





INSTITUT PASTEUR

In an enlightening interview with *International Innovation*, **Professor Christian Bréchet**, President of the Institut Pasteur, reveals the tremendous progress made by the world-leading research organisation, which continues to pave the way to enhanced scientific understanding and better public health

Named after renowned chemist and microbiologist, Louis Pasteur, how does the Institut Pasteur support the advancement of science, medicine and public health?

Although there are many high-quality research institutes worldwide, the Institut Pasteur has three unique differentiating qualities. The first is its name; people around the globe know of Louis Pasteur and his legacy. There is therefore an expectation of excellence associated with our work – and, to date, 10 of the Institut's scientists have been awarded the Nobel Prize.

The second is that we have a blend of activities; the Institut supports basic research across medicine and public health in a multidisciplinary way. We conduct research on microbiology, as its part of our heritage and history, but we also dedicate our efforts to immunology, neuroscience, developmental biology, genetics and cancer. Additionally, we support public health related activities and, in particular, the surveillance and monitoring of infectious diseases. The Institut Pasteur is also a major education centre; we have a high number of undergraduates, Master's and PhD students as well as postdocs. The Institut is also an important partner for industry, and we collaborate extensively.

The third is our international perspective; though based in France, the Institut Pasteur is not a French organisation, it is global. This has been the vision of our Founder from the very beginning. The Institut was founded in 1888, and as soon as 1891, Pasteur sent someone to create the first institute in Saigon (now Ho Chi Minh City). The headquarters in Paris is at the heart of a network of 33 institutes in 26 countries over five continents; we are presently creating another institute in Guinea, West Africa, following the Ebola crisis. So far, we have 10 institutes in Africa, nine in Asia, two in South America, and many in different parts of Europe and New Caledonia.

In what manner are scientists at the Institut endeavouring to accelerate understanding of the many physiological and pathological processes involved in disease pathogenesis?

It is important to emphasise that we are in a very exciting period of science, where interdisciplinarity is somehow fashionable; but it is also at the heart of modern science and medicine. In fact, the key to

understanding disease lies at the interplay between humans (the host), the animal (the vector and origin of many infectious disease transmitted from animal to human, known as zoonoses), and the environment. Our centres are working in Paris and throughout the entire network to explore this interplay of host genetics and how it affects our sensitivity to and severity of disease. They are working on viruses, bacteria, fungi and parasites. This is highly interdisciplinary research, which benefits greatly from the expertise of our institutes in Africa, Asia and South America.

Could you describe the Institut's approach to developing methods of diagnosing and treating disease?

From the very beginning, the Institut Pasteur has been dedicated to creating new concepts and knowledge with very basic research, but always with the intention of transferring this knowledge to medicine, public health and industrial partnerships.

During the Ebola crisis, for example, I set up a taskforce within the 33 institutes to address this major epidemic. In fact, we have been at the forefront from the very beginning in the fight against Ebola, because we were the first to describe (in March 2014) the virus at the origin of the epidemic. We created the taskforce with the idea of merging the forces within Pasteur working on diagnosis and treatment – even if they were not working on Ebola or infectious disease at that time, in order to focus their efforts on this crisis. We have been able to generate a novel approach for diagnostic tests for immediate testing on the ground in Senegal, Guinea and the Ivory Coast. This is the way we work; we start from basic knowledge on some proteins of the virus and nucleic acids, then we transfer that knowledge to diagnosis. We don't want to do this by ourselves, we want to work with industrial partnerships.

Before I took up the position of President of the Institut Pasteur in 2013, I was Vice President of a global holding of several companies. One of these was bioMérieux, which is dedicated to diagnostics. I have been convinced for a long time of the necessity of partnerships for diagnosis and therapeutics. At the Institut Pasteur, we have a portfolio of around 300 family patterns and around 80 per cent of these are focused on diagnosis. I'm now working with my colleagues to investigate new patterns for treatment; we are dedicating a lot of time to chemistry-based research.

From medical student to President of the Institut Pasteur

Why did you decide to dedicate your career to medicine and its associated fields?

I started off as an MD, but I have always been interested in research. I was very fortunate in that my military service enabled me to work as an MD in Tunisia, North Africa. Because of this, I was exposed very early in my career to liver disease. This was around 1975, and I was very much intrigued and stimulated by cirrhosis and chronic hepatitis, which were, at that time, of unknown origin. Now, we know that they are related to hepatitis B and C viral infections. When I came to Paris and started working as a resident, I wanted to work in research, so I took a number of courses. These were the very early days of molecular biology understanding, and I had been very fortunate to have the opportunity to work at the Institut Pasteur as a PhD student. This led me to apply this young discipline to virology and cancer, where I focused on hepatitis and liver cancer. Then, I went on to work both in the clinic, where I was Head of the Liver Department at the Necker-Enfants Malades and Head of the Cell Biology Department at the Necker School of Medicine (where I set up my own laboratory), which is 500 metres from the Institut Pasteur. Now, of course, my role is that of President of the Institut.

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What role does interdisciplinary collaboration play at the Institut Pasteur?

I have three key points to emphasise about our interdisciplinary work ethic. The first is that we have embarked on significant reinforcement to attract and recruit new scientists with an interdisciplinary mode of thinking who can interact with those from other disciplines.

Secondly, we created flexible structures that span across our 11 departments and the 33 institutes, and aim to merge expertise on these major challenges. More specifically, we have four centres: the Center for Bioinformatics, Biostatistics and Integrative Biology; the Center for Translational Science; the Center for Global Health; and the Center for Innovation and Technological Research.

Thirdly, we have developed transversal research programmes, which provide financial incentive and support for research activities across the 11 departments. This work includes explaining the link between microbes and noncommunicable diseases, which is a very interesting and

important prospect for the future. Noncommunicable diseases concern cancer, neurodegenerative disease, obesity and diabetes on the one hand and microbes, infectious diseases and microbiology on the other. We have much evidence that points to the role of microbes in a substantial fraction of so-called noncommunicable diseases. In fact, 25 per cent of cancers worldwide are associated with pathogens. There is also growing evidence for the important role of intestinal bacteria in metabolic disorders (obesity and diabetes) and possibly, cancer and neurodegenerative disease.

What are the Institut's key short- and long-term scientific priorities for 2014-18?

We have four general transversal scientific priorities. As a first priority, we have set up the very important development of integrative biology, bioinformatics and quantitative biology. This is at the heart of modern science and many institutes worldwide are also setting this up as a priority, which is excellent. We want to integrate this into the international network. The second priority is epigenetics and how there are mechanisms beyond our knowledge of the human genome that drive bacterial and viral infections and development, which is very much an interdisciplinary theme. The third priority is to work at the interplay of microbes, microbiology and noncommunicable disease. Finally, as mentioned previously, the fourth is the interplay between host genetics, the pathogen, the vector and the environment. We have more focused priorities on the renewal of some departments; for example, we need to reinforce our work on antibiotic resistance, tuberculosis and neuroscience, which are, of course, very important issues.

Can you outline the ways in which the Institut enables R&D?

I would like to emphasise the cultural aspect of science, and the blend between basic research and R&D to address the challenges of the future. We have adjusted funding from our industrial partnerships, which now represents 20-25 per cent of our overall budget – which is very significant. More importantly, we know that there are a number of projects that you can only achieve in the context of industrial partnerships.

When I started as a student at Pasteur, we set up the first diagnostic test to detect the hepatitis B virus in blood, which at the time was a new technology. We did this in partnership with Abbott Laboratories, as we had the early conviction that we would benefit from this association.

I was recently in a meeting in the US and I was discussing the formation of strategic partnerships with presidents and CEOs of several high-level pharmaceutical and diagnostic companies, in order to understand each other's priorities. This is a major part of private-public partnerships, academies and companies; it's important to share the objectives from the start of a project to avoid the very frequent misunderstandings that unfortunately complicate research institute partnerships.

Ten Institut Pasteur scientists have received the Nobel Prize in Physiology or Medicine, the first of which, Alphonse Laveran, discovered the parasite that causes malaria. How does the Institut itself celebrate research excellence?

We ensure that we celebrate when our scientists are awarded prizes, and emphasise how significant this is for the Institut. There are specific celebrations for these prizes for the entire scientific community to attend. We evaluate our scientists at regular intervals to assess their accomplishments; those with a high level of achievement also receive financial rewards. We are creating what will be called the 'Chairs of Excellence' to award bonuses on top of permanent salaries in recognition of the quality of work and attainment of specific missions within basic research, public health, education, international activities and industrial partnerships. We make a clear distinction between those who have average results and those who have excellent results. Recognition of excellence is one of the most difficult activities for all research institutions; it is especially difficult at the Institut Pasteur, because we have to recognise excellence across the diversity of all our missions. We must understand that excellence at Pasteur is not only excellence in basic research, but also work being undertaken at our institutes in Africa or Asia, for example.

More recently, what have been some of the organisation's biggest breakthroughs?

It's hard to choose because there have been so many! We have had HIV breakthroughs, which led to the Nobel Prize in 2008. There have also been the long-standing successes of vaccination against hepatitis B, which was the first vaccine based on genetic combination – a landmark success. Another achievement was the research into intestinal microbiota and bacteria and the discovery of how it profoundly affects the pattern of immune response. This is an emerging field and it is crucial to understand how normal intestinal bacteria can modulate the impact of external pathogens, viruses and bacteria and how this interplay modulates the severity of disease and the type of response. In neuroscience, there have been many breakthroughs in the genetics of autism; our scientists have been at the forefront of identifying how some genes might be predisposing factors to the condition. Regarding neuroscience, I would also like to raise the fact that even in the adult brain, there is a degree of plasticity in neuronal cells, which means that we have a capacity for neuronal regeneration and adjustment. The Institut has not been the only one to investigate this, but our scientists have been at the helm of these discoveries. I could give many more examples!

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INSTITUT PASTEUR'S 11 RESEARCH DEPARTMENTS:

- Structural Biology and Chemistry
- Developmental Biology and Stem Cells
- Cell Biology and Infection
- Immunology
- Infection and Epidemiology
- Genomes and Genetics
- Microbiology
- Mycology
- Neuroscience
- Parasite and Insect Vectors
- Virology

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We have been at the forefront from the very beginning in the fight against Ebola, because we were the first to describe the virus at the origin of the epidemic

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