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EDITORIAL

Understanding immune decline

Pr Yasmine Belkaid,
Director General
of the Institut Pasteur

Ageing is inevitable, but research in this field is ongoing. It offers a fascinating area of scientific exploration.

Thanks to recent advances, we know that age-related immune decline, or immunosenescence, is not simply a consequence of the passage of time, but the result of complex mechanisms: weakening of lymphocytes, chronic inflammation, and increased vulnerability to infections and cancers.

These discoveries open up new perspectives. Research on immunity conducted on our campus reveals that each individual ages differently and that personalised therapies can slow down this process.

The stakes are high: by 2050, 10% of Europeans will be over 80 years old. Faced with this challenge, precision medicine, which considers each person's immune characteristics, is emerging as a revolution. By identifying biomarkers and developing tailored vaccines, scientists are charting a new course: not only living longer but living healthier lives.

Your support for this research is essential to better understand the mechanisms of ageing and adapt our approaches to everyone's immunity.

SPECIAL REPORT

Understanding our immunity to age better

—> A natural phenomenon that affects us all, ageing is not simply a matter of accumulating years. With life expectancy increasing, particularly in industrialised countries, the question of the quality of ageing has become central. Today, nearly 10% of the European population will be over 80 by 2050, and the number of centenarians is expected to increase 18-fold compared to 2000. This development raises major medical and social challenges.

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In this issue



Anticipating the **seasonal flu** epidemic through science



Measles: why is it reappearing?



New **Franco-Brazilian** Alliance for global health research



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We are all different in terms of our DNA and our immune defences

Although ageing is universal, it never occurs in the same way for everyone. Everyone has a unique immune heritage, inherited from their ancestors, which profoundly influences how their body functions. The immune system also retains a memory of the pathogens it has protected us against. Its composition, effectiveness and ability to adapt vary considerably from one person to another.

In addition to this genetic diversity, there are differences related to biological sex. Women and

• • •



UNDERSTANDING

What is epigenetics?

Epigenetics studies reversible and heritable modifications that influence gene activity without altering the DNA sequence itself.

It explores how external factors, such as the environment, lifestyle, diet or stress, can activate or deactivate the expression of certain genes, like a switch. These epigenetic modifications play a crucial role in the development of organisms and their adaptation to their environment.

This discipline sheds light on the origins of diseases (cancer, neurological disorders, diabetes) and paves the way for personalised treatments.

Milieu Intérieur
Vers une médecine personnalisée

ACTION PASTEUR



The “Milieu Intérieur” project: a unique study to decipher our immunity



Launched in 2011 at the Institut Pasteur and led by **Darragh Duffy** and **Lluís Quintana-Murci**, the “Milieu Intérieur” project studies the variability of the immune system in healthy individuals. Unlike research focused on specific diseases, it follows a cohort of 1,000 volunteers – 500 women and 500 men, aged 20 to 70 – over more than ten years, combining genetic and immune analyses with environmental data.

This approach has made it possible to identify disease predictors, immune differences related to gender or age, and the impact of factors such as smoking or viral infections. The results open prospects for more personalised medicine: tailored treatments (such as for tuberculosis), early detection of metabolic complications, and understanding the mechanisms of ageing. The project is now exploring the links between immunity, ageing

and epigenetics in greater depth.

By making its data available to the scientific community, the “Milieu Intérieur” project is helping to shape the future of healthcare, where prevention and precision are becoming central.

PROJECT DURATION

15 years (2012-2027)

IMPACT

More than 80 projects authorised based on the data generated

STUDY FACTORS

11 factors influencing our immunity identified (age, biological sex, genetics, CMV infection, smoking, epigenetics, microbiota, BMI, diet, social status, body temperature and hormone treatments)

PARTNERSHIP

12 academic partnerships and 4 industrial companies (4 patents filed)

APPLICATIONS

20 clinical studies (lupus, type 1 diabetes, multiple sclerosis, etc.)



Annual meeting of the LabEx “Milieu Intérieur” on 24 October 2025.



men do not have the same immune defences, nor the same ageing trajectories.

Women generally have a stronger immune response but are also more susceptible to certain autoimmune diseases. Men, on the other hand, experience a sometimes earlier or more pronounced decline in immunity, with specific consequences for long-term health.

“LabEx Milieu Intérieur” is a large-scale French research project to understand the variability of the immune response

It is precisely to better understand this diversity that the “LabEx Milieu Intérieur” programme was launched. This vast French research project, bringing together 45 laboratories, aims to define what constitutes a “healthy” immune system and to measure its natural variability within a cohort of 1,000 healthy adults (see box on previous page).

In 2021, ten years after the programme was launched, the same cohort was studied again. This longitudinal approach offers a rare opportunity to observe how the immune system evolves over time in individuals who were initially healthy. And thus, to better understand the complex mechanisms that link ageing and the immune system. They first show that immune ageing is neither linear nor uniform. It is based on the interaction of several biological phenomena that evolve at different rates depending on the individual.

The four main lessons concerning ageing

One of the major findings concerns the gradual onset of **low-grade chronic inflammation** (or inflamm'aging). This diffuse inflammation, which is not very noticeable clinically, develops with age and creates a favourable environment for the development of many chronic diseases, such as cardiovascular disease and type 2 diabetes or certain neurodegenerative diseases. It also acts as a factor in the exhaustion of the immune system, constantly taxing the body's defences.

Autoimmune diseases are another important lesson. As we age, the immune system can become dysregulated and less able to distinguish between what belongs to our body and what is truly foreign to it, such as viruses or bacteria. It may then mistakenly attack healthy cells, causing unnecessary inflammation. These malfunctions promote the onset or worsening of autoimmune diseases, the frequency and intensity of which vary from person to person, particularly depending on gender and heredity.

Persistent viral infections, particularly those caused by viruses of the herpes family, such as cytomegalovirus, also play a key role. These viruses, which can remain dormant for decades, mobilise the immune cells responsible for controlling them on a long-term basis. In the long term, this constant mobilisation contributes to the depletion of the reservoir of immune cells capable of responding to new infectious agents.



“Milieu Intérieur” study

Biological sex shapes our immunity

Molly Ingersoll

Mucosal Inflammation and Immunity Unit

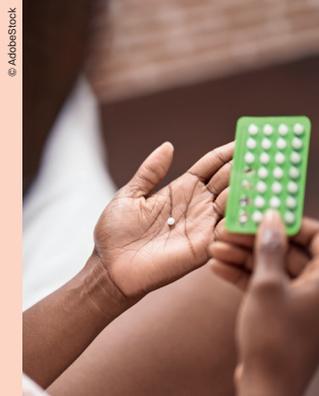


© M. Ingersoll

The differences between women and men when it comes to disease are striking; for example, 50% of women will suffer from a urinary tract infection during their lifetime, compared to only 10 to 15% of men. Conversely, bladder cancer affects three times more men, but when women do develop it, they are often diagnosed at a more advanced stage and have a poorer prognosis. These disparities raise a fundamental question: why do immune responses and health trajectories differ between the sexes?

Molly Ingersoll's team is tackling this very puzzle by studying under-explored mucosal sites such as the bladder. Their hypothesis is based on the influence of hormones. Steroids (oestrogens, progesterone, androgens, cortisol), which act as powerful modulators of the immune system.

To answer this question, the team collaborated with the “Milieu Intérieur” consortium and analysed 17 different hormones in the blood of volunteers from the cohort, around 500 of whom returned to provide samples again ten years later. This longitudinal follow-up provides insight into hormonal changes over the course of ageing.

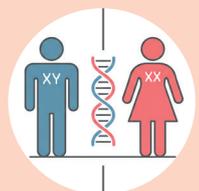


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Their results are revealing. Female hormonal contraception alters almost the entire steroid landscape, including cortisol and cortisone, which regulate stress and immunity. This little-known systemic impact raises questions about the long-term effects on metabolism and resistance to infections or other diseases. Menopause proves to be a critical turning point: the rapid decline in oestrogen and progesterone

is associated with increased susceptibility to bladder infections and changes in the tumour characteristics of bladder cancers. In male smokers, an unexpected correlation appears between smoking and androgens, which does not exist in women, revealing a relationship between specific levels of male hormones and environmental disruptors. Finally, the ten-year follow-up shows that, surprisingly, a marked decrease in progestogens is associated with an increased risk of disease only in male donors.

This study has its limitations: it establishes correlations, not causalities. But its strength lies in the quality of the data sets, and in its rare and valuable nature. The data will serve as a global reference. Future projects aim to separate the effects of hormones from those of X/Y chromosomes and to personalise treatments according to gender. The challenge is to adapt medicine to the actual biology of women and men, for fairer and more effective care for everyone.



Étienne Patin

↳ Director of Research, Human Evolutionary Genetics Unit at the Institut Pasteur



© P. Imbert / Collège de France

“Ancient DNA acts as a temporal microscope for observing how human populations have responded to pathogens over thousands of years”

The “Milieu Intérieur” project is a unique scientific adventure. What is your role in this project?

“Milieu Intérieur” is an ambitious project that aims to understand the variability of the human immune system by integrating immunological, genetic, epigenetic and environmental data. We aim to identify the main genetic and environmental factors affecting the variation in immune response in the general French population. Within the consortium, I am seeking to determine the causes of immune ageing and to better understand how DNA alterations influence the immune response with age. I also coordinate the analysis and management of the very large volumes of data generated, through the programme, ensuring that the results are robust and usable.

How is ancient DNA sequencing revolutionising our understanding of the immune system?

For geneticists, ancient DNA sequencing is equivalent to the discovery of the microscope in microbiology. We can now directly observe how human populations and their pathogens have evolved over millennia, rather than relying on theoretical models.

This approach reveals the causes of historical pandemics such as the Black Death. By comparing the genomes

of victims and survivors buried in Toulouse in the 14th and 15th centuries, we found that several genes suspected of being involved in susceptibility to the plague do not appear to be involved. This suggests that non-genetic factors (nutrition, conditions life) played a key role in this pandemic, which killed between 30 and 60 per cent of the European population.

Was agriculture really the major turning point in the evolution of the human immune system?

In science, certain plausible hypotheses, such as the epidemiological transition linked to agriculture, become dogma. However, our data show that the Bronze Age was much more decisive for the immune system in Europe. This can be explained by urbanisation, mass migration and increasing population sizes, which promoted the spread of pathogens and made natural selection more effective. Reevaluating these theories is crucial to better understand the causes of the demographic crises that have marked the history of our species, and the evolutionary mechanisms that have shaped our immunity.

You also work on Polynesian populations. What lessons have you learned from these studies, particularly regarding metabolic diseases?

Together with my colleagues Lluís Quintana-Murci and Van-Mai Cao-Lormeau, we sequenced 1,800 modern genomes to study the history of settlement and susceptibility to metabolic diseases. Contrary to popular belief, our results do not support the idea that the current obesity epidemic is due to an increased genetic risk in Pacific populations. It is clearly linked to recent environmental

factors, such as sudden changes in diet. Polynesians now consume ultra-processed foods, and their obesity rate has risen from 0% in the 1950s to 50% today. This result raises questions about the impact of gene-environment interactions in modern diseases.

Your research shows that mutations that promote resistance to infections also increase the risk of autoimmune diseases. How do you explain this paradox?

This paradox ceases to be one when understood in the light of evolutionary theory: the mutations that have protected us from infections can become harmful in a less infectious environment. For example, a mutation in the TLR1 gene, which increases resistance to pathogens, is also associated with an increased risk of allergies and asthma. In a hygienic environment such as ours, these mutations no longer confer a selective advantage and may even promote autoimmune diseases. This phenomenon could contribute to the prevalence of allergies and autoimmune diseases in modern societies.

What are the future challenges for your research?

To better understand our health history, we need to develop new approaches to trace the causes of death of our ancestors, such as estimating age at death from ancient DNA using markers linked to ageing. We also want to study other epidemics, such as those that wiped out up to 90% of the Polynesian population when Europeans arrived, or smallpox and Spanish flu, even though this poses technical (ancient viral genomes are difficult to sequence) and ethical challenges (the descendants of recently deceased individuals are identifiable). Each ancient skeleton is a piece of the puzzle of our biological history. Our health is the result of a complex history, where genes and environment intertwine.



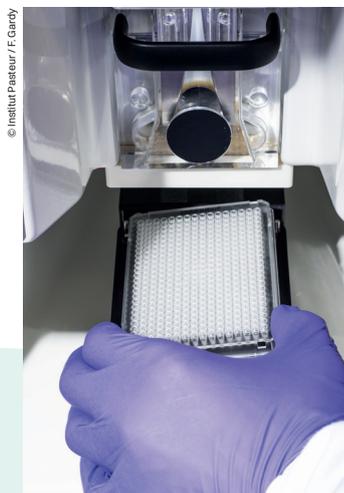
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UNDERSTANDING

Single-cell sequencing

Single-cell sequencing is a cutting-edge technology that analyses RNA cell by cell, revealing their diversity and individual functioning.



© Institut Pasteur / F. Gandy

Thanks to advances in microfluidics, the genomic content of a single cell can be sequenced.

Using microfluidic systems, it identifies cell subpopulations, such as tumour cells that are resistant to treatment, or rare subpopulations that appear with age and are undetectable by conventional methods.

In oncology, it makes it possible to distinguish healthy cells from malignant cells and refine therapeutic targets.

This approach is revolutionising diagnostics, personalised treatments and understanding of diseases.

Finally, the concept of the **epigenetic clock** sheds new light on ageing. It shows that chronological age does not always reflect the actual state of our cells. Environmental, behavioural or infectious factors can accelerate or slow down biological ageing. The epigenetic clock is therefore a promising tool for assessing the individual trajectory of immune ageing and anticipating the risks of age-related diseases. It can be used to estimate the actual biological age of cells, regardless of chronological age. Two people of the same age may therefore experience very different cellular ageing, depending on genetic, environmental or behavioural factors. This clock is a valuable tool for anticipating changes in the immune system and identifying possible courses of action.

Towards the emergence of personalised medicine for ageing

All of these observations point to one clear conclusion: a uniform approach to health is no longer sufficient given the diversity of immune profiles and ageing trajectories. Understanding ageing now requires considering each individual's biological age, genetic makeup, infectious history and lifestyle.

Continued on p.6



"Milieu Intérieur" study

Unlocking the secrets of immunity according to age, gender and vaccination

Marwan Sharawy

Human Evolutionary Genetics Unit at the Institut Pasteur



© J. Ono

Our immune system is not static: it evolves throughout our lives, shaped by factors such as age, gender and vaccination history. Thanks

to cutting-edge technologies such as single-cell sequencing (see definition above), these variations can be analysed, revealing the mechanisms of age-related immune decline.

By exposing the blood cells of 380 individuals from the "Milieu Intérieur" cohort to pathogens such as SARS-CoV-2 or the influenza virus *in vitro*, it was demonstrated that older people have a weakened immune response, particularly due to reduced production of interferon alpha, a protein crucial for blocking viral replication. "At the same time, analysis of all genes shows that CD4 T lymphocytes are the cell type most affected by age", adds the researcher.

Their work also confirms that women have a stronger immune response than

men, a paradox known as the mortality-morbidity paradox: although they live longer on average, they are also more prone to autoimmune diseases. "In women, innate immune cells, such as myeloid cells, react more vigorously to viruses, with increased expression of pro-inflammatory genes", explains the researcher.

This superiority can be explained in part by their two X chromosomes: certain genes escape inactivation of the second X chromosome, giving them an immunological advantage.

Conversely, men over the age of 60 often lose their Y chromosome (up to 50% in some cases), a phenomenon that the team has linked for the first time to a weakened immune response.

"This loss could explain why men are more vulnerable to severe infections as they age", says Marwan Sharawy.



CD4 T lymphocyte viewed under a scanning microscope.

© Institut Pasteur / O. Schwartz and Microscopy Platform / Electron Microscope Platform

These discoveries open promising prospects for maintaining robust immunity despite age. "If we can understand why some elderly people maintain a strong immune system, we may be able to replicate these conditions in others", hopes Marwan Sharawy. His findings could inspire new therapeutic approaches, such as targeted stimulation of interferon alpha. "The goal is not just to live longer, but to age in better health", he summarises.



“Milieu Intérieur” study

Smoking leaves lasting traces on our immune system

Violaine Saint-André

Translational Immunology Unit at the Institut Pasteur & Bioinformatics and Biostatistics HUB



© Institut Pasteur / T. Lang

Smoking leaves a lasting mark on the immune system, even up to 40 years after quitting.

Cigarettes influence our defences as profoundly as age or gender, by altering the production of cytokines, key proteins in the immune response.

This mark persists due to epigenetic modifications – alterations in gene expression without changes in DNA – affecting immunomodulators. Thus, for certain immune responses, former smokers retain an immune profile like that of active smokers, despite years of abstinence. The message is clear: it is never too late to quit smoking, although it is best not to start in the first place.

Analysis of the “Milieu Intérieur” cohort also revealed two other factors that strongly influence our immune system. The first is human cytomegalovirus (HCMV), a very common virus that permanently alters certain immune cells. The second

is being overweight: a high body mass index (BMI) disrupts the production of important immune messengers, such as interleukin-2.

To isolate these effects, the researchers stimulated blood cells with pathogens and cross-referenced the results with 136 variables (socio-demographic, lifestyle habits, etc.). Advanced statistical analyses confirmed that smoking, CMVH and BMI influence immunity independently of age and gender, with persistent DNA alterations in former smokers.

These discoveries open major prospects for public health.

The team is now studying the influence of the exposome (everything we are exposed to in our lives: pollution, food, stress, chemicals, viruses, etc.) on immunity and seeking to identify the metabolic and epigenetic pathways involved. *“Understanding how our environment shapes our immunity will enable more*



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targeted prevention strategies”, emphasises Violaine Saint-André. *“The expression of our genes is highly regulated”,* the researcher explains. Our choices and our environment matter, and identifying the right levers, such as quitting smoking and eating a balanced diet, allows everyone to influence their health capital.

... This awareness paves the way for more personalised medicine based on the identification of specific biomarkers¹. These markers make it possible to assess the state of the immune system, detect imbalances at an early stage and adapt prevention and management strategies. It is thus becoming possible to offer tailored vaccination schedules, target persistent viral infections more effectively, or implement specific measures to limit chronic inflammation.

Beyond prevention, this personalised medicine also aims to optimise treatments, considering the specific characteristics of each patient. The objective is twofold: to improve the effectiveness of medical interventions and reduce adverse effects, while supporting everyone towards healthier ageing.

The combination of prevention, personalisation and targeted interventions is shaping the future of ageing care.

Given the diversity of immune profiles and ageing trajectories, medicine must become more personalised and offer tailor-made strategies: optimisation of vaccines, personalised nutritional recommendations or targeted lifestyle adjustments. But the innovations don't stop there: promising therapeutic avenues are emerging, such as gene therapy and epigenetic interventions, which could one day enable us to ‘rewind’ our biological clock. By targeting chronic inflammation or stimulating immune cell regeneration, these approaches could prolong our health, far beyond simple longevity.

Living longer... in good health

The combination of prevention, personalisation and targeted interventions is shaping the future of ageing care. Anti-inflammatory and antiviral treatments currently in development, combined with a better understanding of our DNA, could revolutionise the quality of life for older people. Not only will they live longer, but above all they will age in good health, with a resilient immune system and a body better equipped to fight age-related diseases.

REPORT BY THE EDITORIAL TEAM

1. Measurable biological indicators (in blood, tissue or cells) that can be used to assess an organism's state of health, detect disease, monitor its progression or measure the effect of treatment.



PROFILE

Agnes* Ullmann 1927-2019

An iconic and visionary figure in molecular biology

Agnes Ullmann, a French microbiologist of Hungarian origin, embodied passion and courage. A survivor of totalitarian regimes, she became a leading figure in molecular biology at the Institut Pasteur. Her career, marked by exile and a tireless quest for knowledge, illustrates the rare combination of scientific rigour and humanism.

Origins and education

Born in 1927 in Transylvania, a region with shifting borders that was at times Romanian, Hungarian or Ottoman, Agnes Ullmann grew up in a multicultural environment. A polyglot (Hungarian, Romanian, German, French and English), she developed an insatiable curiosity for science and sport. The Second World War broke out when she was only twelve years old, but neither deprivation nor political upheaval dampened her passion for swimming, skiing or chemistry. After studying in Cluj, then in Budapest under Stalinist rule, she obtained a doctorate in microbiology from the University of Budapest in Hungary in 1949.

Exile and meeting Jacques Monod

In 1956, she became actively involved in the Hungarian Revolution, an uprising crushed by Soviet tanks. Under threat, she fled her country in 1960 with the help of Jacques Monod, a French biochemist whom she had admired since his 1948 article denouncing Lysenko's pseudoscientific theories. At the Institut Pasteur, she joined his laboratory, the legendary "attic", which she jokingly called "*Avenue de l'Opéron*"¹. She was referring to the bustling atmosphere of the place and the discovery of the first genetic regulatory system, called the "operon", which earned André Lwoff, François Jacob and Jacques Monod the Nobel Prize in Medicine in 1965. There she made some groundbreaking discoveries: genetic fusion, α -complementation and the study

of allosteric mechanisms in enzymes. Her work on adenosine (cAMP) revealed its role in genetic regulation in *Escherichia coli* and paved the way for vaccine applications, particularly against whooping cough. She ultimately spent 55 years at the Institut Pasteur. "*That's quite a long time*", she said in 2012 on France Culture radio, with her inimitable Central European accent. To those who were surprised by her longevity in scientific practice, she replied: "*I don't know how to do anything else...*"

Scientific and humanistic legacy

A woman of courage and culture, as well as a committed teacher, she chaired the scientific committee of the Jacques Monod Foundation which organises international conferences and trains generations of researchers. His will continues his commitment: an annual prize now rewards a young researcher in molecular biology or microbiology, perpetuating his legacy of high standards and passion.

** No accent due to her Hungarian origin.*



© S. Touillon

KEY DATES

- 14 April 1927:** born in Szatmar (Satu Mare, north-western Transylvania, now part of Romania)
- 1947:** she crossed illegally into Hungary and enrolled at the Faculty of Science in Budapest
- 1956:** political involvement leading to active participation in the Hungarian Revolution
- 1958 - 1959:** internships in the laboratory of Jacques Monod, then head of the Cellular Biochemistry department at the Institut Pasteur
- 1958:** obtained her doctorate in natural sciences at the University of Budapest, where she was appointed lecturer
- 1960:** moved permanently to France as a Rockefeller fellow at the Institut Pasteur. Granted political refugee status
- 1962:** research fellow at the CNRS, then senior research fellow (1968-1986), and director of research from 1986
- 1966:** obtained French nationality
- 1976:** lecturer in general microbiology at the Institut Pasteur
- 1978:** Head of the Cellular Regulation Biochemistry Unit at the Institut Pasteur
- 1982-1995:** Director of Research Applications at the Institut Pasteur
- 25 February 2019:** died in Paris at the age of 92. She donated her body to science and bequeathed all her possessions to the Institut Pasteur

Knight of the National Order of Merit (1984), Grand Cross of the Legion of Honour (1996), Robert Koch Medal (2002), Honorary Doctorate from Sapienza University, Rome (2007).

Archives held at the Pasteur Institute Archives: webext.pasteur.fr/archives/ull1.html

Tribute to Agnes Ullmann in the greenhouse of the Institut Pasteur in Paris on 11 December 2024.

The historic building of the former Institut Pasteur hospital now bears her name.

From left to right: Prof. Yasmine Belkaid, Director General of the Institut Pasteur; Monica Sala, Vice-President of Education at the Institut Pasteur; and His Excellency Georges de Habsburg-Lorraine, Hungarian Ambassador to France.

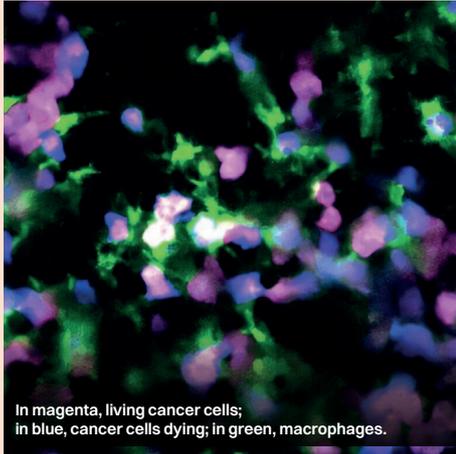
1. An operon is a group of genes that are clustered together and controlled together in bacteria, allowing several proteins to be produced at once.



NEWS

An innovative triple therapy for cancer

Immunotherapies are transforming cancer treatment by mobilising the immune system against tumour cells. A recent breakthrough is a triple therapy capable of reprogramming the death of malignant B cells, triggering an intense immune response. This approach opens up new possibilities for treating blood cancers such as lymphomas and leukaemias.



In magenta, living cancer cells; in blue, cancer cells dying; in green, macrophages.

Using advanced imaging techniques, interactions between immune and cancer cells were analysed in real time, revealing how necroptosis (a form of programmed cell death) transforms tumour cells into warning signals. This study represents a major breakthrough for B-cell lymphomas and leukaemias, which are often resistant to conventional treatments, and paves the way to more effective immunotherapies.

* Work led by Philippe Bousso, head of the Immune Response Dynamics Unit (joint Inserm at the Institut Pasteur).

SEASONAL FLU

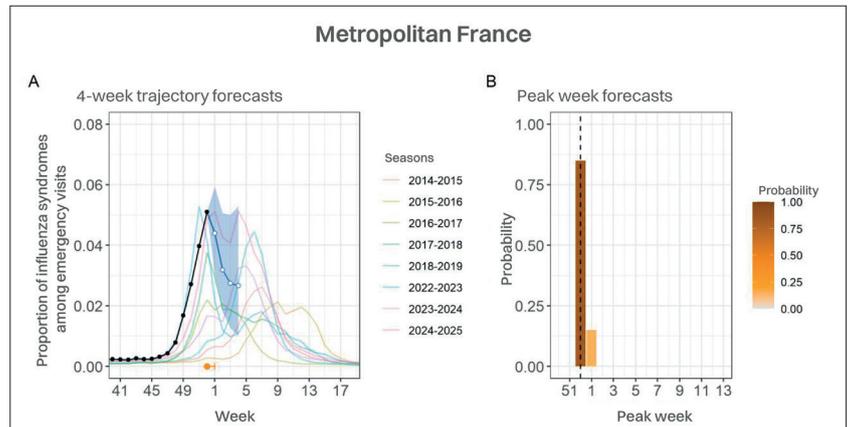
Anticipating the epidemic thanks to science



Seasonal flu, which affects 2 to 6 million people every winter in France, causes tens of thousands of hospitalisations and nearly 9,000 deaths, especially among the most vulnerable. To anticipate its impact, mathematical models analyse factors such as behaviour, viral strains and seasonality.

The Institut Pasteur and *Santé publique France* publish weekly forecasts on the evolution of the epidemic, at national and regional level, enabling its trajectory over four weeks and the probable date of the peak to be estimated. This data helps the authorities to adapt care and preventive measures.

Annual vaccination and protective measures (masks, hand washing, ventilation) remain the best forms of protection. However, forecasts have limitations due to model uncertainties and external factors.



Two visual tools facilitate their interpretation: curves showing the evolution of the epidemic with a confidence interval, and a graph indicating the probability of the peak per week. These tools, although imperfect, are crucial for better preparing the response to this unpredictable disease.

* Provision by the Institut Pasteur of a dedicated space for consulting this work, carried out by the Mathematical Modelling of Infectious Diseases Unit, headed by Simon Cauchemez.

BACTERIOLOGY

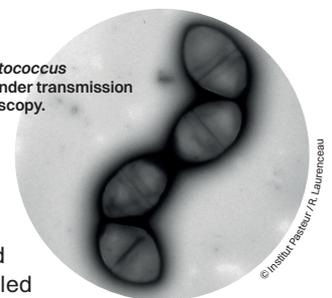
A new class of molecule against resistant bacteria

French researchers have developed a promising innovation to combat pneumococcus (*Streptococcus pneumoniae*), a bacterium responsible for severe pneumonia and meningitis. In the face of growing antibiotic resistance, this discovery opens up new possibilities.

The principle is based on aptamers, small fragments of DNA that function like homing missiles: they are designed to recognise and attach themselves to a specific target, in this case the pneumococcus. Imagine a key that can only open one lock: the aptamer only binds to its target bacterium, ignoring the others.

* Study conducted by Marcel Hollenstein, head of the Bioorganic Chemistry of Nucleic Acids Unit at the Institut Pasteur, Gilles Gasser of the Institute of Chemistry for Life Sciences and Health (Chimie Paris Tech-PSL), and Mélanie Hamon, head of the Chromatin and Infection Unit at the Institut Pasteur.

Chain of *Streptococcus pneumoniae* under transmission electron microscopy.





DISEASES

What is endometriosis?



Endometriosis is a chronic and often painful gynaecological condition characterised by the presence of tissue similar to the endometrium (the lining of the uterus) outside the uterine cavity.

Endometriosis affects approximately 1 in 10 women of childbearing age worldwide, or approximately 180 million people, and represents a major public health issue due to its impact on quality of life, fertility and social costs.

Symptoms vary greatly from person to person: some women have no apparent signs, while others suffer from chronic debilitating pain, intense fatigue, digestive or urinary disorders. Diagnosis is often long and difficult, with an average delay of 7 to 10 years in France, as the symptoms are sometimes confused

with those of other conditions (irritable bowel syndrome, cystitis, etc.). It is based on a clinical examination, a pelvic or endovaginal ultrasound scan, an MRI scan, and sometimes surgery with biopsy to confirm the presence of lesions. Endometriosis is also a major cause of infertility, as it can alter the quality of the eggs, block the fallopian tubes or create an inflammatory environment that is hostile to conception.

The exact causes of endometriosis remain poorly understood, but several theories coexist: retrograde menstruation (where menstrual blood flows back into the fallopian tubes instead of being evacuated), genetic, immune or environmental factors (such as exposure to certain pollutants). There is currently no cure, but there are solutions to relieve the symptoms: painkillers (non-steroidal anti-inflammatory drugs), hormone treatments (contraceptive pill, hormonal IUD to block menstruation), or surgery (removal of lesions). In cases of infertility, assisted reproductive technology (ART) may be offered.

In recent years, campaigning by associations and media coverage have led to greater awareness of the disease, accelerated research and improved care, although progress is still needed, particularly in terms of early diagnosis and innovative treatments.

Measles: why is it reappearing?



Measles, a disease that can be prevented by vaccination, is making a worrying comeback in 2025. According to *Santé publique France*, 858 cases were reported between January and October 2025, compared to 483 for the whole of 2024.

In the United Kingdom, 742 cases were recorded between January and August 2025, following a record peak of 2,911 cases in 2024, the highest level since 2012. In the United States, 1,454 cases were reported between January and September 2025, compared to only 344 in the period 2023- 2024. Across Europe and Central Asia, cases doubled between 2023 and 2024, reaching 127,300 reports.

This resurgence can be explained by three factors. The Covid-19 pandemic disrupted routine vaccinations, creating cohorts of unvaccinated children. At the same time, mistrust of vaccines has grown, fuelled by anti-vaccination movements and misinformation. Finally, as measles is highly contagious, 95% vaccination coverage is required to eradicate it. However, this threshold is no longer being met in many countries.

The measles-mumps-rubella (MMR) vaccine remains extremely effective. In France, two doses (at 12 months and



around 16-18 months) offer nearly 100% protection with immunity sustainable. A study shows that immunity only decreases by 0.22% per year. Since 1974, vaccination has prevented 94 million deaths, according to the Vaccine Alliance (GAVI).

The myth of a link to autism persists, stemming from a fraudulent publication in 1998. Since then, numerous large-scale studies have confirmed that there is no link between the MMR vaccine and autism spectrum disorders.

Measles affects all age groups. In 2025, the median age of cases in France was 17, and in the United States, 34% of cases involved adults over the age of 20. Complications are serious: respiratory in infants under one year of age, neurological with risk of sequelae or death in adults.

This epidemic is a wake-up call. It reminds us of the importance of maintaining high vaccination coverage and combating misinformation. The MMR vaccine is safe, effective and essential for protecting individuals and the community. Without collective action, this preventable disease will continue to spread, putting the most vulnerable populations at risk. Vaccination remains our best defence.



INTERNATIONAL

ASIA-PACIFIC

Sustainable collaboration on emerging infectious diseases



The 25th anniversary of the HKU-Pasteur Centre was celebrated on 26 November 2025 at a symposium bringing together researchers from the Institut Pasteur, the Pasteur Network and their international partners.

Part of the University of Hong Kong's Faculty of Medicine, this centre is a key player in research on emerging infectious diseases in the Asia-Pacific region. During the Covid-19 pandemic, its teams developed diagnostic tests for SARS-CoV-2, which were distributed within the Pasteur Network. The centre also contributes to scientific training with courses in immunology, cell biology and virology, having trained more than 1,000 interns, as well as a scholarship programme for doctoral and post-doctoral students, supported by the Consulate General of France in Hong Kong and Macao, The *Légion D'honneur* Club Hong Kong Chapter Association Limited and the Pasteur Foundation Asia.



From left to right: Darragh Duffy, Head of the Translational Immunology Unit at the Institut Pasteur; Malik Peiris, Co-Director of the Centre for Immunology and Infection (C2i); Yves Saint-Geours, Chairman of the Board of Directors of the Institut Pasteur; Roberto Bruzzone, Co-Director of C2i; Odette Tomescu-Hatto, Director of International Affairs at the Institut Pasteur; Leo Poon, Co-Director of the HKU-Pasteur Research Centre; James Di Santo, Head of the Innate Immunity Unit at the Institut Pasteur; Vincent Rouilly, Research Engineer in the Translational Immunology Unit at the Institut Pasteur.

In 2020, the partnership has been strengthened with the creation of the Centre for Immunology and Infection (C2i), supported by the Hong Kong government. Led by Professors Leo Poon, Roberto Bruzzone and Malik Peiris, the C2i is notably conducting the Healthy Human Global Project, adapted from the "Milieu Intérieur" project set up at the Institut Pasteur in Paris, to develop personalised immune monitoring in Hong Kong.

BRAZIL

New Franco-Brazilian Alliance for global health research

PRISME-Brazil, the International Research Platform for Global Health, was launched on 1st October 2025 in Fortaleza. Led by the Institut Pasteur, in collaboration with the Brazilian Ministries of Health and Science, Fiocruz, CNPq, and French partners (Inserm, ANRS-MIE, IRD, Institut Pasteur of Guyane), this initiative aims to strengthen scientific cooperation between France and Brazil.

Designed since 2022 by ANRS-MIE and its partners, PRISME goes beyond traditional bilateral partnerships to bring together institutions engaged in health research, particularly on infectious diseases. It promotes collaborative projects, scientific events and training courses in support of national programmes to combat HIV/AIDS, hepatitis, tuberculosis and emerging infections, as well as epidemic preparedness and the impact of climate change on health.



From left to right: Olivier Steffen, Head of International Relations, Inserm; Odette Tomescu-Hatto, Director of International Affairs at the Institut Pasteur; Yazdan Yazdanpanah, Director of ANRS-MIE; Mariângela Simão, Secretary of Health and Environmental Surveillance, Brazilian Ministry of Health; Emmanuel Lenain, French Ambassador to Brazil; Maria de Lourdes Aguiar Oliveira, Vice-President of Global Health and International Relations, Fiocruz; Abdel Sifeddine, IRD representative in Brazil; Raquel Coelho, Deputy Scientific Director of CNPq; Christophe Peyrefitte, Director of the Institut Pasteur of Guyane.

This alliance aims to stimulate innovation in global health by bringing together French and Brazilian expertise to respond to current health challenges and future.



BEQUESTS AND LIFE INSURANCE

Support long-term research, through bequests and life insurance

You may have seen us on television, in the press, or on the web. From 12 to 25 January, the Institut Pasteur ran a media campaign on the theme of charitable giving. It is possible to organise your estate by deciding to bequeath all or part of your assets to the Institut Pasteur.

To do so, simply draw up a will, which will only take effect upon your death. Next March, we will also be promoting life insurance online, a savings product that can be a remarkable tool for passing on your

estate in support of our biomedical research. If you have not seen our TV advert, or if you would like to find out more about associating your name with tomorrow's medical advances, visit our website legs@pasteur.fr. You can download our brochure (only in french) on these topics free of charge and with no obligation.

Leaving a bequest or life insurance policy to our charitable foundation provides direct support, free of inheritance tax, to our researchers who are working tirelessly to combat the diseases that threaten us.

We are available to advise you on the options available to you based on your family and financial situation. You can contact our dedicated team on +33 (0)1 40 61 32 03, or by email at legs@pasteur.fr.

Thank you very much for your support.



GENEROSITY

Charity initiative

On the occasion of Epiphany, Intermarché stores joined forces with the Le Roch-Les Mousquetaires Foundation in a large-scale charitable initiative from 6 to 18 January.

For every galette des rois sold, the Foundation donated a portion of the proceeds to support research into food safety.

We would like to warmly thank them for this delicious initiative in support of research at the Institut Pasteur!



AT THE HEART OF PASTEURIAN HERITAGE

Our historic building and its museum are getting a facelift

A major building, both from the point of view of the history of science and the history of architecture, the entire building has been listed as a historic monument since 1981.

It consists of two rectangular buildings connected at their centre by a longitudinal gallery. The first building mainly houses the apartment of Louis and Marie Pasteur, which became a museum in 1936; the Hall of Acts and Louis Pasteur's laboratory on the ground floor. The second building is dedicated to the Institute's three founding missions, as stated in Louis Pasteur's inaugural speech: "Our Institute will be both a dispensary for the treatment of rabies, a research centre for infectious diseases and a teaching centre for studies relating to microbes".

The project aims in particular to integrate the apartment-museum into a redesigned visitor route throughout the building, with new spaces dedicated to exhibitions and mediation.

The project is expected to be completed by the end of 2028, marking the 140th anniversary of the inauguration of the Institut Pasteur.



View of the façade of the historic Institut Pasteur building around 1900-1910.

© Institut Pasteur / Pasteur Museum

Follow the project on video

To recount the museum's transformation and preserve a living record of it, the Institut Pasteur museum has produced a web documentary (only in French) tracing the different phases of the project. The first three episodes can be found on the museum's website www.pasteur.fr/fr/institut-pasteur/musee-pasteur

EPISODE 1:
"Le musée s'emballe"
(The museum gets excited)

EPISODE 2:
"Le musée déménage"
(The museum moves)

EPISODE 3:
"Les archis s'en mêlent"
(The architects get involved)



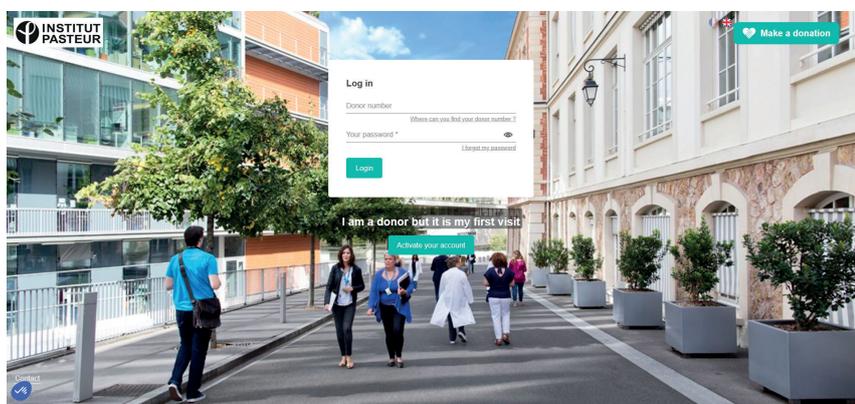


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Please also ensure that you have **provided your email address** to the Institut Pasteur so that your account can be activated.

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Your annual tax receipt for your donations by regular direct debit in 2025 is also available in this space. It will be sent to you by email or post, depending on your communication preferences.

This space also allows you to make an online donation or change your regular payments, view your donation history, update your contact details and easily contact our Donor Relations Department.

Finally, you will find several useful documents to download: our welcome brochure, our annual report and summary of our accounts, as well as the last four issues of *La lettre de l'Institut Pasteur*.

IN MEMORIAM

At the beginning of the year, we learned of the passing of Corinne Jamma, editorial manager of La lettre de l'Institut Pasteur for more than 20 years.

Her commitment and professional standards greatly enriched this quarterly magazine. This issue of La lettre de l'Institut Pasteur is dedicated to her.



Subscription and/or support form

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Please return to:
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