition.

*Source: Pringent et al.*, Cell Reports, *May 2018.*

## PLATELETS ARE CRITICAL PLAYERS IN SEVERE ALLERGIC REACTIONS

Platelets are best-known for their capacity to rapidly form clots at sites of blood vessel injury, thereby restricting excessive blood loss and initiating wound repair. Recently, platelets have gained a lot of attention as immune cells that contribute to inflammation and host defense. Friederike Jönsson from the Antibodies in Therapy and Pathology Unit directed by Pierre Bruhns, in collaboration with the Établissement Français du Sang - Grand Est, has revealed that platelets can also play a role during anaphylaxis, a very severe form of allergic reaction. In the presence of antibody (IgG) aggregates, platelets that express human IgG receptors get activated and release large amounts of a vasoactive substance, serotonin. Serotonin alone can induce anaphylaxis symptoms. These observations suggest that platelets could also contribute to anaphylaxis in humans.

*Source: Beutier et al.*, Science Immunology, *April 2018.*



VISUALIZING THE ACTION OF A STAINED IMMUNE CELL.

## CANCER UNDER PRESSURE: VISUALIZING THE ACTION OF THE IMMUNE SYSTEM IN RESPONSE TO TUMOR DEVELOPMENT

As tumors develop, they evolve genetically. This process allows tumor cells to escape immunity, which complicates therapy. How does the immune system react? How does it exert pressure on the genetic diversity of cancer cells? The Dynamics of Immune Responses Unit directed by Philippe Bousso, in collaboration with the Genome Integrity, Immunity and Cancer Unit directed by Ludovic Deriano, used innovative imaging and a multicolor labeling system to visualize the action of immune cells in response to the proliferation of cancer cells. They demonstrate that spontaneous immune responses and immunotherapies can profoundly reduce tumor diversity and promote the emergence of more genetically homogeneous tumor cells. This research shows that taking into account interactions between immunotherapies and tumor heterogeneity could help optimize therapeutic strategies.

*Source: Milo et al.*, Science Immunology, *November 2018.*

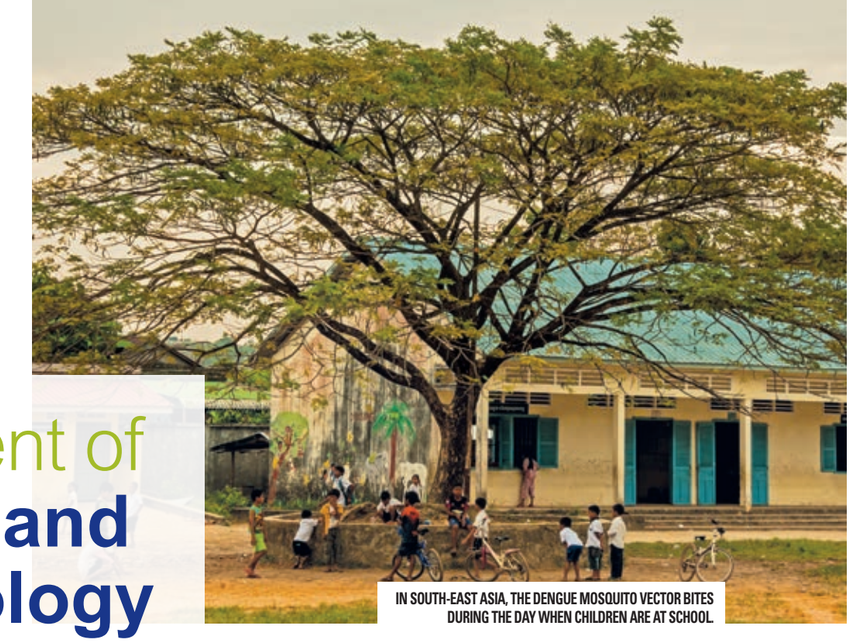
A MINIATURIZED DEVICE PERFORMING PCR THAT ENABLES THE NECESSARY SUCCESSION OF 40 REACTION CYCLES TO BE CARRIED OUT MORE QUICKLY THAN IN A CONVENTIONAL PLATFORM.

## A NEW BEDSIDE SCREENING TEST FOR THE HEPATITIS C VIRUS

A fast and reliable bedside screening test for the hepatitis C virus has been developed by Darragh Duffy's group in the Dendritic Cell Immunobiology Unit directed by Stanislas Pol. This new detection test, accessible to populations in countries with limited resources, will allow immediate diagnosis of the patient – achievable in one hour – and the immediate implementation of treatment against the disease. Chronic hepatitis C affects about 1% of the world's population (71 million people) and is responsible for 400,000 deaths per year, due to the severe progression of the disease to cirrhosis or liver cancer. Early detection is all the more important because most infected people do not know their status, while the most recent antivirals can cure disease in 95% of cases.

*Source: Llibre et al.*, Gut, *April 2018.*

# Department of **Infection and Epidemiology**



IN SOUTH-EAST ASIA, THE DENGUE MOSQUITO VECTOR BITES DURING THE DAY WHEN CHILDREN ARE AT SCHOOL.

**The Infection and Epidemiology Department studies all aspects of emerging and re-emerging infectious diseases: reservoirs and transmission mechanisms of pathogens, virulence factors, pathophysiological processes of the host, the innate immune response and the role of vaccines. This work, which involves both basic and clinical research, draws on the expertise of National Reference Centers (CNRs), in collaboration with the Institut Pasteur International Network. The department is led by Professor Marie-Lise Gougeon.**

## ANTIBIOTIC RESISTANCE: A SURPRISING TIMELINE

Scientists in the Enteric Bacterial Pathogens Unit, led by François-Xavier Weill, retrospectively identified early cases of *Salmonella* resistance to ampicillin, a broad-spectrum antibiotic that is still widely used today. By analyzing the genomes of hundreds of historical samples of *Salmonella* kept in the National Reference Center collection, they demonstrated that approximately 4% of these strains had genes encoding resistance to ampicillin. The oldest strains dated from 1959 and 1960, several years before ampicillin was released on the market for human use. The scientists then demonstrated that ampicillin-resistance genes could be transferred between wild-type strains of *Salmonella* after exposure to relatively low levels of penicillin G, similar to the residual doses found in farms several decades ago. Their research suggests that low doses of penicillin G, routinely fed to livestock in North America and Europe in the 1950s to boost growth, may have encouraged bacteria resistant to this new antibiotic to evolve and spread to humans just a few years later.

*Source: Tran-Dien A et al.,* Lancet Infect Dis., *2018 Feb;18(2):207-214.*

SALMONELLA SPP.

## DENGUE: IDENTIFICATION OF AT-RISK INDIVIDUALS FOR SEVERE DISEASE

The four serotypes of dengue virus co-circulate endemically throughout tropical regions. Infection can be asymptomatic, or in the severest forms cause hemorrhage which can be fatal. The presence of antibodies from infection due to one serotype seems to affect the severity of subsequent infections with another serotype; however, quantifying this risk has not previously been possible. Henrik Salje from the Mathematical Modeling of Infectious Diseases Unit analyzed a large cohort of Thai children exposed to dengue. This study identified a 'risk window', where individuals with antibody titers <1:80 (the detection threshold) had over seven times the risk of having a severe form of dengue if re-infected, compared to seronaive children or those with higher titers. The only current licensed dengue vaccine places previously naive individuals within this risk window, highlighting the need to know an individual's serostatus before deciding to vaccinate.

*Source: Salje H et al.,* Nature., *May 2018; 557(7707):719-723*

A FEMALE *AEDES AEGYPTI MOSQUITO* REARED AT THE VECTOPOLE OF THE INSTITUT PASTEUR DE LA GUYANE.

## CONGENITAL NEUROLOGICAL DEFECTS ASSOCIATED WITH THE ZIKA VIRUS

Previous research in French Polynesia by the teams led by Arnaud Fontanet and Simon Cauchemez suggested that babies born to mothers infected with the Zika virus during pregnancy could suffer from neurological defects, especially microcephaly (an unusually small head associated with delayed brain development). Following up on this research, Arnaud Fontanet's team, working in cooperation with Bruno Hoen, an Inserm scientist based in Guadeloupe, participated in the recruitment of a cohort of 546 pregnant women infected with the Zika virus during the 2016 outbreak in the West Indies and French Guiana, and estimated the risk of neurological damage in fetuses and babies depending on the trimester in which Zika was contracted. The risk was 7.0% overall but rose to 12.7% if the mother was infected during the first three months of pregnancy. The most serious damage (severe microcephaly) was also linked to infection during the first trimester of pregnancy.

*Source: Hoen et al.,* New Eng J Med, *2018 Mar; 15;378(11):985-994.*

## AWARDS

**François-Xavier Weill**
Eloi Collery Prize from the French National Academy of Medicine

**Henrik Salje**
ERC Starting Grant

**Arnaud Fontanet**
Collège de France annual Chair in Public Health

# Department of **Microbiology**

PHOTO REPORT IN THE *HELICOBACTER* PATHOGENESIS UNIT.

**The scientists of the Department of Microbiology study 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 improve our understanding of these microorganisms, and contribute to the development of new therapies or diagnostic tools to treat or prevent bacterial infections. The department is led by Hilde De Reuse.**

MOUSE COLON COLONIZATION BY THE BACTERIUM *STREPTOCOCCUS GALLOLYTICUS*.

## THE *STREPTOCOCCUS GALLOLYTICUS BACTERIUM* TAKES ADVANTAGE OF THE TUMORAL ENVIRONMENT TO ELIMINATE *ENTEROCOCCUS FAECALIS* FROM THE MURINE GUT MICROBIOTA

The colon harbors approximately $10^{13}$ bacteria, forming the gut microbiota, whose composition varies and influences the development of colorectal carcinoma (CRC). In humans, bacteria such as *Streptococcus gallolyticus* subsp. *gallolyticus (Sgg)* are found more frequently when colon tumors are present. Shaynoor Dramsi (Biology of Gram-Positive Pathogens) in collaboration with the team of Philippe Sansonetti (Molecular Microbial Pathogenesis) showed that the number of *Sgg* bacteria found in the colon of mice with tumors was increased 1000-fold with respect to that of healthy control mice, using the *Apc+/− Notch* genetic model. The authors showed that *Sgg* is able to secrete a specific bacteriocin, named gallocin, whose activity is enhanced under tumor conditions, enabling *Sgg* to kill resident enterococci in the murine colon. *Sgg* thus takes advantage of intestinal tumor conditions to eliminate and replace closely related bacteria in the colon. *Sgg* constitute a potential marker for CRC diagnosis.

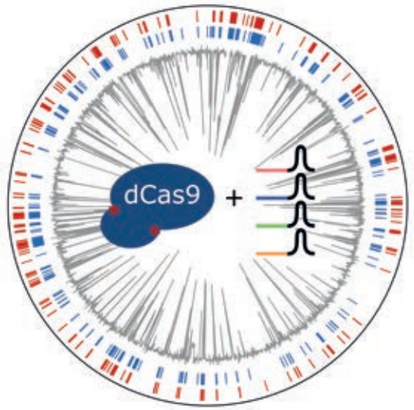
*Source: Aymeric L, et al.*, Proc Natl Acad Sci USA. *2018 Jan 9;115(2):E283-E291.*

## PROTEIN SPLICING IN BACTERIA

Amino acids are the fundamental building blocks of proteins and peptides. Expanding the genetic code beyond the 20 current amino acids is crucial in life science. Many natural products and bacterial-derived antibiotics are characterized by unusual amino acids. How do bacteria accomplish this? Using an innovative approach combining microbiology, omics and chemistry, a collaborative study between Muriel Gugger (Collection of Cyanobacteria) and Jörn Piel (ETH Zürich, Switzerland) has identified a novel bacterial strategy characterized by a post-translational protein-splicing modification to generate unusual amino acids in the protein backbone. This transformation was discovered in strains from the Institut Pasteur Culture collection of Cyanobacteria (PCC), but found to be more widely distributed in bacterial genomes. This work opens multiple avenues for applications in chemistry and biology.

*Source: Morinaka BI, et al.* Science. *2018 Feb 16;359(6377):779-782.*

CYANOBACTERIA OF THE INSTITUT PASTEUR CULTURE COLLECTION OF CYANOBACTERIA (PCC).




GENOME-WIDE DETECTION OF ESSENTIAL GENES IN *ESCHERICHIA COLI* WITH A CRISPR-DCAS9 SCREEN.

## PEEKING INSIDE BACTERIAL GENOMES WITH CRISPR-DCAS9

In recent years, the bacterial immune system known as CRISPR-Cas9 has been diverted to design powerful genetic modification tools. A variant of the Cas9 protein, known as dCas9, can be reprogrammed to specifically attach to a DNA sequence without introducing a modification. This attachment blocks the expression of genes, and it is thus possible to silence any gene in a cell simply and efficiently. In this study, we programmed dCas9 to turn off all of the *Escherichia coli* genes one by one, which allows us to study the genetics of this bacterium in a systematic way and to better understand the role of certain genes essential for the growth of *E. coli*. This new technique could be extremely useful in particular to better understand the resistance of bacteria to antibiotics and find new strategies to combat it.

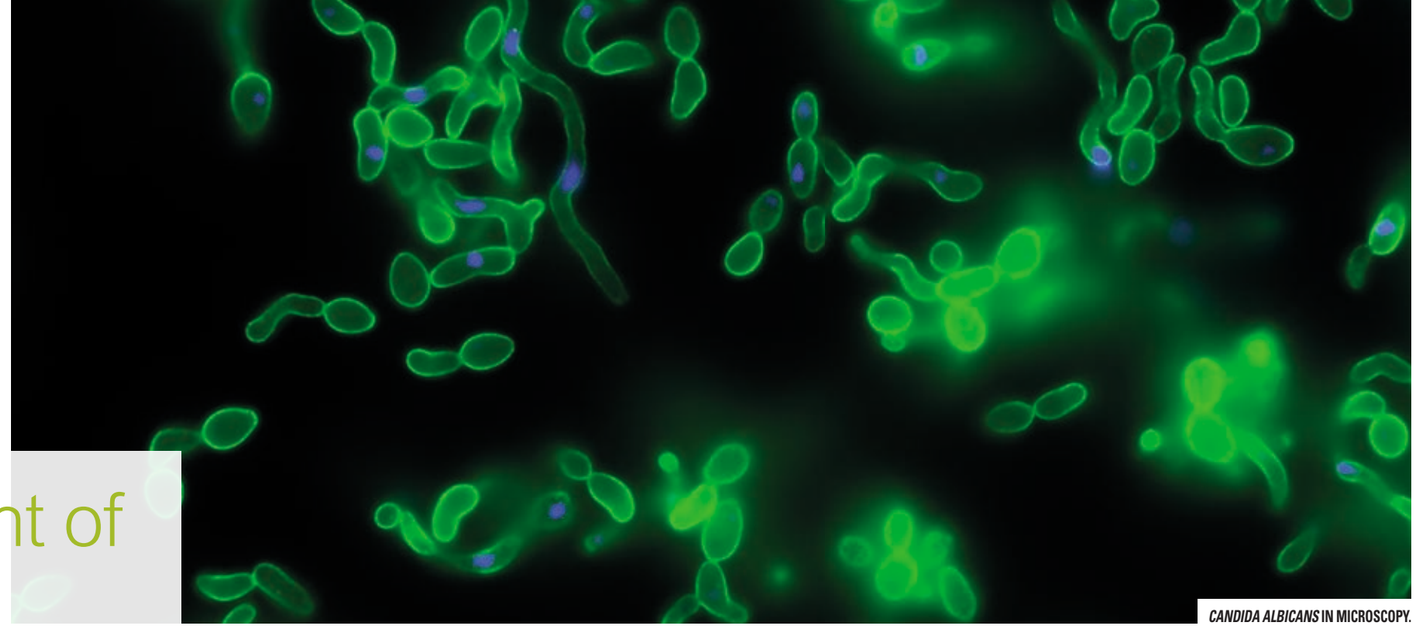
*Source: Rousset F, et al.*, PLoS Genet. *2018 Nov 7;14(11):e1007749.*

## AWARDS

**Sven van Teeffelen and David Bikard**
EMBO Young Investigator Award

**Simonetta Gribaldo**
Elected to Fellowship in the American Academy of Microbiology

**Isabelle Martin-Verstraete**
Elected member of the Institut universitaire de France



*CANDIDA ALBICANS* IN MICROSCOPY.

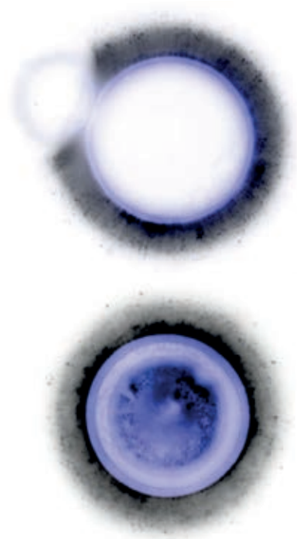
# Department of **Mycology**

**Over the last thirty years, fungal infections have become a major public health concern. The Department of Mycology focuses its research on the three main fungi responsible for invasive infections: *Aspergillus fumigatus*, *Candida albicans* and *Cryptococcus neoformans*. The aim is to shed light on the biology of these pathogenic fungi, identify their virulence mechanisms and develop new strategies for diagnosis, prevention and treatment. The department is led by Françoise Dromer.**

## TITAN CELL FORMATION IN *CRYPTOCOCCUS NEOFORMANS* ELUCIDATED

*Cryptococcus neoformans* is a yeast responsible for meningoencephalitis in patients with immune deficiencies. "Titan cells" in *C. neoformans* are giant (>100 µm) polyploid cells with a thickened cell wall. They are found in small quantities during infection, making them difficult to study. To shed light on the role played by titan cells in the pathobiology of cryptococcosis, scientists from the Molecular Mycology Unit developed and standardized experimental conditions enabling them to generate the cells *in vitro*. They demonstrated that the titan cells generated *in vitro* had the same characteristics as those obtained *in vivo*. This research was carried out in collaboration with four US teams investigating the biology of *C. neoformans*. Adopting a variety of approaches including genetic analysis of reference strains, genome analysis of various clinical strains and the use of series of knockout mutants for a gene of interest, the scientists discovered that the metabolic pathway, involving cyclic AMP and protein kinase A and its regulators, played a role in the formation of these cells. This research opens up significant prospects for investigating the cells' origins and their role in infection.

*Source: Hommel B et al.,* PLoS Pathog., *May 18, 2018.*

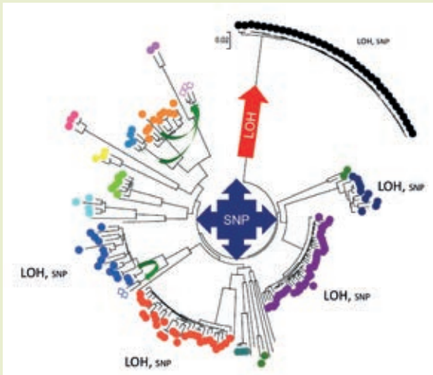


**STAINING OF THE CAPSULE AND WALL OF *CRYPTOCOCCUS NEOFORMANS* BUDDING (OR NON-BUDDING) TITAN CELLS USING ANTICAPSULAR IMMUNOFLUORESCENCE (GRAY) AND CELL WALL STAINING (BLUE).**

## HOMOLOGOUS DSDNA-DSDNA PAIRING AS A NEW SOURCE OF DNA SUPERCOILING IN THE CELL

Repetitive DNA plays an important role in the genome function in many eukaryotes, including humans. Previously, researchers used a fungal-specific phenomenon known as Repeat-Induced Point mutation (RIP) to reveal the existence of a cardinally new kind of a DNA homology recognition process, by which segments of chromosomal (repetitive) DNA are matched as arrays of interspersed base-pair triplets.
Importantly, homologous triplets were recognized efficiently for RIP only if they occurred with a periodicity of 11 or 12 base-pairs, corresponding to moderately unwound (negatively supercoiled) DNA double helices. In this new study researchers have developed a more formal approach to quantifying RIP, by which the propensity of a given base-pair to undergo mutation can be estimated. By applying this approach to a series of test constructs with closely-positioned repeat pairs, scientists now show that the propensity of the intervening DNA (situated between the two repeats) to mutate strongly depends on the repeat orientation (which could be either direct or inverted). Researchers speculate that such profound difference in RIP propensity can be explained by the differential distribution of DNA supercoiling that is generated by the physical pairing of closely-positioned repeats. This idea raises an intriguing possibility that homologous dsDNA-dsDNA pairing can represent a previously unappreciated way of modulating the levels of supercoiling in repeat-rich regions of eukaryotic genomes.

*Source: Mazur AK & Gladyshev E.,* Biophys J., *August 21, 2018.*

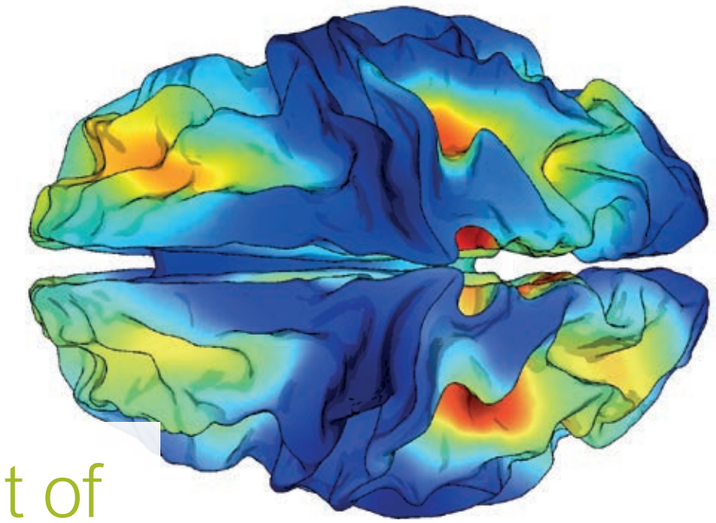



GENETIC TREE REPRESENTING THE DIVERSITY OF ANALYZED *CANDIDA ALBICANS* STRAINS.

## VARIOUS REPRODUCTIVE MECHANISMS REVEALED IN *CANDIDA ALBICANS* POPULATIONS

Understanding how pathogens emerge and spread involves analyzing the structure of their populations. Scientists in the Fungal Biology and Pathogenicity Unit, in collaboration with 12 other teams, sequenced and analyzed the genomes of 182 strains of *C. albicans* isolates, either commensal or responsible for superficial or invasive infections, from around the world. This is the largest population genomics study on the pathogen to date. It confirms the primarily clonal reproduction of this human pathogen – but it also shows traces of introgression in the genome of some strains, indicating the possibility of genetic exchanges between strains in nature and reflecting parasexual reproduction, independent from meiosis, which had previously only been observed in a laboratory setting, or sexual reproduction, hitherto unknown for *C. albicans*. *C. albicans'* use of parasexual reproduction is no doubt crucial for it to generate genetic diversity and adapt to new environments quickly, as well as to rid itself of the deleterious mutations that build up during clonal reproduction and which, if they are not eliminated, would lead to the species' extinction.

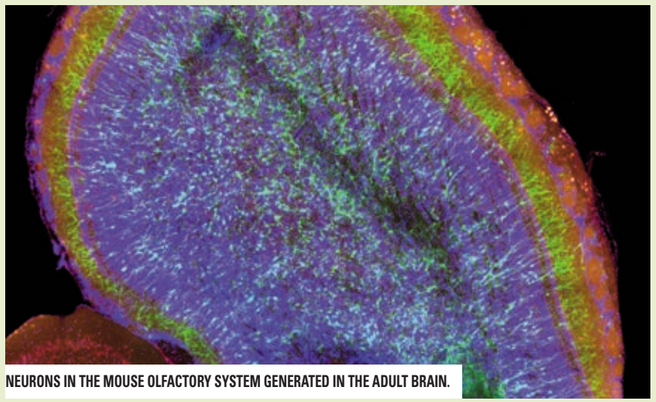
*Source: Ropars J, et al.* Nat Commun., *June 8, 2018.*



SURFACE MAP SHOWING AGE-RELATED CHANGES IN CORTICAL THICKNESS DURING ADOLESCENCE.

# Department of **Neuroscience**

**The Neuroscience Department investigates the organization and workings of the central nervous system at various levels, from molecules to behavior. This work goes hand in hand with research on conditions such as neurological diseases, behavioral disorders and sensory deficits (deafness, autism, addiction, neurodegeneration and mood disorders), all of which represent major research challenges for the department's scientists. The department is led by David DiGregorio.**



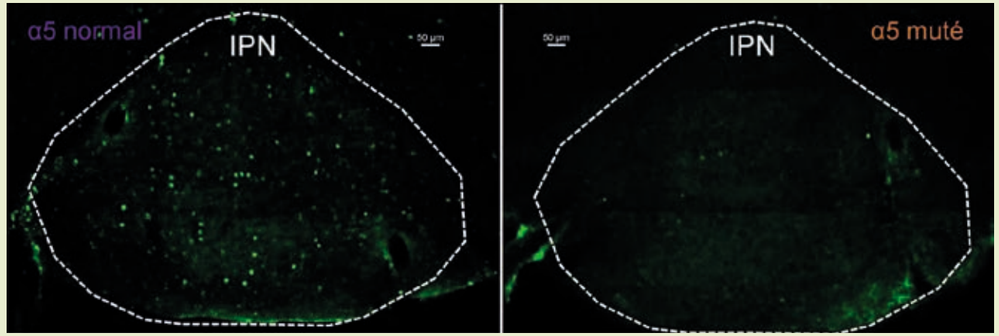
NEURONS IN THE MOUSE OLFACTORY SYSTEM GENERATED IN THE ADULT BRAIN.

## NEW NEURONS HELP US ASSESS THE RELEVANCE OF OUR SENSORY EXPERIENCES

Although we have known for several years that the adult brain can produce new neurons, many questions about the properties conferred by these adult-born neurons were left unanswered. What advantages could they offer that could not be provided by the neurons generated shortly after birth? Scientists in the Perception and Memory Unit looked into the production of new neurons in the brain region responsible for analyzing odors, the olfactory bulb. They demonstrated that the new neurons produced in adults react preferentially to reward-related sensory stimuli and help speed up the association between sensory information and reward. Their research shows that adult-born neurons play an important role in both the identification of a sensory stimulus and the positive value associated with that sensory experience. The neurons generated shortly after birth are unable to perform this function.

*Source: Anne Grelat et al.,* PNAS, *February 19, 2018.*

## SMOKING CESSATION: A GENETIC MUTATION INVOLVED IN RELAPSE




Nicotine dependence, a chronic condition with a high rate of relapse, is the leading preventable cause of death worldwide. Seven million people die from tobacco use every year. Nicotine, the main psychoactive compound in tobacco, causes this addiction by binding to the nicotinic receptors in the brain. In so doing it activates the reward circuit and creates a feeling of well-being. An individual's tobacco consumption is therefore closely linked to the sensitivity of these nicotinic receptors, which are composed of five subunits.

Recently, several large-scale human genetic studies have demonstrated that a mutation in the CHRNA5 gene that codes for the α5 nicotinic receptor subunit is associated with a significant increase in the risk of nicotine dependence. The mutation is highly present in the general population, and approximately 35% of Europeans carry it.

We introduced the mutation into a rat by using a recent molecular genetics technique, and evaluated its effect on various behaviors associated with nicotine dependence. We demonstrated that it resulted in greater nicotine consumption at higher doses, as well as an increased rate of relapse to nicotine-seeking behavior after cessation. Interestingly, the research showed that this effect on relapse was associated with reduced neuronal activation in the interpeduncular nucleus, a brain structure with the highest concentration of α5 nicotinic receptor subunits.

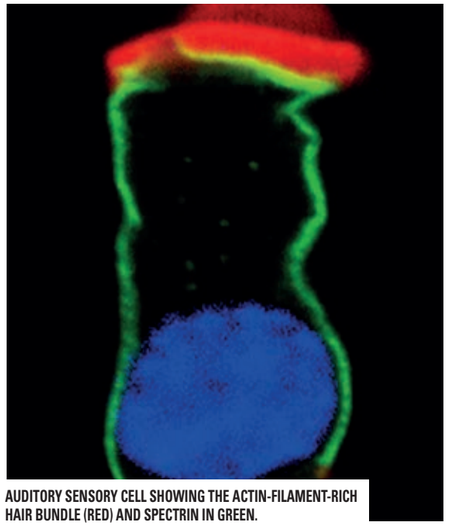
The results suggest that a drug capable of increasing the activity of nicotinic receptors containing the α5 subunit could reduce tobacco consumption and lower the risk of relapse after cessation.

*Source: Forget B et al.,* Curr Biol, *September 26, 2018.*

## GENE THERAPY HELPS MAINTAIN SYNAPTIC TRANSMISSION TO AUDITORY NEURONS

Hearing loss is the most common sensory deficit in humans. In a model reproducing the progressive postlingual hearing loss caused by Usher syndrome type III (USH3), it was demonstrated that, in addition to its involvement in the functioning of the hair bundle, the structure that converts sound into electrical signals, clarin-1 (*USH3A* gene), is also vital for the synapses between sensory cells and auditory neurons. Interestingly, transferring the gene encoding clarin-1 into the ear results in long-term preservation of hearing by maintaining the normal subcellular and molecular organization of the auditory synapses. These results confirm that gene therapy approaches could be used as an effective treatment method for conditions affecting the auditory synapses, to preserve auditory neurons and improve the transmission of signals to the brain.

*Source: Dulon D et al.,* J. Clin. Invest., *August 1, 2018.*



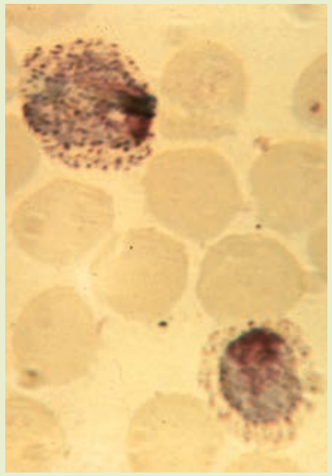
AUDITORY SENSORY CELL SHOWING THE ACTIN-FILAMENT-RICH HAIR BUNDLE (RED) AND SPECTRIN IN GREEN.

CYTOSKELETON OF *TRYPANOSOMA BRUCEI.*

# Department of **Parasites and Insect Vectors**

**The Department of Parasites and Insect Vectors conducts research on the three key eukaryotic parasites responsible for severe diseases of major public health concern that generate an important economic burden in the world's most populous regions. These are: *Plasmodium*, which causes malaria; *Leishmania*, the agent of leishmaniasis; and *Trypanosoma*, responsible for sleeping sickness. The *Anopheles* mosquito, which is the vector of *Plasmodium* and other viruses, is also studied, as well as the tsetse fly, the vector for *Trypanosoma brucei*. The department is led by Gerald Spaeth.**

## MATHEMATICAL MODELING OF *PLASMODIUM VIVAX* CONTROL IN PAPUA NEW GUINEA



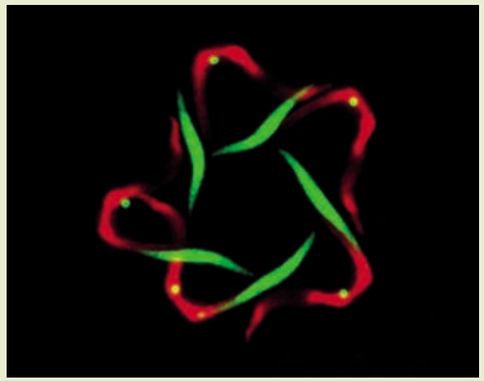
Following advances in computational power and statistical inference, mathematical models can now provide quantitative predictions of the impact of malaria control interventions. After calibration to data from Papua New Guinea (PNG), we simulated the impact of mass distribution of insecticide-treated bed nets and treatment of symptomatic cases on *P. vivax* transmission. In high transmission settings such as New Ireland, existing interventions are not sufficient to reduce *P. vivax* transmission to levels low enough to pursue elimination. However, in many regions of PNG, notably the highlands, continued distribution of bed nets would be sufficient to reduce *P. vivax* to pre-elimination levels. Unfortunately, the past year has seen a resurgence of malaria cases driven by factors not included in the current iteration of our model: interruptions to the supply of anti-malarial drugs, reduced funding, and behavioral and chemical resistance of mosquitoes to insecticide-treated nets. Mathematical models alone will not solve the challenges needed to pursue *P. vivax* elimination, but they provide crucial information to support epidemiologists and malaria control officers in their response to these challenges.

*Source: White MT, et al.,* Nature Commun., *2018; 9(3300); August 17, 2018.*

## UNDRESSING AND KILLING MALARIA PARASITES IN THE HOST SKIN

Malaria is a disease caused by *Plasmodium spp* parasites that still kills more than 400,000 persons a year. Vertebrate infection starts with the inoculation of a few sporozoites (SPZs) into the host skin during a bite by an infected mosquito. The most prominent malaria vaccine candidate, RTS,S/AS01, targets the major SPZ surface protein, the circumsporozoite protein (CSP), but the precise mechanisms of protection are not well known. Using a rodent malaria model, Aliprandini and collaborators showed that sterile protection conferred by anti-CSP antibodies (Abs) is dependent on parasite inoculation in the host skin, where SPZs decrease their speed and surprisingly die displaying a dotty phenotype. Ab cytotoxicity requires the motility-dependent translocation and stripping of the protective CSP surface coat, which renders the parasite membrane vulnerable to the perforin-like protein secreted by SPZs to traverse host cell membranes. The SPZ neutralization by anti-CSP Abs is thus a dynamic process initiated in the skin where SPZs either stop moving, or migrate and traverse cells to progress through the host tissues at the eventual expense of their own life.

*Source: Aliprandini et al.,* Nature Microbiology, *October 2018.*



## "CRISPR IN PARASITOLOGY" SYMPOSIUM

The department organized an international symposium "CRISPR in Parasitology" at the Institut Pasteur, Paris on November 19-20, 2018. Its goal was to facilitate lively discussion and sharing of information/advice about various CRISPR techniques from gene editing to CRISPRi to other dCas9-based technologies in *Leishmania*, *Plasmodium*, *Trypanosoma*, and *Anopheles*. Experts from each field were invited to present on the latest advances and discoveries in CRISPR technology, to a diverse international audience. It has encouraged a community effort in improving/standardizing CRISPR methodology in the parasitology community.

## SETTING THE RIGHT LENGTH

Trypanosomes are extracellular flagellated parasites that are responsible for sleeping sickness in humans and nagana in cattle. They develop in the skin and blood of their mammalian hosts and are transmitted by the bite of the tsetse fly, where they undergo a complex developmental cycle to move from the gut to the salivary glands. Trypanosomes adapt to these changing environments by specific differentiation steps characterized by exhaustive modifications of the length of their flagellum. Bertiaux and co-workers propose a new model termed "grow-and-lock" to explain how trypanosomes control the length of their flagellum. It posits that the organelle elongates at a linear rate until a locking event takes place in a time-defined manner, hence fixing length. The authors show that alteration in the growth rate and/or in the timing of the locking event leads to the formation of flagella of different lengths. This simple model could also be relevant for the control of flagellum length in other eukaryotes, especially in humans where dysfunction of these organelles causes severe genetic diseases.

*Source: Bertiaux, Morga et al.,* Current Biology, *October 2018.*

## OTHER NEWS

**Gerald Spaeth**
2018 Georges Zermati Prize for his work on *Leishmania* evolvability and his efforts to identify new treatment options that are more refractory to parasite drug resistance.

**The LeiSHield-MATI consortium**
*(see page 73 - International)*

EBOLA VIRUS.

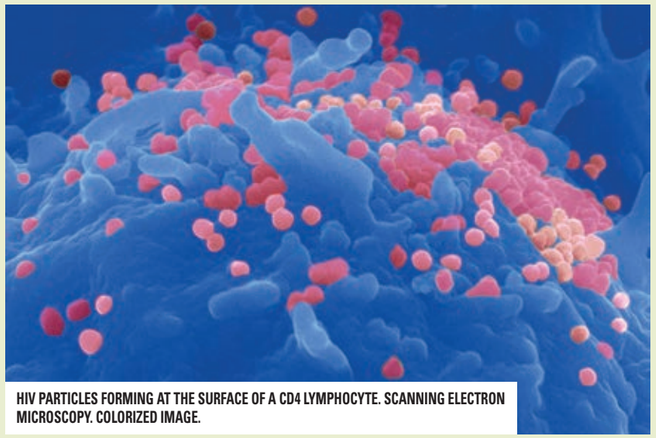
# Department of **Virology**

**The Virology Department focuses its research on viruses – their molecular organization, pathogenicity determinants, multiplication and interactions with host defense mechanisms. The viruses under study include respiratory viruses such as influenza; viruses that cause cancer (papillomaviruses, HTLV, and the hepatitis B and C viruses); retroviruses such as HIV; insect-borne viruses that are responsible for severe diseases including dengue, chikungunya, yellow fever, microcephaly caused by the Zika virus, and Rift Valley fever; and viruses causing hemorrhagic fever (such as the Lassa fever and Ebola viruses).**
**The department is led by Monique Lafon.**

## STARVING HIV-INFECTED CELLS: A NEW ANTIVIRAL STRATEGY

The antiretroviral therapy currently used to treat HIV is capable of blocking infection, but it cannot eliminate the virus from the body. The treatment therefore needs to be taken for life, and the virus remains in the reservoir cells of the infected host, especially in CD4 lymphocytes. Scientists in the HIV, Inflammation and Persistence Unit and their colleagues discovered that these cells were preferentially targeted by HIV because of their high demand for energy and glucose consumption. This finding raises the possibility of eliminating HIV-infected lymphocytes by depriving them of glucose. Scientists managed to block the infection of CD4 lymphocytes *ex vivo* by treating them with metabolic activity inhibitors that have already been investigated in cancer research.

*Source: Valle-Casuso JC et al.,* Cell Metabolism, *2018.*



HIV PARTICLES FORMING AT THE SURFACE OF A CD4 LYMPHOCYTE. SCANNING ELECTRON MICROSCOPY. COLORIZED IMAGE.

## WHAT IF WE COULD MAKE THE INSECTS THAT CONTAMINATE US FALL SICK?

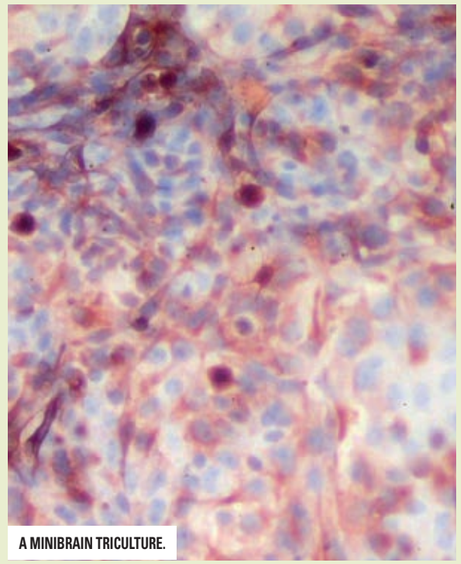
Mosquitoes are effective vectors for diseases such as dengue and Zika because they themselves are not susceptible to these viral infections. Scientists in the Viruses and RNA Interference Unit investigated how mosquitoes resist these infections. Taking vinegar flies as an experimental model, they discovered that after contamination, the viral infection became persistent. They determined that this persistence was a result of the viruses' ability to produce circular DNA molecules that trigger defense mechanisms in insects, and that inoculating this DNA into a non-infected fly induces protective immunity. This research raises hopes that persistent infections in insects could be blocked by reducing the production of viral DNA, which in turn could limit the spread of insect-borne viral infections.

*Source: Poirier E et al.,* Cell Host and Microbes, *2018.*

THE VINEGAR FLY, OR ***DROSOPHILA MELANOGASTER.***

### AWARD

**Nadia Naffakh**
A molecular virologist and Research Director at the CNRS, who works in the Virology Department's Molecular Genetics of RNA Viruses Unit, has received the Georges, Jacques and Elias Canetti Prize for her research on influenza viruses aimed at elucidating the molecular mechanisms used by the virus to proliferate. This research paves the way for the identification of new therapeutic targets and the development of novel antiviral treatments.



A MINIBRAIN TRICULTURE.

## "BBB-MINIBRAIN", A 3D CULTURE MODEL MIMICKING THE BLOOD-BRAIN INTERFACE IN HUMANS – A NOVEL TOOL FOR INVESTIGATING VIRAL ENTRY INTO THE BRAIN

*In vitro* modeling of tissues and organs is a valuable research tool, not only because these models make it easier to examine complex interactions but also because they will ultimately reduce the need for animal testing. A model mimicking the interaction between the blood vessels in the brain and the brain parenchyma in humans, known as the BBB-Minibrain, has been developed in the Viral Neuro-Immunology Unit. A pilot study using a live yellow fever vaccine strain that was banned in the 1980s because of a high number of neurological events demonstrated that the BBB-Minibrain could be used to isolate the rare mutants that had developed the ability to enter the nervous system and multiply there. The BBB-Minibrain therefore represents a promising alternative for performing neurovirulence tests on live vaccines without the need for animal testing.

*Source: Da Costa A et al.,* Biologicals, *2018*

# Center for Global Health (CGH)

**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 established in September 2014 and is directed by Prof. Arnaud Fontanet.**

## THE PASTEUR OUTBREAK INVESTIGATION TASK FORCE (OITF)

The Pasteur OITF, created in 2015, comprises staff in the Institut Pasteur International Network (IPIN) who are committed to participating in outbreak responses, through the World Health Organization's Global Outbreak Alert and Response Network (GOARN) or in support of requests for assistance from other institutes in the IPIN. The mission of the OITF is to increase capacity for outbreak response locally and internationally by providing training and hands-on field experience, promote collaboration within the IPIN and among partners to enhance knowledge about epidemic-prone infectious diseases, and contribute to the detection, response, and control of public health threats worldwide.

- **Pasteur OITF Deployments.** Starting from a cohort of 50 scientists from 10 institutes in the Institut Pasteur International Network in 2015, the Pasteur OITF expanded during 2018 under the leadership of its new Director Dr. Eileen Farnon, to comprise over 90 volunteers from 18 institutes. During 2018, the Pasteur OITF deployed a total of six staff through the WHO Global Outbreak Alert and Response Network (GOARN) to four outbreak responses (Listeriosis in South Africa; Ebola in Equateur Province, Democratic Republic of Congo (DRC); the Rohingya refugee crisis in Cox's Bazar, Bangladesh; and Ebola Readiness and Preparedness in Rwanda and Burundi).

- **INCEPTION funding awarded to the OITF**. The Pasteur OITF was awarded its first grant, from the INCEPTION Program, consisting of €83,500 per year, for three years (2018-2020). This grant provides funding for preparedness and capacity-strengthening, and for outbreak response, including applied public health research. During 2018, this grant allowed OITF to award four small project grants of €10,000 each to Institut Pasteur scientists and IPIN collaborators to conduct research on epidemic-prone emerging infectious diseases. It also provided salary support to extend a social scientist's contract who was engaged in the Ebola outbreak in Equateur Province, DRC; supported shipping of monkeypox outbreak specimens from the Pasteur Center in Cameroon to the Institut Pasteur for sequencing; supported shipping of reagents from the Institut Pasteur to Rwanda to support the Ministry of Health's Ebola preparedness activities in response to the Ebola outbreak in North Kivu and Ituri Provinces, DRC; and supported travel for IPIN scientists in the AFRO region to attend the first International Conference on (Re-) Emerging Infectious Diseases, the annual conference of Africa CDC.

## DEVELOPING A PAN-AFRICAN CAPACITY STRENGTHENING PLATFORM

The Pan-African capacity strengthening platform will be built around the best match between Pasteur's strengths and the relevant research and training needs within African Higher Education Institutions. For this purpose, three priority areas have been selected:

- emerging and re-emerging diseases,
- antimicrobial resistance,
- malaria.

During 2018, Dr. Hans Hagen, Deputy-Director of the CGH, consulted a wide range of stakeholders, covering a number of IPIN institutes on the continent, selected universities and research institutes across several French-speaking and English-speaking countries, as well as other relevant organizations and initiatives. Based on the feedback received, the two following strands of activities were retained for the program:

- **Pan-African Research Networks:** strengthening intra-African research collaboration with a specific focus on linking French-speaking scientists (in particular those based at the 10 Pasteur Institutes on the African continent) with their non-French-speaking peers.
- **Beyond excellence in science:** developing practical strategies for the conversion of research into (early) development across diagnostics, drug discovery, and vaccine development, akin to the H3D drug discovery platform established by Prof. Kelly Chibale at the University of Cape Town. (http://www.h3d.uct.ac.za/)

The focus of any capacity strengthening program is on skill acquisition, especially for young researchers: in addition to the bespoke training activities embedded in each research consortium, a complementary training program will be established across the important subject matters of data sciences, vocational and entrepreneurial skills, as well as in science policy. These complex training platforms can only be managed in partnership with other initiatives, for example in bioinformatics with the African Institute for Mathematical Sciences, and the African Bioinformatics Network, H3ABionet. The delivery of the overall program will be done in collaboration with the African Academy of Sciences.



## INTRA-AFRICA MOBILITY SCHEME ON SCIENCE AND LANGUAGE

A first round of applications for the Science and Language Mobility Scheme, which aims to boost researchers' mobility in Africa, has been finalized. Dr. Soanandrasana Rahelinirina from the Institut Pasteur de Madagascar is one of the six successful grant holders. The Institut Pasteur de Dakar is hosting Dr. Kevin Ochieng' Opondo from the Medical Research Council Unit at the London School of Hygiene and Tropical Medicine, in Gambia. This scheme is a collaboration between the Institut Pasteur, the Wellcome Trust, and the African Academy of Sciences.

## GLOBAL HEALTH E-ACADEMY

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. As part of the project to develop the platform for the Global Health e-Academy, in 2018, the CGH carried out a survey across four African Higher Education Institutions to evaluate the role and perceptions of MOOCs among university lecturers and students. The surveyed institutions were the *Université Cheikh Anta Diop de Dakar*, Dakar, Senegal; the University of Ghana, Accra, Ghana; the Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; and the *Université d'Antananarivo,* Antananarivo, Madagascar.

## 2019-2023 STRATEGIC PLAN: A STEP TOWARDS INTEGRATED GLOBAL HEALTH

We will adjust the sphere of activity of the Institut Pasteur's departments and centers – like the CGH – so that they are more closely in line with current scientific realities and can enable us to achieve our strategic priorities.

# Department of Technology and Scientific Programs (DTPS)

**The Department of Technology and Scientific Programs (DTPS) was set up on June 1, 2018 to give new impetus to the Institut Pasteur's research via a state-of-the-art technological environment.**

The Department of Technology and Scientific Programs meets the various key requirements of Institut Pasteur research teams. It provides access to state-of-the-art resources and expertise in the fields of technology and animal testing (a priority of the 2019-2023 Strategic Plan), and incentive funding in line with the Institut Pasteur's scientific strategy.
In addition, the DTPS manages technological investment policy and rolls out digital technologies to the campus in collaboration with the Information Systems Department.

over **150** people work at the DTPS
- **85%** engineers and technicians
- **15%** administrative staff

## THREE CENTERS OF EXPERTISE

- **The Center for Technological Resources and Research (C2RT)** is home to four technology and service units (UTechS) and 12 technological platforms. Thanks to the expert staff working in these facilities, research teams can access state-of-the-art technologies, be trained in their use and keep up to date with technological and methodological developments. Fields as varied as omics (particularly at single-cell level); design and production of biomolecules and their structural analysis; imaging; cell sorting and phenotyping; phenotypic screening; microfluidics and 3D cell culture are covered. 2018 saw the arrival of three new platforms – the Biomaterials and Microfluidics Platform *(see inset on page 44)*, the Biological NMR Technological Platform and the Nanoimaging Platform *(see inset on following page)*.
- **The Center for Animal Resources and Research (C2RA)** meets the animal testing requirements of research teams and houses the Central Animal Facility (AC), the Mouse Genetics Engineering Center (CIGM) and the Center for Production and Infection of Anopheles (CEPIA).
- **The Center for Scientific Incentive Programs (SPIS)** runs incentive programs via calls for proposals, including Transversal Research Programs (PTRs), Inter-Pasteurian Concerted Actions (ACIPs) and Targeted Incentive Initiatives (AICs) (*see inset on this page*).

## LAUNCH OF A NEW SESSION OF PTR AND ACIP INCENTIVE PROGRAMS – 2019 SESSION

To identify topics and talents within the Institut Pasteur and the Institut Pasteur International Network, in late 2018:
- the DTPS launched a 2019 PTR call for proposals to support collaborative, interdisciplinary and ambitious research projects in the priority scientific areas of the 2019-2023 strategic plan,
- and a 2019 ACIP call for proposals in partnership with the Department of International Affairs to support Inter-Pasteurian collaborative projects in the field of public health.



## CREATION OF THE NANOIMAGING TECHNOLOGICAL PLATFORM

The Nanoimaging platform opened in late 2018 following the arrival of the most powerful electron microscope to date at the Institut Pasteur, the Titan Krios™. Directed by Matthijn Vos, and under the scientific supervision of Dorit Hanein, this platform will provide the scientific community with technological and methodological assistance for high-resolution imaging of biological samples (single particle imaging and cell cryo-electron tomography).

**20** DTPS units
- **16** C2RT units
- **3** C2RA units
- **1** SPIS unit

**6** units are ISO9001 certified

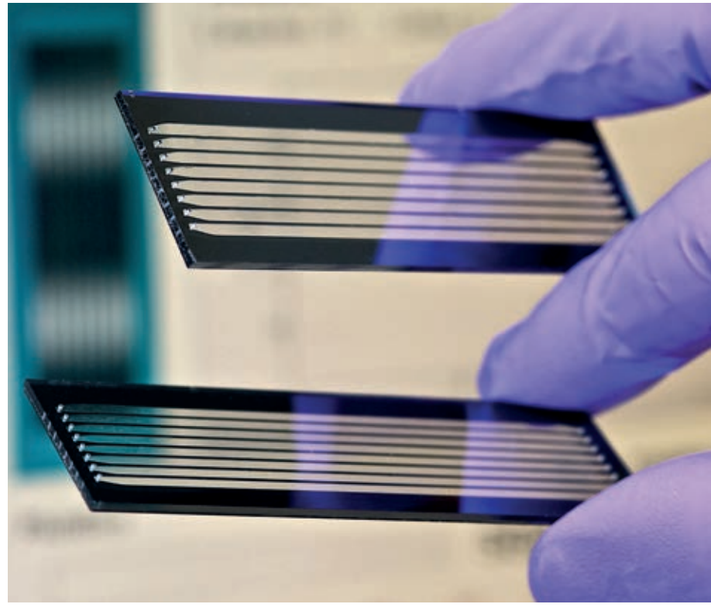
**8** units have IBISA accreditation

The DTPS faces considerable challenges:
- **maintaining a range of state-of-the-art equipment** in a context of rapidly developing technology,
- **developing and offering new services** to research units dependent on cutting-edge technology,
- **increasing contributions from the C2RT and C2RA** in campus unit research projects,
- **identifying strategic equipment requirements** with scientific departments, by prioritizing a pooling and partnership policy.

## NEW TOOLS AND METHODS

In 2018, the C2RT and C2RA implemented several new tools and methods. The Central Animal Facility produced various mouse strains with diverse genetic heritage, providing new models for studying diseases and enabling genotype-phenotype association studies (Zhang et al., *BMC Genomics*).
In collaboration with the Integrative Neurobiology of Cholinergic Systems Unit, the Mouse Genetics Engineering Center developed its first nicotine-dependent transgenic rat model (Forget et al., *Current Biology*).

The Cytometry and Biomarkers UTechS rolled out a transcriptomic pipeline at single-cell level in collaboration with the Genomics and Epigenomics of Vertebrate Development Unit (Sebé-Pedrós et al., *Cell 2018*). Finally, the Image Analysis Hub created MaMuT, a software tool for analyzing very large multi-view images (Wolff et al., *E-Life*).



## LAUNCH OF THE ORGAN-ON-CHIP CENTER IN PARTNERSHIP WITH EMULATE

This partnership, led by the Biomaterials and Microfluidics Technological Platform directed by Samy Gobaa, gives scientists special access to Organ-On-Chip technology, and enables them to develop new types of cell-based assays, mimicking the physiology of a human organ, through projects developed at the Institut Pasteur or in collaboration with Emulate.

## NEW TECHNOLOGICAL AND EXPERIMENTAL RESOURCES

The C2RT and C2RA also provided the campus with several new technological and experimental resources.
The Photonic BioImaging UTechS added two light sheet fluorescence microscopes to its range of optical microscopy equipment. They enable detailed low phototoxicity imaging of thick samples.
The Ultrastructural BioImaging UTechS acquired a Cryo CLEM microscope to combine fluorescence microscopy and cryogenic electron microscopy and obtain ultrastructural visualization of protein dynamics and interactions.
The Production and Purification of Recombinant Proteins platform automated selection of expression host/vector pairs and culture parameters, speeding up the identification of optimal conditions for producing and purifying proteins of interest.
The Biomics Technological Platform unveiled an open-access room featuring all the equipment required to perform high-throughput sequencing independently, including Illumina ISeq100 and NextSeq500-type sequencers.
The Central Animal Facility provided new anesthesia equipment to make it easier to train users.
The C2RT and C2RA units are part of an international environment. In 2018, the Mass Spectrometry for Biology UTechS became the only French laboratory to integrate EPIC-XS, the European Proteomics Infrastructure Consortium.

## 2019-2023 STRATEGIC PLAN: THE TECHNOLOGICAL OBJECTIVES OF THE DTPS

- Expand our nanoimaging initiative by acquiring additional electron microscopes to optimize our use of the Titan Krios™.
- Develop optical imaging methods for the multi-scale study of host-pathogen interactions.
- Optimize our facilities to consolidate our structural biology resources.
- Offer shared metabolomics resources for sample preparation and analysis.
- Boost our ability to identify novel diagnostic and therapeutic solutions.
- Develop high-throughput approaches for antibody identification and production.
- Implement shared electronic data collection and analysis (ELN, LIMS).



(C3BI)

# The Center for Bioinformatics, Biostatistics and Integrative Biology

**Following almost four years of successful operation, the C3BI – one of France's largest bioinformatics centers – moved to new premises on the Institut Pasteur Paris campus in 2018. It published close to one hundred scientific papers during the year.**

Biology is now a computational science that uses modeling, statistics and informatics to analyze and exploit omics (genomes, transcriptomes, proteomes, etc.) data efficiently. It has wide-ranging applications, especially in the field of health. The Center for Bioinformatics, Biostatistics and Integrative Biology (C3BI), based at the Institut Pasteur, is a joint research and service unit with the CNRS (USR 3756). It is housed in the Omics building, which opened on September 13, 2018 *(see inset on following page)*.
The C3BI is a national and international reference center for bioinformatics, related disciplines and their applications in biology and health. Its activities are multidisciplinary and cross-sectoral: basic research, services for experimental units and platforms, and training to improve the skills at the Institut Pasteur (and especially its junior scientists) in these fields.

## THE TWO MAIN FACILITIES AT THE C3BI

**The research area** hosts 12 units whose skills range from mathematical modeling to algorithms, statistics and machine learning:
- Structural Bioinformatics,
- Mathematical Modeling of Infectious Diseases, Imaging and Modeling,
- Human Evolutionary Genetics,
- Human Genetics and Cognitive Functions, Microbial Evolutionary Genomics,
- Spatial Regulation of Genomes,
- Evolutionary Bioinformatics,
- Cellular Processes Modeling,
- Statistical Genetics G5[1],
- Decision and Bayesian Computation G5[1],
- Sequence Bioinformatics G5[1].

The Sequence Bioinformatics G5[1] (directed by Rayan Chikhi) was set up in 2018 as part of the Inception project. This G5 works on the fundamental aspects of sequence algorithms and applications in genomics, metagenomics and proteomics.


OMICS BUILDINGS.

ANDRÉE GILLOT, A GENEROUS DONOR WHO HELPED FUND THE CONSTRUCTION OF THE OMICS BUILDINGS.

## OPENING OF THE OMICS BUILDINGS

An omics center of expertise was opened on the Institut Pasteur Paris campus on September 13, 2018. It occupies two buildings. The Alexandre Yersin building houses several C3BI research teams and the Bioinformatics and Biostatistics Hub. The Simone Veil building is home to the Biomics Pole, the shared microbiology platform (P2M), and the Pathogen Discovery laboratory. This center brings together outstanding multi-disciplinary research teams and state-of-the-art technologies, which consolidate the Institut Pasteur's position as a major global player able to generate and analyze big health data to advance our understanding of the living world and improve healthcare.

**The Bioinformatics and Biostatistics Hub** performs analyses, develops applications and data processing pipelines, and provides training for units and platforms on the Paris campus and in the Institut Pasteur International Network.
In 2018, the Hub worked on more than 84 new projects (330 since inception). The Hub is involved in 7 new long-term projects, i.e. 18 long-term projects in total, including "Milieu Intérieur" (immune system and personalized medicine), Afribiota (child malnutrition) and PIBnet (analysis of microbial genomes, discovery of new pathogens or new pathogen combinations, etc.).
The Hub completed its team in 2018 with the arrival of 40 engineers. It also hosts two engineers from the French Institute of Bioinformatics (IFB) and one engineer funded by ELIXIR, the European bioinformatics network.

## C3BI SCIENTIFIC PAPERS

In 2018, the C3BI units published 96 papers in leading international scientific journals, such as: Science, Nature, Nature Communications, Nature Biotechnology, Elife, PNAS, American Journal of Human Genetics, Genome Biology, Nucleic Acids Research, Bioinformatics, PLoS Computational Biology and PLoS Pathogens. These papers covered various fields, including:

- antibiotic resistance: three-dimensional modeling of proteins to predict antibiotic resistance, distinguishing between resistance and resilience for more effective antibiotic use, etc.,
- contribution of machine learning in recognizing bipolar disorder, in relationships between cell metabolism and HIV infection, and in an RNA signature for diagnosing and predicting the severity of dengue,
- data analysis: a new phylogenetic bootstrap technique to reveal the signals contained in large datasets (such as omics data), and a new integrative approach for analyzing human data efficiently, presented at the American Society of Human Genetics Meeting.

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

MEMBERS OF THE BIOINFORMATICS AND BIOSTATISTICS HUB IN THE OMICS BUILDING ENTRANCE HALL.

ORLAN, *LES PHAGES D'ORLAN,* 2018, AN ORGANOÏDE/INSTITUT PASTEUR CREATION. THIS WORK IS EXHIBITED IN THE ENTRANCE HALL OF THE SIMONE VEIL AND ALEXANDRE YERSIN BUILDINGS.

## THE INCEPTION PROJECT

The Inception[2] project ("Convergence Institute", launched in 2017 as 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. Allocated €12 million over ten years, it aims to enhance synergies and cooperation between the various partners. The C3BI teams are actively involved in the projects and training supported by Inception. 2018 stands out for the creation of an experimental GPU laboratory for scientific computing, the development of training courses (Analysis of biological data, Molecular phylogenetics, Linking gene and function: Comparative genomics tools for biologists, Introduction to Python programming), support for numerous workshops, the creation of a rapid response unit in the event of a major pandemic outbreak, and recruitments (PhD students, post-doctoral fellows, and a new G5).

## OVERVIEW AND PROSPECTS

In the coming years, the Institut Pasteur C3BI will continue to work with the CNRS, Inria and Paris-Sciences-Lettres (PSL) University, and will also be involved in the Institut PRAIRIE (set up in March 2018), a center of excellence dedicated to artificial intelligence and bringing together many academic and industrial partners. In addition to the initiatives already taken, this will help to bolster the expertise of the center, recognized by an international site visit committee chaired by Hugues Roest Crollius of the ENS, in 2018: "The C3BI enables Institut Pasteur research units to draw on the expertise of a large group of qualified engineers, and to excel in computational biology research." The committee adds: "The C3BI can provide reliable and agile services to support biomedical research projects, and develop new areas of research in bioinformatics and computational biology at the Institut Pasteur."

*2. The Inception Convergence Institute involves academic partners that contribute directly to the project: the Institut Pasteur and its CNRS/Inserm-associated joint research units, the CEA with its National Genotyping Center (CNG), Paris Diderot University with its SPHERE laboratory, PSL Research University, Paris Public Hospital Network (AP-HP), INRA and the "Frontières du Vivant (FdV)" Doctoral School.*

## What they have to say about us

*"The C3BI enables Institut Pasteur research units to draw on the expertise of a large group of qualified engineers, and to excel in computational biology research."*

**International site visit committee chaired by Hugues Roest Crollius of the ENS**

## MEASURES OF THE 2019-2023 STRATEGIC PLAN

With the help of the Information Systems Department (DSI), the C3BI has a key role to play in processing multi-omics data and incorporating these data into predictive models. The Institut Pasteur intends to strengthen its expertise in artificial intelligence to analyze and interpret the vast quantities of data generated by its teams and external partners.

Priorities for state-of-the-art technological development will enable us to:

- perform imaging of living systems, from molecules to organisms,
- explore the metabolome, a new frontier in understanding biological systems,
- expand our capacities for single-cell analysis,
- provide an environment for the comprehensive study of vector-borne diseases,
- identify novel diagnostic and therapeutic approaches,
- enhance data management and collaboration at global level.

# Academic partnerships **within France**

**The Institut Pasteur has a long history of research and/or teaching partnerships with institutions and universities in the Greater Paris region. One of the objectives of the 2019-2023 Strategic Plan is to consolidate and develop partnerships to drive scientific excellence within the Institut Pasteur.**

These partnerships with other institutions enable the Institut Pasteur to pursue four broad aims.

- **To formalize and consolidate** links with regional partners that facilitate the creation of joint units based at and/or outside the Institut Pasteur.
- **To provide** a framework for researchers from these institutions to come and work on the Institut Pasteur campus and also for Institut Pasteur researchers to spend time at external research organizations, schools and universities, in some cases accompanied by post-docs or engineers.
- **To identify** potential scientific research organizations, teams and projects that could be associated with these partnerships and lead to opportunities for joint research units and researcher mobility.
- **To promote** outstanding teaching and enhance the Institut Pasteur's appeal to future generations of scientists.

Partnerships are governed by specific agreements, sometimes in connection with existing framework agreements, that set the terms for cooperation *(see inset)*.

## PARTNERSHIPS WITH EPSTs

The Institut Pasteur's longest-standing partners among France's Public Scientific and Technical Research Establishments (EPSTs) are the CNRS and Inserm. A number of research structures are currently based at the Institut Pasteur campus, including accredited research teams (ERLs), joint research units (UMRs) and service and research units (USRs). These structures are jointly affiliated, either to the Institut Pasteur and the CNRS (2 ERLs, 8 UMRs and 2 USRs, including the Center for Bioinformatics, Biostatistics and Integrative Biology (set up in 2015)), or to the Institut Pasteur and Inserm (1 ERL and 11 units). A team from the UMR Inserm 1163, based on the Necker Campus, is jointly affiliated to the Institut Pasteur and the Institut Imagine. The Institut Pasteur also hosts a joint Institut Pasteur-INRA (French National Institute for Agricultural Research) unit. Two joint units were recently set up on the Institut Pasteur campus to promote interdisciplinary research combining experimental approaches and methodological developments, one in partnership with the French National Research Institute for the Digital Sciences (Inria) and the other with the École Polytechnique and CNRS.

## BASIS FOR RESEARCH PARTNERSHIPS

- Research field, program and length of the partnership.
- Scientific leaders of the project and staff involved.
- Allocation of skills, staff, human and financial resources and equipment.
- Expenditure forecast and funding of the partnership.
- Commercialization of results (publications, intellectual property, etc.).

## BASIS FOR TEACHING PARTNERSHIPS

- Course title, program and length, qualification(s).
- Course coordinators and composition of organizing committees.
- Student selection process and numbers.
- Allocation of skills, staff, human and financial resources and equipment among the parties.

## PARTNERSHIPS WITH UNIVERSITIES

These partnerships cover both research – five joint units are hosted on the Institut Pasteur campus, mainly jointly affiliated with Paris Diderot University – and teaching. Fourteen Institut Pasteur courses lead to the award of a university diploma, and 20 courses are recognized as doctoral school modules. Most of them are run jointly with Paris Descartes, Paris Diderot, Sorbonne, Paris-Saclay and PSL universities. The Pasteur/CNAM School also awards the Advanced Master's in Public Health, accredited by the French *Conférence des Grandes Écoles*. The "Médecine-Sciences" program is run in partnership with the École normale supérieure (ENS), Institut Curie and PSL.

## PARTNERSHIPS WITH THE PARIS PUBLIC HOSPITAL NETWORK

To support research projects that associate the basic research conducted by the Institut Pasteur's teams with translational and clinical research, the Institut Pasteur and the Paris Public Hospital Network (AP-HP) annually publish joint calls for proposals to host hospital-based physicians (as guest researchers or via a partnership contract) or to set up joint units on the Institut Pasteur campus. Three joint units were set up in 2016 for a five-year period. A dual-site Institut Pasteur/AP-HP/Paris-Sud University joint research unit was set up in 2013.

## HOSTING SCIENTISTS FROM EXTERNAL RESEARCH ORGANIZATIONS (OREX)

The joint units hosted at the Institut Pasteur are partly composed of OREX scientists and engineers from EPSTs, universities, and the AP-HP, etc. The Institut Pasteur currently hosts 150 scientists and 40 engineers employed by partner institutions, mainly from the CNRS (85 scientists and 22 engineers), Inserm (39 scientists and 15 engineers), Paris Diderot University (13 scientists/lecturers) and Paris Descartes University (5 university hospital scientists/lecturers).

# Health

**A key challenge facing the Institut Pasteur is how best to address today's public health issues and anticipate future health needs. It is committed to strengthening the link between scientists and patients through epidemiological surveillance and clinical research.**

*"At the Institut Pasteur, a temple for science and progress, scientists work for the common good. Both in France and worldwide, this collaborative approach to science and medicine is achieving great things. One only needs to look at the amazing strides made in human health over the past 10, 20 or 30 years. And that's why humanity should be so grateful to scientists like those at the Institut Pasteur. […] The Pasteurian community is well aware of the great esteem our mother, Simone Veil, had for the Institut Pasteur – not just because she came to its rescue,[1] but because it was truly at the heart of her work as a minister. For what's the use of being Minister for Health if not to advance science, and to advance what is most crucial to humankind – life itself?"*

**JEAN AND PIERRE-FRANÇOIS VEIL,**
sons of Simone Veil
**Inauguration of the Omics building on September 13, 2018**

*1. On June 12, 1975, Simone Veil, French Minister of Health and Family, informed Institut Pasteur President Jacques Monod and Board Chairman Jean Royer that the government would be increasing its grant to 50.5 million francs. This substantial government contribution enabled the Institut Pasteur to overcome a major financial crisis.*

# Center for Translational Science (CRT)

**The Center for Translational Science (CRT) promotes 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 ideas, improve our understanding of disease and enhance patient care.**

## LAUNCHING TRANSLATIONAL PROJECTS

The CRT's Open Desk scheme provides guidance for scientists embarking on research projects involving human subjects by anticipating the ethical, regulatory and administrative procedures required with the assistance of a committee of internal and external experts. After briefly presenting their projects, scientists are given a clear idea of the procedures involved and are pointed to the relevant people and departments who can help them develop and implement their projects from start to finish. In 2018, the CRT reinforced its support for project leaders after the Open Desk phase, and a scientific illustrator helped to inform the Institut Pasteur's scientists about the translational research process.

## FORGING PARTNERSHIPS AND ATTRACTING PHYSICIANS

In addition to close partnerships with the Paris Public Hospital Network (AP-HP) and Necker and Sainte-Anne hospitals, the CRT provides funding for junior and experienced hospital professionals (doctors and pharmacists) to carry out translational research projects in the Institut Pasteur's research units.

## DEVELOPING NEW TRANSLATIONAL PROJECTS

The CRT runs a wide variety of scientific events to promote dialog and encourage collaboration between clinicians and scientists. At the monthly Pasteur Medicine Quarter-Hour sessions, doctors come to campus to speak about their work. Recordings of the sessions are available online on the CRT's YouTube channel (▶ CRT Pasteur).

This year, the first two-week observation placement took place at a partner hospital. The topic of aging was the focus of both the annual Translational Science Day and a "storm" session between clinicians and scientists in which each gave a brief presentation of their expertise.

## DEVELOPING LINKS WITH PATIENT ASSOCIATIONS AND RESEARCH PARTICIPANTS

In 2018, the CRT organized two major events. At the first, patient volunteers involved in the Institut Pasteur's research were invited to a presentation of findings based on their samples. The second event compared how different institutes in Europe maintain links with patient associations. An agreement was also signed with Thellie to facilitate public funding of research projects via an online platform.

**49** **translational projects were presented at Open Desk sessions in 2018**

## ADVANCING CLINICAL RESEARCH WITHIN THE INTERNATIONAL NETWORK

The INCREASE program (International Network Clinical Research Sustainable Initiatives) helped launch clinical and translational research projects involving the Institut Pasteur International Network, such as the EU-funded ALERRT[1] project to strengthen clinical research capabilities during outbreaks, and specific projects on topics including whooping cough and Zika virus. It also worked with the Information Systems Department to implement a data capture system (REDCap).

*1. https://www.alerrt.global.*



## THE THREE CRT STRUCTURES

- **The CRT Clinical Core** provides support for research projects led in France and worldwide after their initial presentation via Open Desk sessions. A satisfaction survey demonstrated that 94% of project leaders were satisfied with the support received in 2018. The survey also highlighted the need for the Clinical Core to explain its work more clearly and to adapt its support to cover research risks. In 2018, the team and its scientific partners received funding from the Bill & Melinda Gates Foundation to pursue the clinical development of a vaccine candidate for bacillary dysentery.

- **The ICAReB platform** coordinates two prospective cohorts of volunteers and manages the related collections of biological resources, which are available to the scientific community. ICAReB also serves as a biobank for research projects led both by Institut Pasteur teams – such as the Afribiota project, which is examining the gut flora of malnourished children –, and in collaboration with external teams – such as OHTicks, which aims to identify tick-borne pathogens.

- **The CRT Technical Core** is jointly affiliated with the Center for Technological Resources and Research. It offers a unique array of sophisticated technologies that can be used in translational research. This year, the BSL2+ containment laboratory for experiments on human material or infectious agents was expanded, and the platform acquired a new image cytometer and developed new single-cell gene expression analysis methods.

## 2019-2023 STRATEGIC PLAN: MEASURES INVOLVING THE CRT

- Develop projects in partnership with the Paris Public Hospital Network (AP-HP) via a joint call for proposals in the Institut Pasteur's priority areas (antimicrobial resistance, brain connectivity and neurodegenerative diseases).
- Foster international links with public health experts and clinicians on infectious diseases.
- Bring together and pool strengths in the area of vaccinology by involving immunologists, microbiologists and epidemiologists.

# National Reference Centers (CNRs)

**The Institut Pasteur hosts 14 National Reference Centers (CNRs) in mainland France (12 in Paris and two in Lyon) and four associated CNR laboratories in French Guiana. The current five-year term for CNRs, assigned by the French National Public Health Agency (Santé publique France or SpF), began on April 1, 2017 and will run until 2022.**

CNRs provide support for health authorities and work in association with their host research units to fulfill four key public health missions:

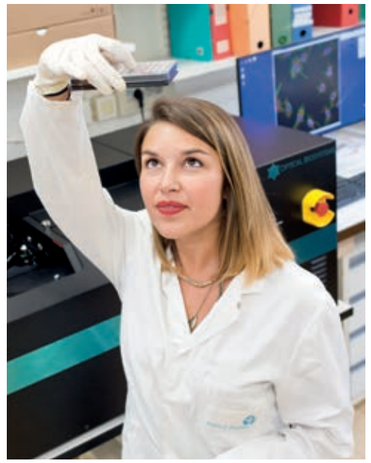
- diagnosis and microbiological expertise;
- advising healthcare professionals and authorities;
- contributing to epidemiological surveillance;
- contributing to the alert system.

The CNRs' activities – highly visible to the general public during major health crises – draw on the expertise of the Institut Pasteur's scientists and its ability to transfer innovative scientific and technological research to the field of public health.

## P2M, A STATE-OF-THE-ART MUTUALIZED PLATFORM FOR MICROBIOLOGY OPEN TO EXTERNAL CNRs

The Mutualized Platform for Microbiology (P2M), up and running since 2015, performs genome sequencing[1] on the bacterial, viral and fungal strains received by CNRs and World Health Organization Collaborating Centers (WHOCCs) for the purpose of infectious disease surveillance.
In 2018, just over 22,000 strains were sequenced at P2M, 73% related to foodborne infection surveillance. Genome sequencing increases the sensitivity threshold for outbreak detection. When an outbreak is identified at an early stage (clustered cases in a short space of time caused by the same pathogen), epidemiologists can immediately get to work to determine the origins of the outbreak, and authorities can order the removal of the contaminated product from the shelves (in foodborne outbreaks). P2M is also available to external CNRs for sequencing. In 2018 it worked with three CNRs based outside the Institut Pasteur. The platform sequences bacteria, viruses and fungi. Building on the experience gained over the past four years, P2M offers a highly efficient service, as shown by a first-pass success rate (i.e. a high-quality sequence providing comprehensive information on the entire genome) of more than 98% in 2018. Sequence production takes between 3 days (for emergencies) and 10 days.

*1. Genome sequencing: a technique used to determine the sequence of genes comprising the genome of microorganisms such as bacteria, parasites, fungi and viruses.*





## MENINGITIS: EFFECTIVE SURVEILLANCE AND ALERT RAISED IN CÔTE-D'OR

The Invasive Bacterial Infections Unit at the Institut Pasteur hosts the CNR for Meningococci and *Haemophilus influenzae* and the WHOCC for Meningitis. In 2018, the CNR used whole genome sequencing to characterize strains of cases of invasive infection with serogroup W meningococcal disease in Dijon. One case revealed that the disease had spread from elsewhere in Europe.
This led to a new vaccination campaign among people aged 17 to 24 living, studying or working in one of the 153 affected towns and villages in the Côte-d'Or department.
In 2018, the CNR revealed that the initial signs of serogroup W meningococcal infections can be abdominal symptoms such as stomach pains and diarrhea. Since these clinical signs are not recognized as being associated with invasive meningococcal infections, this may delay treatment. A press release was issued to inform the public and healthcare professionals about the symptoms, previously unknown to the medical community.
Research conducted at the WHOCC in collaboration with institutes in the Institut Pasteur International Network enabled scientists to describe the emergence of serogroup W in the Central African Republic and serogroup B in Morocco in 2018.

## TOWARDS ELIMINATING MALARIA IN FRENCH GUIANA AND NEIGHBORING COUNTRIES

In 2018, the Malaria CNR launched a public health research project in close cooperation with Cayenne Hospital to test approaches for eliminating malaria on the Guiana Shield. The project, ELIMALAR (Malaria Elimination in French Guiana), addresses several questions: Who are the carriers of malaria? Does treating these carriers reduce disease spread even if they don't display any symptoms? Are the drugs based on artemisinin derivatives prescribed today still effective? If so, should we be concerned about the rapid selection of resistant parasites? Supported by EU funding, WHO and Santé publique France, this program has already demonstrated the heterogeneous nature of malaria transmission foci in French Guiana. Some clearly defined areas far from healthcare structures are severely affected. The study on resistance to antimalarial drugs is drawing on the expertise of the WHO Collaborating Center for Surveillance of Anti-malarial Drug Resistance, which was redesignated for the period 2018-2021. It covers all the countries in the Guiana Shield including Venezuela, French Guiana, Suriname and Brazil. The scientists are looking for *in vitro* resistance to artemisinin drugs by *P. falciparum* in French Guiana. The situation is less severe in neighboring countries.

**More than 22,000** strains sequenced in 2018, 73% for foodborne infection surveillance

**3** non-Institut Pasteur CNRs made use of the P2M platform, now open to external CNRs

**98%** an extremely high performance rate for P2M, confirming that quality sequences can be obtained in just a few days

## 14 NATIONAL REFERENCE CENTERS

- Anaerobic bacteria and botulism
- Whooping cough and other Bordetella infections
- Corynebacteria of the diphtheriae complex
- Escherichia coli, Shigella, Salmonella
- Viral hemorrhagic fevers
- Hantaviruses
- Leptospirosis
- Listeria
- Meningococci and Haemophilus influenzae
- Invasive mycoses and antifungals
- Plague and other Yersinia infections
- Rabies
- Vibrios and Cholera
- Respiratory viruses (including influenza)

## 2019-2023 STRATEGIC PLAN: PROSPECTS FOR CNRs

1. Step up links between the diagnostics activities of National Reference Centers and the basic research carried out in the research units.
2. Continue raising awareness of these activities among the general public.
3. Reflect on how the organizational setup and business model of CNRs should develop in line with the development of the Institut Pasteur's service platforms.
4. Share the experience of the P2M platform with health authorities to consolidate the model and make it a pilot for similar structures at national and international level.
5. Boost research potential by applying to host CNRs for the next term (from 2022) in areas related to the Institut Pasteur's strategic priorities.

# Medical Center (CMIP)

**The Institut Pasteur Medical Center (CMIP) is where the Institut Pasteur comes into direct contact with patients in Paris. It offers a range of services including a vaccination center; consultations for infectious and tropical diseases, travel medicine and allergies; and an Anti-Rabies Center. In 2018 it was awarded ISO 9001 v2015 certification.**

The Institut Pasteur International Vaccination Center (CVI) is a leading center for people traveling to countries with a different environment and health and hygiene conditions. It has an outstanding reputation and attracts high numbers of people seeking vaccinations and specific information for trips abroad.

## VACCINATIONS AND TRAVEL MEDICINE

Two categories of travelers make use of the International Vaccination Center and the travel clinic: those who attend privately prior to family holidays or trips abroad, and those from public institutions, companies and especially NGOs going on foreign business trips, who come on the basis of contracts concluded with the Institut Pasteur. These travelers are seen before their departure and sometimes also when they return to France. Travel medicine is often closely linked with recent outbreaks of emerging infectious diseases at the international level, an area in which the Medical Center's expertise is widely recognized. This was the case in late 2018, when an Ebola virus outbreak occurred in the Democratic Republic of the Congo. Many of the humanitarian volunteers traveling to the country were treated at the CMIP before setting off.

## CONSULTATIONS

As well as providing vaccinations and advice for travelers, especially vulnerable patients (those with HIV, organ transplants or other immune deficiencies) and humanitarian aid workers, much of the Medical Center's work involves managing diseases imported by returning travelers (malaria, dengue, rickettsial infections, leishmaniasis, amebiasis, etc.), HIV or hepatitis virus infection, and widespread infectious diseases such as Lyme disease. Some of these conditions are monitored in collaboration with Necker-Enfants Malades Hospital, via the Necker-Pasteur Infectiology Center (CINP). Most of the physicians from the Infectious and Tropical Diseases Department at Necker Hospital hold clinics at the CMIP, alongside physicians from the Institut Pasteur. Their work includes treating a high caseload of patients infected with HIV or viral hepatitis, which also serves as the basis for clinical research.

One focus of the Medical Center is dermatology, especially hidradenitis suppurativa. The CMIP monitors a large number of patients and is internationally recognized for its expertise in this condition. The Anti-Rabies Center treats patients that have been exposed to the rabies virus (through a bite, a scratch, the licking of a wound or a mucous membrane), usually during a trip abroad. The multidisciplinary allergy team has expertise in all types of allergies.

## What they have to say about us

*"As a humanitarian aid worker, it's very reassuring to be monitored before and after my field missions by such knowledgeable, dedicated doctors, who recognize any medical conditions and related diseases. Well done, and thank you!"*

*"I would like to commend you for your vaccination service. I know the Institut Pasteur and I have been coming for the past 30 years to update my immunizations so that I can travel all over the world knowing that I am completely safe. That's something you can't put a price on! The actual cost is very reasonable and I'm more than happy to pay it. Well done for all the lives you are saving. I'm proud of my country and the Institut Pasteur!"*

**Word-for-word accounts (originally in French) from forms filled out by Medical Center users as part of ongoing efforts to improve the quality of service and treatment offered to patients.**

## CLINICAL RESEARCH

The Medical Center is involved in clinical research in its areas of medical specialization: cohorts in the field of HIV infection, most often in conjunction with the French Agency for Research on AIDS and Viral Hepatitis (ANRS); the pathophysiology of hidradenitis suppurativa (genetics and immunology, in collaboration with the ICAReB platform, Institut Pasteur research units and Necker Hospital); and allergies (research on the immune phenotypes of patients with allergies to wasp stings or penicillin, in cooperation with an Institut Pasteur research unit). In 2018, a proposal for a comparative therapeutic trial for hidradenitis suppurativa was submitted and accepted. The aim is to endorse the treatment currently recommended by the CMIP's dermatologists. It is due to begin at the end of 2019.

Finally, a retrospective study published in 2018 demonstrated good tolerance and a satisfactory immune response to yellow fever vaccination following bone marrow transplantation, a situation for which very little data had previously been published.
The new insights generated by these projects fully justify the CMIP's role within the Center for Translational Science and the future Vaccinology Center envisaged in the new Strategic Plan.

### 2019-2023 STRATEGIC PLAN: A KEY ROLE FOR THE CMIP

Draw on the expertise of the International Vaccination Center as part of efforts to pool strengths in the field of vaccinology, involving immunologists, microbiologists, epidemiologists and vaccine specialists, and the Cochin-Pasteur Vaccinology Clinical Investigation Center (CIC).

**71,000** vaccines administered

**53,000** visits to the International Vaccination Center (CVI)

**12,000** consultations for infectious and tropical diseases and travel medicine

**3,300** consultations at the Anti-Rabies Center

**2,700** consultations for allergies

# Innovation

**The Institut Pasteur is at the forefront of innovation. It is constantly developing applications for its research and pursuing its mission of technology maturation and transfer through industrial partnerships, start-ups and invention disclosures.**

*We cannot separate basic research from research applications," said Louis Pasteur. The Institut Pasteur embodies this reality, proving that advancing the boundaries of science and serving contemporary society are one and the same thing. For the Institut Pasteur's scientists, technology transfer is a perfectly logical way of improving human health – the 290 industrial contracts signed by the Institut Pasteur in 2018 and the 31 companies set up since 1997 based on discoveries from its laboratories speak for themselves. The Institut Pasteur fosters this culture of application by hosting start-ups on its Paris campus and developing research partnerships at its Carnot Institute, a highly effective structure whose funding I will be increasing once again in 2019."*

**JÉRÔME SALOMON,**
French Director-General for Health
**Closing ceremony for the Institut Pasteur's 130th anniversary on November 13, 2018**

# Research applications **and technology transfer**

**The Research Applications and Industrial Relations Department (DARRI) develops applications for the Institut Pasteur's research. It works with industry partners in France and worldwide to detect, promote, support, protect and transfer inventions arising from scientific findings.**

In developing research applications and transferring technological solutions to industry, the Institut Pasteur is able to respond to global public health challenges and also to secure part of its funding. Novel vaccine and therapeutic approaches are vital in tackling the challenge of antimicrobial resistance and embracing the potential of theranostics and precision medicine. With its high-caliber research teams, strategic industrial partnerships and new start-ups, the Institut Pasteur plays a leading role in technology transfer.
The Research Applications and Industrial Relations Department (DARRI) is pursuing an effective strategy. Its teams are constantly developing their expertise to support every stage of the innovation process, enabling initial ideas to become mature inventions and ultimately to result in new medical solutions and products being brought to market.
Industry partnerships are a source of short-term income for the Institut Pasteur, with the potential to generate long-term income from R&D cooperation and license revenue.

## INTELLECTUAL PROPERTY – A KEY STRATEGIC ISSUE

In 2018, the rate of innovation remained high, with 57 invention disclosures registered, resulting in 19 new priority patents being filed and 32 provisional applications (software, expertise and biological material). One major event was the settlement of the litigation proceedings initiated in 2017 between the Institut Pasteur/Bio-Rad and Abbott/Alere over the strategic portfolio of HIV2 patents in the United States. The resolution of this dispute with a settlement agreement will enable the Institut Pasteur to continue receiving royalties from HIV2 and HIV1+2 immunological diagnostic kits until the US patents expire. The favorable conclusion of this case demonstrates the lengths the Institut Pasteur is willing to go to to defend its industrial property rights and generate funding for its research.

## NEW INNOVATION DEPARTMENT

The aim of the new Innovation Department is to identify Institut Pasteur inventions with the long-term potential to provide solutions for patients, and to identify the phases needed for their successful development, which systematically involves bringing products to market. In the current climate, especially when it comes to less profitable markets, inventions often need to be taken a step further before they can be transferred to industry or attract venture capitalists. The department's scientists, with their extensive experience in industrial R&D, can spearhead this maturation process at the Institut Pasteur. The department also offers guidance for scientists looking for external funding for these development phases. In 2018, a support framework for development projects related to technologies and vaccines was set up. This has already given rise to considerable success for two development programs, one for the Lassa vaccine based on the measles vector, carried out with the company Themis, to be funded by the Coalition for Epidemic Preparedness Innovations (CEPI), and the other for the Shigella vaccine, funded by the Bill and Melinda Gates Foundation.
Identifying new opportunities involves fostering an ongoing two-way dialog with scientists. At the Institut Pasteur, a proactive approach based on a thorough understanding of basic research can reveal opportunities to turn new findings into applications with a major impact on society. The department also works closely with the business development team to identify the needs and expectations of industry partners, enabling the Institut Pasteur to propose targeted scientific partnerships and ambitious development plans.

**57** **invention disclosures**

**19** **new priority patents and 32 provisional applications**

**290** **industrial contracts signed in 2018 (a 40% increase)**

**254** **industrial contracts in place**

## DEVELOPING NEW PARTNERSHIPS

In the Technology Transfer & Entrepreneurship Department, the joint activities of the two strategic divisions, Business Development and Contract Negotiations, have resulted in:
- **a 40% increase in the number of contracts signed** this year with industry partners;
- **discussions on a new process for creating and supporting spin-offs** based on the Institut Pasteur's research, which will be introduced in 2019. The spin-off Neurophoenix, led by scientist Monique Lafon, was also set up with the aim of developing innovative therapeutic solutions to treat neurodegenerative diseases, especially sensory disorders *(see inset)*.


## What they have to say about us

*"The biotech company Neurophoenix was launched from the Viral Neuro-Immunology Unit in the Institut Pasteur's Virology Department in August 2018. We are proud to draw on the Institut Pasteur's expertise and outstanding research. The aim of the company is to develop a drug candidate to treat optic neuropathies based on a molecule from a virus that has the remarkable property of reactivating survival mechanisms and regenerating damaged neurons."*

**Tom Shepherd, co-founder of the start-up Neurophoenix**

## PASTEUR MICROBES AND HEALTH CARNOT INSTITUTE

Carnot Institutes are public research bodies recognized by the French Ministry of Research for their commitment to developing R&D that drives industrial innovation. The main objectives of the Pasteur Microbes and Health Carnot Institute, composed of six Institut Pasteur departments (Cell Biology and Infection, Infection and Epidemiology, Microbiology, Parasites and Insect Vectors, Virology and Mycology) are to support research into the impact of microbes on health, and to encourage the industrial development of innovative products in the areas of therapeutics, diagnostics and vaccines.

In 2018, the Pasteur Microbes and Health Carnot Institute identified and supported long-term biology and technology projects with potential for applications, and provided funding for maturation programs and interdisciplinary projects, especially with the France Futur Elevage Carnot Institute. In line with the Institut Pasteur's new strategic priorities, the Carnot Institute is focusing on the development of professional skills to encourage public-private technology transfer.

The Neurophoenix start-up project, supported by Pasteur Microbes and Health for several years, was launched in 2018. Based on research conducted in the Viral Neuro-Immunology laboratory led by Dr. Monique Lafon, Neurophoenix is developing an innovative molecule with neuroprotective and neuroregenerative properties. Its aim is to develop a therapeutic treatment for optic neuropathies such as glaucoma.

In addition to R&D cooperation with our long-standing partners (Sanofi, Sanofi Pasteur, bioMérieux, Bio-Rad and Moderna), several promising new industrial agreements were concluded in 2018.

- A new collaboration agreement was signed for the creation of an Organs-on-Chips center in the Biomaterials and Microfluidics Technological Platform led by Samy Gobaa. This partnership will give scientists privileged access to Emulate technology with the aim of developing novel cell assays that mimic the physiology of human organs.
- In acquiring the Institut Pasteur start-up Axenis, Genoway became an exclusive Institut Pasteur licensee for the use of several humanized mouse lines. Alongside this license, a cooperation agreement is currently being finalized for the improvement and development of new humanized mouse models, especially for infectious diseases and liver disease, in collaboration with the laboratory led by Professor James Di Santo.
- Professor Christine Petit's internationally recognized expertise in the physiology and molecular pathophysiology of the auditory system has led to the signing of a letter of intent by the Institut Pasteur and Sensorion which provides for collaboration on several research programs with the aim of developing and marketing gene therapy drug candidates to restore, treat and prevent hearing problems.

### CONSOLIDATING KEY PARTNERSHIPS

- Following the framework agreement signed with Hoffmann-La Roche in 2017 to facilitate cooperation with the group's companies (Genentech, Roche Pharma and the Roche Institute), a further R&D collaboration agreement was signed between Hugo Mouquet's laboratory and Roche Pharma for the development of novel immunotherapy approaches to treat hepatitis B. A second agreement on neurology is set to be signed, and talks are being held with Genentech to explore shared areas of interest.
- Two epidemiological studies with long-standing partner Sanofi Pasteur have been launched in Africa, the first in Côte d'Ivoire to analyze whooping cough vaccine coverage in collaboration with Fabien Taïeb, and the second to determine the etiological agents of pediatric acute bacterial meningitis and the distribution of *Neisseria meningitidis* serogroups in Algeria, Morocco and Tunisia, in close collaboration with scientist Muhamed-Kheir Taha.
- A call for tenders for vaccine development launched by CEPI boosted the Institut Pasteur's existing partnership with Themis Bio for measles vector-based vaccines (licensed from the Institut Pasteur), with a new cooperation agreement for the development of a Lassa virus vaccine candidate in collaboration with Sylvain Baize's team.



- The Institut Pasteur has worked closely with Meiji since 2011 and is actively pursuing this partnership to elucidate the immunomodulating properties of probiotic bacteria, which play a key role in stimulating the immune system, in collaboration with the laboratories led by Gérard Eberl and Ivo Boneca.

### OUR LICENSED PARTNERS CONTINUE THEIR CLINICAL TRIALS

In connection with a collaborative research project launched in 2011, followed by an exclusive license granted by the Institut Pasteur in 2014, the STRAGEN group announced this year that it had enrolled its first patient in the phase I clinical trial of STR-324, a non-opioid painkiller discovered by Catherine Rougeot's teams.
A partnership launched in 2011 with FERRING Pharmaceuticals culminated in FDA approval in 2018 to start phase I clinical trials on treating inflammatory gut conditions with a phage cocktail developed with Laurent Debarbieux's team.
The development of measles vector technology led to excellent phase II results for partner Themis Bio with the vaccine for chikungunya, a mosquito-borne disease for which there are currently no treatment or prevention options.

## PROGRESS IN BIOASTER

BIOASTER, set up in 2012 by the Institut Pasteur and the Lyon-biopôle competitiveness health cluster, develops and applies technological innovations in microbiology that meet industry needs, with the aim of boosting the development of medical and nutritional solutions for human and animal health.
The founders, a group initially composed of Sanofi-Pasteur, the Institut Mérieux and Danone Nutricia Research, were joined by bioMérieux and Boehringer Ingelheim in 2018, demonstrating BIOASTER's attractiveness for industry. Following a proposal by the Institut Pasteur, the University of Lyon also joined the founders as an academic partner to boost BIOASTER's visibility at its two sites, Paris and Lyon.

Cooperation with the Institut Pasteur was stepped up in 2018 with joint participation in consortia for large-scale EU calls for proposals with the potential to fund collaborative research for several years on topics such as tuberculosis.

### 2019-2023 STRATEGIC PLAN: DEVELOP TEACHING PROGRAMS IN LINE WITH SCIENTIFIC PRIORITIES

1. Foster closer cross-disciplinary involvement in the development of research applications among scientists on campus and all relevant stakeholders.
2. Set up a Consultative Innovation Committee and appoint business development correspondents in the departments and centers.
3. Pursue a more proactive policy to detect and support innovative projects.
4. Identify innovative solutions to get external stakeholders (investment funds, industry partners, Bpifrance investment bank, etc.) involved in all stages of the innovation process, especially the upstream phase (proof of concept).
5. Support start-up projects before they get off the ground.
6. Develop partnerships with incubators so that they can take over as soon as start-ups reach setup phase.
7. Create spin-offs.

# Education

**On the Institut Pasteur campus, a cosmopolitan community of Master's and PhD students, and healthcare professionals, receive state-of-the-art scientific and medical teaching. The aim is to train up a new generation of scientists who are actively engaged in global public health issues.**

*"Without researchers, there would be no research. Defending research is also, crucially, about inspiring young people, providing them with outstanding teaching and giving them the opportunity to thrive in a profession that, while very challenging, is incredibly rewarding. Education and training have always been an essential part of the Institut Pasteur's activities. We continue to rely on public support to fulfill this mission and train up new generations of scientists who will advance the frontiers of science for the benefit of human health. I sincerely hope that one day they may become Nobel laureates themselves."*

**FRANÇOISE BARRÉ-SINOUSSI,**
Laureate of the 2008 Nobel Prize in Medicine for her identification of HIV at the Institut Pasteur in 1983
**October 10, 2018, ten years after the announcement of her Nobel Prize win (October 6, 2008)**

# Transferring and sharing **scientific knowledge**

**Education and training are an essential part of the Institut Pasteur's activities, continuing the legacy of its founder, Louis Pasteur. For the past 130 years, ever since the first microbiology course taught by Émile Roux in 1889, the Institut Pasteur has played a key role in teaching life sciences at the international level.**

Each year, over 1,200 students, PhD students and healthcare professionals from around 70 countries attend one of the 60 courses and workshops run at the Institut Pasteur in Paris or at one of the 32 institutes in the Institut Pasteur International Network. More than 600 young scientists (300 PhD students and 300 Master's students) also receive training at laboratories on the Paris campus, where they complete their undergraduate, Master's and PhD research projects.

## A UNIQUE SETTING FOR TRAINING IN SCIENCE AND RESEARCH

The Institut Pasteur's reputation for excellence in research provides a unique, hands-on environment for young French and international scientists, who come to complete internships from undergraduate to PhD level in its laboratories. 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 (including Paris Descartes and Paris Diderot universities – which together formed the Université de Paris in 2019 –, Paris-Saclay and Paris Sciences & Lettres universities, the Institut Curie, the CNRS and Inserm) and at the international level. The regular involvement of expert scientists in Institut Pasteur courses is pivotal to the success of our teaching, giving students access to the very latest developments in research, especially in life sciences and public health. Experimentation and practical work are a particular strong point of the Institut Pasteur's educational approach, setting it apart from other institutions. The development of the Institut Pasteur International Network has had a major impact on teaching, in terms of both the scientific subjects taught and the international makeup of the students.
The Institut Pasteur is constantly striving to consolidate its reputation and enhance its teaching by placing more emphasis on online courses (MOOCs[1] and SPOCs[2]), opening up courses to younger students, encouraging multidisciplinarity and links with medicine, and promoting entrepreneurship and business development.

## ONLINE COURSES IN LIFE SCIENCES AND HEALTH

The Institut Pasteur develops online teaching activities as a way of extending the reach of the courses taught at its Education Center or at institutes in the International Network. In 2018, just three years after the distribution of its first MOOCs, the Institut Pasteur launched 15 online courses in life sciences and/or health which proved hugely successful in terms of numbers (1,500 to 4,800 students enrolled per session) and international visibility (95 to 151 countries). To promote its MOOCs in China, the Institut Pasteur signed an agreement with a Chinese distribution platform, XuetangX, via the France Université Numérique (FUN) platform. At the Institut Pasteur, MOOCs have now taken over from CNAM video lectures as the main way of distributing recorded content.

**300** **PhD students on the Institut Pasteur's Paris campus**

Four new MOOCs, developed in 2018, were launched in late 2018 and early 2019: HIV Science (4,455 learners), Viruses and Human Cancers (3,020 learners so far), Advances in Stem Cell Biology (launched on February 18, 2019) and Medical Entomology (launched on March 18, 2019). The first three are brand new courses, but the Medical Entomology course is an updated version of one of the Institut Pasteur's most internationally successful MOOCs.
In 2019, four MOOCs will be produced: a complete update of the Vaccinology MOOC first distributed in 2015, and MOOCs on Epigenetics, Human Population and Evolutionary Genetics, and Emerging and Re-emerging Viruses. The Resistance to Antibacterial Agents MOOC, distributed via FUN in 2018, was also accepted for distribution on XuetangX, the leading Chinese MOOC platform. Through its MOOCs, the Institut Pasteur is able to share scientific knowledge in virtually all its areas of expertise with an international audience.
The Institut Pasteur currently produces 24% of the life science MOOCs and 20% of the health MOOCs available on the FUN platform. In these two fields, the Institut Pasteur is the leading MOOC creator in France.

The Institut Pasteur MOOC team has developed an effective approach by setting clear guidelines, responding to student feedback and organizing virtual meetings that are attended by students from all over the world. Online teaching is a way of developing new courses without the need for instructor-led sessions. It has the potential to become a key part of a "flipped classroom" approach, whereby students learn theoretical background via MOOCs and only come to the Institut Pasteur for lab work or to explore specific concepts in more depth in small groups.

*1. MOOC – massive open online course. 2. SPOC – small private online course.*



Just like in research, the Institut Pasteur is also leading the way in innovative teaching approaches.

## PROGRAMS FOR INTERNATIONAL UNDERGRADUATE AND MASTER'S STUDENTS

The Institut Pasteur is keen to offer more training for students at earlier stages in their academic career. Several predoctoral programs have been developed at undergraduate and Master's level for students from all over the world. The Amgen Scholars Program, for example, gives around 20 students from European universities and higher education institutions the opportunity to 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 has partnerships with several European universities and hosts interns via the EU's Erasmus+ program. Following recent agreements concluded with Columbia, Stanford and South Florida universities in the United States and the University of Cambridge in the UK, it also welcomes Master's students from these universities. A program run by the Pasteur Foundation gives five or six undergraduate students from the US the opportunity to carry out research placements at the Institut Pasteur every summer.
The Institut Pasteur set up its own International Genetically Engineered Machine (iGEM) team in 2015 as a way of varying its predoctoral courses and consolidating its position at the forefront of innovation in synthetic biology. Since the Massachusetts Institute of Technology (MIT) launched the iGEM competition in 2004, teams worldwide have competed to develop the most innovative synthetic biology projects. The 2018 Institut Pasteur team was composed of

## What they have to say about us

*"The Institut Pasteur is one of France's leading producers of MOOCs in life sciences and health, with scientific content aimed at specialists and professionals. In the space of just four years, it has become a key player in online life sciences teaching in France. Through its MOOCs, it is able to reach a huge number of learners from a wide range of countries."*

**Catherine Mongenet, Director of France Université Numérique (FUN)**

FUN FRANCE UNIVERSITÉ NUMÉRIQUE

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 the partnership with Sorbonne and Paris Diderot universities, the program has been boosted by new links with ESPCI Paris, ENSCI-Les Ateliers design school, the Faculty of Law at Paris-Sud University, Central Supélec, Chimie ParisTech and the École Polytechnique.

## 2018 PPU YEAR GROUP NAMED AFTER CHEMIST THÉRÈSE TRÉFOUËL

The 2018 "Tréfouël" year group, the tenth since the Institut Pasteur's PPU program was set up, was composed of 14 students: seven from Europe (Croatia, Denmark, France, Germany, Russia, Switzerland and the United Kingdom), four from North and South America (Argentina, Canada, the United States and Uruguay) and three from Asia (China). A higher proportion of European PhD students were selected compared with previous years.
The Welcome Day for this year group was a chance to celebrate the 10th anniversary of the PPU program and look back over its highlights:
- 117 PhD students supervised (66 completed their PhD at PPU),
- two satellite programs set up in 2016: PPU-CNBG (China National Biotec Group) and PPU-EMHE (Enhancing Mobility Between Latin-American and Caribbean Countries and Europe),
- significant EU co-funding secured for the 2016 and 2017 year groups, in addition to other one-off funding,
- prestigious international awards won by PPU PhD students (five in 2017 and two in 2018).

Once again in 2018, the students worked in a variety of disciplines, coming together for joint activities such as seminars, oral presentations and the annual retreat, guided by a dedicated scientific committee. Several activities were open to all PhD students on campus, confirming the role of the PPU program as a framework for testing novel teaching approaches.

## TRAINING THROUGH RESEARCH FOR PHD STUDENTS

With 130 research units in Paris and a network of 32 institutes worldwide, the Institut Pasteur is a higher-education hotspot for many young scientists. Each year, around 85 PhD students complete their studies in laboratories on the Paris campus. Students may be eligible for funding from their home university, from the laboratories themselves under regional, national or European funding programs, from non-governmental organizations or via the Institut Pasteur's International Doctoral Program *(see inset)*. The Institut Pasteur offers scientific supervision for PhD students through thesis committees, as well as personal support with a post-doctoral tutoring and career development program.

**1,200** **students each year on the Paris campus and in the International Network**

The Institut Pasteur in Paris runs specific PhD programs, like the Pasteur-Paris University (PPU) international doctoral program, open to students with a Master's degree (or equivalent) from a non-French university who 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 and Paris-Diderot universities (which formed the Université de Paris in 2019), Sorbonne University and Université Paris-Saclay (since 2015). The three-year program, led by Susanna Celli since November 2015, culminates in a PhD from a French university.

Each year, the Institut Pasteur Department of International Affairs also awards 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 in a doctoral school at a French or non-French university.

The Institut Pasteur, Institut Curie and École Normale Supérieure (ENS) are continuing their "Médecine-Sciences" program, which reflects the major changes in medical practice and biomedical research brought about by scientific and technological progress. The program was set up in 2015 to train up a body of professionals with both scientific and medical expertise. It offers an advanced dual curriculum in medicine and science, including an introduction to research. Students are recruited through a competitive examination at the end of their second year of medical or pharmacy studies. The program offers comprehensive interdisciplinary training, top quality teaching, lectures and internships. The many advantages include guaranteed funding for the first three years, expert scientific and medical supervision, a prestigious ENS qualification and a PhD in Science. Graduates of the Médecine-Sciences program can enjoy excellent career prospects in academia or the healthcare industry, in France or at the international level.



## TRAINING IN RESEARCH APPLICATIONS AND SCIENTIFIC ENTREPRENEURSHIP

In keeping with its vocation, the Institut Pasteur has always been committed to finding applications for its research, and this is reflected in its teaching. To this end, several initiatives were developed during 2018, including the "Creating your own company" series, now the Startup Breakfast – informal monthly events for Institut Pasteur scientists interested in business development, with guest speakers including successful biotechnology entrepreneurs, funding bodies or heads of business incubators –, and a start-up workshop in July 2018 with practical sessions on specific projects led by junior Institut Pasteur scientists.
Over the years, the Institut Pasteur has developed highly structured teaching activities at the local, national and international level, enhanced by the involvement of leading experts and professionals. The courses and undergraduate and continuing training on offer at the Institut Pasteur enjoy an outstanding international reputation, attracting promising young scientists from all over the world and helping to build an international network of researchers. The Institut Pasteur trains these young scientists in basic research, while also providing guidance in business development and company creation.

## TO FIND OUT MORE:
## WWW.PASTEUR.FR/EN/EDUCATION

## 2019-2023 STRATEGIC PLAN: TEACHING ACTIVITIES THAT REFLECT SCIENTIFIC PRIORITIES

The Institut Pasteur has identified seven broad measures in the areas of teaching and training:

1. Set up courses that reflect the Institut Pasteur's scientific priorities.
2. Produce three MOOCs per year.
3. Set up a digital Pasteur diploma in public health.
4. Expand the distribution of MOOCs and related partnerships to strategic regions (Africa and China).
5. Increase the revenue of the Institut Pasteur International Doctoral Program (foundations, EU funds, sponsorship, LabEx).
6. Host two students from the "Médecine-Sciences" program each year as interns or as part of their PhD.

# Cooperation

**The Institut Pasteur International Network is composed of 32 institutes united by Pasteurian values and missions in the service of public health. This unique network is an outstanding base for the development of international scientific cooperation.**

*One thing that makes the Institut Pasteur unique is its international reach. This approach goes right back to its early days; the institute had been in existence for just three years when it opened a center in Vietnam to provide vaccinations against rabies and smallpox for the local people. Two institutes were soon opened in Africa – in Madagascar in 1900 and Tunisia in 1905. The Institut Pasteur International Network is currently composed of 32 institutes in 25 countries on every continent. Its departments are united by a sole mission: to advance international research on infectious diseases and the ability to overcome them. It is for all these reasons that, in my view, the Institut Pasteur is ideally placed to show the way and tackle the major global challenges facing us in the 21st century, for the benefit of human health."*

**TREVOR MUNDEL,**
President of Global Health at the Bill & Melinda Gates Foundation
**Ceremony to mark the Institut Pasteur's 130th anniversary on November 13, 2018**

# International highlights **of 2018**

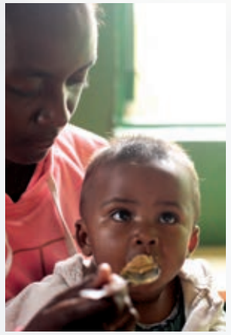

## JANUARY

**Twelve new species of *Leptospira* discovered in New Caledonian soils** 1
A group of researchers from the Institut Pasteur International Network coordinated by the Institut Pasteur de Nouvelle-Calédonie described 12 new species of the genus *Leptospira*. Leptospirosis is a re-emerging zoonosis that affects over one million people and claims close to 60,000 lives a year worldwide.

**A platform for malaria infections in vector Anopheles in Madagascar** 2
A new platform for *Plasmodium falciparum* and *Plasmodium vivax* infection in Anopheles was set up in the northwest of the island, an area with medium to high prevalence of malaria. The platform operates from November to May and plans to analyze the vector competence of malaria-carrying Anopheles populations.

## FEBRUARY

**Initial findings of the BIRDY project on the incidence of neonatal infections**
In 2012, the Institut Pasteur in Paris and the Institut Pasteur de Madagascar launched the BIRDY program to document neonatal infections in the community and assess the status of antibiotic resistance. The initial findings, released in February 2018, show an extremely high incidence of these infections, i.e. 40 times greater than the rate observed in the US.



## MARCH

**Global mapping of Zika virus mosquito vectors**
A group of entomologists from five institutes in the Institut Pasteur International Network (Institut Pasteur in Paris, Institut Pasteur du Cambodge, Institut Pasteur de Nouvelle-Calédonie, Fiocruz, Institut Pasteur de Dakar) published a review of the literature on the main vectors of the Zika virus in urban and sylvatic (jungle) areas on all continents, in *Microbes and Infections*.

**Scientists from the Institut Pasteur de Lille investigate the origins of the BCG**
Almost 100 years after Albert Calmette and Camille Guérin discovered the BCG, scientists from the Institut Pasteur de Lille (Inserm, CNRS, University of Lille) opened tubes containing the original strains to sequence the genome. Their aim is to advance knowledge and develop a new, more effective, vaccine against tuberculosis.

Discovery · Scientific event · Public health · Event · Award

## APRIL

**Inauguration of Sciensano, a One Health research institute in Belgium** 3
Resulting from the merger between the former Scientific Institute of Public Health (ISP, member of the Institut Pasteur International Network) and the Veterinary and Agrochemical Research Center (CERVA), Sciensano entered the Belgian public health arena on April 1, 2018. Its work is guided by the inextricable link between human and animal health and their environments.

**The WHO recommends the Institut Pasteur du Cambodge vaccination regimen against rabies** 4
On the basis of immunogenicity and clinical efficacy data, the World Health Organization (WHO) recommends the Institut Pasteur du Cambodge's post-exposure rabies vaccination regimen, which is based on three appointments including two intradermal injections on days 0, 3 and 7. The Institut Pasteur du Cambodge opened its second rabies prevention center in Battambang in July 2018 in collaboration with the Battambang provincial health department with the aim of vaccinating 10,000 bitten people per year.

## MAY

**A Pasteur-USP platform in Brazil to combat neurological disorders** 5
A group of scientists set up an initial research team in Brazil following the University of São Paulo/Institut Pasteur/Fiocruz tripartite agreement signed in 2015. This scientific platform will use a One Health approach to address neurological disorders caused by either infectious agents or degenerative/ progressive diseases.

**Launch of the H2020 LeiSHield-MATI project in Tunis** 6
This project, coordinated by the Institut Pasteur in Paris, is funded by the European H2020 program and focuses on cutaneous leishmaniasis. It aims to improve scientific knowledge of parasite-vector-host interactions and develop new preventive and therapeutic measures. Four institutes in the Institut Pasteur International Network (Algeria, Morocco, Tunis and Iran) are partnering the project.

## MOBILITY AND EXCHANGE PROGRAMS BETWEEN INSTITUT PASTEUR INTERNATIONAL NETWORK SCIENTISTS

**55 network scientists**
received training through the Calmette & Yersin program; among them were 2 post-doctoral fellows and 14 PhD students

**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

**12 internships**
for young French researchers in the International Network funded by the Pierre Ledoux-Jeunesse Internationale Foundation

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

**3 4-year research**
groups (G4)

**10 international courses**
funded by the Pasteur International Network Association

# International highlights **of 2018**


## JULY

**Cooperation in Hong Kong to set up a biomedical research center** 1
The University of Hong Kong, the Institut Pasteur in Paris, and Hong Kong Science and Technology Parks Corporation signed a memorandum of understanding in Paris to create a joint biomedical research center under the direction of a high-level delegation chaired by Carrie Lam, Chief Executive of Hong Kong, and Nicholas W Yang, Secretary for Innovation and Technology.

## AUGUST

**Chronic malnutrition in children – a new gut microbial signature**
The Afribiota project, led by several member institutes of the Institut Pasteur International Network (Paris, Madagascar and Bangui) aims to advance understanding of the underlying mechanisms of chronic malnutrition. Scientists revealed the existence of a microbial signature in the gut of malnourished children, characterized by the unexpected and widespread presence of bacteria that are normally found in the nose and mouth.

## SEPTEMBER

**12 years of collaboration with the US DHHS regarding surveillance and response to outbreaks**
With the support of the US Department of Health and Human Services (DHHS) via the ASIDE (Alerting and Surveillance for Infectious Disease Epidemics) project, the Institut Pasteur in Paris and the Institut Pasteur International Network support public health infrastructures in six countries in Africa and South-East Asia to develop and boost their ability to prepare for and respond to outbreaks of influenza and emerging and re-emerging infectious diseases, in application of the International Health Regulations (2005).
During a meeting held in Washington D.C. in September 2018, the various parties took stock of the 12 years of partnership and considered the future of their collaboration.

## NOVEMBER

**The Institut Pasteur de Guinée opens its first laboratory in Conakry** 2
The first laboratory at the Institut Pasteur de Guinée was officially opened on October 22, 2018 at a ceremony attended by four Guinean government ministers and the French Ambassador to Guinea and Sierra Leone. Housed free of charge at Gamal Abdel Nasser University of Conakry, the Pasteur Laboratory will mainly focus on public health, monitoring and research activities. With the support of the French Ministry of Europe and Foreign Affairs and the Expertise France agency, in connection with the LAB-NET program, a 230m$^2$ space has been turned into a modern training and research center for the benefit of Guinea. This laboratory, which has expertise in molecular diagnosis of emerging pathogens, will support the national network of laboratories.

**Didier Koumavi Ekouevi won the 2018 Dedonder-Clayton Award**
During the 4$^{th}$ Institut Pasteur International Network symposium, Dr. Didier Koumavi Ekouevi was presented with the 2018 Dedonder-Clayton Award. Dr. Ekouevi is head of the Department of Public Health at the University of Lomé (Togo) and was congratulated on his research on the epidemiology of human papillomavirus infection and sexually transmitted infections associated with the virus, as well as for his studies on HIV in Africa.

**Combating Resistance: microbes and vectors symposium** 3
The 4$^{th}$ Institut Pasteur International Network symposium, held at the Institut Pasteur (Paris) on November 15 and 16, 2018, was attended by close to 350 delegates from all over the world. The program included various talks on the theme of microbial and vector resistance given by members from all over the network. The annual Council of the Directors of the Institut Pasteur International Network took place beforehand from November 13 to 14, 2018 in Paris. Over two days, representatives from the 32 member institutes discussed the main areas of development for the International Network.

## DECEMBER

**Partnership to rebuild the National Health Laboratory in Myanmar**
The French Development Agency (AFD), the Institut Pasteur and the Mérieux Foundation joined forces for a €27 million national reference biosafety laboratory in Rangoon, Myanmar (Burma). The laboratory will strengthen diagnostic capabilities, improving protection against outbreaks and emerging diseases for the local population, especially vulnerable groups. The AFD and the Institut Pasteur signed a €5 million EU grant delegation agreement for the Institut Pasteur on December 21, 2018, and an MoU for the project was concluded between the Mérieux Foundation and the AFD.

Discovery | Scientific event | Public health | Event | Award

# Support

**Public generosity has always been crucial to the Institut Pasteur's success. And the Institut Pasteur is committed to optimizing its resources to support scientists and pursue a stable, human-centered business model that will underpin its long-term development.**

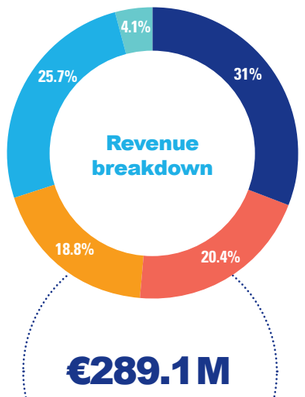
*When I was 24, I came to the Institut Pasteur Vaccination Center before going on a trip abroad. On my way out, as I went through the gate, I said to my husband – and I remember it as if it were this morning – "If we don't have any children, this place will become our child." And the decision we made that day was one that we have never once regretted. We have done our absolute utmost to honor the promise that we made. We were desperate to do something, to give our lives a purpose. I feel honored and overjoyed, because the Institut Pasteur is universally recognized for its outstanding contribution to improving health for everyone, everywhere."*

**ANDRÉE GILLOT,**
Institut Pasteur donor, whose generous contribution helped fund the Omics building, a new facility to explore the potential of big data
**Inauguration of the Omics building on September 13, 2018. On that day, Andrée Gillot celebrated her 94th birthday**

# Financial review of 2018

**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.**

## RESOURCES




As indicated in the Institut Pasteur 2018 *Use of resources* statement, the revenues reported in the profit-and-loss account amounted to €289.1 million, with the following breakdown.

**€89.6 M Public fundraising**
*Donations and legacies collected directly and earnings from assets and real estate derived from public donations*

**€58.9 M Public subsidies**
*Grant from the French Ministry of Higher Education, Research and Innovation and funding for the 14 National Reference Centers managed by the Institut Pasteur, which is provided by Santé publique France*

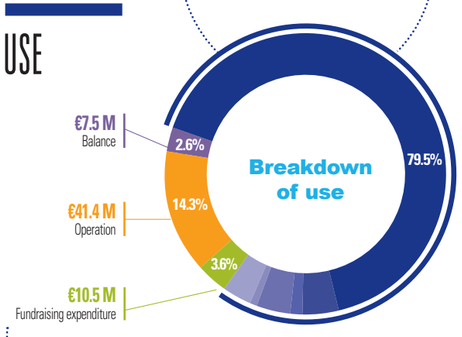
**€54.4 M Other public funding**
*Research contracts from public funding bodies*

**€74.3 M Own revenue**
*Industrial revenue (€29.1 M), sales and services (€16.2 M), other financial revenue (€23.6 M), other revenues (€5.4 M)*

**€11.8 M Other private funds**
*Sponsorship agreements (€6.7 M) and other agreements with private funding bodies*

## USE

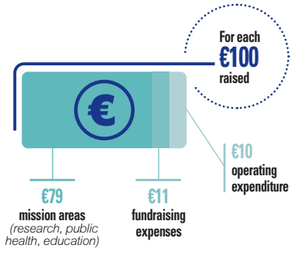
The revenues reported in the profit-and-loss account are earmarked as follows: Institut Pasteur mission areas €229.7 M, operation €41.4 M, and fundraising expenses €10.5 M. The remainder is used to fund initiatives and long-term investments.




**Mission areas**
**€190.6 M** Research
**€11.7 M** Public health initiatives
**€4.2 M** Education
**€11.3 M** Development of research applications
**€2.9 M** Payments to other organizations
**€8.9 M** Initiatives abroad

## 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. €89.6 M was raised in 2018[1]. In addition to its mission areas, the public gifts and donations received in 2018 covered the Institut Pasteur's fundraising expenses and operating expenditure.




*1. See chart above and Institut Pasteur 2018 Use of resources statement in the financial report.*



## 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.

| IN 2018 | €M | % |
|---|---|---|
| **Total** | **780** | 100 |
| Property | **166** | 21 |
| Securities | **569** | 73 |
| Private equity | **6** | 1 |
| Cash | **39** | 5 |

Productive assets account for the equivalent of 2.3 times the Institut Pasteur's annual operating costs (ratio set out in late 2018).
These assets generated €34.8 M during the 2018 fiscal year, reported in the profit-and-loss account, representing a reduction of €2.4 M in relation to 2017.

## EARNINGS FROM ASSETS

| IN 2018 | €M |
|---|---|
| **Total** | 34.8 |
| Property | **6.5** |
| Securities | **25.4** |
| Cash | **3** |

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 de la Guadeloupe and the Institut Pasteur de la Guyane.

| REALIZED IN 2018 | €M |
|---|---|
| Institut Pasteur operating revenue | **294** |
| Institut Pasteur operating expenses | **332** |
| Contribution to IP Guadeloupe and IP Guyane | **- 1.6** |
| Operating income | - 39.5 |
| **Institut Pasteur financial result** | **29.3** |
| Contribution to IP Guadeloupe and IP Guyane | **- 0.0** |
| Financial income | 29.3 |
| Recurring operating income | - 10.3 |
| **Institut Pasteur non-recurring income** | **- 20.3** |
| Contribution to IP Guadeloupe and IP Guyane | **- 0.0** |
| Non-recurring income | - 20.3 |
| **NET INCOME** | **- 30.6** |

Recurring operating income showed a deficit of €10.3 M as against €8.9 M for 2017. €1.6 M of this deficit is due to the institutes outside mainland France, and €8.7 M to the Institut Pasteur Paris campus. This current account deficit is a result of increased costs, which neither operating revenue nor financial revenue from short and long-term investments were able to cover over the fiscal year; and this was despite the rise in financial resources from legacies and donations.
Non-recurring income was down €20.3 M due to negative market growth in the latter months of 2018. This translated to a latent loss on stable stock investments reported at 12/31/18 and provisioned for an amount of €40.9 M.

Due to this deficit, the Institut Pasteur recorded net income of €-30.6 M as against €0.1 M in 2017.

# Promoting
# **sustainable development**

**In its 2019-2023 Strategic Plan, the Institut Pasteur reiterates its commitment to sustainable development, maintaining the momentum built over the past decade.**

In 2018, the Institut Pasteur published its first ten-year retrospective of sustainable development initiatives, with a particular focus on two projects, Green Campus and Responsible Campus, led by the Environment and Sustainable Development Unit within the Quality, Environment and Sustainable Development Department.

Green Campus was launched in 2010 to promote and consolidate environmentally friendly practices at the Institut Pasteur. The initiative is based around three main objectives: preserving resources, preventing pollution, and sharing ideas and best practices. New ideas and suggestions from Institut Pasteur employees are regularly incorporated into the Green Campus strategy.
Since 2014, Green Campus has become the environmental component of a broader strategy to encourage sustainable development, known as “Responsible Campus”.

## WINNER OF THE “STUDENT FOR GREEN WATTS” COMPETITION

From April 1 to 30, 2018, the Institut Pasteur, along with EM, ISCOM, Paris Business School and ESSCA, took part in the “Student for Green Watts” competition organized by Origo, a young start-up which provides Renewable Energy Guarantees of Origin (REGOs). The competition was supported by the “Responsible Campuses” network of French universities and higher education institutions committed to sustainable development. REGOs are a way of tracking electricity from producer to end consumer. After the month-long competition, the Institut Pasteur finished in first place with 123 “likes”, earning two months of REGOs beginning on May 1, 2018. It was closely followed by EM, which came second with 103 votes.

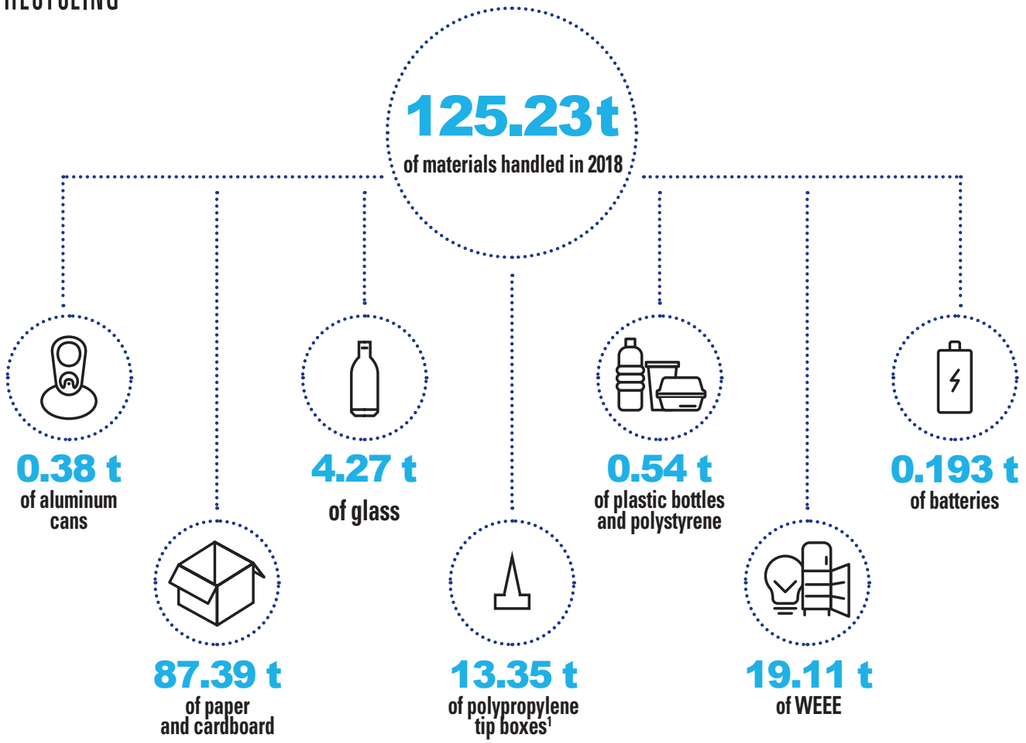
## VOLUNTARY RECYCLING OF OFFICE WASTE

In June 2018, the Institut Pasteur launched a voluntary recycling scheme for office waste in two of its buildings. The aim is to give teams a role to play by introducing a new method for collecting and disposing of office waste. Paper is sorted separately from other non-hazardous waste, with two recycling bins set up in communal recycling areas on each floor (in the social space or near the photocopier).
After six months, the volume of paper collected was a staggering 128.7kg, or the equivalent of 25,740 A4 pages! Since there were hardly any unwanted materials in the paper stream, the company in charge of recycling at the Institut Pasteur was able to recover the material effectively.

### 2019-2023 STRATEGIC PLAN: SUSTAINABLE DEVELOPMENT MEASURES

Sustainable development is part of the Institut Pasteur’s DNA and central to its missions of research, public health, education and development of research applications. Sustainable development is addressed in the Strategic Plan through issues such as quality of working life, ethics and the development of interactions between the Institut Pasteur and civil society. As indicated in Objective 8 of the plan (“Pursue the ongoing improvements to the campus”), real estate policies will be aligned with principles of sustainability to ensure that environmental standards and regulatory requirements are taken into account from the design phase of all building and renovation projects.


## RECYCLING




## OTHER RECOVERY

**7.67 t**
of dried organic waste

## REUSE

**18.62 t**
of pallets

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

# An HR team supporting **the Institut Pasteur community**

**In 2018, the Human Resources Department pursued its mission to provide effective day-to-day support for Institut Pasteur staff and create a healthy working environment.**

The Institut Pasteur's HR teams continued recent efforts to modernize and simplify procedures with a series of measures to meet campus needs more effectively in 2018.

## ASSISTANCE AND GUIDANCE FOR STAFF

- **New digital tools** were implemented to help managers and assistants with their requests to host interns and Orex staff.[1] An application that assesses hosting requests and a specific vacancy request module were introduced to facilitate processing.
- **A number of tools** aimed at non-French scientists were created to help them through the many administrative procedures they have to deal with (visas and residence permits, social security, accommodation, banks, income tax, etc.).
- **Ongoing efforts to optimize HR** processes also resulted in a new calendar for annual HR campaigns, which include annual appraisals and career development reviews (with new online forms), training, recruitment requirements, pay and promotions.
- **The MAASCC welcome, support and career development structure for scientists** continued to provide Master's and PhD students, scientists and engineers with personalized support for their professional growth and future career plans. Some 40 events – including after-work career sessions, start-up breakfasts, the "Start me up" school (with the Department of Education) and the company start-up program (with the DARRI) – were held in addition to personalized career reviews and meetings with the Careers Committee.

## IMPROVING THE QUALITY OF WORKING LIFE

- **The Human Resources Department was involved** in drafting the 2019-2023 Strategic Plan, which includes an ambitious HR priority for Institut Pasteur staff: to work more effectively together and empower each individual so as to create an attractive, collaborative working environment (*see inset*).
- **In late 2018, efforts to improve the quality of working life** led to talks with management and unions to develop arrangements for working from home. The resulting agreement, unanimously signed by all parties, will be implemented in 2019 and will help Institut Pasteur staff achieve a better balance between their professional and personal lives.
- **The Institut Pasteur reiterated** its commitment to health in the workplace, launching an initiative for the prevention of musculoskeletal disorders (MSDs), in partnership with the Massage and Physiotherapy Training Institute in the Paris Public Hospital Network (IFMK-APHP), for the Logistics Department and the mediums/equipment and technological platforms. Practical workshops led by trainee physiotherapists were held to teach employees simple exercises and easy movements that they can repeat at work to prevent the emergence of symptoms associated with MSDs.
- **In the area of labor relations,** the terms of elected members of staff representative bodies were extended in 2018 so that new members can be elected in 2019 and elections can be held for the new combined staff representative body, the Social and Economic Committee.

*1. Employees from external research organizations.*

### 2019-2023 STRATEGIC PLAN: AMBITIOUS HR TARGETS

- Secure the EU's "HR Excellence in Research" award.
- Recruit wisely and support organizational structures.
- Introduce a strategy for forward-looking management of jobs and skills, initially for scientists.
- Continue to offer training for managers.
- Contribute to the quality of working life (behavioral principles that encourage success, right to disconnect, working from home, labor relations).
- Promote gender equality.



## ON CAMPUS

**2,784** staff members on campus *(as at 12/31/2018)*

- **2,206** IP employees *71.9% with permanent contracts*
- **528** employees from external research organizations *(OREX)*
- **50** interns

Of the **2,734** employees *(excluding interns)*

- **12.2%** administrative and technical managers
- **27.8%** non-managerial staff
- **60%** senior scientists and health officers

## DIVERSITY ON CAMPUS

- **42.8** average age of employees
- **58.6%** of staff members are women
- **68** nationalities on campus

## FOCUS ON RECRUITMENT

**462** people hired in 2018 *(excluding fixed-term to permanent contracts)*

- **57.6%** women hired
- **40.7%** researchers hired *(excluding engineers)*
- **18.2%** employees under 25 hired

### PROFESSIONAL CATEGORIES AT THE INSTITUT PASTEUR

**Of the 2,206 IP employees, percentage per category**
*(as set out in the Jobs and Skills Guide)*

- **65.8%** Research
- **2.3%** Health
- **31.9%** Administrative and Technical

### DEVELOPMENT OF SKILLS
*(training)*

- **4,050 courses,** including **930** for employees of external research organizations or interns
- **€4,047k invested** in professional training *(costs including time spent on training and compulsory contributions)*
- **49,000 training hours** (including **9,000** for members of external organizations and interns)

### CAREER SUPPORT FOR SCIENTISTS

- **70 state-employed researchers and engineers** met with the Careers Committee
- **134 scientists** followed the career guidance program at the MAASCC welcome, support and career development structure for scientists
- **34 career events** (round tables, sessions, etc.) held including 10 skills workshops


BANNER SHOWING THE PASTEURDON 2018 PRESENTERS ON THE RAILINGS OF THE INSTITUT PASTEUR CAMPUS.

# Donations, sponsorship and legacies
# Your support humbles and inspires us

**In 2018, nearly a third of the Institut Pasteur's resources came directly from individual and corporate donations and legacies. This vital support has a direct impact on our work.**

In 2018, the Institut Pasteur received financial support from almost 205,000 individual donors, despite new tax measures and a social climate that discouraged donations from individuals in France – the effects of which were also felt by the Institut Pasteur. We therefore particularly want to extend our thanks once again to our loyal donors and commend them for their commitment to our work. 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, optimize its impact and explore new avenues for research. In 2018, total donations came to €26.2 million.

More than 43,000 new donors joined the Institut Pasteur's loyal supporters in 2018, with nearly 26,000 choosing to set up a direct debit which enables them to spread their donations over the entire year.

For the 12th year in a row, our donors showed extraordinary generosity in supporting the Institut Pasteur's research during Pasteurdon, which ran from October 10 to 14, 2018. Loyal Pasteurdon patron Alexandra Lamy demonstrated her continued commitment to research and to its key protagonists, the Institut Pasteur's scientists, who were the focus of this year's campaign. The campaign film "Defending research together" subtly illustrated the threats facing scientists, emphasizing the urgent need for action to give medical research the resources it requires to move forward.

## DONATIONS FROM COMPANIES AND FOUNDATIONS

2018 saw the seventh edition of the Sanofi-Institut Pasteur Awards, 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 among populations and individuals. Once again in 2018, the Institut Pasteur's sponsors and partners rallied to the cause for the 12th edition of Pasteurdon. The Le Roch-Les Mousquetaires Foundation, which provides direct funding for two research programs on food safety, elicited the support of the Les Mousquetaires group via the launch of two charity-linked products. In 2018, ASSU 2000, a Pasteurdon partner for the fifth year running with its ongoing support for research on cardiovascular diseases, launched its first charity-linked product for Pasteurdon, with a donation made for every new insurance policy taken out. The social welfare company AG2R LA MONDIALE, a loyal and generous Pasteurdon partner with its sport-based fundraising campaign *"Vivons Vélo"*, once again set the bar high, raising a total of nearly €90,000 for the Institut Pasteur. Finally, Axa Atout Cœur and Tarifold offered their support for Pasteurdon as they do every year, organizing fundraising campaigns for the Institut Pasteur on their sites.

In 2018, a number of new sponsors joined the Institut Pasteur's supporters: the BTP Plus Foundation, Groupe Pasteur Mutualité, the Fondation pour l'Audition, the SCOR Corporate Foundation for Science, SACEM, Gilead, the Groupama Foundation, the Janssen Horizon endowment fund and VolkswagenStiftung.

The Institut Pasteur was also one of three beneficiaries from the sale of the "Pièce des Présidents" at the 158th Hospices de Beaune wine auction. In total, donations from companies and foundations raised almost €7 million.

## LEGACIES OFTEN SHARED

2018 saw 139 new legacies submitted to the Board of Directors, representing a total of €47.3 million. The Institut Pasteur shares most of the legacies bequeathed to it with several other institutions.

Life insurance policies continued to represent a leading source of recurring income and remained stable in 2018, raising €16.2 million. These policies, like legacies and gifts, offer favorable tax arrangements in that they are exempt from transfer duties.

## What they have to say about us

*"The Institut Pasteur is at the forefront of French and international biomedical research. Groupe Pasteur Mutualité and all its Directors are very proud to contribute to its work and support it in its missions. This partnership raises hopes of major medical discoveries and advances, both for us as healthcare professionals and for the patients we treat."*

**Dr. Michel Cazaugade, President of Groupe Pasteur Mutualité, an active player in the field of health which joined the Institut Pasteur's sponsors in 2018**

## What they have to say about us

*Congratulations to all the Institut Pasteur's staff for their efforts on a daily basis and their dedication to improving the lives of others. I salute you!"*

**Mr. N.D.**

*"I sincerely hope that the Institut Pasteur will receive many donations so that it can continue its work – its work for humanity!"*

**Mr. B.A.**


NATHALIE BAYE, EMMANUELLE BÉART AND ERIK ORSENNA AT THE 158TH HOSPICES DE BEAUNE WINE AUCTION.


PASTEURIANS AT THE 2018 EDITION OF THE "20 KM DE PARIS" RACE TO RAISE MONEY FOR PASTEURDON.


ON JUNE 21 AND 22, IN COOPERATION WITH THE SCOR CORPORATE FOUNDATION FOR SCIENCE, THE INSTITUT PASTEUR ORGANIZED AN INTERNATIONAL CONFERENCE ON THE EMERGENCE, SPREAD, DETECTION AND CONTROL OF INFECTIOUS DISEASES.

## QUALITY STRATEGY: PIONEERING CERTIFICATION RENEWED

The Institut Pasteur's Legacies and Real Estate Assets Management Office is still the only department of its kind in France to have applied quality procedures to all its activities. Following the annual audit, AFNOR Certification renewed the Institut Pasteur's ISO 9001:2015 certification for 2018.

## COMMUNICATIONS ACTIVITIES

In 2018, for the fourth year in a row, the major annual promotional campaign for legacies and gifts was launched on radio stations and TV channels, on the web and in the mainstream and legal press, to raise awareness of these important long-standing funding sources for the Institut Pasteur. The number of people seeking information about legacies, life insurance and donations, as well as gift notifications, continued to rise. Questions concerning more innovative schemes, such as the temporary transfer of usufruct rights and posthumous gifts, have also become more frequent. To manage all these new contacts, the Legacies and Real Estate Assets Management Office employs two dedicated staff members in charge of legator relations. Benefactors can contact them for advice and guidance or speak to one of the office's three legal experts. The six-monthly "Legacies and Gifts" newsletter is the main means of communication with legators. The eighth edition was sent out at the end of 2018. The newsletter focuses on a specific aspect of gifts, legacies or life insurance policies in each issue, generating substantial feedback and many personal testimonials.

The Think Tank on Philanthropic Trusts, set up by the Institut Pasteur following the success of its first Conference on Philanthropic Trusts in 2009, continued its work and issued a series of opinions. The experts in this think tank include notaries, lawyers and bankers. It is currently the only platform where experts from a variety of disciplines can come together to discuss questions relating to generosity and philanthropy.

### MAJOR SPONSORS

SANOFI

MSD AVENIR

### SPONSORS

AG2R LA MONDIALE
ASSU 2000
BILL AND MELINDA GATES FOUNDATION
CONNY-MAEVA CHARITABLE FOUNDATION
CRPCEN
DENNIS AND MIREILLE GILLINGS FOUNDATION
FLORENCE GOULD FOUNDATION
FONDATION BETTENCOURT SCHUELLER
FONDATION BTP PLUS
FONDATION COGNACQ-JAY
FONDATION DANIEL ET NINA CARASSO
FONDATION GROUPAMA
FONDATION LE ROCH-LES MOUSQUETAIRES
FONDATION ORANGE
FONDATION POUR L'AUDITION
FONDATION SCOR POUR LA SCIENCE
FONDS AXA POUR LA RECHERCHE
GILEAD
GROUPE PASTEUR MUTUALITE
JANSSEN HORIZON
LHW STIFTUNG
MUTUELLE DU PERSONNEL AIR FRANCE
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NOUVELLE CASSIUS FONDATION
ODYSSEY REINSURANCE COMPANY
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SANOFI PASTEUR
TARIFOLD
VOLKSWAGENSTIFTUNG
VON DUHN STIFTUNG

### PARTNERS

AXA ATOUT COEUR
BNP PARIBAS
SOCIÉTÉ GÉNÉRALE

# Board of **Directors**

APRIL 2019

**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

**Christian Vigouroux**
**CHAIRMAN**
French Council of State Department Head

**Hubert du Mesnil**
**VICE-CHAIRMAN**
Ponts et Chaussées engineer and Tunnel Euralpin Lyon-Turin Board Chairman

**Artur Scherf**
**VICE-CHAIRMAN**
Head of the Biology of Host-Parasite Interactions Unit

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

**Alban Hautier**
**TREASURER**
Representative of the French Minister for Action and Public Accounts

**Antoine Triller**
**PERMANENT GUEST OF THE BUREAU**
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

**Gérard Berry**
Professor at the Collège de France, Chair of Algorithms, Machines and Languages

**Gilles Bloch**
Chairman and Chief Executive Officer of Inserm (French National Institute for Health and Medical Research)

**Stéphanie Fougou**
General Counsel at AccorHotels Group

**Muriel Hilaire-Soule**
Curator of the Pasteur Museum

**Isabelle Lamothe**
CEO of ManpowerGroup Solutions

**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

**Anne Paoletti**
Scientific Director for Biology and Health at the Directorate-General of Research and Innovation, French Ministry of Higher Education, Research and Innovation

**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**

APRIL 2019

**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

**Arnaud Echard**
Head of the Membrane Traffic and Cell Division Unit

**Jean-Marc Ghigo**
**SECRETARY**
Head of the Genetics of Biofilms Unit

**Aziz El Amraoui**
Head of Laboratory in the Genetics and Physiology of Hearing Unit

**Michaela Müller-Trutwin**
**VICE-CHAIR**
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

## 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

**Gillian M. Griffiths**
Prof. Immunology and Cell Biology, Department of Medicine, Cambridge Institute for Medical Research, University of Cambridge, UK

**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

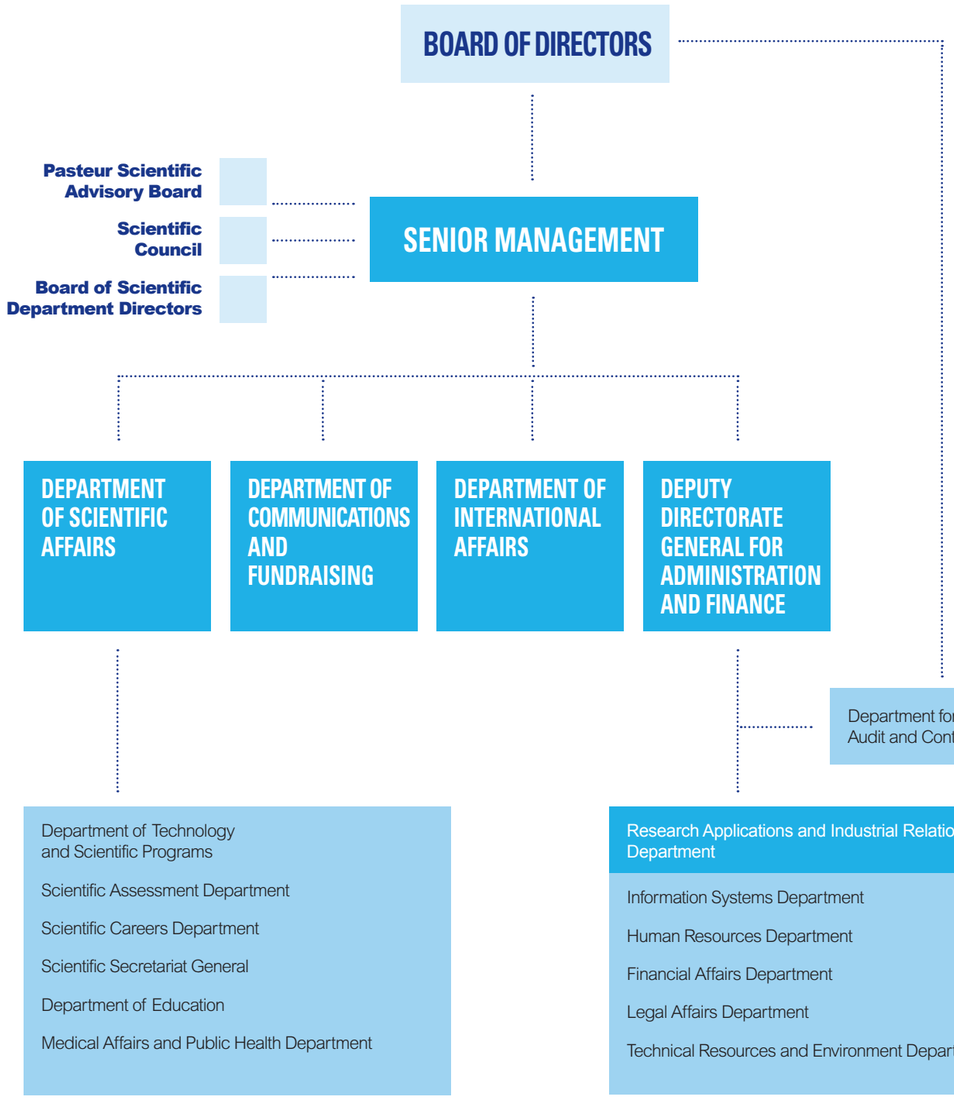
**Nicholas Hastie**
Prof. MRC Human Genetics Unit, MRC Institute of Genetics and Molecular Medicine at the University of Edinburgh, Edinburgh, UK

**Julian Parkhill**
Prof. Genomics of Bacterial Pathogens, Sanger Institute, Cambridge, UK

**Claudio D. Stern**
Prof. Department of Cell & Developmental Biology, University College London, UK

# Governing **bodies**

APRIL 2019






# Management of the **Institut Pasteur**

APRIL 2019

**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.**

**Stewart Cole**
President

**François Romaneix**
Senior Executive Vice-President Administration and Finance

**Olivier Schwartz**
Scientific Director

**Isabelle Buckle**
Vice-President Research Applications and Industrial Relations

**Jean-François Chambon**
Vice-President Communications and Fundraising

**Pierre-Marie Girard**
Vice-President International Affairs and International Network

**Pascal Masse-Navette**
Director for Internal Audit and Control

**Isabelle Cailleau**
Acting Vice-President Medical Affairs and Public Health

**Nathalie Denoyés**
Vice-President Technical Resources and Environment

**Christophe D'enfert**
Vice-President Technology and Scientific Programs

**Stéphane Fournier**
Vice-President Information Systems

**Odile Hermabessière**
Vice-President Human Resources

**Alain Israël**
Vice-President Scientific Assessment

**Nathalie de Parseval**
Scientific Secretary General

**Françoise Perriolat**
Vice-President Financial Affairs

**Monica Sala**
Director of the Education Department

**Patrick Trieu-Cuot**
Vice-President Scientific Careers

**Samuel Valcke**
Vice-President Legal Affairs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