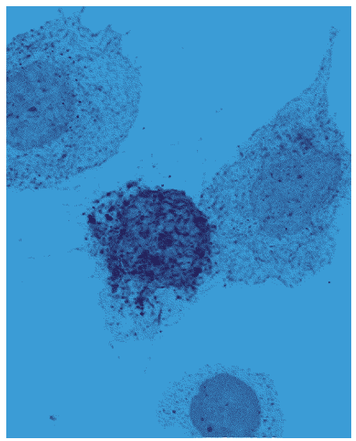
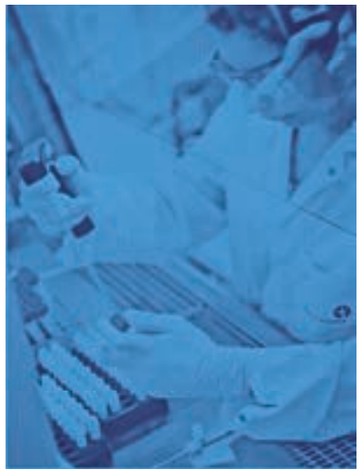
INSTITUT PASTEUR

ANNUAL REPORT 2022

“SENTINEL”

Monitoring and analyzing circulating pathogens, advancing research and protecting public health





THE INSTITUT PASTEUR *IN NUMBERS*

The Institut Pasteur is committed to conducting 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.

€367.9
million budget in 2022

78
nationalities (as at 12/31/2022)

142
research structures including 96 research units, 10 five-year units (U5s), 18 five-year groups (G5s), 11 laboratories, 7 Hearing Institute teams
(as at 12/31/2022)

2,934
staff members (as at 12/31/2022)

32
research support core facilities

Thanks to our
239,000
individual donators, legators, sponsors and partners.
With your help we have advanced research. For further information see pages 56 and 57.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT OUR INSTITUTE.

INTERNATIONAL: *INITIATING AND STRENGTHENING* PARTNERSHIPS AND SCIENTIFIC *COLLABORATIONS*

The Institut Pasteur has been conducting its missions internationally since its creation in 1887. A policy of openness informs the Institut Pasteur's strategic partnerships and scientific cooperation throughout the world, putting scientific excellence at the service of the health of populations. Also, as a co-founder of the Pasteur Network, the Institut Pasteur plays a key role in the co-construction of projects alongside its members, to contribute to the network's international influence.

In 2022, the Institut Pasteur's international focus was on initiating and strengthening partnerships and scientific collaborations, especially with organizations in the United States, Japan, India, and Brazil but also thanks to regional projects in collaboration with the Pasteur Network.

United States: Launching Center of Excellence in Emerging Infectious Diseases with UCSF-QBI

In a ceremony on October 21, the Institut Pasteur and the University of California, San Francisco-affiliated Quantitative Biosciences Institute (UCSF QBI) announced a partnership for the joint establishment of a Center of Excellence in Emerging Infectious Diseases.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE NEW COLLABORATION WITH UCSF QBI.

India: Research collaboration with the Council of Scientific & Industrial Research of India

A memorandum of understanding was signed on January 25 between the Institut Pasteur and the Council of Scientific & Industrial Research of India, CSIR, during a hybrid ceremony. This agreement aims to strengthen collaboration with the CSIR laboratories, in particular the Centre for Cellular & Molecular Biology (CCMB).

Japan: Institut Pasteur Japan Office's presentation during a Japanese delegation visit

During the France-Japan Joint Committee on Cooperation in Science and Technology on July 27, a high-level Japanese delegation was welcomed at the Institut Pasteur. The group attended presentations, including one on the Institut Pasteur Japan Office (IPJO), whose scientific strategy is based on three pillars – immunology/infectious diseases, global health and epidemic preparedness.

Strengthening historic entrepreneurship

partnership with Fiocruz

A two-day workshop was held on April 11 and April 12 in Rio De Janeiro by the Institut Pasteur and its longtime partner, the Brazilian public health institution, Fiocruz. This was an opportunity for both organizations, who share a commitment to modern health innovation and to transferring science-based knowledge to society, to compare innovation and entrepreneurship strategies.

Royal Society: a tribute to Louis Pasteur in London

A series of high-level presentations were given in chemistry, biotechnology, infectious diseases and vaccinology by Institut Pasteur and UK scientists on October 28 in London at the Royal Society's celebration of Louis Pasteur's bicentenary.

Progress of three international projects

- **"SARS-CoV-2 in Wastewater"**: project gathering 10 countries (mostly African), funded *by the Agence française de Développement* (AFD) aiming to support the implementation of SARS-CoV-2 surveillance in wastewater.
- **"PerMedina"**: innovative project funded by the French Ministry of Foreign Affairs, leading to creation of a Maghrebin consortium on precision medicine.
- **"MediLabSecure"**: the 3rd phase of the project funded by the EU CBRN Centre of Excellence Initiative aims to strengthen institutional capacities of reference laboratories and public health institutions in 22 non-EU countries around the Mediterranean, Balkan, Black Sea and Sahel regions to face vector-borne diseases, and emerging threats.

SCAN THE QR CODE TO LEARN MORE ABOUT OUR INTERNATIONAL ACTIVITY IN 2022.

PASTEUR NETWORK: *A UNIQUE SCIENTIFIC* NETWORK

The Institut Pasteur is part of the Pasteur Network. The Pasteur Network is a human and scientific community with more than 30 members in over 20 countries working together to help improve global health. Located in the heart of endemic areas, the Network has privileged access to a large number of pathogens that it monitors and studies on all five continents. This exceptional diversity makes the Pasteur Network a unique global actor in public health, science, innovation, and education, especially in the fight against infectious diseases.

45

SCIENTISTS in the Pasteur Network received training through the Calmette & Yersin program, including 4 postdoctoral fellows and 9 PhD students

11

INTERNSHIPS for French early career researchers in the Pasteur Network funded by the Pierre Ledoux–Jeunesse Internationale Foundation

3 G4s,

or 4-year research groups, set up in Pasteur Network institutes

7

Pasteur joint international research units (PIUs)

A new management team for the Pasteur Network

In June 2021, the Pasteur Network reviewed its governance to make it more participatory and egalitarian. With the consent of all its members, an executive board was set up to translate these changes into specific actions. The reorganization of the Pasteur Network began in late June 2022 with the appointment of a new Executive Director, Rebecca F. Grais, who advocates joint action to unlock the network's potential as a global player.

In late December 2022, just days after the bicentenary of Louis Pasteur's birth, Rebecca F. Grais, Amadou A. Sall and Stewart T. Cole co-authored a commentary in *The Lancet* charting the network's key developments from its inception to the present day. The Pasteur Network's overarching vision is now stronger than ever and effective in promoting the diversity of its members and Pasteur's legacy in research and public health.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE PASTEUR NETWORK.

Pasteur Network members share strategic priorities such as:

- epidemic and pandemic intelligence and preparedness;
- support for research and development and the innovation ecosystem;
- support for various multidisciplinary knowledge communities by facilitating global and regional mobility;
- promotion of excellence in basic and translational research.

New tools facilitating information sharing

SCAN THE QR CODE TO FIND OUT ABOUT THE PASTEUR NETWORK IN THIS VIDEO.

SCAN THE QR CODE FOR THE PASTEUR NETWORK LINKEDIN PAGE.

SCAN THE QR CODE FOR THE PASTEUR NETWORK MONTHLY NEWSLETTER.

SNAPSHOT OF 2022

A look back at twelve months of activities embodying the Pasteur ethos in honor of Louis Pasteur's bicentenary and demonstrating scientific progress in the areas of cancer, infectious diseases, the role of the microbiota and neuroscience.

THE BICENTENARY OF LOUIS PASTEUR'S BIRTH

A year to celebrate the "Pasteur ethos"!

Louis Pasteur was born on December 27, 1822, so 2022 was an opportunity to reflect on the legacy of the Institut Pasteur's founder. With the French Academy of Sciences, the Institut Pasteur launched a bicentenary label that would bring the various commemorative initiatives under the same banner. These included:

- Conferences at the Institut Pasteur *(Epidemics, pandemics: a never-ending story?)*, the Institut de France *(Pasteur, a visionary)*, the Institut français in Greece, the Danish Pasteur Society in Copenhagen, the Royal Society in London, the Deutsches Hygiene-Museum in Dresden, the Copernicus Science Center in Warsaw, etc.;
- Exhibitions at the Petit Palais and the National Archives and a traveling exhibition designed by the Institut Pasteur which was hugely popular in French town halls and schools;
- A dozen books published about Louis Pasteur.

Finally, to celebrate the Pasteur ethos, a Louis Pasteur Bicentenary Prize was awarded to five outstanding scientists.

FIND OUT MORE ABOUT THE BICENTENARY OF LOUIS PASTEUR'S BIRTH.

JANUARY

Cancer: bacteria provide a target for treatment

Scientists researching a neglected tropical disease identified a vulnerability in cancer cells that could be exploited to overcome their resistance to treatment.

EMBO Molecular Medicine, January 11, 2022.

FEBRUARY

SARS-CoV-2-related viruses found in bats

Viruses capable of recognizing human cells with similar efficacy to the original SARS-CoV-2 strain were identified in bats in northern Laos.

Nature, February 16, 2022.

Legionnaires' disease: bacteria bypass immune defenses

Scientists revealed a mechanism used by the bacteria responsible for Legionnaires' disease to bypass cells' immune response by secreting a small regulatory RNA.

Nature Communications, February 9, 2022.

Innate immunological memory in the intestine

Some innate immune cells can be trained to develop a form of memory that can protect the host during reinfection.

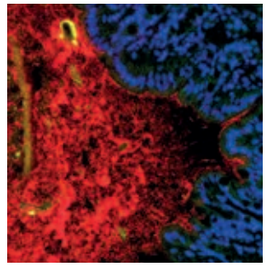
Science, February 25, 2022.

APRIL

Dialog between the gut microbiota and the brain

Scientists pooled their expertise to understand how bacteria in the gut can have a direct effect on the activity of certain neurons in the brain.

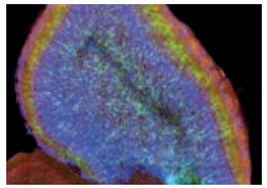
Science, April 15, 2022.



Therapeutic avenues for the psychological consequences of infection

The brain can respond to inflammation by secreting hormones like cortisol. But this message can be ill adapted and lead to immunological and psychological disorders.

Brain, April 20, 2022.

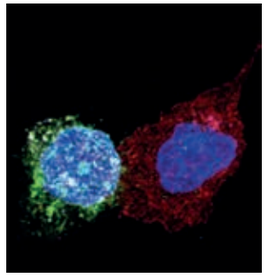


HIV: how to mimic patients able to control infection

The Institut Pasteur is investigating the rare cases of patients who can control infection naturally without treatment. One team successfully reprogrammed immune cells from non-controllers to give them properties found in controllers' cells. Another team observed that some controllers develop an effective, robust humoral immune response that can help control infection in the absence of treatment.

The Journal of Clinical Investigation, April 5, 2022.

Nature Communications, April 11, 2022.



MAY

Phage therapy: predicting its effectiveness against pathogenic bacteria

Since the mechanisms of action of bacteriophages remain poorly understood, several scientists are involved in the development of a mathematical model to predict their effectiveness.

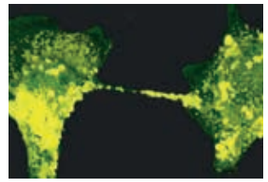
Cell Reports, May 17, 2022.

JULY

How SARS-CoV-2 infects neurons

Neurological symptoms are often associated with COVID-19, both during the acute phase of the disease and over the long term. But how does the virus enter brain cells?

Science Advances, July 22, 2022.



Towards a treatment for preeclampsia

As an effective treatment for preeclampsia, scientists propose administering aspirin with BH4, a cofactor involved in nitric oxide metabolism.

Redox Biology, July 30, 2022.

OCTOBER

Emerging diseases: international collaboration with UCSF QBI

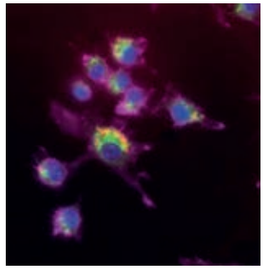
The Institut Pasteur and UCSF QBI (University of California) signed an agreement on October 21 to establish a Center of Excellence for Emerging Infectious Diseases.

Why are sounds not perceived under anesthesia?

Even under anesthesia, the neurons in the auditory cortex are still stimulated by external sounds, but the brain is unable to interpret them.

Nature Neuroscience, September 28, 2022.

The Black Death may have shaped the evolution of immunity genes



Yersinia pestis bacteria, responsible for bubonic plague, are believed to have shaped our current response to autoimmune diseases.

Nature, October 19, 2022.

COVID-19: start of clinical trials for a monoclonal antibody

SpikImm, the biotech founded by Truffle Capital based on a license granted by the Institut Pasteur, announced the start of clinical trials on SPK001, its monoclonal antibody targeting SARS-CoV-2.

17 Ukrainian scientists on campus

In view of the ongoing war in Ukraine, the Institut Pasteur hosted 17 Ukrainian scientists in its research laboratories in 2022.

OUTSTANDING RESULTS IN A TURBULENT GLOBAL CONTEXT

The Institut Pasteur achieved outstanding results in 2022 by securing prestigious European funding and joining forces with internationally renowned partners. Its National Reference Centers were awarded new terms of office in recognition of its expertise as a "sentinel for health." 2023 will be a year of transition before new management takes over in 2024. The task now is to complete the major goals in the Strategic Plan developed by President Stewart Cole, with the support of Yves Saint-Geours, the new Chairman of the Board of Governors.

"We need to ensure that our social bonds remain strong, so that our community – our greatest asset – continues to be an effective force."

Yves Saint-Geours,
Chairman of the Board of Governors.

As the new Chairman of the Board of Governors, how are you approaching 2023?
Yves Saint-Geours: I would like to thank all those who have given me such a warm welcome, especially the President. I have familiarized myself with the specific governance of the Institut Pasteur, with its new Board of Governors, the General Meeting board – who I have had the pleasure of meeting –, the Scientific Council and the Social and Economic Committee. My arrival comes at a turning point for the Institut Pasteur's governance, with the appointment of the future President. Like my predecessor Christian Vigouroux, whom I hold in the highest esteem, I am convinced that our governing bodies and the Pasteur Network, of which we are members, place the Institut Pasteur in a uniquely strong position and guide us in the choices we have to make regarding its future.
Stewart Cole: I am delighted that we have been able to establish such an effective working relationship between the Board and the senior management team. I welcome the fact that Yves Saint-Geours is committed to supporting a policy that is both ambitious and realistic to promote the excellence of our research, in keeping with the policy pursued by the previous Chairman.

What is your overall assessment of 2022?
SC: 2022 was an eventful, memorable year, with excellent results in the calls for proposals issued by the French National Research Agency and the European Research Council, the success of the DURABLE consortium, which will improve the European Union's preparedness for future health crises, our concerted action to tackle the COVID-19 pandemic, the renewal of our National Reference Centers by Santé publique France, and more than 50,000 people vaccinated by our Medical Center. Nearly 70 students defended their PhD thesis at the Institut Pasteur, and we plan to establish a Graduate School for Emerging Infectious Diseases. Our research applications are wide-ranging, with 25 patents filed and more than 250 collaboration agreements signed, and I should also mention the progress of our startup SpikImm on monoclonal antibodies that target SARS-CoV-2.
YSG: As well as these remarkable achievements, 2022 was an opportunity for us to celebrate the bicentenary of Louis Pasteur's birth. The commemoration was not an excuse to indulge in self-glorification but rather a chance to reconnect with Pasteurian values in the light of today's debates and struggles. The global geopolitical, economic and environmental context is one in which truth itself is called into question, and this raises serious questions for science and also for peace. We need to make every effort to ensure that science is used across the world as a diplomatic tool for peace.

"The 2023 budget pursues an ambitious policy of investment. Our goals continue to be those laid down in our Strategic Plan."

Stewart Cole, *President.*

What areas require particular attention in the global context you have described?
SC: The global situation is having an impact on the Institut Pasteur, but we are keeping things under control. The management team has taken significant wage measures to support staff while preserving our financial health. And the 2023 budget pursues an ambitious policy of investment to underpin our scientific strategy and our real estate assets.
YSG: The Board is working with the senior management team to ensure the long-term sustainability and independence of the Institut Pasteur. Sustainability creates independence, and independence creates sustainability. Guaranteeing our independence is about preserving scientific freedom. Part of that independence is financial, and the Institut Pasteur's governing bodies are constantly working to ensure that our finances are balanced and that we maintain our ability to invest where needed.

What are the Institut Pasteur's ambitions in 2023?
SC: We are preparing for the launch of the Vaccinology and Immunotherapy Center, which is key to our ambitions in terms of pandemic preparedness and response. We also need to continue to boost our profile to attract talented scientists – and that means pursuing our modernization efforts. I have also launched a capital campaign with the target of raising an additional €100 million over five years to fund our strategic projects.
YSG: The Board fully supports all these strategic priorities. They will safeguard the Institut Pasteur's future, maintaining our position in the global research landscape so that we can attract the best and the brightest talents, especially early career researchers, and identify new sources of funding. We are also continuing to consolidate our international outlook, which reflects the universality of science at a time of increasing globalization and demonstrates the appeal of the "Pasteurian ethos" for talented researchers. Our recent partnerships with the University of California San Francisco, the Indian Council of Scientific & Industrial Research and the Abu Dhabi Public Health Center are in line with this strategy and we need to continue to work to develop further large-scale scientific partnerships.

So you believe that the "Pasteurian ethos" that you alluded to, which was celebrated in 2022, is still relevant today.
YSG: Yes. Our first priority is science, which we pursue with rigor and excellence, because basic research leads to improvements for human health. But in a typically "Pasteurian" way, we also seek to develop links with society, to communicate about our research. I would add that, on the Institut Pasteur campus, now that the pandemic period is behind us, we need to rethink the way in which we work together, our sense of community. This collective spirit should underpin our measures to promote gender equality and help improve female representation in senior scientific positions.
SC: Gender equality is one of our priorities, and the Gender Equality Plan was a new milestone in our commitment in this area. We are continuing to make structural and cultural changes that promote a fair, inclusive working environment. It was this community spirit, as mentioned by Yves Saint-Geours, that led me to establish the Explorer initiative for early career scientists to reflect on the future of the Institut Pasteur. This project will help generate ideas to boost the Institut Pasteur's profile.

“We are prioritizing the most effective collective measures for carbon footprint reduction. Work carried out in 2022 with the Hearing Institute will help us make objective choices.”

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

PRESERVING THE ENVIRONMENT, OUR CAPABILITIES AND OUR FUTURE

The Institut Pasteur pursues a “sustainable economy” strategy that seeks to reconcile efforts to protect the planet’s resources with financial equilibrium. Recent years have seen rising numbers of sustainable development initiatives with an increasingly strong commitment on campus. In 2022, the management team confirmed its ambitions with an emphasis on sustainable management, which combines effective action on protecting the planet with efforts to secure the Institut Pasteur’s scientific capabilities and long-term financial future. Nathalie Denoyés, Vice-President Technical Resources and Environment, and Françoise Perriolat, Vice-President Financial Affairs look back at a pivotal year that provides impetus for the future.

When did the Institut Pasteur first become involved in sustainable development?
Nathalie Denoyés: We were the first research organization to join the United Nations Global Compact in 2010. Every two years, we publish a report on progress made. This ambition instilled by senior management is part of our DNA as a non-profit foundation with recognized charitable status.
Françoise Perriolat: It also makes perfect sense for an institute that has studied living organisms for the past 135 years to adopt such a strategy. That’s why we are committed to implementing the most effective measures for protecting the environment while also preserving research activities. This is the focus of our approach to a “sustainable economy”.

What has been done in 2022 to further the Institut Pasteur’s sustainability goals?
ND: As part of our sustainable development master plan, we conducted an initial “advanced” carbon inventory at the Hearing Institute, our center in Paris’ 12th *arrondissement*. This revealed that purchasing is our primary source of carbon emissions. We are also aware that travel is a contributing factor. This has prompted our policies on sustainable mobility (1) and business travel, which was reviewed in 2022 with the Department of Financial Affairs.
FP: Our travel policy is a key tool for reducing our carbon emissions and spending. Plane fares or mileage can no longer be claimed for journeys of under 4 hours that can be undertaken by train.
ND: The Hearing Institute’s carbon inventory also justifies our action on heating use this winter and in other areas such as air conditioning, which is aimed at keeping the Institut Pasteur running in an inflationary climate.
FP: By cutting our consumption by 10%, we can save approximately €500,000 in energy expenditure. We have achieved a 6% reduction since the start of the year. Although not insignificant, these savings do not offset rising energy costs. The ecological impact is positive, though we are unable to measure it precisely. We are working with Nathalie Denoyés’ teams to identify extra-financial indicators to assess economic AND ecological impacts and thus prioritize the most effective measures.

Extra-financial indicators aside, what other sustainability measures are you developing?
FP: Consolidated purchasing is effective both from an economic and environmental perspective. Suppliers are prepared to grant us discounts on grouped deliveries and tangible benefits are achieved in terms of reduced transport. We therefore strongly encourage all requesters to group their purchases and avoid small orders of less than €50.
ND: We’ve also looked at rolling out bulk deliveries of consumables such as pipettes and test tubes to reduce the quantities of associated packaging and plastic waste [see p.53]. However, counterintuitively, deliveries are often more expensive in bulk than by the unit.
FP: Discussions with the procurement department and scientists have given us a better understanding of the price of certain consumables. While choosing such products currently generates extra costs, a broader shift in habits and higher purchasing volumes will allow greater scope for future price negotiations.

“It is important to establish extra-financial performance indicators to measure the true effectiveness of our measures.”

Françoise Perriolat, *Vice-President Financial Affairs.*

ND: Our Information Systems Department joined forces with the Sustainable Development Department to hold a Digital Cleanup Month aimed at cleaning up mailboxes, etc. Paperless processes sometimes result in overuse of digital technology and therefore excessive energy consumption.

Do these steps amount to a culture change for employees?
ND: These are major changes. However, more and more scientists are receptive to these issues. Such measures also appeal to young people who are also encouraged to take action by their professional environment. For instance, the management team has put together a group of young scientists (the EXPLORER group) to consider these issues for the future of the Institut Pasteur. Calls for grant applications increasingly require them to provide a carbon inventory for their unit. We have approached the Labos 1.5 collective to access tools specific to research and refine measurements of greenhouse gas emissions generated by our activities. By the end of 2023, we will offer units an ad hoc tool to help them with their carbon inventories.
FP: Time is required in each situation to identify an appropriate response and avoid slipping into greenwashing. Measurable, appropriate and effective measures are essential if we are to set an example. This approach is reflected in the way we manage our financial assets, and we therefore score highly on environmental, social and governance criteria considered by investors when assessing companies’ extra-financial performance.

Are these sustainability goals applied to real estate projects?
ND: Energy sufficiency is essential for major future real estate projects. Numerous environmental criteria will be applied to construction work on the future Vector-Borne Diseases Center (CMTV), which is due to start in 2023. Suppliers with a good environmental record have been selected and some of the demolition materials will be reused.
FP: We are considering how to ensure our buildings meet environmental criteria, which will entail extra costs. Research laboratories are inherently environmentally unfriendly spaces (contained rooms, air circulation, temperature control, etc.). To meet environmental criteria, the CMTV has become a major, costly real estate project for which we will need to diversify our financial resources.

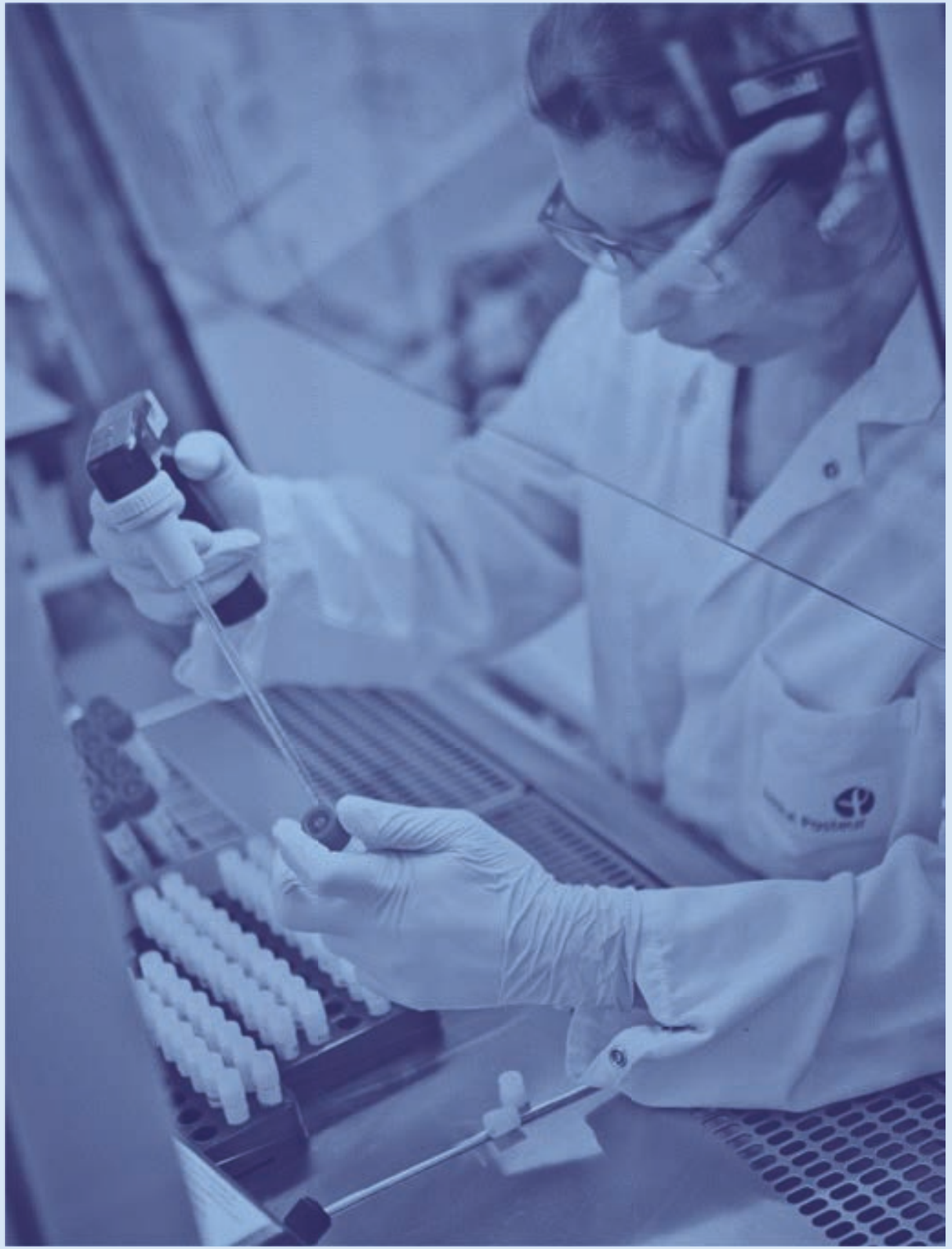
So the transition to a sustainable economy does not necessarily generate savings?
FP: All the steps the Institut Pasteur is taking on sustainable development are commendable and make sense for the foundation. Wherever possible, we need to make financial savings on the measures we take. Although the green transition comes at a price, our performance in this area will attract young talent with a personal and professional interest in these issues.
ND: Our management team firmly believes that the green transition movement is set to gain pace. Support from the Department of Financial Affairs is valuable and allows ourselves and the other support departments to become involved in work that is stimulating both intellectually and from a human perspective.

(1) Business travel by train encouraged, sustainable mobility payment for employees who travel to work by bicycle/scooter, charging stations for electric vehicles with a system for scheduling charging times, etc.

NATIONAL *REFERENCE* CENTERS, *SENTINELS* GUARDING AGAINST *PATHOGENS*

On December 31, 2022, Santé publique France renewed its trust in the Institut Pasteur for its National Reference Centers (CNRs). Nineteen laboratories are currently involved in the CNRs. Their role is to monitor and analyze circulating pathogens, advance research and protect public health.

SCAN THE QR CODE TO READ THE ONLINE REPORT.



INTRODUCTION

with Muhamed-Kheir Taha, Head of the Invasive Bacterial infections Unit and the National Reference Center (CNR) for Meningococci and *Haemophilus Influenzae*, a designated WHO Collaborating Center for bacterial meningitis.

While National Reference Center (CNR) status can only be acquired once scientific expertise has been proven in a specific field, it is nevertheless clear that this expertise develops through “real world” contact with the pathogens targeted by CNRs.

Through its research on the biology of living organisms, the Institut Pasteur works with known microorganisms, which provide genuine test tube models. Alongside the research units, the CNRs monitor and analyze circulating pathogens on a daily basis. This work tests our hard-won knowledge, significantly increasing its reliability and validity by confronting it with an enormously diverse range of pathogen-patient pairings.

The CNRs derive crucial knowledge from this mutual enrichment between basic research and public health. As such, the Institut Pasteur’s involvement in 17 of around 40 CNRs operating in France is an undeniable strength, enabling it to advance research and protect public health. CNRs play a key role in health crises. This role as sentinels reflects a specific view of our value.

From its inception, the Institut Pasteur played a major role in public health as a dispensary for rabies treatment as well as a research center for infectious diseases. This role now finds its direct expression in the CNRs’ activities. They reflect recognition of our scientific expertise and ability to collaborate within the epidemiological surveillance ecosystem. In recent years, the CNRs have become bona fide decision-making tools for the public authorities, extending their role as sentinels to become key stakeholders in a coordinated response to pathogenic threats.

As recognized by the scientific community and public, the CNRs continue to prove their worth by responding early to emerging health crises and helping to prevent many others. We can only be proud of contributing to their success and thus continuing to pursue the Institut Pasteur’s original mission.

DEFINITION

WHAT IS A *SENTINEL?*

with Isabelle Cailleau, Institut Pasteur Medical Department, coordinator of the National Reference Centers.

Romaine lettuce contaminated with *E. coli*.

IN PUBLIC HEALTH TERMS, THE WORD “SENTINEL” REFERS TO A SURVEILLANCE PROCESS. National Reference Centers (CNRs) are watchtowers that gather, analyze and interpret signals of potential future outbreaks.

CNRs offer specific expertise in terms of identification, characterization and vigilance. They are required to analyze, contextualize and interpret large volumes of data and link them to existing scientific knowledge. The alert mechanism is therefore just a first step, triggering a process that is honed to ensure an immediate and effective response.

A CNR is an interface. It is a place in which knowledge of microorganisms and their hosts gained through basic research is confronted with pathogen strains sent by medical test laboratories as part of epidemiological surveillance. A place where the controlled laboratory environment meets unpredictable crisis situations. Each side benefits from the other in a cycle enabling the continual improvement of knowledge of diseases, their vectors and modes of transmission. Expertise and models are compared, bounced off each other, shaken up and refined by sentinels, which represent a strength and asset, not just for public health but also research.

sentinel, noun: *something that guards, protects, keeps watch; whose task is to provide surveillance and thus prevent any surprises. With its origins in military terminology, the term “sentinel” conjures images of an outpost or strategic position enabling the detection of changes or anomalies indicative of things to come. The sentinel stands guard, a beacon in the mist of a potentially hostile “other” against which protection is sought.*

CNRs: SENTINELS *AGAINST THE UNSEEN*

with Isabelle Cailleau, Institut Pasteur Medical Department, coordinator of the National Reference Centers.

Handling at the CNR for Rabies.

NATIONAL REFERENCE CENTERS (CNRs) are early warning stations for outbreaks, sweeping French national territory in their role as look-outs for threats with potential public health implications. Supported by research units, they draw on the expertise of leading scientists and access state-of-the-art technologies. All this enables them to constantly update existing knowledge of the virulence and transmission mechanisms of infectious agents and methods of detecting them. Their value to the health ecosystem and our ability to understand, anticipate and respond to unseen threats has been clearly demonstrated by the key role they have played in managing recent health crises.

A long-standing surveillance system

The designation "National Reference Center" (CNR) made its first appearance in France in an order published in the Official Journal of April 18, 1972. However, the notion of "reference centers" had already been used since the 1950s to describe the activities of Institut Pasteur research units in response to issues raised by physicians or the French Ministry of Health regarding the diagnosis or treatment of certain infectious diseases.

Going back even further, the Institut Pasteur has, since its very early days, naturally assumed a role as sentinel for numerous communicable diseases. Its original articles of association provided for: *"creation and management of laboratories for referral, testing and monitoring, and for collections of microbial strains"*, which fully encapsulates the CNR concept.

Obviously, the system has since been developed to keep pace with the speed and scale of these pathogenic threats and harness progress in detection techniques. Official recognition of CNRs in 1972 brought confirmation of their role as sentinels and harmonization of their remit at national level. There are currently 43 of them following the renewal of their term of office in early 2023. Thirteen of these are coordinated by the Institut Pasteur (see list on page 14), each specializing in a pathogen or pathogen family.

An extended remit in the post-pandemic landscape

The CNRs' response to recent health crises (see timeline p.18) has confirmed their key role in the outbreak alert and response process. Their ability to combine basic research, expertise gained in medical biology through the CNR remit, and scientific breakthroughs in predictive epidemiology makes them the first link in the chain of a coordinated response. The SARS-CoV-2 outbreak perfectly illustrates the value of concurrent interactions between research and its applications, including large-scale, real-time data collection and analysis to track the development of the outbreak, the introduction of screening tests, and support for national health agencies with assessments of diagnostic tests, all of which proved the CNRs' key role in managing this most recent health crisis.

The call for applications to renew CNRs published in March 2022 extended the remit (see diagram p.16) of some CNRs including the Center for Respiratory Infection Viruses, which was tasked with developing a range of techniques and methods to enhance its expertise on coronaviruses and respiratory syncytial virus responsible for respiratory infections such as bronchiolitis, very severe forms of which can occur in infants.

Research and public health: sharing best processes

Having long been confined to their role as observatories for pathogens, CNRs have gradually been upgraded as key interfaces between basic research and public health. By logging and analyzing thousands of pathogen strains every year, CNRs accumulate substantial, constantly updated collections that can be used to track the spread of a disease over time and characterize successive mutations of a microorganism, thus providing a valuable record of diseases and outbreak development. This, for instance, enabled teams from the CNR for Vibrios and Cholera to investigate the genomes of 172 strains in 2020 to elucidate the source of cholera outbreaks since 1970 and confirm the role of humans in their spread. These databases form the bedrock of epidemiological surveillance, and analysis of them supports modeling work used to forecast the development of outbreaks and guide health authorities on introducing protective measures to limit their spread. Moreover, samples collected by CNRs provide research units with valuable material with which to conduct their basic

CNRs
AT THE INSTITUT PASTEUR

The Institut Pasteur hosts 19 laboratories (13 coordinating and 6 associated laboratories). These monitor the following 17 pathogens:

Viruses
- Respiratory infection viruses including influenza and SARS-CoV-2
- Rabies virus
- Viruses causing hemorrhagic fevers such as Lassa and Ebola
- Hantaviruses spread by rodents
- Arboviruses (see article at the end of this special feature)
- Enteroviruses and parechoviruses, particularly those causing poliomyelitis

Bacteria
- The genus *Clostridium* including the bacterium causing botulism
- The genus *Yersinia* including the plague bacillus
- The genus *Corynebacterium* including the bacterium causing diphtheria
- The genera *Shigella, Salmonella* and *Escherichia coli* responsible for foodborne infections
- The genus *Leptospira* that can cause kidney failure
- The genus *Listeria* including "refrigerator bacteria" that cause listeriosis
- Meningococci and *Haemophilus influenzae*, which cause meningitis
- Vibrios including the cholera agent
- The genus *Bordetella* including the whooping cough bacillus

Fungi
- Candida, aspergillus, cryptococcus and other invasive mycoses

Parasites
- The genus *Plasmodium* that causes malaria

"The CNRs play a central role in our public health system, working closely with Santé publique France. They provide essential microbiological support to strengthen our ability to respond to developments in pathogen spread. Besides acting as sentinels, they are also interfaces between research and public health and forums for vital discussions between all stakeholders, both at local and national level."

Prof. Christophe Burucoa, ***Chairman of the CNR Committee, Santé publique France.***

research and studies. Scientific papers and discoveries at the Institut Pasteur are furthermore increasingly based on data collected by CNRs.

CNRs' affiliated laboratories also offer expertise that brings significant public health benefits, particularly with regard to technical progress. In one recent example, the source of a salmonella contamination of powdered milk that infected nearly 200 infants between 2005 and 2017 (for which an alert was issued by the CNR for *Escherichia coli, Shigella* and *Salmonella*) was identified thanks to progress on high-throughput genome sequencing, a technique used in the Institut Pasteur's Enteric Bacterial Pathogens Unit.

The CNRs' missions

- **Expertise** concerning the microbiology and pathology of infectious agents, the development, optimization, validation and distribution of medical biology examinations; the identification and confirmation of pathogens;
- **Scientific or technical advice** in response to any request from the French Health Minister, Santé publique France (SpF) and health professionals;
- The contribution to **epidemiological surveillance:**
  - by leading a network of laboratories responsible for handling examinations and subsequently transmitting results,
  - by carrying out the analyses necessary for the monitoring of pathogens.
- **Immediately alerting** Santé publique France, the French Ministry of Health, and, where applicable, the Regional Health Agency to any finding likely to present a risk or threat to public health.

Operation and remit

CNRs are appointed for a five-year period by the French Ministry of Health on the basis of proposals from Santé publique France following an assessment of applications by a committee of experts. Specifications are drawn up setting out specific missions for each CNR. To conduct certain missions, a CNR can rely on one or more laboratories (no more than three) known as "associated laboratories." To ensure their missions are performed optimally, CNRs are involved in numerous national and international collaborations, particularly with public and private medical test laboratories, physicians from the "Sentinelles" network, Santé publique France for epidemiological surveys, health authority departments, research laboratories and organizations (Inserm, CNRS, Anses, Ifremer, etc.) and industrial laboratories. Most CNRs are also members of European networks (including the European Centre for Disease Prevention and Control – ECDC) or international networks (the World Health Organization (WHO) – see below). ●

OTHER

PUBLIC HEALTH SENTINELS

Like pathogens themselves, surveillance systems are unconfined by geographic borders! International health institutions throughout the world have formed sentinel networks composed of reference laboratories. **World Health Organization (WHO) Collaborating Centers** coordinate international efforts under the aegis of the organization. The Institut Pasteur hosts seven of these centers in France (Enterovirus, Listeriosis, Meningitis, Rabies, Salmonella, Antimalarial Drug Resistance and Yersinia), while Pasteur Network members host 17 worldwide.

The WOAH (World Organization for Animal Health) operates by the same principle of a network of collaborating centers. The Institut Pasteur hosts the center for the detection and identification in humans of emerging animal pathogens and development of tools for their diagnosis.

Finally, the Institut Pasteur set up a **Laboratory for Urgent Response to Biological Threats (CIBU)** in 2002 at the instigation of the French General Directorate of Health. With its 24/7 on-call system, the team can respond to microbiological emergencies both in France and worldwide at the request of the French General Directorate of Health. It supports the CNRs as seen in the early days of the COVID-19 pandemic and the H1N1 influenza pandemic in 2009. The CIBU is a World Health Organization partner whose remit also includes tackling emerging diseases such as Ebola in Guinea and the Democratic Republic of the Congo.

ARBOVIRUSES: AN EXAMPLE *OF CROSS-DISCIPLINARY* SURVEILLANCE

DENGUE, CHIKUNGUNYA, YELLOW FEVER AND ZIKA are severe diseases caused by the same virus type: "arboviruses". These viruses spread to vertebrates through bites from blood-feeding vectors (insects or ticks). Carriers include mosquitoes mainly from the genus *Aedes*, such as *Aedes albopictus* (the tiger mosquito) and *Aedes aegypti*. Their eggs are able to survive for several months in dry environments and, in the case of the tiger mosquito, even in cold environments. They are identified as invasive species.

ORIGINS AND EMERGENCE

The Zika virus was first detected in a monkey in Uganda in 1947. The first outbreak hit Micronesia in 2007 and was followed by further outbreaks in French Polynesia in 2013 and 2014, and Brazil in 2015.
Dengue is most prevalent in intertropical regions. Cases have been regularly reported in France since 2010, proving that transmission is a genuine risk, even in temperate zones.
Yellow fever was rife in the Americas between the 17th and 19th centuries. It is now most prevalent in Africa, with 95% of cases reported in this continent.

Since the first chikungunya outbreak in Tanzania in 1952, the disease has gained ground in Africa and Asia. The virus emerged in Europe in 2007, subsequently spreading to the West Indies and Polynesia, with major outbreaks between 2013 and 2014.

TRANSMISSION

A bite by a mosquito of the genus *Aedes*, the virus vector. A single mosquito can carry nearly 10 billion viral particles without suffering any harmful effects itself. Once infected, the mosquito can transmit the virus throughout its lifespan with every bite.

EXPERTISE and SURVEILLANCE

Almost 60% of the units in the Institut Pasteur Department of Virology in Paris work on vector-borne diseases.
The Laboratory for Urgent Response to Biological Threats (CIBU) is part of the WHO Collaborating Center for Arbovirus and Viral Hemorrhagic Fever Reference and Research. It is particularly involved in diagnosing and researching Zika virus.

The Institut Pasteur de la Guyane hosts the associated laboratory for the National Reference Center for Arboviruses.
A medical entomology course has run since 1988, providing training in this discipline to experts from around the world. The course runs every two years, alternating with a course via the Pasteur Network. A MOOC version is also available.

The Institut Pasteur and other Pasteur Network members are part of the Arbo-france French multidisciplinary and multi-institutional monitoring, surveillance and research network on human and animal arboviruses (arbo-france.fr). ●

KEY FIGURES

100 M

symptomatic cases of dengue per year worldwide, including 500,000 hemorrhagic cases (source: WHO)

200,000

cases of yellow fever per year worldwide with mortality rates ranging from 20% to 60% depending on the outbreak (source: WHO)

1

chikungunya vaccine candidate produced by the Viral Genomics and Vaccination Unit, which is ready to enter Phase III

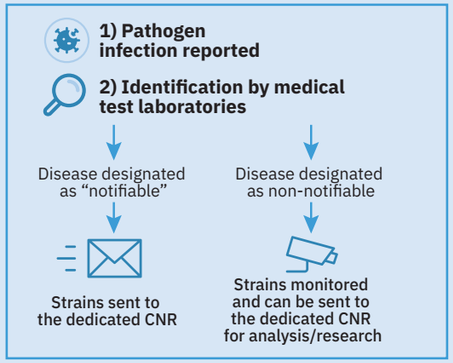
ANATOMY *OF AN ALERT*

with François-Xavier Weill, Director of the CNR for Escherichia coli, Shigella and Salmonella.

Prologue

CNRs play a pivotal role in a well-established system governing the surveillance of pathogens. What is the process for switching from sentinel to alert status? Here is a close look at one potential scenario...

Step 1: the threat

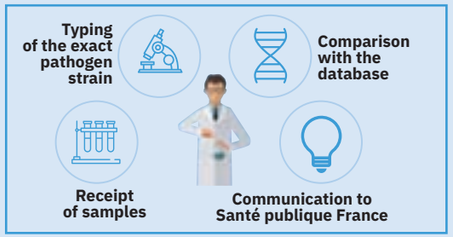


Cases of infection with a pathogen that is under surveillance are reported in various parts of the country. These have been identified by both hospital-based and non-hospital-based medical test laboratories that have diagnosed one or more patients. Two scenarios:

- either the disease in question is designated as notifiable (there were 36 such diseases in 2022), in which case any samples taken from patients are sent to the dedicated CNR for analysis of the responsible strains;
- or it is not designated as a notifiable disease but strains are submitted for microbiological surveillance and may be sent to the CNR for characterization and typing to identify the source of an infection or detect a chain of infection.

Step 2: expert assessment

Any samples received are identified using advanced technologies (genome sequencing since 2017) to precisely type the exact strain of the responsible pathogen. This microbiological work involves comparing the sampled pathogen with a genome database to determine other genetically related strains and thus trace



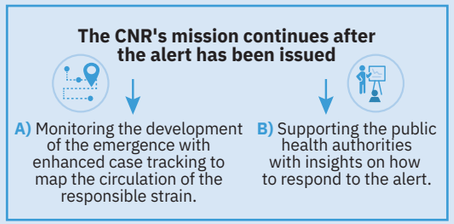
the outbreak’s origins. The results of these analyses are then passed on to Santé publique France, so it can assess the epidemiological situation. This is done in real time for notifiable diseases and at regular intervals for other diseases. For foodborne infections, any samples taken from potentially contaminated food or subject to systematic surveillance are passed on to the CNR for comparison of strains taken from clinical samples with strains taken from food samples in an attempt to identify the source of contamination.

Step 3: the alert

In most cases, the identified pathogen is known. Sometimes, a new strain or variant is identified, adding to knowledge of the associated disease. An alert is issued once the situation exceeds known parameters for normal circulation. This occurs in cases where a new, more aggressive and/or more communicable and/or more antibiotic-resistant strain is identified. Sometimes, case numbers rise quickly or their geographic concentration suggests a common source of infection. All situations are closely monitored to prevent a potential outbreak. The CNR teams immediately alert Santé publique France, which may decide to expedite an epidemiological survey to ascertain the source of contamination. Other institutional stakeholders may also become involved depending on the pathogen type. These include the general directorates of ministries (of agriculture/food, health, the economy, etc.) if the investigation relates to a foodborne infection.

Step 4: monitoring and advice

Once the alert has been issued, the CNRs continue their work in two parallel areas. The first involves monitoring the development of the emergence with enhanced case tracking to map the circulation of the responsible strain. The second involves supporting the public health authorities with insights on how to respond to the alert, for example by recommending the most appropriate diagnostic testing methods for the identified strain.



Epilogue

The outbreak has been contained, its source identified, and measures taken to prevent its resurgence. However, the CNR’s role as a sentinel does not stop there. It continues to monitor circulating pathogens and keeps records of this latest alert, which constitute a vital tool for quickly identifying any future re-emergences of infection. Some CNRs store all the strains they receive over periods spanning decades (for example, the CNR for *Escherichia coli, Shigella* and *Salmonella* has retained hundreds of thousands of strains since 1947). This valuable knowledge supports the work of research units, shedding light on pathogens’ genetic diversity and evolution over time. Some CNRs also conduct cohort tracking surveys, which involve monitoring a defined population over time to study the incidence of health events in order to improve our understanding of diseases.

TRACKING RABIES

IN REAL TIME

with Laurent Dacheux, Deputy Director of the CNR for Rabies.

Rabies is the type of pathogen we like to monitor closely. Every year, the CNR for Rabies (CNRR) analyzes between 1,200 and 1,300 samples from animals as part of its surveillance work. In October 2022, an alert was triggered by a case of canine rabies in the Greater Paris Region. Here is an hour-by-hour summary.

Tuesday 10/25, 15:00
Initial contact with DDPP 91 (the departmental authority for the protection of populations for Essonne). Dog died at 14:00 with clinical signs strongly indicating rabies. It was taken in by an animal refuge in Évry several weeks earlier, probably imported from North Africa. First clinical signs on 10/22. At least 3 individuals bitten, treated at the Institut Pasteur Anti-Rabies Center (post-exposure rabies prophylaxis).

Wednesday, 10/26, 11:00
Videoconference between the General Directorate of Health, Santé publique France, the Regional Health Agency, the General Directorate for Food and the DDPP.

Wednesday 10/26, 13:00
Receipt of the sample by the CNRR.

Wednesday 10/26, 16:00
Partial diagnosis made and reported.

Thursday 10/27, 17:30
Final diagnosis made and reported.

Friday 10/28, 10:00
Press release from the General Directorate of Health.

Saturday 10/29, 18:00
Molecular typing, virus source confirmed (Morocco) based on viral genetic sequence data available to the CNRR, results sent.

Subsequent days
epidemiological and legal investigation ongoing, individuals exposed to the animal and contacted by the Regional Health Authority treated at the Institut Pasteur Anti-Rabies Center.

RESEARCH *ADVANCES*

SCIENCE AT THE INSTITUT PASTEUR IN 2022

"Ten ERC grant winners in 2022 – that's our best result in years for this prestigious European funding. We have a proactive recruitment policy for early career researchers, with a highly selective process with over a hundred candidates for three or four jobs. These recruits often win ERC Starting Grants. They may then win an ERC Consolidator Grant, which was the case for Romain Levayer in 2022 and David Bikard in 2021. This reflects our highly dynamic long-term scientific policy. To date on our campus almost one in four lab heads currently holds an ERC Grant."

Christophe d'Enfert,
Senior Executive Scientific Vice-President

1,140
papers published
Source: Web of Science (articles, reviews and letters excluding preprints, extraction from April 7, 2023)

9
new research units (hearing/language/speech, microbiology, virology, immunology, aging)

4 G5s,
or junior groups, converted to units (chemistry, genetics, chromatin and infection, age-related pathologies)

19
CNRs (National Reference Centers), including 1 new center, operating under Institut Pasteur supervision over a five-year period (2023-2027)

45
invention disclosures registered, resulting in **25 patents** being filed

Major international collaborations including with
UCSF QBI
(Quantitative Biosciences Institute, University of California, San Francisco)

56
awards and prizes won by Institut Pasteur scientists including **10 ERC Grants** awarded *(3 Synergy Grants, 4 Consolidator Grants and 3 Starting Grants)*

ADVANCES MADE *UNDER THE 2019-2023* STRATEGIC PLAN

SCAN THE QR CODE TO LEARN MORE ABOUT THE STRATEGIC PLAN'S PROGRESS.

EMERGING INFECTIOUS DISEASES

2022 was marked by the COVID-19 and monkeypox pandemics. The Institut Pasteur confirmed its key role in tackling emerging infectious diseases through its 450 scientific papers on COVID-19 and the action taken by teams on campus from the outset of the monkeypox pandemic. Work in this area was ramped up through the funding of 6 research projects led by early career Institut Pasteur scientists and the launch of 2 five-year units (U5s). Finally, the international collaboration signed between the Institut Pasteur and University of California (UCSF QBI) to establish a dedicated Center of Excellence marked a further highlight in the field of emerging infectious diseases for 2022.

"Epidemics, pandemics: a never-ending story?" conference

The *Emerging infectious diseases* priority area in numbers:

10 scientific departments
—
90 teams
—
3 platforms/core facilities
—
4 biological resources
—
19 National Research Centers
—
1 WOAH (World Organization for Animal Health) Collaborating Center – WOAHCC
—
3 LabEx laboratories
—
1 Pasteur International Center for Research on Emerging Infectious Diseases

Interaction between *Aspergillus fumigatus* and *Pseudomonas aeruginosa*, two microorganisms in the lung microbiota, observed using scanning electron microscopy.

ANTIMICROBIAL RESISTANCE (AMR)

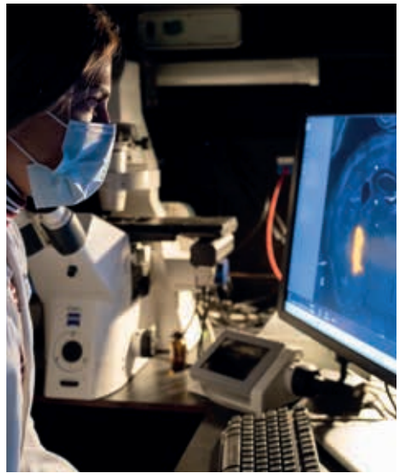
Numerous Institut Pasteur teams were involved in research on antimicrobial resistance (AMR). Every year, the Institut Pasteur strengthens its partnerships and participates in several national bodies (the antibiotic resistance priority research program (PPR), ABRomics, etc.) and international bodies in this area, thus uniting stakeholders to step up the fight against AMR. Symposia on AMR were held with Université Paris Cité, the University of Oxford, Inserm and the French Ministry of Higher Education and Research (MESRI), and the Pasteur Network. A five-year unit was established to ramp up phage therapy research in this area.

The *Antimicrobial resistance* priority area in numbers:

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

BRAIN CONNECTIVITY AND NEURO-DEGENERATIVE DISEASES

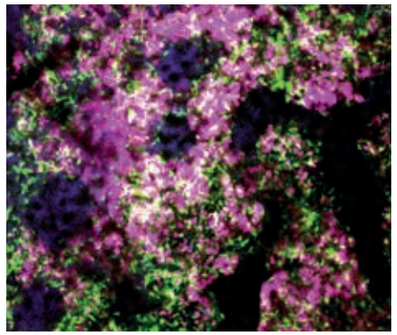
Substantial efforts were made to further develop the Brain Connectivity and Neurodegenerative Diseases community, which draws its diversity and strength from its multidisciplinary composition. Research excellence in this area is reflected in a series of major publications, in particular those on the discovery of novel mechanisms in SARS-CoV-2 infection and decoding the dialog between the gut microbiota and the brain. Collaborations also featured prominently this year, with existing links to the Paris Brain Institute strengthened through competitive bilateral projects and discussion days, and efforts made to reach out globally.



Observing the results of a stereotactic injection.

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

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



Cancer cells and macrophages attacking tumor cells.

CANCER

The Cancer Initiative stood out for its excellence and dynamism this year, securing numerous external grants and publishing over 70 studies in international journals. This initiative also took active steps to unite its scientific community on campus, organizing various events including the first Cancer Initiative symposium in December 2022. Moreover, through cross-disciplinary and collaborative efforts, it enabled the Targeted Technological Action (ATC) on "Drug Discovery and Screening" to update and supplement its bank of oncology-specific compounds, benefiting numerous projects on campus.

The *Cancer initiative* in numbers:

9 scientific departments
—
53 teams
—
4 technology core facilities

VACCINOLOGY AND IMMUNOTHERAPY

2022 was an eventful year for vaccinology and immunotherapy (IT) projects at the Institut Pasteur. The highpoint of the year was the announcement of a new Vaccinology and Immunotherapy Center, which will focus on the transition from discovery to clinical research. As regards vaccine candidates, a quadrivalent *Shigella* vaccine is currently under development; a vaccine for diarrheal diseases caused by *Shigella flexneri 2a* has reached Phase II; and a Lassa fever vaccine has completed a Phase I trial. In terms of immunotherapy, broadly neutralizing antibodies for SARS-CoV-2 (SPK001, SPK002) have quickly reached Phase II trials.

Report in the Translational Immunology laboratory.

The *Vaccinology and Immunotherapy initiative* in numbers:

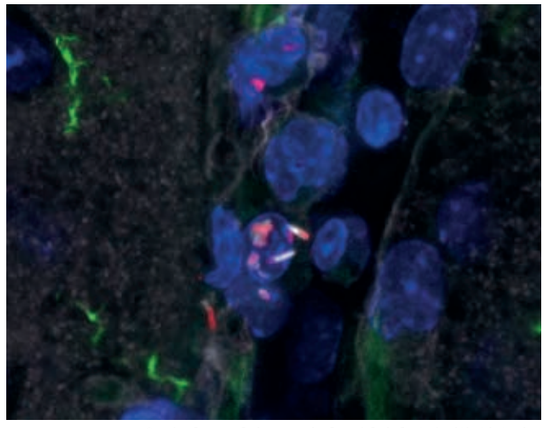
15 teams dedicated to basic research
—
20 teams and projects dedicated to innovation – vaccine candidates
—
16 teams and projects dedicated to clinical research
—
5 teams of experts including immunologists, microbiologists, virologists, epidemiologists, vaccine and immunotherapy specialists in collaboration 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 react during infection or in disease conditions 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.

Acting director: Guillaume Duménil.
17 teams



Cerebral vessel in an animal model infected with *Listeria*.

The gut movements help bacterial invasion

A gut-on-a-chip can mimic the complex interactions between biological and mechanical signals occurring when pathogens infect the gut epithelium. Aleix Boquet-Pujadas *et al.* developed state-of-the-art live microscopy and computer modeling to create tissue stress maps and track infections. They discovered the central role played by the contractile movement of the intestine in the penetration and virulence of two enteric pathogens, a bacteria and a parasite.

Science Advances, October 21, 2022.
Doi: 10.1126/sciadv.abo5767.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Tracking cells with machine-learning and deep-learning segmentation algorithms

TrackMate is a software platform for tracking cells and organelles in live-cell microscopy images, developed in the Image Analysis Hub, that grew a large user-base worldwide. Jean-Yves Tinevez and his collaborators released an entirely reshuffled version to integrate a wide range of machine-learning and deep-learning algorithms. This makes it possible to follow single-cell dynamics over a wide range of imaging conditions and cell types.

Nature Methods, June 2, 2022.
Doi: 10.1038/s41592-022-01507-1.

Listeria escapes the immune system to infect the brain

Upon ingestion of contaminated food, *Listeria monocytogenes* can reach the central nervous system causing neurolisteriosis, which is fatal in 30% of cases. The Biology of Infection unit has uncovered a new mechanism by which *Listeria* protects infected monocytes from CD8+ T lymphocyte-mediated killing. Carried by monocytes to the brain, *Listeria* ultimately invades the brain parenchyma. This also favors *Listeria* release in the environment through fecal shedding, favoring its transmission to a new host.

Nature, March 16, 2022.
Doi: 10.1038/s41586-022-04505-7.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

InBio laboratory meeting.

EXPLORING *BIOLOGICAL* DATA

DEPARTMENT OF COMPUTATIONAL BIOLOGY

This department specializes in data science and computational modeling. It combines expertise in mathematics, statistics, computer science, physics and imaging to address complex biological questions relating to genomes, cells, cancers, brain function and epidemiology. Its teams are developing quantitative methods and novel models to help understand and make use of the data generated by sequencing, experimental biology, public health, and clinical research. The department is accumulating expertise on artificial intelligence and machine learning, both key tools for gaining deeper insights in the fields of biology and health. The Department of Computational Biology is part of the Institut Pasteur's Paris campus and maintains close ties with the institute's other teams. It liaises closely with the Bioinformatics and Biostatistics Hub, houses two Inria teams, and pursues international collaborations, particularly with the Pasteur Network.

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

Innovative genomic data analysis method leads to the discovery of novel coronavirus families

Despite concerted planetary efforts to sequence and analyze SARS-CoV-2, our understanding of the virus is limited by a lack of genomic data on coronaviruses. Scientists from the "Sequence Bioinformatics" team who worked with an international team at a hackathon have discovered a number of novel coronaviruses by analyzing all the RNA sequencing data that is publicly available at global level (5.7 million sequencing samples).

Nature, January 26, 2022.
Doi: 10.1038/s41586-021-04332-2.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Artificial intelligence: an online platform to improve molecular-level analysis of living systems

Super-resolution microscopes are commonly used in life sciences to observe biological structures at molecular level. The Imaging and Modeling team has developed the ShareLoc platform, which provides access to large collections of images produced with this equipment. The data accumulated over time on ShareLoc can be used to train artificial intelligence, especially to speed up super-resolution imaging.

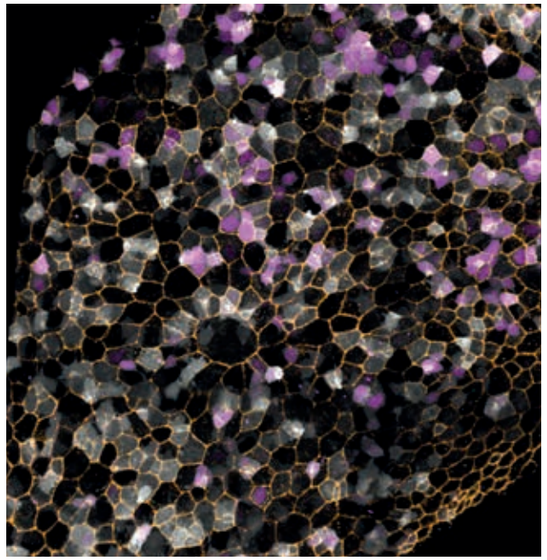
Nature Methods, November 22, 2022.
Doi: 10.1038/s41592-022-01659-0.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

ReacSight: a flexible, responsive and low-cost software solution for automating lab experiments

Scientists from the InBio team developed the ReacSight software solution in Python designed to enhance the utility of sensitive measurement equipment (plate readers, cytometers, etc.) with pipetting capabilities, and to create reactive bioreactor-based platforms with real-time sampling and analysis capabilities. Automation improves throughput and experiment reproducibility.

Nature communications, June 11, 2022.
Doi: 10.1038/s41467-022-31033-9.



A layer of neural stem cells lining the cerebral ventricle of an adult zebrafish (Danio rerio).

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 is tissue produced and repaired? This department covers a wide range of study topics, from individual cells to whole organisms and from embryo to adult. Its research on development also examines stem cells and their potential role in tissue regeneration.

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

Understanding the formation of the niche surrounding stem cells in the brain

In the brain, the neural stem cells interact with different neighboring cell types, forming what is called a “niche” displaying a highly hierarchized 3D architecture. In a study published in *Nature Communications*, Pauline Spéder and her team show in the larval *Drosophila* brain the central role of glial cells: they go through an elaborate dynamic, growing and fusing together, ultimately forming structural modules spatially partitioning the neural stem cell population.

Nature Communications, August 25, 2022.
Doi: 10.1038/s41467-022-32685-3.

How senescent cells can help tissue repair

When a cell goes through senescence, it stops dividing, which prevents its ability to reprogram and acquire a new identity. Han Li and her team have showed that, through the secretion of soluble factors, senescent cells can nonetheless improve other cells’ capacity to reprogram and have identified amphiregulin as a key molecule in this process. The secretory factors produced by senescent cells could then play an important role in tissue repair.

Cell Reports, July 12, 2022.
Doi: 10.1016/j.celrep.2022.111074.

Mechanics of digit formation

How do digits form during development? Jérôme Gros’ team recently demonstrated that the mechanical forces allowing limbs to lengthen also locally activate the genes responsible for digit emergence. These findings revealing the importance of the interaction between molecular and mechanical signals will enable a clearer understanding of congenital limb malformations, which are among the most common types in humans.

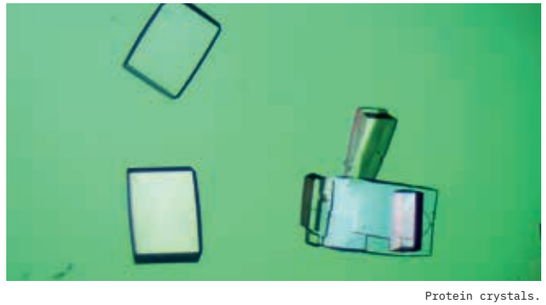
Developmental Cell, April 11, 2022.
Doi: 10.1016/j.devcel.2022.03.004.

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

DEPARTMENT OF STRUCTURAL BIOLOGY AND CHEMISTRY

A molecule’s structure is closely linked to its function. This department’s units and technology core facilities focus their research on the three-dimensional organization, properties, functions and dynamics of macromolecular complexes and the synthesis of molecules relevant to human diseases. Through integrative structural biology approaches and interdisciplinary projects combining chemistry, biology and technology, the department plays a key role on campus in developing novel therapeutic, diagnostic and vaccine strategies. The department is led by Paola B. Arimondo.

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



Protein crystals.

EpiCBio

Malaria treatment resistance is spreading urging development of new drugs. Researchers isolated from the plant *Cocculus hirsutus* compounds active against the malaria parasite. The compounds address unconventional targets for antimalarial drugs resulting in potent inhibitors of multiresistant clinical isolates. The lead compound, chemically optimized, was active in a mouse model of malaria and on all the parasite’s lifecycle stages, including transmission.

iScience, February 17, 2023.
Doi: 10.1016/j.isci.2023.105940.

Bacterial pathogenicity: improving understanding of an essential process – molecule secretion

The type 2 secretion system is a nanomachine assembled in the envelope of Gram-negative bacteria and used for the secretion of virulence factors. To understand its mechanism of assembly and secretion, researchers showed how the atomic structure and the dynamic of key components promote the assembly of the nanomachine during secretion. The results are highly useful for future development of antimicrobial therapy and biotechnological tools.

Structure, December 30, 2022.
Doi: 10.1016/j.str.2022.12.003.

SCAN THE QR CODE
FOR MORE INFORMATION
ABOUT THIS PUBLICATION.

InDeep: 3D fully convolutional neural networks to assist *in silico* drug design on protein-protein interactions

InDeep is a tool for predicting functional binding sites within proteins that could either host protein epitopes or future drugs. Leveraging deep learning on a curated dataset of PPIs, *InDeep* can proceed to enhanced functional binding site predictions either on experimental structures or along molecular dynamics trajectories. The benchmark of *InDeep* demonstrates that it outperforms state-of-the-art ligand binding site predictors.

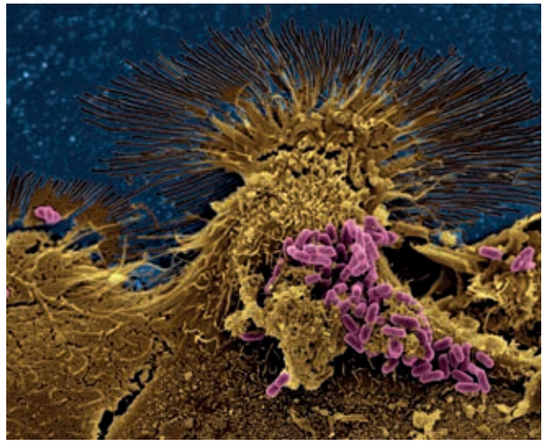
Bioinformatics, February 7, 2022.
Doi: 10.1093/bioinformatics/btab849.

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 adaptive selection 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: Romain Koszul;
Deputy Director: Micheline Fromont-Racine.
12 teams.



Escherichia coli O104:H4 bacteria interacting with human intestinal epithelial cells.

Origins of transfer establish networks of functional dependencies for plasmid transfer by conjugation

In several plasmids of pathogenic bacteria, scientists have identified a sequence that enables bacterial conjugation to take place via a hitchhiking mechanism. This discovery is important as it sheds light on the process and its role in antimicrobial resistance. It also suggests that complex networks of interactions between different plasmids exist in cells.

Nucleic Acids Research, November 29, 2022.
Doi: 10.1093/nar/gkac1079.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

High resolution microfluidic assay and probabilistic modeling reveal cooperation between T cells in tumor killing

Immune responses to tumors largely vary among individuals, but very few studies examine the contribution of intrinsic behavior of the T cells to this heterogeneity. Using a microfluidic-based *in vitro* method (to track the outcome of antigen-specific T cell activity on many individual cancer spheroids simultaneously, researchers show that both T cell accumulation and killing function rely on collective behaviors rather than simply reflecting the sum of individual T cells.

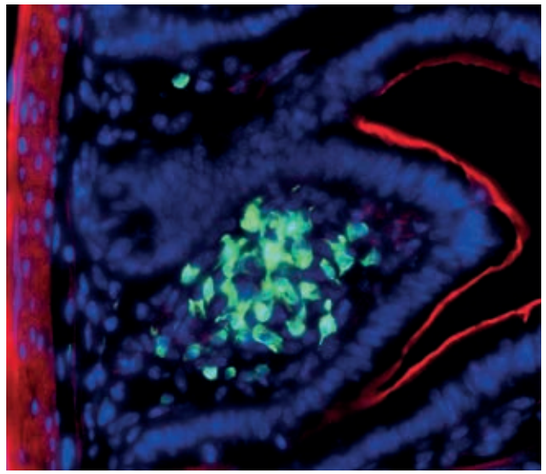
Nature Communications, June 3, 2022.
Doi: 10.1038/s41467-022-30575-2.

The immune factors driving DNA methylation variation in human blood

The nature and respective contribution of factors that drive epigenetic variation in humans remain to be fully characterized. In their study, researchers show that DNA methylation differs substantially between naïve and memory T cells and highlight the key role played by latent cytomegalovirus infection. Their results indicate that blood cellular composition and DNA sequence variation are the strongest predictors of DNA methylation, highlighting critical factors for medical epigenomics studies.

Nature communications, October 6, 2022.
Doi: 10.1038/s41467-022-33511-6.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.



Immunofluorescence staining of ILC3s (green) in the intestine (nuclei in blue and actin in red). Group 3 innate lymphoid cells (ILC3s) play an essential role in the innate immune response, especially in the gut mucosa.

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. It provides the exclusive focus of this department's work. Teams here research the development of the immune system, its protective and pathological immune 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.
15 teams.

The innate immune system displays a memory response against infection

While the adaptive immune system generates memory responses to previous infections, little is known whether the innate immune system develops these attributes. Scientists from the Innate Immunity Unit demonstrated such a memory response from intestinal group 3 innate lymphoid cells (ILC3s; which the team first identified in 2008). In their recent work, the researchers showed that a primary bacterial infection 'trains' ILC3 to more efficiently fight a subsequent infection that occurs later in life.

Science, February 24, 2022
Doi: 10.1126/science.aaz8777.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Broadly SARS-CoV-2-neutralizing antibodies

Antibodies are a very powerful weapon enabling the immune system to fight off infectious agents such as the SARS-CoV-2 virus. Hugo Mouquet's team has produced and characterized some hundred human monoclonal antibodies that target the SARS-CoV-2 spike protein. The scientists identified two broadly neutralizing antibodies that were effective against all variants circulating at the time. These are currently being clinically developed by the biotech firm SpikImm.

Journal of Experimental Medicine, June 15, 2022.
Doi: 10.1084/jem.20220638.

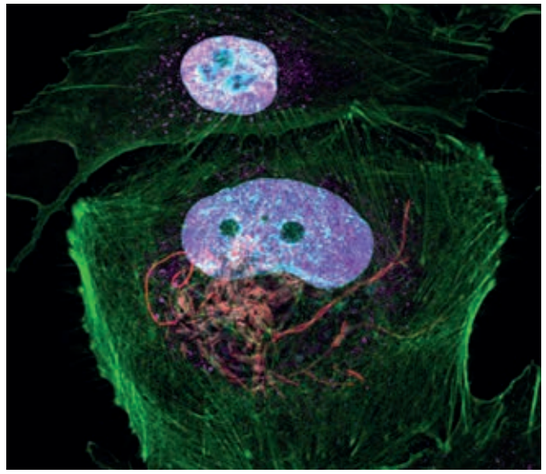
SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Stromal cells, maestros of the intestine

The intestine plays a key role in nutrient absorption and defense against pathogens, a task performed by a complex intestinal barrier. The unit of Lucie Peduto identified a population of tissue-resident cells known as stromal cells which are crucial for the development of a functional intestinal barrier in the first weeks after birth. Absence of these cells prevents normal postnatal growth and increases susceptibility to intestinal inflammation.

Cell Stem Cell, May 5, 2022.
Doi: 10.1016/j.stem.2022.04.005.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.



Intracellular replication of *Legionella pneumophila* (in red) in lung epithelial cells.

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.

Legionellosis: a novel mechanism by which the bacterium *Legionella pneumophila* regulates the immune response of its host cells

Legionellosis is an emerging disease caused by *Legionella pneumophila* bacteria. Scientists from the Department of Microbiology and their colleagues have revealed a mechanism enabling *L. pneumophila* to target the immune response of the cells it infects by secreting a small regulatory RNA. This mechanism facilitates the survival and proliferation of *L. pneumophila* during infection. The research provides new information on the tactics used by bacteria to manipulate host cells.

Nature communications, February 9, 2022.
Doi: 10.1038/s41467-022-28454-x.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Phage therapy: a model to predict its efficacy against pathogenic bacteria

Understanding the mechanisms governing the therapeutic efficacy of bacteriophages used to tackle antibiotic-resistant bacteria remains a challenge. Scientists from the Department of Microbiology and their colleagues have used experimental data to develop a mathematical model to evaluate several key efficacy parameters including dosage, route of administration and bacteriophage interaction with the host's immune system.

Cell Reports, May 17, 2022.
Doi: 10.1016/j.celrep.2022.110825.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Iron-sulfur cluster biosynthesis: a much earlier origin than previously thought

Iron-sulfur (Fe-S) clusters are protein cofactors that are essential for life. It has generally been thought that the molecular machineries catalyzing Fe-S cluster biosynthesis emerged in response to the Earth's oxygenation. An alternative scenario is now being put forward by scientists. Two new synthesis machineries have been identified in numerous bacteria and archaea. These machineries were present in the last universal common ancestor and therefore predate the appearance of O_2 on Earth.

Nature Ecology & Evolution, October 6, 2022.
Doi: 10.1038/s41559-022-01857-1.

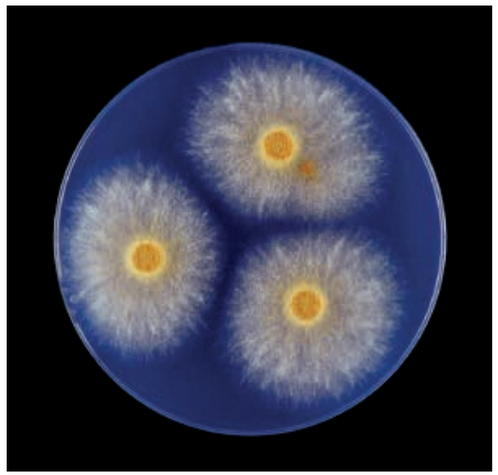
SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

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.



Aspergillus flavus culture.

Surfactant protein D inhibits growth, alters cell surface polysaccharide exposure and immune activation potential of *Aspergillus fumigatus*

This study led by researchers from the department of Mycology demonstrates that surfactant protein-D (SP-D), a humoral immune component and a pattern recognition receptor of the collectin family, has direct growth inhibitory activity on *Aspergillus fumigatus*, an airborne fungal pathogen. SP-D recognizes polysaccharides exposed on this fungal surface, alters fungal cell wall organization and permeability, thereby increasing the efficacy of antifungal drugs, which suggests its therapeutic potential.

The Cell surface, January 10, 2022.
Doi: 10.1016/j.tcsw.2022.100072.

Antifungal therapy: Csa6 protein, a potential target for treatment development

A team of scientists has revealed a gene (CSA6) that regulates genome stability in *Candida albicans* and other related fungi. The protein produced by this gene, Csa6, therefore represents a potential target for antifungal therapy, at a time when there is an urgent need for the development of novel treatments for fungal infections.

Nature communications, July 23, 2022.
Doi: 10.1038/s41467-022-31980-3.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Tackling fungal infections more effectively through surveillance

The French National Reference Center for Invasive Mycoses and Antifungals leads an active and sustained nationwide surveillance program on probable and proven invasive fungal diseases (IFDs) to determine their epidemiology in France. Between 2012 and 2018, a total of 10,886 IFDs were recorded. Analysis of those IFDs underlines the interest of an active surveillance involving mycologists and clinicians to describe the global incidence and that of the main IFDs, notably in light of the lack of improvement in the global survival rate despite the new diagnostic tools and drugs.

mBio, May 2, 2022.
Doi: 10.1128/mbio.00920-22.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

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 multiple scales, from molecules to behavior. We also seek to understand how the brain works through its interactions with other systems including the microbiome and immune system. Our work provides a fundamental basis for accelerating translational research focused on the mechanisms, pathophysiology and clinical implications of psychiatric disorders (autism spectrum disorder, dyslexia, addiction, mood disorders) and neurological disorders (neurodegenerative diseases), which present developed countries with a plethora of major health challenges. The department is led by Pierre-Marie Lledo.

Director: Pierre-Marie Lledo;
Deputy Director: Uwe Maskos.
10 teams, and 1 award-winning team.

Meeting in the Human Genetics and Cognitive Functions laboratory.

Gut microbes regulate appetite and body temperature

With more microbes than cells in our body, it's not surprising that bacteria and other invisible "guests" influence our metabolism, immune system, and even our behavior. Our team studying mice have worked out how bacteria in the mammalian gut can ping the brain to regulate appetite and body temperature – and guess what? It involves the same molecular pathway the immune system uses to detect bacterial pathogens.

Science, April 15, 2022.
Doi: 10.1126/science.abj3986.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Amortized inferences of synaptic receptors

Bayesian inferences are challenging and computationally intensive procedures. They can be even more complex when multiple models can describe the data and various parameters are associated with each model. Researchers have shown that they could simplify this procedure massively by teaching a neural network on a graph to reproduce the entire procedure with linear complexity and applied it to synaptic receptor dynamics.

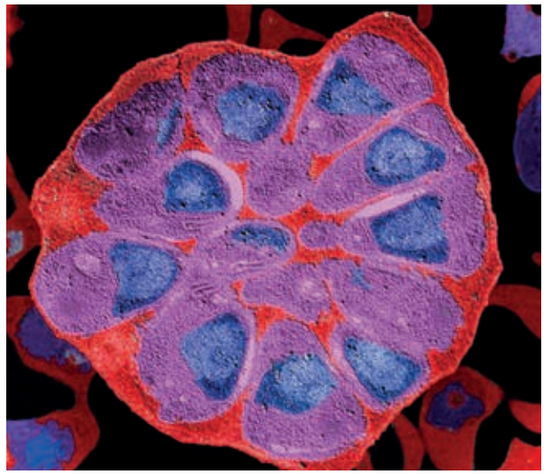
Physical Review E, November 22, 2022.
Doi: 10.1103/PhysRevE.106.055311.

Autism: how genetics influences symptoms

In collaboration with Cambridge, scientists at the Institut Pasteur studied the genetic and phenotypic profiles of 24,000 autistic individuals. For the first time at this scale, they shed light on the effect of different genetic architectures on the components of autism. These results provide relevant information to better identify more appropriate support for each autistic individual. The paper won the 2022 ISPG Gershon Paper of the Year Award.

Nature genetics, June 2, 2022.
Doi: 10.1038/s41588-022-01072-5.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.



Red blood cell infected with *Plasmodium falciparum*.

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 sandfly, the vector of *Leishmania*, and the tsetse fly, the vector of *Trypanosoma*. The department is led by Gerald Spaeth.

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

Malaria: blood stage of the parasite recreated *in vivo* to help tackle the disease

Plasmodium vivax, one of the causative agents of malaria, exhibits characteristics that make it difficult to control, eliminate and study in the lab, since it cannot be cultured for long periods *in vitro*. By engrafting human hematopoietic stem cells into mice, scientists were able to maintain the parasite *in vivo*. This constitutes a major breakthrough in research, as it paves the way for testing new drug and vaccine candidates.

Nature communications, July 15, 2022.
Doi: 10.1038/s41467-022-31864-6.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

A New Drug Target against Malaria

Plasmodium falciparum, which causes the deadliest form of malaria, is increasingly resistant to the frontline drug, artemisinin. Researchers have found that a membrane repair enzyme called PRDX6, which is present in red blood cells, is taken up by the parasite along with hemoglobin and is essential for parasite growth. PRDX6 inhibitors that target the human enzyme kill the parasite and can serve as novel anti-malaria drugs that could help eradicate malaria.

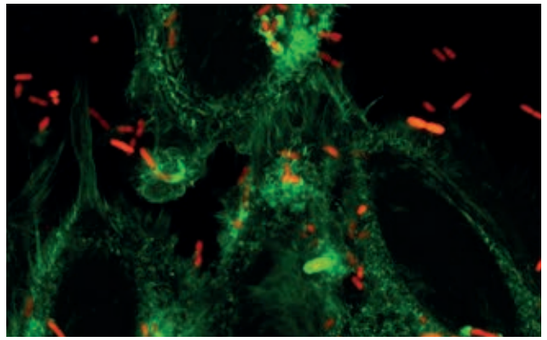
Cell Report, June 14, 2022.
Doi: 10.1016/j.celrep.2022.110923.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

SHERLOCK4HAT: A new highly sensitive and specific diagnostic toolkit for African Trypanosomiases

Elimination of Human African Trypanosomiasis (HAT) requires new highly sensitive diagnostics. We have developed a CRISPR-based molecular detection toolkit using SHERLOCK (Specific High-sensitivity Enzymatic Reporter unLOCKing) that distinguishes between the three *T. brucei* subspecies with a higher sensitivity than existing tools. It is adaptable to a field-based setting and can be used for HAT diagnosis or epidemiological surveillance.

EBioMedicine, October 27, 2022.
Doi: 10.1016/j.ebiom.2022.104308.



Shigella flexneri infecting HeLa cells.

ANTICIPATING *EMERGENCE*

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 and WHO Collaborating Centers 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.

Diagnosis during plague epidemics: the contribution of statistics

During an epidemic, it can happen that no diagnostic test offers perfect performance and so different tests are used, making interpretation of the results more complex. Scientists in the Mathematical Modeling of Infectious Diseases Unit have developed a method for characterizing the performance of the various tests and estimating prevalence in these situations. This method, published in *PLoS Biology*, has been applied to the study of plague in Madagascar.

PloS Biology, August 15, 2022.
Doi: 10.1371/journal.pbio.3001736.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

A new method for identifying and typing *Shigella* strains

Research conducted in the Enteric Bacterial Pathogens Unit has led to the modernization of shigellosis surveillance through bacterial genome sequencing. Using this new standardized technique, bacteria can be accurately classified and uniquely high-resolution typing is possible. The method is now routinely used at the National Reference Center for surveillance of *Shigella* infections in France.

Nature communications, January 27, 2022.
Doi: 10.1038/s41467-022-28121-1.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Understanding how the whooping cough bacterium has evolved in response to vaccination

The Biodiversity and Epidemiology of Bacterial Pathogens Unit has demonstrated the potential of phylogeographic methods for understanding pathogen evolution. These findings will prove useful for the vaccination strategy for whooping cough, a disease that currently affects over 24 million people per year. The study sheds light on pathogen spread and the evolutionary pressure of vaccines, a particularly topical issue given the COVID-19 pandemic.

Science Translational Medicine, April 27, 2022.
Doi: 10.1126/scitranslmed.abn3253.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

BETTER *UNDERSTANDING* VIRAL THREATS

DEPARTMENT OF VIROLOGY

This department's research focuses on understanding the molecular mechanisms that are involved in various viral cycle stages and cause related diseases. Major efforts are under way to elucidate and analyze the biological and epidemiological determinants of infectious disease emergence. Research activities include studies on transmission, animal reservoirs and vectors, viral epidemiology and evolution, and host immune response. Emerging respiratory viruses, oncogenic viruses, retroviruses and arboviruses are scrutinized 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.
23 teams.

In the Virus and Immunity laboratory.

Considerable escape of SARS-CoV-2 Omicron to antibody neutralization

The Virus and Immunity Unit studies the replication of SARS-CoV-2 variants and their interaction with the host immune response. The authors developed rapid high-throughput assays to study neutralizing antibodies. They report that the SARS-CoV-2 Omicron variants display considerable escape to neutralizing antibodies generated by vaccination and by infection with previously circulating variants. Omicron variants also escape most currently available therapeutic monoclonal antibodies.

Nature, December 23, 2021.
Doi: 10.1038/s41586-021-04389-z.

Structural basis of synergistic neutralization of Crimean-Congo hemorrhagic fever virus by human antibodies

The tick-borne Crimean-Congo hemorrhagic fever virus causes severe disease in humans. The Structural Virology team previously identified a combination of two antibodies targeting protein Gc, the main antigen, yielding postexposure protection in animal models. This paper describes the structures of Gc in its trimeric postfusion form and in its monomeric pre-fusion form in complex with these two antibodies, showing how they act synergistically to block membrane fusion.

Science, January 7, 2022.
Doi: 10.1126/science.abl6502.

Innate immune pathways act synergistically to constrain RNA virus evolution in *Drosophila melanogaster*

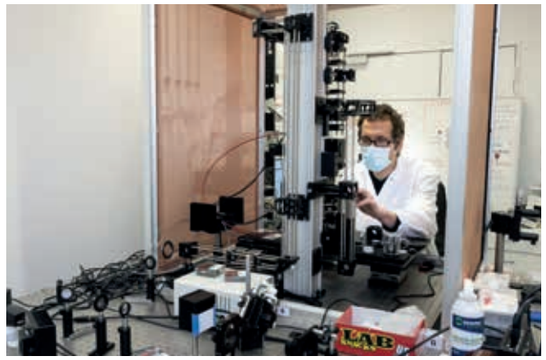
A recent study led by the Viruses and RNA interference Unit showed that the innate immune pathways act synergistically to constrain RNA virus evolution in insects. Experiments conducted on flies infected by the *Drosophila C* virus confirmed that there is not a main immune defense mechanism against a particular virus, but instead a repertoire of defense mechanisms that are triggered after infection and that interact with each other.

Nature Ecology & Evolution, May 6, 2022.
Doi: 10.1038/s41559-022-01697-z.

AUDITORY *SYSTEM EXPERTS*

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;
Deputy Director: Anne-Dominique Lodeho-Devauchelle.



Development of a microscope for imaging and optical stimulation of the peripheral auditory system using two-photon microscopy. Report at the Hearing Institute in January 2021.

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

Anne-Lise Giraud, new Director

Anne-Lise Giraud was appointed as Director of the Hearing Institute in January 2022. Her unit "Neural coding and neuroengineering of human speech functions" grew during the year with the recruitment of eight people. Their research involves exploring the neural mechanisms underpinning the implementation of the language processing network in the human brain, investigating dysfunction in hearing and language disorders such as aphasia, dyslexia and stuttering, and developing therapeutic solutions.

Why are sounds not perceived under anesthesia?

DFNB1, a severe to profound form of congenital sensorineural hearing loss that is by far the most frequent worldwide, is caused by variants in the GJB2 gene – which is also responsible for presbycusis. The Auditory Therapies Innovation team is working on preventing and treating these forms of hearing loss. In collaboration with Sensorion, a number of key milestones have been reached on the path to identifying an effective therapeutic candidate.

By monitoring the activity of nearly a thousand neurons in the auditory cortex during the transition from wakefulness to anesthesia, the team revealed a novel neural mechanism that accompanies the transition from a state of conscious perception to a state of unconsciousness. The results indicate that under anesthesia, the neuron groups that respond to sounds are indistinguishable from spontaneously active neurons. The cerebral cortex masks sensory inputs with its own "spontaneous" activity.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

CERIAH comes to the Institut Pasteur campus

The Center for Research and Innovation in Human Audiology (CERIAH) has moved into its spacious new premises in the Medical Center wing. CERIAH is a platform that performs research protocols involving human subjects entailing minimal risks and burdens (RIPH2 and 3, not RIPH). This new space on the campus in Paris' 15th *arrondissement* is crucial for the future development of the center, enabling the introduction of new research protocols in a controlled acoustic environment with the aim of scaling from scientific proofs of concept to real-world applications.

DEVELOPING *CUTTING-EDGE TECHNOLOGY*

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.

Mouse Genetics Engineering Center (CIGM).

EMPOWERING RESEARCH TEAMS with a supportive technological environment to help advance their discoveries is a key priority for the Institut Pasteur. The Department of Technology provides access to high-level shared resources as well as expert consultation and other services to scientists through a unique continuum of facilities, technologies and biological resources. The Department of Technology constantly invests in the development of these resources.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE DT'S OBJECTIVES.

These resources are divided into 4 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 Center for Resources and Research in Scientific Informatics (C2RI).

C2RT: core facilities driving innovation

After the disruption of the pandemic, 2022 witnessed C2RT re-engage scientific R&D and innovation activities, re-establishing scientific seminars, symposia and technology training events. For example, the technological seminars of the *Action Thematique Concertee* included seminars on high-throughput and spatiotemporal molecular analyses of organoid and spheroid tissue models; a mini-symposium organized by the Single Cell Resources Initiative; and the 1st Drug Discovery & Screening Symposium. Acting in concert, the C2RT facilities that pivoted their activities amidst the pandemic providing front and center technological resources supporting COVID researchers yielded a plethora of important research publications reinforcing the fundamental understanding necessary to fight the virus. Among them, especially solicited because of their transversally concerted and coordinate actions were the platforms providing know-how in protein-production, antibody-engineering, crystallography, and molecular, chemical and ultrastructural analyses; culminating in exceptional publications (e.g. Temmam S, et al., Nature. 2022; Bruel et al., Nature Medicine. 2022). Such activities were further driven by both generous contributions from donors, and coordinated grant funding recognizing excellence of C2RT teams with significant awards from *ANR, Region Ile de France* and other agencies. This success enabled investment supporting implementation of powerful new image-detectors and software for ultrastructural analyses, and mass-spectrometry software for top-down proteomics. Finally, in the wake of the success of the C2RT innovative diagnostic development technology platform a collaborative planning with UPC proposed creation of a new joint technology platform for therapeutics discovery.

C2RA: animal models to aid research

C2RA continued to grow with the addition of a new Histopathology Core Facility in early 2022. This new facility is available to meet needs in experimental analysis of tissues from animal models used on campus for different research topics including infectious diseases, cancer, immunotherapy and inflammation. In partnership with the Image Analysis Hub (C2RT/C2RI centers), it is also involved in a digital

pathology development project. Several C2RA facilities contributed to COVID-19 research efforts with the development of novel murine models (CIGM/Mouse Genetics Engineering Center) and technical assistance with animal testing (CAF/Central Animal Facility) for various units on campus. CEPIA was involved in the InfraVec2 project to provide vectors for units outside the Institut Pasteur and expanded its in-house services with the implementation of new *Anopheles* breeding facilities. The Human Disease Models (HDM) core facility, launched in 2021, moved to new premises and developed its first mice with a "humanized" immune system. From an operational perspective, all animal facilities (CAF, CEPIA and Hearing Institute) achieved renewal of their accreditation and also filed accreditation applications for GMO handling to conform to a regulatory change in January 2022. C2RA also actively contributed to working groups for the future center on vector-borne diseases.

Production and Purification of Recombinant Proteins Technological Platform.

CRBIP: biological resources on hand

CRBIP continued to grow its collections of bacteria and human biological specimens for distribution to users both within and off campus, notably via the European One Health EJP-CARE project (CIP) and within the COVID-19 topic area (ICAReB-Biobank). A collection of 800 live cyanobacteria strains is available within the PCC. In parallel, CRBIP instigated a project to resurrect the Institut Pasteur legacy collection of fungal specimens. It was involved in several partnerships, including with the EVA-g virus collection network, and the European IS_MIRRI21, ISIDORe and HoloZcan projects for the assessment of an experimental holographic platform. CRBIP contributed to the development of a monkeypox collection within the CIBU for the management of new outbreaks. As regards operational aspects, CRBIP continued its strain sequencing efforts in collaboration with the Mutualized Platform for Microbiology (P2M) and to offer genome taxonomy services (BIGSdb-Pasteur). Development projects led to the installation of a lyophilizer and an aliquoting system, as well as digitization operations for 15,000 bacterial strain files. In addition to the distribution of numerous samples, CRBIP also actively contributed to scientific research with 25 journal papers.

C2RI: supporting computational biology

The year 2022 saw the creation of a new Center affiliated to the Department of Technology, the Center for Resources and Research in Scientific Informatics (C2RI), with Michael Nilges as its interim head. Its primary mission is to facilitate the processing and analysis of vast amounts of data generated by the institute's research units and core facilities, and to develop customized algorithms. The C2RI regroups expertise in a wide range of topics, including phylogenetic analysis, genomics, statistics, systems biology, image analysis, data management, and high-performance computing. Data come from genomics, proteomics, photonic and electron microscopy, and other advanced technologies.

With the creation of this center, we will enhance the integration of the institute's existing informatics strengths, alongside other support groups of the Department of Technology and national and international organizations, and foster synergies between computational approaches employed for different types of data. Data management is central to virtually all scientific research and is crucial for a number of high profile research programs at the institute.

The C2RI, in particular its largest entity, the Bioinformatics and Biostatistics Hub, provides basic and advanced training and support to researchers new to bioinformatics, equipping them with the skills and knowledge necessary to work with complex data sets. ●

330

staff

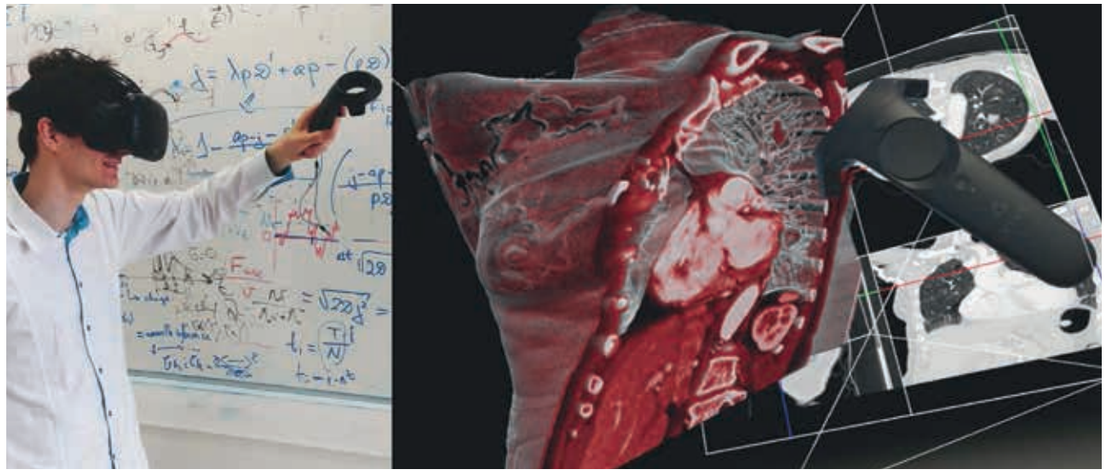
22 C2RT units
6 C2RA units
4 CRBIP units
4 C2RI units
1 PAD unit
13 units are ISO 9001 certified
9 units have IBISA accreditation

NEW C2RI

The C2RI, launched in 2022, aims to support research teams and core facilities with the computational biology aspects of their projects. This includes data analysis in a wide range of fields, development of custom algorithms and web applications, data management and high-performance computing. —

SPEEDING UP INNOVATION, *FOR THE BENEFIT OF HEALTH*

The Technology Transfer and Industrial Partnership Department (DARRI) seeks to promote translational research in order to boost the impact of basic research on tackling public health challenges. The DARRI identifies scientific projects with high innovation potential and supports them through the innovation process to enable the commercialization of innovative health products and services developed from academic research through industrial partnerships, licenses or the launch of startups.



Visualization with DIVA, software for microscopy and biomedicine.

IN 2022, the DARRI continued to roll out its strategy based on the following principles: cross-disciplinary organization of activities to cover the entire innovation process, an Innovation Accelerator supporting the most promising applications, optimized positioning of patents in strategic fields, and increased efforts to promote the Institut Pasteur's inventions.
With 21 new collaboration agreements (and 14 new patent and biological material licenses) secured and a new startup launched based on Institut Pasteur research (V4C), the DARRI has facilitated technology transfer to industry while continually ensuring that products and services can be accessed by as many people as possible, particularly in low-income countries.

The DARRI also coordinated 330 management agreements and its activities generated a total of €38.2 M in revenue from industry partnerships, of which €13.1 M related to collaboration agreements.
In 2022, the DARRI also played an active role in the Pasteur Network, sharing its expertise and fostering future collaborations at the "innovation" workshops organized by Fiocruz (Brazil) and the Institut Pasteur Korea.

Identifying disruptive projects and providing innovation training

A series of individual meetings was held (with nearly 25% of unit heads on campus) to raise scientists' awareness of industrial applications of their findings. In 2022, the DARRI also joined forces with the HR Department to set up a new course entitled "De la découverte scientifique à la start-up en passant par le transfert de technologie" ("From scientific discovery to startup via technology transfer"), which can be accessed by the whole campus.

Protecting inventions

In 2022, 45 invention disclosures were registered, resulting in 25 new priority patents being filed and 19 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.

Mouse cardiomyocytes (orange) and mitochondria (blue).

Two new selected projects within the Innovation Accelerator

The Institut Pasteur Innovation Accelerator launched in 2019 seeks to support the most promising research applications and boost their socio-economic transferability. The project engineering approach taken combines funding strategies, technical support and professional expertise from the DARRI. This support helps selected projects to mature and brings them in line with industrial requirements and needs.

Two new projects were selected in 2022: Tailor-made inhibitors of the Sec61 translocon for Oncology, PI: Caroline Demangel, High-throughput multimodal imaging screening of therapeutic compounds for mitochondrial diseases in human cells, PI: Timothy Wai.

Networking with other health ecosystem stakeholders

In 2022, the Institut Pasteur stepped up its collaboration with Argobio through its decision to launch two joint maturation programs.
The Institut Pasteur also forged links with Paris Biotech Santé by signing a new partnership agreement aimed at ramping up cooperation.

Moreover, the Institut Pasteur took part in the AI for Health Challenge launched by the Greater Paris Region with the Foch Hospital and Medicen. This marks the next concrete step in the Phoenix project aimed at standardizing data production and sharing practices to facilitate data usage and partnership building.

2022 saw the launch of the MOPEVAC NEXT project which won the “Emerging Infectious Diseases and CBRN Threats” call for expressions of interest. Its aim is to develop and preclinically assess a new vaccine platform based on a live attenuated viral vector.

Developing strategic partnerships

To provide favorable conditions in which to bring products based on Institut Pasteur research to market, it is essential to increase interaction between the Institut Pasteur and industry and establish synergies between their respective scientific teams.

In 2022, this ambition led to the signing and extension of 57 R&D collaboration agreements with long-standing and more recent partners, including the following:

- 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** concerning the signaling pathways involved in chronic inflammatory diseases. A key milestone was reached in 2022 with the start of enrollments of psoriasis and ankylosing spondylitis patients in the AP-HP.
- The framework agreement signed in 2022 between the Institut Pasteur and **Moderna** provides scientists on campus with access to Moderna’s mRNA technology platform and expertise for testing novel antigens or antigen combinations.
- Six new R&D projects emerged from the partnership between the Institut Pasteur and **Sanofi** in 2022. In particular, a specific mRNA program was put in place following Sanofi’s creation of an mRNA Center of Excellence.

- In 2022, a license agreement was signed with **eTheRNA**, a Belgian company specializing in the development of RNA vaccines, thus building on the collaboration initiated in 2020 with the Malaria Infection and Immunity Unit.
- The 10th anniversary of the collaboration between the Institut Pasteur and **Meiji Holdings** was also marked in 2022.

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 2022, 16 innovative new research projects at an early or advanced stage – 5 within the Carnot scope – were funded by the DARRI/Carnot Emergence, Maturation, Partnership & Innovation and Consolidation programs.

A successful year for our spin-offs SpikImm and AVATAR MEDICAL

In 2022, SpikImm, a company set up jointly by Truffle Capital and the Institut Pasteur in 2021, was granted substantial funding through the France 2030 plan. This will be used to speed up the clinical and industrial development of its broadly neutralizing monoclonal antibodies designed to prevent COVID-19 in immunocompromised patients: SPK001, the first drug candidate which demonstrated outstanding tolerability in a Phase I clinical trial and SPK002, which is due to enter clinical trials in the second quarter of 2023.

In addition to this, Institut Pasteur and Institut Curie spin-off, AVATAR MEDICAL, which seeks to place medical imaging at the heart of surgical practice, was announced the winner of the European EIC Accelerator program.

“Through this first Pasteur Innov Day, we wanted to show that there can be no innovation without technology.”

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

45
invention disclosures

10
projects in the Innovation Accelerator

269
agreements signed

€38.2 M
in revenue

First edition of Pasteur Innov’Day.

“A SUCCESSFUL FIRST *PASTEUR INNOV’DAY*”

The first Pasteur Innov’Day, held on campus on July 7, 2022 and organized by the Department of Technology, the DARRI and the management team at the Pasteur Microbes and Health Carnot Institute, was attended by around a hundred industrial and academic partners. Its purpose was to introduce industrial stakeholders to the institute’s outstanding expertise and technological know-how, providing them with the potential to overcome their technological barriers.
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ACADEMIC *PARTNERSHIPS*

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 and international academic partnerships to drive scientific excellence within the Institut Pasteur. Thus, having formed an association with Université Paris Cité in 2022, the Institut Pasteur forged a partnership with UCSF QBI in 2023 (see inset).

Signing of the new framework agreement for collaboration between the Institut Pasteur and INRAE.

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 two Units 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. Joint units can host scientists from these organizations. The Institut Pasteur currently hosts 73 scientists and 27 engineers from the CNRS, 35 scientists and 14 engineers from Inserm, 17 scientists/lecturers and 17 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

…

BASIS FOR RESEARCH PARTNERSHIPS

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

BASIS FOR TEACHING PARTNERSHIPS

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

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THE INSTITUT PASTEUR ALSO DEVELOPS NUMEROUS INTERNATIONAL PARTNERSHIPS (SEE P.2)

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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) and Paris Psychiatry and Neurosciences University Hospital Group (GHU)

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 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 AP-HP.

The Institut Pasteur and GHU Paris have furthermore renewed an agreement to strengthen relations between the two institutions in the fields of research, training, education, and scientific events. ●

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 postdoctoral 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 implementing specific agreements that can be linked to framework agreements defining the terms of such collaborations with regard to research or education.

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ADVANCES IN *PUBLIC HEALTH*

COMMITTED TO SERVING *PUBLIC HEALTH*

The status of National Reference Center (CNR) is awarded by Santé publique France. CNRs have four missions, as laid down in the French Public Health Code: 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; and advising and training public authorities, health safety agencies and health professionals.

BOTULISM is a human and animal neurological disease caused by bacterial neurotoxins known as botulinum toxins. The disease induces flaccid paralysis that can result in respiratory paralysis and heart failure. Botulism is rare in humans, with an average of ten outbreaks reported each year, mainly caused by the consumption of contaminated food. But because of its potentially severe impact on health, botulism is closely monitored in France. In 2022, Christelle Mazuet, Head of the CNR for Anaerobic Bacteria and Botulism, published her research on routine botulism surveillance in humans and animals in France. The study, conducted in collaboration with ANSES, INRAE and SpF, was based on a "one health" approach. It involved compiling all the botulism surveillance data collected for humans and animals between 2008 and 2019. With the exception of botulinum toxin type E, which was detected throughout the period in wild birds, the study demonstrated that the types of botulism found in animal outbreaks are different from those identified in human outbreaks over the past decade in France, and concluded that none of the human botulism outbreaks investigated was linked to animal botulism.

19 laboratories
involved in 17 national reference centers (CNRs) at the Institut Pasteur.

The team in the Laboratory for Urgent Response to Biological Threats (CIBU) was actively involved in the response to the monkeypox outbreak that occurred in France in May 2022. The virus is classified as a pathogen with high infectious risk, meaning that diagnosis could only be performed by teams authorized to handle it in a high-BSL laboratory. The CIBU was chosen as the national biobank for samples tested positive as part of the MOSAIC clinical trial, in partnership with trial sponsor ANRS-Emerging Infectious Diseases.

Between May and October 2022, the CIBU received 57 samples of suspected cases, two of which had been identified by the Institut Pasteur Medical Center team in connection with its patient consultations. Of these 57 samples, 23 were confirmed to be positive for monkeypox. These diagnostic activities for the 2022 outbreak, in conjunction with the AFRIPOX research project that has been under way for several years with the Institut Pasteur de Bangui, led to new research on viral inactivation so that the virus can be handled safely in the lab, research on viral persistence in the environment, a study on circulation of the virus in domestic animals and small mammals in France with an ANSES laboratory, and the development of innovative serology techniques by the Institut Pasteur's Virus and Immunity Unit. ●

SCAN THE QR CODE TO VIEW THE LIST OF INSTITUT PASTEUR CNRs (IN FRENCH).

CLINICAL RESEARCH *REORGANIZED*

To optimize scientific activities at the interface of basic and clinical research, a vast reorganization program is underway at the Center for Translational Science (CRT). The long-term aim is to focus CRT research on two core divisions that report directly to the Medical Department.

Report in the Translational Immunology laboratory with the "Milieu Intérieur" LabEx team.

THE YEAR 2022 saw a reorganization of the Center for Translational Science (CRT), with entities offering technological expertise and services being transferred to the Technology Department. The Cytometry and Biomarkers UTechS was affiliated with the Center for Technological Resources and Research, and the Institut Pasteur Biological Resource Center was given responsibility for tasks related to the receipt, treatment, preservation and distribution of collections of biological samples of human origin. The clinical and translational research activities previously carried out under the aegis of the Medical Department are now affiliated with two platforms:

- The Clinical Research Coordination Office (PC-RC), which supports scientists in managing projects and compliance with ethical and regulatory requirements.
- ICAReB-Clin, which performs clinical research on healthy volunteers and certain cohorts in projects sponsored by the Institut Pasteur.

Eighty-nine health research proposals were submitted by the Institut Pasteur's scientists to the "guichet unique" (one-stop shop) for an initial assessment of the project type and the regulatory procedures required. Half of these were research projects involving human subjects, and 75% required a thorough analysis involving partner teams able to offer ethical, legal and other skilled expertise to identify potential future applications in the fields of diagnostics, treatment or vaccination. On process completion, the Clinical Research Coordination Office, which is responsible for project development, monitoring and regulatory compliance, took on 25 new research projects, bringing the total number of projects given expert biomedical research support in 2022 to 172.

89
health research proposals were submitted by the Institut Pasteur's scientists to the "guichet unique" (one-stop shop)

ICAReB-Clin is in charge of the organization and operational implementation of the clinical investigation aspects of research projects. In 2022, ICAReB-Clin took responsibility for the cohorts in pilot studies linked with research and education activities, and it supported various health research projects through its cohort of healthy volunteers. ICAReB-Clin is coordinating clinical investigations for the CORSER 5 study, aimed at examining the humoral immune response in the early days after SARS-CoV-2 infection and estimating pre-existing immunity. To this end it organized 417 visits, mostly to participants' homes. The team was responsible for nearly a quarter of the visits for the CORSER 4 study, which looked at the humoral and cellular immune response to COVID-19 vaccination in subpopulations depending on the vaccination schedule applied. Finally, working in collaboration with the team from the Medical Center, ICAReB-Clin was in charge of inclusion visits for the PoxVac22 study, a descriptive study exploring clinical and biological kinetics in people treated for monkeypox. ●

PATIENT-CENTERED *CARE*

The Institut Pasteur Medical Center (CMIP) is where the Institut Pasteur comes into direct contact with patients in Paris. It houses an International Vaccination Center and the Anti-Rabies Center for the Greater Paris Region, and it offers consultations for infectious and tropical diseases, travel medicine and allergies. It received ISO 9001:2015 certification in 2018.

Consultation at the Institut Pasteur Medical Center (CMIP).

44,082
visits to the Vaccination Center

61,409
vaccines administered

12,407
consultations for infectious and tropical diseases and travel medicine

1,757
consultations at the Anti-Rabies Center

647
consultations for allergies

Medical activities

With the COVID-19 epidemic on the wane, there has been a resurgence in international travel and the Medical Center has resumed its work in the area of travel medicine. In preparation for trips abroad, there has been high demand for international vaccinations and travel medicine, both among the general public and for certain categories such as humanitarian aid workers. And for those returning from foreign travel, the Medical Center treats individuals exposed to a risk of rabies abroad or presenting with travel-related illnesses such as malaria, dengue and chikungunya – offering an emergency walk-in clinic to diagnose patients with fever –, as well as rickettsial infections, infectious diarrhea, respiratory infections and skin conditions (leishmaniasis, etc.). The Medical Center was also actively involved in the response to the international mpox outbreak, treating multiple cases of this emerging disease that hit Europe in mid-2022 and offering dedicated vaccination to people at risk. At the same time, it continued to treat patients for chronic infection with HIV or hepatitis viruses, in collaboration with Necker Hospital, as well as chronic skin conditions such as hidradenitis suppurativa, and allergies.

Clinical research

The Medical Center took the opportunity of the mpox outbreak to launch the PoxVac22 study on immune response to the smallpox vaccines administered during the vaccination campaign. It also performed a retrospective analysis on its humanitarian aid workers, confirming that this population is at high risk of health problems, especially malaria. 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 Institut Pasteur campus and Necker Hospital. A comparative therapeutic trial for hidradenitis suppurativa is set to begin in late 2023, with the aim of endorsing the treatment currently recommended by the CMIP's dermatologists. The new insights offered by these projects fully justify the Medical Center's central role in the Institut Pasteur's translational research activities.

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

TRANSFERRING AND *SHARING 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. Every year, over 1,200 students, PhD students and professionals from around 80 countries attend one of the 50 courses and workshops run at the Institut Pasteur. More than 700 early career scientists are also hosted by laboratories on the Paris campus to receive training in research and complete their undergraduate, Master's and PhD research projects.

A unique setting for training in science and public health

The Institut Pasteur provides a unique hands-on environment for young scientists from undergraduate to PhD level. It also runs outstanding courses for Master's and PhD students, as well as vocational courses in science and public health 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 Institut Pasteur and online courses in life sciences and health

The Institut Pasteur is continuing to develop its online teaching as a way of reaching more people with the courses taught at its Education Center. Within the space of just eight years, the Institut Pasteur has become 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 proven remarkably successful with the public in terms of registrations and international visibility.

“The aim of the teaching provided by the Institut Pasteur is to train up outstanding scientists to work all over the world.”

INSTITUT PASTEUR 2022 PHD GRADUATION CEREMONY

THE ANNUAL PHD graduation ceremony took place on December 9, 2022. Since 2013, this ceremony has become a showcase for the Institut Pasteur’s excellence in research and education. The guest speaker at the ceremony was Professor Uğur Şahin, Chief Executive Officer of BioNTech, which developed one of the COVID-19 vaccines. —

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

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 interns 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 postdoctoral career development. The Institut Pasteur in Paris offers specific international doctoral programs (PPU) 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.

Scientific entrepreneurship training

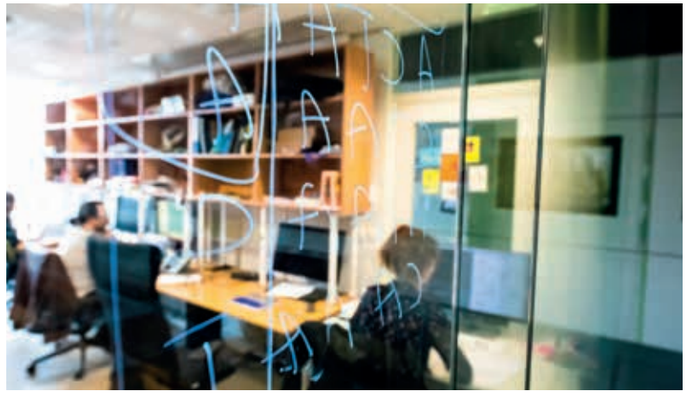
The Institut Pasteur is committed to finding applications for its research, and this is reflected in its teaching. Several such initiatives took place throughout 2022. These included the continuing “Start-up Breakfast” series – informal monthly events for Institut Pasteur scientists interested in business development, with guest speakers including successful biotech business leaders, representatives of funding bodies and heads of business incubators – and a startup workshop in June 2022 with practical sessions on specific projects led by junior Institut Pasteur scientists.

Major teaching consortia

In 2022, the Institut Pasteur joined three major teaching consortia on infectious diseases (CAIDERA), emerging infectious diseases (EUR 1H-EID) and antimicrobial resistance (PROMISE). This demonstrates national and international recognition for the Institut Pasteur’s teaching among academic and private partners and national funding bodies (e.g. DAAD and PIA). ●

THE CENTRAL ROLE OF INFORMATION *TECHNOLOGY IN RESEARCH*

Research in life sciences is imposing an increasing load on information systems. Computing power and data storage capacity requirements are constantly growing, especially with the ubiquitous application of artificial intelligence and also the use of nanoimaging, which in the Institut Pasteur’s case is performed with the Titan microscope. Ethical and environmental concerns and issues related to sustainable development and open science are also adding additional hurdles, meaning that meticulous planning is needed when implementing investments to ensure that the Institut Pasteur’s approach reflects the principles of responsible computing.



The Bioinformatics and Biostatistics Hub.

Data: FAIR principles, challenges, responses and infrastructures

Science depends on data, which are used to perform research, develop theories and answer complex questions. Data quality is crucial to avoid drawing the wrong conclusions and skewing research results. Data must be accompanied by detailed documentation explaining the collection method, variables, codes and units. Metadata are also important in finding and understanding data. Sensitive information like health data must be protected to guarantee confidentiality and personal protection. The FAIR (Findable, Accessible, Interoperable, Reusable) principles provide a framework to assess the quality of scientific data and encourage reuse. By adopting and implementing the FAIR principles, research institutes like the Institut Pasteur can improve the quality and impact of their research, while also contributing to a more open, collaborative and innovative research environment. Several units are working together to develop methods and tools to promote these principles, including the CeRIS, the Data Management Core Facility and the Information Systems Department. The TODAY project, funded by the Inception program and based on the OWEY data lake, is one example of an initiative aimed at making data findable, accessible and reusable in line with the FAIR principles, using metadata, unique identifiers and appropriate documentation.

Infrastructure security

In 2022, the Institut Pasteur’s Information Systems Department took the strategic decision to strengthen the security of its IT infrastructure by outsourcing data hosting to a sovereign French data center. This decision followed a thorough analysis of the risks and opportunities associated with data and information systems security. Measures taken also include training for staff and scientists and the introduction of processes to detect, prevent and manage security incidents.

Computing infrastructures

In 2022, the Maestro HPC cluster exceeded 15,000 CPU cores. Its GPU capacities have also been increased to 70 GPU acceleration modules, enabling it to handle new disciplines like nanoimaging and protein folding calculations. Maestro also has a dedicated ultra-high performance storage space to meet growing data management needs.

Efforts have been made to develop integration with scientific workflows so that scientists can access and analyze data quickly and easily. The Institut Pasteur’s HPC platform is focused on offering support, guidance and expertise to users and also helping them prepare resource allocation applications for national and European computing platforms. ●

AWARDS AND APPOINTMENTS 2022

APPOINTMENTS

Paul Avan
Director of the Center for Research and Innovation in Human Audiology
Elected a member of the French National Academy of Medicine

Laure Bally-Cuif
Head of the Zebrafish Neurogenetics Unit
Elected a member of the French Academy of Sciences

Frédéric Barras
Head of the Stress Adaptation and Metabolism in Enterobacteria Unit
Elected a member of the Academia Europaea

Françoise Barré-Sinoussi
Laureate of the 2008 Nobel Prize in Medicine for co-discovering HIV, the virus causing AIDS
Appointed Honoris Causa *member of the French National Academy of Medicine*

Olivier Dussurget
Leader of the Bacterial Pathogenesis and Antibacterial Agents Group within the *Yersinia* Unit
Appointed 'exceptional class' university professor

Simonetta Gribaldo
Head of the Evolutionary Biology of the Microbial Cell Unit
Elected a member of the European Academy of Microbiology

Guilhem Janbon
Head of the RNA Biology of Fungal Pathogens Unit
Elected a member of the American Academy of Microbiology

Romain Koszul
Head of the Spatial Regulation of Genomes Unit
Elected a member of EMBO

Mart Krupovic
Head of the Archaeal Virology five-year unit
Elected a member of the Academia Europaea

Jean-Christophe Olivo-Marin
Head of the Biological Image Analysis Unit
Appointed Fellow of the international learned society in optics, Optica

Eduardo Rocha
Head of the Microbial Evolutionary Genomics Unit
Elected a member of the American Academy of Microbiology

Maria-Carla Saleh
Head of the Viruses and RNA Interference Unit
Appointed Distinguished International Fellow of the American Society of Tropical Medicine and Hygiene (ASTMH)

HONORS AND PRIZES

Paola Arimondo
Head of the Epigenetic Chemical Biology Unit
Seqens Prize, French Academy of Sciences

Charles Baroud
Head of the Physical Microfluidics and Bioengineering Unit
Jaffé Prize, French Academy of Sciences

Aude Bernheim
Head of the Molecular Diversity of Microbes junior group (G5)
Collège de France young researcher prize

Thibaut Brunet
Head of the Evolutionary Cell Biology and Evolution of Morphogenesis junior group (G5)
French Society for Cell Biology (SBCF) young researcher prize

Thomas Bourgeron
Head of the Human Genetics and Cognitive Functions Unit
2022 Gershon Paper of the Year Award (ISPG, International Society of Psychiatric Genetics)

Simon Cauchemez
Head of the Mathematical Modeling of Infectious Diseases Unit
Officer of the Legion of Honor & Scientific grant from the Simone and Cino Del Duca Foundation

Germano Cecere
Head of the Mechanisms of Epigenetic Inheritance Unit
Pasteur Vallery-Radot Prize, National Library of France

Jean-Pierre Changeux
Emeritus Professor at the Department of Neuroscience
Erasmus Medal, Academia Europaea

Guilherme Dias De Melo
Scientist in the Lyssavirus Epidemiology and Neuropathology Unit
International Prize in Global Health, Franco-German University (FGU)

Francesca Di Nunzio
Head of the Advanced Molecular Virology five-year unit
Pasteur Vallery-Radot Prize, National Library of France

James Di Santo
Head of the Innate Immunity Unit
Clarivate Highly Cited Researcher 2022 (Cross-Field)

Jérémy Dufloo
Scientist in the Virus and Immunity Unit
"Prix solennel de la Chancellerie" in "science all specialties"

Violaine Esnault
Scientist in the Immunology of Fungal Infections Unit
Villa M medical research grant

Sandrine Étienne-Manneville
Head of the Cell Polarity, Migration and Cancer Unit
René Turpin Cancer Research Prize, Institut de France Foundation

Arnaud Fontanet
Head of the Epidemiology of Emerging Diseases Unit
Officer of the Legion of Honor Jean Valade Prize, Fondation de France & Senior Scientist Institut Pasteur Prize (Louis Pasteur Bicentenary Prize)

Pierre Garcia
Scientist in the Evolutionary Biology of the Microbial Cell Unit
Monod Prize, Fondation de France

Tamara Giles-Vernick
Head of the Anthropology and Ecology of Disease Emergence five-year unit (U5)
Stars of Europe Trophy

Pablo Guardado-Calvo
Head of the Structural Biology of Infectious Diseases junior group (G5)
Thérèse Lebrasseur Prize, Fondation de France

Marion Guérin
Postdoctoral fellow in the Dynamics of Immune Responses Unit
Hélène Starck Oral Prize, ARC Foundation for Cancer Research

Mélanie Hamon
Head of the Chromatin and Infection Unit
Junior Scientist Institut Pasteur Prize (Louis Pasteur Bicentenary Prize)

Ghizlene Lahlou
Scientist in the Technologies and Gene Therapy for Hearing Loss team (Hearing Institute, an Institut Pasteur center)
2022 Scientific Emergence Prize for Clinical Research, Fondation Pour l'Audition

Isabelle Louradour
Scientist in the Molecular Parasitology and Signaling Unit
H2020 Marie Skłodowska-Curie Actions (MSCA) & Springboard to Independence Fellowship, Labex IBEID

Jean-Baptiste Masson
Head of the Decision and Bayesian Computation five-year group (G5)
Île-de-France Region Innovators Award & European Innovation Council Accelerator Award

Lucienne Nouchikian
Scientist in the Mass Spectrometry for Biology technology and service unit (MSBio UTechS)
2022 L'Oréal-UNESCO "For Women in Science" French Young Talent award

Gérard Orth
Guest researcher, former Head of the Department of Virology
Thomas A. Waldmann Memorial Award 17th International Symposium on Inborn Errors of Immunity

Annick Perrot
Honorary Curator of the Pasteur Museum
Edmond Nocard Award, French Veterinary Academy

Leo Lit Man Poon
Co-Director of the HKU-Pasteur Research Pole, University of Hong-Kong
Pasteur Network Prize (Louis Pasteur Bicentenary Prize)

Olaya Rendueles Garcia
Scientist in the Microbial Evolutionary Genomics Unit
Georges, Jacques and Elias Canetti Prize

Félix Rey
Head of the Structural Virology Unit
Clarivate Highly Cited Researcher 2022 (Cross-Field)

Philippe Sansonetti
Guest researcher, former Head of the Molecular Microbial Pathogenesis Unit
Abarca Prize - Senior Scientist Institut Pasteur Prize

Maxime Schwartz
Molecular biologist, former President of the Institut Pasteur
Edmond Nocard Award, French Veterinary Academy

Olivier Schwartz
Head of the Virus and Immunity Unit
Duquesne Prize

Nader Yatim
Scientist in the Translational Immunology Unit
Villa M medical research grant

ERC FUNDING

Laure Bally-Cuif
Director of the Department of Developmental and Stem Cell Biology, Head of the Zebrafish Neurogenetics Unit and CNRS Director of Research
ERC Synergy Grant

Massimiliano Bonomi
Head of the Integrative Structural Biology of Dynamic Systems group in the Structural Bioinformatics Unit and CNRS research associate
ERC Consolidator Grant

Rayan Chikhi
Head of the Sequence Bioinformatics junior group (G5)
ERC Consolidator Grant

Aleksandra Deczkowska
Head of the Brain-Immune Communication junior group (G5)
ERC Starting Grant

Caroline Demangel
Head of the Immunobiology and Therapy Unit
ERC Synergy Grant

Romain Levayer
Head of the Cell Death and Epithelial Homeostasis Unit
ERC Consolidator Grant

Liliana Mancio Silva
Group Leader in the Biology of Host-Parasite Interactions Unit and Inserm research associate
ERC-Consolidator Grant

Sarah Hélène Merkling
CNRS research associate in the Insect-Virus Interactions Unit
ERC Starting Grant

Jakob Ruess
Inria research associate in the joint Inria/Institut Pasteur unit InBio: Experimental and Computational Methods for Modeling Cellular Processes
ERC Starting Grant

Gerald Spaeth
Head of the Molecular Parasitology and Signaling Unit
ERC Synergy Grant

FUNDAMENTALS.

PROMOTING A HEALTHY *WORKING ENVIRONMENT*

In 2022, the Institut Pasteur delivered on its commitment to providing an attractive and responsible working environment, thanks to work carried out by teams in the HR Department.

A GENDER EQUALITY PLAN was adopted in early 2022, marking a new step aimed at **supporting the Institut Pasteur's equality, diversity and inclusion policy**. It sets out a series of commitments and specific actions promoting equality in the workplace at the Institut Pasteur. The introduction of an employee ambassadors' group, special training and awareness-raising events are just some of the measures implemented.

The HR Department has also continued its **digitization** process with an online platform that features 600 answers to the most frequently asked employee questions.

Keen to **reward Institut Pasteur staff for their hard work** and address union concerns, management also introduced adjusted salary measures in 2022 in response to an economic climate characterized by high inflation.

Finally, special emphasis was placed on **protecting the mental health** of early career scientists. A confidential internal questionnaire was used to evaluate perceived stress levels and their impact on daily routines and propose specific improvements, thus applying a collective prevention approach as well as addressing individual cases.

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

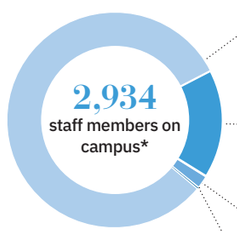
FIND OUT MORE ABOUT THE GENDER EQUALITY PLAN AT PASTEUR.FR

Diversity on campus

42.3
average age of employees

78
different nationalities on campus* (Institut Pasteur employees & OREX)

479
people hired in 2022 (excluding fixed-term to permanent contracts), 40.7% of whom scientists and 30.9% in the research engineering sector



2,388
Institut Pasteur employees (69.4% on permanent contracts)

483
OREX staff (from external research organizations)

57
interns

6
scientists with grants

57.5%
scientists and research engineers out of the total of **2,871** employees & OREX

Gender equality in the workplace,
a key priority of the Strategic Plan

59.5% female staff at the Institut Pasteur

61.4% of people hired in 2022

49.2% of researchers and 60% of research engineers are female

98% Gender Equality Index in 2022

Skills development and career support

€3,295,000
invested in professional training *(teaching costs, time spent training and compulsory contributions)*

37,550 hours
of training completed

7,152
staff registered on training courses (Institut Pasteur staff, Orex and interns)

164
scientists supported by the MAASCC** (over 800 sessions)

* figures on December 31, 2022
** Welcome, support and career development structure for scientists
Sources: HR Department – HR management control, MAASCC, Training Center – March 2023

A CAMPUS COMMITTED TO *SUSTAINABLE DEVELOPMENT*

The issue of sustainable development is promoted by the management team and numerous Institut Pasteur employees, who are involved in ramping up responsible practices within their entities.

2022 Sustainable Development Forum.

Renewed commitment to the Paris Climate Action Biodiversity Pact

The new Paris Climate Action Biodiversity scheme adopted by Paris City Council in July 2022 is based on a Pact of Commitment and a raft of specific operational measures set out in advance by the local authority. Having first signed up to the scheme in September 2020, the Institut Pasteur renewed its commitment on November 22, 2022 alongside 52 other signatories.

In line with this undertaking, the foundation is seeking to improve its energy performance, preserve biodiversity, and adapt its practices to address climate change, thus fully embracing the impetus created by this Pact.

CLICK HERE TO ACCESS THE PACB PACT.

Reducing environmental impact

As well as renewing sustainable development commitments made several years ago, the management team published a decision memo in November 2022 to step up existing measures aimed at reducing the foundation's environmental impact, particularly with regard to energy sufficiency and sustainable mobility. Prior to this, the measures were presented at a forum for all staff held during European Sustainable Development Week.
Various initiatives have also been instigated by staff, including the Make Pasteur Greener movement introduced in 2020 and the CSE sections on cycling and community vegetable plots. Every year, the Sustainable Development Challenge is well attended by staff who use it as an opportunity to pitch new projects.

Recycling in 2022

66.142 t
paper and cardboard

2.97 t
Paper archives and other paper

0.24 t
Metal packaging

12.330 t
Plastic packaging

3.07 t
Glass

21.091 t
Waste electrical and electronic equipment including light bulbs

0.156 t
Batteries

0.501 t
Ink/toner cartridges

Other recovery

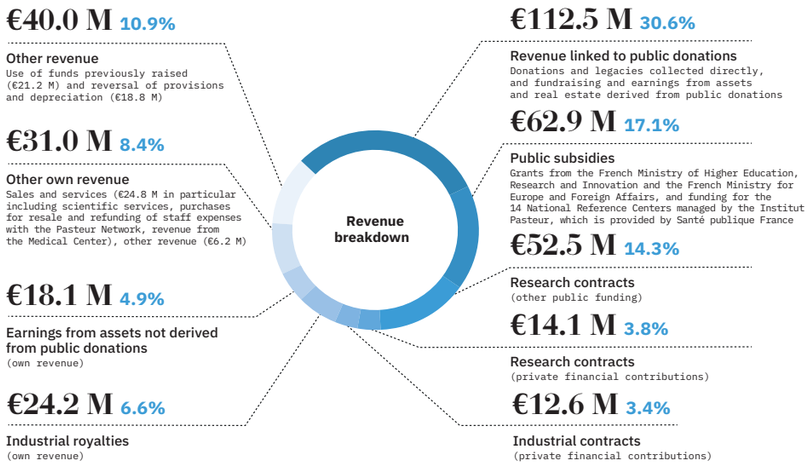
2.665 t
Organic waste

HOW OUR REVENUE *WAS USED IN 2022*

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.

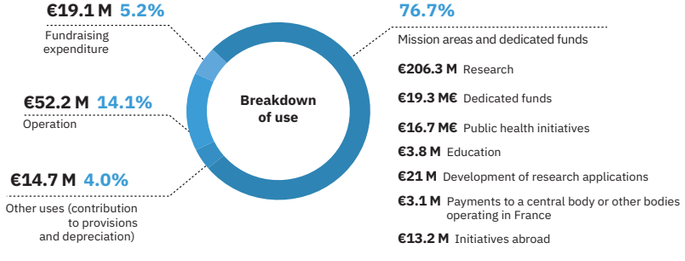
Revenue

As indicated in the Institut Pasteur 2022 *Statement of source and application of funds*, the revenues reported in the income statement amounted to €367.9 million, with the following breakdown.



Use

The revenues reported in the income statement are earmarked as follows: Institut Pasteur mission areas €264.1 M, fundraising proceeds not used during the fiscal year earmarked for mission areas €19.3, operation €52.2 M, fundraising expenses €19.1 M and contribution to provisions and depreciation €14.7 M, implying a deficit of €1.5 M.



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

€367.9 M

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 level of growth comparable with the previous year; €112.5 M was raised in 2022[1].

1. See adjacent chart and Institut Pasteur 2022 Use of resources statement in the financial report.

For each

€100

raised

€74
Mission areas *(research, public health, education)*
—
€15
Fundraising expenses
—
€11
Operating expenditure

View of the entrance to the Duclaux building.

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 2022	€M	%
Total	**997**	**100**
Property	240	24
Securities	587	59
Private equity/strategic partnerships	76	8
Cash	94	9

Productive assets account for the equivalent of 2.8 times the Institut Pasteur's annual operating costs (ratio set out in late 2022).

These assets generated €9.9 M during the 2022 fiscal year, reported in the income statement and representing a sharp decline in relation to 2021 (€-29.7 M) due to non-distribution of revenue from long-term investments.

Earnings from assets

In 2022	€M
Total	**9.9**
Property	6.8
Securities	2.4
Cash	0.7

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, Institut Pasteur de la Guadeloupe, Institut Pasteur de la Guyane and Institut Pasteur de Nouvelle-Calédonie.

In 2022	€M
Institut Pasteur operating revenue	318.3
Institut Pasteur operating expenses	354.5
Contrib. from IP Guadeloupe, Guyane and N. Calédonie	-1.5
OPERATING INCOME	**-37.7**
Institut Pasteur financial result	**-6.2**
Contrib. from IP Guadeloupe, Guyane and N. Calédonie	0.4
FINANCIAL INCOME	**-5.8**
Institut Pasteur non-recurring income	**38.9**
Contrib. from IP Guadeloupe, Guyane and N. Calédonie	3.0
NON-RECURRING INCOME	**41.9**
Profit sharing	-0.1
NET INCOME	**-1.5**

In 2022, net income showed a deficit of €1.5 M as against a surplus of €12.2 M in 2021 – a fall of €13.7 M. This is primarily explained by an increase in operating deficit of €15.6 M.

€-3.4 M of this result is due to the Institut Pasteur's Paris campus and €+1.9 M to the institutes outside mainland France.

DONATIONS, *SPONSORSHIP* AND LEGACIES

Research is advancing through your generosity

The public has continued to demonstrate its generous support this year, despite a challenging economic and political climate.

In 2022, 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 2022, the Pasteurian values of humanism, perseverance and rigor were particularly in evidence during the celebrations for the bicentenary of Louis Pasteur's birth. Year after year, these values continue to provide a solid foundation for the outstanding research performed at the Institut Pasteur thanks to your generous support. In 2022, the Institut Pasteur received financial support from more than 239,000 individual donors. Public support is vital if the Institut Pasteur's scientists are to continue making major scientific and medical breakthroughs and tackling key research priorities such as infectious diseases, cancer, neuroscience and antimicrobial resistance.

More than 30,000 of our donors have chosen to set up a direct debit, which enables them to spread their donations over the entire year.

After living through the pandemic for two years, we were pleased to be able to welcome many more of our donors and benefactors to campus for scientific conferences this year.

The 16th Pasteurdon campaign, a special edition for the bicentenary year held from October 5 to 9, 2022, was yet another reminder of the importance of public generosity for the research conducted by scientists at the Institut Pasteur on topics such as cancer, emerging infectious diseases, brain connectivity and neurodegenerative diseases, antimicrobial resistance, vaccinology and artificial intelligence.

Pasteurdon 2022 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 once again received vital support through donations from companies and foundations.

Our loyal partners all got involved in the 16th 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 with the launch of a dozen charity-linked products in the Intermarché and Bricomarché store chains. A practical brochure, "Fewer germs on our plates," was also distributed in Intermarché stores, offering a host of tips and advice on food hygiene. ASSU 2000, a Pasteurdon partner for the ninth year running with its ongoing support for research on cardiovascular diseases, continued its charity-linked product campaign, with a donation made for every new car, motorcycle, health or 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.

New sponsors also joined us in 2022, including the Optic 2000–Lissac–Audio 2000 Foundation and the Lefoulon-Delalande Foundation. We were proud to be supported once again this year by MSDAVENIR and the Axa Research Fund.

2022 also saw the launch of the first editions of the Benefactors Circle, "Les rendez-vous de Louis," to which all the Institut Pasteur's sponsors and friends were invited to find out more about the Institut Pasteur's research. This enjoyable event was much appreciated by all those who came along!

MAJOR SPONSORS

Fondation Bettencourt Schueller
Reconnue d'utilité publique depuis 1987

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

Fondation pour l'audition
À l'écoute de la vie

Groupe Pasteur Mutualité

Janssen Horizon

MTRL
Une Mutuelle pour tous

MSD Avenir
Améliorer la Vie Ensemble par l'Innovation et la Recherche

PASTEURDON PARTNERS

Fondation Le Roch les Mousquetaires

ASSU 2000

AG2R LA MONDIALE

SPONSORS

- AG2R LA MONDIALE
- AGIPI
- Allianz
- Aosis Consulting
- Assu 2000
- Biostime Institute Nutrition & Care
- Boehringer Ingelheim Fonds
- Cercle FSER
- Crédit Agricole Mécénat IDF
- Fondation Air Liquide
- Fondation Btp+
- Fondation CFM pour la Recherche
- Fondation d'entreprise Michelin
- Fondation d'entreprise Optic 2000-Lissac-Audio 2000
- Fondation d'entreprise SCOR pour la science
- Fondation Groupama
- Fondation Ipsen
- Fondation Jacqueline Beytout
- Fondation Lefoulon-Delalande
- Fondation Le Roch-Les Mousquetaires
- Fondation NRJ
- Fondation Suez
- Fondation Total Energies
- Fondation Veolia
- Fonds Axa pour la recherche
- Fonds de dotation Perfumum
- Gilead
- Groupama Nord Est
- ICADE
- Mutuelle du Médecin
- Natixis
- Nouvelle Cassius Fondation
- Odyssey Reinsurance Company
- Pfizer
- Sacem
- SANOFI Aventis Recherche et Développement
- The Joe W. and Dorothy Dorsett Brown Foundation

International fundraising

In 2022, we enjoyed continued support from our international donors and our sister foundations in the United States and Switzerland, which also rally local donors to support the Institut Pasteur's major research projects.

A new International Development Unit was also established in the Philanthropy Department in 2022, with the aim of boosting international financial support for the Institut Pasteur. One of the team's first missions was to work with the Department of Scientific Affairs on the strategic "Pasteur Pandemic Preparedness" project, which was presented for the first time to our supporters in the United States in November. In connection with this major project, we will be visiting all our international donors in Europe, the United States and Asia over the next five years.

Donations, legacies and life insurance policies

In 2022, 170 new legacies were submitted to the Board of Governors, amounting to €36.9 M. Life insurance gifts amounted to €14.9 M. Five 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 Gifts Office have been assigned to testator development and relations with a view to promoting legacies among the public. The office publishes a six-monthly "Gifts" newsletter. The media campaign to promote gifts was run in August using the existing TV spot. Information videos on gifts can also be found at www.pasteur.fr. The Institut Pasteur Gifts Office is the only one 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.

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 DIRECTORS BUREAU

Chair: Yves Saint-Geours,
Senior Minister Plenipotentiary, former Ambassador

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

Vice-Chair: Stéphanie Fougou,
General Counsel at Technicolor

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

Treasurer: Louis de Franclieu,
Deputy Director (3rd sub-directorate) in the Budget Division

Permanent guest of the Bureau:
Patrick Charnay, Professor at the École Normale Supérieure (ENS), Inserm Emeritus Director of Research

OTHER MEMBERS

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

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

Christine Clerici, President of Université Paris Cité

Delphine D'Amarzit, Chairman and CEO of Euronext Paris

Jean-Claude Manuguerra, Head of the Environment and Infectious Risks Research and Expertise Unit, Institut Pasteur

Inès-Claire Mercereau, Chief Advisor to the French Government's Accounting Office

Antoine Petit, Chairman and CEO 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

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

Bertrand Schwartz, Deputy Scientific Director Biology and Health Department, Directorate General for Research and Innovation, French Ministry of Higher Education and Research

Fabiola Terzi, Institut Necker-Enfants Malades Director, Inserm Director of Research

Catherine Touvrey, CEO of Harmonie Mutuelle

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

Virginie Ponticelli, Head of the Administrative Coordination of Education: Courses, Projects and Innovation Section, Institut Pasteur

Agnès Raymond-Denise, Head of the Scientific Information Resources Center, Institut Pasteur

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

Henri Pitron,
Vice-President Communications

Fernando Arenzana-Seisdedos,
acting Vice-President International Affairs

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

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

Vice-Chair: Michaela Müller-Trutwin,
Head of the HIV, Inflammation and Persistence Unit
Caroline Demangel, Head of the Immunobiology and Therapy 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*

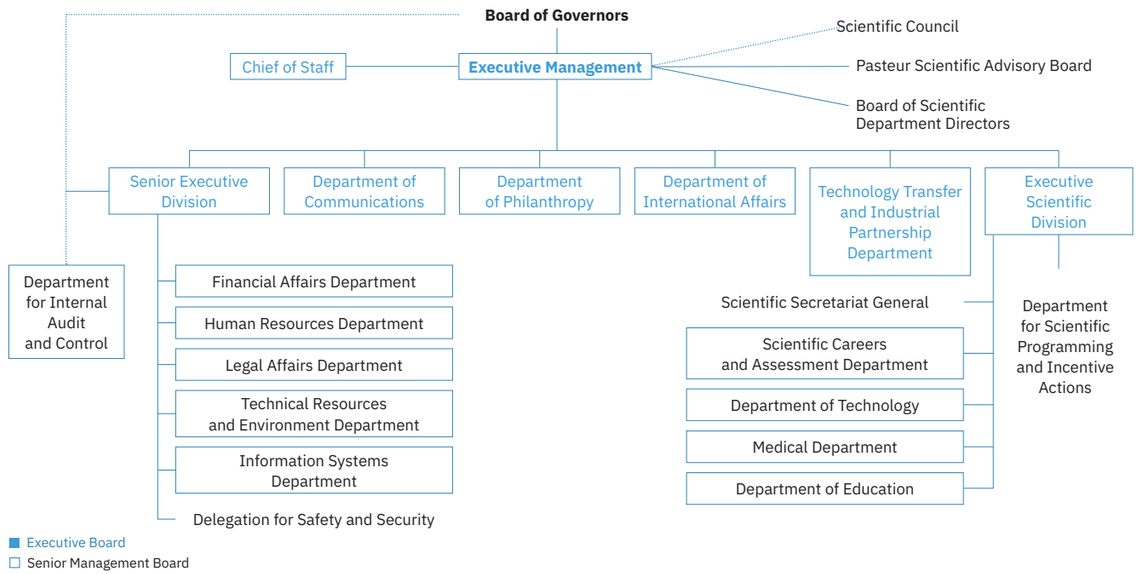
Yvonne Jones, *Prof. Division of Structural Biology, Henry Wellcome Building for Genomic Medicine, University of Oxford, UK*

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



This annual report was designed and produced by Bergamote, an agency certified by AFNOR (confirmed grade**) and Ecovadis (silver badge) and a Global Compact member like the Institut Pasteur.

The report was printed by an Imprim'vert and ISO 14001 certified supplier on paper made from ECF pulp and a minimum of 40% recycled fibers and produced from sustainably managed forests (FSC® certified). This paper is also fully biodegradable and recyclable. Vegetable inks were used. Fewer copies were printed to conserve paper.

This report was produced in line with the Institut Pasteur's procurement policy, which is guided by a buyers' code of ethical conduct and part of the Institut Pasteur's Charter for the Prevention and Management of Conflicts of Interest. This procurement policy implements environmentally friendly practices and promotes sustainable initiatives; it defines the missions of the Procurement Department and sets out the Institut Pasteur's values and commitments in its dealings with suppliers.

Head to pages 9 and 53 of this annual report for our sustainable development commitments, and to our dedicated web page for our broader commitments:

SCAN THE QR CODE FOR OUR COMMITMENTS.

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