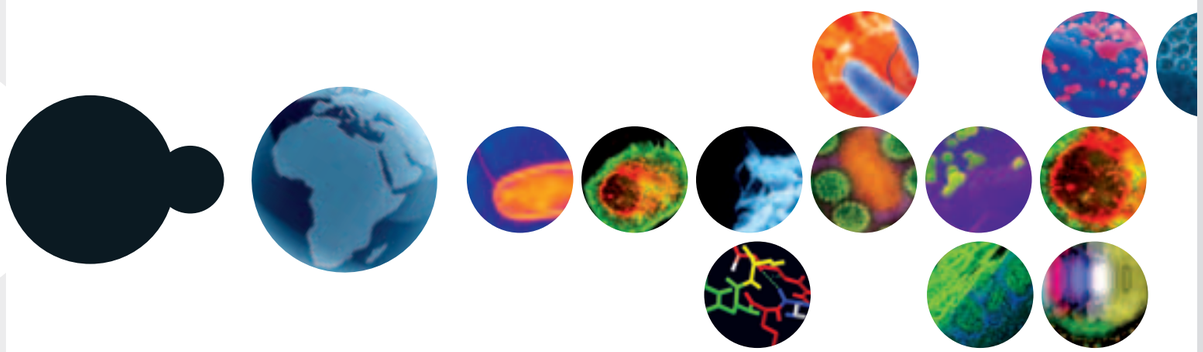
Institut Pasteur

excellence in research

ANNUAL REPORT 2010

the essence of the Institut Pasteur



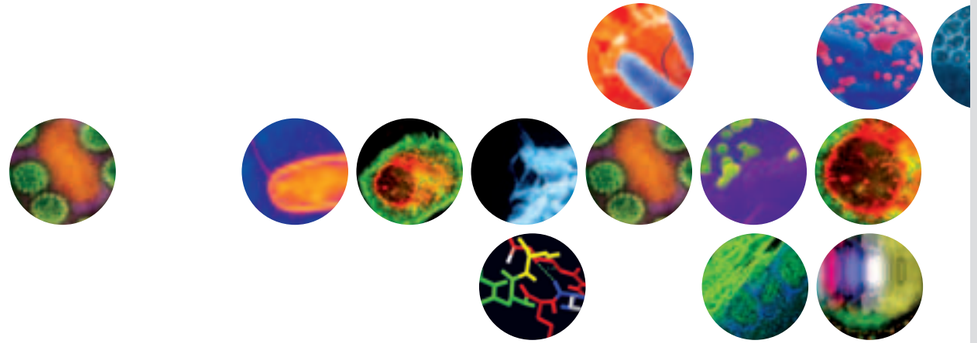
14 technological platforms

130 research entities

I so wish I could have known Mr. Pasteur...

Hawa Yaffa – Laboratory Aide

at the **heart** of global challenges



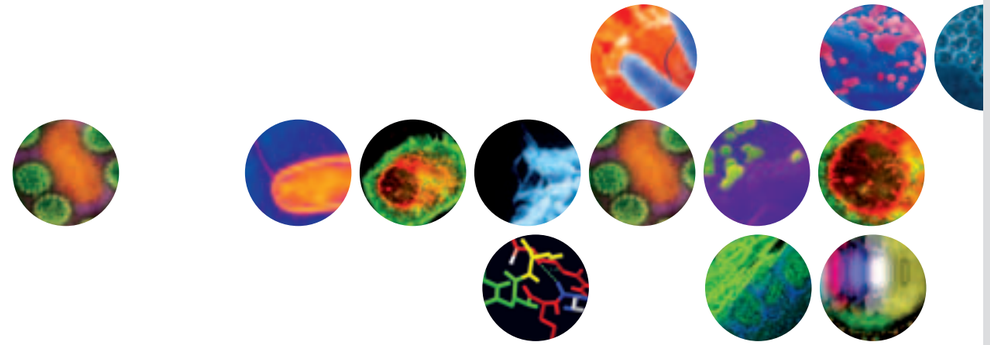
Determined to find answers to the problems raised by the emergence of new diseases, the Institut Pasteur applies all its expertise in the areas of infectious diseases, neuroscience, developmental biology, genetics, and genomics to research and global public health. Its laboratories, along with the National Reference Centers and WHO Collaborating Centers they host, often in cooperation with leading international players, are committed to making progress in life sciences, and more particularly to furthering knowledge of viruses, bacteria, parasites, and fungi.

10 Nobel laureates

I came to work at the Institut Pasteur inspired by the words of Jacques Monod: "What is true for bacteria is also true for elephants." Here, everyone can give their best.

Didier Mazel – Unit and Department Head

at the **forefront** of biomedical research

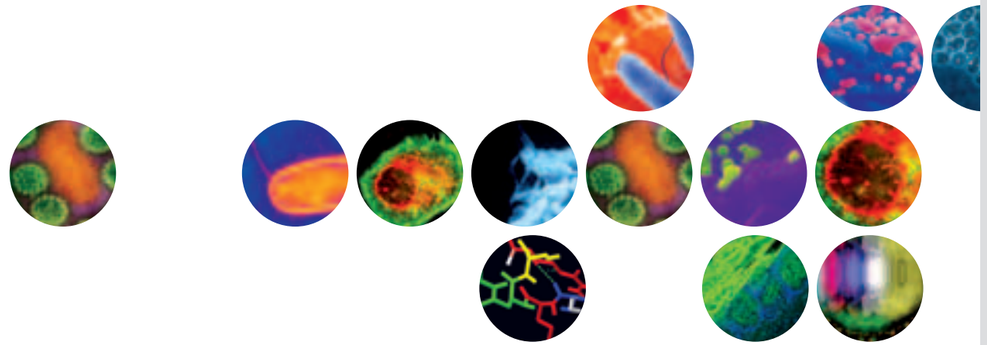


The scientific strategy of the Institut Pasteur is focused on developing new areas for research, fostering multidisciplinary approaches, and encouraging the transfer of scientific discoveries to applications. By providing its teams with the technological resources that are so vital for their research, the Institut Pasteur works tirelessly to fulfill its overriding ambition: making progress in biomedical research to improve health and human welfare.

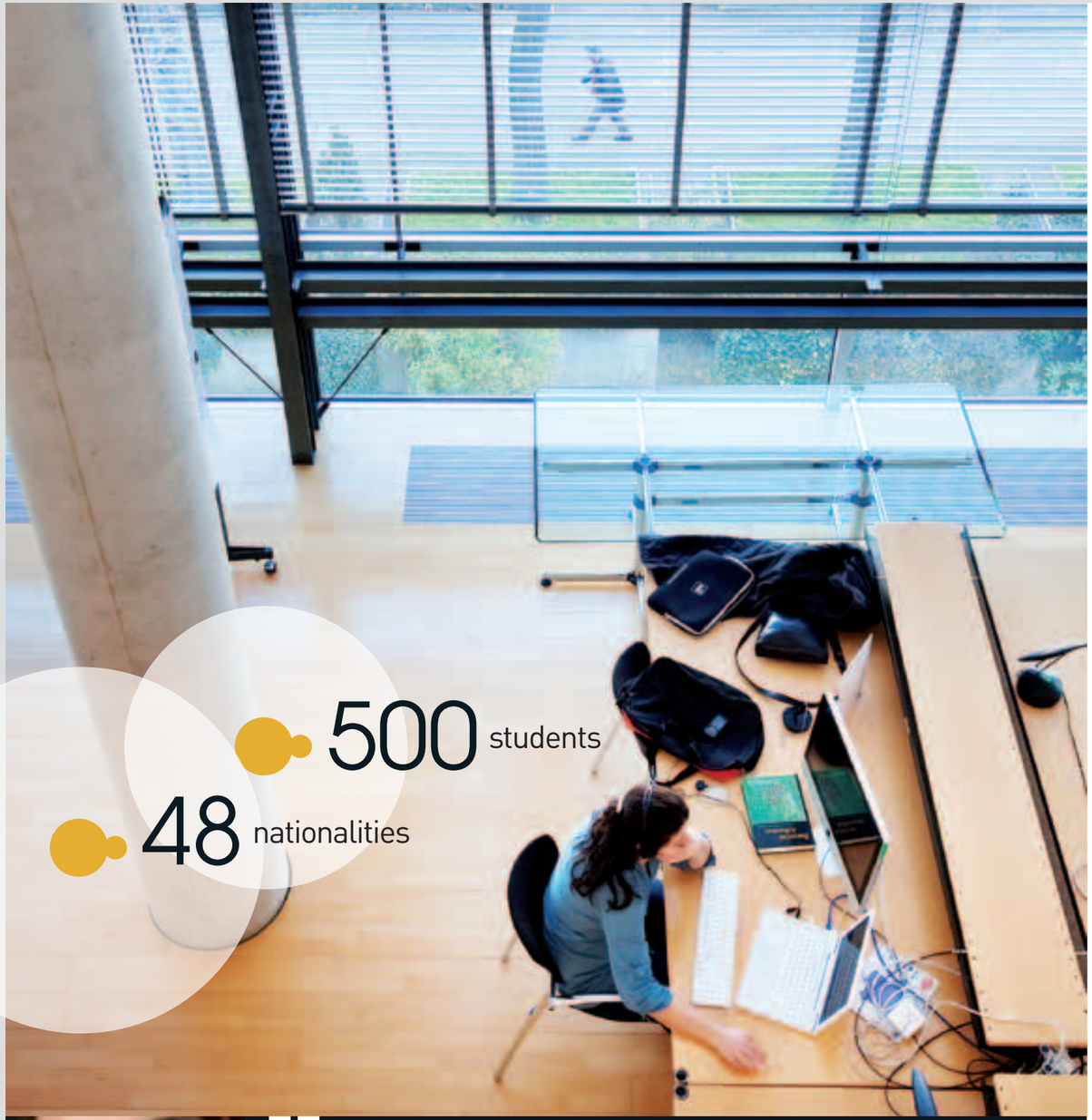
The Institut Pasteur invests its intelligence in life...
and I have the honor of being part of that.

Catherine Adjutor – Assistant

setting the international standard



As well as the many partnerships and projects developed in cooperation with major international scientific bodies such as the World Health Organization and universities and research institutes from around the world, the Institut Pasteur is at the heart of an international network of 32 institutes located worldwide. They have all signed a charter declaring their commitment to Pasteurian values and are united in the fight against infectious diseases.



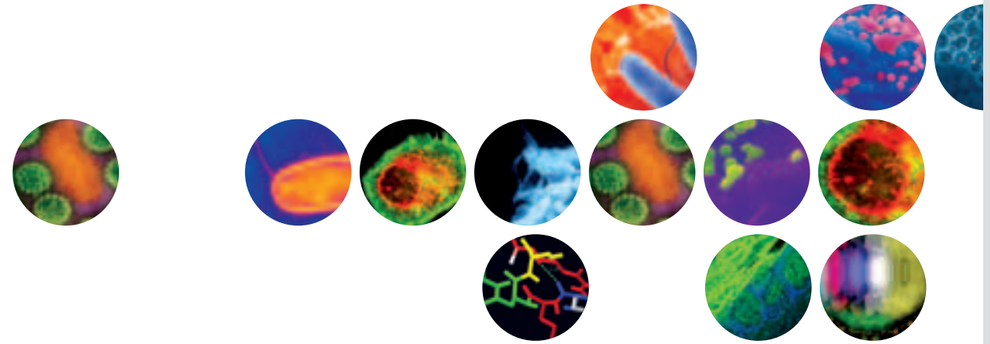
500 students

48 nationalities

For me, the Institut Pasteur is an institution with a humanist outlook whose research work is known and recognized worldwide.

Charlène Blanchet – Researcher

teaching
students from around the world

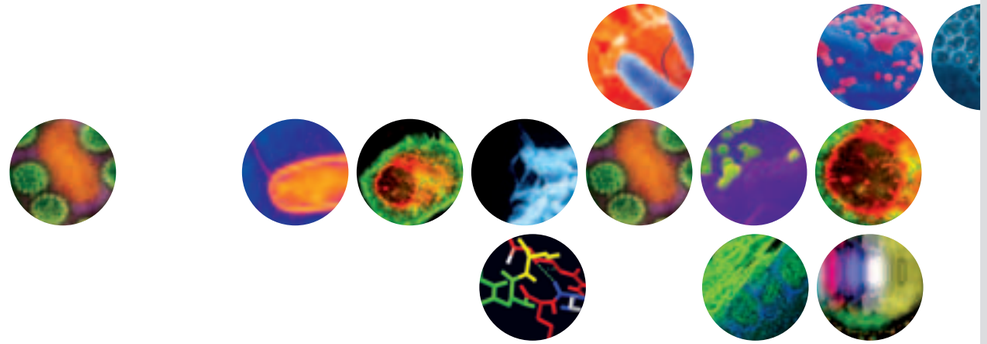


Each year, students from all over the world come to further their knowledge or to supplement their degree programs at the Institut Pasteur Teaching Center. Twenty-five courses with a strong emphasis on practical work are structured around three main subject areas: Mechanisms of Living Organisms, Biology of Microorganisms, and Epidemiology and Public Health. These courses can be taken as part of Masters degree programs at various universities or the specialized Masters degree program run by the Pasteur-CNAM School of Public Health.

Having been at the Institut Pasteur since 1993, I am happy to be working for science and proud to be able to say "I work at the Institut Pasteur" when I'm on the other side of the world.

Christine Phan – Assistant

a unique economic model



The budget of the Institut Pasteur is based on four sources of funding – public generosity, government contributions, the development of business based on Pasteurian research, and research grants – a feature that guarantees the independence of the research policy pursued by this private, state-approved foundation.

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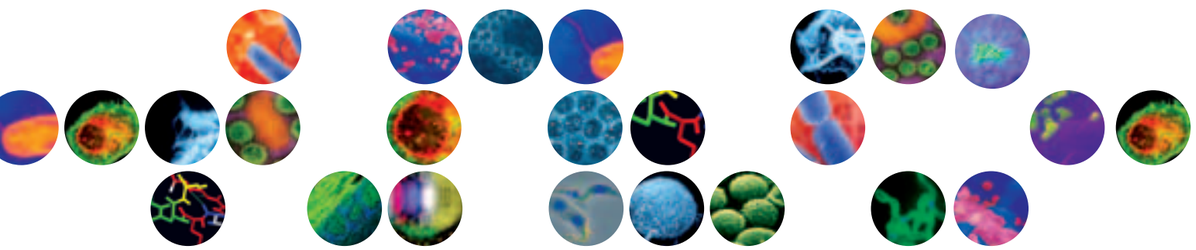
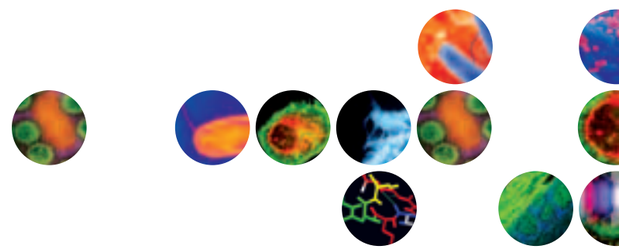




interview with François Ailleret 5

Chairman of the Board of Directors

What were the main issues addressed by the Board of Directors in 2010?
Each year there are a number of "compulsory" issues that are particularly important, such as the approval of the budget, the closure of the accounts for the previous financial year, and also internal appointments, investment decisions, the implementation of various procedures, etc. Added to these issues are various specific strategic questions.

Can you give us some figures that sum up the financial situation?
The 2010 budget took into account foreseeable financial constraints and the financial year ended on a high note with a positive operating result of €0.8 M and a positive net result of €35.1 M due to high non-recurring income. This is a sign of good management and responsiveness, because the Institut Pasteur was affected by the financial crisis and had to deal with unforeseen events. As for the 2011 budget, it is tight but reasonable. The management is carrying out extensive work on our medium-term prospects, with significant input from the Finance and Audit Committee and detailed and constructive discussions within the Board of Directors. In short, I would say that the next few years will be difficult but the financial situation will remain healthy. Particular effort will have to be made to develop resources, in conjunction with a constant drive to increase productivity.

What other subjects have been dealt with by the Board?
Alice Dautry was reappointed as President of the Institut Pasteur for a four-year term in 2009, and at the beginning of 2010 the Board devoted an entire session to the "mandate" of the general management, which establishes guidelines for the priorities and main institutional balances of the Institut Pasteur for this period, in line with the future-oriented and strategic reflections carried out periodically by the Board of Directors and the general management.
A consultative committee for investments, guided by recognized experts, was set up to propose an allocation strategy for our financial and real estate investments and to advise us on monitoring the implementation of this strategy so that we are in a position to react rapidly if necessary.
We particularly addressed the question of the management of the Institut Pasteur's real estate assets. These include the site on rue du Docteur-Roux, entirely dedicated to the activities of the institute, which has undergone significant reconstruction and modernization in recent years. But the real estate assets also include income property – accommodation or offices – that mostly comes from legacies. The initial reallocation guidelines were examined by the bureau and the Board. Discussions were also held on research contracts, which are developing both in volume and value terms. Furthermore, as requested, by the Board members, we heard from the Chairman of the Scientific Council, Olivier Schwartz, who presented his analysis of the current research situation and future prospects in this area.

Aside from these major issues, were there any particular events or projects in 2010 that you would like to mention?
I would simply mention the think tank that was set up to study risk analysis in all areas; the partnerships with leading companies that were created or renewed; the many awards and distinctions received by Pasteur researchers; and the concerted efforts made to submit applications for the "Investing in the Future" programs launched by the French Government.

What about the International Network, to which you are particularly attached?
My attendance at the meeting in Hong Kong for the Directors of the member institutes confirmed for me the sheer quality of this network, whose work resonates with the philosophy of Louis Pasteur himself. I salute the courage and action of those working as part of this network, who fulfill their tasks to the best of their ability, sometimes in countries where conditions are very difficult.
In terms of particular breakthroughs, I would mention the change in status of the Institut Pasteur in Dakar, which has now become a private foundation under Senegalese law, and the newly created Institut Pasteur in Laos, which will take up residency in its new premises, currently under construction in Vientiane, at the end of 2011.
I would also like to thank those who work tirelessly in the Pasteur foundations and associations in the USA, Japan, and Canada to strengthen the links between these countries and the Institut Pasteur in Paris.
A project in which I have been personally involved for the last five years is the partnership between the Institut Pasteur and EDF for the building of the Nam Theun 2 hydroelectric dam in Laos. The quality of the Institut Pasteur scientific and medical input, along with the willingness of EDF to be involved in this large-scale energy project and offer its valuable support, meant that the project – a global first – could be brought to a successful conclusion. The beneficiaries of the project are the inhabitants of this still very impoverished country: yet another example of the Pasteurian spirit in action.

"The Institut Pasteur has strong assets: the expertise of its researchers, its doctors, and all its staff…"

In June 2011, your term as Chairman of the Institut Pasteur Board of Directors will come to an end. What are your thoughts on the Institut's future?
For the past six years, the Institut Pasteur has been an important part of my life, and I will of course remain very attached to it.
It has strong assets: the expertise of its researchers, its doctors, and all its staff; the Pasteurian values that bind all this together and set it on the right course; the faithful support of donors; the financial backing from the government; the growing importance placed on research and research applications in France; and the International Network, which is unique, the only infrastructure of its kind in the world.
But all the excellent "foundations" of the Institut Pasteur should not lessen the vigilance that is so vital in a world that is changing ever more rapidly. Progress will always depend on respect for people and values, rigorous management, a clear and transparent strategy, adaptability, human relationships based on trust, awareness of the needs and views of society, and the development of new partnerships.
I am very confident. The Institut Pasteur has a bright future ahead of it.

interview with Alice Dautry

President

How do you rate the year 2010?
The year 2010 was a complex one, marked by a generally gloomy atmosphere in France against a backdrop of economic crisis and important reforms in the areas of research and university education. This context had an impact on the Institut Pasteur. The government also launched the call for projects for its "Investing in the Future" program and our teams put in a concerted effort to submit proposals. We have had to cope with a year of challenges, but despite various uncertainties, the Institut Pasteur put its depth of talent to work and was able to achieve further success!

What were the main highlights of this year?
One of the main highlights was without doubt the call for projects for "Investing in the Future". The three laboratories of excellence (Labex) projects submitted by the Institut Pasteur were all selected in March 2011. Three successes for our teams, who made concerted efforts to put together particularly innovative projects. Six of our researchers were recognized by the European Research Council (ERC), four in the Starting Grants category and two in the Advanced Grants category. These distinctions demonstrate the quality and creativity of Pasteurian research.
New agreements have been signed or renewed. We have signed an R&D agreement with bioMérieux, a recognized global leader in diagnostics, and we have also strengthened our links with Danone, Bio-Rad, and L'Oréal. The Institut Pasteur continues to support company start-ups piloted by our scientists to develop applications for their research. Housed on the Institut Pasteur campus, the start-ups created in 2010 such as Pathoquest, Affilogic, Axenis, Invectys, and VaxiTech should contribute to the future development of our innovative technologies.
I also want to emphasize the generosity of individuals and companies, which reached even higher levels than in 2009. After signing a first agreement in 2005, the Total Foundation renewed its commitment for the period 2010-2014. Sanofi is also a valuable long-standing partner for us. Finally, we signed a partnership agreement with the Banque Privée Européenne, which has chosen to support us for the development of a therapeutic vaccine candidate for certain cancers.

What have been the major achievements of the Institut Pasteur's scientific policy in 2010?
At a scientific level, the Institut Pasteur has achieved significant results in all its departments.
Examples include discovering that hematopoietic stem cells – which give rise to all the body's blood and immune cells – can be formed from cells from the aortic wall; demonstrating that the parasite that causes malaria can develop in the skin; clarifying the structure of the surface protein of the chikungunya virus; discovering a strategy used by *Listeria* bacteria to infect and control the host cell; and developing a tool using DNA microarray technology that is able to detect the presence of a known virus or bacteria, or one of their emerging variants, within 24 hours, even given a combination of viruses.
But 2010 also witnessed important developments in clinical research. The Institut Pasteur made the decision to promote clinical trials, particularly in gene therapy treatment for Sanfilippo syndrome, a rare disease that affects children.

You have also adopted a sustainable development strategy…
In 2010, the Institut Pasteur signed on to the United Nations Global Compact and to its principles in the areas of human rights, labor rights, environmental protection, and the fight against corruption. This commitment has also been backed up by a change in organization, an audit process, and procedures to comply with ISO 26000.

The campus is still undergoing major building works…
Construction work on the new building for emerging diseases will be completed in early 2012 and when finished will provide space for some 400 scientists at the very heart of the campus. This Integrative Biology of Emerging Diseases Center will house multidisciplinary teams in cutting-edge technological premises, open to everyone on campus, with the aim of developing a comprehensive approach to research. It is also a place that has been designed to stimulate and promote discussions and ideas between different departments.

The Institut Pasteur also has a truly global reach…
Whether in Niger, Tunisia, Ivory Coast or Egypt, the on-site teams have encountered major difficulties. Remarkably, however, and despite challenging conditions, the staff working in these countries have continued to carry out their work. I would also like to emphasize the success of the cooperation between the Institut Pasteur and the US Department of Health, geared towards the rapid detection of a new avian or human influenza epidemic.
Finally, partnership agreements have been signed with the Principality of Monaco. Prince Albert II initiated this cooperation, which has given rise to a framework agreement and three specific agreements. The framework agreement, lasting five years, provides for the funding of joint projects to fight against emerging diseases and to provide access to training for scientists and healthcare professionals in the least developed countries.

What challenges lie ahead for 2011?
The coming year will see the completion of work on our new building for emerging diseases. We will also pursue our policy for the recruitment of top-level researchers, both those starting out on their career and those with more experience, at international level, through the creation of new units and new five-year groups. The modernization and extension of the institutes in the International Network will be continued, with developments including the official opening of the biosafety laboratory at the Institut Pasteur in Bangui and the completion of building works for a new Institut Pasteur in Laos.
In 2011, the Institut Pasteur will rely more than ever on anticipation and responsiveness in its research to combat health problems, striving to offer solutions while remaining faithful to its missions and values.

"In 2010 we had to cope with a year of challenges, but despite various uncertainties, **the Institut Pasteur put its depth of talent to work** and was able to achieve further success."

personal accounts

Sponsors, artists, writers… for more than a hundred and twenty years, the Institut Pasteur has enjoyed the support of a wide range of committed individuals. Keenly aware of the combat being led against infectious diseases, each of them, in their own way, has been a standard-bearer for the Institut Pasteur message: *"Advancing biomedical research to improve health and human welfare."*

Researchers are the keepers of the lighthouse

Marc Levy, writer

> At the Institut Pasteur, I was introduced to a woman in a white coat. When I realized that it was in fact Françoise Barré-Sinoussi, winner of the Nobel Prize for Medicine, I said to the journalist: "You're crazy – it's not me you should be following; all I do is write books."

"I dreamed of being like him…" As a child, Marc Levy was always fascinated by Louis Pasteur, one of his own pantheon of great historical figures. He also admires Pasteur's working method, akin to that of a detective, blending observation, deduction, and rigor, but also intuition. *"Research is the work of intelligence and devotion to nurture hope and serve the cause of humanity,"* he affirms.

As Ambassador for the Institut Pasteur, he is now lending his voice to Pasteurdon and is filming a short program on influenza. When interviewed on programs such as RTL's *Le Journal Inattendu* or France 2's *Thé ou Café*, he speaks about the Institut Pasteur. *"Despite all the controversy surrounding the distribution of the vaccine for influenza A(H1N1), I was struck by the fact that even before the emergence of the pandemic, researchers at the Institut Pasteur had developed a test that could detect the new A(H1N1) virus within twelve hours… It's extraordinary!"* he exclaims.

For Marc Levy, pandemics are far from being a thing of the past: *"The fight against the threat of emerging global pandemics has always inspired the efforts of the Institut Pasteur's researchers. They are the keepers of the lighthouse!"* He is firmly against reality TV shows that give a false image of existence and human relationships. *"It's a form of culture that derives from a lack of intelligence, where strutting nonentities are promoted to the ranks of stars while we ignore the researchers who are working to develop vaccines and saving thousands of lives,"* he deplores.

On a visit to the Institut Pasteur, Marc Levy feels a sense of history, a pride in belonging, a true identity. *"When we 'give' to the Institut Pasteur, it truly reflects the notion of Louis Pasteur, of his 'house' in which all the stones are the sign of a generous thought, coming together to build a future for humankind."*

So can we look forward to a new novel set at the Institut Pasteur? *"If only it were true…"* – in a nod to his bestseller of the same name…

Hitch your wagon to a star

Catherine Ferrant, Managing Director of the Total Foundation

Furthering science, but also acting to reduce the number of people who are suffering.

Having worked alongside the Institut Pasteur since 2005, Catherine Ferrant now speaks with a distinct Pasteurian accent. *"Sponsorship is a true partnership based above all on osmosis, working together and sharing,"* she explains. With a presence in several countries confronted with pandemics, Total, via its Foundation, was keen to play a major role in the field of public health. *"We naturally turned to the Institut Pasteur to draw up a first sponsorship agreement in 2005 for the strengthening of local capabilities for the prevention, diagnosis, and treatment of infectious diseases,"* recalls Catherine Ferrant.

Five years on, innovative programs are being conducted in Cameroon to support the families of babies born seropositive, in Madagascar and shortly in Bangui, Central African Republic, to study and treat infant diarrhea, and also in Morocco, to raise awareness among truck drivers about AIDS and sexually transmitted infections (STIs).

In 2010, a new sponsorship agreement was signed with increased funding of €10 million. *"It is important to hitch your wagon to a star,"* affirms Catherine Ferrant. *With the Institut Pasteur, we know that we can count on a guarantee of quality, on an institute that is firmly rooted among local communities, and on sustainable services."* These funds will be used to create a Barré-Sinoussi Chair for HIV/AIDS training and research, to finance research programs to combat infectious diseases, and to support public health initiatives in the countries in which Total operates.

"As we were starting to get to know each other well and to work well together, the Institut Pasteur suggested that our network of filling stations be used as a center and collection point for Pasteurdon. This campaign to raise awareness demonstrates that the Institut Pasteur has become a family friend…" she concludes.

The spirit of Pasteur haunts us

Fabrice Hyber, artist

In this place which is rarely used to display art, the researchers, always receptive to new ideas, take the time to think. They have no preconceptions.

In this unusual exhibition venue, Fabrice Hyber has strewn his works all around, creating a dialog between his universe, the laboratory equipment, and Pasteur's vision. The Institut Pasteur is above all a dynamic, outward-looking environment, a meeting place for intellectual effervescence and research. But are not all scientists also unknowing artists, and all artists also researchers striving to find themselves? *"Both are constantly seeking new ways to look at the world. Scientists pursue an objective, even if they explore tangents from time to time, whereas artists have no limits."* Strangely, did you know that Fabrice Hyber is a former mathematician turned artist, and that Louis Pasteur, highly gifted in all fields, produced several portraits in pastels, charcoal and pencil from the age of 11? The lines between the two worlds are blurred: *"I always think that there is a link between artistic creation – art – and all types of creation. I imagine that Pasteur might have thought that the body was composed of microparticles in the same way as his pastels. It led him to identify microorganisms, and along with them our hygienic, modern, contemporary world."*

Through the exhibition "Pasteur' Spirit", Fabrice Hyber wanted to display inventions, in a veiled reference to the idea that we are haunted by Pasteur's spirit and attitude. *"I always intended to express a vision through my artistic approach. My idea? To show the body differently, the shadows that one can produce, the climate that one can generate, the atmospheres that one can make, the attitudes or non-attitudes that one might have."* His favorite piece? The three-pan balance. *"Generally there are the pros and the cons, and sometimes we would like to have a third solution. So I invented a third pan. It was a concept that I developed for children. I even made a 20-pan scale for a G20 summit."*

In this place which is rarely used to display art, how would Louis Pasteur have reacted? *"I think he would have been intrigued, but he would have tried to understand."*

highlights

In addition to the rich scientific activity that characterizes the daily routine at the Institut Pasteur and upholds its prestigious reputation, life at the institute is also marked by various events that support and illustrate this vibrant research dynamic. Here is a summary of the year's most significant episodes.

2010

Monaco joins forces with the Institut Pasteur

The Institut Pasteur is increasing its research partnerships with the aim of encouraging progress in biomedical research. The signing of a cooperation agreement with the Principality of Monaco reflects this humanist approach.

On Tuesday, December 21, 2010, partnership agreements were signed between the Principality of Monaco and the Institut Pasteur. The ceremony, held in the presence of HSH Prince Albert II, followed the Sovereign Prince's visit to the Institut Pasteur on June 28. During this first visit, HSH Prince Albert II met scientists specializing in emerging diseases and spoke with Professor Alice Dautry. He also visited research laboratories, notably that of Professor Françoise Barré-Sinoussi, co-discoverer of the AIDS virus and laureate of the Nobel Prize in Medicine.

"The Institut Pasteur is delighted to welcome Your Highness today and hopes that this meeting will mark the beginning of a partnership, one we hope will be long and fruitful and, I have no doubt, will enable us to win new battles against disease," stated Professor Alice Dautry.
During his address, HSH Prince Albert II emphasized that public health had become one of the Principality's priority areas for action in terms of international aid. He went on to invite his government to develop closer relations with the Institut Pasteur with a view to considering a formal, long-term partnership.

This joint reflection eventually led to a framework agreement and three specific agreements.
The five-year framework agreement provides for the funding of joint projects to combat emerging diseases, access to training for scientists and healthcare professionals in the least developed countries, and the organizing of scientific charity events related to environmental protection.

Three specific agreements were also signed.
The first is a memorandum of understanding between the Institut Pasteur, the Monaco Scientific Center and the Prince Albert II of Monaco Foundation to organize a biennial conference in Monaco on environmental change and its effects on health, to award an international prize recognizing the work of a researcher on this topic, and to hold a charity gala to support the partnership.

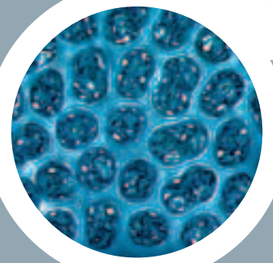
Two agreements between the Institut Pasteur and the Department of External Relations.
The first agreement is geared towards fighting against severe bacterial meningitis in Niger through a better understanding of the impact of climatic, environmental, health-related, and socio-demographic factors on the dynamics of the epidemics. The second is to combat antibiotic-resistant infections in children in low-income countries. One million euros will be allocated from the Monaco Office of Cooperation for the implementation of these two projects from 2010 to 2013.

May

Franck Riboud, Chief Executive Officer of Danone, and Muhammad Yunus, laureate of the Nobel Peace Prize in 2006, winners of the 2010 Pasteur Foundation Award. Inspired by the biomedical research carried out for over a hundred and twenty years at the Institut Pasteur, the Pasteur Foundation in New York honors figures whose outstanding work contributes to improving health across the world. The 2010 Pasteur Foundation Award honored the joint commitment of Franck Riboud and Professor Muhammad Yunus for the creation of Grameen Danone Foods, a social enterprise that aims to reduce poverty and malnutrition among children through the local production and sale of yogurts enriched with micronutrients in rural regions of Bangladesh.

June

Creation of a Françoise Barré-Sinoussi Chair with the Total Foundation. After a first sponsorship agreement signed in 2005, the Total Foundation renewed its commitment to Institut Pasteur work to combat infectious diseases by extending the support it has provided over the last five years. This new agreement demonstrates the shared dedication of the Total Foundation and the Institut Pasteur to pursue their partnership in the fight against infectious diseases. The new funds will be used over the next five years to create a Françoise Barré-Sinoussi Chair for HIV/AIDS training and research, to finance research programs to combat infectious diseases, and to support public health initiatives, notably against emerging and re-emerging diseases.



June

The Institut Pasteur launches Green Campus. The Institut Pasteur has adopted a comprehensive sustainable development strategy and in 2010 became the first French foundation to adhere to the United Nations Global Compact. In so doing, the Institut Pasteur undertakes to contribute to sustainable development in a voluntary and comprehensive way, through its actions in the field of human rights, labor relations and conditions of employment, the environment, best business practices, consumer issues, and societal commitment. The first section of its strategy focuses on environmental questions. Green Campus aims to promote and consolidate the Institut Pasteur's action in favor of the environment. It is based around three priority areas for action: preserving resources, preventing pollution, and sharing ideas and best practices. To support this strategy, a letter of commitment was drafted by the general management, accompanied by an action plan based on the three priority areas.

July

The Institut Pasteur opens its doors to artist Fabrice Hyber and launches "Campus Philanthropes". With the "Pasteur' Spirit" exhibition, the French artist, known internationally for his installations combining new behaviors, arts, science, and business, set up his works around the campus. This was an opportunity for the Institut Pasteur to open its doors to contemporary art and to the general public. The Institut Pasteur also chose this occasion to launch its new program for major sponsors known as "Campus Philanthropes", which offers personal support and advice for those wishing to invest in the Institut Pasteur.

October

"All researchers for one weekend!" That was the watchword of Pasteurdon 2010, which saw more than a million pledges made in support of the Institut Pasteur's research. The Institut Pasteur's annual campaign to raise awareness and collect donations was organized in partnership with digital terrestrial TV channels and France Inter radio station. The face of this year's campaign was actress and singer Sandrine Kiberlain. The Institut Pasteur took this opportunity to open its laboratories to the general public.

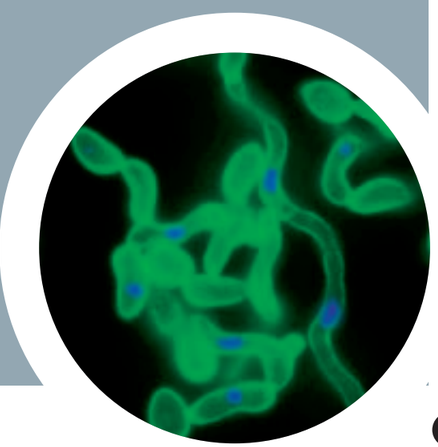
November

The Institut Pasteur launches the first think tank on philanthropic trusts. The Institut Pasteur has stepped up its structural support for philanthropic trusts with the creation of a think tank and an online platform entirely dedicated to this topic. In November 2009, the Institut Pasteur launched the first conference on philanthropic trusts. The think tank was set up to further the work carried out at this annual meeting of asset management experts, attended by over 300 specialists in the field, to assess the current situation and identify the prospects for this dynamic and rapidly evolving sector.

Fondation Pasteur Suisse

December

The Institut Pasteur creates the Pasteur Foundation Switzerland. This new structure, a recognized public service that continues the Institut Pasteur's tradition of international development, has its origins in the numerous scientific partnerships and philanthropic relationships between the Institut and the Swiss Confederation. Based in Geneva, the Foundation's missions are to raise funds to support the activities of the Institut Pasteur and to contribute to the development of links with research structures pursuing similar aims.



> Each stone that, as researchers, we bring to the edifice of science might one day allow us to construct an unscalable wall around some diseases...
>
> **Christophe Beloin** – Researcher

scientific discovery for sustainable health

The research infrastructure at the Institut Pasteur is geared towards providing the resources required for the implementation and materialization of ambitious, varied scientific projects. Ongoing investment in cutting-edge technologies, regular cooperation with the Institut Pasteur International Network, the application of discoveries from Pasteurian research, and the dissemination of knowledge and expertise all help foster quality research.

RESEARCH

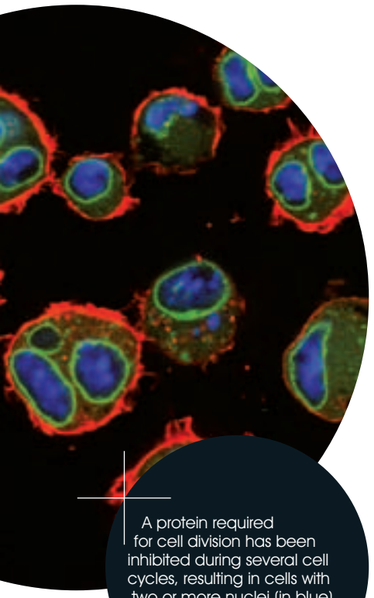
effective multidisciplinary research

I am attached to my Institute, to its heritage and culture; it's what inspires me and instills in me a passion for science.

Corinne Jallet – Senior Technician

The department's research focuses on interactions between hosts and pathogens. This is complemented by work on the cell biology of pathogens and studies to gain a detailed knowledge of the cell in a physiological context.

Cell Biology and Infection



A protein required for cell division has been inhibited during several cell cycles, resulting in cells with two or more nuclei (in blue).

Developing a comprehensive understanding of host-pathogen interactions and the factors involved therein requires research in a physiological and tissue context using approaches incorporating spatio-temporal dynamics and complex signaling pathways. The Cell Biology and Infection Department has defined three priorities to develop the analysis of the interface between microorganisms/cells and tissues: to strengthen the integration of cell biology, cell microbiology, genomics, and imaging for a more effective analysis of bacterial, viral, parasitic, and prion infections; to analyze at systemic level the molecular and cell interactions required for the establishment, dissemination, and maintenance of pathogenicity; and finally, to foster close links with immunologists and cell biologists in other departments. These activities are closely related to the development of new techniques such as imaging, image analysis, genomics, and post-genomics.

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

MEMBRANE TRAFFIC AND CELL DIVISION

For a cell to be able to multiply, it must first replicate its genetic material and then distribute it on either side of the cell in two identical batches. Once this operation has been completed, the parent cell can then begin the actual process of cell division, during which it contracts at its center until it forms two daughter cells which are only linked by a thin tube, which is eventually cut to separate the two cells permanently.
The Membrane Traffic and Cell Division five-year group, created on January 1, 2010, focuses on the very last stage of this process, cytokinesis, the process during which the two new cells are physically separated from one another. The researchers are studying the membrane traffic – molecular exchanges between the different cell compartments – involved in this process, using human and Drosophila cells as models. Their aim is to understand how this filiform bridge is stabilized and then cut. They are particularly studying how a new protein that regulates membrane traffic, protein Rab-35, orchestrates the remodeling of the proteins and lipids in the bridge, a process that is essential for cytokinesis. The inhibition of Rab-35 prevents the cells from separating and leads to the formation of binucleate cells.
This highly fundamental research sheds new light on the mechanisms required for cell division and could be particularly useful, especially in cancer research to block the uncontrolled division of tumor cells.

THE "NUE" PROTEINS OF *C. TRACHOMATIS*

Infection by *Chlamydia trachomatis* in developing countries is responsible for trachoma, the primary infectious cause of blindness. Bacteria of this species are also the agents of widespread sexually transmitted diseases and are one of the main causes of sterility in women.
The Biology of Cell Interactions Unit is focusing on the interactions between *C. trachomatis* and the host and on the proteins secreted by this pathogen in the cells in which the bacteria develop. One of these proteins, termed NUE, particularly caught the attention of the unit's researchers because it uses a secretion mechanism known to be a virulence factor in pathogens. This mechanism enables the protein to be transferred from the bacterium to the cell, and the researchers have discovered that NUE then moves towards the nucleus of the infected cell. They have also demonstrated that NUE has an enzyme activity known to play a role in controlling the opening of compacted DNA, therefore also controlling access to genes and their expression. This enzyme activity, which is yet to be demonstrated *in vivo*, suggests that *Chlamydia* has the potential to control the host directly at epigenetic level, via NUE.

S. FLEXNERI'S NEED FOR OXYGEN

Bacillary dysentery is a severe diarrheic disease that is endemic in economically disadvantaged regions of the world. This disease, caused by an invasive bacteria, *Shigella,* affects some 150 million people each year and causes hundreds of thousands of deaths, mostly children under the age of 5.
The Molecular Microbial Pathogenesis Unit is attempting to identify the virulence genes and their mode of regulation, and also to unravel the mechanisms used by the bacteria to survive *in vivo* in the intestine. Researchers have discovered that *Shigella flexneri* is able to modulate its virulence according to the level of oxygen in its environment. Working with a team from Imperial College London, the team demonstrated that oxygen was essential for the functioning of the type III secretion system, which represents the major virulence factor of *Shigella*. This secretion system is required for the secretion of the effectors and toxins that enable the bacteria to rupture and invade the intestinal barrier. The researchers demonstrated that this level of oxygen was high near the intestinal walls. *S. flexneri* uses it to optimize the secretion of its effectors at the site at which it invades the intestine.
Understanding the regulation of the virulence mechanisms of *S. flexneri* at the infection site *(in vivo)* will serve in the long term to optimize treatments and vaccine prophylaxis against bacillary dysentery. The scientists are currently looking into the role played by oxygen in the activation of the immune response against *S. flexneri*.

2 technological platforms

12 research entities

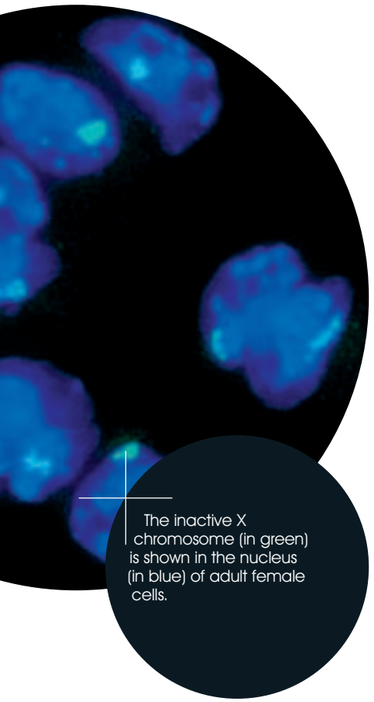
The Institut Pasteur, my home from home for 37 years...
Dario Giorgini – Senior Technician

A Pasteur scientist wins the L'Oréal-UNESCO Award

Each year, five outstanding women scientists, selected from Africa, the Americas, Asia, Australia, and Europe respectively, are recognized by the L'Oréal-UNESCO Awards for Women in Science, which showcase women's scientific excellence. The 12th Award (for Europe) was awarded to Prof. Anne Dejean-Assémat, Director of the Nuclear Organization and Oncogenesis Unit, for her elucidation of the molecular and cellular mechanisms at the origin of some leukemia and liver cancer in humans.

How can a highly integrated and sophisticated multicellular organism develop from a fertilized egg? This is a vast question, one to which the Developmental Biology Department is attempting to provide some answers.

Developmental Biology



The inactive X chromosome (in green) is shown in the nucleus (in blue) of adult female cells.

The research areas of the Developmental Biology Department can be divided into four main missions:
• identifying the cell movements and migrations in the embryo needed for organ and tissue formation, and the informational exchanges used during this process;
• determining how the identity of each cell is established and maintained through specific programming mechanisms;
• establishing the role of stem cells, which play a dominant part not only in embryogenesis but also in the regulation and maintenance mechanisms of adult tissues;
• clarifying the respective roles of innate and non-genetic factors in the phenotype developed by the individual, and their genetic contributions to the host's resistance to infectious diseases and/or congenital and metabolic diseases.

11 research entities

2 technological platforms

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

MALE INFERTILITY: GENETICS COULD BE A KEY

Researchers from the Human Developmental Genetics Unit have identified a gene whose mutations explain certain cases of severe infertility in men.
The study was conducted on 315 men affected by unexplained infertility. The team particularly focused on mutations in the NR5A1 gene, which had previously been identified by the researchers as being responsible for cases of severe ovarian failure in 2009. Sequencing of the NR5A1 gene revealed in all seven mutations, responsible for 4% of severe cases of infertility thereby constituting the most frequent "monogenic" cause of infertility known to date.
In vitro functional studies performed for each of the mutations demonstrated that they reduce the expression of key genes vital for testicle development, particularly genes involved in the biosynthesis of certain hormones.
This discovery paves the way for early diagnosis of forms of male infertility associated with these mutations and could help medical professionals offer advice to affected individuals and couples regarding procreation or freezing of sperm and egg cells. Given that in some cases infertility can constitute a risk factor in the emergence of cancer, this research could also help medical professionals by identifying people carrying these mutations for intensified medical monitoring.
This research was performed in cooperation with Tenon Hospital, Paris, and the Germetheque biobank for research on human reproduction, which supplied the samples required for the study, as well as with a team from University College London.

CUSTOM-MADE STEM CELLS FOR TREATING LEUKEMIA

Two researchers from the Macrophages and Development of Immunity Unit have used a high-resolution imaging technique to demonstrate that hematopoietic stem cells (HSCs), which are responsible for the lifelong production of blood cells, are formed from the cells of the embryo's aortic wall. This study, performed on zebrafish, has enabled the researchers to give a precise description of the stages in the birth of these stem cells and to clarify the question of how they come into being.
The research shows how some endothelial cells separate and detach at the surface of the aorta, while preserving the integrity of the blood vessel. These endothelial cells then become "traveling" stem cells, which go on to divide so that they can give rise to all the different blood cell types. This discovery shows that cells which are already specialized, such as those which make up a blood vessel, can naturally reprogram themselves to become multipotent stem cells.
This research has potential therapeutic applications, particularly for the treatment of patients with leukemia, whose HSCs are destroyed by radiotherapy or chemotherapy: it would simply be necessary to generate HSCs *in vitro*, in a laboratory, using a biopsy sample from the blood vessels of the patients, and to reintroduce them in these patients to replace the old cells. These new custom-made HSCs could then be used to restore the functioning of the blood and immune systems.

GENETIC PROGRAMMING AND REGULATION

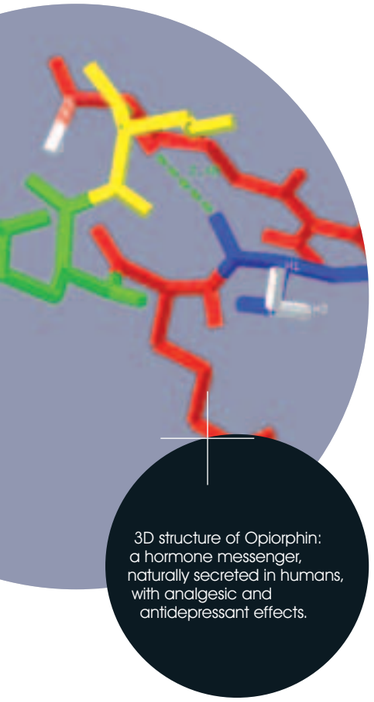
The future of all living organisms depends on the establishment and smooth operation of their genetic programs. The decoding of genetic information and its regulatory mechanisms are key elements in the process by which a genome is expressed. Two of the department's units have been looking closely into these questions.
The Drosophila Developmental Genetics Unit has developed a method that identifies the regulatory sequences for gene expression within the genome. These sequences determine the transcription factors that initiate the reading of the genome. This method uses statistical tools to identify regulatory sequences with characteristics similar to those of known sequences, in genomes from closely related species. Developed for *Drosophila* and applicable to all living species whose genomes have been sequenced, the method will help improve understanding of how the genome works.
The Mouse Molecular Genetics Unit has identified regulators that control one of the essential processes in embryo development in female mammals: the silencing of the genes of one of the two sex chromosomes. These regulators are involved in maintaining the ability of embryonic stem cells to give rise to different tissues: the skin, nails and liver. They can also "reprogram" the genome of mature cells to make them lose their specialization (returning them to the state of stem cells). Characterizing the fundamental mechanisms involved in development is vital if new therapeutic strategies based on stem cells are to be implemented safely.

Philip Avner – Head of Department

He emphasizes the importance of research carried out on stem cells: *"In the next few years, stem cells will become increasingly central in the development of new therapeutic strategies. They are critical elements for our understanding of embryonic development and homeostasis in adults. They play a vital role in the establishment of the immune and nervous systems. The department is leading a range of initiatives that encourage interaction between the various groups on the campus working on adult and embryonic stem cells."*

Identifying links between the structure and function of molecules of biological interest is essential to determine their role in human pathology and develop new therapeutic strategies. The Structural Biology and Chemistry Department carries out in-depth research in this area.

Structural Biology and Chemistry



3D structure of Opiorphin: a hormone messenger, naturally secreted in humans, with analgesic and antidepressant effects.

Studying the structure of molecules can improve our understanding of their functions and role in the development of infectious diseases, genetic diseases, and cancers. To perform this research, the Structural Biology and Chemistry Department uses and develops cutting-edge technologies such as molecular modeling, which plays a key role in determining structures and making use of them; crystallography, which displays the 3D structure of a molecule and makes it possible to carry out drug-design studies on potential targets; and finally nuclear magnetic resonance, which enables researchers to access the structure of smaller molecules and provides information on their movements and the molecular interactions studied. The department combines structural, biochemical, and biophysical approaches to reveal the molecular mechanisms involved in pathological and infectious processes and to design chemical tools that are able to interfere with these processes.

11 research entities

6 technological platforms

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

PAINKILLER, ANTIDEPRESSANT – AN "ALL-IN-ONE" MOLECULE

The Structural and Cellular Biochemistry Unit* has characterized the analgesic and antidepressant effects in animals of Opiorphin, a hormone messenger naturally secreted in humans that was discovered at the Institut Pasteur in 2006.

In vivo, for the same doses, Opiorphin exhibits an analgesic potency comparable to that of morphine, with considerably milder side effects: Opiorphin does not induce tolerance (doses do not have to be increased to obtain the same antinociceptive or "painkilling" effect) or cause constipation, and it has much lower addictive potential (the potential to induce psychological dependence). Its antidepressant properties are also particularly potent – the molecule is as effective at the same doses as imipramine, an active compound used for treating depressive syndromes, but does not have the same side effects, which may include hyperactivity, sedation, and long-term-memory disruption.

A drug based on Opiorphin, effective at the same doses against pain and depression, two disorders that are often linked, would therefore be beneficial. Before initiating clinical trials to assess the actual therapeutic potential of Opiorphin, researchers are currently working on optimizing a synthetic Opiorphin in order to make it more stable and increase its bioavailability and duration of action.

** Institut Pasteur Unit/URA2185-CNRS in cooperation with a team from the ETAP-Applied Ethology neuropsychopharmacology research center based in Vandœuvre-lès-Nancy.*

A NEW PLATFORM SPECIALIZING IN PROTEINS

In November 2010, a new entity, known as the Proteopole, was created with the aim of bringing together the instrumentation as well as the technical and methodological expertise on the Institut Pasteur campus in the area of (bio)chemical, biophysical, and structural research on biological macromolecules. This center federates a number of technological platforms with specialties ranging from the production of recombinant proteins to their analysis at an atomic scale using crystallogenesis and X-ray diffraction, and including mass spectrometry and a host of other molecular-scale biophysical approaches. In 2010, the members of the different platforms participated in more than a hundred research projects involving Institut Pasteur laboratories and several external academic and industrial teams (in France and abroad), which led to the co-authoring of 25 scientific publications. The Proteopole created as a result of this pooling of expertise represents a unique and powerful tool in France which will gradually be developed by incorporating other cutting-edge physico-chemical approaches such as nuclear magnetic resonance, cryo-electron microscopy, and high-throughput molecular screening.

INNOVATIVE, THERAPEUTIC, AND "MOVING" TARGETS

Once discovered purely by chance, new therapeutic molecules are now generally identified through the systematic screening of collections of natural extracts or synthetic molecules. For a number of years, computer-aided rational drug design has been used to design chemical compounds that bind as effectively as possible to a known site on an enzyme of the pathogen so as to block the infectious process.

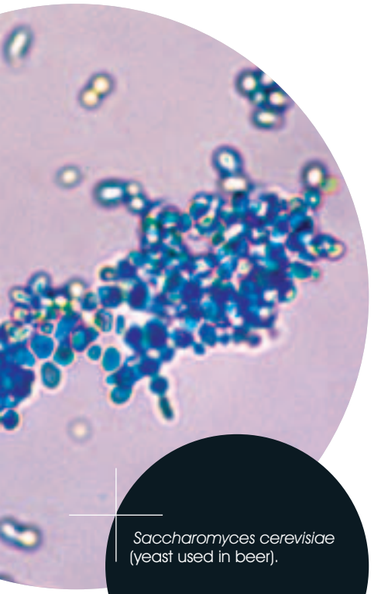
More fundamentally, the Structural Bioinformatics Unit has devised a new approach to identify how to block pathological processes by targeting not only an active enzyme site but also the molecular movements required for these processes to operate. To demonstrate the usefulness of this strategy, they used it to design a molecule to block an enzyme, called EF, an essential toxin produced by *Bacillus anthracis*, the pathogenic agent of anthrax. The approach is based on the detailed reconstitution of the molecular movements of the EF enzyme as it interacts with a key protein cofactor present in the host cells. To achieve this reconstitution with the necessary detail, researchers in the unit needed to develop an innovative algorithmic approach. The aim was to identify a cavity that appears along the conformational transitions of EF, and then to identify molecules that upon binding to this cavity would block the enzyme activation – as a grain of sand in the gears – and thus prevent the development of the pathogenic processes.

> Mastering research in biology, communicating it, and applying it for the benefit of everyone – I've found that the Institut Pasteur is a length ahead of the rest!
>
> **Deshmukh Gopaul** – Researcher

The discovery of new genes is constantly revealing new biological functions, the interpretation of which falls upon researchers in the Genomes and Genetics Department whose work attempts to give us a better understanding of the world around us.

Genomes and Genetics

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS



Saccharomyces cerevisiae (yeast used in beer).

The work of researchers in the Genomes and Genetics Department mainly involves the study of human, bacterial, and yeast genomes. The in-depth analysis of genetic information in tuberculosis bacilli, streptococci, Vibrio, and Legionella genomes aims to improve our understanding of the life and pathogenic determinants of these organisms. Yeasts are also studied, both for their own properties and as models to help us understand human genetics. The department is also thoroughly investigating the evolution of infectious agents and the selective pressures they have exerted on human genes over time. All this research relies on advanced sequencing and genotyping techniques available at the Genopole.

BACTERIAL COLONIZATION TACTICS REVEALED

The "Evolutionary Microbial Genomics" five-year group studies the organization and composition of bacterial genomes to shed light on the physiology and ecology of these species through metagenomics. This innovative approach involves sequencing genomes from a given ecosystem, such as the intestine, in all species. The advantage of this method is that it provides access to the genomes of 99% of bacterial species that are currently impossible to cultivate under laboratory conditions.

The team analyzed the complete genomes of 214 microbial species and was therefore able to identify indicators that permit them to establish the optimal growth time of the microbe based on DNA sequences alone, rather than on the entire genome. When combined with metagenomics, this provides information on the microbial diversity and distribution of the environment studied, and also on the relevant growth time for each species represented.

These data are highly valuable for understanding the strategies adopted by bacteria to colonize human ecosystems that are untouched (at birth) or damaged following an infection or antibiotherapy. Determining the growth rate of species is also beneficial for the development of therapeutic strategies, making it possible to adapt doses and to direct treatments against the pathogens responsible for the infection, while preserving or encouraging the development of the commensal species required for the regeneration of the environment.

15 research entities

3 technological platforms

1 software and databases group

THE SMALL STEPS STRATEGY

The Physics of Biological Systems Unit focuses on the chemotaxis of bacteria, in other words their ability to direct their movements according to the chemical elements in the environment, be it nutrients that attract them or toxins that cause them to flee.

Using mathematical models, the unit has demonstrated that bacteria are able to adapt the length of their "steps" to the environment that surrounds them. Bacteria need to move when they enter the stationary growth phase, a critical stage when bacterial colonies become very dense and the surrounding environment is depleted of nutrients. It becomes vitally important for the bacteria to search for nutrients, which they do by employing a mechanism that involves moving in straight lines for 1 to 2 seconds, stopping and turning back on themselves to set off in another random direction. In theory, bacteria can change the length of their "steps" depending on the concentration of chemical substances in the environment. However, experiments show that they do not choose the length of step that enables them to approach the source of nutrients as quickly as possible. They remain "cautious".

This "small steps" strategy, observed in both commensal bacteria and pathogens, is an optimal approach in a fluctuating environment that is hostile and depleted of nutrients. It is currently the focus of laboratory experiments in which bacteria are made to grow in controlled environments to test whether the length of their "steps" increases when the environmental constraints are reduced.

YEASTS: A REVIEW

Yeast, a unicellular fungus whose evolutionary lineage branches off from that of the animal world, is a research model that is widely studied across the world. Over the past ten or so years, yeast comparative genomics has developed considerably, to such an extent that this group of organisms, which includes over 1,500 described species that are very distant from one another at an evolutionary level, is one of the best studied of all eukaryotic groups in terms of evolutionary genomics.

Professor Bernard Dujon, Head of the Yeast Molecular Genetics Unit and a pioneer in this research field, conducted a review of current knowledge in this area at the request of the scientific journal *Nature Reviews Genetics*.

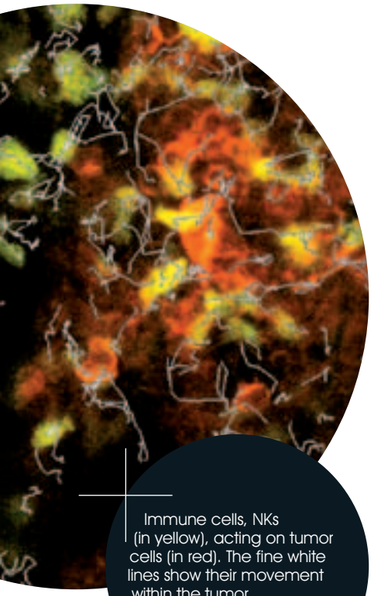
In addition to standard genomic processes common to species with exclusively sexual reproduction such as humans, yeast has been used to demonstrate phenomena of genetic exchanges between species (such as the formation of hybrids, the existence of long introgressed segments, and horizontal gene transfers) that appear to give rise to the rapid formation of new lines. Moreover, the mechanisms for duplication of the genome or of long chromosome segments which have equivalents in other genomes have been studied with an extremely high degree of precision in yeast, which serves as a useful experimental model for significant genetic impairments, including in humans.

Louis Forest Prize awarded to Guillaume Cambray

Each year, the Chancellery of the Universities of Paris offers eight science awards from the donations and legacies made to the former University of Paris. These awards recognize the scientific excellence of a PhD thesis completed during the year. In 2010, the Louis Forest Prize was awarded to Guillaume Cambray for his thesis entitled *Evolvability: the integron case and the use of synonymous sequences for directed evolution*. This research, supervised by Didier Mazel, Head of the Bacterial Genome Plasticity Unit, demonstrates how a particular genetic system is able to sense conditions that are hostile to the organism and to increase the mutation rate accordingly.

The Immunology Department studies all the facets of the immune system – development, regulation, and protective or pathogenic immune responses – using innovative technological approaches and tools.

Immunology



Immune cells, NKs (in yellow), acting on tumor cells (in red). The fine white lines show their movement within the tumor.

The work of the Immunology Department can be divided into three main research areas. The first is research into the development of the immune system, with teams focusing in particular on the differentiation of immune cells, the formation of lymphoid organs, and cell dynamics during the immune response. Other groups work on the complementarity of the immune responses induced by innate immunity (non-specific and immediate) and acquired immunity (adaptive, specific and acquired). They look at response processes, the cells responsible, and their interactions. Finally, the research area based on immune responses and pathologies involves teams studying protective, anti-infectious, and anti-cancer immunity, as well as those focusing on immune disorders such as allergies or autoimmune diseases.

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

HEPATITIS C: A PREDICTIVE MARKER FOR RESPONSE TO THERAPY

Hepatitis C is currently one of the leading causes of chronic viral liver disease. With more than 170 million chronic carriers of the hepatitis C virus in the world, this infectious disease represents a serious public health problem.
For the past ten years, treatment has been based on interferon in combination with the antiviral drug ribavirin. This long treatment (24 to 48 weeks) has considerable side effects (high risk of depression), and only 50% of patients are completely cured.
This is the context in which an Institut Pasteur/INSERM team studied the immune response of chronic hepatitis C patients and particularly looked at the protein IP-10, which if found in high levels in the patients' plasma is predictive of ineffective treatment. This observation was both disconcerting and paradoxical, as IP-10 is considered to be a molecule that facilitates the migration of anti-HCV-specific T lymphocytes to the liver. After several years of research it was found to be a truncated form of IP-10 that causes the inhibition of T lymphocyte recruitment and is therefore responsible for the failure to respond to treatment in 50% of patients.
On this basis, a prognostic test to distinguish between the different forms of IP-10 from a simple blood sample, developed by a biotechnology company, will be marketed to health institutions in the first semester of 2011.

This research was conducted under the direction of the Joint Institut Pasteur/INSERM Unit Immunobiology of Dendritic Cells and the team from Paris Descartes University, Institut Cochin INSERM U1016 and Hepatology Department, AP-HP – Cochin Hospital.

11 research entities

Flow Cytometry Platform

Center for Human Immunology

THE IMMUNE CELL BATTLE PLAN

The immune system is a dynamic system composed of cells that can move and exchange information between themselves and also with the other cells in the body (healthy cells, tumor cells, or infected cells). The Dynamics of Immune Responses Unit considers these characteristics as it carries out research on immune system responses when confronted with tumors or pathogens. Using *in vivo* imaging techniques such as two-photon microscopy, an innovative technique, they view the cells located deep inside an organ and film the immune response process in the organ in question (spleen, skin, etc.), or in a tumor, in real time.
In this way, the researchers try to understand how immune cells are activated and destroy diseased or infected cells. In 2010, their research shed light on the defense strategy of two cell types involved in the elimination of tumors: T lymphocytes and NK cells. Studies revealed that their complementary mode of action and the quality of the contacts that they establish with diseased cells provided an effective response. It was found that T lymphocytes attach themselves to tumor cells for long periods of time and remain on the surface of the tumor, while NK cells prefer very short contacts and act deep inside the tumoral mass. This plan of attack could prove useful for the development of therapeutic strategies.
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HIV: EXPANSION OF REGULATORY CELLS

The main pathological hallmark of HIV infection is the severe lack of CD4+ T lymphocytes, cells which constitute the backbone of the immune system. Restoring the level of CD4+ T lymphocytes in HIV-positive patients remains a central concern for doctors. It had been demonstrated that therapy combining effective antiretroviral treatment and cytokine interleukin-2 (IL-2), a protein partly responsible for inducing the proliferation of CD4+ T lymphocytes, resulted in a significant increase in the number of CD4+ T lymphocytes in patients infected with HIV. But recent phase III clinical trials have revealed that this treatment does not exhibit a favorable clinical effect in the long term.
In an attempt to explain these disappointing results, the Immunoregulation Unit studied the long-term effects of IL-2 therapy in these patients. Researchers analyzed their CD4+ T lymphocytes and discovered that the main effect of this therapy was the expansion of populations of "regulatory" CD4+ T lymphocytes, which are characterized by a high immunosuppressive potential, in other words, an ability to prevent autoimmune reactions or even to inhibit the immune response to pathogens. This explains the failure of IL-2 therapy in HIV-positive patients. On the other hand, the expansion of regulatory CD4+ T lymphocytes induced by IL-2 may be beneficial in autoimmune diseases or may improve the body's tolerance to organ transplants. An avenue to be explored...

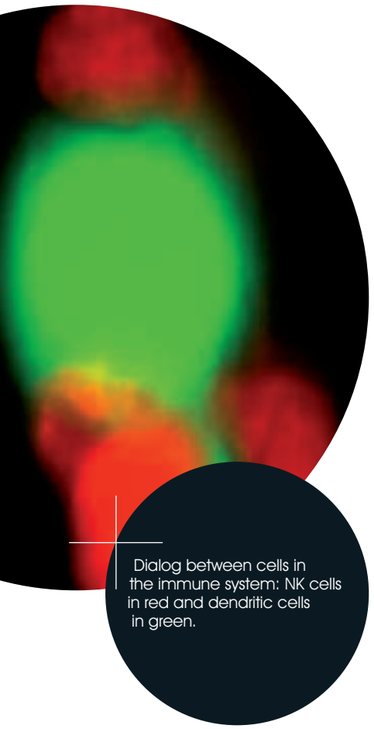
This research was conducted in cooperation with Paris Public Hospital Network (AP-HP), Georges Pompidou European Hospital, and the Henri-Mondor Albert-Chenevier Group.

Ignacio Moraga Gonzales – PhD student

He is one of the eight students in the Immunology Department who defended their thesis in 2010. His thesis is entitled *Study of the signaling pathways activated by the alpha and beta interferons leading to differential activities*. Based in the Cytokine Signaling Unit, he used cellular models that he had created himself to study how two similar molecules that attached to a single receptor could induce different responses. His work enabled him to join Stanford University (USA) in 2010 to continue his training as a postdoctoral researcher. He emphasizes that *"My time at the Institut Pasteur helped shape my scientific interests in an environment of international excellence."*

The Infection and Epidemiology Department is constantly seeking to stay in touch with clinical realities, remaining attentive to public health issues while conducting quality fundamental research on infectious diseases.

Infection and Epidemiology



Dialog between cells in the immune system: NK cells in red and dendritic cells in green.

This multidisciplinary department studies all aspects of infectious diseases, whether bacterial, viral, parasitic, or fungal: reservoirs, transmission modes, and virulence factors of pathogens, physiopathological processes, the immune response of the hosts and the impact of vaccines. In addition to its fundamental research, the department plays an active role in public health, hosting two epidemiology units, nine National Reference Centers, and three WHO Collaborating Centers. The Laboratory for Urgent Response to Biological Threats (CIBU) attached to the department provides an emergency response to potential epidemics. The department also conducts a number of clinical and epidemiological studies with clinicians from partner hospitals so that its research can be successfully applied in humans.

16 research entities

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

DENDRITIC CELLS, HIV RESERVOIRS

Dendritic cells (DCs) are one of the first targets for HIV when it enters the body. These cells, which form part of the immune system, are able to produce viral proteins (antigens) at their surface. These antigens are then recognized by T lymphocytes and a specific adaptive response is induced.
In theory, when they are infected by a virus, dendritic cells are destroyed by other cells, known as NK (natural killer) cells. The Antiviral Immunity, Biotherapy, and Vaccines Unit has demonstrated that, in the case of infection by HIV, this defense mechanism – intended to limit viral propagation – is hijacked so that it works to the advantage of the virus. The DCs become resistant to NK-mediated destruction by apoptosis and thus constitute viral reservoirs. It is the cell protein HMGB1, responsible for activating immune system effectors against a pathogen, which induces resistance to apoptosis in infected DCs. Moreover, this protein stimulates the replication of HIV in these cells, thereby contributing to the persistence and dissemination of the virus.
This research has led to the filing of two patents. The first protects the operating system which involves using HMGB1 antagonists to reduce viral replication in HIV-positive patients; the second protects the operating system which involves silencing the genes coding for the identified anti-apoptotic proteins in infected DCs.

GEOGRAPHICAL SPREAD OF RABIES MAPPED

Africa is currently the second continent most affected by rabies, after Asia. This disease, which is still fatal if untreated, causes almost 24,000 deaths each year in this region of the world, where it remains a major public health problem. 98 to 99% of human cases result from contact with dogs.
A study carried out by the Lyssavirus Dynamics and Host Adaptation Unit has shown the importance of human intervention in the spread of rabies in dogs in North African countries. By using cartographic and phylogenetic tools and comparing data from strains collected on specific dates and in specific geographical positions over a period of almost twenty years in Morocco and Algeria, researchers demonstrated that the contemporary geographical distribution of the canine rabies virus had spread beyond the limits established by simple dog-to-dog transmission (between 30 and 70km per year) and followed the architecture of the road network, keeping within administrative borders.
This shows that by transporting dogs during the incubation period, humans play a fundamental role in the spread of a virus that is a major pathogenic agent. This information is important as it helps explain the failure of current public health policies. The results can also be used to gear these policies more successfully towards prevention and raising awareness among dog owners. In addition, this research demonstrates the efficacy of what are termed Bayesian techniques, using spatial dynamics and temporal data in conjunction with traditional epidemiological techniques to study the effects of human behavior on the development of zoonotic viruses.

CHIKUNGUNYA: A NEW BREAKTHROUGH

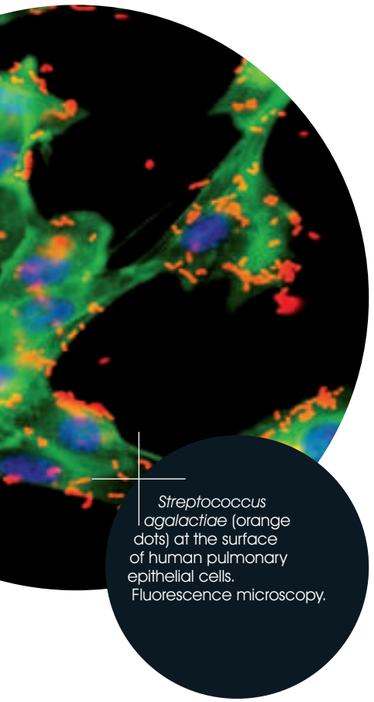
The chikungunya virus, transmitted by bites from mosquitoes of the *Aedes* genus, causes fever and joint pain in infected individuals. The massive reemergence of this virus, known since the 1950s, triggered a severe epidemic on Reunion Island in 2005-2006 and is causing major public health problems in India and South-East Asia. The virus recently also emerged in Italy and mainland France.
Researchers have been investigating the host responses during infection by this virus. Given that the viral load of patients declines before the emergence of neutralizing antibodies (therefore before the specific immune system is activated), the teams focused on the role of type I interferon (IFN-I) in controlling the infection, as IFN-I is one of the key proteins for the establishment of antiviral immunity. The researchers were able to demonstrate that, unlike other viral species for which IFN-I controls infection by acting on immune cells, chikungunya is controlled by IFN-I acting on the main target cells of this virus, fibroblasts.
This study improves understanding of the infection mechanism of the virus and the way in which the infected host controls the infection. This knowledge will be important for the introduction of effective therapeutic strategies against this disease.

This work is the result of joint research by the Dendritic Cell Immunobiology Unit and the Microbes and Host Barriers group at the Institut Pasteur.

> My attachment to the Institut Pasteur dates back to my very first day there. The "Pasteurian spirit" continues to be the motivating force behind my work each day.
>
> **Bruno Cailleux** – Head of the Scientific Equipment Department

Bacteria are associated with a vast number of infectious diseases and have always been the subject of major research efforts at the Institut Pasteur, in particular in the Microbiology Department.

Microbiology



Streptococcus agalactiae (orange dots) at the surface of human pulmonary epithelial cells. Fluorescence microscopy.

Bacteria and archaea are studied in the Microbiology Department to learn how they live and interact with the environment.
The researchers study the mechanisms that enable some of them to be virulent and to evade the host immune system and/or to develop resistance to antibiotics.
Understanding the molecular mechanisms of virulence is essential for the development of new diagnostic tools and new therapies (antimicrobial agents and vaccines).
The department also studies microorganisms and their viruses as model systems for fundamental research in areas such as genomics, genetics, and metabolism.

15 research entities

1 Biology Resource Center

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

ORGANIZED RESISTANCE TO ANTIBIOTICS

Researchers in the Antibacterial Agents Unit have been working on the mechanism of resistance to vancomycin in enterococci. In recent decades, these bacteria, the main cause of nosocomial infections, have developed multiple antibiotic resistance, and vancomycin is a last-resort treatment. This recent study explains why the genes responsible for resistance to vancomycin have spread so effectively throughout the world.
When they are expressed, these genes, which can be transferred to other microorganisms, confer a high level of resistance by remodeling entirely the bacterial cell wall. However, the high fitness cost associated with this remodeling slows bacterial growth considerably. To avoid this loss of fitness, the resistance genes are only expressed in the presence of the antibiotic and in the absence of antibiotics, this mechanism has no fitness cost and does not penalize the resistant bacteria. Both *in vitro* and *in vivo*, they retain the same characteristics as their vancomycin-susceptible counterparts, in terms of growth rate, ability to colonize, and spread from animal to animal.
This result highlights a new dimension in the fight against antibiotic resistance. It is the first demonstration of a complex and costly resistance mechanism that can disseminate among bacteria without putting them at a competitive disadvantage. This observation will incite researchers to strive for a better understanding of resistance mechanisms and their "biological cost" for the bacterial host.

A MAJOR BREAKTHROUGH IN OUR UNDERSTANDING OF NEONATAL MENINGITIS

Group B streptococci *(S. agalactiae)*, a bacterium normally present in the intestinal microbial flora of adults, is the main cause of neonatal meningitis. This severe disease is caused when these bacteria cross the intestinal and hematoencephalic barriers that protect the host from microbial dissemination in the blood and the brain.
Epidemiological studies have demonstrated that a clone of group B streptococcus known as ST-17 was responsible for most neonatal infections and almost all cases of meningitis. By experimentally reproducing the human neonatal infection, researchers have demonstrated that a specific surface protein of the ST-17 clone known as HvgA was responsible for its hypervirulence. This protein enables the streptococci to adhere *in vitro* to the cells that compose the intestinal and hematoencephalic barriers. Moreover, the researchers showed that the HvgA protein promotes intestinal colonization and the crossing of the intestinal and hematoencephalic barriers in the animal models developed for this study.
The discovery of this protein and its crucial role during infection could have major implications in the development of new diagnostic tools. This protein could also be a vaccine target for the prevention of group B streptococcal meningitis.

This research was the result of cooperation between the Institut Pasteur (Biology of Gram-Positive Pathogens Unit and Microbes and Host Barriers five-year group), the National Reference Center for Streptococci, the Institut Cochin, Paris Descartes University, INSERM, and AP-HP.

USING VIRUSES TO COMBAT BACTERIA

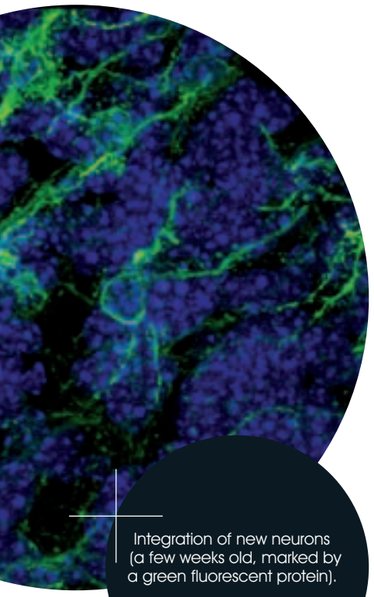
Even though we can easily imagine viruses as being responsible for diseases that are dangerous for living beings such as animals and plants, we rarely think of them as being infectious agents for bacteria. Such viruses are known as bacteriophages. Discovered in the early 20th century, bacteriophages are among the most common viruses on the planet. They have long been studied and used by scientists for the development of molecular biology tools.
Yet bacteriophages were first used for medical purposes. In the 1920s, the Pasteur researcher Félix d'Herelle demonstrated that these viruses could be used to treat bacterial infections. But when antibiotics were discovered in the 1930s, bacteriophages fell into disuse. Today, given the development of antibiotic resistance, there is renewed interest in the medical use of bacteriophages. A group in the Molecular Biology of the Gene in Extremophiles Unit has been researching this area since 2006 and has demonstrated that phage therapy (therapy using bacteriophages) could become a solution in the fight against antibiotic-resistant bacteria. Using animal models, researchers have demonstrated that bacteriophages can be used to treat pulmonary infections – a promising discovery, but one that requires further advanced research if we are to fully master the medical application of these viruses as well as their physiology and their ecology.

What I particularly value in my profession is having to combine creativity and rigor.

Fabrice Lemaitre – Assistant Engineer

The cells in the nervous system communicate with each other through billions of synapses, which gather, transfer, and retain information. The research carried out in the Neuroscience Department focuses on the biology of communication at molecular, cell, and social level.

Neuroscience



Integration of new neurons (a few weeks old, marked by a green fluorescent protein).

The department's focus on communication means that it takes a particular interest in how the information gathered by sensory organs is perceived. Major progress in the understanding of auditory and olfactory mechanisms has been made by the department in recent years. In the same vein, the department is particularly recognized for its work on the biological bases of language, the difficulties involved in understanding and acquiring language, and the consequences of diseases affecting the intellectual development of young children on social interaction. The department's teams are also involved in studying behavior associated with addiction. These issues are explored from the perspective of their biological bases, with researchers looking into questions relating to the production, transmission, and modulation of signals, how understanding these signals can affect behavior and how the signals can deteriorate in pathological situations.

7 research entities

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

LIGHT-CONTROLLED NEWBORN NEURONS

The Perception and Memory Unit has demonstrated for the first time that it is possible to use light to stimulate and specifically study the new neurons that form in the adult brain in an animal model. Until now the existing methods of stimulation did not permit this. Electrical stimulation affects all cells without discrimination and chemical stimulation concerns only neurons mature enough to have surface receptors for active molecules.
By introducing and inducing expression of photo-sensitive proteins in new neurons, the scientists have been able to control their activity with the use of luminescent flashes. This has enabled them to see, stimulate and specifically record the activity of new nerve cells. They have proved that new neurons formed in the olfactory bulb of the adult brain are integrated into preexisting nervous circuits. They have also shown that, against all expectations, the number of contacts between young cells and their targets greatly increased over several months.
This work constitutes an essential step in characterizing the functions fulfilled by neo-neurons. It opens new avenues for investigation to understand the connectivity between "newly formed" neurons and their host circuits. This is a crucial stage on the way to envisaging the use of neural stem cells as part of new therapeutic protocols for repairing brain damage, notably in the realm of neurodegenerative diseases.

AUTISM: NEW GENES DISCOVERED

Autism is a complex neurobiological disorder that affects the ability to communicate and establish social relationships. It is accompanied by repetitive behavior and restricted interests. Diagnosed in one child for every 110, autism affects four times more boys than girls. The developmental disorders generally set in before the age of 3.
The Autism Genome Project is a vast consortium on the genetics of autism involving 177 scientists from more than 60 institutions in 11 different countries, with the aim of pooling their samples, data, and expertise to thereby facilitate the identification of the genes involved in autism. This group of researchers, which includes the Human Genetics and Cognitive Functions Unit, recently presented the results of phase 2 of the consortium. They were able to demonstrate insertions and deletions of genetic sequences, a phenomenon known as "variations in the number of copies". Their work has enabled them to identify new genes involved in autism. Some of these genes act on the contacts between neurons (synapses), while others are involved in cell proliferation or the transmission of intracellular signals. The identification of these biological pathways opens new avenues for research and provides potential targets for the development of original treatments.
These discoveries support an emerging consensus within the scientific community that autism is partly triggered by several "rare variants" or genetic modifications detected in some affected individuals.

DEAFNESS: THE ROLE OF CELL JUNCTIONS

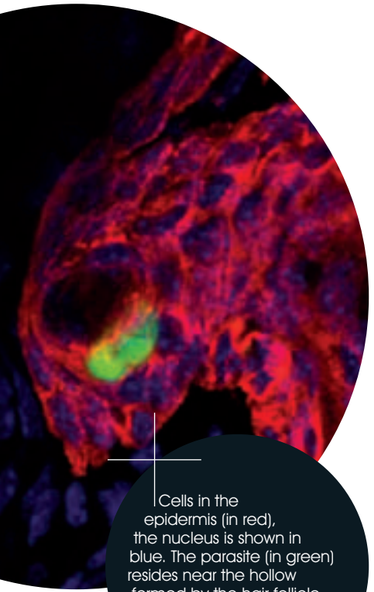
The sensory cells responsible for hearing are topped with a tuft of stereocilia within which sound vibrations are transformed into electrical signals. A very intense and/or long sound can cause these cells to die, leading to irreversible auditory damage. The Genetics and Physiology of Hearing Unit carried out research into a protein in cell junctions, vezatin, which it discovered in the year 2000. In mice lacking this protein, the team demonstrated that even moderate sound exposure (105 dB for one minute) causes a loss of hearing which, unlike that observed in wild mice in the same conditions, is irreversible. It is accompanied by a disorganization of the ciliary tuft followed by the death of these cells after a few days. This research has revealed the critical role of junctions in the resilience of the auditory sensory epithelium to sound trauma. Late recruitment of vezatin in the formation of intercellular junctions plays an essential role in their stability.

"Our daily life is about studying, understanding, and sharing."
Sarah Dubrac – Research Fellow

The Parasitology and Mycology Department conducts research on the life cycle of parasites and their vectors, and the survival strategies of some pathogenic fungi, key issues in global public health.

Parasitology and Mycology

FOCUS ON 4 SIGNIFICANT HIGHLIGHTS



Cells in the epidermis (in red), the nucleus is shown in blue. The parasite (in green) resides near the hollow formed by the hair follicle, shown in a darker color.

The department conducts research into three key eukaryotic parasites responsible for severe diseases of major burden in developing countries in terms of both public health and economic impact. *Plasmodium* spp, which cause malaria, *Leishmania* spp, the agents of leishmaniasis, *Trypanosoma brucei*, responsible for sleeping sickness, and their vectors are the focus of fundamental research efforts along with biomedical research, field work and clinical trials of vaccines. *Aspergillus fumigatus*, responsible for mycoses which are often fatal in immunodeficient patients and *Cryptococcus neoformans*, which causes severe respiratory infections, are also studied. Novel experimental models and tools are developed to better understand the dynamic interactions between eukaryotic microorganisms and their host, to identify the fundamental bases of parasitism and transmission by vectors, to reveal the mechanisms by which fungi invade the host, and to determine the virulence factors, pathology, and survival strategies of these organisms.

NEW POPULATIONS AFFECTED BY MALARIA...

Malaria kills nearly one million people per year across the world. It is caused by a blood parasite, the two main species of which are *Plasmodium falciparum*, highly prevalent in Africa, and *Plasmodium vivax*, mainly found in Asia and South America. So far, epidemiological and experimental data showed that *P. vivax* could not infect people whose red blood cells lack a surface protein called the Duffy protein, a receptor that enables the parasite to invade red blood cells.

Researchers in the Parasite Molecular Immunology Unit* have demonstrated that the Duffy receptor is not, or is no longer essential for *P. vivax* to infect red blood cells. The study showed that in Madagascar, where Duffy-positive populations of Indonesian or Asian origin have mixed with Duffy-negative populations of African origin, *P. vivax* infected the red blood cells of people with a Duffy-negative blood group and caused malaria attacks. This indicates that the parasite has broken through its dependence on the Duffy receptor and uses another as-yet-unknown pathway to invade the target cell.

These unexpected findings challenge the current vaccine research strategies targeting the parasite's Duffy binding protein, and alert on the threat of possible spread of the parasite to Duffy-negative populations in regions where it was virtually absent until now.

** In cooperation with the Institut Pasteur in Madagascar and the School of Medicine in Cleveland (USA).*

... AND A WIDELY HELD THEORY CHALLENGED

The malaria parasite is transmitted to humans by the *Anopheles* mosquito and undergoes a complex maturation cycle in the host organism, particularly in the liver then in the blood, causing this terrible disease. Until now, the scientific community believed that after injection into the skin by the mosquito, the parasites traveled rapidly to the liver, thought to be the only site of their transformation into parasites capable of infecting red blood cells. The Malaria Biology and Genetics Unit has recently called this theory into question. Using *in vivo* real-time imaging techniques developed in the laboratory, researchers monitored the progress of the parasites injected into the skin of mice and observed that 50% of them remained there. For ten percent of cases, the parasites even pursued their development cycle up to the infectious stage in the skin, without invading the liver. The study also showed that the lymph node draining the bite site receives antigens, not only from the parasite form injected by the mosquito but also from its intracellular developmental forms, indicating that this site triggers a complete immune response. Monitoring of the immune response in the skin and in the draining lymph node should be easier than in the liver, in particular to study the mechanism and efficacy of vaccine strategies. The scientists are now devoting efforts to develop this research in "human" conditions, in which human parasites infect "humanized" mice on which human skin has been grafted.

REGULATION FOR *LEISHMANIA*...

Besides the research on malaria, the department also performs research into other parasites such as *Leishmania*, responsible for severe infections transmitted to humans by hematophagous insects belonging to the genus *Phlebotomus*. Almost 12 million people are infected throughout the world (source WHO). The Parasitic Virulence five-year group focuses on the differentiation factors enabling the parasite to progress from the promastigote stage present in infected insects to the amastigote stage infectious for humans. The scientists used a sophisticated proteomic approach to demonstrate that the parasite has developed a highly specific differentiation system that does not involve the regulation of gene expression but implicates molecular modifications (phosphorylation) of some stress-response proteins. This finding is a major breakthrough for the design of therapeutic strategies against leishmaniasis.

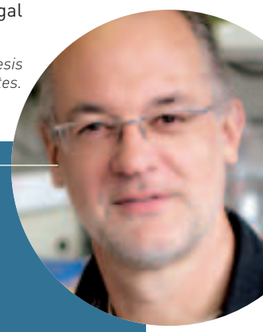
... AND CRYPTOCOCCOSIS

Cryptococcus neoformans is a fungus responsible for cryptococcal disease, a severe infection mainly affecting immunodeficient patients, in particular AIDS patients and proves fatal for one third of them. The *Aspergillus*** Unit investigates the regulation of gene expression of *C. neoformans* and showed that, among a number of regulation factors, RNAi promote stability and integrity of the *C. neoformans* genome. The scientists are now working to better understand how the complex metabolism of the RNAi pathways influences fungal virulence.

*** In close collaboration with the Center for Fungal Pathogenesis in Seoul and Duke University Medical Center in the United States.*

9 research entities

1 Center for the Production and Infection of Anopheles

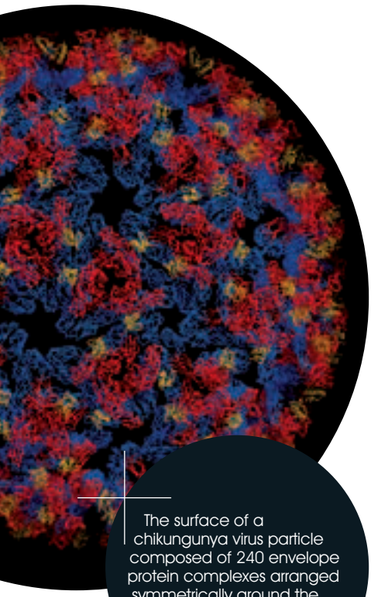


Funding granted to the BHPI Unit

The research activities performed at the Biology of Host-Parasite Interactions Unit under the direction of Artur Scherf focus on the blood stages of the malaria parasite *Plasmodium falciparum*. The team specializes in the study of virulence factors involved in the pathogenesis of severe malaria and immune evasion strategies as well as biology of the nucleus. This year, the project "PLASMOESCAPE – Monoallelic Gene Expression in Malaria Parasites: Key Mechanisms in the Pathogen's Survival Strategy" received funding from the "Ideas" program of the European Research Council (ERC), part of the 7th Framework Program for Research and Development, in the category "Advanced Investigators".

Viruses are infectious microorganisms whose genome is composed of DNA or RNA. They multiply by using the cellular machinery of the hosts that they infect. Many viruses are pathogenic for humans, and they represent a vast field of investigation for the department.

Virology



The surface of a chikungunya virus particle composed of 240 envelope protein complexes arranged symmetrically around the viral membrane.

The viruses studied by the Virology Department include arboviruses, transmitted by insects and responsible for severe diseases such as chikungunya, dengue, yellow fever, and Rift Valley fever; retroviruses such as HIV and HTLV; respiratory viruses; and viruses that cause cancer such as papillomaviruses or the hepatitis B and C viruses. All the research units base their studies on the molecular organization of viruses, their interactions with their host, and their pathogenicity determinants. To improve the understanding of the infection mechanisms of these viruses and their modes of propagation in an organism, the virologists are developing a number of partnerships with other departments at the Institut Pasteur and with the Institut Pasteur International Network. The department also hosts several of the Institut Pasteur's 21 National Reference Centers, which play a major role in the epidemiological monitoring of infectious diseases.

22 research entities

FOCUS ON 3 SIGNIFICANT HIGHLIGHTS

A DNA MICROARRAY TO DETECT EMERGING VIRUSES

As part of the DEVA TRP*, which involves several units on campus and particularly the Virology Department, a DNA microarray that can detect and identify a virus or bacterium from a very broad range of infectious agents in complex clinical situations has been developed. Researchers in the Oncogenic Virus Epidemiology and Pathophysiology Unit and the Laboratory for Urgent Response to Biological Threats (Infection and Epidemiology Department) applied this microarray in the context of the influenza A(H1N1) epidemic, which began in April 2009. In just 24 hours, the technique revealed the presence of the viral variant in clinical samples.

A DNA microarray is a solid surface on which specific nucleic acid probes are placed in a particular spatial arrangement. When these probes come into contact with the test sample, if they are complementary to the viral or bacterial nucleic acids (DNA or RNA) in the sample, they bind tightly to them. By using powerful means of molecular amplification and bioinformatic analysis tools, the signal that is emitted enables these nucleic acids to be identified, even if they are only present in small quantities.

The microarray developed by the researchers therefore makes it possible to test simultaneously for a wide range of target genes defined prior to the test for one or more pathogenic agent(s), in a single operation. Although these tools have not yet been designed for diagnostic purposes on an individual level, they could nevertheless prove useful in the context of future epidemics as they can be employed for the rapid identification of the pathogenic agents involved, something that could help health authorities in their decision making, particularly as regards public health measures and treating patients.

**TRP: transversal research program.*

Working at the Institut Pasteur helps me to develop my scientific approach, and living abroad is a character-building experience that opens my eyes to new horizons.

Inès Subota – PhD student

A PROTEIN, A TRAP, AND HIV

Characterizing the mechanisms by which the HIV virus moves from one cell to another can help us understand how the virus spreads through the body. In this context, the Virus and Immunity Unit has been studying virological synapses, those contact points between infected cells and cells not yet affected by the virus, where viral material accumulates and where viruses are able to move to the neighboring cell. The researchers are looking at the role of the cellular and viral proteins involved in this junction. They have particularly focused on a cellular protein known as tetherin, which is capable of blocking the release of new viruses at the cell surface. They have demonstrated how tetherin affects the constitution and function of synapses.

Tetherin accumulates at the cell surface, at the precise location where new viruses are formed. These viral particles are then trapped by tetherin and prevented from spreading to neighboring cells. The virus defends itself from this antiviral effect by destroying the tetherin protein. Now that the precise role of tetherin is more fully understood, we can envisage new therapeutic possibilities that can help stop the virus from destroying tetherin.

The Virus and Immunity Unit is also working to understand the immunological development of these aggregates of viral particles with tetherin and to characterize the other cellular proteins involved in the spread of HIV from cell to cell and in the formation of synapses.

WHIM SYNDROME AND PAPILLOMAVIRUS

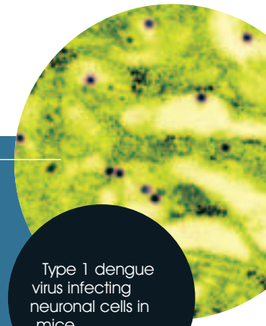
WHIM syndrome is characterized by a rare hereditary immune deficiency, passed on as a dominant trait. Its sufferers are subject to severe bacterial infections and chronic papillomavirus infections. Viruses in this family cause widespread and recurring warts and condylomata, which often become cancerous.

WHIM syndrome is the result of a change in a chemokine receptor (CXCR4) that is essential for the development and organization of the cellular traffic of immune cells. This alteration increases the activity of the receptor after the binding of its ligand (CXCL12). The Viral Pathogenesis Unit has demonstrated a link between the abnormal activation circuits that cause this syndrome and the keratinocytes, which are the target cells of the papillomavirus. The binding of the ligand to CXCR4 creates an environment that is favorable to the biological cycle of the virus and which the virus's regulatory proteins help maintain.

One therapeutic angle to consider for treating this disease would be to use molecules that inhibit this ligand so as to prevent the constant activation of the receptor and thereby hinder the action of the papillomavirus.

Dengue and chikungunya under close surveillance

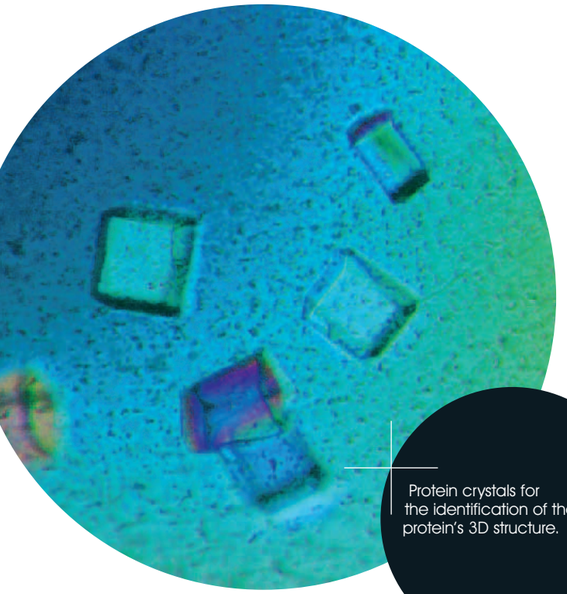
The mission of the National Reference Center (CNR) for Arboviruses is to issue epidemiological alerts, to offer expertise in viral diagnosis, and to investigate human arboviruses, throughout mainland France and its overseas territories. The CNR is an expert entity affiliated to the World Health Organization and the World Organization for Animal Health. It helps monitor emerging arboviruses in different regions of the world, in close cooperation with the Institut Pasteur International Network. The CNR is the reference laboratory for the diagnosis of imported cases in France of dengue and chikungunya, two diseases that are being closely monitored in south-east France. In 2010, the CNR diagnosed the first autochthonous cases of these two notifiable diseases in this region.



Type 1 dengue virus infecting neuronal cells in mice.

Technological Platforms

With 14 technological platforms organized into three clusters – the Genopole, Imagopole and Proteopole –, as well as the Central Animal Facility, the Mouse Genetics Engineering Center, and the Center for the Production and Infection of Anopheles, the Institut Pasteur provides its teams with all the resources required to perform cutting-edge research.



Protein crystals for the identification of the protein's 3D structure.

GENOPOLE

New sequencing techniques are revolutionizing the analysis of genetic information, from microorganisms to humans. They allow the sequencing of hundreds of genomes and the characterization of polymorphisms on a very large scale. Sequencing is applied to characterize microbial virulence and antibiotic resistance traits in a single operation. Metagenomic and metatranscriptomic data mining enables the discovery of new pathogenic agents, particularly viral agents, and helps prevent their emergence. Large-scale transcriptional analysis combining sequencing and DNA microarrays has improved our understanding of the physiology of microorganisms and the host response to infection. These new techniques enable researchers to address fundamental questions in the study of genetic and epigenetic programming during embryo development, throughout the cancer process, and during stem cell differentiation. The teams are developing and implementing computing methods to analyze and manage the genomic and post-genomic data produced by high-throughput approaches so as to facilitate the analysis of this information using multiple algorithms. The application of new-generation sequencing requires developments in the area of IT that have been carried out in close cooperation with research teams on the campus. These two operations are currently incorporated into the Scientific Computing Division within the new Information Systems Department.

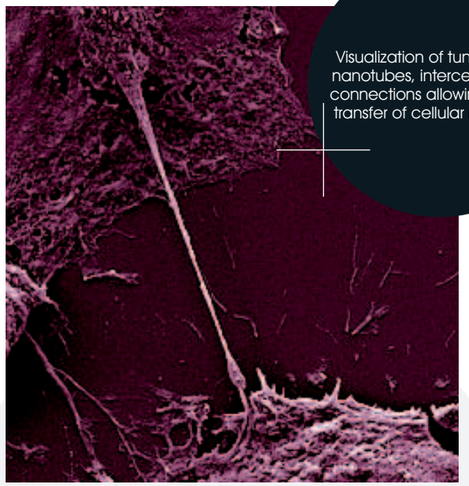
The five Genopole platforms contribute to the development and application of methodologies and computing that are vital for generating and analyzing data from high-throughput sequencing. Forty researchers, engineers and technicians with a wide variety of skills are involved in fundamental research and public health projects. The Genopole platforms are officially accredited by the GIS IBiSA (Scientific Interest Group–Infrastructure for Biology, Health and Agronomy).

PROTEOPOLE

The Proteopole offers a full range of technologies for the analysis of macromolecules, from the production of recombinant proteins in prokaryotic or eukaryotic systems to their characterization using physico-chemical methods. Various proteomic and analytical biochemistry techniques are used to address a wide range of questions such as post-translational modifications of proteins, analysis of complex mixtures of macromolecules and other compounds, intracellular traffic, and the organization of macromolecular complexes. Fully automated crystallogenesis of biological macromolecules has contributed to the development of structural biology at the Institut Pasteur. The energetics and dynamics of biological macromolecules, their assembly into complexes and interaction with ligands can be studied using 15 biophysics instruments. Thirty-three researchers, engineers, and technicians with wide-ranging skill, are involved in fundamental research projects in close cooperation with the research teams on the campus and elsewhere. The Proteopole platforms are also officially accredited by the GIS IBiSA.

IMAGOPOLE

The Imagopole is a center dedicated to research into life sciences. It brings together four technological platforms: Dynamic Imaging, Ultrastructural Microscopy, Flow Cytometry and the Center for Human Immunology. The Imagopole mission is to provide conventional and sophisticated qualitative and quantitative imaging technologies, particularly for the study of infectious, systemic, and tumoral diseases, at both molecular and functional level. The Imagopole currently has 30 research engineers, experts in ultrastructural microscopy, optical microscopy, cytometry, cell culture, molecular biology, and imaging, from the cell to the animal. Officially accredited by IBiSA (2009-2013), it has around forty imaging systems that are used for 40,000 hours each year. The Imagopole is used by several hundred researchers at the Institut Pasteur and in France, and its international reputation has generated many close collaborations with researcher groups outside of France. The Imagopole has recently renewed its ISO 9001:2008 certification, which guarantees its commitment to constantly improving the quality of its services and relations with its users.



Visualization of tunneling nanotubes, intercellular connections allowing the transfer of cellular material.

Infection imaging

Methods are developed and applied for research into host-pathogen interactions at molecular and cellular level, and also at the level of tissues or even of entire organisms.

The Institut Pasteur has "that little something extra" that makes doing a PhD a life-changing experience...

Julien Gallaud – PhD student

This research includes analysis *in situ* of sub-cellular dynamics, such as spatio-temporal parameters based on the observation of fluorescent and/or bioluminescent tracers. Data analysis is facilitated by the development and management of mathematical, informatic, and statistical approaches. The main examples of pathogens currently targeted by the Imagopole's imaging technologies include parasites such as *Plasmodium* (responsible for malaria) and *Leishmania* (responsible for visceral leishmaniasis). Infection by viruses such as the AIDS virus (HIV), the hepatitis C virus, and human papillomaviruses is also studied. Researchers also focus on infections by bacteria such as *Listeria* and *Shigella* and the mycobacteria responsible for tuberculosis. Moreover, imaging technologies are used in research into emerging diseases such as SARS, avian influenza, and chikungunya.

Some examples of technological development projects

Development of a correlative microscopy approach
This correlative approach makes it possible to combine data obtained from fluorescence (cryo)microscopy with structural information obtained in 2D using transmission (cryo)electron microscopy and in 3D using (cryo)electron tomography. Fluorescence cryomicroscopy is used to localize fluorescence-marked structures in frozen samples, a development being applied to research into isolated pathogenic bacteria and host-pathogen relations.

Imaging systems for high-throughput screening
Research into infectious disease processes requires analysis of the dynamics of host-pathogen interactions at both molecular and cellular level. Imaging techniques provide significant new information for understanding mechanisms at the molecular, functional, and structural levels. Since 2009, new high-throughput and high-resolution imaging systems for screening adherent and non-adherent cells have been available for scientists. These screening systems are also linked to a database used to view, analyze, and share biological images within the Institut Pasteur. This project is partly funded by the Greater Paris region (SESAME 2007 project).

MOUSE GENETICS ENGINEERING CENTER (CIGM)

The discovery of new genes, new promoters or new regulatory regions opens up the possibility of generating new transgenic mice. These tools are highly effective research aids to improve understanding of biological functions and to confirm genetic regulatory mechanisms in an overall genomic context.
Since it was set up in 2003, the Mouse Genetics Engineering Center has generated many genetically modified mice each year using "traditional" transgenesis techniques. Lentiviral additive transgenesis is also carried out and has been optimized for the genetic modification of rat embryos. Genetic modification via "targeted" transgenesis, using the technique of homologous recombination in embryonic stem cells, has enabled the precise manipulation of the mouse genome, providing a large number of mutant mice for the required genes.
The four members of the CIGM team have wide-ranging and highly specific skills in biology and embryonic stem cell culture, in microsurgery and in embryo microinjection, as well as in the manipulation of mice at all stages of development, whether embryo, fetus, or adult. The platform is involved in fundamental and applied research projects conducted by various Institut Pasteur units and by other research institutions in France and abroad.

CENTRAL ANIMAL FACILITY

The use of animal models remains a necessity for the Institut Pasteur research programs. The Central Animal Facility houses almost all the resources deployed for working on small rodents. The total capacity is 15,000 cages, 1,200 of which are used for rodents infected by class 2 and 3 biological agents so that research can be performed on the diseases caused by these agents. The 47-strong team is supervised by four veterinarians. The Central Animal Facility also carries out technical activities such as cryopreservation and the decontamination of strains, the development of genetically modified strains, and the production of mice strains with defined microbial flora.

CEPIA

The activities and organization of the Center for the Production and Infection of Anopheles (CEPIA) are geared to research on the interactions of the *Plasmodium* parasite, the malaria agent, with its mammalian hosts (mice or cell lines) and insect hosts (mosquitoes of the *Anopheles* genus). The platform mass-produces two species of *Anopheles* (*An. gambiae*, the African vector, and *An. stephensi*, the Asian vector). It is the only French structure specialized in the experimental infection of mosquitoes with the human parasite *P. falciparum*. A range of equipment and facilities are provided for studying interactions between *Anopheles* and *Plasmodium* (cell biology and functional genomics) and for the production of sporozoites, the infectious stages of the parasite for the mammal host. Each week, the platform is used by more than 15 researchers and technicians from the Institut Pasteur.
The platform is a partner of several collaborative programs on and off the campus, including a European project called INFRAVEC. CEPIA also responds to external requests from the Greater Paris region, from elsewhere in France and from abroad, and regularly hosts foreign interns. The platform has adopted a quality approach with the aim of being awarded ISO 9001 certification.
Alongside its *P. falciparum* mosquito production activities, the CEPIA is committed to improving and developing new tools. The *in vitro* production of the ookinete stage of *P. falciparum* has been developed and is currently being perfected. The platform is also strongly committed to the development of an effective transgenesis technology for *An. gambiae,* in cooperation with the Genetics and Genomics of Insect Vectors Unit.

For me, research is a long-term commitment.
Marc Monot – Engineer

National Reference Centers and WHO Collaborating Centers

The National Reference Centers and WHO Collaborating Centers housed within the Institut Pasteur's research units are effective observatories for communicable diseases. Every day they work to diagnose and identify the agents of several infectious diseases for which they carry out epidemiological surveillance.

Salmonella typhimurium (pink bacilli) on the surface of a mouse intestinal epithelium

Given that expert laboratories serve as microbiological observatories for communicable diseases, 21 National Reference Centers (CNRs) and two associated laboratories, supported by Institut Pasteur research units, have been accredited by the Ministry of Health, on a proposal from the French Institute for Public Health Surveillance (InVS), for six years (2006-2011 period).

Seven of these 21 National Reference Centers (CNRs) are also WHO Collaborating Centers (WHOCCs), and one CNR/WHOCC has been designated as a reference laboratory for the OIE (World Organization for Animal Health). They play a role similar to that of CNRs but at international level.

The CNRs and WHOCCs draw on the scientific environment of their host units and the various support structures, particularly the Genotyping of Pathogens and Public Health Platform (PF8) and the Laboratory for Urgent Response to Biological Threats (CIBU), to develop tools and perform research in connection with their given missions.

NATIONAL REFERENCE CENTER FOR ARBOVIRUSES

The National Reference Center and its associated laboratory at IRBA Marseille are involved in surveillance systems for dengue and chikungunya, two notifiable diseases, carrying out first-line diagnosis for all suspicious cases identified. This mission gave rise to a huge volume of activity in 2010 following the dengue epidemic outbreak in the French departments of the Americas. The possibility of an outbreak of these two diseases in mainland France became a reality in August-September 2010 with the identification of the first cases on the mainland. These two arboviruses are currently being closely monitored by health authorities at European and national level as the departments in south-east France have been infested by the mosquito vector since 2004.

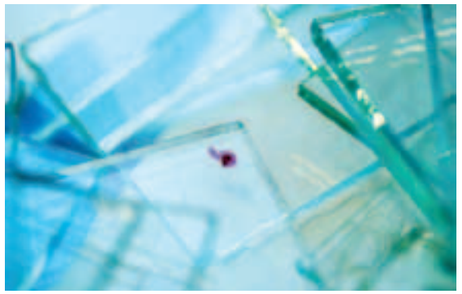
The Genotyping of Pathogens and Public Health Platform (PF8) performed more than 100,000 analyses of sequences for its recipient laboratories (CNRs, WHOCCs, CIBU) in 2010. It offered particular support to the Arboviruses CNR (Institut Pasteur and Pharo) for the emergency analysis of autochthonous arboviruses (chikungunya and dengue) in mainland France. A "second-generation" HiSeq 2000 sequencing system has been installed at the Pasteur Genopole. This equipment is used to characterize emerging pathogens in cooperation with the CNRs and hospital laboratories.

NATIONAL REFERENCE CENTER FOR PERTUSSIS AND OTHER BORDETELLA

This National Reference Center pursued its research on the evolution of species of the *Bordetella* genus following the replacement of the whole-cell pertussis vaccine with an acellular vaccine that contains only a few detoxified proteins of *Bordetella pertussis*, the primary agent of pertussis, or whooping cough. The hypothesis that, given sufficiently high vaccine coverage of the population, immunity induced by this new type of vaccine could lead to an increase in the circulation of *B. pertussis* isolates that do not express one of the vaccine antigens seems to be playing out. In recent years, the proportion of such isolates has increased regularly. However, the data obtained by the Molecular Prevention and Therapy of Human Diseases Unit indicates that these different isolates seem to remain sensitive to vaccine-induced immunity. Moreover, an increase in *B. parapertussis* isolates not expressing a vaccine antigen has also been noted, an unexpected observation given the antigenic differences in the proteins expressed by the two bacteria. This data demonstrates the importance of monitoring microbial species targeted by vaccination and closely-related species that can be modified depending on the immunity of the population.

NATIONAL REFERENCE CENTER FOR *SALMONELLA*

This CNR was able to sound the alert and take part in the investigation into two national epidemics in 2010. The first, caused by consumption of raw milk cheese, was due to *Salmonella* Typhimurium, which is ultra-resistant to antibiotics. An equine reservoir was identified (in cooperation with ANSES, the French Agency for Food, Environmental and Occupational Health and Safety). The second epidemic, caused by consumption of dried pork sausage, was due to a monophasic variant of Typhimurium. The CNR was also involved in investigating three collective foodborne infections (including one in Poitiers with more than 750 cases caused by consumption of beef in schools).



In 2010, the results of the national survey into cases of human salmonellosis in France, conducted with AFSSAPS (the French Health Products Safety Agency) and InVS, enabled scientists to pinpoint at 15,665 the number of isolated strains in France in 2008. Consequently, the level of overall completeness of the CNR was evaluated at 66% of the isolated strains in France. Serotyping remains a specialized technique given that only 3.4% of the laboratories in France are able to perform it completely. The CNR has introduced the routine, real-time application of a new method for subtyping *S. Typhimurium* and its variants, CRISPOL, a method it developed and patented (in parallel with ANSES, whose technology was transferred, TRP 2010). The CNR was twinned with CERMES in Niger with the aim of creating surveillance networks and increasing their laboratory capacity.

NATIONAL REFERENCE CENTER FOR RESISTANCE TO ANTIBIOTICS

The main activity of this National Reference Center in 2010 was to characterize the mechanisms of resistance to ß-lactams in Enterobacteriaceae, particularly in *Klebsiella pneumoniae* and *Acinetobacter baumannii*. The National Reference Center received a total of 145 strains from various hospitals and laboratories from towns in mainland France and overseas. The year 2010 was marked by a significant increase in consulting and expertise for isolates from systematic screening and from infections exhibiting antibiotic resistance, including resistance to carbapenems. It is often difficult for hospital-based and private medical biology laboratories to detect such resistance, so they often make use of the services provided by the CNR. In this context, an improvement in biologists' awareness of the health risk represented by carbapenemase-producing bacterial strains is required. Moreover, the circular issued by the French General Directorate of Health (DGS) on December 6, 2010, regarding the implementation of measures to monitor imported cases of carbapenemase-producing Enterobacteriaceae, led to greater involvement of the CNR in the analysis of these strains.

NATIONAL REFERENCE CENTER FOR TOXIGENIC CORYNEBACTERIUM

This year, the National Reference Center was involved in the development of a new molecular typing technique for isolates from the species *Corynebacterium diphtheriae*, the diphtheria agent. The most widely recognized technique had previously been ribotyping, a precise technique but one that is highly subjective as to its interpretation. This new technique involves sequencing of seven conserved genes and comparing them. This method, which has recently been published, is reproducible and its results can very easily be exchanged between laboratories across the world without any risk of error. The National Reference Center is looking to develop this technique to analyze isolates of *C. ulcerans*, another species that can cause diphtheria, transmitted by pets. This bacterium needs to be monitored as several cases of infection have been recorded in recent years in France. These infections are due to *C. ulcerans* isolates carrying the tox gene, the gene encoding the diphtheria toxin. On the contrary, the *C. diphtheriae* isolates currently collected by the National Reference Center in mainland France are mostly isolates that do not carry this gene.

Research is a constant gift.

Marie Thibonnier – Researcher

Clinical research and the Medical Center

The synergy established between fundamental and clinical research is one of the Institut Pasteur's major assets, helping it ensure that its research findings lead to applications in the field of public health.

The year 2010 was particularly marked by:
• the conclusion of large-scale contracts that will enable vaccine development projects and a gene therapy project to progress to phase I clinical trials beginning in 2012-2013;
• the growing interest of several teams on the campus and within the Institut Pasteur International Network in the ethical questions associated with research on human beings in the light of the requirements for publications and international funding;
• the development of the PATHODISC program in cooperation with teams from the Institut Pasteur and the Paris Public Hospital Network (AP-HP).

I – WIDE-RANGING AND ETHICAL CLINICAL RESEARCH

In 2010, the Clinical Research Committee examined the regulatory, legal and ethical compliance of 35 research projects on human beings or healthcare products. The Institut Pasteur was the promoter/legal sponsor of 49% of these projects. This growing role as institutional promoter demonstrates the Institut Pasteur's desire to commit to translational and clinical research and to accept the responsibilities associated with this type of research as regards the human subjects involved.
The Institutional Review Board (IRB) reviews all the projects submitted to it by scientists seeking ethical information or an official opinion in order to access US federal funding.

A – Progress in vaccine candidates and the gene therapy project

The year 2010 saw considerable progress made on several large-scale projects:
• the project on Mag Tn3, a breast cancer vaccine candidate; the preclinical development phases of this candidate in laboratory conditions have enabled it to be adapted to industrial-scale production;
• the RMV-HIV project, launch of phase I with the first administration to humans of an HIV vaccine candidate;
• the Anthrax project, with the entry into preclinical operational phase of a vaccine candidate against anthrax in partnership with the DGA (the French defense procurement agency);
• the Sanfilippo B project: the development of a gene therapy project focusing on a rare lysosomal disease, Sanfilippo B syndrome, with the production launch of the vector of interest in partnership with the AFM (the French Muscular Dystrophy Association).
The Clinical Research Center (PIRC) also helped bring to maturity two European anti-infective therapy projects, against shigellosis (STOPENTERICS) and influenza (ANTIFLU).

B – Training… and informing

For the second consecutive year, the "Research on Human Beings and Applied Ethics" program was used to train researchers in the regulations for research on human beings. Targeted educational measures have been implemented to train PhD students and researchers in ethics.

15,443 consultations for infectious and tropical diseases and travel medicine

Medical Center **55,014** vaccinations

The Clinical Research Center Workshops, a new series of six annual training and information sessions, are designed to help scientists improve their understanding of the regulations supporting the development of clinical research protocols and to meet the growing demands that govern the submission of publications and access to national and international funding.

C – The PATHODISC (PaTHOgen DISCovery) program

This program, supported by a medical committee, focuses on the identification of pathogens using very high-throughput sequencing and complementary methods. It relies on the complementary nature of the various units and platforms at the Institut Pasteur. The program studies infectious syndromes of unknown etiology in France (such as those recorded in immunodeficient children, joint research with Necker Hospital, funding from the National Research Agency (ANR)) and in Asia (cooperation between the Instituts Pasteur in Cambodia and Shanghai), and also tumoral diseases thought to be of infectious origin.

D – Quality strategy

In its efforts to successfully carry out its tasks directly involving human beings (clinical research and healthcare activities), the Medical Department has adopted a number of measures to improve the reliability of its interventions and to meet national and international standards relating to best clinical practices:

- the Clinical Research Center has updated the "standard operative procedures" in the field of biomedical research with or without healthcare products;
- the "quality assurance" strategy at the ICAReB platform was pursued following its certification in 2009 (standard NFS 96-900);
- non-opposition procedures were introduced for the secondary use of human biological samples by Institut Pasteur teams;
- the Institut Pasteur Medical Center implemented a certification procedure on the basis of the guidelines of the French Health Authority (HAS) and under the aegis of AFNOR.

II – THE INSTITUT PASTEUR MEDICAL CENTER

The Institut Pasteur Medical Center offers access to various types of healthcare, including vaccinations and consultations for rabies, infectious and tropical diseases, travel medicine, and allergology.

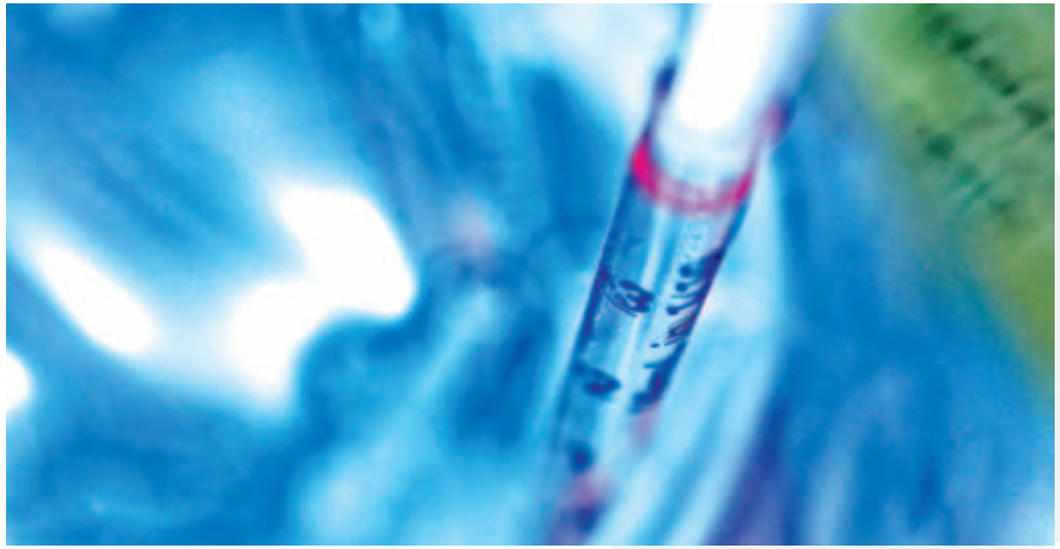
Infectious and tropical diseases, travel medicine

As well as vaccinations and advice to travelers, particularly for fragile patients (i.e. those with HIV or organ transplants), and the treatment of imported diseases on their return, a major part of the Medical Center's activities is dedicated to HIV infection, infectious diseases such as Lyme disease, treatment for rabies, and dermatology, particularly through the treatment of hidradenitis suppurativa (over 320 patients being treated). Some of these diseases are monitored in cooperation with Necker-Enfants Malades University Hospital.

> The desire to understand, the joy of sharing, the hope of improving our future.
>
> **Patrick Trieu-Cuot** – Unit and Department Head

2,052 consultations for rabies

Medical Center **7,589** consultations for allergies



Allergies

The rate of general allergy consultations for adults is the highest in France, with some 8,000 patients analyzed each year. The largest national cohort is also treated for hereditary angioedema.

Clinical research

Clinical research is directly linked to the Center's medical focus areas: cohorts and therapeutic studies on HIV infection; the physiopathology of hidradenitis suppurativa (in cooperation with Necker Hospital and the ICAReB platform); vaccinology (interaction of the yellow fever and measles vaccines in children); treatment of imported malaria; the physiopathology of post-infectious anosmia.

III – CLINICAL INVESTIGATION AND ACCESS TO BIOLOGICAL RESOURCES PLATFORM

The Clinical Investigation and Access to Biological Resources platform (ICAReB) has continued to step up its cooperation with the research teams in 2010:

- over 20 research teams using the platform (10 in 2007);
- participation in two transversal research programs (TRPs) – PATHODISC and anosmia-dysgueusia – and in a hospital clinical research program on listeriosis;
- 900 samples distributed for the DIAGMICOLL project (new methods for diagnosing infectious diseases) as against 400 in 2009;
- continued management of the WHO biobank on trypanosomiasis;
- establishment of a new CoSImmGen cohort (immunogenetic study of healthy subjects).

This platform has also launched a research initiative on bioresources (optimization of the preparation and preservation methods for biological samples/IBiSA project).

BUSINESS DEVELOPMENT

research applications

The scientific results of the Institut Pasteur's research lead to the filing of patent applications and the creation of partnerships that give rise to industrial developments. These activities are not only vital for the transfer of research carried out by the Institut Pasteur's researchers but also contribute as much as €40 M to its annual budget.

200 industrial contracts, including 70 license agreements

55 invention disclosures

12 priority patents

The Research Applications and Industrial Relations Department (DARRI) was set up for the protection and transfer of the Institut Pasteur's scientific discoveries. Its strength lies in the complementary nature of Pasteurian expertise, and it creates an effective link between the worlds of research and industry. Strengthening the partnerships between these two communities, both major players in the pursuit of progress, serves the needs of public health and patients – a concept close to Louis Pasteur's heart and a core objective that generates revenue which is in turn reinvested in the campus. The DARRI is therefore constantly striving to identify the needs of the scientific community so that it is well-positioned to meet its expectations in terms of technology transfer and business development.

SERVING THE INTERESTS OF THE SCIENTIFIC COMMUNITY THROUGH PARTNERSHIPS WITH INDUSTRY

The main missions of the DARRI consist of transferring innovation and technologies resulting from Institut Pasteur's research activities by establishing commercial licenses and by developing partnerships with industry. This implies the prior processes of identification and protection of the inventive activities in the Institut Pasteur.
In 2010, the DARRI managed 200 industrial contracts, including 70 license agreements, representing a 25% increase compared with 2009. These contracts were mostly related to diagnostics. The contracts signed in 2010 included 23 research and development or expertise agreements and 36 biological material agreements.

OPTIMIZING A WEALTH OF INTELLECTUAL PROPERTY

The DARRI's business development strategy aims at raising the number of patents offering real potential for industrial development, in order to increase the royalties collected by the Institut Pasteur.
In 2010, 55 invention disclosures were submitted, 12 priority patents were filed, 24 extensions were decided, 86 patents were issued, and 45 deposits of biological material were made. It should also be noted that 58 patents were surrendered during this year, enabling the portfolio to be optimized. At the end of 2010, the Institut Pasteur owned a portfolio of 3,609 active patents.

MORE COMPANY START-UPS

In 2010, Pasteur BioTop celebrated its tenth anniversary. Since its creation, the Institut Pasteur business incubator has nurtured 22 new companies, 17 of which are still operating. The year 2010 saw a significant increase compared with previous years with the setting up of four new companies: Affilogic, Axenis, Invectys, and Vaxitech. 2010 also marked the first year of activity of Kurma Biofund, a venture capital fund whose aim is to bring to maturity the scientific work carried out by the research units: the start-up Pathoquest was set up within this framework. A total of six young companies were created in 2010; they will follow in the footsteps of previous start-ups by generating economic value and jobs.

STRENGTHENING RESEARCH PARTNERSHIPS

For the Pasteur Infectious Diseases Carnot institute (Pasteur MI), 2010 was a year of assessment marked by a request for renewal. Each of the 33 Carnot institutes submitted a report to the French National Research Agency (ANR) detailing their activities over the past four years since their setting up. Pasteur MI was able to submit very positive results, having achieved 92% of its objectives. On the basis of 12 indicators of progress, the objectives were exceeded for four indicators and achieved for seven. During this period, research partnerships increased by an average of 72% each year. Pasteur MI is currently preparing its application to renew its Carnot label, to be submitted in early 2011. In 2010, the Carnot programs carried on, with three new programs launched in the fields of imaging, neuroprotective viral peptides and high-content screening.
Alongside these Carnot programs, the Institut Pasteur is pursuing promising programs aiming at bringing innovations to maturity over periods from one to two years, in areas as wide-ranging as zebrafish screening, innovation in the treatment of autoimmune diseases, antivirals, and original DNA polymerases...

45 deposits of biological material

24 extension decisions

TEACHING

the transfer of values

The theoretical and practical courses offered at the Institut Pasteur Teaching Center are organized and taught by French and international scientists from the Institut Pasteur as well as other scientific organizations. Meeting the needs of biologists and healthcare professionals is important, which is why the Institut Pasteur is constantly developing and updating the content of its courses and training programs.

500 students

250 PhD students

In 1889 the Institut Pasteur offered the world's first microbiology course, "Technical Microbiology", and has made teaching a priority ever since. Today the Institut Pasteur is truly a higher education hotspot. In 2010, 500 students took courses at the Teaching Center, 40 students completed their Masters internships, and 250 PhD students conducted research projects in Institut Pasteur laboratories.

40 Masters students

25 courses

A DEDICATED ENVIRONMENT AND VARIED COURSE SELECTION

The Teaching Center, based at the former Pasteur hospital, offers both practical biology and theory courses. These courses are separated into three main areas of study: Epidemiology and Public Health, Mechanisms of Living Organisms, and Biology of Microorganisms. They cover a wide range of topics including microbiology, genomics, immunology, vaccinology, neuroscience, epidemiology, cell biology, and topics related to public health. They are aimed at current students, graduates from French and foreign universities, university teaching hospitals, and French *grandes écoles*, as well as working professionals – scientists, doctors and veterinarians – wishing to supplement their training. Twenty-five courses were offered during the 2009-2010 academic year.

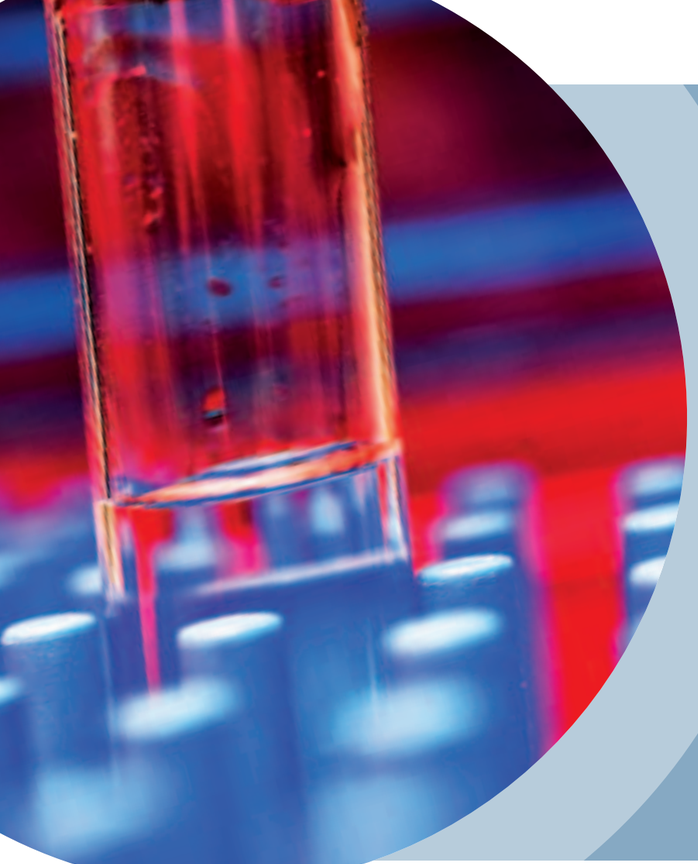
Many of these courses can be counted as part of a Masters degree program, either as second year teaching units for the Masters offered at Paris Descartes, Pierre and Marie Curie, Paris Diderot, Paris-Sud 11, and Versailles-Saint-Quentin universities, or as part of the specialized Masters in Public Health run by the Pasteur-CNAM School of Public Health. Outside these university programs, they can be taken as part of degree programs from partner universities. Most courses can also be taken by PhD students as part of their doctoral studies.

TEACHING STUDENTS FROM AROUND THE WORLD

The Teaching Center welcomes students, scientists, doctors, pharmacists, engineers, and veterinarians from all over the world. In 2010, 144 international students represented 48 nationalities. Courses are generally taught in French, but with the growing number of foreign students and lecturers the Institut Pasteur is adopting a more international approach. Certain courses are taught alternately in French and English from one year to the next and an increasing number are taught exclusively in English.

The year 2010 also welcomed the second class of doctoral students for the Pasteur-Paris University International Doctoral Program. This program, which involves agreements with Paris Descartes, Pierre and Marie Curie, and Paris Diderot universities, is open to students who have completed studies at a foreign university. It is a three-year program leading to a PhD. The "Jacques Monod" class of 2010 includes six students from Germany, the United Kingdom, the United States, India, and Taiwan.

The specialized Masters in Public Health, recognized by the French *Conférence des Grandes Ecoles*, is run in partnership with the French National Conservatory of Arts and Trades (CNAM) at the Pasteur-CNAM School of Public Health. After six months of theoretical training, students must complete a six- to eight-month internship. In 2010, all 13 students from the second class completed their oral defense, nine with specializations in "Infectious Risks". These students addressed subjects such as malaria in Senegal, hepatitis C in Egypt, acute encephalitis in Cambodia, chikungunya in Madagascar, and research priorities for infectious diseases in Laos.



INTERNATIONAL global reach

The Institut Pasteur has established an effective cooperation network that serves human development and health. This Institut Pasteur International Network, spread over every continent involving 32 institutes, has developed various partnerships with international research teams on scientific and medical issues.

67 grants from the International Division (28 study grants and 39 internship grants)

8 International Network grants (9 PhD grants and 4 conference grants)

The Institut Pasteur's excellent relations with the research community have enabled it to develop a number of international partnerships on scientific and medical topics. This approach has led to the signing of partnership agreements with the Centers for Disease Control and Prevention (CDC) in the United States, the Wellcome Trust in the United Kingdom and several other institutions across the world. Each year, around half of the Institut Pasteur's scientific publications are the result of joint international efforts. With its worldwide presence through the Institut Pasteur International Network (RIIP), the Institut Pasteur is a major strategic partner of the World Health Organization (WHO) in the area of infectious diseases. In addition to the seven WHO Collaborating Centers (WHOCCs) in Paris, the International Network hosts 11 WHOCCs and over 30 National Reference Centers recognized by the WHO.
Born out of Louis Pasteur's desire to fight infectious diseases, the International Network is a partnership of research and public health institutes with a presence on all continents. These institutes are mainly independent institutions rooted in their national contexts. The sustainability of these institutes is guaranteed by the training of local researchers.

11 grants co-funded with the Pierre Ledoux-International Youth Foundation

10 Amsud-Pasteur grants

The activities of the International Network cover the three central Pasteurian priorities – scientific research, public health and teaching – with a particular focus on infectious and emerging diseases, resistance to anti-infectious treatments, neglected diseases and research for new vaccines and treatments. For each of these areas, the institutes in the International Network are recognized as key partners by the Health Ministries in France and abroad, the WHO, leading national and international research institutions and public health organizations.

INTERNATIONAL AGREEMENTS

• In 2010, all the institutes from the Institut Pasteur International Network signed a new partnership agreement that confirms their commitment to the International Network.
• In April, the IRD (Development Research Institute) and the Institut Pasteur signed a partnership agreement to develop joint research projects. The first joint research team Institut Pasteur-IRD, named "Young Team Associated with the IRD", was set up at the Pasteur Centre in Cameroon for research on Buruli ulcer.
• The Institut Pasteur of Shanghai signed two new partnership agreements to fight against infectious diseases: the first for a research partnership with the Children's Hospital of Fudan University focusing on hand, foot and mouth disease, the second most deadly infectious disease in China in 2010; the second with the Institute for Glycomics at Griffith University, Australia, to strengthen cooperation in the research and development of new therapies and to consolidate the institutes' expertise in research into anti-infective and antiviral agents.

EVENTS

• Roselyne Bachelot, French Minister for Health and Sports, and Valérie Pécresse, French Minister for Higher Education and Research, visited the Institut Pasteur of Shanghai respectively in May and July 2010. Yves Jégo, French State Secretary for Overseas Affairs, held a meeting for the Directors of French Guiana-based research bodies in April 2010 at the Institut Pasteur in French Guiana.
• To mark the Year of France in Russia and the Year of Russia in France in 2010, the international conference on 'Scientific research and monitoring of infectious diseases' was organized by the Institut Pasteur in Saint Petersburg in May 2010.
• The RIIP Annual Scientific Meeting was organized by the HKU–Pasteur Research Centre at the campus of the University of Hong Kong's Faculty of Medicine in November 2010. The Council of the Directors of the RIIP was held on November 24-25 in the presence of the partners.
• To mark its 70th anniversary, the Institut Pasteur in French Guiana opened its doors to the public in December 2010.
• In December 2010, the Institut Pasteur in Madagascar hosted the closing meeting of the project aimed at "Building and strengthening core capacity for influenza preparedness and response", led jointly by the Institut Pasteur, the Institut Pasteur International Network, and the United States Department of Health and Human Services (HHS).

COMMUNICATIONS

• The online bibliographic archive HAL-RIIP, which also serves as a platform for the online submission of scientific publications from the International Network, has been operational since June 2009, and a new website, www.pasteur-international.org, has been launched.

EXAMPLES OF PROJECTS DEVELOPED BY THE INTERNATIONAL NETWORK

• The US Department of Health and the Institut Pasteur have signed a cooperation agreement for support, training, and capacity building in connection with influenza monitoring in Southeast Asia and Africa.
• The French Development Agency is funding the regional SISEA project (Surveillance and Investigation of Epidemic Situations in Southeast Asia).
• The Total Foundation is funding projects on infant diarrhea in Madagascar and Central African Republic.
• A program focusing on bacterial meningitis in Africa and a program on influenza in Asia and Africa are being supported respectively by the French Ministry of Foreign Affairs and the French Ministry of Health.

International teaching

Each year, more than 100 scientists from the Institut Pasteur International Network supplement their training with courses or internships in Paris. In 2010, 18 courses and workshops funded by the International Network were taught in nine countries – two in Africa, four in Asia, five in Latin America, two in Europe, and five in North Africa. Four courses and workshops were also taught in the framework of the Amsud-Pasteur partnership.

Research at the Institut Pasteur is about making constant progress while addressing society's needs.

Michel Débarbouillé – Researcher

expertise & resources

human resources

Skills development, "plan seniors" policy for older staff members, stress prevention, and e-learning are the themes that the Human Resources Department's teams have been particularly focusing on this year.

LABOR RELATIONS

Labor relations in 2010 began with the implementation of staff representative bodies, which for the first time were renewed within the framework of the new trade union representation law. The merger of two trade unions (one trade specific, one general) following new legislation has affected, in a small but noticeable way, the Institut Pasteur's trade union dynamics. Following the aforementioned renewal, the five trade unions now present on campus all exceeded the minimum 10% of votes required for representation.
Although the annual negotiations for 2010 ended in disagreement, given an uncertain budgetary context which made it difficult to enter into any long-term commitments, other negotiations were brought to a successful conclusion. These included the negotiations for a "method agreement" *(accord de méthode)* on the prevention of psychosocial risks, signed unanimously and which provides for the establishment of a working group composed of members of trade unions, the CHSCT (Committee for Health, Safety, and Working Conditions), the Workplace Health, Hygiene and Safety Department, and the Human Resources Department, tasked with making proposals for action in this field. The annual negotiations for 2011, organized at the end of the year, were also successful and included provisions for several pay-related measures for the coming year and a one-time bonus for all staff in recognition of the work achieved in 2010.
The year 2010 also saw the implementation of the "plan seniors" policy for older staff members at the Institut Pasteur, providing a series of measures in support, anticipation and preparation for retirement, in conjunction with the goal of keeping workers in employment. The agreement on telecommuting also came into force on an experimental basis in sectors that mainly use computer resources. After a one year trial period, 15 employees out of 80 who were eligible to opt for this arrangement chose to do so.
Finally, in the area of welfare/medical expenses, the Institut Pasteur agreed to re-examine the question of contract funding in order to standardize and streamline regulations concerning managerial and non-managerial staff contributions. A statement of conclusions signed by four out of five trade unions finalized this decision and resulted in a working group that met regularly in 2010.

ORGANIZATION

The year was also marked by the reorganization of several supporting units with the aim of optimizing their operational efficiency for the use of the laboratories. These changes, which did not affect staff numbers, targeted the purchasing, logistics, building works, scientific equipment, and IT resources sectors. For the IT resources sector, an Information Systems Department, serving as an umbrella structure for all the IT activities on the campus, was set up.
Particular efforts were also made in terms of training to support the professional development of staff members concerned by these structural reorganizations. Within the Human Resources Department, efforts particularly focused on welcoming, informing, and managing young researchers. A targeted communication strategy was carried out on internal procedures, steps to be taken, and key information. The Human Resources Department also strengthened the team responsible for welcoming young researchers and stepped up its relations with international funding bodies to ensure that each researcher's case can be properly dealt with on an individual basis.

2,434 staff *Institut Pasteur workforce as of December 31, 2010*

1,854 Institut Pasteur employees (81% on permanent contracts)

508 employees from research and higher education organizations

72 interns

EMPLOYMENT, CAREERS AND SKILLS MANAGEMENT

Several aspects of skills development were investigated in 2010, including the material used for the annual appraisal system, which has been redesigned to focus more on past and future achievements in conjunction with skills acquired or to be improved. A major study was also launched on preparation laboratories with the aim of being ready for future developments in this sector as a result of new requirements (health and safety, quality, ergonomics, etc.) and future organizations.
In the area of training, 2010 also saw the launch of the first e-learning training modules on chemical risk prevention. Devised in cooperation with an external organization, this new training approach will facilitate compliance with all the regulatory requirements in this particularly complex field. The course is available to all employees from their desktop and is available in French or English. A record is kept of training modules completed, making it easier to keep up with compulsory refresher training, every three or five years depending on the particular risks. This training course was an instant hit, with 846 training programs successfully completed during the year. Other modules are already being planned in the areas of general risks, biological risks, and radiation protection.

RECRUITMENT

The policy to control workforce numbers launched in 2009 was pursued in 2010. This policy, based on the fact that many Pasteurians are nearing retirement age, stipulates that departing employees are not systematically replaced. With this policy, the Institut Pasteur's workforce can remain generally stable at around 1,900 employees (monthly average across the year), owing to the arrival of a large number of young PhD students and post-doctoral researchers on fixed-term contracts. The main bases for these contracts, specific to the research sector, are research training grants, the hosting of researchers under an international agreement, or the hosting of foreign researchers.

53.3% of managerial posts and **71%** of technician, supervisor and employee posts are held by women

financing structure

Current income in 2010 €250.4 M

€99.5 M
Revenue from own activities

45.1%(1)

€39.5 M
Research contracts

€22.8 M
Sales and services

€37.2 M
Industrial royalties

Industrial royalties (€37.2 M and 16.9% of income) are essential for the Institut Pasteur. They are a direct result of the research carried out on campus. The increase this year is a result of the resolution of litigation cases with companies regarding HIV-1 and HIV-2 licenses. These negotiations, which took place during 2010, had a major impact on accounts.

Sales and services (€22.8 M) comprise activities linked to business development (expert assessments, advice for industry, etc.), public health activities carried out at the Medical Center, and the provision of services, particularly to institutes in the International Network. This income remains stable.

Research contracts (€39.5 M) are stable, both public contracts and European and foreign funding. The number of major programs aimed at institutes in the International Network has fallen slightly this year.

€60.2 M
Fundraising and patrimony incomes

27.3%(1)

€18.1 M
Donations

€1.5 M
Apprenticeship tax

€23.8 M
Legacies

€16.8 M
Patrimony incomes

Patrimony incomes (€16.8 M) include current financial revenue, rent from income property and agricultural revenue from estates registered among the Institut Pasteur's assets.

Fundraising (€43.4 M) includes all donations and legacies, and apprenticeship tax. Donations continued their upward trend in 2010, reaching €18.1 M, compared with €16.4 M in 2009. The overall total collected, including donations stated as operating income, non-recurring income, and equipment grants, has stabilized, reaching €19.7 M in 2010 as against €19.8 M in 2009. Legacies, as regards the share allocated to current revenue, are stable compared with 2009. The sums recorded as resources correspond to completed legacies, the majority of which were bequeathed in previous years.

€60.9 M
Government contributions

27.6%(1)

€5.8 M
French Institute for Public Health Surveillance (InVS)

€55.1 M
French Ministry of Research

These are mostly made up of the grant from the French Ministry of Research, which totaled €55.1 M in 2010, up by €3 M from 2009.

They also include the **annual grant from the French Institute for Public Health Surveillance (€5.8 M),** which covers some of the costs of the activities carried out by the National Reference Centers.

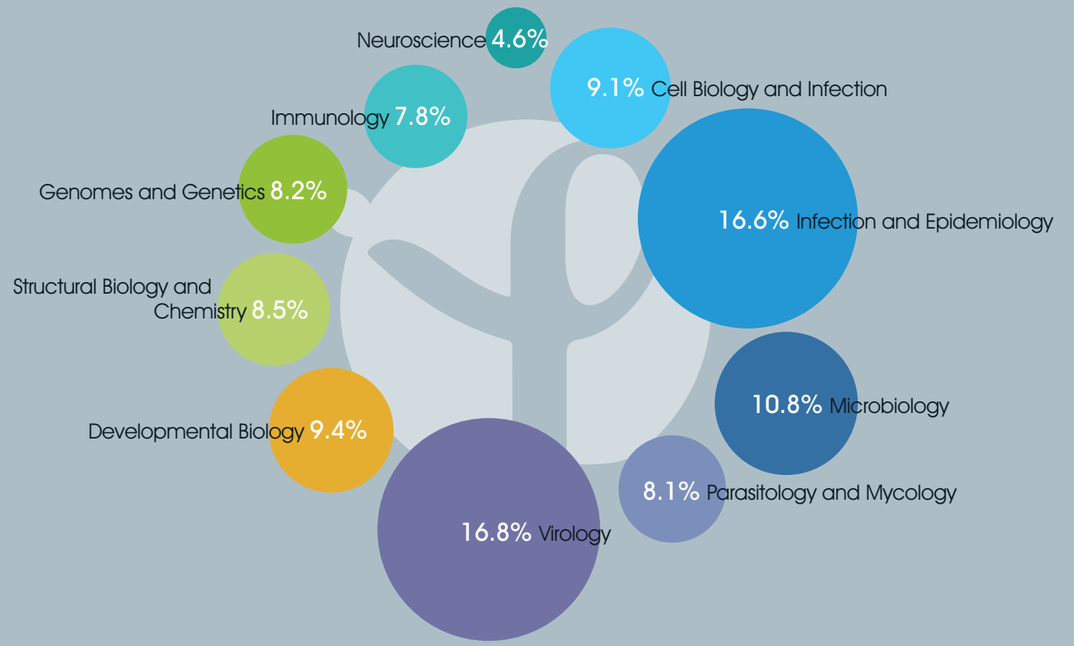
€29.8 M
Non-allocated

€29.8 M
Carry-over income

This is carry-over of unused income from previous years and recovery of provisions.

(1) Percentages calculated excluding carry-over of unused income from previous years and recovery of provisions.

Current expenditure in 2010 €249.6 M



€114.4 M
Personnel expenditure

€85.7 M
Operating costs

€13.4 M
Depreciation

€36.1 M
Provisions and future commitments

financial situation

In 2010, the current-account surplus totaled €0.8 M. This can be broken down into operating deficit (€10 M), structurally loss-making, and financial surplus (€10.8 M), mostly comprising income from long-term investments.

CURRENT OPERATIONS

Current revenue increased by 8% on average in relation to 2009, with contrasting developments for various items. Government grants, revenue from own activities, and income from fundraising increased, while patrimony incomes fell. The operating result, structurally loss-making, demonstrates that the balance of the Institut Pasteur's operating result is linked with the optimization of movable and immovable assets management. In a difficult global economic climate, our competitiveness is also reliant on government support.
Current expenditure also rose by 8.2% compared with 2009, with an increase in total operating expenditure.

NON-RECURRING OPERATIONS

The surplus in non-recurring operations, composed partly of legacies and income from the management of long-term investments, stands at €34.3 M and structurally comprises the largest share of the annual net surplus.
As laid down in the articles of association, the share of each gift (donation or legacy) under €300,000 is recorded in the accounts as current income. The share which exceeds this amount is reported as non-recurring income (apart from the amount transferred to operating income in accordance with article 19 of the articles of association (€4 million in 2010)). In 2010, the total recorded in the accounts as non-recurring income was €12.2 M (compared with €16.6 M in 2009). In total, legacies recorded in the accounts in 2010 as both current income and non-recurring income amounted to €35.9 M, compared with €40.5 M in 2009.
The overall situation of the global financial markets meant that, for the second year running, net non-recurring income could be recorded in the long-term investment portfolio (€21.5 M). The Institut Pasteur's assets are managed by several specialist financial institutions on the basis of management agreements. The long-term allocation of assets corresponds to a balance between shares and bonds. The performance of the portfolio stands at 5.4% in 2010 against a benchmark of 3.7%.

donations and legacies

The generosity of individuals and companies, as demonstrated through donations, legacies, and sponsorship, has always been one of the pillars of the Institut Pasteur's budget, and most importantly has guaranteed its independence. The year 2010 saw a real boost in this generosity as a result of specific fundraising measures.

DONATIONS

Upward trend confirmed with greater funding

With €21.14 M collected in 2010 (donations and apprenticeship tax), the upward trend that began in 2006 is continuing. Specific campaigns aimed at individuals subject to the solidarity tax on wealth (ISF) raised more than €1 M through the provisions of the law in favor of labor, employment, and purchasing power (TEPA), and the apprenticeship tax paid by companies to the Institut Pasteur Teaching Center reached a record high this year (€1.48 M). Fundraising was also stepped up for the building of the new Integrative Biology of Emerging Diseases Center. Highlights of 2010 included the Business Gift program launched by BNP Paribas Corporate and Investment Banking; several research teams in around twenty countries and at the Institut Pasteur enjoyed the benefits of this scheme in 2010.

Attracting new donors

In recent years we have seen a new generation of donors seeking to invest in a cause to give a sense of purpose to their professional success. They look for a certain level of excellence when selecting and assessing programs to invest in. To provide a suitable framework to meet the requirements of these sponsors, a space for specialist expertise and dialog between the Institut Pasteur and potential sponsors was set up in 2010. Known as Campus Philanthropes, this new service adopts a fully personalized approach, with the aim of putting together a custom project in line with the priorities and aims of each sponsor. A dedicated website is available at www.campusphilanthropes.fr.

Welcoming the public: from Pasteurdon to "Pasteur' Spirit"

For the first time since the launch of Pasteurdon, last October members of the general public were invited to follow a discovery trail set up on the Institut Pasteur campus and touring some twenty laboratories, scientific workshops, stands and lectures. Delighted visitors flocked to this event, organized with the help of volunteers from the "AXA Atout Coeur" foundation. Other visitors had already become acquainted with the Pasteurian universe through the original, innovative approach of artist Fabrice Hyber, whose exhibition "Pasteur' Spirit" was held on the Institut Pasteur campus in July 2010.

Exhibition by artist Fabrice Hyber at the Institut Pasteur in July 2010.

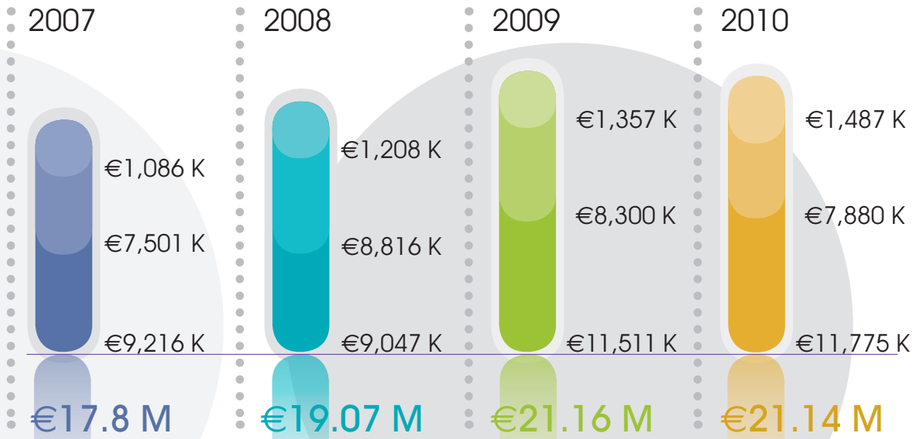
LEGACIES AND GIFTS

Legacies and gifts: a year of contrasts

The year 2010 was marked by a significant fall in new legacies received, fewer than 100, confirming the slow-down observed in this sector over the past three years. Nevertheless, the total amount of legacies and gifts given to the Board of Directors was slightly higher than 2009, reaching €29.1 M as opposed to €26.6 M in 2009 (a rise of 9.2%).
The legacies bequeathed to the Institut Pasteur are most often shared with other institutions which therefore affects the calculated average volume.
The institute did receive an exceptional legacy of almost €12 M, including various works of art, which will be processed over the coming financial years.

Development of fundraising in €M

(from top to bottom: Apprenticeship tax, Businesses, Individuals)



The amount received from life insurance policies once again confirmed the importance of this major resource, totaling almost €5 M. This resource, a recent source of revenue for the Institut Pasteur, has developed considerably in under a decade and is exempt from tax, in the same way as legacies and gifts which are exempt from transfer duties.

Quality strategy: certification on the horizon

The legacies and real estate assets management department pursued its quality strategy, launched by the Institut Pasteur general management some years ago. This department now has a quality policy for the management and processing of gifts and applies specific operating rules according to a well-defined process. It is also constantly aiming to improve the department's expertise and to assess the satisfaction of its main partners, which particularly include notaries. These efforts to ensure security and transparency were rewarded with AFNOR certification in 2011.

A new communication strategy

Many people contact the legacies department each year for information on how to give to the Institut Pasteur, whether in the form of a legacy or a gift.

These people require advice from the legal experts working in this department, which specifically deals with these questions relating to the transfer of assets.

The information brochure containing technical guidelines and above all practical and simple advice has been completely remodeled to engage more effectively with readers and make it as easy as possible to make a legacy or gift to the Institut Pasteur.

A promotional campaign calling for legacies and gifts has been launched in the mainstream and specialist press to raise awareness of the continued importance of the public generosity upon which the Institut Pasteur was built.

The Institut Pasteur has also set up a think tank on philanthropic trusts as a continuation of the first conferences on the subject. This platform for discussion and sharing ideas over the Internet, organized around two groups of recognized experts from a wide range of fields gathers together legal and assets management professionals keen to deal with the requests of their clients regarding the fiscal, civil, and patrimonial aspects of giving. In 2010, the think tank provided information on donations and tax loopholes, posthumous gifts, and temporary transfer of usufruct rights.

communications and fundraising

In 2010, the Department of Communications and Fundraising emphasized the Institut Pasteur's position in the landscape of biomedical research, clarified what the Institut Pasteur "brand" represents and improved conditions to promote fundraising.

In 2010 the Department of Communications and Fundraising consolidated its efforts among all sectors of the public to raise awareness of the action and values of the Institut Pasteur, to publicize its latest news and its successes, to promote its humanist model (commitment, scientific excellence and selflessness) and to further emphasize its need for donations with the development of Pasteurdon. The aim of improving the Institut Pasteur's visibility is particularly to encourage fundraising, a vital activity which has its own specific strategy. To this end, a corporate communications campaign was launched in the first half of the year to raise public awareness of the Institut Pasteur's missions. This campaign was based on core values and principles: determination, dedication and action for the sole purpose of furthering research.

PASTEURDON BECOMES A FIRM FIXTURE

Pasteurdon 2010 enjoyed the support of major French companies and was organized in partnership with all French digital terrestrial network channels, providing major media impact. As well as the 12 digital terrestrial channels that broadcast short programs free of charge, France Inter radio station also offered its airwaves to this fourth Pasteurdon. The Institut Pasteur opened its doors to the public for the event over the weekend of October 25, inviting people to come and meet its scientists. This helped raise awareness among the general public of science and biomedical research, and of the need for donations. Several Institut Pasteur employees were involved in the event, along with volunteers from the "AXA Atout Coeur" foundation.

COMMITTED SPONSORS

Large numbers of partner companies and corporate donors are continuing to support the Institut Pasteur, a recognized leader in its areas of expertise. Alongside loyal partners such as Danone and the Le Roch-Les Mousquetaires Foundation, new sponsors have rallied to the Institut Pasteur's cause, including the Banque Privée Européenne and the company Reckitt Benckiser. The extension of the agreement with the Total Foundation for a further five years has led to the creation of the Françoise Barré-Sinoussi Chair for HIV/AIDS training and research and will serve to finance research programs to fight infectious diseases and public health initiatives, notably against sexually transmitted diseases.

Arnaud Ardoin (LCP-AN), Rebecca Fitoussi (NT1), Sonia Mabrouk (Public Sénat), Matthieu Delormeau (NRJ12), Alexandre Devoise (W9), Cyril Hanouna (France 4),

Sandrine Kiberlain, the face of this year's Pasteurdon, and 11 digital terrestrial TV presenters agreed to be part of a video supporting Pasteurdon 2010.

Sandrine Kiberlain, Laurence Boccolini (TMC), Audrey Pulvar (i-Télé), Ruth Elkrief (BFM TV), Adrienne de Malleray (Direct 8) and Joan Faggianelli (Gulli).

A NEW SERVICE FOR MAJOR DONORS

The Institut Pasteur has developed a new service for major donors known as Campus Philanthropes. This initiative was launched in July 2010 at the opening of artist Fabrice Hyber's exhibition. The service offers dedicated, customized support. Institut Pasteur advisers help donors to devise the broad outlines and stages of their investment projects. The donors are fully involved in their programs, taking part in all the key stages of project implementation and sharing in the achievements and successes with the researchers themselves. Each donor therefore receives customized support that meets his or her needs and expectations, and becomes an integral part of the team that he or she has chosen to support.

DEVELOPING INTERNATIONAL SPONSORSHIP

As well as its foundation in the United States, based in New York, in 2010 the Institut Pasteur also set up a foundation under Swiss law, the Pasteur Foundation Switzerland. It is composed of volunteer members and aims to develop scientific partnerships and to raise the funds needed to put them into action. Its headquarters are in Geneva. In 2011, a communications and development strategy will be launched to raise awareness of the aims and social objectives of the new foundation. In June 2010, the Institut Pasteur also had the honor of welcoming HSH Prince Albert of Monaco to its headquarters with the aim of establishing a long-term partnership between the Institut Pasteur and the Principality of Monaco.

WEB-BASED SUPPORT FOR TARGETED COMMUNICATION

The Institut Pasteur makes use of the instant, interactive, and free services offered by the Internet. In 2010, Facebook and Twitter pages and a YouTube channel were set up. The first Web-based fundraising campaign took place during Pasteurdon, with a fun-to-use application. Increasing numbers of donors are choosing to give over the Internet. A user-friendly, simple, and informative space has been set up for this purpose at aiderpasteur.fr.

"Research at the Institut Pasteur is about the thrill of searching, the joy of finding, and the pleasure of sharing!"

Tarek Msadek – Head of Laboratory

BRINGING SCIENCE TO THE GENERAL PUBLIC

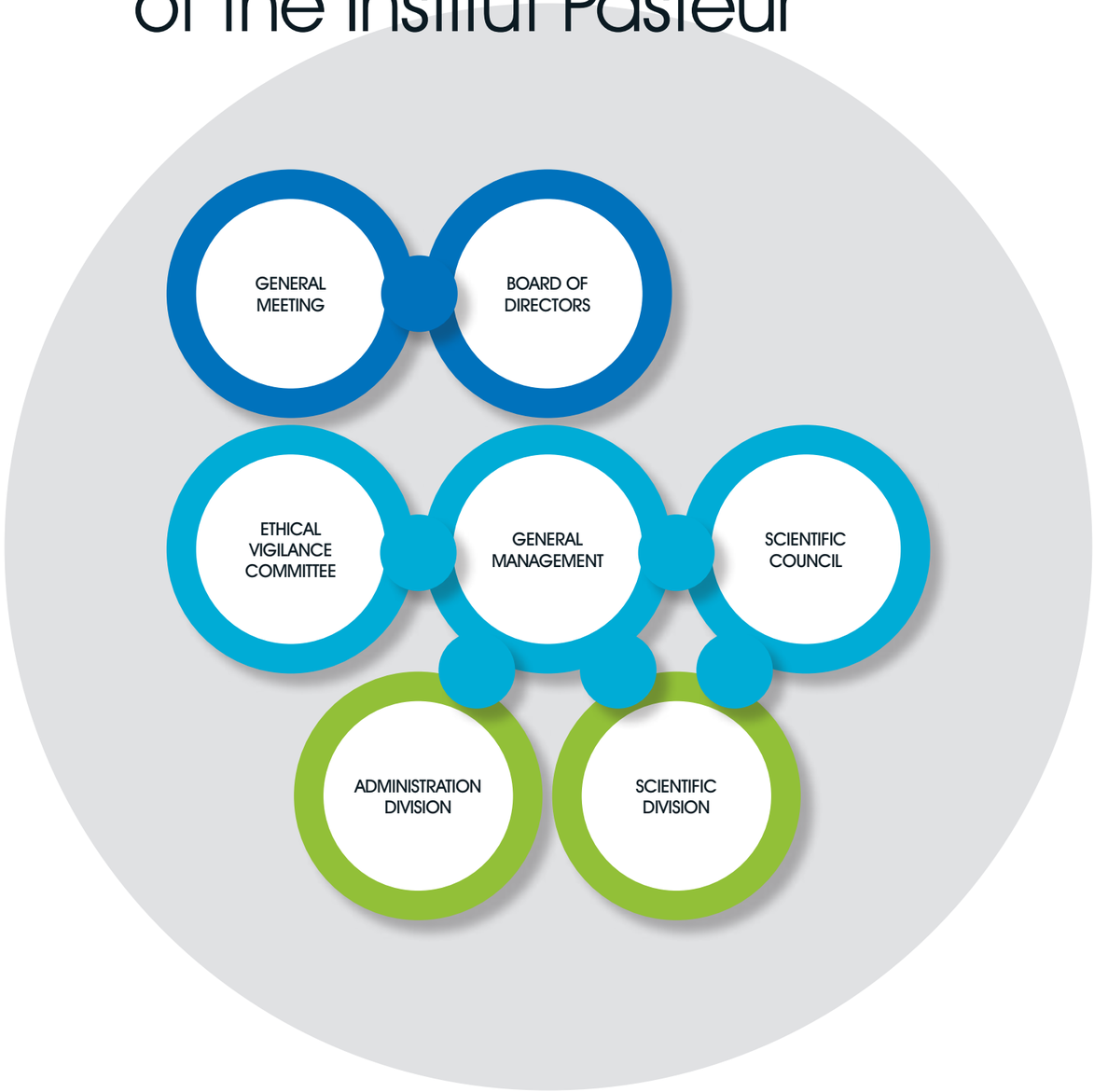
The Institut Pasteur continued to promote and explain its research to the public. Of the 30 press releases published this year, 20 focused on advances in research. Several talks were also organized for the general public in Paris and throughout France. The "Mysteries of Science" and "Mr. Pasteur's Way" lectures, in particular, met with great success.
The Pasteur museum, which preserves the memory of Louis Pasteur's life and work in the apartment where he lived for the last seven years of his life, helps promote and raise awareness of Pasteurian history. The museum received 9,600 visitors in 2010. The cultural seminars on the theme "Mr. Pasteur's Way" were attended by 580 people, and 12 exhibitions were provided via loans of collections in France and abroad. The Pasteur museum is also popular among young people. It hosted the prize-giving ceremony for the "Science et Vie Junior" trophy for young inventors. The ceremony not only gave budding scientists a chance to demonstrate their inventions but was also an opportunity for them to visit the museum and learn about Pasteurian culture.

My job contributes to HIV research efforts and helps improve the lives of men and women affected by this virus in developing countries.

Yoann Madec – Researcher

general organization

general organization of the Institut Pasteur



board of directors

up to July 2011

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Antoine Gessain
Head of the Oncogenic Virus Epidemiology and Pathophysiology Unit, Institut Pasteur

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General Council for the Environment and Sustainable Development, French Ministry of Ecology, Sustainable Development, Transport, and Housing

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Patricia Tortevoye
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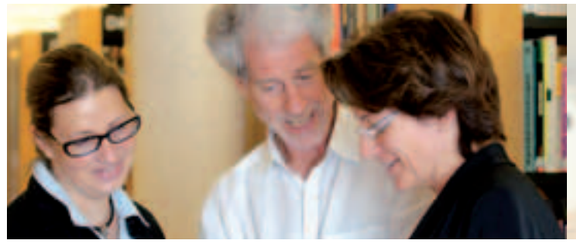

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scientific council

June 2011

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Head of the Lymphocyte
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Christophe d'Enfert
Head of the Fungal Biology
and Pathogenicity Unit

Frédéric Tangy
Head of the Viral Genomics
and Vaccination Unit - Vice-President

Pedro Alzari
Head of the Structural
Biochemistry Unit

APPOINTED PASTEURIAN MEMBERS

Ana Cumano
Head of the Lymphocyte
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Arnaud Fontanet
Head of the Epidemiology
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Antoine Gessain
Head of the Oncogenic
Virus Epidemiology
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Institut Pasteur
Department of Communications and Fundraising
25-28, rue du Docteur-Roux
75724 Paris Cedex 15, FRANCE
www.pasteur.fr