Institut Pasteur

Review of activities 2013-2017

INTERIM REVIEW OF THE 2014-2018 STRATEGIC PLAN

July 2017

Preamble

The 2014-2018 strategic plan implemented by the Institut Pasteur and the 33 institutes in the Institut Pasteur International Network, based in 26 countries, enabled the Institut Pasteur to respond more effectively to the challenges and possibilities raised by progress in modern science and to incorporate these new developments into a comprehensive medical and public health strategy based on an international approach.

Since 2014 the Institut Pasteur has implemented an ambitious strategic plan drawn up by the President, Christian Bréchot, working closely with the Board of Directors and with the support of all the units of the Institut Pasteur and the Institut Pasteur International Network (IPIN). This plan set out several key priorities.

It aimed to:

1. strengthen the attractiveness of jobs and careers at the Institut Pasteur;
2. position the Institut Pasteur International Network at the center of the Institut Pasteur's strategy;
3. develop and modernize education activities, improving interdisciplinarity and drawing on the potential of digital technologies;
4. reaffirm the major role of medicine and public health for the Institut Pasteur;
5. strengthen bioinformatics and integrative biology at the Institut Pasteur;
6. improve the organization of research and strengthen scientific synergies;
7. improve the Institut Pasteur campus;
8. devise new models for cooperation with industrial partners;
9. strengthen the Institut Pasteur's image and fundraising activities.

The key priorities of an ambitious plan

1_ Strengthening the attractiveness of jobs and careers at the Institut Pasteur

To boost the attractiveness of jobs and careers at the Institut Pasteur, the management team has made efforts to enhance job offers with the aim of attracting high-level scientists. Major changes have also been made to career guidance and development procedures for existing staff. Between 2013 and May 2017, 19 research units and laboratories, and 16 junior research groups (five-year groups) were set up (30 entities were closed over the same period). This led to an overhaul of more than a quarter of the Institut Pasteur's scientific entities.

At the same time, efforts were made to enhance career possibilities for existing staff by improving recognition of the value and diversity of different career paths. This involved creating group head and research director positions; offering significant pay rises to post-doctoral fellows and, recently, PhD students; and setting up Chairs of Excellence for high-level scientists. Significant measures have also been taken to improve career guidance and support. A new welcome and support structure for contract researchers (MAASCC) is now available for scientists arriving from abroad, and provides support to scientists at all stages of their career to assist them in their professional development. The Careers Committee was set up to support this career development, to identify and promote talent, and to help employees avoid demotivation and feelings of failure. Against this backdrop, the introduction of a profit-sharing agreement shows that the management is keen to recognize the efforts and contributions of all staff on an equal basis.

2_ Positioning the Institut Pasteur International Network at the center of the Institut Pasteur's strategy

The Institut Pasteur has reaffirmed the central role of the Institut Pasteur International Network in its strategy, with the aim of creating a fully functioning community of institutions that share the same values and goals and work together on joint projects.

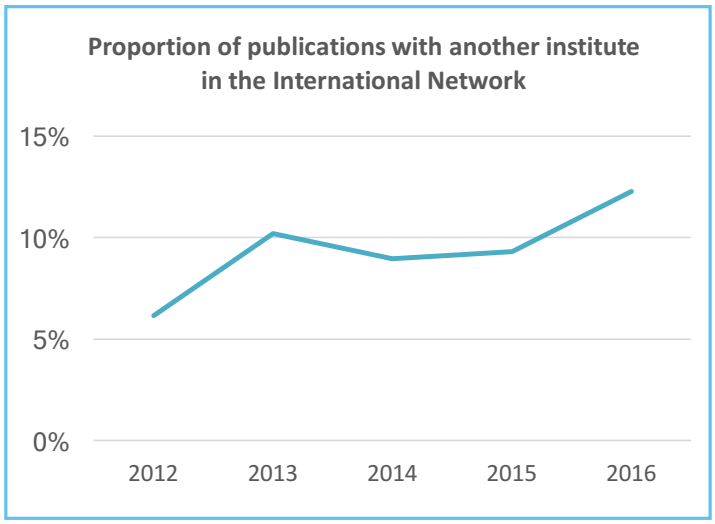
A global scientific vision and a charter signed by all the institutes have been drawn up, illustrating the vision and shared values of the 10,000 people working within this network on public health, education and research activities. The past four years have also seen the launch of an annual Symposium of the Institut Pasteur International Network, attended by a large number of scientists from the entire network as well as the directors of many of the institutes. Several other vital measures designed to strengthen the unity of the network have been introduced or consolidated, including the creation of joint research units between the Institut Pasteur and other institutes in the network, greater staff mobility within the network (now compulsory for young scientists recruited on permanent contracts), and training. Four-year research groups (G4s) have also been set up, giving young scientists the opportunity to develop ambitious research projects in institutes within the International Network (not including Paris), often in their home country. Efforts to identify talent and offer career guidance within the network will ensure its future success.

A scientific strategy has been developed, combining the local strategies of each of the institutes with regional strategies and a global approach. Major scientific consortiums have been set up, enabling comparisons to be made between the epidemiological situations in Asia, Africa and Latin America/the Caribbean. One of these large-scale projects resulted in the first global map of resistance to artemisinin, the most commonly used antimalarial medication.

A dedicated outbreak investigation task force has also been set up to provide assistance, when requested by national and international authorities, in responding to the risks of pandemics. This task force was deployed in response to the outbreaks caused by Ebola and Zika, resulting in both large-scale, effective action and also several high-level publications. The Institut Pasteur International Network is the institution that has published the most articles on the Zika virus since the outbreak began in 2015 – ahead of the Centers for Disease Control and Prevention in the United States – reflecting the extensive involvement of its scientists. The united front exhibited by the institutes in the International Network during the Ebola virus epidemic demonstrated the wide-ranging nature of the Institut Pasteur's expertise, from identification of the strain responsible for the epidemic to hands-on support for local authorities in the field. Moreover, its outstanding research on Ebola also resulted in the publication of high-level papers in a third of the institutes in the network. These large-scale actions also led to the creation of front-line laboratory in Macenta (Guinea) and then to the creation of an Institut Pasteur in Guinea, the 33rd member of the International Network. The response to this crisis illustrated that the Institut Pasteur and the International Network are capable of stepping up in the event of health emergencies and also making a long-term commitment – confirming that the Institut Pasteur can now be considered as a major partner for WHO in health crises. The Pasteur International Network Association, the official entity which represents the network, has been admitted into official relations with WHO and now has a seat in the World Health Assembly, indicating the extent to which the network is recognized for its unique role in global health.

These initiatives within the International Network are part of a more wide-ranging, long-term strategy, resulting in the addition of a new Institut Pasteur in Guinea (see above) and in the development of an ambitious project in Brazil, in close cooperation with the *Fundação Oswaldo Cruz* (Fiocruz), a long-standing partner of the Institut Pasteur, and the University of São Paulo. This broad strategy has also led to several scientific partnerships across the world (including in Myanmar and the Philippines), to the creation of joint research units outside the network – in Japan, Australia and the United States – and to the implementation of training / education initiatives with Qatar.

Stronger links with the Institut Pasteur International Network have also produced nearly a doubling of the number of joint publications between the Institut Pasteur and at least one other institute in the International Network (60 in 2012 and 117 in 2016). The proportion of Institut Pasteur publications produced with another International Network institute also doubled from 6 to 12% between 2012 and 2016, reflecting a significant rise in scientific cooperation among the institutes.



3_ Developing and modernizing education activities

The Institut Pasteur has also strengthened and modernized its education activities, one of its major missions, adopting a more interdisciplinary and international approach and working in partnership with universities and higher education and research institutions in France and around the world. The number of courses run by the Institut Pasteur rose from 24 for the 2013-2014 academic year to 42 for 2016-2017. The Institut Pasteur's education activities have also been modernized with the introduction of Massive Open Online Courses (MOOCs) in a variety of disciplines including epidemiology, immunology, neuroscience, entomology, vaccinology, and developmental biology. A Medicine-Science program has been set up in partnership with the École Normale Supérieure and the Institut Curie, with the aim of attracting more doctors to the Institut Pasteur. A number of outstanding predoctoral programs have also been developed (Amgen Scholars, iGEM, Erasmus +), opening the Institut Pasteur to younger students, and several doctoral programs have been expanded, such as the Pasteur-Paris University International Doctoral Program.

In response to the scientific developments currently under way at the Institut Pasteur, a new bioinformatics and integrative biology course was introduced in 2017. This course, which is compulsory for all new PhD students at the Institut Pasteur, reflects the fast-growing data analysis needs of laboratories and will boost the quality of training available at the Institut Pasteur.

4_ Reaffirming the major role of public health and medicine for the Institut Pasteur

Since 2013, the Institut Pasteur has taken steps to reaffirm the vital role of medicine and public health in its strategy. This has resulted in the creation of two new transversal centers: the Center for Global Health, which draws on the International Network to improve understanding of major global health challenges by combining scientific expertise, interdisciplinarity and cutting-edge technology to serve public health; and the Center for Translational Science, which aims to ensure that medicine plays a central role in discussions on research areas that need to be developed, while facilitating the transfer of discoveries made in laboratories to new diagnostic and therapeutic tools in hospitals. One goal of this center is to "remedicalize" the Institut Pasteur by attracting greater numbers of doctors, pharmacists and veterinarians to our research units on the basis of specific contracts that enable them to combine research and healthcare activities. This policy has also led to affiliation with hospitals to facilitate transfers between research and medical activities, and to the organization of monthly events where scientists and doctors can come together to discuss key public health issues.

In addition to these new measures, the Institut Pasteur has stepped up its pathogen surveillance efforts; it hosts fourteen National Reference Centers and eight World Health Organization Collaborating Centers. The creation of PIBnet (the Pasteur International Bioresources Network), a large-scale project to harmonize, optimize and make effective use of microorganism collections and analytical methods in Paris and throughout the International Network) and the modernization of technological methods have made the Institut Pasteur more competitive in the area of surveillance.

5_ Strengthening bioinformatics and integrative biology at the Institut Pasteur

The consolidation of bioinformatics, biostatistics and integrative biology over the past four years is the result of unprecedented efforts to position the Institut Pasteur at the forefront of a field that will play a vital role in the future of biomedical research. Three research units directed by leading scientists and a transversal research center specializing in these topics (the Center of Bioinformatics, Biostatistics and Integrative Biology (C3BI), an Institut Pasteur–CNRS joint service and research unit) have been set up. Thirty high-level engineers have also been recruited, and the initial target of forty new staff should be reached in early 2018.

One visible result of this concerted policy to boost staff and infrastructures came in 2016 with the success of the Institut Pasteur's project proposal, INCEPTION, in the highly selective "Convergence Institute" call.

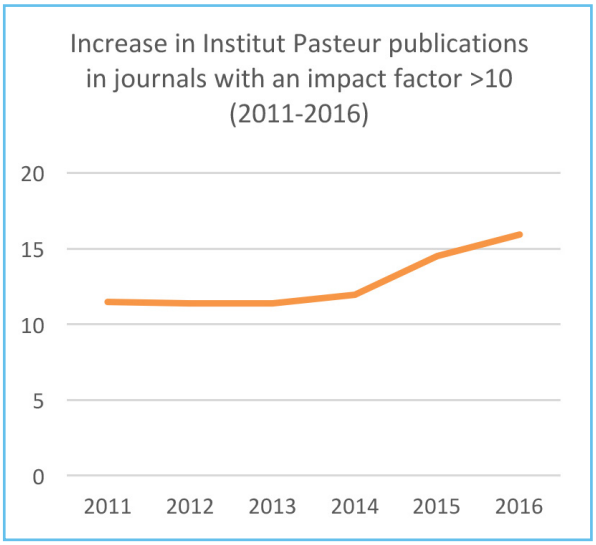
6_ Improving the organization of research and strengthening scientific synergies

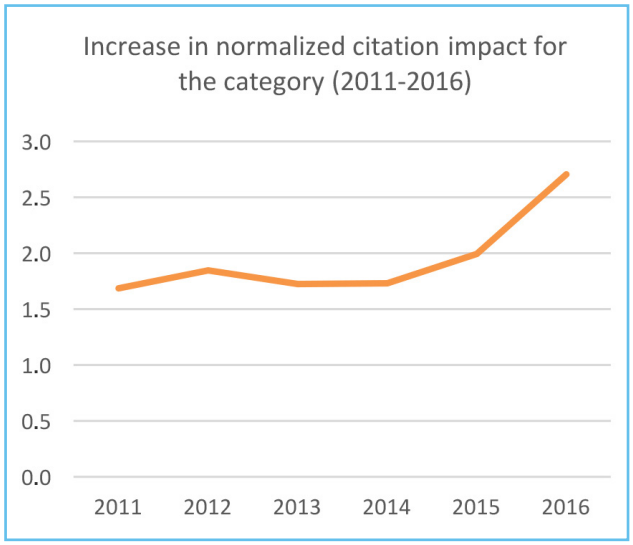
A truly interdisciplinary scientific approach is essential for the practice of biomedical research today. To strengthen scientific synergies, four transversal research centers have been set up to complement the eleven existing research departments: the Center of Bioinformatics, Biostatistics and Integrative Biology, the Center for Global Health, the Center for Innovation and Technological Research, and the Center for Translational Science.

In addition to these activities, maintaining quality research at the Institut Pasteur also means stepping up technological research and providing scientists with the best possible infrastructures for their research activities. Cutting-edge equipment, such as the Titan cryo-electron microscope and an 800 MHz NMR spectrometer, have boosted existing infrastructures. The central role of technological research in the scientific strategy has been confirmed with the creation of the Center for Innovation and Technological Research (Citech), facilitating the incubation of new technologies and the development of partnerships with institutions involved in high-level technological research. The Institut Pasteur is now planning to continue these efforts with an ambitious plan to invest in new facilities and staff.

The will to improve the organization of research and to enhance the career perspectives of the researchers contributed to a significant progress in scientific publications: in 2016, approximately one in six (16%) of the Institut Pasteur's publications were published in journals with an impact factor higher than 10, compared with 11.5% in 2011.

There has been a marked increase in publication impact: the normalized citation impact (the number of citations in relation to comparable articles – same journal category, publication year and document type) was 2.7 in 2016, compared with 1.7 in 2011. Several major scientific discoveries have been made over these four years, a selection of which are described in the appendix.





7_ Improving the Institut Pasteur campus

Over the past four years, the Institut Pasteur has embarked on major building works to improve its five-hectare campus in the center of Paris. A building has been constructed to house the Titan Krios™ new-generation cryo-electron microscope, which will be used to investigate viruses and bacteria at atomic level and study the molecular processes at work during infection.

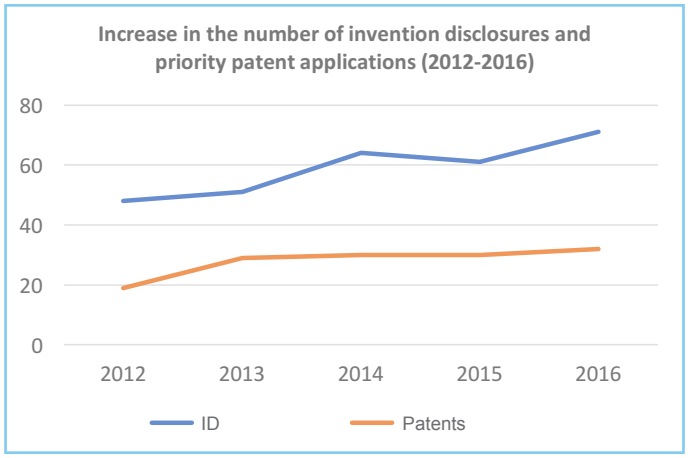
A new 1,600m² OMICS Center will house teams working on bioinformatics, “dry” biology, genomics and proteomics from the first half of 2018.

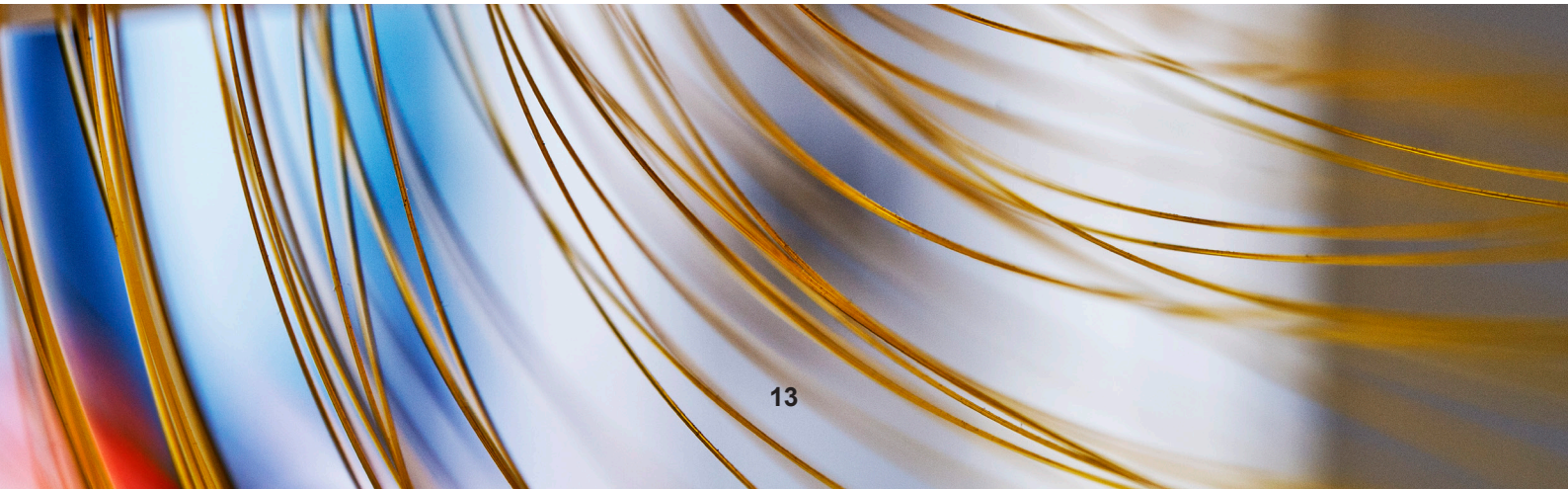
8_ New models for technology transfer and industrial partnerships

In 2013, the Institut Pasteur was facing a period of uncertainty in terms of revenue from technology transfers and industrial partnerships, caused by challenging circumstances: the gradual expiry of the most lucrative patents (the hepatitis B patent in 2015 and gradually those associated with HIV) led to a fall in industrial revenue. The period from 2013 to 2014 was also a difficult phase for research and development contracts, and changes in industry payment models led to a gradual drop in upfront payments. This challenging situation forced the Institut Pasteur to devise new models for collaboration with industry. Relations with industrial partners have now been redefined with a new focus on shared strategic priorities. Non-exploited patents in the Institut Pasteur's portfolio have been identified and analyzed, and a committee of experts has been set up to assess invention disclosures. These measures have helped reboost the Institut Pasteur's industrial partnerships, partly reflected in R&D contracts, after a less successful phase.

The Institut Pasteur has improved its ability to generate highly innovative new patents by boosting its innovation identification methods and stepping up support to scientists. Efforts have also been made to encourage the creation of biotechnology companies in life sciences, especially by improving incentives for scientists with a more attractive invention remuneration policy, organizing events focusing on entrepreneurship at the Institut Pasteur, and supporting company start-up projects. This proactive approach has led to the creation of three start-ups since 2014 and to continued support for start-ups already based on campus.

There has also been a significant increase in the number of inventions arising from the Institut Pasteur's research, leading to a rise in the number of invention disclosures and patent applications. The Institut Pasteur's scientists registered 71 invention disclosures in 2016 (compared with 51 in 2013) and filed 32 patent applications (compared with 19 in 2012).





9_ Improving the Institut Pasteur's image and boosting fundraising

Several measures have been adopted to improve the Institut Pasteur's visibility and image in France and across the world, leading to a rise in donations and legacies.

The Institut Pasteur has recently developed a strategic platform for brand communications, emphasizing the modernity of the Institut Pasteur and presenting scientists' discoveries in a way that resonates with the public. An alumni community was also set up in 2016 to contribute to the Institut Pasteur's reach and reputation in France and abroad, to promote networking between members and to support fundraising activities.

In a further bid to boost visibility, Erik Orsenna was appointed Institut Pasteur Ambassador, and he has already helped raise awareness of the Institut Pasteur's work. Partnerships with radio stations and television channels have been stepped up each year with Pasteurdon, the Institut Pasteur's annual fundraising campaign. Twenty four television channels and fourteen radio stations now support the event.

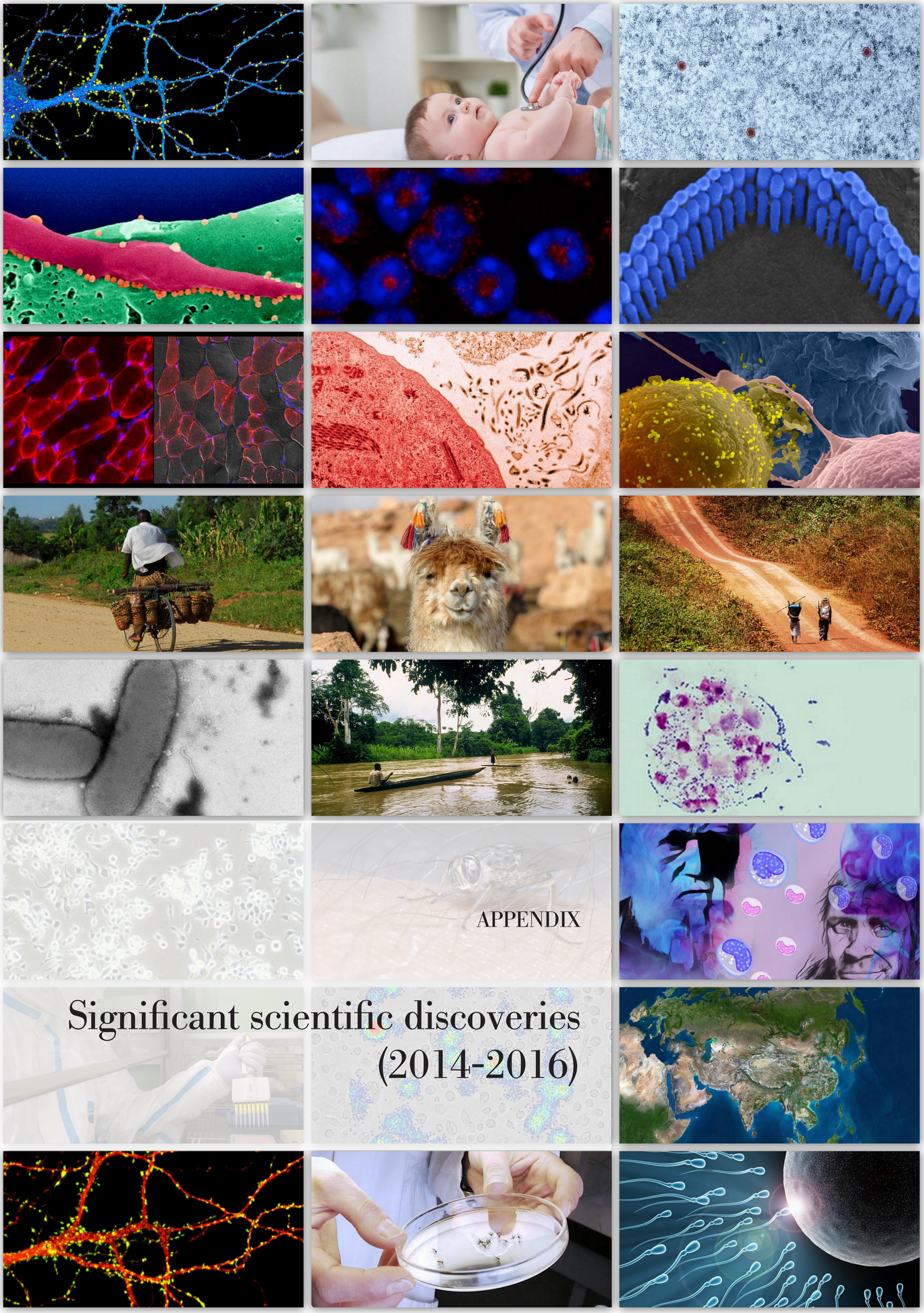
The Institut Pasteur's digital communication strategy, a key contributor to visibility, has been revamped to improve the clarity of the Institut Pasteur's image and guarantee consistency and continuity in communications.

An ambitious fundraising strategy for donations and legacies has been pursued in France and abroad. At national level, major strides have been made in fundraising, positioning the Institut Pasteur among the best-performing institutions in France. These efforts resulted in a 25% increase in funds raised by the Institut Pasteur between 2013 and 2016, and a significant rise in legacies (+28%), making a major contribution to the Institut Pasteur's research projects. The cumulative growth in fundraising between 2014 and 2016 was €20 million, enabling the Institut Pasteur to step up its activities.

These improvements have also led to a new, more ambitious approach to international fundraising, especially in the United States, China and Switzerland. The international fundraising campaign, whether direct or indirect, during the year 2016 raised more than 8 million euros, including 2.7 millions which were effectively given to the Institut Pasteur in 2016.

The future: discussions on a scientific vision for 2025, campus improvements and a possible extension at the Saclay research cluster

The 2014-2018 strategic plan was developed on the basis of a future scientific vision – but that vision needs to be regularly updated, a task that was carried out in 2016 under the coordination of Lluis Quintana-Murci, Scientific Director of the Institut Pasteur. The resulting document should be used as a basis for future recruitments and strategic action. This process of reflection was also incorporated into the discussions launched in summer 2015 on the possibility of setting up an Institut Pasteur center at the Saclay research cluster. Given the complexity of this topic, the management team has proposed that the question should be examined carefully and thoughtfully via a stage-by-stage process. A major internal consultation, ad hoc working groups and several discussions with the higher education and research institutions in the University of Paris-Saclay have enabled significant progress to be made. The question of the feasibility and desirability of extending the Institut Pasteur to the Saclay research cluster has also been discussed on a regular basis with the Scientific Council and the Institut Pasteur Board of Directors.



APPENDIX

Significant scientific discoveries (2014-2016)

2014

Inserm and the Institut Pasteur identify a new variant of Ebola virus in Guinea

Inserm and the Institut Pasteur published their initial findings on the characteristics of the Ebola virus discovered in Guinea. Initial virological investigations enabled them to identify Zaire ebolavirus as the pathogen responsible for this epidemic.

Mild hearing impairment may indicate greater underlying problems

Scientists from the Institut Pasteur, Inserm, Collège de France, and Pierre and Marie Curie University, in collaboration with a team from the University of Auvergne, identified mouse models that mimic high-frequency hearing impairment in humans, with a strong low-frequency sound interference.

Predicting mutations that lead to epidemics

Using the 2005-2006 chikungunya virus epidemic that occurred in the Indian Ocean islands as a study model, researchers at the Pasteur Institute have succeeded in developing an approach that can predict the virus mutations most likely to emerge in the short-term, with strong epidemic potential.

The emergence of neonatal group B streptococcal infections explained

Scientists from the Institut Pasteur and the CNRS, in collaboration with teams from the CNRS/Inserm/Paris Descartes University–Sorbonne Paris Cité (based at the Institut Cochin) and the Wellcome Trust (Sanger Institute), have recently revealed the cause behind the emergence in the 1960s of neonatal infections due to group B streptococcus and which resulted from the widespread use of an antibiotic, tetracycline, from the 1950s onwards.

Autism: SHANK gene may indicate the severity of the disorder

The Institut Pasteur, the French National Center for Scientific Research (CNRS), Paris Diderot University and the FondaMental Foundation succeeded in mapping the clinical incidence and impact of certain genetic mutations linked to the cognitive and intellectual abilities of the patients. Mutations affecting the SHANK3 gene were shown to coincide with the most severe cases of autism and are associated with 1 out of 50 children with autism and intellectual deficits.

Genomics challenges long-held beliefs surrounding the role of agriculture in African history

An extensive genomic study of pygmy hunter-gatherer populations and agricultural village communities, conducted in Central Africa by scientists from the Institut Pasteur and the French National Center for Scientific Research (CNRS), in collaboration with the French National Museum of Natural History (MNHN), the University of Montreal and the University of Lyon 2, challenges the established understanding of the role played by agriculture in African Neolithic history. It would appear that agriculture was not directly responsible for the demographic success of populations that adopted it or for the high level of genetic mixing between agricultural and pygmy populations.

2015

Identification of an Achilles heel in the dengue virus gives new hope for vaccine development

In association with Imperial College London, scientists at the Institut Pasteur and CNRS have identified a vulnerable site on the surface of the dengue virus which is targeted by the only broadly neutralizing antibodies identified to date.

Chambéry babies – Official recognition of the new bacterium identified by the Institut Pasteur, *Rouxiella chamberiensis*

Following the death of three newborns at Chambéry hospital (France) in December 2013, scientists at the Institut Pasteur quickly drew connections to a previously unknown bacterium responsible for the contamination of parenteral nutrition bags.

First case of prolonged remission (12 years) in an HIV-infected child

A young woman now aged 18 and a half, who at birth was HIV-infected via mother-to-child transmission (during pregnancy or at delivery), is in virological remission, despite not having taken any antiretroviral therapy for the last 12 years.

Following maternal transmission, group B strep mutates to sicken infants

Group B *streptococcus* (GBS), a mostly benign inhabitant of healthy adults, is one of the leading causes of neonatal sepsis and meningitis. Researchers from the Institut Pasteur and Inserm have now shown that these pediatric cases might occur when the bacteria mutates within the infant following transmission from the mother.

Sepsis: cell therapy to repair muscle long-term impairment

Scientists from the Institut Pasteur, Paris Descartes University, Sainte-Anne Hospital and the CNRS have published a paper in *Nature Communications* which proposes a therapeutic approach based on mesenchymal stem cell transplantation, which has produced encouraging results and has proved successful in restoring muscle capacity in animals.

2016

Zika: Confirmation of a causal link between the Zika virus and Guillain-Barré Syndrome

Using data collected in French Polynesia, researchers from the Institut Pasteur, the CNAM (Conservatoire national des arts et métiers), the Institut Louis Malardé, the French Polynesia Hospital Centre, and the Public Hospitals of Paris (AP-HP), have shown that infection by the Zika Virus (ZIKV) increases the likelihood of contracting Guillain-Barré Syndrome (GBS), a severe form of limb paralysis that is often accompanied by respiratory impairment.

Zika and microcephaly: first trimester of pregnancy most critical

A new analysis of data from the 2013-2014 Zika epidemic in French Polynesia, using innovative mathematical modeling techniques, by scientists from the Institut Pasteur, Paris, and their French Polynesian colleagues has confirmed the incidence of grouped cases of microcephaly and quantified the risk of microcephaly associated with the virus.

Antibodies capable of eliminating HIV-infected cells

Researchers from the Institut Pasteur, CNRS and Vaccine Research Institute (ANRS/Inserm) have recently shown that some effective antibodies recognize cells infected by the human immunodeficiency virus (HIV) and trigger their destruction by the immune system. This discovery sheds new light on the mechanism of action of these specific antibodies, which are currently undergoing clinical trials.

Confirmation of the persistence of the Ebola virus in the sperm of survivors of the epidemic

An international study conducted by scientists from the IRD, Inserm and the Institut Pasteur, together with their Guinean partners at Donka University Teaching Hospital, Macenta Hospital, the National Institute of Public Health and the University of Conakry, has confirmed the persistence of the Ebola virus in the sperm of survivors of the Guinea epidemic for at least nine months after recovery.

Malaria - a mapping of artemisinin resistance confirms that resistance is confined to Southeast Asia and has not spread to sub-Saharan Africa

The first global mapping of artemisinin resistance (the KARMA study) has definitively confirmed that resistance to the main drug currently used in the treatment of Plasmodium falciparum malaria is for the moment confined to Southeast Asia and has not spread to sub-Saharan Africa. Led by researchers from both the Institut Pasteur in Paris and the Institut Pasteur in Cambodia, KARMA gathers a large consortium of institutions including 13 members of the Institut Pasteur International Network.

Sleeping sickness: parasites found hiding in the skin

Scientists from the Trypanosome Cell Biology Unit (Institut Pasteur/Inserm), working in collaboration with scientists from the University of Glasgow, have demonstrated the presence of a large quantity of trypanosomes – the parasites responsible for sleeping sickness – in the skin of individuals with no symptoms. This discovery should refocus the screening strategy for this disease.

Africans and Europeans have genetically different immune systems... and Neanderthals had something to do with it

In the prestigious journal *Cell*, scientists from the Institut Pasteur and the CNRS decoded the immune responses of 200 African and European individuals. They show that there is indeed a difference in the way these populations respond to infection, that this response is largely controlled by genetics, and that natural selection has played an important role in shaping such immune profiles. They also offer proof that the genetic legacy passed on by Neanderthals to Europeans has significantly influenced their ability to respond to viral challenges.

Diagnosis of Alzheimer's disease: llama antibodies detect cerebral lesions

The major challenge facing physicians treating Alzheimer's is the ability to detect markers of the disease as early as possible. These markers, located in the brain, are difficult to access, hampering diagnosis. Using two types of llama antibody capable of crossing the blood-brain barrier, a non-invasive approach to reach brain cells was developed in a mouse model of the disease. Once in the brain, these llama antibodies can specifically mark and show amyloid plaques and neurofibrillary tangles, the two types of lesions that characterize Alzheimer's disease.

2017 (January - May)

How nicotine acts on the brains of schizophrenic patients

Several studies have indicated that schizophrenic patients are likely to show a high level of nicotine dependence. Scientists from the Institut Pasteur, the CNRS, Inserm and the ENS used a mouse model to elucidate the mechanism of action of nicotine on cells in the prefrontal cortex.

Why does bronchiolitis only affect infants?

Researchers from the Institut Pasteur in Paris and in Shanghai, Bicêtre Hospital (AP-HP), Paris-Sud University and the CNRS (French National Center for Scientific Research) reported on the discovery of a new group of B lymphocytes, which are only present in infants and are the preferential target of the virus responsible for bronchiolitis. This shows why this infection of the lower respiratory tract mainly affects newborns so severely, in contrast to older children.

Link between a virus and sexual reproduction on Earth

By formally identifying the main player in the fusion between male and female sex cells, researchers from the Institut Pasteur, the CNRS and Paris Descartes University, together with American and German teams, have revealed the probable viral origin of this fusion process, which is common to a vast number of living organisms on Earth. In addition, the study provides new lines of research for therapeutic possibilities, aiming to block sexual reproduction in certain pathogens, such as the malaria agent.

The migration history of Bantu-speaking people: genomics reveals the benefits of admixture and sheds new light on slave trade

Using data from a vast genomic analysis of more than 2,000 samples taken from individuals in 57 populations throughout Sub-Saharan Africa, scientists from the Institut Pasteur and the CNRS, together with a broad international consortium, have retraced the migratory routes of these populations, previously a source of debate. By analyzing the genomes of more than 5,000 African-Americans, the scientists have identified the genetic origins of African populations deported as slaves, and confirmed that the Bight of Benin and West-Central Africa were the main ports used for the slave trade to North America.

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