

ANNUAL REPORT 2023

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Resistance, resilience. In an ever-changing world, adaptability is crucial.

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Resistance, resilience.

In an ever-changing world, adaptability is crucial.

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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.

million budget

in 2023

nationalities

(as at 12/31/2023)

99 research units,

10 laboratories,

(as at 12/31/2023)

research structures including

12 five-year units (U5s),

14 five-year groups (G5s),

7 Hearing Institute teams

facilities







research support

Thanks to our almost

individual donors, legators,

sponsors and partners. With your help we have advanced research. For further information see pages 56 and 57.

INTERNATIONAL: BUILDING AND STRENGTHENING SCIENTIFIC PARTNERSHIPS AND COLLABORATIONS

The Institut Pasteur has been operating at the international level since it was founded in 1887.

Its strategic partnerships and research cooperations worldwide are guided by a policy of openness with the aim of applying scientific excellence to serve the health of populations. As co-founder of the Pasteur Network, the Institut Pasteur also plays a key role in developing joint projects with member institutes that contribute to the network's global reach.

DURABLE, a European project tackling emerging diseases

The European project DURABLE coordinated by the Institut Pasteur was launched in February 2023. DURABLE (Delivering a Unified Research Alliance of Biomedical and Public Health Laboratories Against Epidemics) is a network primarily aimed at establishing a onestop shop to improve the preparedness of health laboratories for emerging diseases. This large-scale four-year project will contribute to the establishment of more effective, resilient and accessible health systems.



New Pasteur International Unit – "Fungal Extracellular Vesicles"

In June 2023, the Institut Pasteur established the "Fungal Extracellular Vesicles" Pasteur International Unit, in collaboration with the Oswaldo Cruz Foundation

(Fiocruz) in Brazil and the University of Birmingham in the United Kingdom. Pasteur international joint research units are established in conjunction with two or more research teams working together within the Pasteur Network.



Launch of the Pasteur Foundation – UK

In November 2023, the Institut Pasteur announced the launch of the Pasteur Foundation - UK, a private non-profit foundation aimed at raising awareness and funds for scientific cooperation between the Institut Pasteur in Paris and research institutions in the UK.



Strengthening international collaboration

The aim of the Operations Unit in the Department of International Affairs is to strengthen the Institut Pasteur's international collaboration by capitalizing on the Pasteur Network. Two projects supported by the French Ministry for Europe and Foreign Affairs have been launched to establish sustainable skills networks in Africa, drawing on the expertise and national presence of Pasteur Network member institutes.

• SARA is a surveillance network to monitor antibiotic resistance in Benin, Cameroon, Central African Republic, Madagascar, Morocco and Senegal, targeting the main pathogens that impact public health. The Institut Pasteur de Madagascar and the Institut Pasteur are providing scientific coordination for the project, which is particularly focused on capacity-building, strengthening genomic surveillance and standardizing protocols within multi-country partner organizations.

• Alliance SHS Afrique is a consortium of experts in social anthropology from Côte d'Ivoire. Madagascar. Niger. Senegal and Tunisia who can be mobilized rapidly in the event of an epidemic. Drawing on a qualitative study about the impact of COVID-19 vaccination on routine vaccination programs, the experts are learning how to better incorporate the sociocultural dimensions of disease outbreaks and develop appropriate tools.

TODAY'S GLOBAL HEALTH CHALLENGES DEMAND OPEN COLLABORATION ACROSS A ROBUST AND RESILIENT NETWORK

The Institut Pasteur is part of the Pasteur Network.

The Pasteur Network is an alliance of 30+ institutes with a crucial role in tackling global health challenges through science, innovation and public health. Its distinctive strength lies in its diversity and extensive geographic reach, spanning 25 countries across 5 continents, fostering a dynamic community of knowledge and expertise. In 2023, the Network renewed its commitment to acting not just as a global entity, but as a cohesive and responsive unit that elevates regional perspectives with an emphasis on collective action.

IN 2023, the Pasteur Network continued to prioritize its collaborative governance framework and strengthened its board with two new co-opted members: Isabella Ovier from KEMRI-Wellcome Trust. and Linda Venczel from PATH.

With over 200 participants, the **Pasteur** Network Annual Meeting was hosted by the Institut Pasteur de Tunis with the support of Wellcome Trust and included rich discussion around the Pasteur Network's strategic pillars:

. The future of pandemic **prepared**ness in a context rapidly evolving with climate change and climate sensitive diseases.

2. The Pasteur Network's role in the future of innovation and R&D ecosystems in LMICs.

J. Identification of needs for continued improvements to the Network's knowledge sharing and communities of practice. as well as celebration of the contribu-

tions of young scientists such as Dr. Ngu Abanda from the Pasteur Center in Cameroon who received the Pasteur Network Talent Award 2023.

+•The importance of improving **equity** across the Network with regards to access to information, representation, and equitable financing to name a few.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THE PASTEUR NETWORK'S STRATEGIC PILLARS.

We expanded our commitment to building global knowledge communities, with 5 new courses selected for funding ranging from advances in genome editing to innovation and technology transfer to the One Health approach. In addition, 3 Pasteur Network PhD grants were allocated to Joël Doté (Institut Pasteur de Bangui), Swaélie Sauthier (Institut Pasteur de la Guyane) and Loeïza Rault (Institut Pasteur de Nouvelle-Calédonie).





The Pasteur Network has also been strengthening partnerships, including joining the Grand Challenges initiative, exploring opportunities to address the repercussions of climate change on human health with the Rockefeller Foundation and the Institute of Philanthropy – The Hong Kong Jockey Club. and the appointment of Rebecca F. Grais. the Executive Director of the Pasteur Network to WHO's Strategic Advisory Group of Experts on Immunization (SAGE).







SNAPSHOT A look back at some of the highlights of 2023, with a series of events to matter 40th appivorsers of the differentiation. OF 2023

of 2023, with a series of events to mark the 40th anniversary of the discovery of HIV and major scientific advances in cancer research and neurodegenerative and infectious diseases.

JANUARY

Emergence of extensively drugresistant Shigella *sonnei* strain in France

Shigellosis is a highly contagious diarrheal disease caused by Shigella bacteria. Scientists from the Institut Pasteur who have been monitoring Shigella in France for several years have detected the emergence of extensively drug-resistant (XDR) strains of Shigella sonnei. Bacterial genome sequencing and case characteristics suggest that these strains, which originated in South Asia, are mainly spreading among men who have sex with men.

Nature Communications, January 26, 2023.

FEBRUARY

New breakthrough in the development of an effective vaccine for allergic asthma

Scientists from Inserm. the CNRS and Université **Toulouse III-Paul Sabatier** in the Infinity Laboratory, the Institut Pasteur and the French company NEOVACS are developing and testing a new vaccine to tackle allergic asthma. In their

latest study, the teams showed that the vaccine was effective in producing antibodies capable of neutralizing proteins in the human immune system that play a key role in triggering allergic asthma. The findings, published in the journal Allergy, pave the way for the organization of a clinical trial. Allergy, February 17, 2023.



AN THE OR CODE TO O OUT MORE ABOUT PUBL TCATTON

MARCH Using evolutionary biology to identify

the origin of disease outbreaks

Identifying the pathogens responsible for a disease outbreak can be a complicated task. Each pathogen can mutate from one generation to the next, and it can soon become difficult to identify the common ancestry of a group of strains. Scientists from the Institut Pasteur have developed an approach inspired by evolutionary

biology for more precise identification of the starting point of potential bacterial disease outbreaks. The Lancet Microbe, March 29, 2023.

APRIL

Identification of tunnels connecting neurons in the developing brain

In a recent study, a team from the Institut Pasteur and the CNRS, in collaboration with Harvard University, revealed novel insights into how cells in the outer layers of the brain interact immediately after birth during formation of the cerebellum, the brain region towards the back of the skull. The scientists demonstrated a novel type of connection between neural precursor cells via nanotubes, even before the formation of synapses, the conventional junctions between neurons. Science Advances, April 5, 2023.

MAY

Parkinson's: connections in the brain identified as therapeutic targets

For the first time, scientists at the Institut Pasteur have identified

connections between neurons and microglia, a type of immune cell in the brain. This discovery should help elucidate the role of inflammation in neurodegenerative diseases, potentially revealing new therapeutic targets.

Cell Death & Disease, May 18, 2023.





JUNE

Genetic variants implicated in autism detected in the general population

Scientists from the Institut Pasteur, the CNRS, the Institut universitaire de France, Université Paris Cité and the Paris Public Hospital Network (AP-HP) compared

genetic data from 13,000 individuals with autism and nearly 200,000 individuals from the general population. While 4% of those with autism were found to carry strong genetic variations implicated in autism, the same variations were also observed in nearly 1% of individuals from the general population, who were also found to have poorer cognitive performance and a lower socioeconomic status. Nature Medicine, June 26, 2023

AUGUST

How the respiratory tract microbiome influences the severity of bacterial pneumonia

Pneumonia is an infection of the lung alveoli caused by bacteria, viruses or fungi. It is one of the leading causes of morbidity and mortality worldwide, representing a global public health problem The microbial ecosystem (or microbiome) of the human respiratory tract colonizes different niches. Scientists from the Institut Pasteur and the CNRS have demonstrated that microbiome composition, pathogen load and clinical interventions influence the severity of bacterial pneumonia caused by Legionella pneumophila. Cell Reports Medicine, August 25, 2023.

OCTOBER

Discovery of cells around tumors that regulate antitumor immunity

A team from the Institut Pasteur has discovered a new population of cells that develops around a tumor mass. The discovery

opens up a new avenue for treating solid tumors, offering hope for improved treatment of cancers for which immunotherapies are often ineffective, such as pancreatic, breast and prostate cancer. Nature Immunology, October 5, 2023.





The impact of neonatal listeriosis on children's health

A team of scientists and physicians from the Institut Pasteur, Université Paris Cité, the Paris Public Hospital Network (AP-HP) and Inserm monitored the development up to age 5 of children who had been infected with *Listeria* monocytogenes bacteria, and compared their development with that of non-infected gestational age-matched children. The study demonstrated that the long-term outcomes of neonatal listeriosis can mainly be attributed to prematurity. The results will enable parents to be informed in more detail about how the health of their children may develop and should help anticipate the potential onset of sequelae.



The Lancet Child and Adolescent Health, October 20, 2023



NOVEMBER

Visit by Anthony Fauci for the conference "40 years of HIV science"

The culmination of the year's events to mark the 40th anniversary of the discovery of HIV was the conference "40 years of HIV science," with guest of honor Anthony Fauci. The US immunologist took the opportunity to look back at the history of HIV/ AIDS from his perspective as a scientist and physician, as well as discussing his role during the COVID-19 Director of NIAID also took the time to chat to several of the Institut Pasteur's young scientists, emphasizing the importance of improving communication with the general public and the need to transmit knowledge to future generations of scientists.

> AN THE QR CODE TO E ANTHONY FAUCI'S ITNG ADDRESS

DECEMBER

An oral pathogen associated with colorectal cancer epigenetically reprograms human colonocytes

Recent research has revealed the potential role of Parvimonas micra, a bacterium in the mouth, in colorectal cancer. Phylotype A of the bacterium was strongly associated with colorectal cancer, with higher abundance in feces and tumoral tissue compared with normal tissue. The scientists demonstrated that P. micra phylotype A epigenetically modifies colorectal cells, influencing genes associated with tumor suppression and cell transition. The results suggest a link between this oral bacterium and the development of colorectal cancer, paving the way for future research.

Gut Microbes. December 15, 2023.



"Our solid foundations and independence enable us to take risks [...]. That is why we will keep investing in major projects that prepare us for

Yves Saint-Geours, Chairman of the Board

> In 2023, the Institut Pasteur finalized the new composition of its management team. What is the outlook as this new chapter begins?

Yves Saint-Geours: In 2023, the Strategic Plan that we adopted in 2019 came to a conclusion. The plan resulted in significant progress, despite the impact of the COVID crisis. Our scientific expertise remains very strong, with nearly 1,300 publications each vear and a total of 550 national and 92 European grants in recent years. These achievements would not have been possible without the work of Stewart Cole. and I commend his efforts. We are now embarking on a new chapter, with the appointment of a new President, Yasmine Belkaid, who took office on January 1, 2024. We are approaching this new phase with confidence and enthusiasm.

Yasmine Belkaid: I would like to thank Yves Saint-Geours and all the members of the Board of Governors for their decision to appoint me as President of the Institut Pasteur. After spending many years in the United States. I am coming back to my roots - it was here that I earned my PhD 28 years ago. I want to pay tribute to the work accomplished by my predecessor and the previous management team. The scientific output of the past few years has been impressive, especially efforts in the field of clinical research. I am thinking in particular of the development of vaccine candidates for HPV and Lassa fever, the support given to hospital departments treating patients with severe COVID to help them choose the most effective monoclonal antibodies on the market, and the development of novel monoclonal antibodies, for example with the startup SpikImm. The future Vector-Borne Diseases Center is a key project for the future of the Institut Pasteur. Drawing on all these strengths and achieve-



"At the Institut Pasteur, we are lucky to be able to attract extraordinary young talent. We need to provide the best conditions so that they can fully express their potential and their voices can be heard."

Yasmine Belkaid, President.

ments, I am more than ready to tackle the challenges that lie ahead.

What are those challenges?

YB: I believe that we need to reflect on who we are so that we can propose a new plan that brings together the Institut Pasteur's four missions: research, public health, education and innovation. This participatory process to develop the Pasteur 2030 Strategic Plan is already under way. It will enable us to identify our priority scientific areas and to respond to the major challenges of our time, which are both scientific and societal: tackling climate change and its consequences for human health, deepening our understanding of the living world by studying neglected subjects related to women's health and genetic diversity, and also exploring the technological revolution

in health innovation, with the development of messenger RNA applications and immunotherapies.

YSG: The Institut Pasteur's strong position, including in financial terms, has been consolidated in recent years. Our solid foundations and independence enable us to take risks, to embark on bold steps, despite the fact that research is becoming increasingly costly and competitive. That is why we will keep investing in major projects that prepare us for the future – the Vector-Borne Diseases Center and the Research Center in Vaccinology and Immunotherapy particularly come to mind. The Institut Pasteur needs to maintain an outward-looking approach as it pursues these initiatives, by working in collaboration with its partner institutions (especially Inserm, the AP-HP

RENEWED AMBITION TO TACKLE MAJOR SCIENTIFIC AND SOCIETAL CHALLENGES

The 2019-2023 Strategic Plan, which recently came to a conclusion, boosted the Institut Pasteur's scientific excellence and attractiveness through a dynamic policy of investments and partnerships. In 2023, Yasmine Belkaid was appointed as the new Institut Pasteur President, marking the start of a six-year term at the helm of the institution.

- with which we signed a framework agreement in late 2023 -, the CNRS and Université Paris Cité). And it goes without saving that our international partners and the Pasteur Network are also crucial. Finally, I share Yasmine Belkaid's firm belief that major scientific challenges are also societal challenges. The Institut Pasteur must play its part in tackling these challenges and leading by example.

This duty to lead by example, what exactly does it involve?

YB: It is crucial that we reaffirm the Institut Pasteur's values and that we continue to strive to defend our principles. The Institut Pasteur must uphold its commitment to protect public health as part of a more participatory, multilateral approach. We need to do so by working on an equal footing with our partners in other world regions, starting with the members of the Pasteur Network. On the issue of gender equality, we now have a Department for Diversity, Equity and Inclusion, which reports directly to the senior management team. The Institut Pasteur is the first research institution in France to establish a department of this kind. The Institut Pasteur has also just published its first carbon footprint assessment. This is a key step in helping us to develop a low-carbon strategy for the coming years as we seek to reduce our carbon emissions and foster a more responsible, sustainable approach to research. The department working in this area has been renamed the Department of Corporate Social Responsibility and Technical Resources, as these environmental issues are part of a broader societal movement. Finally, we have created a Department for Transformation to coordinate the structural developments that will be part of the Pasteur 2030 Strategic Plan.

Any final thoughts?

YSG: We need to promote the potential of young people and help build the future. As well as constantly seeking scientific excellence and striving to serve public health, this means that we need to uphold our principles: scientific integrity, exemplary institutional conduct, clear action, and a commitment to resolving the problems facing society. And we must defend science and freedom.

YB: I want us to place our trust in the next generation! At the Institut Pasteur we are lucky to be able to attract extraordinary voung talent. We need to provide the best conditions so that they can fully express their potential and their voices can be heard. For we have a collective responsibility to build their future.

CONVERSATIONS



COMBINING EQUITY AND SCIENTIFIC EXCELLENCE

The Institut Pasteur is doubling down on its efforts

to offer all its staff a fully inclusive working environment as well as optimal conditions for conducting their research. We speak to Christophe d'Enfert, Senior Executive Scientific Vice-President and Mariana Mesel-Lemoine, Director of Diversity, Equity and Inclusion.

"20 to 25% of Institut Pasteur" laboratory heads are ERC grant winners, which allows them to develop ambitious research projects."

Christophe d'Enfert, Senior Executive Scientific Vice-President.

> Given the highly competitive environment in which academic research operates, what recruitment policies has the **Institut Pasteur put in place?**

> Christophe d'Enfert: The Institut Pasteur is supported by a strong, long-term recruitment strategy. Young scientists can put together their own research teams thanks to the "5-year group" (G5) program introduced around twenty years ago. This scheme allows the Institut Pasteur to recruit young talent. Over the years, other programs have been added, including G5+ programs for recruiting mid-career scientists and U5 programs allowing people who already work at the Institut Pasteur to open a research unit. These schemes enable us to strike a balance between bringing in new talent and research topics and the need to ensure scientists' career progression.

Mariana Mesel-Lemoine: These schemes also promote diversity in research teams, which is an important factor. We can see that the more diverse a team is, the higher the intrinsic quality of its research tends to be! The concept of diversity is underpinned by multiple criteria that need to be taken into account, and further steps are required to promote a fairer working environment.

In terms of support for scientific careers, what other schemes already contribute to the Institut Pasteur's appeal?

MML: The Career Development Service for Scientists (now known as CARE) has been in place for 10 years. It offers quite a unique service within the global academic landscape, in which careers advisors support scientists with whatever career plans they might have at any stage in their careers. A whole host of careers events are held, offering young scientists the opportunity to talk to professionals from various sectors. Assistance is also provided with preparing oral presentations for academic recruitment processes (COMESP, Inserm, CNRS). Several partnerships have been set up with other academic stakeholders, including the Imagine Institute, as well as with private-sector players such as L'Oréal. In 2023, CARE conducted 800 interviews and closely monitored 110 scientists.

CdE: Scientists can also access support with applications for funding offers. A high-quality Grant Office widely recognized by other foreign institutions is available to them. The Grant Office plays a key role in helping scientists to write funding applications and prepare oral presentations. As a result, 20 to 25% of Institut Pasteur laboratory heads are ERC grant winners, which allows them to develop ambitious research projects.

Equity and Inclusion.

Mariana Mesel-Lemoine, you are the Director of Diversity, Equity and Inclusion. Why do we need a DEI department? MML: DEI reflects a desire to go the extra mile by offering a new way of engaging in collective action based on outstanding human resource management. Change is needed in the scientific ecosystem. Science is not immune to its historical, social and political context which mirrors the prevailing prejudices and power structures in our society. Although progress has been made, unconscious bias and cultural, social and economic barriers continue to hamper representation and equal and active participation of the diverse range of individuals who make up the community of women and men in research. If we overlook female talent, we overlook half the population. In 2019, for example, only 27% of research directors and 19% of university professors in science were women

"By embracing diversity, the Institut Pasteur will improve its ability to innovate, enabling it to [...] tackle the major public health challenges ahead."

Mariana Mesel-Lemoine, Director of Diversity,

CdE: While gender parity has largely been achieved on recruitment, it is true that numbers of women applying for schemes such as the G5 program are low. We must also empower women to apply for senior positions, such as director of research, for which there is currently a glass ceiling. To achieve this, we must build on steps initiated in recent years to ensure equality on pay and tackle sexism. This requires a joint effort involving both the DEI Department and the whole of the Institut Pasteur.

In concrete terms, how are efforts to further promote diversity, equity and inclusion incorporated in the Institut Pasteur's activities?

CdE: Steps to address these issues more effectively require a different outlook on research conducted both now and in future. Issues relating to women's health, neglected diseases and the study of under-investigated populations will thus be given a more prominent place in the Pasteur 2030 strategic plan currently being drawn up.

MML: A diverse and inclusive community is one that encompasses the broadest range of talent, backgrounds, perspectives and experience. It provides us with the means to maximize innovation, scientific creativity and performance in research. This is a challenge that relates both to value and also our appeal and efforts to improve our scientific output. By embracing diversity, the Institut Pasteur will improve its ability to innovate, enabling it to push back the boundaries of knowledge and tackle the major public health challenges ahead. The new DEI Department underpins this engagement with a future in which each individual, regardless of their origin, gender, culture or any other characteristic, will contribute fully to the Institut Pasteur's missions.

RESISTANCE, RESILIENCE. IN AN EVER-CHANGING WORLD, ADAPTABILITY IS CRUCIAL.

Adaptation is a universal phenomenon. It occurs whenever anything exceeds its natural limit - examples include microbial resistance, scientific innovation and the evolution of the human immune system. This special feature highlights the incredible complexity of adaptation processes.

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TO READ THE ONLINE



INTRODUCTION

With Erik Orsenna, French novelist, member of the Académie Française and Ambassador of the Institut Pasteur



Adaptation, the secret to survival

As vertebrates, we are vastly outnumbered by insects, of which there are 8 million species compared to our 8,000 ... Why are they so successful?

Every time I have a question about the living world, I ask Professor Gilles Bœuf*.

In my view, there are six reasons for insects' success, which can be summed up by the following equation: Small + eat anything + live anywhere + reproduce intensively + like to live in communities + diversity = skilled adapters.

That's the secret to survival: adaptation!

Insects aren't the only creatures that use this kind of agility to survive. All living beings and populations are constantly adapting. This of course also applies to those peskiest of lifeforms: pathogens.

Words are also constantly adopting disguises, pairing up and evolving. In fact the reason that languages adapt from generation to generation is that they too are living things!

DEFINITION

WHAT IS **ADAPTATION?**

With Simonetta Gribaldo, Head of the Evolutionary Biology of the Microbial Cell Unit



Petri dishes with cultures of different fungi

For living beings,

adaptation is also a necessary biological process, a beneficial adjustment, a way of fully making the most of one's environment, of getting the best out of it. Adaptation reflects an ability to reinvent oneself. It is

adaptation, noun: the process of changing to suit different conditions (Cambridge Dictionary). Adaptation is a reaction. a necessary development. We adapt to adjust to a situation or to our environment

Scientists.

are no exception to this rule – they also regularly demonstrate adaptability. The scientific approach is one of constant adaptation: we adapt our knowledge, our theories, our processes, our view of the world. Adaptation forces us to face up to the fleeting nature of things and prompts us to respond with agility, humility and invention. For while it is necessary and inevitable, adaptation is also a driving force, underpinned by the interdependence that characterizes our existence.



an iterative process that permanently challenges the status quo in an ever-changing world. It is a reaction by individuals to everything that surrounds and shapes them – and is shaped by them in turn.

A TALE OF RESISTANCE

With Paola B. Arimondo, Head of the Epigenetic Chemical Biology Unit, and Philippe Glaser, Head of the Ecology and Evolution of Antibiotic Resistance Unit

Microbes and antimicrobials: a never-ending battle

Antimicrobial resistance is growing at a dramatic rate and raising concern in every corner of the planet. In 2019 it was included in WHO's list of the ten greatest threats to global public health. Antibiotic-resistant bacteria alone were responsible for 1.3 million deaths in 2019. That same year, the Institut Pasteur made antimicrobial resistance one of the three priorities of its Strategic Plan. Although antibiotic resistance grabs all the headlines, the problem is much broader: every category of drugs used to prevent and treat infections in humans, animals and even plants – including antivirals, antifungals and antiparasitics – is facing growing resistance.

While the situation is alarming, it is not surprising: it is only natural that microorganisms will evolve over time to thwart strategies aimed at eradicating them. But antimicrobial resistance is rendering treatments ineffective and jeopardizing our ability to contain infections over which we had temporarily gained the upper hand. Resistance has wide-ranging consequences: it drives epidemic spread, opens the way to a resurgence in "forgotten" infectious diseases, complicates treatment for patients and leads to soaring costs for health systems.

In Sub-Saharan Africa, 50% of HIV-positive infants are infected with a virus that is resistant to common antivirals. After South-East Asia and the Western Pacific. the Institut Pasteur has revealed that the malaria parasite is resisting state-of-the-art antimalarial drug artemisinin in Eritrea. Elsewhere, mosquitoes are evading insecticides, and fungi like *Candida auris*, a common problem in hospitals, are no longer responding to common antifungals. Whenever a new area of resistance develops, the scientific community tries to understand, prevent and innovate in a bid to come up with new strategies in this never-ending battle.

Why and how do bacteria become resistant?

Antibiotics represent one of the most important breakthroughs in modern medicine, starting with the discovery of penicillin by Sir Alexander Fleming in 1928. Antibiotics may be broad or narrow spectrum, and they are used to kill bacteria or stop them proliferating. But bacteria are like any living organism – when faced with

BACTERIA

PUBLIC ENEMIES

The seven bacteria responsible for the most cases of antibiotic resistance in hospitals:

Enterococcus faecium, gut bacteria known to have developed resistance to vancomvcin.

Staphylococcus aureus, normally present in the pulmonary tract and on the skin, increasingly resistant to methicillin and more rarely to vancomycin.

Klebsiella pneumoniae, naturally present in the soil and in the skin, mouth and gut microbiomes, has developed resistance to carbapenems.

Acinetobacter baumannii, responsible for a great number of hospital-acquired infections. resistant to multiple antibiotics including all **B**-lactam antibiotics.

Pseudomonas aeruginosa, lives in soil and in damp and extreme environments. Very hard to treat as resistant to multiple antiseptics and antibiotics.

Enterobacter spp., causes many urinary and lung infections but still sensitive to colistin and tigecycline.

Escherichia coli, gut bacteria that are often harmless and even beneficial, but some strains are pathogenic and multidrug resistant.

a threat to their survival, they evolve. Just as natural selection enabled animals, including humans and their immune system, to adapt to their pathogenic environment, bacteria have developed resistance to our attempts to eradicate or at least contain them. This is what we now refer to as antimicrobial resistance. Bacteria can acquire resistance in two ways. The first is mutation. In this case, bacteria develop mutations that mean they are no longer susceptible to a given antibiotic, and natural selection enables these resistant

bacteria to reproduce more effectively and become dominant. This is the only mechanism used by the tuberculosis agent *Mycobacterium tuberculosis* and the main mechanism employed by *Pseudomonas aeruginosa*, bacteria that infect the lungs of people with cystic fibrosis. Escherichia coli's resistance to fluoroguinolones is also essentially caused by mutations. Bacteria can also develop resistance by acquiring resistance genes. Bacteria exchange plasmids, a type of genetic material that confers resistance. Plasmids can be transferred between bacteria in different genera, and between pathogenic and non-pathogenic bacteria. This is the main mechanism by which Escherichia coli and Staphylococcus aureus became resistant to methicillin, for example.

Reservoirs of antibiotic resistance, frequently created by "friendly" commensal bacteria in our microbiota, are fueled by widespread use of antibiotics, especially indiscriminate broad-spectrum antibiotics. The more we eliminate non-resistant bacteria, the more we make room for those resistant bacteria that manage to survive. We are at risk of losing hard-won progress through dosage errors, wrongly using antibiotics to treat viral infections, stopping antibiotic treatment early and using out-of-date or fraudulent products. Antibiotics are a double-edged sword that need to be handled with caution and used in a targeted way.

Resistant bacteria are responsible for infections that are difficult or impossible to treat. Some are resistant to several antibiotics and are known as multidrug-resistant (MDR) bacteria. They can even be resistant to all existing antibiotics ("pan-resistant") and lead to a therapeutic impasse. The most alarming MDR bacteria include Enterobacteriaceae family members Escherichia coli and Klebsiella pneumoniae (bacteria in the digestive tract responsible for a large number of infections); Mycobacterium tuberculosis; and Staphyas mentioned above.

Fighting back

HOW ANTIBIOTIC RESISTANCE HAPPENS



resistant

0



Normal bacterium
 Resistant bacterium
 Dead bacterium

lococcus aureus and Pseudomonas aeruginosa, both frequently responsible for hospital-acquired infections. Some resistant bacteria can cause large-scale epidemics, like in Yemen, which is dealing with the most severe cholera outbreak in modern history. The Institut Pasteur has identified the plasmid conferring multiple antibiotic resistance on Vibrio cholerae for this outbreak. Antimicrobial resistance also concerns resistance to antiparasitics, antivirals and antifungals,

Antimicrobial resistance is a worldwide phenomenon that is affecting all living species. In 2015, WHO launched its Global Antimicrobial Resistance and Use Surveillance System (GLASS), and several databases have been compiled to record every occurrence of antimicrobial resistance worldwide. In 2002, the European Union banned all growth-promoting antibiotics used in animal feed, a measure that reflects the "One Health" approach that has developed since the early 21st century, based on the idea that the health of humans, animals and the environment is interlinked. In France, a national antibiotic resistance strategy was adopted by the Ministry for Solidarity and Health in 2022. But although there is widespread awareness of the problem, there are huge disparities and discrepancies from one country to the next: the phenomenon of antimicrobial resistance is by no means the same everywhere. A multidisciplinary team from the Institut Pasteur has developed a statistical model to analyze the data collected since 2004 in 51 countries. Their conclusion was that there are multiple determinants of antimicrobial resistance, ranging from socio-economic factors (GDP per capita) and climatic aspects (exposure to extreme meteorological events, average temperature in the country) to the quality of the health system and the volume of antibiotics consumed. Anti-





Drug-resistant bacteria are now allowed to grow and take over



Some bacteria give their drug resistance to other bacteria



microbial resistance prevention strategies need to be adapted to the local context and the infectious agents targeted.

But despite the need for a targeted approach, there are several key objectives that systematically apply. The first is a need to better understand the emergence and spread of resistance by drawing on epidemiology, genomics, statistics, evolutionary biology, structural biology, chemical biology and modeling. This research can help calibrate and rationalize the use of existing antimicrobials. The second is to identify new drugs and therapeutic strategies in response to resistance, by synthesizing specialized chemical molecules, exploring new targets (such as elements involved in host-microbe interactions and the life cycles of infectious agents), carrying out phenotypic and molecular screening, and phage therapy (discovered at the Institut Pasteur in 1917). Prevention (vaccines, health measures, training and education), surveillance and diagnostic development are also key to tackling antimicrobial resistance. Every avenue needs to be explored. The use of artificial intelligence to process huge volumes of data and identify novel molecules and biomarkers is particularly promising. The final objective is to **improve prevention** by adopting guidelines on the use of antimicrobials worldwide, for all aspects of human and animal health. We also need to introduce more effective wastewater treatment measures and restrict human-animal interactions. The goal is clear: we have to do all we can to delay the arrival of a post-antibiotic era in which everyday infections once again become life-threatening.

Weapons

Some of the research avenues to tackle antibiotic resistance at the Institut Pasteur:



Bacteriophages on an Escherichig coli bacterium

"Antimicrobial resistance is a global phenomenon that is much bigger than just antibiotics, although they tend to grab all the headlines. It is continually pushing us to try to understand the adaptation processes used by pathogens and parasites that affect humans, animals and plants so that we can develop effective strategies to tackle antimicrobial resistance in an ever-changing world."

Didier Fontenille, Research Director and Head of the RIVE RIVOC initiative at the IRD, and former Director of the Institut Pasteur du Cambodge.

Novel treatments and phage therapy

Scientists from the Institut Pasteur and the CNRS have demonstrated in vivo that bacteria are capable of regulating their gene expression to evade the many bacteriophages in the gut environment (Cell Host & Microbe, April 13, 2022). The same team has developed a mathematical model to predict the effectiveness of phage therapy in treating lung infections (Cell Reports, May 17.2022).

Understanding antibiotic resistance

Plasmids are DNA molecules outside the chromosome that can carry antibiotic resistance genes. They can move between bacteria via a process known as bacterial conjugation. Scientists in the Microbial Evolutionary Genomics Unit have revealed that some plasmids contain sequences enabling them to hijack proteins from other plasmids so they can be transferred from one bacterium to another - what we might call conjugation by hitchhiking. Their research means that we can now predict the transfer mechanisms in 90% of the known plasmids in bacteria (Nucleic Acids Research, November 29, 2022).

Another team, composed of scientists from the Genetics of Biofilms Unit and Rakuno Gakuen University in Hokkaido, Japan, has demonstrated that the biofilms formed by bacteria to survive in their environment encourage the emergence of antibiotic resistance (Communications Biology, March 16, 2023).

FOCUS

MOSQUITOES – *ADEPT AT ADAPTING*

With Anna-Bella Failloux, Head of the Arboviruses and Insect Vectors Unit

MOSOUITOES transmit several epidemic diseases that are progressing at an alarming rate. The aim of the vector control strategies employed to tackle them is always to try to keep one step ahead. But the adaptation and resistance developed by both mosquitoes in the genus *Aedes* and the pathogens they and other insects transmit represent a challenge for prevention, screening and treatment protocols. Two studies published by Institut Pasteur teams in 2023 shed light on these developments.

EXPANSION OF THE TIGER MOSOUITO TO TEMPERATE REGIONS

The tiger mosquito (Aedes albopictus) has come a long way from its native South-East Asia. Although originally a tropical species, it can now be found in large numbers in temperate regions from America to Europe, including mainland France, where it has already spread to four-fifths of the country. And Aedes *albopictus* has not come alone: it is one of two vectors of the chikungunya virus and is responsible for a number of indigenous cases reported far from endemic areas since 2007, including in Europe.

A team of scientists from the Institut Pasteur and Université Paris Cité focused on the impact of climate, especially temperature, on the transmission of pathogens by mosquitoes. Although the tiger mosquito is used to an average of 28°C, lower temperatures do not seem to prevent it from spreading the virus.

The results of the study, published in the Journal of *Travel Medicine*¹, reveal an example of mutual adjustment between the virus and its vector in response to the environment. Temperature profoundly alters the gene expression and bacterial microbiome of mosquitoes and the genetic diversity of the chikungunya virus. But although lower temperatures result in different molecular processes, the mosquito is capable of transmitting the virus just as effectively at 20°C as at 28°C. This adaptation raises fears of a spread of chikungunya in the absence of vaccines and treatments.



Head of a female Aedes albopictus mosquito, the vector for dengue and chikungunya. Scanning electron micro-photograph, colorized image.

Malaria under the radar in Eritrea

In recent years, Plasmodium falciparum, the parasite responsible for the most severe forms of malaria. has become increasingly resistant to rapid screening techniques and artemisinin-based therapy. A study² coordinated by scientists from the Institut Pasteur has revealed a new focus of resistance in Eritrea, the most worrying to date because it shows that the parasites are capable of evading rapid tests and that their vectors are becoming resistant to insecticides. The conclusions of this research support the urgent introduction of novel vector control strategies in response to these adaptations.

(1) "Climate change and vector-borne diseases: a multi-omics approach of temperature-induced changes in the mosquito," Journal of Travel Medicine, April 25, 2023. (2) "Increasing Prevalence of Artemisinin-Resistant HRP2-Negative Malaria in Eritrea," New England Journal of Medicine, September 28, 2023.



18 / ADAPTATION 2023

FACT SHEET

TIMELINE

ADAPTATION OF OUR IMMUNE SYSTEM

With Lluis Quintana-Murci, Head of the Human Evolutionary Genetics Unit

IN THE 1950s, the scientist J.B.S. Haldane theorized that the genetic mutation responsible for abnormalities in red blood cells observed in some African populations had persisted in those populations because it provided protection against malaria. The theory that pathogens are among the strongest selective pressures faced by humans has since been confirmed by several studies. But how does this selective pressure affect the immune system? And what are the consequences for the risk of developing inflammatory or autoimmune diseases? In a study led by a team from the Institut Pasteur, scientists analyzed genetic mutations in hundreds of individuals living in Europe over the past 10.000 years to reconstitute the evolution of the human immune system.

An age-old mystery finally solved

The scientists from the Institut Pasteur, Université Paris Cité, the CNRS and the Collège de France used paleogenomics to go back over 10,000 years of human history and try to trace the evolution of hundreds of thousands of genetic mutations over time. The study, published in the journal Cell Genomics, involved analyzing the genome variability of more than 2,800 individuals who lived in Europe over a period covering the Neolithic, the Bronze Age, the Iron Age, the Middle Ages and the present.

This detective work revealed a series of mutations that the past 10,000 years. had occurred in response to "positive" natural selection, reducing the risk of developing infectious diseases. These mutations, which demonstrate a genetic



Dendritic cells.

"The results of our study suggest that the two phenomena are linked: the risk of inflammatory or autoimmune disorders has increased, at least in large part, because of a positive selection of mutations improving resistance to infectious diseases."

explains Lluis Quintana-Murci.

adaptation to the pathogenic environment, began relatively recently in the grand scheme of human history, in the Bronze Age, around 4,500 years ago. The "sudden" acceleration in adaptation can be explained by the population growth during this period and the spread of infectious diseases as a result of increasing contacts between populations. At the same time, the scientists observed that mutations associated with a higher risk of inflammatory disorders, including Crohn's disease, have become more frequent over

WHAT IS **PALEOGENOMICS?**

Paleogenomics is a relatively recent discipline that studies the DNA from fossil remains of humans, animals, plants or even microbes. It has already led to major discoveries about the history and evolution of humans and human diseases, and even resulted in the 2022 Nobel Prize in Medicine being awarded to Svante Pääbo for his sequencing of the Neanderthal genome. At the Institut Pasteur, paleogenomics has been used to reconstitute the history of tuberculosis and elucidate its impact on the human genome.



With Yusuke Shimakawa, a scientist in the Epidemiology of Emerging Diseases Unit

HEPATITIS IS A LIVER INFLAMMATION generally caused by viruses, or more rarely by toxic substances. These viral infections are triggered by five pathogens identified by the letters A to E. Hepatitis B is one of the most common human diseases - it has already affected more than two billion individuals. In Sub-Saharan Africa, a highly endemic area, scientists from the Institut Pasteur are developing screening models to optimize treatment for infected individuals and limit disease spread.

Origins

The first outbreak to be recorded probably occurred in 1883, in a shipyard in Bremen where the workers had been vaccinated against smallpox with lymph from other people carrying the as yet unidentified hepatitis B virus. The antigen that causes hepatitis B was identified in

KEY FIGURES



More than



first vaccine licensed

The most affected countries are also those with the most limited resources for screening and treatment. While many people are asymptomatic carriers of the virus, some end up developing chronic diseases that can lead to cancer. A universal approach to diagnosis and treatment may seem a good idea if access to tests determining treatment eligibility is limited. But given the cost and the difficulty in offering lifelong access to treatment, it may not be an appropriate option. The Institut Pasteur's teams have developed the first mathematical model to determine optimal eligibility for antiviral treatments for the Gambia. The result suggests a simplified, targeted strategy using the diagnostic test TREAT-B, which combines the hepatitis B e antigen (HBeAg) and alanine aminotransferase. This strategy would reduce cases of cirrhosis and hepatocellular carcinoma and would cost just half as much as a universal treatment approach.

1964 by Baruch Blumberg, a US scientist and laureate of the 1976 Nobel Prize in Medicine for his discovery.

Symptoms, transmission and treatment

The virus is transmitted through bodily fluids and secretions. The main transmission routes are from mother to child during childbirth and through sexual contact or close contact with an infected person, use of contaminated syringes and unscreened transfusions. The virus is extremely infectious and affects more than 5% of the general population in Sub-Saharan Africa, East Asia and the Pacific. Some 254 million people worldwide live with chronic HBV infection. The disease is often asymptomatic, or it may cause symptoms similar to flu or other liver inflammation. There are no specific treatments for acute hepatitis; the main defense is the body's own immune system. Chronic infection is treated with specific antivirals in people at high risk of chronic liver disease. Vaccines were developed in the early 1980s and have a very high effectiveness rate for 98% of the population.

Adaptation to the Sub-Saharan context



RESEARCH **ADVANCES**

SCIENCE AT THE INSTITUT **PASTEUR IN 2023**

papers published Source: Web of Science (articles, reviews and letters excluding preprints) queried on 04/30/2024

new research units (structural biology, viruses and immune control, viruses and cellular stress, respiratory viruses, immunology)







or junior groups, converted to units (epigenetics, parasitology, tissue plasticity, bioinformatics, the brain's adaptation to environmental changes, fungal genetics, innate immunity)

laboratories involved in National Reference Centers (CNRs), **13** coordinating and **6** associated laboratories, for the period 2023-2027

invention disclosures

Launch of the IHU

re-Connect

led by the Hearing Institute, an Institut Pasteur center, and the IHU InovAND partnered by the Institut Pasteur



awards and prizes won by Institut Pasteur scientists including **10 ERC Grants** awarded

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.

> Director: Guillaume Duménil; Deputy Director: Thomas Wollert. 17 teams



Human microglial cells connecting via tunneling nanotubes (TNTs)

An immune memory against bacterial infection

Mélanie Hamon and her team uncover a new role for specific cells of the immune system during a bacterial infection. Studying infection by Streptococcus pneumoniae (also known as pneumococcus), they showed that Natural Killer (NK) cells directly detect bacteria and retain a memory of previous encounters to help protect against secondary infections through mechanisms depending on cytotoxic molecules. This study offers new insights on antibacterial responses to pathogens.

PLOS Pathogens, July 24, 2023. Doi: 10.1371/journal.ppat.1011159.



A key protein to form functional cellular cilia

The unit led by Arnaud Echard has identified a key role for a protein called MiniBAR in the formation of primary cilia. These protrusions, present on the surface of most of our cells, are involved in the reception of chemical and mechanical signals, particularly during development. Depletion of MiniBAR in vivo in a zebrafish model leads to the formation of non-functional cilia and kidney cysts and disrupts the left-right asymmetry that normally emerges during development, all characteristic signs of ciliopathies in humans.

Developmental Cell, October 23, 2023. Doi: 10.1016/j.devcel.2023.09.010.

The formation of intercellular nanotubes elucidated

Tunneling nanotubes (TNTs) are long membranous channels formed between cells to transport material, including amyloid proteins in neurodegenerative diseases, over distances of dozens of microns. Combining biophysical approaches and cutting-edge microscopy, Chiara Zurzolo's team has uncovered key molecular players driving the assembly of actin, an essential component of these structures. Their research sheds light on how actin forms elongated communicating protrusions and could lead to insights for treating diseases involving TNTs.

EMBO Journal, November 27, 2023. Doi: 10.15252/embj.2023113761.



Report on the "Milieu Intérieur" LabEx project.

EXPLORING BIOLOGICAL DATA

DEPARTMENT OF COMPUTATIONAL BIOLOGY

The department specializes in data science and computational modeling of biological processes. It combines expertise in mathematics, statistics, computer science, physics and imaging to answer complex biological questions concerning genomes, cells, cancers, brain function, epidemiology and more. The teams develop guantitative methods to analyze and understand data from sequencing, experimental biology, public health or clinical research. The department is currently strengthening its know-how in artificial intelligence, an essential tool for furthering knowledge in biology and health. It maintains close collaboration with many other teams within the institute. In particular, it has strong links with the Bioinformatics and Biostatistics Hub, has two

joint teams with Inria and pursues collaborations

abroad, notably with the Pasteur Network.

Director: Gregory Batt; Deputy Director: Hugues Aschard. 8 teams

Pangenomics, an approach for comparing human genomes

virulence.

Diversity of vaginal microbiota and pregnancy

A healthy vaginal microbiota is generally a low-diversity environment populated primarily by lactic acid-producing Lactobacillus species. A study conducted on a diverse cohort of 749 women enrolled in the inSPIRe cohort in their final trimester of pregnancy revealed that lactobacilli, including L. crispatus, play a major role in maintaining low diversity, and that a decline in this key community is linked to premature delivery.

Scientific Reports, June 4, 2023. Doi: 10.1038/s41598-023-36126-z.

For the first time, a sequence graph has been constructed in which around fifty human genomes are simultaneously represented. This enables variations in human genomes to be analyzed collectively, a new discipline known as pangenomics. This article outlines existing methods and presents analyses of genes linked to immunity.

Genome Biology, November 30, 2023. Doi: 10.1186/s13059-023-03098-2.

Identifying the origins of virulence

Sequencing technology has dramatically expanded the sources from where genomic data can be obtained. As a case in point, ancient DNA data has been obtained for a number of pathogens from thousands of years ago, and it has improved our understanding of when and how these pathogens emerge. This article describes novel advances in evolutionary modeling to uncover how pathogens become more virulent or transmissible over time. It showcases a key concept, the molecular clock of infectious microbes, a statistical technique that can estimate the precise time when pathogen lineages diverge from each other and acquire important traits, such as mutations that increase

Science, December 14, 2023 Doi: 10.1126/science.adl6094.

Polymerases are enzymes involved in DNA replication during which nucleotides, the building blocks of DNA, are added one by one by these enzymes. In this article, we explored the possibility of synthesizing modified DNA three-by-three using artificial trinucleotides. This approach is very promising to synthesize therapeutic oligonucleotides in a more efficient and sustainable manner and for applications in synthetic and chemical biology. Chemical Communications, November 15, 2023. Doi: 10.1039/d3cc04933g.

Neural stem cells (zebrafish brain).

UNDERSTANDING THE MECHANISMS **INVOLVED IN BUILDING THE** LIVING WORLD

DEPARTMENT OF DEVELOPMPENTAL 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 Levaver. 17 teams.

A new stem cell model to study gonad formation in humans

Anu Bashamboo and collaborators in Ken McElreavey's unit have created a new in vitro model of human gonad formation. Using human pluripotent stem cells, they devised protocols to generate somatic gonad cells. These were used to understand how a genetic variant can lead to testicular disease. This model provides a powerful tool for understanding gonad development and its disorders, and a scaffold for in vitro gametogenesis.

Science Advances, January 4, 2023. Doi: 10.1126/sciadv.abn9793.



A spatiotemporal exploration of gene regulation

Gene regulation requires the physical encounter of different genetic elements, but what happens when they are far away from each other on the same chromosome? Coupling high-precision microscopy to provide real-time visualization of gene transcription and physical models of the 3D dynamics of the DNA molecule, Thomas Gregor and his colleagues showed that gene regulation is less sensitive to genomic distance than anticipated, allowing rapid contacts over long distances. Science, June 29, 2023. Doi: 10.1126/science.adf5568.

Genetic and embryological origin of a rare cardiac malformation

Sigolène Meilhac and her team, in collaboration with Necker-Enfants Malades hospital, investigated a rare congenital heart disease of unknown origin, called crisscross heart, where the inflow streams of the two ventricles cross. Identifying the first murine model of the disease, they have shown that the Grebl1 gene is involved in this malformation. This research sheds light on the developmental mechanisms transforming the embryonic heart tube into a four chambered heart.

Developmental Cell, November 6, 2023. Doi: 10.1016/j.devcel.2023.09.006.

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

DEPARTMENT OF STRUCTURAL BIOLOGY AND CHEMISTRY

The structure of a molecule is intricately linked to its function. The units and technological platforms in the Department of Structural Biology and Chemistry focus their research on the three-dimensional organization, properties, functions and dynamics of macromolecular complexes and machineries, as well as the synthesis of small molecules and biomolecules of biological interest, especially those relevant for human diseases. This interdisciplinary research reveals vital information for the development of new therapeutic, diagnostic and vaccine strategies.

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



Macrophages infected with Mycobacterium tuberculosis

Elucidation of the corynebacterial cell cycle

Joint work between the Institut Pasteur in Paris and Institut Pasteur de Montevideo led to a breakthrough in the understanding of the bacterial cell cycle vital for some bacterial pathogens, offering new potential tools to combat infectious diseases like tuberculosis. leprosy or diphtheria. The discovery shows that a metabolic protein conserved in all organisms acquired new functions in those pathogens to link the essential cell division and growth machineries, showcasing life's remarkable adaptability.

Nature Microbiology, September 7, 2023. Doi: 10.1038/s41564-023-01473-0.

Artificial codons for DNA synthesis

Molecular basis for proofreading by family-D DNA polymerases (or PolD)

Reliable, heat-stable DNA polymerases are required for PCR, a technique widely used in human health research. The team led by Ludovic Sauguet is investigating PolD, a DNA polymerase isolated in ocean hot springs. In collaboration with New England Biolabs, the scientists have determined the structure of PolD at atomic level, revealing a novel fidelity mechanism which paves the way for the design of new biotechnological tools.

Nature Communications, December 14, 2023. Doi: 10.1038/s41467-023-44125-x.

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: Camille Berthelot. 12 teams.



In the Bacterial Genome Plasticity Unit

Who were the first ancestors of present-day fish?

Understanding the family tree of species is crucial for studying evolution. By analyzing the mutational and chromosome evolution patterns in newly sequenced genomes from early-branching fishes, we resolved a long-standing debate on the early evolution of teleost fishes, one of the most species-rich clades of vertebrates, including several model species for biomedical research (zebrafish, killifish).

Science, February 9, 2023. Doi: 10.1126/science.abg4257.



SARS-CoV-2, how the history of human populations influences their immune response

SARS-CoV-2 infection induces highly variable immune responses. Through single-cell RNA sequencing, this study reveals the role of cellular composition and genetic factors in this variability and enables the identification of variants under selection that contribute to disparities in the risk of severe COVID-19 between human populations.

Nature, August 9, 2023. Doi: 10.1038/s41586-023-06422-9.



Predisposition to Zika virus susceptibility

Zika virus is responsible for human infections with variable severity. To identify susceptibility genes, we used mice of the genetically diverse Collaborative Cross. By combining genetic mapping, RNAseg and the quantitative complementation test, we showed that the high susceptibility of the CC071 strain results from a mutation in the Irf3 gene and other loci under investigation.

PLOS Pathogens, September 21, 2023. Doi: 10.1371/journal.ppat.1011446.



Cell undergoing apoptosis.

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.



treatment.



How the brain communicates with our immune system to fight infection

The immune system is a key player to help our body deal with infection, but it does not act alone: our brain is also involved. Gérard Eberl's team, in collaboration with the department of Neuroscience, identified the cerebral area central to two-directional communication between the brain and immune system: this area integrates inflammatory signals present in the blood and in response releases a neurohormone that will regulate the immune response to infection. Neuron, June 5, 2023. Doi: 10.1016/j.neuron.2023.05.009.



A resident T cell population mediates immune memory against recurrent bladder infections

A study led by Matthieu Rousseau in Molly Ingersoll's team uncovered a population of immune cells that are not only necessary, but also entirely sufficient to fight recurrent urinary tract infections (UTI). These memory T cells appear in the bladder after a first UTI and reside there to fight subsequent infections. Importantly, this study shows that rapid antibiotic treatment can limit immune memory, providing a rationale to develop new vaccines or novel immunotherapies to prevent recurrent UTI.

Science Immunology, May 26, 2023. Doi: 10.1126/sciimmunol.abn4332.

> SCAN THE QR CODE OR MORE INFORMATION BOUT THIS PUBLICATION.

Immunotherapy as a long-range weapon against tumors

CAR T cells represent a promising new immunotherapy for treating some blood cancers. Using cutting-edge microscopy techniques, Philippe Bousso's team observed in real time how these cells act against cancer cells, discovering that most of the killing events mediated by a subset of CAR T cells occur without direct contact but at a distance, through the production of IFN-y by the CAR T cells. They then showed that sensitivity to IFN-y is a key factor for predicting the success of an immunotherapy

Nature Cancer, May 29, 2023. Doi: 10.1038/s43018-023-00570-7.

> SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

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Extracellular vesicles (EVs) are membrane-enveloped particles that are released by cells into the extracellular space. Fungal EVs can mediate community interactions and biofilm formation, but their functions remain poorly understood. Here, the scientists report the identification of the first regulators of EV production in the major fungal pathogen Cryptococcus neoformans, and they describe a novel role of EVs in modulating antifungal drug resistance. mBio, June 13, 2023. Doi: 10.1128/mbio.00870-23.

Fungi are responsible for over 1.5 billion infections each year worldwide. Unfortunately, fungi are increasingly resistant to commonly used drugs such as azoles. To address this issue, the scientists identified several small molecules that can restore the susceptibility of Candida isolates to antifungal drugs. Novel antifungal potentiators represent a powerful strategy for addressing the growing resistance of fungi to clinically approved drugs. mBio, June 16, 2023. Doi: 10.1128/mbio.00479-23.

ment strategies.

In the Biology and Genetics of the Bacterial Cell Wall Unit.

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. The team investigates 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

Off-target effects of Cas9 on bacterial gene expression

Powerful genetic manipulation tools derived from the CRIS-PR-Cas9 system can be used to modify gene expression. Gene specificity represents a key challenge, since so-called off-target effects can lead to non-specific effects, skewing the interpretation of experimental results. This study conducted on bacteria revealed an unexpected effect: Cas9 can block gene expression unpredictably by binding non-specifically upstream of genes.

Nucleic Acid Research, April 24, 2023. Doi: 10.1093/nar/gkad170.

How the respiratory tract microbiome influences the severity of bacterial pneumonia

Scientists analyzed the inter-kingdom (bacteria, archaea, fungi, protozoa) diversity and composition of the respiratory tract microbiome (RTM) of patients with pneumonia due to Legionella pneumophila. After antibiotic treatment, the empty RTM niche is rapidly occupied by other bacteria. Thus, high biomass emerges as a biomarker for secondary/co-infections. The interplay of RTM equilibrium, pathogen load dynamics, and clinical interventions plays a critical role in the recovery of pneumonia patients.

Cell Reports Medicine, September 19, 2023. Doi: 10.1016/j.xcrm.2023.101167.



A bridge for phospholipid traffic

Understanding how bacteria build and maintain their cell envelope is a major area of investigation in the fight against pathogens. However, current knowledge is mostly based on a handful of models. Using the diderm *Firmicute V. parvula*, scientists have identified a novel mechanism responsible for phospholipid trafficking that forms a trans-envelope bridge between the inner and outer membrane and is widely distributed in Gram-negative bacteria.

Nature Communications, November 23, 2023. Doi: 10.1038/s41467-023-43411-y.



INVESTIGATING THE BIOLOGY **OF PATHOGENIC** FUNGI

DEPARTMENT OF MYCOLOGY

Fungal infections are a major public

health concern linked to nearly 3.8 million deaths throughout the world every year. The Department of Mycology adopts multidisciplinary approaches to explore the biology of fungal pathogens and fungal pathogenesis with a view to offering novel diagnostic, preventive and therapeutic strategies. Director: Guilhem Janbon; Deputy Director: Jessica Quintin.

Regulation of extracellular vesicle production in Cryptococcus neoformans

A way of restoring antifungal drug activity

Gut aging clock correlated with health

Candida albicans is a commensal yeast present in the gut of most healthy individuals. In this study, scientists assess how the microbiota, lifestyle or genetics influence gut colonization by C. albicans in healthy adults. They show that the load of C. albicans in the gut correlates with certain genetic traits and dietary habits. Notably, the authors show that a higher load of C. albicans in the gut induces a stronger immune response to new challenges by this yeast, paving the way to new treat-

Gut Microbes, November 28, 2023. Doi: 10.1080/19490976.2023.2287618.

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 seek to understand how the brain works both through its functional characteristics and by elucidating its interactions with other systems including the microbiota 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.

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



Thin section of the vagus nerve lymph node.

Gut microbiota involved in depressive disorders

The link between a healthy mind and healthy microbiota has already been established. This study demonstrates that the gut's bacterial population exhibits a specific profile in cases of depression. When this bacterial population is transferred to healthy mice, they show all the signs of depression within a few days. What mechanism is at work here? This study reveals that the body's longest nerve, the vagus nerve, plays an essential role in direct communication between the gut microbiota and brain.

Molecular Psychiatry, May 2, 2023. Doi: 10.1038/s41380-023-02071-6.



Genetic variants implicated in autism detected in the general population

Autism is a clinically and genetically heterogeneous condition, characterized by atypical social communication and restricted or repetitive interests. Investigating 185 genes robustly associated with autism, this study indicates that genetic variants associated with autism can be identified in 1% of undiagnosed individuals, suggesting that genetic and environmental contexts play a crucial role in autism.

Nature Medicine, June 26, 2023. Doi: 10.1038/s41591-023-02408-2.



A mechanism to stimulate and target nicotinic receptors

A specific class of nicotinic receptors in the brain is involved in higher cognitive functions such as memory and executive functions, which are impaired by diseases such as schizophrenia and Alzheimer's disease. This study describes the mechanism of action of molecules that not only effectively stimulate these nicotinic receptors, but also precisely target them. These agents with therapeutic potential are alpaca single-chain antibodies.

Nature Communications, September 25, 2023. Doi: 10.1038/s41467-023-41734-4



Human red blood cell infected with Plasmodium falciparum.

EXPLORING PARASITES AND **THEIR VECTORS**

DEPARTMENT OF PARASITES AND INSECT VECTORS

The PIV department conducts research on three key eukaryotic parasites and their vectors 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 *bruce*i – 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 currently led by Lucy Glover.

> Director: Lucy Glover: Deputy Director: Chetan Chitnis. 10 teams.

Brain activity influences the vector competence of mosquitoes

How the Leishmania pathogen evolves inside the host insect

During insect infection, vector-borne pathogens show a reduction in population heterogeneity, which limits their adaptive potential. Conducting experimental sandfly infection with the protist pathogen Leishmania donovani, scientists provide the first evidence that these parasites regain genetic heterogeneity and thus evolvability inside their vector in response to DNA-damaging oxidants. These results may be applicable to other pathogens that infect insect hosts.

Proceedings of the National Academy of Sciences, February 27, 2023. Doi: 10.1073/pnas.2220828120.

How protective antibodies eliminate malaria parasites

Monoclonal antibodies hold promise for malaria prevention. This study shows that protective antibodies mainly target malaria parasites in the skin and can directly kill parasites. Notably, the researchers developed a novel in vitro assay that mimics skin protection and strongly correlates with protection, emerging as a promising tool to identify new potent prophylactic antibodies.

Cell Reports, July 25, 2023. Doi: 10.1016/j.celrep.2023.112681.

The insect brain sodium channel, para, is a target of pyrethroid class insecticides. In this study, scientists show that normal para activity in the malaria mosquito vector. Anopheles coluzzii. limits development of the human malaria parasite. Plasmodium falciparum. These results pave the way for studying how the activity of the mosquito nervous system through its receptors could influence vector competence for Plasmodium or other microbes.

Scientific Reports, September 4, 2023. Doi: 10.1038/s41598-023-40432-x.





Journal of Travel Medicine, April 25, 2023.





The tiger mosquito can transmit the chikungunya virus in temperate conditions

Arboviruses such as chikungunya (CHIKV) first emerged in Europe in 2007. By combining three approaches (transcriptomics, metagenomics and genomics), scientists have identified temperature as a modifying factor in mosquitoes' immunity gene expression and microbiota, and also in the genetic diversity of CHIKV, although it does not affect transmission efficiency.



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 and oncogenic viruses, retroviruses and arboviruses are scrutinized using state-ofthe-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; Deputy Director: Sarah Merkling. 24 teams



Human respiratory tissue with ciliated cells stained green (anti-TMPRSS2 antibodies), nuclei in dark blue and cell membranes in light blue



Ciliated cell infected with SARS-CoV-2

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: Michael White 13 teams

The impact of variants and circumstances of infection on the COVID-19 incubation period

The ComCor study investigates the circumstances of SARS-CoV-2 infection. Using data from 20,000 individuals who had a single encounter with an infected person, scientists discovered that the COVID-19 incubation period was one day shorter for Omicron than for the historical variant, and when the contact person was symptomatic, suggesting that a higher infectious dose of the virus could shorten the incubation period.

The Lancet Microbe, April 18, 2023. Doi: 10.1016/S2666-5247(23)00005-8.



Enteric viruses with similar genomes in humans and great apes

This study has revealed a high degree of convergence between the genomes of enteric eukaryotic viruses in humans and great apes in a Cameroonian forest. Fields were identified as a platform for viral sharing between humans and great apes in the central African forest. Observations made in the field in Cameroon were compared to a European zoo. This research was coordinated by Tamara Giles-Vernick in collaboration with the CNRS. the Pasteur Center in Cameroon and Saint-Louis Hospital.

Nature Communications, June 21, 2023. Doi: 10.1038/s41467-023-39455-9



The SARS-CoV-2 virus can migrate within neurons and infect the brain

Scientists at the Institut Pasteur and Université Paris Cité have demonstrated a characteristic common to several SARS-CoV-2 variants: the ability to infect the central nervous system. The study also confirms that SARS-CoV-2 is capable of infecting human neurons in vitro and migrating into nerve cell projections that carry information.

Nature Communications, July 26, 2023. Doi: 10.1038/s41467-023-40228-7.



Nature, October 25, 2023.



Development of a pentavalent vaccine against New World arenaviruses

New World arenaviruses cause fatal hemorrhagic fever in South America. MOPEVAC NEW is a pentavalent live attenuated vaccine for the Junin, Machupo, Chapare, Guanarito and Sabiá viruses. It induces sterilizing immunity against the Machupo and Guanarito viruses in cynomolgus monkeys due to high titers of antibodies, including neutralizing antibodies, demonstrating the efficacy of this vaccine for several of these viruses.

Nature Microbiology, January 5, 2023. Doi: 10.1038/s41564-022-01281-y.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

Doi: 10.1093/jtm/taad062.

SCAN THE QR CODE FOR MORE INFORMATION ABOUT THIS PUBLICATION.

New discovery concerning receptors used by coronaviruses to enter human cells

The gateway used by a seasonal coronavirus, HKU1, to enter human cells has been identified. HKU1 binds to a different receptor than SARS-CoV-2, which may partly explain the difference in severity between these two coronaviruses. Receptors provide a useful means of elucidating coronavirus transmissibility and pathology as part of surveillance work on viral evolution.

Doi: 10.1038/s41586-023-06761-7.

SCAN THE QR CODE FOR MORE INFORMATION BOUT THIS PUBLICATION.

ADVANCES

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: Anne-Lise Giraud; Deputy Director: Anne-Dominique Lodeho-Devauchelle. 10 teams



Posture test at CeRIAH.

The re-Connect IHU – a hub for all hearing health stakeholders

On May 16, 2023, the French President, Emmanuel Macron announced the launch of the re-Connect IHU (university hospital institute) as part of the France 2030 Plan, following the IHU3 call for tenders. Its remit is to improve the detection and treatment of hearing and speech disorders and to make the transition from compensatory medicine to reparative medicine. It is led by the Hearing Institute in collaboration with the Institut Pasteur, Paris Public Hospital Network (AP-HP), Université Paris Cité, Inserm and the Fondation Pour l'Audition, with Anne-Lise Giraud at its head.



Gene therapies: new hope for curing hearing loss

Scientists at the Hearing Institute have produced the first gene expression atlas of the cochlea in mice. They have also successfully classified the genes involved in hearing loss and/or cochlear development according to their different expression profiles in various cochlear cell types. Based on these discoveries it should be possible to identify cell types affected by pathogenic gene variants faster and develop targeted therapies aimed at restoring hearing.

Proceedings of the National Academy of Sciences, June 20, 2023. Doi: 10.1073/pnas.2221744120.



CeRIAH: inauguration of premises

In October, the Center for Research and Innovation in Human Audiology (CeRIAH) was inaugurated in the presence of representatives from the Fondation Pour l'Audition, Paris City Hall, Inserm, and the Hearing Institute and Institut Pasteur community. The event also provided an opportunity for the hearing community to come together and forge ties. The day was interspersed with various highlights, including a tour of the new premises, a press conference and a ceremony, which all culminated in the unveiling and signing of the inaugural plaque.



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DEVELOPING **CUTTING-EDGE TECHNOLOGY**

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



Photonic Bioimaging Technology Platform.

ONE OF THE INSTITUT PASTEUR'S PRIOR-ITIES IS TO CREATE A TECHNOLOGICAL **ENVIRONMENT** that benefits and stimulates its research teams. Teams within the Department of Technology provide access to high-level shared resources including a unique range of expertise, facilities, technologies and biological resources. The Department of Technology is committed to constantly investing in the development of

these resources, which are organized into four 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

In 2023 the C2RT provisioned support to over 1,000 users, across more than 900 unique projects. In this same year, the C2RT yielded >200 publications, and was instrumental in hosting dozens of advanced training and teaching courses,





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seminars and symposia. Among these, the "single-domain antibodies 2023" congress alone hosted 350 participant scientists from 30 countries, a testimony to C2RT's unique contribution to this dynamic field of biomedical research.

C2RA

In 2023, C2RA continued to adapt its services to campus requirements by implementing new technologies/models: freezing rat sperm and introducing dedicated isolation units to perform behavioral analyses on infected animals (Central Animal Facility); developing automated analysis of histology slides - digital pathology project (C2RT Histology and Image Analysis Hub); using CRISPR/Cas9 to create new transgenic rat models (Mouse Genetics Engineering Center - CIGM); adding a gene to improve yield when transplanting human hematopoietic stem cells in proposed immunodeficient mouse models (CIGM and Human Disease Models core facilities); introducing a climatic chamber and opaque cages with their own programmable

The C2RT reinforced transversal activities facilitating sophisticated cross-disciplinary research workflows, e.g. single-cell genomics, ultrastructural microscopy, high-content screening, proteomics and metabolomics. Such activities included protein molecule isolation, and structural analysis using combinations of protein purification, crystallography, antibody pro-

duction, macromolecular biophysical analysis and cutting-edge technologies in chromatography, nuclear magnetic resonance, structural cryo-electron microscopy and mass-spectrometry.

In addition, great strides have been made in cell and tissue phenotypic analysis, including correlative light electron microscopy revealing the subcellular anatomy of single cells impacted by viruses and bacteria and allowing screening for therapeutics. These achievements have attracted significant regional, government and industry funding for C2RT platforms.

lighting systems to perform experiments at different temperatures and/or on modified biological rhythms. C2RA has also modernized its facilities and helped plan future facilities including a new animal facility specializing in "tick" vectors; modifications to part of the animal facility in the Gnotobiology Center enabling work to be performed in BSL-2 conditions, particularly when using oligo-mouse-microbiota (OMM12) flora; and involvement in working groups (Center for the Production and Infection of Anopheles and Central Animal Facility) for the future Vector-Borne Disease Center.

CRBIP – robust biological resources for robust research

In 2023. CRBIP launched a 10-year strategic plan aimed at modernizing its infrastructure, increasing use of biological resources placed under its responsibility, and developing services for Institut Pasteur scientists. To enhance its services. CRBIP has been allocated a project management office, whose remit includes ensuring the regulatory compliance of human sample collections for the whole of the Institut Pasteur.

In 2023 the center further developed its infrastructure with the implementation of professional software for managing microbial collections and the installation of new sample preparation and characterization equipment for high-throughput aliquoting, lyophilization and measuring the viability of human and microbial cells. A new cross-disciplinary quality management system concept was developed, and the three units responsible for managing collections of bacterial strains, cyanobacterial strains and human samples were





awarded ISO 9001 certification. Conditions ensuring safe storage of collections under CRBIP responsibility have been tightened. Bioinformatics services relating to genome taxonomy have been enhanced and the GIPhy group has joined CRBIP.

In terms of leveraging data, 2,300 whole genome sequences (WGS) of strains in the CIP collection have been added to the BIGSdb and can be accessed by Institut Pasteur scientists. A further group of 2,000 bacterial strains has been prioritized for sequencing using a tool that has been specifically developed in-house. An initial group of 50 strains from the Fungi Culture Collection has been qualified. The phylogenetic tree for cyanobacteria is currently being restructured.

Lastly, 28 scientific articles were published with CRBIP team members as co-authors or cited in the acknowledgments. Moreover the European IS_MIRRI project was successfully completed.

C2RI

Consolidation of C2RI launched in 2022 continued in 2023. On taking the reins in September, Laurent Essioux and his team worked hard to enhance support for computational biology and data management at the Institut Pasteur, while also increasing the impact of these two areas. C2RI

continued to provide the campus with scientific support through over 250 projects with research units from all departments and 120 co-authored publications covering its vast field of expertise which spans everything from data management to biostatistics, image analysis and computational biology. In partnership with C2RA and C2RT, the team has developed its knowledge, particularly within the fields of deep learning, spatial transcriptomic data analysis, integration and analysis of multimodal data, and digital pathology. It has expanded its involvement in data management and FAIRification through new National Reference Center (CNR) projects, which have seen it step up its support with data management for Institut Pasteur biological collections held by CRBIP and offer specific assistance to the Hearing Institute. In line with the key priority areas included in its mission. C2RI continued its educational initiatives, offering all Institut Pasteur PhD students a course focusing on bioinformatics, biostatistics and image analysis as well as data management training.

In 2023, it ramped up its scientific outreach work by joining The French Gut initiative and increasing its contribution to the France-BioImaging infrastructure, assuming joint management of its image processing and data management node.

INNOVATION FOR HEALTH

The Technology Transfer and Industrial Partnership Department (DARRI) seeks to

promote translational research in order to boost the impact of basic research on public health challenges. The DARRI works with the scientists to identify projects with high innovation potential and supports them through the innovation process to bring innovative health products and services to market by means of industrial partnerships, licenses and startups. The Institut Pasteur has been part of the Carnot network since the accreditation was first introduced in 2007.



Human macrophage infected by the Lassa virus (arenavirus).

IN 2023, the DARRI continued to roll out its strategy based on the following principles: cross-disciplinary organization that covers 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 14 new collaboration agreements and seven new patent licenses, 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 coordinated 349 management agreements and its activities generated a total of €32.84 M in revenue from industry partnerships.

In 2023, the DARRI also contributed to the activities of the Pasteur Network through its participation in the workshop on innovation organized by the Hellenic Pasteur Institute in Athens.



INTERVIEW WITH VALÉRIE HÉLIN,



The Global Alliance Manager, a key role for strategic industry partnerships

Valérie Hélin joined the Institut Pasteur in 2022 as Global Alliance Manager in the DARRI – a position that is often seen in major corporations but rarely in the academic arena. The DARRI chose to open up this global alliance management position in response to the challenging new health industry landscape, and the role has become crucial for the success of our industry partnerships.

What is the role of a Global **Alliance Manager?**

V.H.: The Global Alliance Manager is involved in the Institut Pasteur's strategic partnerships once they have been set up. He or she has three main duties: first, coordinating partnerships by organizing launch meetings and establishing governance structures; second, monitoring the financial and operational aspects of projects in association with the team's financial coordinators (achieving deliverables and anticipating potential problems); and last but not least, creating the conditions for suc-

cessful projects by developing a relationship of trust with partners. The Global Alliance Manager carries out these tasks by establishing effective communication channels, liaising with decision-makers to deal with issues and identifying the right person or people to resolve any difficulties.

Communication is a major part of my role: on the one hand I keep scientists informed about the obligations related to partnerships, and on the other I analyze requests from industry, ensuring that the interests of our scientists and the Institut Pasteur are protected. The challenge is to bring together two very different spheres, each with its own aims and objectives.

The Global Alliance Manager position is inevitably an interdisciplinary role, and that's what appeals to me! I obviously work with all the DARRI departments. but I also work with the Institut Pasteur's other departments - the Legal Affairs, Medical and Scientific Departments, for example. In industry, I liaise with a wide range of people, including other alliance managers, external innovation managers and scientists for major corporations, as well as CEOs, CFOs and CSOs for smaller companies.

Why was it so important to create this position?

V.H.: Alliance management is something that has been around for many years in large corporations to manage strategic partnerships on several levels: financial, research and development, joint marketing, etc. More recently, biotech companies, especially in the field of medicine, have also recognized the importance of having someone to facilitate and manage partnerships.

The DARRI was a pioneer in this respect, as one of the first academic technology transfer departments to create an alliance management position. The role is so important in enabling the Institut Pasteur to adapt to the specific circumstances of its industry partners and to pursue successful, long-term partnerships.

Can vou tell us a little more about the strategic partnerships you manage? V.H.: The first category to mention is industry partners with which we have framework agreements.

In the area of vaccines, for example, we have a dozen ongoing collaboration projects with Sanofi Vaccines.

In diagnostics, we are embarking on a new framework agreement with bioMérieux. This should open up a number of possibilities, with one or two collaborative projects expected at the end of the year.

In the field of instruments and equipment, we are in discussions with ThermoFisher on various potential collaborative projects, ranging from the establishment of reference centers with our platforms to the conclusion of license agreements.

I am also responsible for monitoring the startups spun off from the Institut Pasteur with which we have license agreements or ongoing research and development collaboration. I would particularly mention Theravectys and Oncovita, which have a joint laboratory with the Institut Pasteur.

"The excellence of our scientists is and will continue to be the key to innovative applications!"

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

Focus on Mopevac, one of the 10 projects in the Institut Pasteur **Innovation Accelerator**

The Mopevac project led by Sylvain Baize (Biology of Viral Emerging Infections Unit, a joint Pasteur-Inserm unit at the International Center for Infectiology Research in Lyon) was selected for the Institut Pasteur Innovation Accelerator in 2021. The aim of the project is to develop an innovative, versatile platform for live-attenuated viral vector vaccines that can be used to express antigens from pathogens. The main aim is to generate vaccine candidates for arenaviruses that are endemic in South America and West Africa, like the Lassa virus. Infections with these viruses cause hemorrhagic fevers that can be fatal, and few effective drugs are available. Vaccination is the most promising approach.

Multiple success stories for Institut Pasteur startups

The biotechnology company Theravectys has developed a vaccine candidate for cervical cancer and oropharyngeal cancer caused by human papillomavirus (HPV). The vaccine candidate, based on lentiviral vector "Lenti-HPV-07" and administered by intramuscular injection, is the result of work carried out in the joint Institut Pasteur-Theravectys laboratory.

On June 8, 2023, Avatar Medical, a spin-off from the Institut Pasteur and the Institut Curie, was granted authorization from the US Food and Drug Administration (FDA) for its virtual-reality surgical planning solution. Avatar Medical instantly converts scans and MRIs into patient avatars, in other words detailed 3D representations. With FDA certification under its belt, this innovative spinoff can now market its solution in the United States.

Oncovita is an Institut Pasteur spin-off that is developing an immunotherapy cancer vaccine, MVdeltaC, using a genetically modified

Artificial intelligence for health data

On September 26, 2023, the winners of the AI 4 Health Challenge, launched in November 2022 by the Greater Paris region and its partners Medicen and Startup Inside, were announced. The principle is to apply artificial intelligence to health data with the aim



reality representations of patients' medical images.

of improving health care for people living in Greater Paris. The Institut Pasteur challenged participants to come up with a proiect to identify factors that contribute to the variability of immune responses in populations and the risk of developing immune diseases. The consortium composed of the company Scienta Lab and the Mathematics and Computer Science Laboratory for Complexity and Systems (MICS) at Centrale-Supélec was selected to take up the challenge. Their mission is to develop algorithms to predict the detailed blood cell composition, inflammation level and serological status of several vaccines and infections based on the DNA methylome.

Avatar Medical converts scans and MRIs into patient avatars, in other words detailed 3D and virtual

HIGH-LEVEL ACADEMIC PARTNERSHIPS TO **ADVANCE RESEARCH**

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 was to consolidate and develop national and international academic partnerships to drive scientific excellence within the Institut Pasteur.



Signing of a new framework agreement between AP-HP and the Institut Pasteur

Partnerships with Public Scientific and Technical **Research Establishments** (EPSTs)

The Institut Pasteur campus currently hosts several research units that are jointly affiliated with the CNRS (9 UMRs (joint research units), 1 EMR (joint research team) and 1 UAR (support and research unit)) and Inserm (6 Us (units), 3 UAs (support units) and 1 ERL (accredited research team)). The Institut Pasteur also hosts two units under contract

(USCs) with the French National Research Institute for Agriculture, Food and Environment (INRAE) and three joint units respectively 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 permanent scientists from these organizations. The Institut Pasteur currently hosts 65 scientists and 16 engineers from the CNRS, 31 scientists and 8 engineers from Inserm, 17 scientists/lecturers and 6 university hospital scientists/ lecturers.

University and teaching partnerships

These partnerships cover aspects of research that enable the Institut Pasteur to host scientists/lecturers and develop teaching activities. The Institut Pasteur has 13 courses that can be included as part of a first- or second-year Master's program at our partner



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

universities (Université Paris Cité, Sorbonne University, Ecole normale supérieure/Université PSL, Paris-Saclay), 17 courses that lead to the award of a university diploma (DU) from Université Paris Cité (15) or Sorbonne University (1), and more than 20 courses that count as doctoral school modules.

Moreover, 10 Institut Pasteur courses are included in the Université de Paris European Master's in Genetics and 12 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), the Institut Curie and Université PSL.

The Institut Pasteur also manages its own international PhD program (PPU) in close partnership with Université Paris Cité, Sorbonne University, Université Paris-Saclay, the University of Oxford and the Institut Imagine.

Partnerships with the AP-HP and Paris Psychiatry and **Neurosciences GHU**

The framework agreements with the Paris Public Hospital Network (AP-HP) and Paris Psychiatry and Neurosciences University Hospital Group (GHU) were renewed in 2023 with the aim of supporting 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 publish joint calls for proposals every year 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. Two new university hospital institutes (IHUs) involving the Institut Pasteur and the AP-HP - re-Connect (for hearing disorders) and InovAND (for pediatric neurodevelopment) – were set up in 2023. 🔴

WHY DO WE NEED **PARTNERSHIPS?**

- To formalize and consolidate links with partners through the creation of joint units based at and/or outside the Institut Pasteur.
- To encourage researchers from these institutions to come and work on the Institut Pasteur's campus and offer opportunities for the Institut Pasteur's scientists to spend time at external research organizations, schools and universities, accompanied by post-docs and engineers where appropriate.
- To identify scientific research organizations, teams and projects that can come under the umbrella of these partnerships, leading to opportunities for joint research units and researcher mobility.
- To promote outstanding university teaching and enhance the Institut Pasteur's appeal to future generations of scientists.

HOW DO WE FORGE **PARTNERSHIPS?**

 By implementing specific agreements that can be linked to framework agreements defining the terms of collaboration in the area of research or education.

ADVANCES IN PUBLIC HEALTH

THE CNRs SERVING PUBLIC HEALTH

In 2023, terms were renewed for the 18 National Reference Centers (CNRs) - including 5 associated laboratories – placed under IP responsibility for a 5-year period. A new application submitted by Maël Bessaud led to the launch of a second laboratory associated with the Enteroviruses-Parechoviruses CNR. This will reap the benefits of its internationally recognized expertise on polioviruses. 2023 saw 3 key events in relation to the CNRs.

The CNR for Anaerobic Bacteria and Botulism on the front line during the Rugby World Cup

On September 10, 2023, three suspected cases of botulism were reported to the Gironde Regional Health Agency. The patients, who were admitted to Bordeaux University Hospital, had all been to the same restaurant and said they had eaten its home-canned sardines. The three patients had been visiting France to attend the Rugby World Cup. The CNR quickly confirmed the presence of botulinum toxin both in the patients and in the cans under investigation, which triggered an inquiry to identify, contact, monitor and offer immediate care to any individuals who had visited the restaurant during this period. The CNR diagnosed a total of 15 cases of botulism affecting nationals of 7 different countries.

A surge in workload for CNR-ESS in 2023

Supported by the Enteric Bacterial Pathogens Unit, also a designated WHO Collaborating Center for Salmonella, the CNR for Escherichia coli, Salmonella and Shigella (CNR-ESS) received and tested 15,478 strains of all three pathogens in 2023, marking an exceptional quantity of strains for a second consecutive year and the center's highest annual workload in the past 20 vears. In 2023. CNR-ESS was involved in 48 European epidemiological surveys and the investigation of over 22 episodes of clustered cases nationwide, including 2 major outbreaks caused by Salmonella-type bacteria. The first of these was linked to the consumption of farmhouse cheeses made with raw milk and accounted for over 90 cases. Around 50 cases were identified for the second outbreak, which was likely caused by the consumption of locally produced pork. In terms of international operations, in November 2023 the French Ministry for Europe and Foreign Affairs commissioned CNR-ESS to investigate an outbreak of febrile diarrhea among participants in a sporting event - the "Trek Rose" - held in the Moroccan desert. Over 300

cases were reported among the 800 exclusively female participants. The assessment submitted by the CNR revealed that this digestive infection was a form of shigellosis caused by Shigella sonnei bacteria and that this epidemic strain (genotype 3.6.2) was also emerging in France.

The National Reference Center (CNR) for Meningococci and Haemophilus Influenzae – a key player in developing the French national vaccination strategy

Every year, around 500 cases of invasive meningococcal infections are reported in France, leading to some fifty deaths. Through monitoring and microbiological characterization work at the CNR for Meningococci and Haemophilus Influenzae, the center's team and members of the Invasive Bacterial Infections Unit to which it reports were able to trace the evolution of invasive meningococcal disease cases in France between 2015 and 2022, revealing an unprecedented resurgence in the disease after the easing of control measures imposed during the COVID-19 epidemic. Recently reported cases have mainly been caused by meningococcal serogroups that were less prevalent before the pandemic. Although group B infections are still in the majority, the incidence of group W and Y infections has risen significantly since 2022. The individuals most affected by this new wave of meningitis are young people aged 16 to 24.

This analytical work and the results published in the Journal of Infection and Pub*lic Health* in 2023 have helped guide the health authorities' decision-making on developing the national vaccination strategy for this fatal disease. As of January 1, 2025, it will be compulsory for infants to be vaccinated against meningococcal serogroups A, C, W, Y and B. 🔴

PROMOTING CLINICAL RESEARCH

In 2023, efforts to reorganize the clinical research conducted by the Clinical Research Coordination Office (PC-RC) and ICAReB-Clin in the Medical Department continued. Several projects were launched following expert guidance from the teams on coordinating and conducting clinical trials.



IN JULY 2023, AFNOR renewed ISO 9001 certification for the Institut Pasteur's translational and clinical research. This certification covers three operational components that provide support for scientists and physicians conducting projects: the One-Stop Shop, which assesses regulatory and ethical aspects; the Clinical Research Coordination Office (PC-RC) and the for the PC-RC. First, following a significant ICAReB-Clin platform.

Over the course of 2023, the One-Stop Shop approved 135 new projects (52% more than in 2022): 45 clinical research projects involving human subjects, with a treating hidradenitis suppurativa at the third led by the Institut Pasteur and twothirds by mainly academic external project leaders; and 90 translational projects on

the use of human biological resources (samples or data). Once the projects were validated, the relevant departments were tasked with preparing and coordinating them in accordance with ethical and regulatory requirements.

The year 2023 saw two major milestones investment in staff, the PC-RC secured authorization for a Phase III clinical trial, in accordance with EU regulation 536/2014. The trial will assess the effectiveness of a combination of antibiotics for Institut Pasteur Medical Center. The first patients are expected to join the trial in 2024. A dedicated project manager was

135

new health-related research projects approved by the One-Stop Shop (52% more than in 2022)

assigned to the research projects at the Hearing Institute, speeding up the approval process and the delivery of several favorable ethical opinions in 2023. These opinions are a necessary first step before setting up centers and launching research (REFINED, RnDys in 2023, COM-PRESSED, AV-SSR-I in 2024).

Since September 2023, the ICAReB-Clin platform has been led by Dr. Hélène Laude. The organizational structure has developed with the arrival of a second clinical research nurse to assist the platform's physician investigator and help with the research activities of the physicians in the Medical Center.

In collaboration with the PC-RC, ICAReB-Clin set up the COSIPOP cohort to give the scientific community access to samples and data from people in a good general state of health. The individuals are informed via dedicated web pages about the research they are participating in and the entire process from recruitment to the publication of scientific results. At the same time, the COVARIANT and PRE-GASIGN trials, led respectively by Professor Sylvie van der Werf and Dr. Eliette Touati, got under way. In 2023, 54 subjects were recruited for these trials, aimed at developing diagnostic tests for COVID-19 and stomach cancer. 🔴

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.



Vaccination at the Institut Pasteur Medical Center.

Medical activities

The Medical Center is mainly involved in providing medical assistance for foreign travel. In preparation for trips abroad, there is high demand for international vaccinations and travel medicine, both among the general public and for certain categories such as humanitarian aid workers and immunocompromised individuals. 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



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

(leishmaniasis, etc.). This has led to the Medical Center being integrated into the worldwide GeoSentinel network for the surveillance of travel-related illnesses. The Medical Center also treats patients for chronic infection with HIV or hepatitis viruses, in collaboration with Necker Hospital, as well as chronic skin conditions such as hidradenitis suppurativa - for which the center's medical team is internationally recognized – and allergies.

Clinical research

The Medical Center is involved in clinical research in its areas of medical specialization: cohorts with HIV infection in conjunction with ANRS-MIE, and the pathophysiology of hidradenitis suppurativa in collaboration with the Institut Pasteur campus and Necker Hospital. A comparative therapeutic trial aimed at endorsing the hidradenitis suppurativa treatment currently recommended by the Medical Center's dermatologists will start enrolling visits to the International Vaccine Center

vaccines administered

consultations for infectious and tropical diseases

and travel medicine

consultations at the Anti-Rabies Center

consultations for allergies

patients in 2024. The continuation of the PoxVac22 trial, which analyzes the natural or post-vaccine immune response to mpox virus infection, meant that a patient was able to be included long after the initial outbreak, indicating at least some persistence of transmission. The Medical Center also performed a retrospective analysis on travelers seen for post-exposure examination at the Anti-Rabies Center, which helped characterize the types of animals responsible for exposure in certain categories of the population and highlighted the important role of monkeys in Asia and cats in North Africa, as well as the usual canine reservoir. The new insights offered by these projects confirm the key role played by the Medical Center in the Institut Pasteur's translational research activities.

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 900 students, PhD students and professionals from around 85 countries attend one of the 40 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 nine 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

AWARDS AND **APPOINTMENTS 2023**



Valérie Masson-Delmotte at the 2023 PhD graduation ceremony

INSTITUT PASTEUR 2023 PHD **GRADUATION** CEREMONY

THE ANNUAL PHD

graduation ceremony took place on December 8, 2023 Since 2013, this ceremony has become a showcase for the Institut Pasteur's excellence in research and education and an opportunity to highlight the PhD research conducted at the Institut Pasteur and in the institutes selected to represent the Pasteur Network. The guest speaker at this year's ceremony was Dr. Valérie Masson-Delmotte, a climatologist, CEA Director of Research and Co-Chair of Working Group I of the Intergovernmental Panel on Climate Change (IPCC). During her fascinating lecture, Valérie Masson-Delmotte spoke about the alarming realities of climate change that we have to address as a matter of urgency and the possible measures that can be taken to reduce their impact.

(DNM2IP), launched by the Institut Pasteur in 2019, have proven remarkably successful with the public in terms of registrations and international visibility. The Institut Pasteur's decision to specialize in high-level online learning in life sciences and health, with 24 MOOCs to date including recent additions on neglected tropical diseases and emerging viral diseases and pandemics –, is positioning it as a key partner in major national and international teaching consortia.

Maior 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).

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 Euro-

"The aim of the teaching provided by the Institut Pasteur is to train up outstanding scientists to make an impact across the globe."

pean 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 specific PhD supervision, as well as personal support with a dedicated office for doctoral students. It also has a dedicated 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.

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

APPOINTMENTS

Aude Bernheim Head of the Molecular Diversity of Microbes five-year group Elected a member of the European

Academy of Microbiology Hervé Bourhy Head of the Lyssavirus.

Epidemiology and Neuropathology Unit Elected a member of the Academia

Margaret Buckingham Visiting researcher Promoted to the rank of Grand

Officier of the Legion of Honor

Prof. Sir Stewart Cole Former President of the Institut Pasteur

Promoted to the rank of Officier of the Legion of Honor

Arnaud Échard Head of the Membrane Traffic and Cell Division Unit

Elected a member of the Academia Europaea, & Mercator Fellow (DFG – Deutsche Forschungsgemeinschaft, German Research Foundation)

Simonetta Gribaldo Head of the Evolutionary Biology of the Microbial Cell Unit Elected a member of EMBO

Mart Krupovic Head of the Archaeal Virology five-vear unit

Elected a member of the European Academy of Microbiology

Louis Lambrechts Head of the Insect-Virus Interactions Unit

Elected a member of the Academia Europaea

Marc Lecuit Head of the Biology of Infection Unit

Elected a member of the European Academy of Microbiology

Lluis Ouintana-Murci Head of the Human Evolutionary Genetics Unit

Knight of the National Order of Academic Palms

Carla Saleh Head of the Viruses and RNA Interference Unit Elected a member of the Academic

Olivier Schwartz Head of the Virus and Immunity Unit

Elected a member of the Academia

Chiara Zurzolo Head of the Membrane Traffic and Pathogenesis Unit

HONORS

AND PRIZES

Scientist in the Structural

Head of the Stress Adaptation

Marija Backovic

Agnes Ullmann Prize

Frédéric Barras

and Metabolism in

Enterobacteria Unit

Fondation de France

Brice Bathellier

Pour l'Audition

Aude Bernheim

Thérèse Lebrasseur Prize,

Head of the Dynamics of

the Auditory System and

Scientific Emergence Prize

Multisensory Perception Unit

for Basic Research. Fondation

Head of the Molecular Diversity

of Microbes five-year group

EMBO Young Investigator

Rosalind Franklin Young

Program (YIP) Award

Camille Berthelot

Head of the Comparative

Schlumberger Foundation

Functional Genomics five-year

for Education and Research (FSER)

Investigator Award

group

endowment

Virology Unit

Elected a member of the Academia

Science Medal, French Academy of Sciences

Award



Svlvain Brisse Head of the Biodiversity and Epidemiology of Bacterial Pathogens Unit

Georges, Jacques and Elias Canetti Prize

Thibault Brunet Head of the Evolutionary Cell Biology and Evolution of Morphogenesis five-year group Vallee Scholar Grant

Jean-Pierre Changeux Neurobiologist, visiting researcher at the Institut Pasteur Erasmus Medal, Academia

Furopaea

Rayan Chikhi Head of the Sequence Bioinformatics five-year group Mme Victor Noury/Fondation

Aleksandra Deczkowska Head of the Brain-Immune Communication five-year group

2023 Joël Ménard Award for basic research (Alzheimer Foundation)





Thomas Bourgeron Head of the Human Genetics and Cognitive Functions Unit 2023 René & Andrée Duquesne

Philippe Bousso Head of the Dynamics of Immune Responses Unit Human Biology and Medical



de l'Institut de France (French Academy of Sciences) Prize

Ludovic Deriano Head of the Genome Integrity, Immunity and Cancer Unit 2023 Pasteur Vallery-Radot Prize

Arnaud Fontanet Head of the Epidemiology of Emerging Diseases Unit Senior Scientist Louis Pasteur **Bicentenary Prize**

Anne-Lise Giraud Director of the Hearing Institute - Head of the Neural Coding and Engineering of Human Speech Unit

Lamonica Neurology Prize (French Academy of Sciences)

Simonetta Gribaldo Head of the Evolutionary **Biology of the Microbial** Cell Unit

Impulscience® Grant, Bettencourt Schueller Foundation

Mélanie Hamon Head of the Chromatin and Infection Unit

Junior Scientist Institut Pasteur Prize

Romain Koszul Head of the Spatial Regulation of Genomes Unit

Molecular and Cellular Biology. Genomics Medal (French Academy of Sciences)

Marc Lecuit Head of the Biology of Infection Unit

Highly Cited Researcher. Cross-Field, Clarivate Web of Science

Romain Levayer Head of the Cell Death and Epithelial Homeostasis Unit

Pasteur Vallery-Radot Prize

Leo Lit Man Poon Co-Director of the HKU-Pasteur Research Pole, University of Hong-Kong, a Pasteur Network member

Pasteur Network Prize

Jean-Baptiste Masson Head of the Decision and Bayesian Computation Unit

Ile-de-France Innovator Award and French Technology Academy Innovation Award (with the founders of Avatar Médical)

Paola Minoprio Head of the Trypanosomatids Infectious Processes Unit French Senate Medal

Marie Robert Scientist in the Translational Immunology five-year unit

Junior Prize from SPILF (French Language Infectious Disease Society)

Brice Rotureau Scientist in the Trypanosome Cell Biology Unit Léon Launois Prize

Arantxa Rojas Scientist in the Mechanisms of Epigenetic Inheritance Unit

Marie Skłodowska-Curie fellowship

Núria Ros i Rocher Scientist in the Evolutionary Cell Biology and Evolution of Morphogenesis five-year group

Marie Skłodowska-Curie fellowship

Mathilde Ruggiu PhD student in the Dynamics of Immune Responses Unit

2023 L'Oréal-UNESCO "For Women in Science" French Young Talent award

Anavaj Sakuntabhai Head of the Ecology and Emergence of Arthropod-Borne Pathogens Unit

Grand Prize in the 2020 i-Lab innovation competition run by the French Ministry of Research ("Le Point" 2023 top innovators list)

Ludovic Sauguet Scientist in the Architecture and Dynamics of Biological Macromolecules Unit Agnès Ullmann Prize

Gérald Spaeth Head of the Molecular Parasitology and Signaling Unit

Visiting Professorship at the University of Bari

Xiaoyue Wang Scientist in the Neural Coding and Engineering of Human Speech Unit First Prize for Scientific Research, 5 senses for Kids

ERC FUNDING

ERC-Advanced Grant

Guillaume Duménil Head of the Pathogenesis of Vascular Infections Unit Project DESTOP – Destabilizing Vascular Colonization to Stop Meningitis

ERC-Consolidator Grant

Massimiliano Bonomi Head of the Computational Structural Biology five-year unit Project bAIes - Integrative, AI-aided Inference of Protein Structure and Dynamics

Rayan Chikhi Head of the Sequence Bioinformatics five-year group Project IndexThePlanet - Planetary-Scale Indexing of Sequencing Data

Romain Levayer Head of the Cell Death and Epithelial Homeostasis Unit Project PrApEDoC – Predicting Apoptosis Engagement Downstream of Caspases

Liliana Mancio Head of the Biology of Plasmodium Infection and Transmission five-vear unit

in vivo

Project DEXES – Mechanisms of Dormancy, Activation and Sexual Conversion in Pre-erythrocytic Malaria Parasites

ERC-Synergy Grant Thomas Gregor

Head of the Physics of Biological Functions Unit Project DynaTrans – Transcription in

4D: the dynamic interplay between chromatin architecture and gene expression in developing pseudo-embryos

Roberto Toro Head of the Applied and Theoretical Neuroanatomy five-year unit

Project UNFOLD – Unfolding the dynamic interaction between mechanical and molecular processes in brain folding

ERC-Starting Grant Daria Bonazzi

Scientist in the Pathogenesis of Vascular Infections Unit Project HOMEPATH – Control of Host

Mechanics by a Bacterial Pathogen and Functional Impact Laura Cantini (G5)

Head of the Machine Learning for Integrative Genomics five-year group Project MULTIview-CELL –

Integration of single-cell multiomics data across space and time to unlock cellular trajectories

ERC Proof of Concept Lucie Peduto Head of the Stroma, Inflammation

and Tissue Repair Unit Project REACT – Reprogramming of Tumor Stroma to Enhance Cancer Immunotherapy

AMR DATA CHALLENGE AWARDS

Scientists in the Epidemiology and Modeling of Bacterial Escape to Antimicrobials Unit selected as awardees in the Vivli AMR Surveillance Open Data Re-Use Data Challenge funded by Wellcome.

Aleksandra Kovacevic **Quentin Leclerc** Lulla Opatowski Eve Rahbe



INSTITUT PASTEUR YOUNG SCIENTIST PRIZE

Morgane Boulch PhD student in the Dynamics of Immune Responses Unit

Marine Cazaux PhD student in the Dynamics of Immune Responses Unit

Claire Maudet-Crépin Postdoctoral fellow in the Biology of Infection Unit

Delphine Planas Postdoctoral fellow in the Virus and Immunity Unit

Francois Rousset PhD student in the Synthetic Biology Unit

Jerzy Witwinowski Postdoctoral fellow in the Evolutionary Biology of the Microbial Cell Unit

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A campus committed to sustainable development

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MAJOR EFFORTS TO PROMOTE AN ATTRACTIVE AND RESPONSIBLE WORKING ENVIRONMENT

The key moments of 2023 were all underpinned by a common theme of guiding, helping and supporting Institut Pasteur staff in their career, while promoting a high-quality working environment.

Eager to provide a high-quality working environment, the Institut Pasteur renewed its commitment to greater diversity and inclusion.

Key steps in 2023 included:

- The continuation of awareness-raising and training initiatives to promote and reinforce the notion of gender equality among all staff on campus;
- The launch and implementation of a structured disability policy following on from a review and action plan conducted with Agefiph*.

Reflecting a firm commitment to supporting and encouraging its postdoctoral community, the Institut Pasteur has stepped up its support by creating an Office of Postdoctoral Affairs within CARE. the Career Development Service for Scientists.

In 2023, a comprehensive and coherent range of scientific training was put together, meeting skills requirements mainly identified by a GEPP** study on developments in scientific professions. Finally, the Institut Pasteur once again renewed its commitment to rewarding its staff for their work this year through

2.449

510

64

interns

Institut Pasteur employees (69% on permanent contracts)

OREX staff (from external

99%

Gender Equality

Index in 2023

research organizations)

appropriate measures on pay (index rises, salary review for PhD students and postdoctoral fellows, 75% coverage of travel expenses, etc.).



FOR FURTHER INFORMATION ON THE INSTITUT PASTEUR'S COMMITMENTS ON DIVERSITY, EQUALITY AND INCLUSION, SCAN THE OR CODE

Diversity on campus



average age of employees

86

different nationalities on campus (Institut Pasteur employees & OREX)

people hired in 2023 (excluding fixed-term to permanent contracts), 41.3% of whom scientists

3.032staff members on campus 57.5%

0 scientists with grants scientists and research engineers out of the total of 2.959 Institut Pasteur employees and OREX

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

59% 58.7% 48.9% of researchers, 59.3% female staff of people hired at the Institut in 2023 of research engineers Pasteur and 69% of research technicians are female

Skills development and career support

€3.590.000

invested in professional training (teaching costs, time spent training and compulsory contributions)

42.700 hours

of training completed (including 9,150 for members of external organizations (OREX))

8.132

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

108

scientists supported by CARE. the career development service for scientists

A CAMPUS COMMITTED TO SUSTAINABLE DEVELOPMENT

When rolling out environmental initiatives needed to address the current situation. the Institut Pasteur can rely on two key assets: the commitment of its community and departments, and access to reliable figures specific to its activities.



At the 2023 Sustainable Development Forum.

An engaged community

In March 2023, the Institut Pasteur's Sustainable Development Department set up an employee resources community dubbed the GreenTeam. This new initiative marks the next step in the Institut Pasteur's commitments on the environment and under the Responsible Campus program set up when the organization joined the Global Compact in 2010. With over 60 staff members at the end of 2023, this multidisciplinary group is living proof that sustainability is relevant to most of the Institut Pasteur's professions. Its members have two main remits: firstly as ambassadors (passing on information,



raising awareness of best practices, etc.) and secondly as stakeholders, in particular through 9 working groups (biodiversity, energy, plastic, etc.) set up when the initiative was launched.

Nine GreenTeam members completed training managed by the Institut Pasteur's Sustainable Development Department enabling them to lead Climate Fresk® workshops internally within the foundation. These workshops set up in 2018 use IPCC data and draw on collective intelligence to raise participants' awareness of climate change. Over 175 people attended these workshops in 2023.

Rigorous methodology

Following a pilot phase conducted at the Hearing Institute, the Institut Pasteur launched a carbon footprint analysis of its direct and indirect emissions in September 2023, with a view to drawing up a low-carbon strategy for 2030 in 2024.

* The French association in charge of access to work funding for disability inclusion at work.

** Jobs and careers management strategy.



Recycling in 2023

110 t Paper (including paper archives) and cardboard

0.41 t Metal packaging

13.92 t Plastic packaging

4.05 t Glass

2.7 t Organic waste

0.214 t Batteries

0.548 t Ink/toner cartridges

ENCOURAGING COMPLIANCE OF RESEARCH ACTIVITIES

The standards governing research activities are becoming increasingly stringent and complex, whether the strict rules imposed by French. European or foreign legal systems, regulations required by funding bodies or the standards and values that the Institut Pasteur seeks to uphold.



TO UNDERSTAND THE IMPACT of these standards on the Institut Pasteur's activities and make sure they are interpreted and applied correctly so that they provide a solid grounding for research projects, the Legal Affairs Department offers support in three main areas.

Support for major partnerships and strategic projects

In 2023, while offering day-to-day support for all the research units in securing and implementing their projects, the various branches of the Legal Affairs Department were involved in negotiations and drafted contractual documents formalizing the Institut Pasteur's key institutional partnerships with Inserm and the Paris Public Hospital Network (AP-HP), thereby facilitating collaboration for scientists in both basic and translational research.

In 2023, the legal teams also ensured a solid legal grounding for large-scale strategic projects including the Vector-Borne Diseases Center (CMTV) and two university hospital institutes (IHUs): Re-Connect (which the Institut Pasteur is coordinating via its Hearing Institute) and InovAND. Finally, at international level, the Legal Affairs Department coordinated the legal aspects of the new Institut Pasteur de São Paulo in Brazil.

Support for measures to promote "responsible science"

In compliance with the values promoted by the Institut Pasteur Ethics Charter, the Legal Affairs Department and its Ethics

Unit provide ongoing support for activities and discussions in the various committees aimed at upholding ethics and professional conduct at the Institut Pasteur, while also offering training and information for scientists and staff affected by these issues. In 2023, preparations were made for a new Charter for Scientific Integrity, in conjunction with the Scientific Integrity and Conciliation Committee (CISC), and the ground was laid for the work of the committee responsible for monitoring dual-use research, a subject on which the Institut Pasteur Ethics Committee (CEIP) delivered an opinion to the senior management team.

Finally, in 2023 the Legal Affairs Department continued its efforts to improve compliance, leading to the introduction of an anti-corruption framework (approved by the Institut Pasteur's Board of Governors) and the implementation of data protection procedures in line with the GDPR.

Support for measures to simplify processes and standards

The need to ensure the compliance of the Institut Pasteur's activities in an increasingly stringent regulatory environment is leading the department's legal experts to reflect on ways to simplify some of the processes in place at the Institut Pasteur. The focus in 2023 was on simplifying the procedure for accessing human biological resources and related data.

In conjunction with the senior management team and the Department of Communications, the Legal Affairs Department also offers its support to lobbying efforts by the Institut Pasteur to change standards that it sees as too complex, unsuitable or insufficient. 🔴

MAKING SCIENCE ACCESSIBLE

An interface between Institut Pasteur scientists and its target audiences.

the Department of Communications is committed to promoting knowledge and showcasing the role of science in our society. Its remit also includes increasing the Institut Pasteur's visibility and continually enhancing its image among its various audiences.

2023 saw a series of major events at the Institut Pasteur, all of which received extensive coverage in the traditional and social media, with highlights including the 40th anniversary of the discovery of HIV and the 17th edition of Pasteurdon. In order to forge further links with its audiences and bring its heritage to life, the Institut Pasteur continued the project launched in 2022 to revamp the Pasteur Museum. Such initiatives play an important role in making science more accessible and maintaining links with society.

Our communities

followers (+21.3% in 2023)

on social media

165.000

67.200

61.000

followers (+7%)

14.900

12.300

followers (+23%)

subscribers (+6.4%)

followers (+5%)

in

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40 years since the discovery of HIV

This anniversary was marked with interviews and articles in the media. a series of videos on www.pasteur.fr with charity-sector representatives and prominent global research figures (Dr. Anthony Fauci), a partnership with an influencer known as "the French Virologist", and a film shown in cinemas charting the history of the discovery, all of which showcased the commitment of scientists and charities to tackling the epidemic. This year also provided an opportunity to pay tribute to Françoise Barré-Sinoussi, the co-discoverer of the virus, during a day held in her honor on the Institut Pasteur campus. This was interspersed with contributions from her close collaborators and partners. A special evening event at Paris cultural venue, Ground Control, gave the public a chance to meet Institut Pasteur scientists working on HIV/ AIDS and learn about the latest research breakthroughs.



17th edition of Pasteurdon

Pasteurdon is the Institut Pasteur's annual brand and fundraising campaign aimed at the public. Pasteurdon 2023 provided a further opportunity to share the quality, diversity and progress of the Institut Pasteur's research with the general public. It also played a key part in ongoing efforts to raise funds for the research carried out by the Institut Pasteur's scientists. This year, the focus was on three key areas under the banner of "Research is part of us": tack-

FUNDAMENTALS



ling emerging infectious diseases, cancer research, and investigating neurodegenerative and brain connectivity diseases.

TO ACCESS THE PRESS KIT FOR PASTEURDON 2023, SCAN THE QR CODE (IN FRENCH).

The Pasteur Museum continues its transformation

In 2022, the Institut Pasteur embarked on a project to renovate the historical building that houses the Pasteur Museum, which was established in 1936. The building was listed as a historical monument in 1981 and recognized under the "Maisons des Illustres" scheme in 2012. In connection with this project, the decision was taken to give the museum itself a makeover by developing new exhibition and scientific outreach spaces that will be open to the public.

When the museum reopens in 2028, the aim is to raise awareness of the Institut Pasteur's historical and scientific heritage and to foster informed and constructive dialog between science and society. Two key phases were completed in 2023: the collection review, in which all objects from the museum's collection were inventoried, digitized, photographed and their condition checked, and a second phase in which collections were placed in storage to protect objects during the works.



OUR FINANCIAL RESOURCES IN 2023

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 2023 Statement of source and application of funds, the revenues reported in the income statement amounted to €373.6 million, with the following breakdown.

Revenue

breakdowr

€35.4 M 9.5%

Other revenue Use of funds previously raised (©21.7 M and reversal of provisions and depreciation (©13.7 M)

€24.6 M 6.6%

Other own revenue Sales and services (€20.9 M in particular including scientific services, purchases for resale and refunding of staff expenses with the Pasteur Network, revenue from the Medical Center), other revenue (€3.7 M)

€31.1 M 8.3%

Earnings from assets not derived from public donations (own revenue)

€20.0 M 5.4%

Industrial royalties (own revenue

Use

The revenues reported in the income statement are earmarked as follows: Institut Pasteur mission areas €275.7 M, fundraising proceeds not used during the fiscal year earmarked for mission areas €19.4 M, operation €54.2 M, fundraising expenses €19.3 M and contribution to provisions and depreciation €11.0 M, implying a deficit of €6.1 M.



€111.9 M 29.9%

Revenue linked to public donations Donations and legacies collected directly. and fundraising and earnings from assets and real estate derived from public donations €65.1 M 17.4%

Public subsidies Funct substructs Grants from the French Ministry of Higher Education, Research and Innovation and the French Ministry for Europe and Forcign Affairs, and funding for the 14 Natistry Reference Centers managed by the Institut Pasteur, which is provided by Santhé publique France €57.5 M 15.4%

Research contracts €15.2 M 4.1%

Research contracts (private financial contributions)

€12.8 M 3.4%

Industrial contracts

private financial contributions)

€75

Mission areas (research, public health, education)

€14

Fundraising expenses

€11

Operating expenditure

€373.6M Forecourt and entrance to the Francois Jacob building **REVENUE/USE**

The Institut Pasteur's assets

Havin nized tion ir hold a them

The aim of these assets is to sustain the missions over the long term.

rities.

| In 2023 | €M | % |
|---|-------|-----|
| Total | 1,039 | 100 |
| Property | 226 | 22 |
| Securities | 630 | 61 |
| Private equity/ strategic partnerships | 103 | 10 |
| Cash | 80 | 7 |

Productive assets account for the equivalent of 3.3 times the Institut Pasteur's annual operating costs (ratio set out in late 2023).

These assets generated €38.5 M during the 2023 fiscal year, reported in the income statement and representing a sharp increase in relation to 2022 (€+28.6 M) due to non-distribution of revenue from long-term investments in the past year.

FUNDAMENTALS



Earnings from assets

Cash

| g been a foundation officially recog- | In 2023 |
|--|------------|
| for its charitable status since its incep- | |
| 1887, the Institut Pasteur must also | Total |
| assets, built up over time, and make | Property |
| grow. | Securities |

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

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

| 23 | €M | % | de Nouvelle-Calédonie. | |
|-------------------|-------|-----|--|--|
| | 1,039 | 100 | | |
| erty | 226 | 22 | In 2023 | |
| rities | 630 | 61 | Institut Pasteur operating revenue | |
| te equity/ | 103 | 10 | Institut Pasteur operating expenses | |
| egic partnerships | | | Contrib. IP Guadeloupe, Guyane, NCalédonie | |
| | 80 | 7 | OPERATING INCOME | |
| | | | | |

Contrib. IP Guadeloupe, Guyane, N.-Calédonie FINANCIAL INCOME

Institut Pasteur financial result

Income statement

Institut Pasteur non-recurring income Contrib. IP Guadeloupe, Guyane, N.-Calédonie

NON-RECURRING INCOME

NET INCOME

raised

1. See adjacent chart and Institut Pasteur 2023 Use of resources statement in the financial report.

Public gifts and donations

funding sources relied upon by the

Within the range of different

Institut Pasteur, the proportion

€111.9 M was raised in 2023¹.

covered the Institut Pasteur's

of gifts and donations was stable

compared with the previous year;

In addition to its mission areas, the

public gifts and donations received

fundraising expenses and operating

For each

expenditure.

| €M |
|------|
| 38.5 |
| 8.6 |
| 26.2 |
| 3.7 |

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.

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

| €M |
|--------|
| 321.8 |
| 368.4 |
| - 1.6 |
| - 48.2 |
| 30.3 |
| 0.5 |
| 30.8 |
| 11.4 |
| - 0.1 |
| 11.3 |
| |
| - 6.1 |

In 2023, net income showed a deficit of €6.1 M as against a deficit of €1.5 M in 2022 - an increase of €4.6 M. This is due to a decline in operating income of €10.5 M and an improvement in "non-operating" (financial and non-recurring) items of €6 M.

€4.9 M of this result is due to the Institut Pasteur's Paris campus and €1.2 M to the institutes outside mainland France.

THANK YOU FOR YOUR LOYAL AND GENEROUS **SUPPORT**

We are honored and indebted for the trust you have placed in us. Your support is a huge encouragement for our scientists.

In 2023, 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.

The funds raised through the generosity of our donors, as well as our partner companies and foundations, will enable the Institut Pasteur's scientists to continue their vital work, optimize its impact and explore new avenues for research with the aim of improving our lives. Research is our primary mission and the chief focus for all our scientists. In 2023, we received support from almost 210,000 donors, over 31,000 of whom chose to set up a direct debit, which enables them to spread their donations over the entire year.

The 17th edition of Pasteurdon, held between October 4 and 8, 2023, was supported by large numbers of donors, with an even broader audience than previous editions. Alongside the Institut Pasteur's ambassador Erik Orsenna, 50 presenters and journalists from 50 partner TV and radio outlets joined forces with the Institut Pasteur to explain the importance of the work carried out by our 1,600 scientists. Key topics included neurodegenerative diseases, cancer, emerging infectious diseases and the microbiota.

Donors also attended the launch of this edition at a conference featuring the YouTuber Julien Ménielle. This was held on campus and also streamed online on the Institut Pasteur's YouTube channel.

Our maior donors

The commitment shown by major donors is vital for providing Institut Pasteur scientists with optimal conditions in which to advance biomedical knowledge for the benefit of everyone's health. Their generous longterm support allows the Institut Pasteur to develop in a way that combines a bold, inguisitive and creative approach with rigor and excellence.

We would like to sincerely thank the many people who joined the Institut Pasteur's Major Donors program this year. In particular, we would like to thank the Lefoulon-Delalande Foundation and Mr. and Mrs. Frédéric Janbon for their generous contributions.

As an individual or family foundation joining the Major Donors program, you will be involved throughout the year in the research that you have chosen to support. You will be sent scientific publications of interest to vou as well as the Institut Pasteur quarterly newsletter. Moreover, you will have access to the "Pasteur class" (a biology course for major donors delivered on a monthly basis), regular discussions with scientists, lectures, laboratory tours and "bespoke" meetings. We will listen carefully to your requirements and work with you to put together your project. For further details of this program, please contact Caroline Cutté on +33 (0)1 45 68 81 04 caroline.cutte@pasteur.fr.

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 17th 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 by offering over a dozen charitylinked products in almost 2,000 stores (Intermarché and Bricomarché). ASSU 2000, a Pasteurdon partner for the tenth year running with its ongoing support for research on microbiota, 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", enlisted large numbers of cyclists for a series of fun sponsored bike rides throughout France for the Institut Pasteur. This year, the Fondation Bettencourt Schueller provided the Institut Pasteur and one of its scientists with funding for a project on the evolutionary history of the bacterial cell envelope through its Impulscience® program.

The third edition of the Institut Pasteur's Benefactors Circle, "Les rendez-vous de Louis" gave sponsors and friends of the Institut Pasteur the chance to meet and discuss the issue of climate and health with the paleoclimatologist, Jean Jouzel. During this successful meeting, participants got to grips with the challenges facing us and clearly appraised the current situation, providing potential avenues for action.



For further information, please contact us at mecenat@pasteur.fr.





International fundraising

The new International Development Unit continued to expand in 2023, growing its team both in Paris and in our sister foundations in the United States and Switzerland. Major Institut Pasteur projects also received further support from our international donors and interest from new European foundations, marking increased international support for Institut Pasteur research.

We are proud to announce that a third sister foundation, the Pasteur Foundation – UK in the United Kingdom, was set up in 2023. Its mission is to promote collaborative research projects involving the Institut Pasteur and British research institutes.

Legacies and gifts

In 2023, the Institut Pasteur had the good fortune of receiving 179 new legacies worth €44.8 M and €22 M in life insurance gifts. Our five legal experts are responsible for handling the associated estate

administration in accordance with Apave's ISO 9001-2015-certified procedures, a guarantee of quality. Two members of the Gifts Office have been assigned to testator development and relations with a view to promoting legacies among the public and answering any questions regarding this means of making a final contribution. The media campaign to promote gifts was run in August using the existing TV spot. Our generous testators receive a special sixmonthly "Gifts" newsletter and are invited to scientific conferences for legators. The Institut Pasteur is very grateful to everyone who has chosen to support it with a legacy, donation or life insurance gift.



SPONSORS

- AG2R LA MONDIALE AGIPI Allianz Assu 2000 Carlsberg Foundation • Dennis and Mireille Gillings Foundation via Pasteur Foundation US Fondation Air Liquide Fondation BTP PLUS Fondation CFM pour la Recherche Fondation Chercher et Trouver Fondation Daniel et Nina Carasso Fondation Dassault Systèmes Fondation Del Duca Fondation d'entreprise Michelin Fondation d'entreprise Optic 2000-Lissac-Audio 2000 Fondation d'entreprise SCOR pour la science Fondation Groupama pour la santé Fondation Jacqueline Beytout Fondation Lefoulon-Delalande Fondation Le Roch-Les Mousquetaires Fondation NRJ Foundation S - The Sanofi Collective Fondation Suez
 Fondation TotalEnergies Fonds Axa pour la recherche Fonds de dotation Perfumum Fonds de dotation Villa M Gilead Sciences Groupama Nord Est • ICADE Mutuelle du Médecin Natixis Nouvelle Cassius Fondation Odyssey Reinsurance Company
- Pfizer Innovation France
- Pfizer Inc. USA
- SACEM
- SCOR
- Spastic Paraplegia Foundation, Inc
- The Joe W. and Dorothy Dorsett Brown Foundation

SINCE 2009. THE THINK TANK ON PHILANTHROPIC TRUSTS,

coordinated by the Gifts Office, has been promoting all issues relating to asset management for philanthropic purposes. As well as organizing meetings with experts every guarter, the Think Tank held the sixth edition of the Conference on Philanthropic Trusts at the Institut Pasteur on September 19, 2023 under the high patronage of the French President, Emmanuel Macron. This event addressing the future of philanthropy was attended by almost 350 French and international professionals from the sector. These meetings generated a significant amount of content, leading to the production and distribution of podcasts and articles featuring the main contributions from interviewed experts, which can be found on philanthropie.pasteur.fr and social media.



FOR FURTHER DETAILS OF THE SIXTH EDITION OF THE CONFERENCE ON PHILANTHROPIC TRUSTS, SCAN THE QR CODE (IN FRENCH)

BOARD OF GOVERNORS

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

BOARD OF GOVERNORS BUREAU

Chair: 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

Delphine D'Amarzit, Chairman and CEO of **Euronext Paris**

Grégory Emery, Director-General for Health, French Ministry for Health and Prevention

Edouard Kaminski. President of Université Paris Cité

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

Antoine Petit. Chairman and CEO of the CNRS (French National Center for Scientific Research)

Félix Rey, Head of the Structural Virology Unit, Institut Pasteur

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

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

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: Jean-Marc Ghigo. Head of the Genetics of Biofilms Unit

Vice-Chair: Caroline Demangel, Head of the Immunobiology and Therapy Unit

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

APPOINTED PASTEURIAN MEMBERS

Eduardo Rocha, Head of the Microbial **Evolutionary Genomics Unit**

Gérald Spaeth, Head of the Molecular Parasitology and Signaling Unit

EXTERNAL MEMBER

Galit Alter, Prof. of medicine at Harva Medical School, and group leader at th Institute of MGH, MIT and Harvard, US

Amos Bairoch, Prof. Department of Human Protein Science, Computer and Laboratory Investigation of Protein 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 le 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

GOVERNING BODIES

MANAGEMENT OF THE INSTITUT PASTEUR

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

Yasmine Belkaid,

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 Pierre Buffet.

Medical Director Nathalie Denovés,

Vice-President Technical **Resources and Environment**

Fanny Forgeau. Director for Transformation and Strategic Projects

Stéphane Fournier,

Vice-President Information Systems Frédéric Durand, Vice-President Human Resources

Éric Laclide.

Director for Internal Audit and

Mariana Mesel-Lemoine, Director of Diversity, Equity and Inclusion

Michael Nilges. Vice-President Technology

Françoise Perriolat. Vice-President Financial Affairs

Henri Pitron, Vice-President Communications and Public Affairs

Monica Sala, Director of the Education

Department

Odette Tomescu-Hatto. Executive Vice-Presid International Affairs

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

Samuel Valcke. Vice-President Legal Affairs



| S | |
|---------------------|---|
| ard e Ragon A | Nicholas Hastie, Prof. MRC Human Genetics Unit, MRC Institute of Genetics and Molecular Medicine at the University of Edinburgh, UK |
| 5 | Yvonne Jones, Prof. Division of Structural Biology, Henry Wellcome Building for Genomic Medicine, University of Oxford, UK |
| | Anne O'Garra, Senior Group Leader, Laboratory of Immunoregulation and Infection The Francis Crick Institute, London, UK |
| ader, | Ari Waisman, Chair and Professor of Immunology, Institute for Molecular Medicine |

University Medical Center of the Johannes

Gutenberg University of Mainz, Germany

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. Print copies were limited to reduce paper use to a minimum.

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 page 51 of this annual report for our sustainable development commitments, and to our dedicated web page for our broader commitments:

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