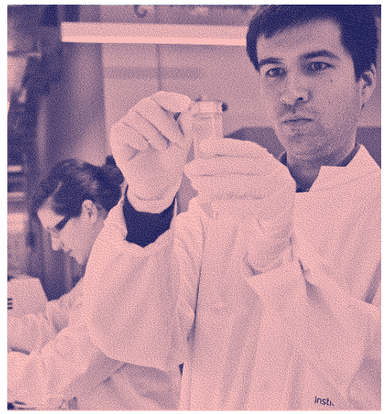
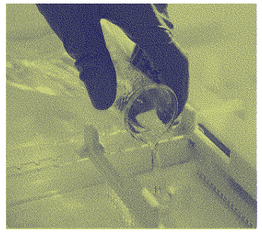
INSTITUT PASTEUR

ANNUAL REPORT 2021

“EMERGENCE”

A historic fight against emerging infectious diseases





WE ARE DRIVEN BY THE PASTEURIAN SPIRIT

Proudly bearing the name of its founder, Louis Pasteur, the Institut Pasteur marks the bicentenary of his birth in 2022 by celebrating the man and scientist, while also promoting the values he embodied. Louis Pasteur pioneered an approach to research focused resolutely on humanist and universal goals and the need to train future generations of scientists.

This "Pasteurian spirit" is rooted in strong scientific and humanist values and fosters three main ambitions: to understand the living world, to improve human health, and to pass on knowledge to future generations. Since the Institut Pasteur was founded in 1888, several generations of Pasteurians have carried on this legacy and successfully sustained and passed on the "Pasteurian spirit." Every year, the Institut Pasteur honors this spirit through its work. Our annual report celebrates the values underpinning this spirit in a new, more condensed format divided into different sections: "Conversations" providing insights on the past year; our special feature on an area of expertise rooted in the "Pasteurian spirit"; "Advances" focusing on key Institut Pasteur missions (research, research applications, public health and education) that form its DNA; and "Fundamentals" addressing its identity, membership of the **Pasteur Network**, resources and governance.

Advances made by the Institut Pasteur focus on priorities set out in its 2019-2023 Strategic Plan. Some of the key developments in 2021 specifically addressed the first priority area of emerging infectious diseases. Other topics will be highlighted in subsequent annual reports towards completion of the plan's implementation period.

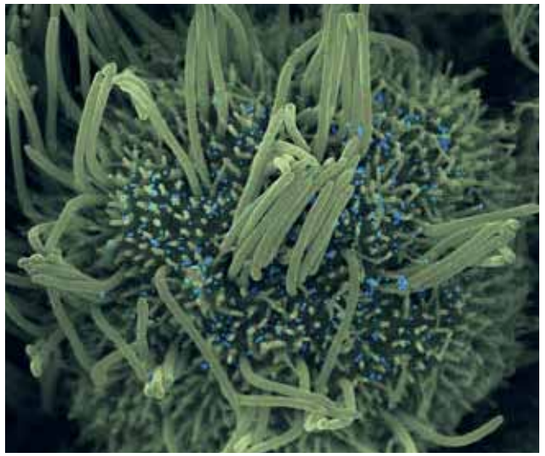
Let's continue to promote the "Pasteurian spirit" which has been inspiring scientists at the Institut Pasteur for over 130 years.

Drawing by artist Fabrice Hyber.

Dr. Jean-François Chambon,
Vice-President Communications - Scientific Outreach

SNAPSHOT OF 2021

Twelve eventful months interspersed with major scientific breakthroughs and key events for the institute in all fields including COVID-19, cancer, neuroscience, genetics, vaccinology and antibiotic resistance.



SPOTLIGHT ON COVID-19

The Institut Pasteur's other work on COVID-19:

In addition to the examples shown on these pages, over 200 scientific publications were produced between 2020 and 2021 on modeling epidemic trends, identifying places of transmission, analyzing immune response and the host-virus relationship, etc.

- The National Reference Center (CNR) for Respiratory Infection Viruses continued its work on genome sequencing and surveillance of variants.

- The Antiviral Molecule Screening Platform (SpikImm startup) developed therapeutic antibodies and 107 technology transfer agreements were signed.

- International response within the **Pasteur Network**.

- Information provided to the public and advice given to the public authorities.

MORE SIGNIFICANT HIGHLIGHTS FOR 2021 CAN BE FOUND ON PASTEUR.FR AND ON THE FOLLOWING SCIENTIFIC DEPARTMENT PAGES.

FEBRUARY

Lymphoma: real-time exploration to improve immunotherapies

Using *in vivo* imaging approaches, scientists visualized in real time how monoclonal antibodies, used to treat B-cell lymphoma, guide the immune system to attack tumor cells.

Science Advances, February 19, 2021.

APRIL

Light shed on the coordination of neural stem cell activation

Scientists visualized and analyzed the spatial and temporal distribution of neural stem cell activation in zebrafish brains.

Cell Stem Cell, April 5, 2021.

Retracing the history of human evolution and admixture in the South Pacific

Using genome sequencing from 320 individuals, scientists deduced how human populations have adapted to the Pacific islands and how this has affected their current state of health.

Nature, April 14, 2021.

APRIL

Description of the biosynthesis pathway of a new DNA nucleobase

Light was shed on the biosynthesis pathway of the Z base, which is the only known exception in the living world to the four DNA bases A, T, C and G.

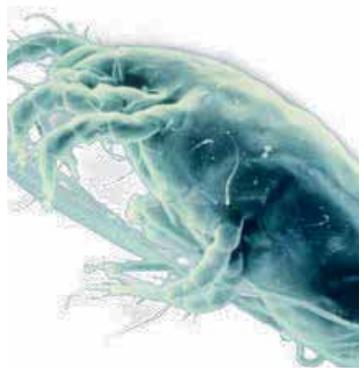
Science, April 30, 2021.

MAY

Asthma: an asthma vaccine that is effective in mice

A vaccine was developed in animals to provide long-term protection against allergic asthma, reducing the severity of symptoms.

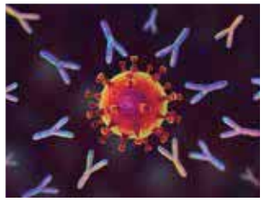
Nature Communications, May 11, 2021.



MAY

Launch of the startup SpikImm to develop monoclonal antibodies

The Institut Pasteur signed an exclusive worldwide license agreement with the biotech startup SpikImm SAS, founded by Truffle Capital, to develop anti-SARS-CoV-2 (COVID-19) monoclonal antibodies for therapeutic and diagnostic use.



JUNE

Partnership with Université Paris Cité

The Institut Pasteur and Université Paris Cité joined forces to develop a scientific strategy for emerging infectious diseases, antimicrobial resistance and vaccinology.

AUGUST

An international collaboration on new antimicrobials

The Institut Pasteur joined IRAADD (the International Research Alliance for Antibiotic Discovery and Development) whose remit is to identify new antimicrobial molecules. Antimicrobial resistance is a major public health issue.

Nature Reviews Chemistry, August 19, 2021.

NOVEMBER

COVID-19: Kamala Harris salutes the Institut Pasteur's response

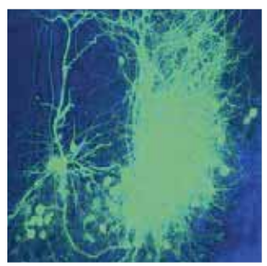
The US Vice President, Kamala Harris, met several of the Institut Pasteur's scientists and saluted the Institut Pasteur community's response in tackling the COVID-19 epidemic.

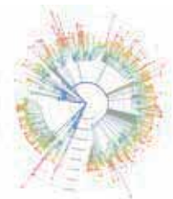
OCTOBER

Intranasal COVID-19 vaccine candidate

In 2021, two publications demonstrated the efficacy of an intranasal lentiviral COVID-19 vaccine. This dramatically reduces viral load and protects the brain and lungs in animals.

Cell Host & Microbe, December 14, 2020. *EMBO Molecular Medicine*, October 15, 2021.





NOVEMBER

COVID-19: results on places of infection and effectiveness of RNA vaccines

One part of the COMCOR study identified sociodemographic factors, places of SARS-CoV-2 infection and behavior linked to risk of infection, and assessed the effectiveness of RNA vaccines against the Delta variant.

The Lancet Regional Health Europe, November 26, 2021.

DECEMBER

COVID-19: Omicron variant resistant to monoclonal antibodies but neutralized by the third vaccine dose

A study revealed that Omicron is much less susceptible than Delta to most neutralizing antibodies used for treating COVID-19, though a third vaccine dose significantly boosts the number of natural antibodies.

Nature, December 23, 2021.

CONVERSATIONS.

A PIVOTAL YEAR FOR THE INSTITUT PASTEUR'S FUTURE

Institut Pasteur Board of Governors Chairman Christian Vigouroux and President Prof. Sir Stewart Cole (see p. 44) share their thoughts on the year's highlights. 2021 was a pivotal year poised between maintaining financial stability and supporting scientific projects.

THE REST OF THIS INTERVIEW ABOUT THE VISION FOR 2030 AND PASTEURIAN VALUES IS AVAILABLE AT PASTEUR.FR.

"The Institut Pasteur is attractive, visited, read and respected. It is the Board of Governors' chief responsibility to ensure that this continues to be so."

Christian Vigouroux

What is your overall assessment of 2021?
Christian Vigouroux: The Board of Governors proved that the Institut Pasteur's historical structure served its purpose, showing determination, restraint and agility in forging relationships built on trust. We established an Ethics and Compliance Committee in addition to the Scientific Integrity Committee, which is now essential for supporting scientific activity. The Institut Pasteur has initiated compliance procedures for data (GDPR) and anti-corruption measures (Sapin II Law of 2016). Partnerships that commenced over two years ago are beginning to yield positive results. This has been the case with Université Paris Cité and also within the **Pasteur Network**. The Institut Pasteur is attractive, visited, read and respected. It is the Board of Governors' chief responsibility to ensure that this continues to be so.
Stewart Cole: In addition to our strength as an institution, we have a string of scientific successes to our name. I would like to pay tribute to our efforts during the COVID-19 crisis. Our research has contributed significantly to the national and international response over the past two years. The CNR (National Research Center) for Respiratory Infection Viruses is conducting a considerable amount of work. I would also mention our fantastic achievements in pathogenesis, long COVID, and diagnostic, vaccine and therapeutic strategies for all variants. Our modeling work has provided vital information for monitoring the outbreak and for guiding decisions. We have also identified and characterized a SARS-CoV-2-neutralizing monoclonal antibody which is effective against Omicron, and fast-track preclinical development is currently underway through our startup SpikImm.

"In an increasingly competitive scientific environment, we are consolidating our national and international standing."

Stewart Cole

Is it true that these successes have not affected the balance of expenditure?
C. V.: Achieving balance is a must for a private foundation with charitable status such as ours. According to the Board of Governors, which is responsible for overall balance, the President and his team have progressed towards developing a balanced budget for the Institut Pasteur in a challenging climate. The current recovery is in line with the target of the 2019-2023 Strategic Plan. Balance holds the key to future breakthroughs in scientific research.

Which scientific objectives were achieved in 2021?
S. C.: We hired five new committed and talented 5-year group leaders. In an increasingly competitive scientific environment, we are consolidating our national and international standing. Our reputation is now more beneficial than ever, as demonstrated by the visit of US Vice President Kamala Harris, and should help boost international philanthropy. The new governance of the **Pasteur Network** has contributed to this standing, as has the Institut Pasteur's enhanced position in the research ecosystem through the historic agreement signed with Université Paris Cité. That's without mentioning our partnerships with the French Research Agency on HIV and Emerging Infectious Diseases (ANRS-MIE), the CNRS, Inserm and the Paris Public Hospital Network (AP-HP). I hope links with the Crick, Oxford and UCSF will be next on the list for us.

Within this ecosystem, what are the Board of Governors' key concerns?
C. V.: We are ambitious and alert to the Institut Pasteur's position in the new scientific landscape and in terms of recruiting the best and brightest scientists. And of course access to funding and programs (e.g. in infectious diseases) is a primary concern. Our institute also needs to be mindful of its ability to change and bounce back, or even redefine its contribution to vaccine research. Let us not forget that our private status enables rapid redeployment where necessary. Lastly, the Board keeps a constant eye on public donations and the strength of our position in terms of contracts and grants.

A word about the future?
S. C.: We won the EU HR Excellence in Research award in 2021 in recognition of our recruitment policy and working environment. We aim to continue offering the best possible research and teaching conditions to ensure we can attract and train young scientists, and pledge to take action to improve female representation in senior scientific roles. On a scientific level, lessons have been learned from the health crisis. In my view, climate change and its impact on future emerging diseases is of critical importance.
C. V.: In future years, it's important for the Institut Pasteur both to maintain its bold and inquisitive outlook with no other limits than its capacities at any given time, and also to change its methods, partnerships and programs whenever improvements are within reach. Pasteur is never more Pasteur than when it embarks on new scientific projects. As regards governance, October 2022 will see the election of a new Board Chairman, and in late 2023 the Search Committee will submit its proposals for a new President. Beyond the people representing it, the Institut Pasteur will remain one of the best conceivable organizations for universal science.

“The significant focus on COVID in labs did not prevent major breakthroughs in other key fields.”

Christophe d’Enfert

CAPACITY BUILDING TO PREPARE FOR THE FUTURE

Institut Pasteur Senior Executive Scientific Vice-President Christophe d’Enfert provides a brief, cross-disciplinary overview of 2021 covering capacity building, enhanced partnerships and future technologies.

What scientific lessons should be learned from two years of pandemic?
The Institut Pasteur achieved a great deal. Modeling enabled us to monitor and forecast the development of the outbreak in France. Through the ComCor study, we gained insights into the epidemiology of the virus.

DISCOVER UNITS AND FACILITIES SET UP IN 2021 AT PASTEUR.FR SCAN THE QR CODE.

The emergence of the Delta and Omicron variants was effectively monitored (p. 48) thanks to the expertise of our CNRs, which play a key role in our organization and are crucial for detecting emerging diseases. We produced monoclonal antibodies effective against all known variants through our startup SpikImm, and developed a nasal vaccine which is entering the clinical phase (p. 45). Progress is being made in pinpointing the origin of the virus through work conducted by the **Pasteur Network** (Paris and Laos) on bats. Moreover, numerous articles were published on humoral immune response, ciliated cells, anosmia, etc. We can all be proud of the work achieved.

Haven’t these successes hampered non-COVID research?
I can honestly say that we spared no effort in other areas despite continuing occasional lockdown restrictions. Within the field of antimicrobial resistance, Institut Pasteur teams joined forces with the off-site Microb’UP institute founded by Université Paris Cité. Neuroscience projects were launched with the Paris Brain Institute. In relation to cancer, an agreement with the Institut Curie will be renewed in 2022. And lastly, a unit will be set up to draw lessons from the pandemic and prepare for subsequent emerging challenges within a global context with our partners including the **Pasteur Network**.

Are partnerships crucial in science?
They have always been important and will become increasingly so in a competitive environment where it is advantageous to share expertise. The partnership with Université Paris Cité opens up opportunities in neuroscience, microbiology and immunology (p. 43). Our Hearing Institute (p. 38), which hosts Institut Pasteur and Inserm teams, is expanding its expertise to include language research. We are also investing in our own units (scan QR code).

What other investments have been made?
Eight long-term “COVID” projects were launched (p. 19) to gain insights into SARS-CoV-2 and COVID-19 over a sufficient period to allow proper analysis. Equipment funded within this context will boost our capacity for future research alongside the numerous technologies in which we are currently investing (single cell analysis, imaging, therapeutic molecule screening, artificial intelligence, etc.). We also have plans to build a vector-borne diseases center with an ad hoc working environment which is due to open by 2026. These projects will prepare us for the future and increase our capacity to respond to future emerging diseases.

“The National Reference Centers’ mission is now fundamental, and will perhaps prove even more so in future.”

Pierre Buffet

HUMAN HEALTH, PART OF THE INSTITUT PASTEUR’S DNA

Pierre Buffet has been the Institut Pasteur’s Medical Director since January 2022. Having managed the Medical Center between 2001 and 2007, he is well aware of the institute’s ability to engage in patient care alongside ad hoc organizational activities to support clinical research.

You are the Institut Pasteur’s new Medical Director. What does the institute’s public health mission involve?
It is one of our long-standing core missions. My task is to continue implementing systems put in place to support clinical research. This support has a significant technical and regulatory component, and consequently also a human side as it involves helping scientists prepare complex applications. We are facilitators in the process, ensuring that clinical research can begin as quickly as possible.

The other aspect of particular importance to me is our medical practice. This is an integral part of the department’s DNA. The CNRs provide diagnostic assessments and therapeutic advice. And the Medical Center (CMIP) is expert in preventive and curative patient care. Public health is the sole focus of our practice.

How important are the National Reference Centers (CNRs)?
We saw just how important the CNRs were during the COVID-19 outbreak [see CNR for Respiratory Infection Viruses]. The fact that we host 14 CNRs tasked with monitoring numerous pathogens is a major asset. The Institut Pasteur has a mutualized platform with powerful sequencing tools. In 2021 we achieved some incredible things with data from the CNRs and biocollections, and also through the EMERGEN consortium (p. 48). The National Reference Centers’ mission is now fundamental, and will perhaps prove even more so in future. Our objective for 2022 – a year in which key roles are due to change hands – is to consolidate our CNR base.

How do you run the Medical Department?
Three key actions provide the basis of my approach: providing support, breaking down barriers, and focusing. Supporting clinical research involves assisting scientists with their projects and supporting medical practice in a broader sense. Breaking down barriers means bringing together various stakeholders within the department [soon to move to a Medical Center building] and within the Institut Pasteur itself, for instance by strengthening links between the CNRs and research units. Lastly, focusing involves identifying the Institut Pasteur’s strengths, areas in which our knowledge has a strong medical impact. This is where we need to make choices and find those areas in which we are competitive, whether it be in epidemiology, microbiology research or vaccine applications. To that end, we work with the Technology Transfer and Industrial Partnership Department, or DARRI (see p. 45) to identify partners.

A HISTORIC *FIGHT AGAINST* EMERGING *INFECTIOUS* DISEASES

Emerging infectious diseases result from contact between microbes and animals, with humans the most parasitized animal species. From the plague in Asia in 1894 to the current COVID-19 crisis, scientists at the Institut Pasteur have long leveraged their expertise and talent to further knowledge creation and benefit humankind.

SCAN THE QR CODE TO READ THE ONLINE VERSION AT PASTEUR.FR

EMERGENCE, AN INEVITABLE *AND UNPREDICTABLE* FACT OF LIFE

with Jean-Claude Manuguerra, head of the Environment and Infectious Risks Unit, Laboratory for Urgent Response to Biological Threats and Hantaviruses CNR, and co-head of the Emerging Animal Pathogens in Humans OIECC (World Organization for Animal Health Collaborating Center).

Between 1918 and 1919, in just a few months a third of the world's population was infected with Spanish flu. While Spain was the first country to report the disease, the outbreak probably started in Asia and subsequently spread to the United States before reaching Europe in a more virulent and lethal form with American soldiers. The risk of pandemics is higher now than in 1918 due to the speed of travel. Viruses can travel the world in a day, compared to a year in the 19th century. While research and public health responses are sometimes slowed by regulations, alert systems have improved and we are now better informed about virus biology. Moreover, laboratory testing capacity has increased following the introduction of the International Health Regulations in 2005.

We also know that the introductory phase (or spillover – see p. 15) is critical for tackling outbreaks. In 2003, rapid identification of the severe acute respiratory syndrome (SARS) virus led to effective containment measures as patients were not infectious prior to symptom onset, and it was thus possible to eradicate the virus. In contrast, COVID-19 spread quickly in 2020 following its introductory phase. WHO thus declared a pandemic, triggering an immediate response from the scientific community. A combination of vaccinations and lockdown measures then helped limit disease severity and spread.

Why are we still faced with such a grave risk? An analysis of key factors in viral emergence since 1940 suggests that changes in land use play a dominant role in 1 in every 4 cases. While climate appears to have less of an impact, except in relation to arboviruses, this situation may well change with global warming.

What are the main causes? By definition, emerging viruses are unpredictable. However, often respiratory and easily transmissible RNA viruses such as influenza and coronaviruses present the greatest risk. In contrast, AIDS was caused by a retrovirus that emerged in the 1980s. The key takeaway is that emergences are an "inevitable fact" in the words of scientist Charles Nicolle. However, let's not be fatalistic as scientific progress is a constant source of hope.

DEFINITION

WHAT IS AN *EMERGING INFECTIOUS* DISEASE?

with Caroline Demangel, head of the Immunobiology and Therapy Unit and co-head of the Emerging infectious diseases priority area (priority area 1 of the Institut Pasteur 2019-2023 Strategic Plan).

IN HUMAN HEALTH, EMERGENCE POINTS TO A REVELATION. *"An emerging disease denotes the sudden appearance within a human population of a novel pathogen from an animal or environmental reservoir or following the genetic modification of an existing pathogen,"* explains Caroline Demangel. *"It may also denote a known disease that reappears by extending its geographical range or becoming more transmissible or severe. This is referred to as a reemerging disease."* Emerging and reemerging infectious diseases are epiphenomena of human existence and our interactions with each other, and with nature. As human societies grow in size and their habitats encroach on natural ecosystems, we create an infinite variety of opportunities for infectious agents to transmit to humans and for new diseases to emerge. The meaning of the term "emergence" implies surprise and a sudden change from a known situation. But how do we prepare for the unknown? That's what scientific research is all about.

emergence, noun.: sudden appearance in a series of events or ideas. By extension, the appearance of a new biological system or new properties. Synonyms: occurrence, appearance, surge. An emergence pre-exists its discovery and only appears to those who encounter it.

WELCOME TO THE AGE *OF EMERGENCE*

with Philippe Sansonetti, microbiologist, professor at the Collège de France, holder of the Chair in Microbiology and Infectious Diseases, and professor at the Institut Pasteur.

On June 15, 1894, Alexandre Yersin landed in Hong Kong with a microscope and autoclave in the midst of an epidemic that was decimating the population. In his straw hut (see photo), he used a bubo specimen taken from a deceased patient to identify the plague bacillus which was later named *Yersinia pestis*. For over 130 years, a whole host of Institut Pasteur scientists have studied endemic and epidemic diseases.

IN 1995, STEPHEN MORSE, Professor of Epidemiology at Columbia University put forward his definition of emerging infectious diseases as "*infections that have newly appeared in a population or have existed but are rapidly increasing in incidence or geographic range.*" His theorization came at the end of a century in which optimistic visions of eradicating infectious diseases encouraged by successes, including the eradication of smallpox declared by the World Health Organization (WHO) in 1979, coexisted with a rise in the number and scale of emerging or reemerging infectious diseases such as Ebola and AIDS. While there is no doubt that our knowledge of these phenomena and ability to respond have improved, this can nevertheless be described as the "age of emergence" due to the dramatic increase in causative factors. No fewer than 335 emerging diseases were detected between 1940 and 2004 affecting all continents. How has this happened?

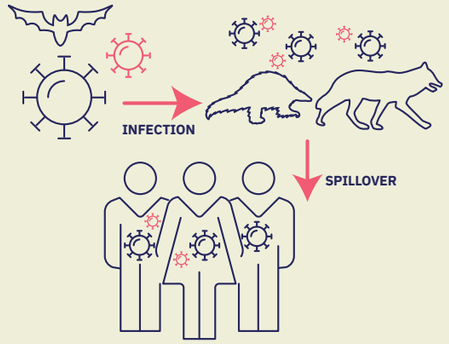
Anthropocene: the fourth upheaval

Emerging infectious diseases are the result of encounters in which humans top all the rankings – 1,400 species of microbes and parasites were listed as potentially affecting *Homo sapiens* at the start of the 21st century (Cleveland et al., 2001), making it the most parasitized animal species. The first upheaval occurred around 75,000 BCE, with the Neolithic Age which marked the start of social and economic organization. Hunter-gatherers began to form small communities and settle. Farming, domestication of animal species, interaction with wild fauna, and proximity among individuals created the first conditions conducive to cross-species transmission. With population spread came increasing opportunities for transmission, heralding the emergence of diseases such as whooping cough, tuberculosis and measles. The second upheaval, which occurred around 1 CE, was driven by urbanization and trade prompted by the rise of the great Roman and Chinese empires. Economic links forged between Europe and Asia precipitated the microbial unification of Eurasia. As caravans traveled the silk roads, people began to mix, enabling the exchange and circulation of goods, ideas and practices, but also of diseases such as plague, smallpox and leprosy. The third upheaval occurred at the turn of the 16th century driven by major naval conquests and the expansion of colonial empires. Microbial unification took on a transcontinental dimension between the old and new worlds. Colonial conquests followed by triangular trade led to infectious diseases such as smallpox, measles, syphilis and malaria spreading on both sides of the Atlantic. The boom in trade and globalization that shaped the history of the 20th century was the final step cementing the advent of the fourth upheaval, the Anthropocene, in which human influences are the primary driver of change in ecosystems. A virus can now switch continents overnight on an international flight... However, while it is possible to interpret the history of humanity through the lens of trade, and therefore understand how its intensification contributed to the emergence of infectious diseases, it is also necessary to examine factors promoting the appearance of pathogens among humans.

How and why do infectious diseases emerge?

While numerous mechanisms are involved in the emergence of infectious diseases, the process can be divided into three main steps.

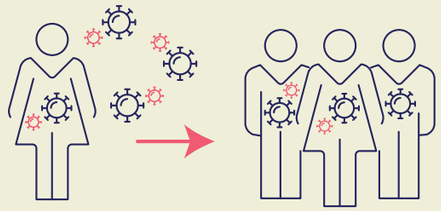
STAGE 1. SPILLOVER



Spillover without secondary transmission: (accidental) infection of a new host without the virus being able to develop in this new human host.

It starts with the accidental infection of a host by a microorganism. The biological agent is introduced to the host (often an animal) or its secretions (saliva, urine, etc.), feces or the contaminated environment. A human then comes into contact with the animal, either directly or through a second animal (vector). Infection subsequently occurs. This is known as spillover, where a virus "spills over" from its usual habitat and is transmitted to humans. In most cases, the virus is unable to develop in its new human host and the story ends there.

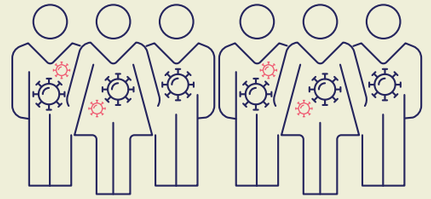
STAGE 2. CROSS-SPECIES TRANSMISSION



The pathogen becomes established in humans (cross-species transmission). Successive spillovers result in a limited chain of transmission in the affected population. If the epidemic ends spontaneously it is referred to as an outbreak.

However, in some rare cases, spillover or successive spillovers lead to a local chain of transmission. The microorganism gradually finds means of adapting and developing in humans. This phenomenon, known as cross-species transmission, or host jump, is where a pathogen becomes established in a new species. The spread of infections from animals to humans is referred to as zoonosis and causes 60% of human diseases according to WHO. The outcome of the infection depends on its transmissibility within the new population.

STAGE 3. CIRCULATION



The epidemic becomes established or even turns into a pandemic through highly efficient transmission within the new host population.

Transmission becomes widespread and an epidemic takes hold due, in particular, to the pathogen's ability to overcome resistance through secondary mutations. Transition of an outbreak to a pandemic is dependent on geographical spread and the basic reproduction number.

The species barrier is normally robust, and although critical, the phenomenon is rare and complex. However, it is possible to pinpoint certain factors that increase the likelihood of occurrence.

The first set of factors relates to biology: microbes adapt in their attempts to thwart tactics used by immune systems. Moreover, hosts' susceptibility to infectious agents varies based on genetic, environmental and social factors. We should also not underestimate the ability of certain animal vectors such as arthropods and mosquitoes to effectively host and then transmit viruses to humans, acting as a link between species, as observed with Zika virus in America in 2016.

The second set of factors relates to human, socio-economic and political issues. The boom in international travel and trade, land use changes and ecosystem deterioration, social inequality particularly with regard to education, and situations involving armed conflict,

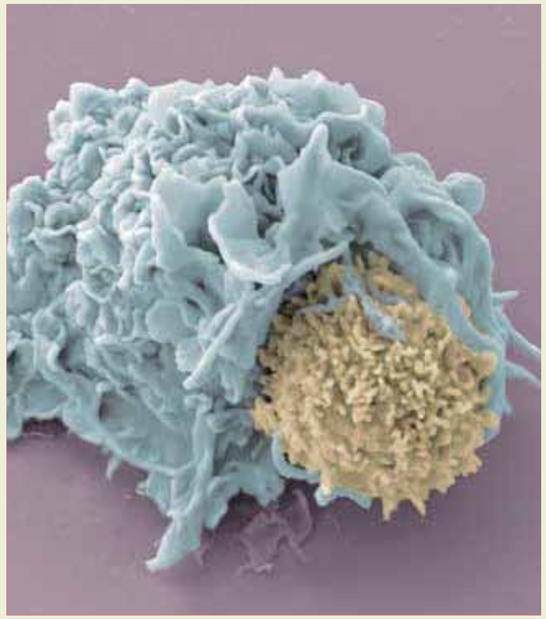
food insecurity and poor governance are all factors providing favorable conditions for these emerging diseases and determining their transmissibility or failure. Recent examples such as the Nipah virus (in Malaysia in 1999) and SARS-CoV-1 (in China and South-East Asia in 2002-2003) clearly demonstrate how a combination of environmental factors (deforestation, habitat loss for animal reservoirs prompting contact with animal vectors) and social factors (consumption of animal vectors) pave the way for cross-species transmission.

Finally, physical factors linked to the increasing frequency of extreme natural phenomena (floods, earthquakes, storms, fires) are changing the balance of ecosystems and disrupting species interactions.

It would be excessively simplistic to identify human impact on the environment as the sole source of emerging diseases. However, it is clear that human-induced changes to natural habitats increase the risk of contact between humans and animal vectors which are reservoirs of infectious agents. This is further compounded by social factors including the boom in international trade which provides the ideal conditions for global expansion of local phenomena.

Can the next emergence be predicted?

We are well aware of the importance of detecting the potential emergence of a disease at the spillover stage. While predicting such phenomena is as complex as the interlinked factors involved, three simple principles may be applied: monitoring, assessment and reporting. Scientific cooperation is more crucial in this field than in any other, as are modeling, sequencing and diagnostic capacity. The challenges faced are cross-disciplinary and require integrated approaches. Although the SARS-CoV-2 pandemic severely tested our systems, they ultimately proved effective, with the virus sequenced in less than three weeks, diagnostic testing rolled out in less than a month, and a vaccine developed in the space of a year. These technical and technological feats should not overshadow the risk we run and the need to guard against it. In particular, we must consider factors that foster the emergence of new diseases by questioning our interaction with ecosystems, as this is where lies the "genius of infectious diseases" in the words of Charles Nicolle, a French physician and microbiologist trained at the Institut Pasteur and laureate of the 1928 Nobel Prize in Medicine. Although difficult to predict with current scientific resources, it is vital that we urgently detect and report any emergence events in order to nip outbreaks in the bud. Monitoring the environment and animal and human populations forms part of the One Health approach of "*one health for humans and animals in one and the same environment*." ●



Interaction between a dendritic cell and a lymphocyte.

INFECTIOUS DISEASES

"THERE WILL THEREFORE BE NEW *DISEASES. THAT IS A FATALITY. (…)*"

Another fact, equally fatal, is that we will never be able to track them down from their origin. When we become aware of these diseases, they will already be completely formed, adult, one could say. How will we recognize these new diseases, how will we be able to suspect their existence before they manifest themselves as symptoms? Knowledge of infectious diseases teaches men that they are brothers and united. We are brothers because the same danger threatens us, united because contagion comes to us most often from our fellow men.

CHARLES NICOLLE, Le destin des maladies infectieuses [The Fate of Infectious Diseases] (1933).

PORTRAIT

A WOMAN IN *PURSUIT OF HIV* FOR OVER 30 YEARS

Michaela Müller-Trutwin considers her encounter with the virus to which she has dedicated her career as the result of a quest to make herself useful. From University of Bonn lecture halls to "Pasteur" laboratories, first in Bangui then in Paris, she has been researching HIV (the human immunodeficiency virus responsible for AIDS) for over 30 years and has always gone where the need for research has been greatest.

"IT ALL STEMS FROM PERSONAL COMMITMENT," she tells us. While studying biology in Germany, she decided to focus her efforts on countries in the southern hemisphere where needs are most critical, and settled on **the Institut Pasteur in Bangui** in the Central African Republic. That was in the early 1990s when the AIDS epidemic was raging in Africa. The HIV variants circulating there appeared very different from those circulating in the United States and Europe. Michaela therefore set out to identify the variants circulating in central Africa. However this was no easy task: "*The PCR tests available were calibrated for American and European variants and sometimes proved ineffective*," she explains. It took her a year to implement the first PCR tests for HIV-related viruses in monkeys living in the Central African Republic. Her research, enhanced by a bioinformatics-based approach, proved crucial in more effectively tracking down circulating variants and helped advance vaccine studies. She also investigated the origin of the virus and, in collaboration with **the Pasteur Center in Cameroon** and a Paris Public Hospital Network (AP-HP) team, she characterized the first SIV (the primate equivalent to HIV) related to HIV-1 in chimpanzees in south-eastern Cameroon.

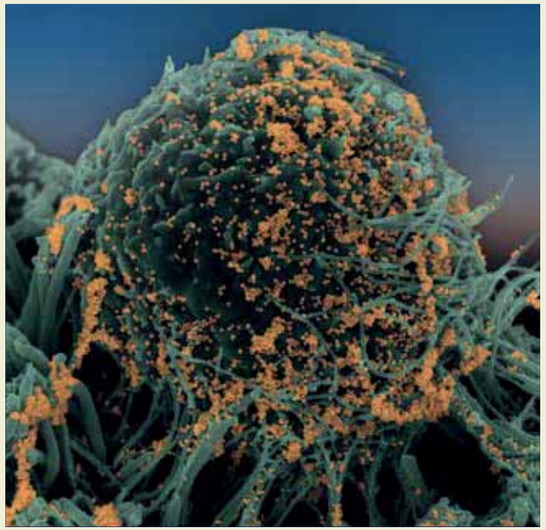
After joining the Institut Pasteur laboratory in Paris led by Françoise Barré-Sinoussi, laureate of the 2008 Nobel Prize in Medicine with Luc Montagnier for their joint discovery of HIV, she continued to work closely with the **Pasteur Network** (Bangui, Dakar and Cameroon) and the International Center for Medical Research in Gabon. Skills and knowledge transfer was a key part of her mission.

While researching African green monkeys infected with SIV from very close quarters in the early 2000s, she noted their failure to develop the disease and attempted to pinpoint the mechanism that conferred natural protection against AIDS. "*We discovered that they are able to control inflammation resulting from the infection, and helped to determine that inflammation plays a major role in immunodeficiency and the development of AIDS in humans*." This discovery of rapid inflammation resolution helped highlight the importance of minimizing time from infection to triple therapy initiation.

However, Michaela did not stop there. She continued her research on the green monkey model and in 2021 discovered the hitherto unknown role of natural killer cells (see p. 36) in controlling viral replication and reducing hidden viral reservoirs in our lymph nodes. This remarkable breakthrough opens up new avenues to find a cure for HIV. One thing is certain: Michaela may not yet be done with HIV but her quest to make herself useful has already been accomplished. ●

THE COVID-19 PANDEMIC *IN THREE ACTS*

with Arnaud Fontanet, head of the Institut Pasteur Epidemiology of Emerging Diseases Unit and co-head of the Emerging infectious diseases priority area (2019-2023 Strategic Plan).



Sample of bronchial cells grown in culture and stained blue. In orange, the SARS-CoV-2 coronavirus.

Prologue

Much has been said and written about the COVID-19 pandemic. Although we still lack the necessary scientific hindsight, it is not the first pandemic the modern world has had to face. Many experts predicted that the risk of an emerging disease with pandemic potential would come from a respiratory virus inherently more transmissible. This one nevertheless outpaced existing alert and response systems, proving the need for a highly connected global scientific community. Here is a look back at the pandemic in three acts.

Act I: identifying the threat

Fact. Research published in the journal *Nature* by **Pasteur Network** teams in Paris and Laos in early 2022 identified a coronavirus in bats in Laos with a human ACE2 receptor binding domain (RBD) that was virtually identical to the SARS-CoV-2 RBD. Bats appear to be the reservoir for the virus but the intermediate host between bats and humans is still unknown, although pangolins were suspected at one point. While determining its origins was important for preventing reintroduction of the virus into the human population, identifying the infectious agent was a matter of public health urgency. With high throughput sequencing, it is now possible to determine the genome of an unknown pathogen in 2 to 4 weeks. The first whole-genome sequence of SARS-CoV-2 was published on January 12, 2020, which was a mere 12 days after the first cases were reported and a testament to the Chinese scientists' strong response. Once the sequence of a pathogen has been characterized, a diagnostic test can be developed to identify the first outbreak clusters and imported cases, and to triage suspected patients. The Institut Pasteur in Paris and its CNR for Respiratory Infection Viruses undertook this task and produced the first testing kits based on the RT-qPCR technique on January 31, 2020. The kits were immediately distributed to hospitals. The first cases had reached France just days previously on January 24, 2020 and the virus was isolated at the Institut Pasteur on January 27. The outbreak then gained pace and all the machinery was set in motion to monitor its development.

Act II: understanding and responding to the outbreak in real time

WHO declared the outbreak a pandemic on March 11, 2020. Escalation to pandemic status was determined by the numbers of cases and their geographical spread. By now the virus was circulating on all continents and nothing seemed to halt its progress.

A task force was appointed at the Institut Pasteur on January 22 with weekly meetings to coordinate overall and multidisciplinary research efforts. On February 12 and March 7, 2020, two calls for research proposals were issued within the **Pasteur Network**, which includes all members of the international network.

All expertise was focused on the pandemic. Each department forged its own approach to tackling the issue within its given remit to deepen understanding of the outbreak unfolding before our very eyes. This massive response and collaboration within the global scientific community was on a virtually unprecedented scale.

In Paris, work began on epidemiological studies of places of SARS-CoV-2 transmission, mathematical modeling of outbreak dynamics, and development of diagnostic and therapeutic approaches – in 2021, this included monoclonal antibody and vaccine therapy with progress made on a potential intranasal vaccine developed with TheraVectys resulting in two publications demonstrating its efficacy in animal models (see p. 3) which should enter clinical trials by late 2022 (see p. 25), and previously in 2020 two other avenues of investigation: a measles vector-based vaccine candidate, which proved insufficiently immunogenic and was discontinued, and a DNA vaccine (see 2020 annual report). Scientific knowledge was useful for monitoring the outbreak and advising the authorities on public health response measures. Nearly a hundred research projects were initiated at the Institut Pasteur in the first months of the outbreak to increase understanding and drive response.

COVID-19

LONG-TERM COLLABORATIVE PROJECTS

- Elucidating the biology of the virus through genetic engineering
- Understanding long COVID
- Examining virus interaction with target cells using structural imaging technology
- Examining SARS-CoV-2 infection through animal imaging
- Examining virus interaction with host cells
- Developing therapeutic strategies
- Examining immune response to infection and vaccination

Act III: a return to long-term scientific research

Although pandemics always come to an end, it is difficult to predict their outcome in advance. How and when will we emerge from this one? With each new emergence the same questions arise. This is perhaps because several timelines coexist. First, there is the short-term public health timeline which occurs in near real time and gives rise to the resources needed for patient management and outbreak response. Then there is the long-term timeline of scientific research aimed at elucidating the biology and emergence of SARS-CoV-2 through a multidisciplinary approach. In 2021, the Institut Pasteur launched collaborative projects, each involving at least four of its research teams, to address key scientific questions regarding this pandemic. The projects will span several years and their findings should provide insights into the SARS-CoV-2 virus and its mutations, which are a source of concern for the coming months, and other coronaviruses, and so expand our knowledge to limit new emergences in the future.

Initial lessons and prospects

The COVID-19 pandemic is not over yet. Research and efforts to discover new ways to control the disease must continue. For instance, clinical trials are planned for the monoclonal antibody developed with SpikImm – see p. 47. The pandemic has also reminded us that outbreaks of this scale can still occur and cannot yet be consigned to the history books. It confirms the epidemic potential of respiratory viruses and the need for vigilance. Moreover, it calls for a concerted effort, both in- and outside the scientific community, to identify and control factors precipitating the emergence of diseases, in particular climate change and human-animal interactions.

The pandemic has also highlighted the need for the Institut Pasteur to build its capacity in response to emerging diseases, especially within the field of vaccinology. This will be a key challenge for future years. On scientific issues, researchers have remained highly connected, sharing scientific knowledge in real time, as well as scientific publications through preprints with commentary on social media platforms such as Twitter. However, this raw scientific data provided via platforms that was inherently complex and in need of peer review required constant monitoring to maintain its quality for the benefit of global health.

FACT SHEET

SHIGELLOSIS, PROFILE OF *AN EMERGING DISEASE*

Shigellosis is a diarrheal disease endemic in several regions of the world. Outbreaks occur during mass gatherings in environments with inadequate hygiene conditions.

The disease is caused by an intestinal bacterial pathogen for which humans are the sole reservoir. It has considerable infectious potential, with only 10 to 100 bacilli required to cause the disease. With the emergence of antibiotic-resistant strains and morbidity due to the long-term consequences of recurrent infections it is under special surveillance.

ORIGINS AND EMERGENCE

- ***Shigella* bacteria,** specialized clones of the *Escherichia coli species*, discovered in 1897 by the bacteriologist Kiyoshi Shiga.
- **Four species:** *Shigella dysenteriae, Shigella flexneri, Shigella boydii and Shigella sonnei. S. sonnei* is the most prevalent species in France (70% of cases) and is an emerging pathogen reported worldwide. *S. flexneri* causes two-thirds of shigellosis cases in Africa and Asia.

TRANSMISSION

Fecal-oral transmission via water or food contaminated by infected feces or flies, and also by infected individuals to their close contacts.

SURVEILLANCE

The Institut Pasteur is responsible for monitoring cases of shigellosis in France (both mainland and overseas) through the Enteric Bacterial Pathogens Unit accredited as a National Reference Center (CNR) for *Escherichia coli, Shigella and Salmonella*.

MORE INFORMATION AT PASTEUR.FR SCAN THE QR CODE.

DEVELOPMENTS

- **Vaccine:** successful Phase I clinical trial in 2021 for a conjugate vaccine candidate derived from synthetic sugars developed by the Institut Pasteur (Chemistry of Biomolecules/Molecular Microbial Pathogenesis units) for the prevalent *S. flexneri* serotype (see p. 29). Phase IIa clinical trial underway in Kenya to establish the efficacy and safety of the monovalent vaccine candidate in the target population of very young children. The results are expected in 2023.
- **Identification:** update of methods for identifying and typing *Shigella* strains using a bacterial genome sequencing approach (Institut Pasteur Enteric Bacterial Pathogens Unit).
- **Diagnostics:** dipstick tests developed for prompt 15-minute diagnosis (**Pasteur Network** and Military Health Department).

MORTALITY

Annual death rate of

200,000

including **65,000** children under the age of 5

LISTED AS ONE OF WHO'S

12

priority pathogens

770

strains identified in 2021 by the National Reference Center (CNR) for *Escherichia coli, Shigella* and *Salmonella* hosted at the Institut Pasteur

THE UNITY OF LIFE

Humans, the environment, animals and diseases

By Erik Orsenna, Institut Pasteur Ambassador

THE COVID-19 OUTBREAK HAS FORCED US TO FACE A SIMPLE TRUTH: LIFE IS UNIQUE. The concept of global health has gained ground throughout the world, both within WHO (World Health Organization) and the Institut Pasteur. If the environment is suffering, how can animals thrive? And within the animal kingdom, how can we humans be the only ones to stay healthy? How can we protect the oceans if we continue to dump our waste in the rivers? The idea of impermeable boundaries between partners of the living world is a misconception, and one that is potentially fatal. Any attack on life is made because other living beings have something to gain. This is probably the first of Louis Pasteur's legacies.

Before Pasteur, medicine was primarily based on observation. Thanks to him and others, we have made progress on discovering causes. It is astonishing to note that lethal infectious diseases are caused by tiny living beings, or even tinier inert particles consisting of a single genome (DNA or RNA) and an envelope – viruses. This crisis reminds us of our vulnerability. The more connected the world is, the more dependent we are on those things that seem most insignificant within it. We are far more dependent on the weakest elements than the strongest ones. Threats are more likely to emerge from the weakest elements. My work on the "geopolitics of mosquitoes" and swine fever has given me a little more insight into the workings of epidemics. Will we learn the lessons of this latest health crisis?

This crisis also forces us to consider our lifestyles. The way we produce food has been a major factor in recent emergences. I have a long-standing interest in agriculture and particularly the transitions required in this area. Food prices are subject to incredible downward pressure, with the proportion of household spending on food falling from 30% to 10% in a very short space of time. Some countries such as China are restructuring their capacities with multi-story farms including units of 28,000 sows spanning nine floors in one building and producing on an industrial scale. How can we think for one second that these systems will guarantee our health and safety?

The health crisis and climate crisis amount to the same challenge. Like life itself, crises are connected. Every year, parasites carried by mosquitoes claim over 700,000 lives. And we couldn't care less because it mainly affects poor countries. Yet I certainly do not view the past through rose-tinted spectacles. Globalization has pulled hundreds of thousands of human beings out of poverty, but it has also come with some horrific epidemics. Our opportunity lies in admitting the need for change.

Unity of life, global economy, planetary connection... How do we reconcile this interconnectedness with an increasingly unequal society? The more devastating a crisis, the harder the poorest are hit. We are faced with a huge challenge. However, with the right energy, we can regain control of our future. Solutions are out there that all require research. In such a context, who would be foolish enough to cut research budgets?

Extract from Erik Orsenna's "Tract de Crise" [Crisis Tract] published by Gallimard in March 2020. Text written by the author based on an interview with Fabrice Moyon for the March 21, 2020 issue of Ouest-France newspaper and adapted for this annual report in April 2022.

ADVANCES.

RESEARCH ADVANCES

2019-2023 STRATEGIC PLAN

EMERGING INFECTIOUS DISEASES

The COVID-19 crisis confirmed the key role played by the Institut Pasteur in tackling infectious diseases in accordance with the Strategic Plan. By late 2021, over 200 studies had been published on modeling of epidemic dynamics, identification of places of transmission, analysis of immune response, host-virus interactions, etc. After SARS-CoV-2 had been isolated and tests developed and assessed, the Institut Pasteur continued its genome sequencing and monitoring tasks.
Its work also involved providing public information and advising the authorities (Scientific Council, French Vaccine Strategy Council, etc.). Two junior teams (G5s) and four units (U5s) were established.

CNR for Respiratory Infection Viruses at the Institut Pasteur.

The *Emerging infectious diseases* priority area in numbers:

10 scientific departments
—
90 teams
—
3 platforms
—
4 biological resources
—
14 National Research Centers
—
3 LabEx laboratories
—
1 Pasteur International Center for Research on Emerging Infectious Diseases

Antimicrobial Resistance Symposium on November 30, 2021.

ANTIMICROBIAL RESISTANCE

Numerous Institut Pasteur teams are active in researching antimicrobial resistance, with a shared focus on three areas: host-directed therapy and host-pathogen interactions; antimicrobial agents and variability of microbial response in terms of persistence, tolerance and dormancy; genomic epidemiology, evolution and resistance. This priority area involves work with several national and international bodies (see IRAADD p. 2-3) and international education and research projects (PPU-Oxford, etc.). Symposia on AMR were held within the **Pasteur Network** in South-East Asia and with Université Paris Cité. Two teams were established to boost research in this priority area (1 G5, 1 U5).

The *Antimicrobial resistance* priority area in numbers:

10 scientific departments
—
91 teams
—
4 platforms
—
3 biological resources
—
12 National Research Centers
—
1 LabEx laboratory

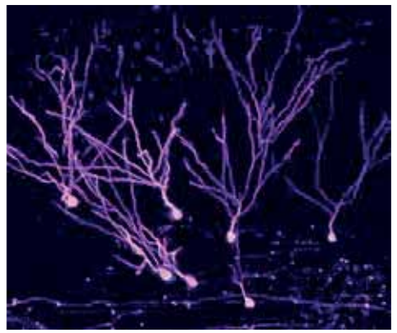
BRAIN CONNECTIVITY AND NEURO-DEGENERATIVE DISEASES

The Brain Connectivity and Neurodegenerative Diseases priority area is involved in numerous partnerships with research institutes in France and throughout the world, notably with the Paris Brain Institute (Neuro-Covid-19 and Big Brain Theory projects) and with **Pasteur Network** member institutes. Several fundraising initiatives are also conducted in this area, particularly with regard to Alzheimer's disease and autism. The Hearing Institute (see p. 38), an Institut Pasteur center, was opened in February 2020 to tackle hearing impairments. Two teams were recruited to advance this priority research area (1 G5 and 1 U5).

Report at the Hearing Institute in January 2021.

The *Brain connectivity and neurodegenerative diseases* priority area in numbers:

8 scientific departments
—
1 Hearing Institute
—
24 teams
—
4 platforms
—
1 Pasteur International Joint Research Unit (PIU) for Neurodegenerative diseases
—
1 partnership with the Paris Brain Institute



New neurons produced in an adult mouse brain.

CANCER

Over €6.1 million of external funding has been secured for the cancer priority research area at the Institut Pasteur since the launch of the Strategic Plan. This funding has been used to initiate three interdisciplinary programs, each involving several teams: Keeping tabs on cancer; Brain tumors; Tomorrow's immunotherapies. Over 60 studies have been published in international journals. Moreover, in 2021 the priority area organized several events on cancer research and was involved in Institut Pasteur courses for major donors and the biology for non-biologists course.

The *Cancer initiative* in numbers:

9 scientific departments
—
49 teams

VACCINOLOGY AND IMMUNOTHERAPY

Progress was made on new vaccinology and immunotherapy projects in 2021, thus building on the Institut Pasteur's historical area of expertise. In a year where the impact of COVID was still being felt, a nasal COVID vaccine candidate was developed with TheraVectys and is due to enter clinical trials by the end of 2022. Two Phase II clinical trials were also initiated for a shigellosis vaccine candidate. The Vaccinology and Immunotherapy priority area was also involved in national and international strategic committees, particularly with regard to the French vaccine strategy, and in WHO working groups on COVID-19.

COVID-19 vaccination at the Institut Pasteur Medical Center (CMIP).

The *Vaccinology and Immunotherapy initiative* in numbers:

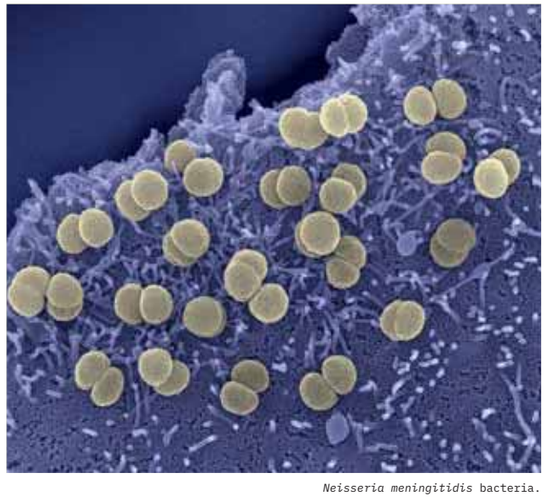
12 teams dedicated to basic research
—
18 teams and projects dedicated to innovation – vaccine candidates
—
14 teams and projects dedicated to clinical research
—
1 team of experts including immunologists, microbiologists, virologists, epidemiologists, vaccine and immunotherapy specialists in collaboration with the **Pasteur Network**, the Institut Pasteur Medical Center and external partners.

UNDERSTANDING *HOW CELLS WORK*

DEPARTMENT OF CELL BIOLOGY AND INFECTION

The work of this department is focused on elucidating the workings of cells – the building blocks of life – to gain a greater understanding of how they behave when faced with infection or diseases such as cancer and neurodegenerative disorders. Its teams pursue an integrative approach that combines expertise in molecular and cell biology, microbiology, physics, mathematics and microscopy to describe dynamic and complex processes on a cellular scale.

Director: Marc Lecuit;
Deputy Director: Guillaume Duménil.
19 teams



Neisseria meningitidis bacteria.

A deeper understanding of the genetic origins of a rare mitochondrial disease

Dominant optic atrophy (DOA), one of the most common forms of mitochondrial disease, causes damage to the optic nerve and in some cases severe neurological disease. Mutations in the gene *OPA1* are associated with the fragmentation of mitochondria. Combining image analysis using supervised machine learning and high-throughput genetic screening, Timothy Wai and his team identified a series of genes blocking mitochondrial defects caused by *OPA1* mutations. Their work shows the genetic complexity of this rare disease.

EMBO Mol Med, May 20, 2021.
Doi: 10.15252/emmm.202013579.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Microtubules contribute to rigidity sensing and mechanosensitive cell behavior

Cells can sense and transduce the physical properties of their environment. Sandrine Etienne-Manneville and her collaborators identified a new player in this phenomenon known as mechanotransduction: microtubules. This cytoskeletal component is post-translationally modified in response to increased substrate rigidity. In turn, modified microtubules promote cell adaptation to the mechanical properties of its environment by controlling cellular functions, such as gene expression, cell adhesion and migration.

Nat Mater, October 18, 2021.
Doi: 10.1038/s41563-021-01108-x.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Meningococci hide from neutrophils inside arterioles

Meningococci are pathogenic bacteria that infect blood vessels and cause meningitis and sepsis. Guillaume Duménil and his team studied the innate immune system's reaction to infection to understand why it fails to control bacterial proliferation inside blood vessels. They found that bacteria can colonize both venules and arterioles while neutrophils only access venules in response to infection thus leaving bacteria freely proliferating inside arterioles.

Nat Commun, July 27, 2021.
Doi: 10.1038/s41467-021-24797-z.

ANALYZING AND MODELING *BIOLOGICAL DATA*

DEPARTMENT OF COMPUTATIONAL BIOLOGY

One of France's largest bioinformatics centers became a scientific department in 2018. It brings together scientists from the quantitative sciences (computer science, mathematics, physics, etc.) and experts in mathematical modeling, algorithms, statistical methods and machine learning. The department carries out work in various fields including genomics, cell biology, structural biology, neuroscience and epidemiology, both on the Paris campus and in the **Pasteur Network**. The Bioinformatics and Biostatistics Hub affiliated with the department provides expertise to units and platforms on campus, analyzing a wide variety of biological data including genomic data. The hub also delivers training and teaching programs.

Director: Christophe Zimmer;
Deputy Director: Gregory Batt.
7 teams.

Deciphering the state of immune silence in severe COVID-19 patients

Using Viral-Track, a recently developed pipeline for the specific analysis of infected cells by the Systems Biology laboratory, a COVID-19 immune signature was identified in bronchoalveolar lavage fluids and blood samples, which is associated with severity. This signature is characterized by lung accumulation of naïve lymphoid cells associated with a systemic expansion and activation of myeloid cells, allowing the characterization of severe COVID-19 as a state of 'immune silence'.

Nature Communications, March 5, 2021.
Doi: 10.1038/s41467-021-21702-6.

Whole-genome assembly on a simple laptop

The Sequence Bioinformatics group and an MIT laboratory developed new software capable of reconstructing a human genome in under 10 minutes (instead of more than 24 hours for traditional techniques). The processing power gain is significant as this can be done on a modest laptop computer. Many areas such as research on the microbiota or antimicrobial resistance will benefit from this breakthrough.

Cell Systems, October 20, 2021.
Doi: 10.1016/j.cels.2021.08.009.

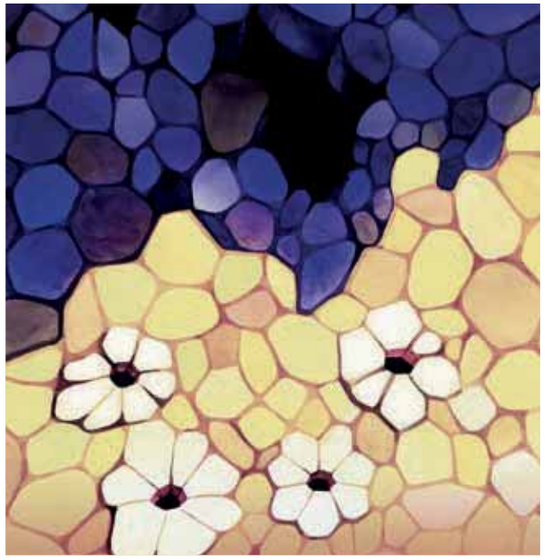
SCAN THE QR CODE FOR MORE INFORMATION (IN FRENCH) ABOUT THIS PUBLICATION.

Characterizing the structure of DNA in human cells

The Imaging and Modeling laboratory developed a method for visualizing individual chromosomes at high resolution in intact nuclei in human cells. Analysis of these images, in comparison with chromosomes generated using computer simulation, indicates that the vast majority of human DNA is enclosed in tens or hundreds of thousands of chromatin loops maintained by cohesin.

Genome Biol, May 11, 2021.
Doi: 10.1186/s13059-021-02343-w.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.



Artist's impression of an epithelium and cell elimination.

UNDERSTANDING THE MECHANISMS INVOLVED IN *BUILDING THE LIVING WORLD*

DEPARTMENT OF DEVELOPMENTAL AND STEM CELL BIOLOGY

How do cells acquire their identity? How do organs form? How are tissues generated and repaired? The department covers a wide range of study topics, from individual cells to whole organisms and from embryo to adult. It also examines stem cells and their potential role in tissue regeneration.

Director: Laure Bally-Cuif;
Deputy Director: Sigolène Meilhac;
Deputy Director: Romain Levayer.
18 teams.

Dying cells protect their neighbors to maintain tissue integrity

Cells constantly die in a tissue as part of its renewal process. Romain Levayer's team showed that this is not a random phenomenon. When a cell dies, it temporarily prevents the death of neighboring cells, thereby avoiding the simultaneous elimination of several adjacent cells, which would compromise tissue integrity. The scientists also identified the molecular pathways involved in this mechanism in Drosophila flies, which are also conserved in humans.

Dev Cell, June 2, 2021.
Doi: 10.1016/j.devcel.2021.05.006.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Embryonic megakaryopoiesis is a two-tier process

How does the embryo build the variety of blood and immune cell types required throughout life, from red blood cells to platelets, lymphocytes and macrophages? In their work published in *Immunity*, Elisa Gomez Perdiguero's team focused on megakaryocytes, the cellular source for platelets. They established that megakaryocytes are produced via two distinct differentiation pathways, both involving the same family of stem cells called erythroid/myeloid progenitors (EMPs) at different stages of embryonic development, before the emergence of hematopoietic stem cells.

Immunity, May 31, 2021.
Doi: 10.1016/j.immuni.2021.04.026.

A pair of core regulators of naïve pluripotency discovered

The maintenance of pluripotency in embryonic stem cells is regulated by a complex network of transcription factors, including Esrrb and Nr5a2. In a new study, Nicola Festuccia and his colleagues described, for the first time, the role of these two factors as a new pair of core regulators acting cooperatively to preserve the activity of the regulatory network of naïve pluripotency in mouse embryos. This work helps improve our understanding of stem cell pluripotency during embryonic development.

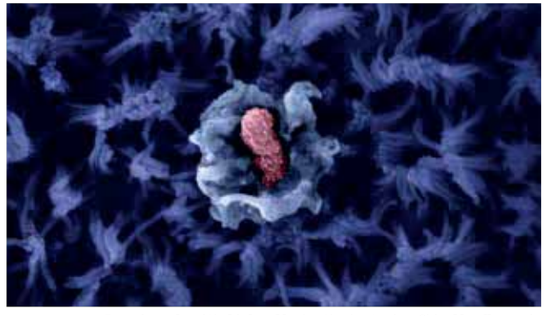
Development, September 10, 2021.
Doi: 10.1242/dev.199604.

OBSERVING LIFE *AT MOLECULAR LEVEL AND* EXPLORING NOVEL *THERAPEUTIC* AND VACCINE-BASED APPROACHES

DEPARTMENT OF STRUCTURAL BIOLOGY AND CHEMISTRY

The structure of a molecule is closely linked to its biological role. The units and platforms of the Department of Structural Biology and Chemistry examine the three-dimensional organization, functions and dynamics of biological macromolecules, and the synthesis of molecules of biological interest involved in cellular processes and human disease. Their multidisciplinary work spanning the fields of structural biology and chemistry provides key data for developing novel therapeutic, diagnostic and vaccine strategies.

Director: Paola B. Arimondo;
Deputy Director: Nadia Izadi-Pruneyre.
17 teams.



Invasion of epithelial cells by the bacterium *Shigella flexneri*.

Surprising features of actinobacterial core metabolic enzymes

The 2-oxoacid dehydrogenase complexes are conserved megadalton machineries involved in key metabolic reactions in aerobic organisms. They are known to be structured around highly symmetric, hollow cores. Researchers have shown that *Actinobacteria* challenge this organization with a trimeric, minimally reduced acyltransferase located at the core of a single mixed super complex. This study sheds new light on the evolution and function of these fascinating enzymatic machineries.

Proc Natl Acad Sci USA, Nov. 30, 2021.
Doi: 10.1073/pnas.2112107118.

Structural basis for the replacement of adenine in the genome of some phages

Genetic information is universally stored in DNA copolymers composed of four basic building blocks (ATGC). In contrast, a group of bacteriophages belonging to families *Siphoviridae* and *Podoviridae* has replaced the adenine (A) with 2-aminoadenine (Z) to counteract the endonucleases of the host. In three publications, researchers have determined the nature and the high-resolution structure of the enzymes necessary to the metabolism and incorporation of the Z-base in the phage DNA, comprising a cluster of three genes and an optional specific polymerase. This work opens the possibility to study and engineer synthetic organisms containing ZTGC-DNA.

Nature Commun, April 23, 2021.
Doi: 10.1038/s41467-021-22626-x.

Nature Commun, August 2021.
Doi: 10.1038/s41467-021-25064-x.

Nucleic Acids Res, Nov. 18, 2021.
Doi: 10.10.1093/nar/gkab955.

A successful Phase I clinical trial for a semisynthetic glycoconjugate vaccine against shigellosis

Shigella bacteria remain one of the four main pathogens responsible for moderate to severe diarrhea in children under the age of 5. No vaccine is currently available for shigellosis. Tackling the challenge of developing an efficacious *Shigella* vaccine with a carbohydrate chemist's vision, the department's scientists produced an original glycoimmunogen featuring a fine-tuned synthetic oligosaccharide as surrogate of the natural polysaccharide antigen. The molecular glycovaccine candidate was safe, well tolerated and strongly immunogenic in a first-in-human study. Data support further evaluation in target populations.

Lancet Infect Dis, April 2021.
Doi: 10.1016/S1473-3099(20)30488-6.

DECODING *GENOMES*

DEPARTMENT OF GENOMES AND GENETICS

This department seeks to decode genome architecture, expression and evolution by exploring genetic information from microorganisms including yeasts and bacteria, and also from humans and mice. It examines how this information is organized in the genome and shaped by cellular processes. Insights are thus gained on how genome evolution reflects selection for adaptation in terms of quality control of cellular processes and antibiotic resistance in microbes, and in terms of immune response in humans. Progress with these research programs is based largely on sequencing, genotyping and microfluidics approaches.

Director: Eduardo Rocha;
Deputy Director: Micheline Fromont-Racine.
11 teams.

South Pacific populations.

The immune response in South Pacific populations

To improve our understanding of diseases and their geographical distribution, knowledge of the genetic diversity of human populations is of vital importance. By analyzing the genomes of 320 individuals from the South Pacific, scientists from the Human Evolutionary Genetics laboratory tracked the different settlement phases in Oceania. They showed the importance of admixture between modern and archaic humans and its consequences for the health of today's populations, in particular their vulnerability to infection.

Nature, April 14, 2021.
Doi: 10.1038/s41586-021-03236-5.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Antibiotic response in bacteria: the role of membrane vesicles

In a study released in 2021, scientists from the Bacterial Genome Plasticity Unit and their colleagues demonstrated that antibiotics actively enhance the properties of extracellular vesicle transport at the surfaces of living microbes: extracellular vesicles are released in greater abundance and travel faster and farther from their origin. The altered extracellular vesicles' behavior may be a generalized response to antibiotic stress linked to the emergence of antibiotic resistance.

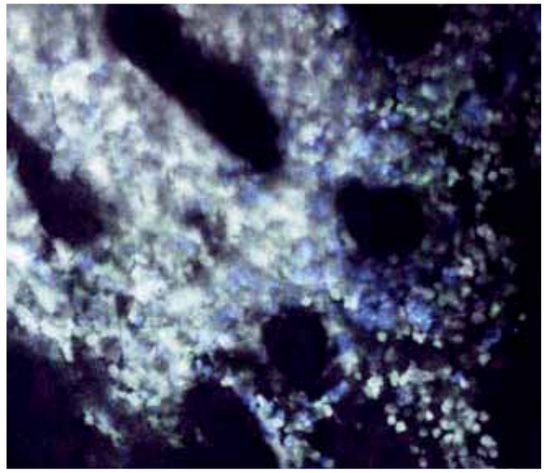
Science Advances, January 20, 2021.
Doi: 10.1126/sciadv.abd1033.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Investigation of RNA metabolism in yeast

Large-scale genetics identifies new factors affecting RNA. Scientists of the Genetics of Macromolecular Interactions laboratory explored hundreds of thousands of yeast mutants to identify genes that affect the stability and translation of messenger RNA in proteins. This allows a better understanding of the conserved mechanisms by which living organisms adapt to changes in the environment and resist viral infections.

Nucleic Acids Research, September 7 2021.
Doi: 10.1093/nar/gkab680.



Cancer: Visualization of CAR T cells in action.

EXPLORING THE WORKINGS OF *THE IMMUNE SYSTEM*

DEPARTMENT OF IMMUNOLOGY

Since its discovery, our immune system has been a constant source of fascination for scientists at the Institut Pasteur, who have been enthralled by its multiple facets. This department's work is focused on the development of the immune system, its protective and pathological responses, and its medical applications. They explore fundamental immunological processes to trace diseases back to their origins, provide ideas for the development of new vaccines, and deliver novel therapeutic strategies.

Director: Philippe Bousso;
Deputy Director: Caroline Demangel.
16 teams.

A promising vaccine against chronic allergic asthma

Allergic asthma is associated with a chronic inflammation of the lungs, notably causing increased production of two mediators of the immune response, IL-4 and IL-13. Pierre Bruhns, Laurent Reber and their colleagues developed a new vaccine targeting both IL-4 and IL-13. Tested on mice, it reduces symptoms and induces a lasting immune response. This dual vaccination could represent an affordable and efficient therapeutic solution against allergic asthma, which needs to be confirmed by clinical trials.

Nat Commun, May 11, 2021.
Doi: 10.1038/s41467-021-22834-5.

SARS-CoV-2: different immune responses observed in nasal mucosa and blood

How does variable mucosal immunity of the infected nasopharynx impact the clinical outcome of people infected with SARS-CoV-2? A large collaborative effort led by the teams of Darragh Duffy and James Di Santo determined that the immune response in nasal mucosa is often different from that in the blood during early acute infection, suggesting different models of immune regulation in the body. They also observed in critical patients increases in pathogenic bacteria often implicated in secondary respiratory infections.

Nat Immunol, September 1 2021.
Doi: 10.1038/s41590-021-01028-7.

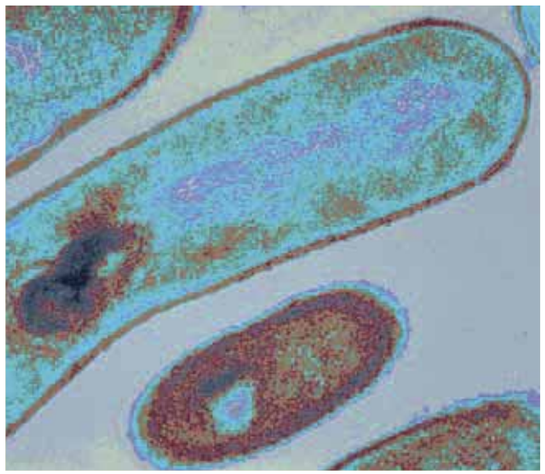
SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Cancer: CAR T cell function scrutinized to improve immunotherapy

CAR T cells represent a promising new anti-cancer strategy, but the mechanisms at play remain elusive. Using intravital imaging, Philippe Bousso and his team identified different cell subpopulations with complementary action: $CD4^+$ CAR T cells specialize in immune activation and $CD8^+$ CAR T cells in the killing of tumor cells. Both subsets rely on an efficient cross-talk with the tumor microenvironment for their therapeutic activity against tumor cells.

Science Immunology, March 26, 2021.
Doi: 10.1126/sciimmunol.abd4344.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.



Section of the *Listeria monocytogenes* bacterium.

A CLOSE LOOK AT *MICROORGANISMS'* LIFE CYCLE

DEPARTMENT OF MICROBIOLOGY

Bacteria, archaea and their viruses are everywhere, potentially causing diseases and/or providing us with research models. Scientists from this department scrutinize microorganisms, examining their basic biological mechanisms using methods such as genomic, genetic and metabolic analyses. They focus on mechanisms that cause some of these microorganisms to be pathogenic and evade the host's immune system or resist antibiotics. This work helps us better understand their life cycle and develop novel diagnostic tools or therapies for treating bacterial infections.

Director: Frédéric Barras;
Deputy Director: Bruno Dupuy.
19 teams.

Z base – the biosynthesis pathway of a new DNA nucleobase elucidated

The purine bases A and G found in DNA are generally synthesized by two different biosynthesis pathways. However, another base, Z, has been observed in the DNA of certain phages. In their study, scientists from the Department of Microbiology and the French Alternative Energies and Atomic Energy Commission (CEA) revealed the existence of a *de novo* purine biosynthesis pathway that leads to the formation of dZTP, illustrating viruses' capacity for biocatalytic innovation.

Science, April 30, 2021.
Doi: 10.1126/science.abe6494.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

A bacterium produces a contact-dependent antibiotic molecule

Listeriolysin S (LLS) is a bacteriocin produced by hypervirulent clones of *Listeria monocytogenes*. LLS targets specific gram-positive bacteria found in the intestine of mammalian hosts, altering the composition of their gut microbiota. Scientists from the *Yersinia* Unit and their colleagues showed that LLS is not secreted and described its mechanism of action – through direct contact between the bacteriocin and target bacteria.

PNAS, Oct. 1, 2021.
Doi: 10.1073/pnas.2108155118.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Insight into the evolutionary mechanisms modifying the importance of genes in *E. coli*

CRISPR-Cas9 technology, which was awarded the Nobel Prize in Chemistry in 2020, offers a novel high-throughput approach to bacterial genetics. Scientists from the Synthetic Biology Unit drew up the list of genes needed to grow an unprecedented number of *E. coli* isolates. This enabled them to identify the evolutionary mechanisms modifying the importance of genes in the bacterium.

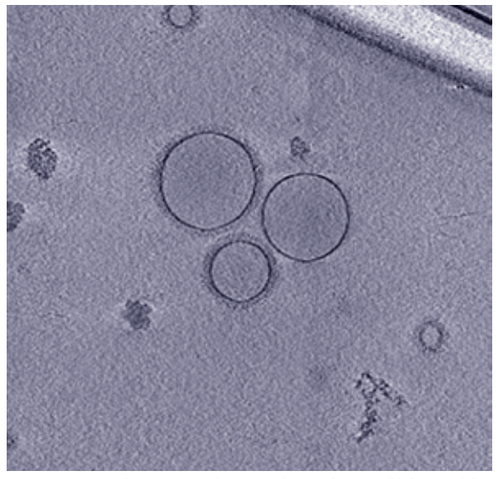
Nat Microbiol, March 15, 2021.
Doi: 10.1038/s41564-020-00839-y.

INVESTIGATING THE BIOLOGY *OF PATHOGENIC FUNGI*

DEPARTMENT OF MYCOLOGY

Fungal infections are a major public health concern linked to nearly 1.5 million deaths throughout the world every year. This department applies multidisciplinary approaches focused on three key fungi responsible for invasive infections: *Aspergillus fumigatus, Candida albicans* and *Cryptococcus neoformans*. The aim is to understand the biology of these pathogenic fungi and their virulence mechanisms, and to develop novel diagnostic, prevention and treatment strategies.

Director: Guilhem Janbon;
Deputy Director: Mélanie Legrand.
6 teams.



Electron cryomicroscopy image of extracellular vesicles produced by *Cryptococcus neoformans*.

Cryptococcus extracellular vesicle properties and their use as vaccine platforms

Extracellular vesicles (EV) have been shown to exist in many organisms, but their structure and composition in fungi, and particularly in fungal pathogens are poorly known. In their study, Rizzo et al. used several cutting-edge approaches to better understand them. They suggest a new EV structural model. For example, *Cryptococcus* EVs resembled the morphology of encapsulated virus structures, suggesting their potential as a vaccine, which was shown in model mice.

JEV, August 2, 2021.
Doi: 10.1002/jev2.12129.

Recombination-independent recognition of DNA homology for meiotic silencing

The initiation of epigenetic silencing remains one of the most poorly understood processes in molecular genetics. We show, in *Neurospora crassa*, that post-transcriptional silencing can be triggered *de novo* by the interactions between intact double-stranded DNA molecules. We also provide an all-atom model of the direct pairing between homologous DNA molecules that is, for the first time, consistent with both genetic and biophysical data.

PNAS, August 12, 2021.
Doi: 10.1073/pnas.2108664118.

Candida albicans isolates exhibit stable colonization of the gastrointestinal tract

Fungal gastrointestinal colonization is recognized as highly relevant to human health. The murine models used to study *Candida albicans* in this niche rely on altering the host microbiome to establish colonization. We characterize two isolates that can colonize without treatment and be used as research tools. This study emphasizes the importance of fungal intraspecies variation as well as host antimicrobial defenses in modulating colonization.

mBio, Dec. 21, 2021.
Doi: 10.1128/mBio.02878-21.

UNRAVELLING THE MYSTERIES OF THE BRAIN AND *UNDERSTANDING ITS DISORDERS*

DEPARTMENT OF NEUROSCIENCE

The Department of Neuroscience investigates the organization and function of the central nervous system across scales, from molecules to behavior. This knowledge about the nervous system forms a basis for studying the pathophysiology, and clinical implications of neurological and psychiatric disorders (hearing loss, autistic spectrum disorders, addiction, neurodegenerative disease and mood disorders) all of which represent major challenges for the department's scientists.

Director: David Digregorio
10 teams,
and 1 award-winning team.

Chronic obstructive pulmonary disease: a genetic mutation as predisposing factor

Chronic obstructive pulmonary disease (COPD) is a progressive chronic respiratory disease characterized by permanently obstructed airways, for which the underlying mechanisms are not fully identified. Researchers at the Institut Pasteur, together with collaborators in Lille and Reims, demonstrated that a single nucleotide substitution in the gene coding for the nicotinic acetylcholine receptor can result in COPD-like symptoms, independent of smoking.

Nature Communications, November 4, 2021.
Doi: 10.1038/s41467-021-26637-6.

SCAN THE QR CODE
FOR MORE INFORMATION
ABOUT THIS PUBLICATION.

COVID-19: discovery of the mechanisms of short- and long-term anosmia

COVID-19's most reported symptom is anosmia. Researchers at the Institut Pasteur, together with the Paris Public Hospital Network, elucidated the mechanism inducing the loss of smell caused by SARS-CoV-2. They discovered that the virus infects sensory neurons and causes persistent epithelial and olfactory nervous system inflammation. Moreover, in patients with persistent clinical signs, they observed enduring presence of the virus in the olfactory epithelium.

Science Translational Medicine, May 3, 2021.
Doi: 10.1126/scitranslmed.abf8396.

SCAN THE QR CODE
FOR MORE INFORMATION
ABOUT THIS PUBLICATION.

Virtual reality helps explore how the brain initiates movements

To escape predators or to acquire rewards, animals need to anticipate movements. How does the brain accomplish this task? Scientists at the Institut Pasteur recorded the activity of neurons in the frontal cortex of mice that were trained to run towards rewards within a virtual reality environment. They found that seconds before the mice start running, neurons show increasing "ramps" of activity.

Cell Reports, November 2021.
Doi : 10.1016/j.celrep.2021.110035.

SCAN THE QR CODE
FOR MORE INFORMATION
ABOUT THIS PUBLICATION.

Leishmania major parasite.

EXPLORING PARASITES AND *THEIR VECTORS*

DEPARTMENT OF PARASITES AND INSECT VECTORS

This department conducts research on three key eukaryotic parasites causing severe diseases that raise major public health challenges and impose a heavy economic burden on the most populated regions of the world: *Plasmodium* – the causative agent of malaria, *Leishmania* – the agent of leishmaniasis, and *Trypanosoma brucei* – responsible for sleeping sickness. The *Anopheles* mosquito, the vector of various *Plasmodium* species and several viruses, is also studied together with the tsetse fly, the vector of *Trypanosoma.*

Director: Gerald Spaeth;
Deputy Director: Kenneth Vernick.
10 teams.

Shedding light on how trypanosomes become infective for mammals

African trypanosomes are parasites responsible for sleeping sickness. They are transmitted by the bite of the tsetse fly, in whose salivary glands they proliferate and mature. Researchers used a novel technique termed "single cell sequencing" to capture the developmental program of trypanosomes in the salivary glands. This revealed key intermediate stages and demonstrated how they trigger the expression of an essential gene to become fully infective.

Plos Pathogens, September 20, 2021.
Doi: 10.1371/journal.ppat.1009904.

New insights into the adaptation mechanisms of *Leishmania* parasites

Leishmania parasites exploit genome instability for adaptation. Applying a new computational pipeline, scientists from the Molecular Parasitology and Signaling Unit led by Gerald Spaeth discovered that *Leishmania* exploits non-coding RNAs to mitigate toxic effects of genome instability by post-transcriptional regulation and the establishment of specialized ribosomes, which opens new avenues for biomarker discovery and anti-microbial intervention.

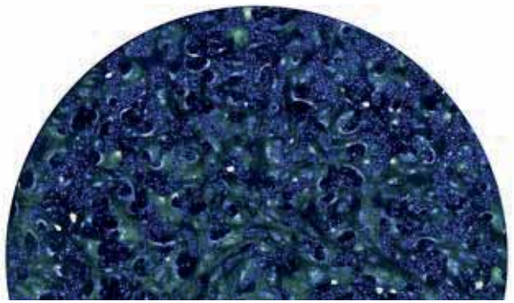
PNAS, December 21, 2021.
Doi: 10.1073/pnas.2113744118.

SCAN THE QR CODE
FOR MORE INFORMATION
ABOUT THIS PUBLICATION.

How the DNA repair response directs antigenic variation in African trypanosomes

DNA double-strand breaks (DSB) are potent drivers of variant surface glycoprotein (VSG) switching, albeit highly toxic. DSBs in highly repetitive regions are poor triggers for antigenic variation. Contrastingly, a DSB that does lead to VSG switching via recombination results in the upregulation of DNA damage linked genes. These results provide new insights into how the position of a DSB influences repair pathway choice and the subsequent gene expression changes.

Plos Pathogens, November 12, 2021.
Doi: 10.1371/journal.ppat.1010038.



Cells infected with SARS-CoV-2 fusing with neighboring cells.

EXAMINING VIRUSES AND MOLECULAR MECHANISMS *THAT CAUSE DISEASES*

DEPARTMENT OF VIROLOGY

This department seeks to gain insights into molecular mechanisms that are involved in various viral cycle stages and cause related diseases, with a significant focus on elucidating virus/host interactions and pathophysiological events linked to viral infection. Its research activities include studies on transmission, animal reservoirs and vectors, viral epidemiology and evolution, and host immune response. It scrutinizes respiratory viruses, oncogenic viruses, retroviruses and arboviruses using state-of-the-art technologies. The department hosts various National Reference Centers and WHO Collaborating Centers for viruses which perform essential epidemiological surveillance of viral infectious diseases.

Director: Jean-Pierre Vartanian.
13 teams.

Zika virus: a higher transmissibility and fetal pathogenicity of African strains over Asian strains

Although Asian Zika virus strains have been incriminated in all documented human outbreaks to date, we found that African Zika virus strains are more transmissible by mosquitoes and more pathogenic in both adult and fetal mice. These results highlight the high epidemic potential of African Zika virus strains and indicate that they could more easily go unnoticed by public health surveillance due to their propensity to cause fetal loss rather than birth defects.

Nat Commun., Feb. 10, 2021.
Doi: 10.1038/s41467-021-21199-z.

Novel natural killer cell induction strategy for controlling HIV

Lymph nodes are a safe haven for HIV where the virus persists despite effective antiretroviral treatment. Scientists from the HIV, Inflammation and Persistence Unit revealed the mechanism whereby natural killer cells learn how to specifically kill infected cells in an animal model. In a preclinical trial they managed to induce these cells and reduce the viral reservoir in the lymph nodes.

Nature Communications, February 2021.
Doi: 10.1038/s41467-021-21402-1.

Nature Communications, May 17, 2021.
Doi: 10.1038/s41467-021-23189-7.

See also page 17.

SCAN THE QR CODE FOR MORE INFORMATION (IN FRENCH) ABOUT THIS PUBLICATION.

Virological and immunological analysis of SARS-CoV-2 variants

The Virus and Immunity Unit studies the replication mechanisms of the different SARS-CoV-2 variants and their sensitivity to neutralizing antibodies. With a rapid, semi-automated assay, the infected cells in culture are detected and turn fluorescent after infection. The results show that the Omicron variant is particularly resistant to the antibodies produced by vaccines, which partly explains its spread to vaccinated individuals. Other studies are seeking to understand the increased transmissibility of the variants.

Delphine Planas et al., Nature, July 2021.
Doi: 10.1038/s41586-021-03777-9.

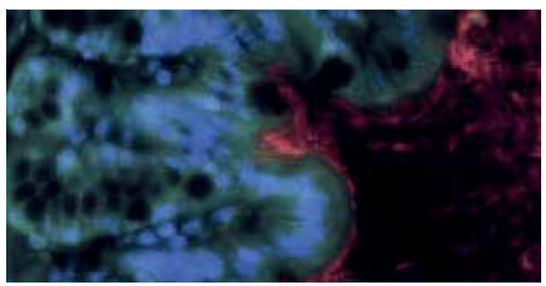
SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

RESEARCHING *EMERGING INFECTIOUS DISEASES*

DEPARTMENT OF GLOBAL HEALTH

The Department of Global Health adopts an interdisciplinary approach aimed at meeting the world's public health challenges. It applies a One Health approach, whereby health is viewed as a whole, with human, animal and environmental health considered interdependent and part of the same system. Scientists in this department research all aspects of interactions between pathogens, vectors and hosts, and their work spans numerous fields: epidemiology, genomic analysis, modeling, medical anthropology, studies of animal reservoirs, transmission and persistence mechanisms of pathogens in their environment, host pathophysiological processes and immune response, virulence factors, analysis of resistance to treatments and vaccinology. The department hosts National Reference Centers (see p. 48) and is involved in an increasing number of international collaborations (including within the **Pasteur Network**).

Director: Hervé Bourhy;
Deputy Director: Muhamed-Kheir Taha
13 teams.



Gut microbiota.

COVID-19: impacts of the pandemic on the human microbiome

An interdisciplinary research group, coordinated by Brett Finlay (University of British Columbia) and Tamara Giles-Vernick (Institut Pasteur), combined medicine and social sciences in an original approach. The researchers studied the effects of the COVID-19 epidemic and ensuing social and health-related disruptions on our microbiome.

PNAS, January 20, 2021.
Doi: 10.1073/pnas.2010217118.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Covid-19 : discovery of the mechanisms of short- and long-term anosmia

See page 34.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

ComCor study: locations of SARS-CoV-2 infection and protective effects of RNA vaccines

The Epidemiology of Emerging Diseases team launched the ComCor study in October 2020. Having included 450,000 cases and 25,000 controls, the circumstances and locations of SARS-CoV-2 infection were monitored in mainland France. The analysis also allowed an estimation of the protective effect of mRNA vaccines against SARS-CoV-2 variants.

The Lancet Regional Health Europe, November 25, 2021.
Doi: 10.1016/j.lanepe.2021.100278.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Diphtheria outbreak in Yemen: an epidemiology study

Diphtheria is a severe infection largely under control but it can re-emerge if vaccination is neglected. A collaboration between the National Reference Center (CNR) for Diphtheria and Yemini doctors and scientists showed an important effect of child vaccination and the concurrent circulation of several pathogenic strains in Yemen.

The Lancet Microbe, May 26, 2021.
Doi : 10.1016/S2666-5247(21)00094-X.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

HEARING *INSTITUTE*

The Hearing Institute, an Institut Pasteur center and France's first center dedicated to hearing research, was founded on the initiative of the Fondation pour l'Audition and the Institut Pasteur in partnership with Inserm. Its aim is to improve understanding of the principles and mechanisms that underpin the development and workings of the auditory system. The center's research areas include auditory perception and cognition, multisensory integration, and interactions between the genome and the acoustic environment. Its teams develop translational approaches aimed at improving patient care, producing diagnostic tools for hearing impairments, and developing innovative therapeutic approaches for children and adults based on advances in basic scientific knowledge.

Director: Prof. Anne-Lise Mamessier Giraud, who took over from Prof. Christine Petit on January 1, 2022.

Deputy Director: Séverine François.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE HEARING INSTITUTE.

Center for Research and Innovation in Human Audiology (CERIAH)

CERIAH, which opened in March 2021, was successful in an ANR/DFG proposal submitted jointly by the Hearing Institute and the University of Oldenburg on phenotyping severe age-related hearing loss (in the most severely affected 7% of cases for their age). The project was launched following approval by the Ethical Research Committee. This study and its environment are representative of other projects, including the Refined project (CERIAH/CEA/INRIA) on embedded artificial intelligence for hearing aids used by patients with auditory neuropathy.

Source: The CERIAH platform for research involving human participants based at the Institut Pasteur (Paris).

Technologies and gene therapy for hearing loss

Targeted inner ear therapies were developed based on identification and selection of viral vectors for gene therapy (Usher syndrome type 1G, otoferlin mutation) and patents were filed. Use of robot-assisted otologic surgery proved its benefit for reducing cochlear trauma when fitting cochlear implants (French National Academy of Medicine Laureate).

Source: Saaïd Safieddine and Yann Nguyen.

Auditory cognition and communication

In 2021, the team formed an industrial collaboration with MyBrain Technologies aimed at developing novel methods for multimodal data acquisition in the home. The researchers are now seeking to incorporate new portable smart recording devices using artificial intelligence for large cohorts that will help usher in a new era of precision telemedicine.

Source: Luc Arnal and Diane Lazard.

Dynamics of the auditory system and multisensory perception

In 2021, the team launched the FET Open-funded European HearLight project which seeks to demonstrate the feasibility of an optogenetic cortical implant for auditory rehabilitation. Further highlights of 2021 included Brice Bathellier's Foulon Prize and the publication of results indicating cortical involvement in the tactile perception of texture orientation in the journal *Science Advances*.

Source: Brice Bathellier.

Plasticity of central auditory circuits

This year, the team was awarded three French National Research Agency grants to study the impact of extended sound exposure and the role of the cerebrovascular system in the link between hearing loss and neurodegenerative diseases, and to fund a project using artificial intelligence to improve hearing aids for people with auditory neuropathy.

Source: Nicolas Michalski and Boris Gourévitch.

AN OUTSTANDING *TECHNOLOGICAL ENVIRONMENT*

The Department of Technology is one of the components of the Department of Scientific Affairs. Its aim is to develop a high-level technological environment to further enhance the Institut Pasteur's excellence in research.

All teams have access to a range of resources to help achieve this goal. The department's staff offers its expertise to provide scientists with access to state-of-the-art technologies, training on how to use them, and advice on technological and methodological developments to address different biological issues.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE DEPARTMENT OF TECHNOLOGY'S OBJECTIVES.

These resources are divided into five centers:

- The Center for Technological Resources and Research (C2RT)
- The Center for Animal Resources and Research (C2RA)
- The Institut Pasteur Biological Resource Center (CRBIP)
- The Data Management Core Facility (PF-DM)
- The Administrative and Quality Center (PAD)

Further resources provided to research laboratories

In 2021, the Department of Technology continued its development with the launch of three new platforms (see adjacent figures). The department pursued its investments in line with the technological strategic objectives outlined in the 2019-2023 Strategic Plan. Thus, by the end of 2021, 75% of planned investments within the remit of the Department of Technology had been made. In collaboration with the Technical Resources and Environment Department and the Information Systems Department, the Department of Technology initiated a project aimed at optimizing the validation process and improving the management of protocols for research entailing an infectious risk.

Under the supervision of the Scientific Secretariat General, the Data Management Core Facility and the Scientific Information Resources Center (CeRIS) introduced a policy on managing and sharing data and software codes which involved numerous Institut Pasteur stakeholders. The policy seeks to facilitate their reuse and improve research quality and reproducibility.

The CRBIP continued its integration within the EU biobank and infrastructure network. The **MIRRI** infrastructure is due to be rolled out by member states. The center is also involved in the **ISIDORe** project for access to infrastructure and the **HoloZcan** project on developing a new microscopy technology for detecting pathogens.

OVER
270
employees

20 C2RT units
4 C2RA units
4 CRBIP units
1 PAD unit
1 Data Management unit
10 units are ISO 9001 certified
9 units have IBISA accreditation

Key projects in 2021

- *A collaboration between the Mouse Genetics Engineering Center (CIGM) and the Institut Pasteur-TheraVectys joint laboratory:* a new transgenic mouse model generated at the CIGM confirmed unprecedented brain permissiveness to SARS-CoV-2 replication in addition to high permissiveness levels in the lungs. Using this animal model, the teams demonstrated the immunization capacity of a lentiviral vaccine candidate, with an initial intramuscular dose followed by an intranasal booster, for achieving full protection of the lungs and central nervous system. It also protects against SARS-CoV-2 variants (Ku et al., 2021, *EMBO Molecular Medicine;* 13: e14459).

- *A project involving a partnership between the Nanoimaging Platform and a group from the Institute for Integrative Biology of the Cell (U Paris-Saclay/CNRS/CEA)* with the assistance of a global expert on helical image processing resolved the structure of the small peptide lanreotide that had been misinterpreted for the past 20 years. This led to a high-impact publication demonstrating its actual structure for the first time (Laura P, et al., *Proc Natl Acad Sci USA*. 2022 Jan 25; doi.org/10.1073/pnas.2120346119).

- *A collaboration between the UBI platform and the Dynamics of Host-Pathogen Interactions Unit:* using a recently developed fluorescent reporter, the Salmonella Intracellular Analyzer, a dormant subpopulation of *Salmonella Typhimurium* (an enteric bacterium) was revealed in vacuoles by correlative microscopy combining fluorescence microscopy and transmission electron microscopy performed on serial sections of infected cells. Intraepithelial dormant *S. Typhimurium* represents an important pathogen niche and offers a new treatment strategy (Luk, C. H. et al., (2021), *PLoS Pathogens, 17*(4). doi:10.1371/journal.ppat.1009550).

- *Proteins pole platforms and other platforms continued to work on several COVID-related projects.* For example, under the coordination of the AI platform, they collaborated on the production of recombinant SARS-CoV-2 nucleoprotein (N) and spike (S) antigens, and the generation of anti-N and anti-S nanobodies for diagnostics (development of serological assays) and therapeutic applications. They contributed to 11 publications including the following:

- Grzelak L, et al., *Sci Transl Med.* 2020 Sep 2;12(559) PMID: 32817357.
- Le Vu S et al., *Nat Commun.* 2021 May 21;12(1) PMID: 34021152.
- Rosado J et al., *Lancet Microbe.* 2021 Feb;2(2), PMID: 33521709.
- Gransagne M, et al., *J Biol Chem.* 2022 Jan;298(1):101290. PMID: 34678315.
- Temmam S, et al., *Nature.* 2022 Feb 16. PMID: 35172323.

NEW PLATFORMS SET UP IN 2021

HUMAN DISEASE MODELS

The Human Disease Models Core Facility affiliated with the C2RA produces mice with human immune systems and offers its expertise on potential applications of this model.
These mice are preclinical *in vivo* models enabling long-term studies in various fields including human immune cell biology, immuno-oncology and infectious diseases (pathogens with human tropism). They are also used to test the efficacy and potential toxicity of new vaccines or immune system modulators.

IMMUNOMONITORING

An immunomonitoring platform was set up in the Cytometry and Biomarkers UTechS. Multidisciplinary expertise available within the UTechS was applied to develop a turnkey solution to support clinical and translational studies through advanced monitoring of immune response tailored to specific projects. In 2021, the "Maison de Famille" project was launched to study anti-SARS-CoV-2 T-cell response in an elderly cohort.

DIAGNOSTIC TESTS

This platform was set up to support the campus with the innovation, development and ultra-high throughput implementation of diagnostic tests for human, animal and environmental health. The LuLISA method developed at the beginning of the COVID pandemic enabled the Institut Pasteur to monitor the rise in infections and the nationwide vaccination campaign in mainland France and overseas territories on behalf of Santé publique France. Through the platform's collaboration with the Laboratory for Urgent Response to Biological Threats (CIBU) and Médecins sans Frontières, it was possible to monitor the spread of the pandemic among disadvantaged communities in the Greater Paris area and tailor support provided to these communities by the authorities and NGOs. This platform will be supported by the Institut Pasteur's Innovation Accelerator.
—

THREE KEY *INFORMATION SYSTEMS* PROJECTS

In addition to ensuring that the Institut Pasteur's IT infrastructure and equipment is fully functional, the Information Systems Department also has an important part to play within a cutting-edge research institute. According to the Strategic Plan, it must "provide a favorable technological environment". In 2021, three projects provided technologies to support the Institut Pasteur in its missions and activities.

Electronic laboratory notebook available for all

Besides being a requirement for funding bodies and industry partners, the introduction of electronic laboratory notebooks (ELNs) primarily represents a technological opportunity and critical tool central to research activities. The eLAB project, whose goal is to equip the entire institute by 2023, was launched in June 2019 under Christophe d'Enfert's leadership, with numerous scientists involved in the selection phases and the final choice of the eLabjournal solution (ElabNext – Eppendorf Group). The three-wave rollout (2021, 2022 and 2023) is well underway with almost two-thirds of research units using the electronic format and all remaining teams due for rollout completion by the end of 2022. A dedicated project team is supporting scientists with this transition from hardcopy to electronic format, which provides them with a scientific, collaborative, and also legal document (when filing for patents).

Digitization of the Education Center's student management system

This project managed by the Director of the Education Department, Monica Sala, with the involvement of her entire team as well as trainers and students, spanned over two years (late 2018 to May 2021). The three key objectives were to:

- Increase productivity in terms of financial resources and administrative management to optimally manage increasing student numbers and new courses.
- Modernize the image of the Institut Pasteur's educational provision using a novel tool with benefits for students, particularly in terms of simplifying the enrollment process.
- Help increase the visibility of the Institut Pasteur's educational provision both in France and abroad.

In its first year of use since going live, the new application has proved effective in allowing all users to meet these various objectives.

New version of the Owey research platform

A new version of the platform has been available since October 2021. Designed for storage and secure transfer of large files in all disciplines, it was developed in consultation with Institut Pasteur scientists in a wide range of fields including the genetics and neurobiological bases of autism (Thomas Bourgeron), antibiotic resistance (Sylvain Brisse), *Candida albicans* (Christophe d'Enfert), and the immune system (Étienne Patin). Owey speeds up international and multidisciplinary collaborations while also ensuring data security.
Aims:

- To provide scientists with virtually instant access to raw and analyzed data.
- To determine who can download files and access data in a few mouse clicks. In 2022, development work on Owey will focus on features enabling data exploration and provision of data to the wider scientific community beyond data gathering partners.

NATIONAL ACADEMIC *PARTNERSHIPS TO DRIVE* SCIENTIFIC EXCELLENCE

The Institut Pasteur has a long history of research and/or teaching partnerships with research institutions and universities in the Greater Paris region. One of the objectives of the 2019-2023 Strategic Plan is to consolidate and develop national partnerships to drive scientific excellence within the Institut Pasteur. In line with this goal, the Institut Pasteur and Université Paris Cité joined forces to forge a world-class partnership (see insert).

Partnerships with Public Scientific and Technical Research Establishments (EPSTs)

The Institut Pasteur campus currently hosts numerous research units that are jointly affiliated with the CNRS (9 UMRs (joint research units), 1 EMR (joint research team), 1 UAR (support and research unit)) and Inserm (8 Us (units), 2 UAs (support units)). The Institut Pasteur also hosts one Unit Under Contract (USC) with the French National Research Institute for Agriculture, Food and Environment (INRAE) and joint units with the French National Conservatory of Arts and Trades (CNAM), the French National Institute for Research in Digital Science and Technology (Inria), and the École Polytechnique.

The purpose of joint units is to host scientists from these organizations. The Institut Pasteur currently hosts 77 scientists and 17 engineers from the CNRS, 32 scientists and 12 engineers from Inserm, 11 scientists/lecturers and 8 university hospital scientists/lecturers.

University and teaching partnerships

These partnerships cover aspects of research that enable hosting of scientists/lecturers and are essential for developing teaching activities. Fourteen courses can be included as part of a Master's program (first- or second-year Master's) at our partner universities (Université Paris Cité, Sorbonne Université, ENS/PSL, Paris-Saclay), 17 Institut Pasteur courses lead to the award of a university diploma (DU) from Université Paris Cité (16) or Sorbonne Université (1), and more than 20 courses count as doctoral school modules. Moreover, 10 Institut Pasteur courses are included in the Université de Paris European Masters in genetics and 14 Institut Pasteur courses are eligible for ECTS (European Credit Transfer System) credits from the Pasteur/CNAM School which awards the Advanced Master's in Public Health. Finally, the "Médecine-Sciences" program is run in partnership with the École normale supérieure (ENS), Institut Curie and PSL. The Institut Pasteur also manages its own international PhD program (PPU) in close partnership with Université Paris Cité, Sorbonne Université and Université Paris-Saclay.

Partnerships with the Paris Public Hospital Network (AP-HP)

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, either as guest researchers or via a partnership contract. This partnership provides the basis for setting up joint units and hosting hospital practitioners from the Paris Public Hospital Network (AP-HP).

WHY DO WE NEED PARTNERSHIPS?

- To identify research institutions, teams and scientific projects for potential collaborations.
- To structure and strengthen links with Institut Pasteur partners by e.g. providing conditions conducive to the formation of joint research units (UMRs).
- To provide a framework for external researchers to work at the Institut Pasteur campus and for Institut Pasteur researchers to spend time at external research organizations, schools and universities (accompanied by post-doctoral fellows, engineers, etc. where appropriate).
- To promote outstanding teaching and enhance the Institut Pasteur's appeal for future generations of scientists.

—

HOW DO WE FORGE PARTNERSHIPS?

- By setting up specific agreements that can be linked to framework agreements defining the terms of such collaborations with regard to research or teaching.

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2021 PARTNERSHIP

A STRATEGIC *SCIENTIFIC PARTNERSHIP* WITH UNIVERSITÉ PARIS CITÉ

The Institut Pasteur's association with Université Paris Cité is a world-class partnership in research and education in the field of biology and health, formally established in June 2021. Through it, the Institut Pasteur has become a research partner and member of the Université Paris Cité community. Research partner status guarantees mutual respect for the institutional, scientific and financial independence of the two partner organizations. Governance of the association is balanced, with the respective Presidents sitting on the Boards of both institutions and reciprocal representation in the Université Paris Cité Academic Senate and the Institut Pasteur General Meeting board.

The two institutions have joined forces to develop a concerted joint scientific strategy based on strengthening and co-developing existing topics within the two institutions in the areas of both fundamental and translational research and training.

- Shared areas of excellence: microbiology, immunology, structural biology and chemistry.
- Synergies will be developed in developmental biology, cellular biology, neuroscience, hard sciences, and humanities and social sciences.

The Institut Pasteur and Université Paris Cité already collaborate on numerous research and training projects, and the sharing of human and technological resources and expertise will further strengthen this collaboration.

The association between the Institut Pasteur and Université Paris Cité also reflects a broader ambition to boost international reach, for which the **Pasteur Network** will be a major asset.

AWARDS AND APPOINTMENTS 2021

APPOINTMENTS

Frédéric Barras
Head of the Stress Adaptation and Metabolism in Enterobacteria Unit
Elected to the American Academy of Microbiology

Simon Cauchemez
Head of the Mathematical Modeling of Infectious Diseases Unit
Appointed to the rank of *Chevalier* of the Legion of Honor

Stewart Cole
or Prof. Sir Stewart Cole, President of the Institut Pasteur (Paris)
Knight Commander of the Most Distinguished Order of Saint Michael and Saint George
For services to Science

Pascale Cossart
Head of the Bacteria-Cell Interactions Unit
Promoted to the rank of *Grand Officier* of the National Order of the Legion of Honor

Marc Delarue
Head of the Architecture and Dynamics of Biological Macromolecules Unit
Elected to the Academia Europaea

Richard Delorme
Human Genetics and Cognitive Functions Unit
Appointed to the rank of *Chevalier* of the Legion of Honor

Hilde de Reuse
Head of the Helicobacter Pathogenesis Unit
Elected to the Academia Europaea

Arnaud Fontanet
Head of the Epidemiology of Emerging Diseases Unit
Promoted to the rank of *Officier* of the Legion of Honor

Didier Mazel
Head of the Bacterial Genome Plasticity Unit
Elected to the Academia Europaea

Didier Ménard
Head of the Malaria Genetics and Resistance five-year unit (U5)
ASTMH Distinguished International Fellow, American Society of Tropical Medicine and Hygiene

Christine Petit
Director of the Hearing Institute
Promoted to the rank of *Commandeur* of the National Order of Merit

François Romaneix
Senior Executive Vice-President of the Institut Pasteur
Appointed to the rank of *Chevalier* of the Legion of Honor

HONORS AND PRIZES

Brice Bathellier
Hearing Institute
Foulon Award, French Academy of Sciences

Christophe Beloin
Genetics of Biofilms Unit
Georges Zermati Prize, Fondation de France

Morgane Boulch
Dynamics of Immune Responses Unit
L'Oréal-UNESCO For Women in Science French Fellowships

Lena Bourhy
Perception and Memory Unit
Villa M Research Fellowship (Groupe Pasteur Mutualité)

Philippe Bousso
Head of the Dynamics of Immune Responses Unit
Grand Prix Charles Oberling-Hagueuneau

Simon Cauchemez
Head of the Mathematical Modeling of Infectious Diseases Unit
Lucien Tartois Prize, French Foundation for Medical Research (FRM)

Jean-Pierre Changeux
Department of Neuroscience
Thomson Reuters/Clarivate "Nobel class" Citation Laureates

Guillaume Dumenil
Head of the Pathogenesis of Vascular Infections Unit
Scientific Grand Prize, Fondation NRJ–Institut de France

Iuliana V. Ene
Head of the Fungal Heterogeneity five-year group
CIFAR Azrieli Global Scholars 2021-2023

Arnaud Fontanet
Head of the Epidemiology of Emerging Diseases Unit
Jean Valade Prize, Fondation de France

Micheline Fromont
Genetics of Macromolecular Interactions Unit
Georges Zermati Prize, Fondation de France

Jérôme Gros
Head of the Dynamic Regulation of Morphogenesis Unit
Pasteur Vallery-Radot Prize, National Library of France

Mélanie Hamon
Head of the Chromatin and Infection five-year research group
EMBO Young Investigator Programme Award

Mart Krupovic
Head of the Genetics of Macromolecular Interactions Unit.
André Goffeau Award, French Genetics Society.
Head of the Archaeal Virology five-year unit
Thérèse Lebrasseur Prize, Fondation de France

Didier Ménard
Head of the Malaria Genetics and Resistance five-year unit (U5)
M^me^ Jules Martin, née Louise Basset Award, French Academy of Sciences

Yann Nguyen
Hearing Institute
Jansen Award, French National Academy of Medicine

Étienne Patin
Human Evolutionary Genetics Unit
Pasteur Vallery-Radot Prize, National Library of France

Olaya Rendueles-Garcia
Microbial Evolutionary Genomics Unit
CNRS Bronze Medal

Marion Rincel
Microenvironment and Immunity Unit
L'Oréal-UNESCO For Women in Science French Fellowships

Étienne Simon-Lorière
Head of the Evolutionary Genomics of RNA Viruses five-year group
Georges, Jacques and Elias Canetti Prize

Gerald Spaeth
Director of the Department of Parasites and Insect Vectors and Head of the Molecular Parasitology and Signaling Unit
"Springboard" award for bilateral research cooperation

Cécile Tran-Kiem
Mathematical Modeling of Infectious Diseases Unit
L'Oréal-UNESCO For Women in Science French Fellowships

Léon Valon
Cell Death and Epithelial Homeostasis Unit
SBCF Junior Researcher Award

Sylvie Van der Werf
Molecular Genetics of RNA Viruses Unit
René & Andrée Duquesne Award

ERC FUNDING

Shahragim Tajbakhsh
Head of the Stem Cells and Development Unit
ERC Advanced Grant 2021 for the project *STENIPATH* – Stem and niche cell dynamics in normal and pathological conditions

Thibaut Brunet
Head of the Evolutionary Cell Biology and Evolution of Morphogenesis five-year group (G5)
ERC Starting Grant for the project *EvoMorphoCell* – From cell shape to organism shape: the cellular basis for the evolutionary origin of animal morphogenesis

David Bikard
Head of the Synthetic Biology Unit
ERC Consolidator Grant for the project *crInSitu* – In situ genetic perturbation of gut bacteria with engineered phage vectors and CRISPR

IP YOUNG SCIENTIST PRIZE

Post-doc category
Fabien Aubry
Insect-Virus Interactions Unit
Microenvironment and Immunity Unit

PhD category
Adrià Sogues
Structural Microbiology Unit

Cécile Tran-Kiem
Mathematical Modeling of Infectious Diseases Unit

ADVANCES *IN RESEARCH* APPLICATIONS

The aim of the Institut Pasteur's Technology Transfer and Industrial Partnership Department (DARRI) is to identify projects with high development potential and promote partnerships to facilitate their transfer to market through licenses or the launch of startups. The department's activities and expertise are wide-ranging, covering the entire innovation life cycle up to technology transfer: identification and protection of potential applications, scientific development, innovation transfer and partnership building.

IN 2021, THE INSTITUT PASTEUR maintained its strong focus on COVID-19-related topics and the DARRI made a significant contribution to this response by enabling rapid technology transfer from academic research to industry through agreements designed to guarantee access to products and services for populations worldwide, with licenses free for low-income countries.

One example that perfectly illustrates the DARRI's strategy and agility is the launch of the startup SpikImm, which occurred in record time (28 days), and the implementation of a new patent license for antibodies developed by the Institut Pasteur's Humoral Immunology laboratory led by Dr. Hugo Mouquet (Inserm joint research unit).

2021 also saw a resumption of "non-COVID" activities, with numerous inquiries from industry partners proving that the Institut Pasteur is recognized as a key stakeholder in the health ecosystem, both in France and throughout the world. This is reflected in the 33 new collaboration agreements (and 13 new patent and biological material licenses) secured.

The DARRI also coordinated 335 management agreements (45% additional agreements since 2016) and its activities generated a total of €39 M in revenue from industry partnerships, of which €12.5 M related to collaboration agreements.

Protecting inventions

In 2021, 45 invention disclosures were registered, resulting in 20 new priority patents being filed and 47 provisional applications (for software, expertise and biological material). In keeping with the maturation of inventions strategy and the policies adopted by the Institut Pasteur Innovation Accelerator, priority was specifically given to projects selected for their high transfer and development potential.

Developing innovation through selected projects

The Institut Pasteur Innovation Accelerator, launched in 2019 to boost the socio-economic transferability of the most promising research applications and mitigate any associated risks, supported over 10 projects in 2021 in an attempt to reduce the time to market of newly discovered health products.

The project engineering approach taken by the Innovation Accelerator combines funding strategies, technical support and professional expertise from the DARRI. This approach is designed to improve the maturity of selected projects and bring them into line with industrial requirements and needs, thereby making them viable, attractive candidates for industry partners, charitable organizations or the launch of start-ups.

Five new projects were selected in 2021:

- Microbiota-based therapies for neurodegenerative diseases, PI: Damien Rei,
- A capture antibody (mAb 1B6) targeting rocuronium to reverse profound neuromuscular blockade, PI: Pierre Bruhns,
- MOPEVAC-NEXT, which seeks to develop and assess an innovative vaccine platform based on a hyperattenuated viral vector derived from the Mopeia virus (MOPV), PI: Sylvain Baize.
  The MOPEVAC-NEXT program won the "Emerging Infectious Diseases and CBRN threats" call for expressions of interest and has received over €5.6 M of government funding through the French national recovery plan and the Investing in the Future program,
- Circulating biomarker signatures for the detection of gastric preneoplasia and cancer, PI: Eliette Touati,
- Development of *in vitro* diagnostic tests to explore sources of allergies, assess severity, guide therapy, PI: Thierry Rose.

Four main criteria were assessed when selecting projects: the science and disruptive aspects of innovations; the strength of related patents and dependence on other technologies; product development with internal resources and via partnerships; and the potential market, its accessibility and rival developments.

Developing partnerships with industry

To provide favorable conditions in which to bring therapeutic, vaccine and diagnostic solutions to market for the benefit of patients, it is essential to increase interaction between the Institut Pasteur and industry and establish synergies between their respective scientific teams. In 2021, this ambition led to the signing and extension of more than 66 R&D agreements with long-standing and more recent partners, including the following two examples.

"The project led by the startup SpikImm on anti-SARS-CoV-2 monoclonal antibodies is a concrete example of the success that is possible with the Institut Pasteur's innovation development model. We were quickly able to transfer the technology to a leading industry partner, Truffle Capital."

Isabelle Buckle, *Vice-President Technology Transfer and Industrial Partnership (DARRI)*

A research collaboration agreement with Janssen
The three-year collaboration agreement signed in 2021 between the Institut Pasteur, the Paris Public Hospital Network (AP-HP) and Johnson & Johnson's pharmaceutical company Janssen paves the way for exploration of the signaling pathways involved in chronic inflammatory diseases. One of the aims of the partnership is to improve our understanding of the biology of disease and to improve treatment of inflammatory diseases through multi-omics research based on patient samples and related detailed phenotypic data.

Sanofi partnership rollout
The framework agreement signed between the Institut Pasteur and Sanofi in 2020 came into full effect in 2021 with the launch of two major programs involving scientists from both parties. One examines the impact of microbiota changes on vaccine response, and the other focuses on immunoprofiling and its impact on immune response.

This strategic partnership is linked to several other projects of interest due for rollout in the coming years.

Carnot, a guarantee of excellence for the Institut Pasteur

The Institut Pasteur has been part of the Carnot network since the accreditation was first introduced in 2007, in recognition of the scientific quality of its research and the professionalism of its technology transfer activities.

In 2021, 23 innovative new research projects at an early or advanced stage – 19 within the Carnot scope – were funded by the DARRI/Carnot Emergence, Maturation, Partnership & Innovation and Consolidation programs. The aim is to support promising projects whose results will contribute to the intellectual property portfolio, applied science projects positioned for product and/or technology transfer and for which an initial invention disclosure has been filed, and also targeted projects (with no call for proposals) jointly developed and pursued by the DARRI and scientists in the departments within the Carnot sphere. The DARRI/Carnot Consolidation program is designed to strengthen patent applications. ●

45
invention disclosures

+5
new selected projects joined the Innovation Accelerator

€39 M
in revenue

330
agreements signed

614
biological material transfers

LAUNCH OF THE STARTUP SPIKIMM

Monoclonal antibody therapy is one of the most novel approaches for treating COVID-19 patients and preventing progression to severe forms of the disease.
The startup SpikImm established by the Institut Pasteur and Truffle Capital in 2021 develops antibodies using an innovative process invented by the Institut Pasteur's Humoral Immunology laboratory (Inserm joint unit) led by Hugo Mouquet, enabling screening and selection of SARS-CoV-2-specific human neutralizing antibodies. The Institut Pasteur filed an international patent application and signed an exclusive global license agreement with SpikImm, under which clinical trials are due to begin in mid-2022.

One of SpikImm's monoclonal antibodies, SPK001, powerfully and effectively neutralizes the original SARS-CoV-2 strain as well as all variants of concern. SPK001 is a high-affinity monoclonal antibody targeting the RBD (receptor-binding domain) of the viral spike protein. —

ADVANCES IN *PUBLIC HEALTH*

NATIONAL *REFERENCE* CENTERS (CNRs)

National Reference Center (CNR) status is awarded by Santé publique France (SpF). CNRs have four broad missions, as laid down in the French Public Health Code, with the aim of: examining infectious agents and their sensitivity to anti-infectives; monitoring their circulation in France; alerting health authorities of the emergence or re-emergence of any pathogens or of an unusually high number of clustered cases that may signal the start of an outbreak; advising and training public authorities, health safety agencies and health professionals.

TO CLOSELY MONITOR the development of the SARS-CoV-2 outbreak and the emergence of new variants, the French health authorities set up EMERGEN (a consortium monitoring and researching infections by EMERging pathogens through microbial GENomics) in January 2021, with a view to rolling out a SARS-CoV-2 genome surveillance system throughout France for public health and research purposes.

35,714
SARS-CoV-2 variants sequenced by P2M in 2021 for the CNR VIR alone through the EMERGEN project.

17,200
samples sequenced in 2019 by P2M, by way of comparison, for the 14 CNRs under Institut Pasteur supervision, of which approximately 4% were conducted for the CNR VIR.

Whole genome sequencing of the virus is the only technique capable of characterizing new emerging variants and identifying their specific mutations and recombinations. Analysis of new variants combined with patients' clinical data at the time of sampling is used to determine variants' functional impact in terms of virulence, infectiousness, and ability to affect vaccinated individuals, etc.

Genomic sequencing of SARS-CoV-2 samples collected nationwide on a given date provides a map of variants in circulation in France on that date. Regular repetition of these large-scale sequencing operations (weekly SpF flash surveys) helps generate a set of genetic data related to the virus, clinical data related to patients, and spatio-temporal data related to the distribution of variants nationwide. Once aggregated, all these data provide the basis for analyses performed by modelers, whose task is to formulate theories and produce projections on the development of the outbreak in France. This knowledge is essential for identifying means of controlling risks related to COVID-19 in the general population, guiding decisions, and helping the health authorities with their strategy to tackle the outbreak.

In 2021, the CNR for Respiratory Infection Viruses (CNR VIR) and the Mutualized Platform for Microbiology (P2M) played a key role in the EMERGEN project. P2M, one of 4 national platforms, tripled its sequencing capacity to meet demand from the health authorities, while continuing to provide sequencing for the other CNRs. It was able to rapidly upscale due to the extraordinary efforts of teams at the CNR VIR and P2M and the solidarity shown by staff at other CNRs and Institut Pasteur research units.

SCAN THE QR CODE FOR OTHER SIGNIFICANT HIGHLIGHTS CONCERNING THE NATIONAL REFERENCE CENTERS (IN FRENCH).

CENTER FOR *TRANSLATIONAL* SCIENCE (CRT)

The Center for Translational Science (CRT) includes two primarily affiliated entities, the ICAReB platform, which performs clinical investigation and biobanking activities, and the Clinical Core (CRT-CC), which designs and coordinates research involving human subjects in accordance with ethical and regulatory requirements. It also encompasses one secondarily affiliated entity, the CB-UTechS, a technology platform for research on biomarkers, cytometry and immunomonitoring.

THE CRT CONTINUED its reorganization initiated in 2020. It continued to develop clinical research activity within the Institut Pasteur by boosting capacity and promoting the transfer of its basic research to applications. In 2021, processes for ethical and regulatory guidance on clinical research programs were optimized with the introduction of the "Guichet Unique" (one-stop shop) designed to facilitate procedures for scientists and minimize any associated risks.
In 2021, projects related to the COVID-19 pandemic continued to be actively pursued, with CRT entities taking operational responsibility for cohorts. These notably included:
- Projects seeking to assess the efficacy of antibodies and immunity against new variants acquired post-vaccination and/or infection within the population and the efficacy of various vaccination regimens: COVIDoise, a longitudinal study of subjects resident in Crépy-en-Valois (800 participants) and CORSER-4 (92 participants).
- The COMCOR project involving a nationwide epidemiological cohort of individuals infected with COVID-19 (316,000 participants), a support study to guide public health decision-making.

The CRT supported the launch and continuation of projects related to other topics, in particular the Glyco-Shig3 vaccine trial aimed at preventing Shigella-induced dysenteric diarrhea (200 participants enrolled in Kenya) and the "Familial Adenomatous Polyposis" project in collaboration with a patient association (24 participants) whose initial findings appear to corroborate the initial scientific theory.

80
research projects involving human subjects were submitted to the "Guichet Unique", in 2021, 50 of which were supported by the Promotional and Monitoring Committee

224,000
samples stored at ICAReB by the end of 2021, of which 73,000 were for COVID-19 projects

80
biological resource requests processed, of which 43% were new in 2021

COVOL led by an Institut Pasteur ethics specialist was established for healthy volunteers included in ICAReB cohorts. COVOL is an advisory body set up to enhance interaction between the Institut Pasteur and individuals participating voluntarily in research, and take account of their opinions and experiences in relation to clinical research issues.

Finally, the CB UTechS now includes an immunomonitoring platform. It provides support and technological expertise for the institute's clinical and translational projects. In 2021, the Maison de Famille project was initiated to study anti-SARS-CoV-2 T-cell response in an elderly cohort. Moreover, the CB UTechS, which is heavily involved in single-cell approaches, was awarded 10x Genomics Service Provider certification recognizing its quality of service and expertise (for transcriptomic studies and immune receptor profiling). With its constant focus on technological developments and scientists' needs, it has implemented a new pipeline for analyzing extra-vesicular and virus particles.

THE INSTITUT PASTEUR *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. It received ISO 9001:2015 certification in 2018.

58,332
visits to the vaccination center, including 39,097 for COVID-19 vaccinations

37,290
vaccines administered

8,427
consultations for infectious and tropical diseases and travel medicine

718
consultations at the Anti-Rabies Center

725
consultations for allergies

Medical activities

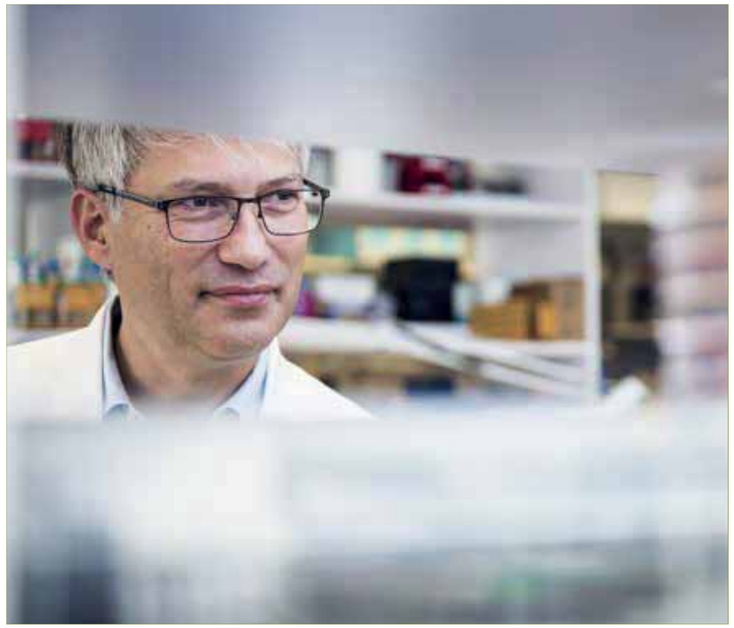
After a decline in the number of international travelers due to the emergence and spread of SARS-CoV-2 that dominated 2020, the Medical Center saw its workload significantly increase again in 2021, when a COVID-19 vaccination center was set up in the building to help with the national effort to vaccinate the population, starting with individuals at highest risk. Although the Medical Center was at first almost exclusively occupied with this work, "non-COVID" work gradually resumed due to increased COVID-19 vaccine coverage and, in particular, the resumption of global travel. This work focused on treating travelers both from a preventive perspective at the International Vaccination Center recognized for its expertise, and from a diagnostic and therapeutic perspective at the Anti-Rabies Center and in consultations for infectious and tropical diseases. In this area, patients continued to receive uninterrupted follow-up for chronic infections with HIV or hepatitis viruses, chronic skin conditions such as hidradenitis suppurativa, and allergies.

Clinical research

The Medical Center was involved in several SARS-CoV-2 seroprevalence studies coordinated by the Institut Pasteur: the CORSER studies, including the CORSER-4 study assessing response to various vaccination regimens, and the Curie-O-SA study in partnership with the Institut Curie. The Medical Center also pursued its involvement in clinical research in its areas of medical specialization: cohorts with HIV infection, and the pathophysiology of hidradenitis suppurativa in collaboration with the ICAReB platform, Institut Pasteur research units and Necker Hospital. A comparative therapeutic trial for hidradenitis suppurativa, funded by the French Hospital Clinical Research Program (PHRC), is due to begin in late 2022 or early 2023. The aim is to endorse the treatment currently recommended by the Medical Center's dermatologists. The new insights offered by these projects fully justify the Medical Center's role within the Center for Translational Science (see p. 49).

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE INSTITUT PASTEUR MEDICAL CENTER

ADVANCES *IN EDUCATION* AND TRAINING



The mission of the Department of Education is to transfer and share scientific knowledge. For more than 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.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT EDUCATION AT THE INSTITUT PASTEUR

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 institutes in the **Pasteur Network** (PN). Over 600 young scientists are also hosted by laboratories on the Paris campus to train as scientists and complete their undergraduate, Master's and PhD research projects.

A unique setting for training in science and research

The Institut Pasteur provides a unique hands-on environment for young scientists from undergraduate to PhD level. It also runs excellent courses for Master's and PhD students, as well as vocational science courses leading to recognized university diplomas. Courses in Paris are coordinated by renowned scientists on campus, with input from professors based at partner institutions in France (Université Paris Cité, Sorbonne University, Université Paris-Saclay, Université PSL, the Institut Curie, the CNRS, Inserm and the CNAM) and abroad. An emphasis on experimentation and practical work is a strength and specificity of the Institut Pasteur's educational approach. The Pasteur Network has a major impact on teaching, in terms of both the scientific subjects taught and the international makeup of the students.

The Institut Pasteur and online courses in life sciences and health

The Institut Pasteur is continuing to develop its online teaching as a way of extending the reach of the courses taught at its Education Center or at institutes in the Pasteur Network. Within the space of just seven years, the Institut Pasteur has become ▶

"First-class lecturers and practical work are notable strengths of the Institut Pasteur's educational approach."

Monica Sala,
Director of the Education Department

INSTITUT PASTEUR 2021 PHD GRADUATION CEREMONY

THE ANNUAL PHD GRADUATION CEREMONY took place on December 17, 2021. Since 2013, this ceremony has become a showcase for the Institut Pasteur's excellence in research and teaching. The next ceremony is due to take place at 3pm on December 9, 2022 with guest speaker Professor Uğur Şahin, CEO of BioNTech (COVID-19 vaccine developer).
—

► France's top producer of MOOCs in the fields of life sciences and health. Pasteur MOOCs and the first global online diploma in infectious diseases (DNM2IP), launched by the Institut Pasteur in 2019, have proved a remarkable success with the public in terms of registrations and international visibility.

Predoctoral programs

The Institut Pasteur also offers training for students at earlier stages in their academic career. It has developed several predoctoral programs for students at school, undergraduate and Master's level. The "Collège 3" program gives middle school students in their fourth year the chance to come and find out about different research professions in a secure, structured environment. The Amgen Program gives around 20 students from European universities and higher education institutions the opportunity to work on a research topic for eight weeks in an Institut Pasteur laboratory. The Institut Pasteur also hosts students under the EU's Erasmus+ program, thanks to its partnerships with several European universities.

Training through research for PhD students

Each year, around 80 PhD students complete their studies in laboratories on the Paris campus. The Institut Pasteur provides scientific supervision for PhD students, as well as personal support with a tutoring program, a dedicated office and a structure for post-doctoral career development. The Institut Pasteur in Paris offers specific international doctoral programs (PPUs) run in close partnership with universities in the Greater Paris region. Each year, the Institut Pasteur also awards grants for the completion of PhDs in the Pasteur Network, outside mainland France. The Institut Pasteur, Institut Curie and École normale supérieure (ENS) run a "Médecine-Sciences" program, which reflects the major changes taking place in medical practice and biomedical research.

Scientific entrepreneurship training

The Institut Pasteur is committed to finding applications for its research, and this is reflected in its teaching. Several initiatives meeting these criteria took place throughout 2021. These included the continuing "Startup Breakfast" series – informal monthly events for Institut Pasteur scientists interested in business development, with guest speakers including successful biotechnology entrepreneurs, representatives of funding bodies and heads of business incubators –, and a startup workshop in June 2021 with practical sessions on specific projects led by junior Institut Pasteur scientists. ●

FUNDAMENTALS.

IN PARIS

The Institut Pasteur is committed to providing outstanding research to improve global health. It is a non-profit foundation with recognized charitable status, and its missions are to help prevent and treat diseases, mainly those of infectious origin, through research, public health, education and training, and the development of research applications.

€ 354.4
million budget in 2021

2,876
staff members (as at 12/31/2021)

77
nationalities (as at 12/31/2021)

1,418
papers published in 2021
Source : Web of Science (articles, early access articles, reviews and letters excluding preprints, extraction from April 4, 2022)

143
research structures including
94 research units,
10 five-year units (U5s),
24 five-year groups (G5s),
8 laboratories, 7 Hearing Institute teams
(including Hearing Institute teams as at January 1, 2022)

25
research support services and technological platforms

33
Pasteur Network member institutes

SCAN THE QR CODE FOR MORE INFORMATION ABOUT OUR INSTITUTE.

IN THE PASTEUR *NETWORK*

41
SCIENTISTS in the **Pasteur Network** received training through the Calmette & Yersin program, including 5 post-doctoral fellows and 13 PhD students

8
INTERNSHIPS for young French researchers in the **Pasteur Network** funded by the Pierre Ledoux–Jeunesse Internationale Foundation

3 G4s
ongoing and 3 new groups selected

9 PIUs
ongoing including 4 units selected for a one-year extension and 3 new units selected

A new system of governance is being introduced for the **Pasteur Network**, formerly known as the Institut Pasteur International Network, and its 33 members, which since 2011 have been part of an association. The network is chaired by Institut Pasteur President Stewart Cole. In June 2021, the network adopted a more participatory, balanced mode of governance and a more structured business model. The articles of association of the association representing the network – rebranded as the Pasteur Network – were amended and a foundation, which is based at the Institut Pasteur, was established as a funding body. This new organizational structure, which constitutes one of the pledges set out in the Institut Pasteur's 2019-2023 Strategic Plan, was presented to and approved by the Institut Pasteur Board of Governors on June 4.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE PASTEUR NETWORK

Strengthening surveillance networks

ANRS | Emerging Infectious Diseases joined forces with the Institut Pasteur, the IRD and laboratories in 13 African countries to launch the AFROSCREEN project. Funded by the AFD, the project addresses an urgent need to build a network monitoring the evolution of SARS-CoV-2 variants and other emerging pathogens by bolstering laboratory genomic sequencing capacity.

In parallel, the SARA project, funded by the French Ministry for Europe and Foreign Affairs and coordinated by the Institut Pasteur, seeks to define strategies to tackle antibiotic resistance through the creation of a dedicated surveillance and research network in 6 African countries.

Strengthening collaborations

The agreement between the IRD and the Institut Pasteur was renewed. A new partnership agreement was signed with the University of São Paulo and the São Paulo Research Foundation to set up four-year research groups (G4s). Three new Pasteur International Joint Research Units (PIUs) were set up with **Pasteur Network** members. The Institut Pasteur and the University of Hong Kong set up the Centre for Immunology & Infection, C2i.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE CENTRE FOR IMMUNOLOGY & INFECTION

Foreign delegations

On November 5, 2021, the Prime Minister of the Socialist Republic of Vietnam, His Excellency Mr. Minh Chinh Pham, visited the Institut Pasteur with his ministerial delegation.

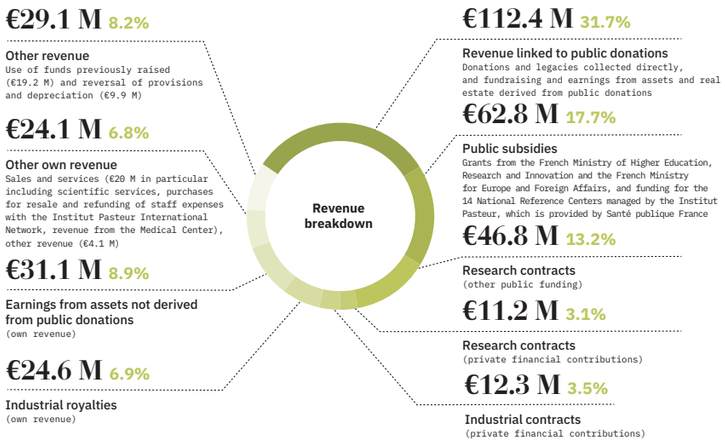
Kamala Harris, Vice President of the United States, visited the Institut Pasteur on November 9, 2021 (see Snapshot p. 2-3).

FINANCIAL REVIEW OF 2021

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, public health initiatives and knowledge transfer activities with a view to finding applications that benefit human health.

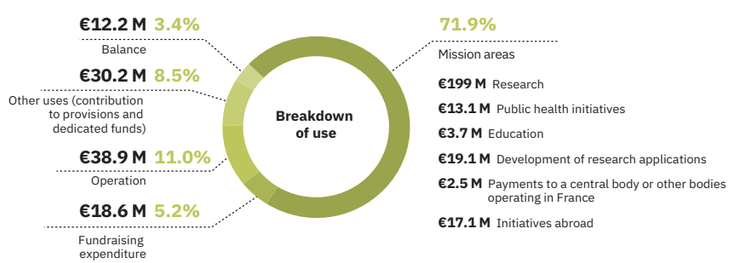
Revenue

As indicated in the Institut Pasteur 2021 *Statement of source and application of funds*, the revenues reported in the income statement amounted to €354.4 million, with the following breakdown.



Use

The revenues reported in the income statement are earmarked as follows: Institut Pasteur mission areas €254.5 M, operation €38.9 M, fundraising expenses €18.6 M, contribution to provisions and depreciation €7.5 M, and fundraising proceeds not used during the fiscal year €22.7 M. The remainder is used to fund initiatives and long-term investments.



SCAN THE QR CODE TO READ THE FULL FINANCIAL REPORT (IN FRENCH) AT PASTEUR.FR.

€354.4 M
FOR REVENUE/USE

Public gifts and donations

Within the range of different funding sources relied upon by the Institut Pasteur, the proportion of gifts and donations maintained a good momentum of growth after an atypical 2020; €112.4 M was raised in 2021[1]. In addition to its mission areas, the public gifts and donations received covered the Institut Pasteur's fundraising expenses and operating expenditure.

1. See adjacent chart and Institut Pasteur 2021 Use of resources statement in the financial report.

For each
€100
raised

€78
Mission areas *(research, public health, education)*
—
€13
Fundraising expenses
—
€9
Operating expenditure

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 2021	€M	%
Total	**1,111**	**100**
Property	229	21
Securities	716	64
Private equity/strategic partnerships	46	4
Cash	120	11

Productive assets account for the equivalent of three times the Institut Pasteur's annual operating costs (ratio set out in late 2021).

These assets generated €39.6 M during the 2021 fiscal year, reported in the income statement, representing a rise of €15.6 M in relation to 2020.

Earnings from assets

In 2021	€M
Total	**39.6**
Property	6.5
Securities	30.7
Strategic partnerships	0.9
Cash	1.6

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 income statement 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.

In 2021	€M
Institut Pasteur operating revenue	307.5
Institut Pasteur operating expenses	330.2
Contribution from IP Guadeloupe, IP Guyane and N. Calédonie	0.6
OPERATING INCOME	**-22.1**
Institut Pasteur financial result	**34.0**
Contribution from IP Guadeloupe, IP Guyane and N. Calédonie	0.2
FINANCIAL INCOME	**34.2**
RECURRING OPERATING INCOME	12.1
Institut Pasteur non-recurring income	**1.3**
Contribution from IP Guadeloupe, IP Guyane and N. Calédonie	0.2
NON-RECURRING INCOME	**1.5**
Profit sharing	1.5
NET INCOME	**12.2**

In 2021, recurring operating income showed a surplus of €12.1 M as against €8.1 M for 2020, a variation of €4.0 M. This surplus reflects a decrease in operating deficit of €12.5 M and an increase in financial surplus of €16.6 M (distribution of revenue from long-term investments on the rise).

€11.3 M of this result is due to the Institut Pasteur's Paris campus and €0.8 M to the institutes outside mainland France.

Profit sharing is provisioned for an amount of €1.5 M.

Net income therefore amounted to €12.2 M in 2021, as against €6.3 M in 2020.

DONATIONS, SPONSORSHIP & *LEGACIES*

MANY THANKS to everyone who put their faith in us and showed great loyalty

In 2021, 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 2021, the Institut Pasteur received financial support from more than 220,000 individual donors. Public support is vital to enable the Institut Pasteur to continue making major scientific and medical discoveries. In 2021, its scientists' exceptional response to the COVID-19 crisis, in which over 450 scientists were directly involved, led to major breakthroughs in research on the virus, its spread, evolution and impact on the body. The Institut Pasteur also continued its research in other key priority areas including cancer, neuroscience and antimicrobial resistance.

Donors

Nearly 32,000 of our donors chose to set up a direct debit, which enables them to spread their donations over the entire year. Despite the extraordinary public health situation in which we continue to find ourselves, we were able to maintain our ties with donors through online scientific lectures on progress made with our research in 2021. The 15th edition of Pasteurdon, held between October 6 and 10, 2021, shone a light on the wide range of research topics covered at the Institut Pasteur including cancer, emerging infectious diseases, brain connectivity and neurodegenerative diseases, antimicrobial resistance, vaccinology and artificial intelligence. The same passionate approach is taken to exploring all these research areas to meet public health requirements. The many donors once again demonstrated their incredible generosity in their support for the Institut Pasteur's research. Pasteurdon 2021 also owes its success to the dedication of actor Alexandra Lamy, loyal patron of Pasteurdon since 2011 and the efforts of nearly 50 media partners – TV channels and radio stations, with even more media partners coming on board this year – who broadcast the campaign film free of charge and rallied their presenters and journalists to the cause.

Donations from companies and foundations

This year, we were once again able to rely on vital support through donations from companies and foundations. Our loyal partners all got involved in the 15th edition of Pasteurdon. The Le Roch-Les Mousquetaires Foundation, which provides direct funding for two research programs on food safety, also elicited the support of the Les Mousquetaires group. It significantly stepped up its sale of charity-linked products (with over 20 products) in the Intermarché and Bricomarché store chains. ASSU 2000, a Pasteurdon partner for the eighth year running with its ongoing support for research on cardiovascular diseases, continued its charity-linked product campaign for Pasteurdon, with a donation made for every new car, health and provident 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 €100,000 for the Institut Pasteur. In total, donations from companies and foundations in France raised over €8 M (see acknowledgments opposite).

Donations, legacies and life insurance policies

In 2021, 165 new legacies were submitted to the Board of Governors, amounting to €53.5 M. Life insurance gifts amounted to €14.4 M. Four legal experts are responsible for handling estate administration. The team has noted that most multiple donors go on to become multiple testators with gifts bestowed split between multiple recipients. Two members of the Legacies Office have been assigned to development and testator relations with a view to promoting legacies among the public. The office publishes a six-monthly "Gifts" newsletter. Two media campaigns to promote gifts were run in 2021 based on a new TV spot. Information videos on gifts can also be found at www.pasteur.fr. Lastly, the team took part in the "Salon des seniors" show for seniors. The Institut Pasteur Legacies Office is the only department of its kind in France to have been awarded ISO 9001-2015 certification by AFNOR. This quality certification provides people with peace of mind when choosing the Institut Pasteur as their legatee. The Institut Pasteur is very grateful to everyone who has chosen to support it.

MAJOR SPONSORS

Fondation Bettencourt Schueller
Reconnue d'utilité publique depuis 1987

Carasso Daniel & Nina
Fondation sous l'égide de la Fondation de France

GROUPE PASTEUR MUTUALITÉ

Janssen Horizon

MTRL
Une Mutuelle pour tous

SPONSORS

- AG2R LA MONDIALE
- Allianz
- Assu 2000
- Biostime Institute Nutrition & Care
- Boehringer Ingelheim Fonds
- Cercle FSER
- Crédit Agricole Mécénat IDF
- Florence Gould Foundation
- Fondation Air Liquide
- Fondation Btp+
- Fondation Cognacq-Jay
- Fondation EDF
- Fondation Groupama
- Fondation Ipsen
- Fondation Jacqueline Beytout
- Fondation Le Roch-Les Mousquetaires
- Fondation NRJ
- Fondation Roquette pour la santé
- Fondation Scor Pour La Science
- Fondation Tourre
- Fondation Veolia
- Fonds de dotation Perfumum
- Gilead
- IBM
- Mutuelle du Médecin
- Mutuelle du Personnel Air France
- Nouvelle Cassius Fondation
- Odyssey Reinsurance Company
- Sacem
- The Joe W. and Dorothy Dorsett Brown Foundation

THINK TANK

A *THINK* TANK ON PHILANTHROPIC TRUSTS

The Think Tank on Philanthropic Trusts, launched by the Institut Pasteur in 2010, remains the leading interdisciplinary research group on the question of philanthropy. It provides a forum for discussion and debate and involves experts from a wide range of different fields (notaries, lawyers, bankers, tax advisors, journalists, scientists, philanthropists, etc.). Its aim is to progress and promote all topics related to asset management for philanthropic purposes. Five working webinars took place in 2021, featuring talks on topics including taxation for philanthropy, the history of 19th century philanthropy, the "Changer par le don" (Change by giving) initiative presented by its founder, Denis Duverne, and the Z-Event fundraising phenomenon. These meetings led to the production and distribution of podcasts and articles featuring the experts' contributions, which are published on philanthropie.pasteur.fr and social media.

SCAN THE QR CODE TO FIND OUT MORE ABOUT HOW TO SUPPORT US

HUMAN RESOURCES: *SUPPORTING AND IMPLEMENTING* STRATEGIC PRIORITIES

In 2021, the Human Resources (HR) teams continued their work on HR projects from the strategic plan aimed at promoting a healthy working environment.

IN 2020, the Institut Pasteur embarked on a process of continuous improvement regarding recruitment and working conditions for scientists to increase its global appeal. In December 2021, it received the EU **HR Excellence in Research** award from the European Commission based on the action plan developed.

The Institut Pasteur strengthened its commitment to quality of working life and a more harmonious workplace. In 2021:

- two new agreements were signed, one on home working and the other on the right to disconnect;
- measures were pursued to promote gender equality (special training, survey on barriers to female career development, "Gender Month" event);
- enhanced measures were implemented on managing and preventing sensitive situations, with numerous awareness-raising sessions for managerial and general staff.

Once again this year, the teams supported Institut Pasteur employees through the health crisis, with the Occupational Health Department in particular implementing preventive and protective measures.

CHECK OUT THE HR EXCELLENCE IN RESEARCH AWARD, AT PASTEUR.FR

DISCOVER THE GENDER EQUALITY PLAN AT PASTEUR.FR

Diversity

42.3
average age of employees

77
different nationalities on campus* (Institut Pasteur employees & OREX)

465
people hired in 2021 (excluding fixed-term to permanent contracts), 48.4% of whom scientists and 27.5% in the research engineering sector

The Pasteurian community

2,364
Institut Pasteur employees (69.2% on permanent contracts)

471
OREX staff (from external research organizations)

41
interns

57%
scientists and research engineers out of the total of **2,835** employees & OREX

Gender equality

58.8%
female staff

57.8%
of people hired in 2021

93%
Gender Equality Index in 2021

Skills development and career support

114
scientists supported by the MAASCC* (over 800 sessions).
** Welcome, support and career development structure for scientists*

€2,996,000
invested in professional training

31,159 hours
of training completed

Quality of working life

2 new agreements
signed in 2021 reflecting a commitment to improving the quality of working life:
- a new home working agreement signed by all parties
- an agreement on the right to disconnect

Sources: HR Department – HR management control, MAASCC, Training Center – March 2022

RENEWED EFFORTS TO PROMOTE *SUSTAINABLE DEVELOPMENT*

In 2021, the management team renewed its commitment to the "Green Campus – Responsible Campus" program, promoting the Global Compact and efforts to rally staff around the foundation's first sustainable development challenge.

An event held during the European Week for Waste Reduction.

Publication of the report on progress in sustainable development

Having joined the Global Compact in 2010, the Institut Pasteur renewed its commitment to the United Nations initiative aimed at encouraging companies and organizations throughout the world to adopt socially responsible attitudes. The Institut Pasteur concurrently published *Institut Pasteur and* ***Pasteur Network*** *– Progress in Sustainable Development*, a report detailing measures taken on the Paris campus and others carried out by **Pasteur Network** members over the past four years.

DISCOVER PROGRESS IN SUSTAINABLE DEVELOPMENT AT PASTEUR.FR

Launch of the first sustainable development challenge

In May 2021, the Sustainable Development Department launched a challenge for all staff in collaboration with the Graduate Office and members of the Make Pasteur Greener group. The aim was to encourage ideas for initiatives to boost sustainable development as part of a broader vision of how the Institut Pasteur will address future challenges. The 11 posters submitted were divided into two categories: Working life and Consumption habits. A feasibility study was conducted to assess how the proposals might be implemented on the Paris campus.

Recycling

0.70 t
Aluminum cans

0.484 t
Plastic bottles

12.41 t
Polypropylene tip boxes

61.89 t
Paper and cardboard

2.229 t
Paper archives

2.01 t
Glass bottles

24.869 t
Waste **electrical and electronic equipment**
including 302 kg of batteries

Other recovery

0.51 t
Organic waste

BOARD OF GOVERNORS

The Board of Governors 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 GOVERNORS BUREAU

Chair: Christian Vigouroux,
French Council of State Department Head

Vice-Chair: Hubert du Mesnil,
Ponts et Chaussées engineer and Chairman of Tunnel Euralpin Lyon-Turin

Vice-Chair: Artur Scherf,
Head of the Biology of Host–Parasite Interactions Unit, Institut Pasteur

Secretary: Sandrine Étienne-Manneville,
Head of the Cell Polarity, Migration and Cancer Unit, Institut Pasteur

Treasurer: Alban Hautier, Representative of the French Minister for Action and Public Accounts

Permanent guest of the bureau:
Antoine Triller, Head of Research at Inserm and Director of the École Normale Supérieure Institute of Biology

OTHER MEMBERS

Geneviève Almouzni, CNRS Director of Research, team leader at the Institut Curie, Paris

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

André Choulika, CEO and Co-Founder of the Cellectis Group

Stéphanie Fougou, Ingenico Group General Counsel

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

Claudia Pena-Rossi, Medical Director, DNDi (Drugs For Neglected Diseases initiative)

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 Solidarity and Health

Marie-Noëlle Ungeheuer, Head of the Clinical Investigation and Access to BioResources Platform (ICAReB), Institut Pasteur

Marie-Hélène Verlhac, CNRS Director of Research, Director of the CIRB (Center for Interdisciplinary Research in Biology), Collège de France

MANAGEMENT OF THE INSTITUT PASTEUR

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

Christophe d'Enfert,
Senior Executive Scientific Vice-President

Antoine Bogaerts,
Director of Philanthropy

Isabelle Buckle,
Vice-President Technology Transfer and Industrial Partnership

Jean-François Chambon,
Vice-President Communications – Scientific Outreach

Pierre-Marie Girard,
Vice-President International Affairs – **Pasteur Network**

Pierre Buffet,
Medical Director

Nathalie Denoyés,
Vice-President Technical Resources and Environment

Stéphane Fournier,
Vice-President Information Systems

Odile Hermabessiere,
Vice-President Human Resources

Pascal Masse-Navette,
Director for Internal Audit and Control

Michael Nilges,
Vice-President Technology

Françoise Perriolat,
Vice-President Financial Affairs

Monica Sala,
Director of the Education Department

Patrick Trieu-Cuot,
Vice-President Scientific Careers and Assessment

Samuel Valcke,
Vice-President Legal Affairs

SCIENTIFIC COUNCIL

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

ELECTED PASTEURIAN MEMBERS

Chair: Arnaud Echard, Head of the Membrane Traffic and Cell Division Unit
Aziz El Amraoui, Head of the Progressive Sensory Disorders, Pathophysiology and Therapy Unit

Secretary: Jean-Marc Ghigo, Head of the Genetics of Biofilms Unit

Vice-Chair: Michaela Müller-Trutwin, Head of the HIV, Inflammation and Persistence Unit

APPOINTED PASTEURIAN MEMBERS

James Di Santo, Head of the Innate Immunity Unit

Carla Saleh, Head of the Viruses and RNA Interference Unit

EXTERNAL MEMBERS

Galit Alter, *Prof. of medicine at Harvard Medical School, and group leader at the Ragon Institute of MGH, MIT and Harvard, USA*

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

Élodie Ghedin, *Senior Investigator and Director of the Systems Genomics Section (NIH), USA*

François Guillemot, *Senior group leader, Neural Stem Cell Biology Laboratory, The Francis Crick Institute, London, UK*

Eva Harris, *Prof. Division of Infectious Diseases and Vaccinology, UC Berkeley School of Public Health, CA, USA*

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

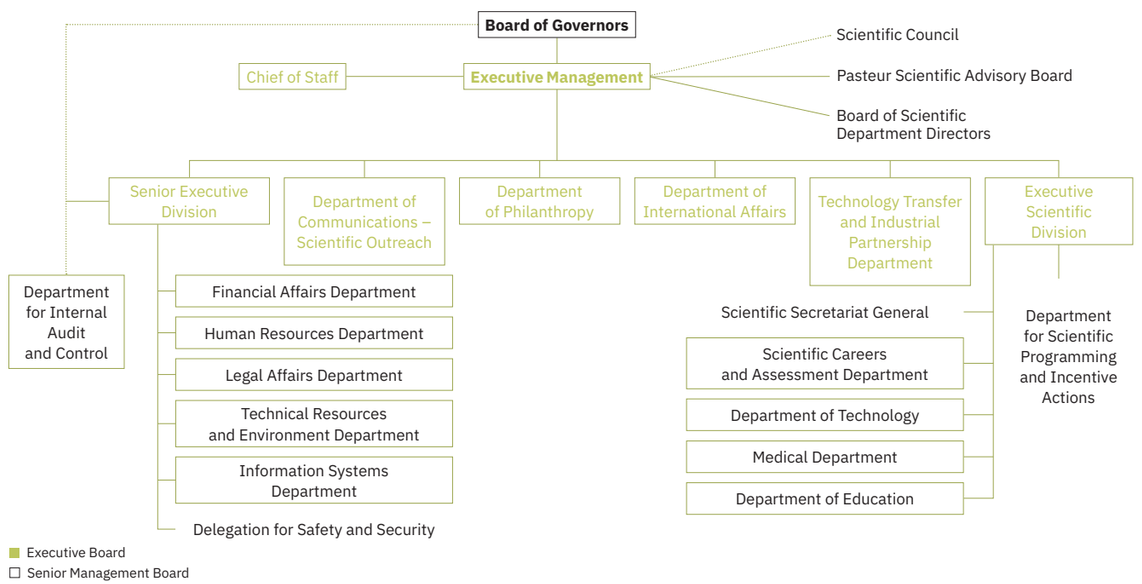
Yvonne Jones, *Prof. Division of Structural Biology, Henry Wellcome Building for Genomic Medicine, University of Oxford, UK*

Dimitri Kullmann, *Prof. of Neurology, UCL Queen Square Institute of Neurology, UK*

Ruth Ley, *Director, Dept of Microbiome Science, Max Planck Institute for Developmental Biology, Tuebingen, Germany*

Anne O'Garra, *Senior Group Leader, Laboratory of Immunoregulation and Infection, The Francis Crick Institute, London, UK*

GOVERNING BODIES



Institut Pasteur / Department of Communications – Scientific Outreach – 25-28, rue du Docteur-Roux – 75724 Paris Cedex 15, France. **Photo credits:** Institut Pasteur. Image by Rémy Robinot, Mathieu Hubert, Vincent Michel, Olivier Schwartz and Lisa Chakrabarti, and colorized by Jean Marc Panaud; Institut Pasteur; AdobeStock/Kateryna_Kon; The White House – Office of the Vice President; William Beaucardet; François Gardy; Olivier Pasquiers; Riccardo Lennart Niels Mayer/iStock; Institut Pasteur/Archives Alexandre Yersin; Institut Pasteur/Olivier Schwartz, Virus and Immunity Unit – Ultrastructural Microscopy Platform – Colorization by Jean-Marc Panaud; Institut Pasteur. Image by Rémy Robinot, Mathieu Hubert, Vincent Michel, Olivier Schwartz and Lisa Chakrabarti. Colorization by Jean Marc Panaud; ozgurdonmaz/iStock; Institut Pasteur – photo Béatrice de Cougny; Institut Pasteur/Pierre-Marie Lledo; Institut Pasteur/Perrine Bomme, Ultrastructural Microscopy Platform, Guillaume Dumenil, INSERM U970, Paris Cardiovascular Research Center, HEGP – Colorization by Jean-Marc Panaud; AdobeStock/catalin; Institut Pasteur/Romain Levayer and Léo Valon – illustration Olga Markova; Institut Pasteur/Perrine Bomme – Ultrastructural Microscopy Platform and Nouara Lhocine – Molecular Microbial Pathogenesis Unit led by Philippe Sansonetti; Marc Dozier; Philippe Bousso/Institut Pasteur; Institut Pasteur/Antoinette Ryter; Jean-Marie Winter; Institut Pasteur/Adeline Mallet, Ultrastructural Microscopy Platform – Pierre Buffet, Parasite Molecular Immunology Unit; Institut Pasteur/Nell Saunders, Delphine Planas, Tim Bruel and Olivier Schwartz. **Design and production:** Agence Bergamote - ISSN: 1632-0115. **Printing:** Sopedi.
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