

## The Pasteur Institute (1887- )

L'Institut Pasteur (The Pasteur Institute) is a non-profit private research institution founded by Louis Pasteur on 4 June 1887 in Paris, France. The Institute's research focuses on the study of infectious diseases, micro-organisms, viruses, and vaccines. As of 2014, ten scientists have received Nobel Prizes in physiology or medicine for the research they have done at the Pasteur Institute. Contrary to the way genetics was studied in US research universities during the mid-twentieth century, the genetic research conducted at the Pasteur Institute at the same time did not rest on a conceptual separation between embryology and evolution. According to historian Michel Morange from the École Normale Supérieure in Paris, France, this difference enabled Pasteurian scientists to develop the concepts of regulatory genes and of developmental genes.

Louis Pasteur served as the Institute's first director until his death on 28 September 1895. Pasteur researched bacteria, contributed to the germ theory of disease, and developed methods of sterilization aimed at reducing pathogens in food, a process eventually called pasteurization. Pasteur also developed a vaccine to control and treat rabies, and he administered it to humans for the first time in 1885 at the École Normale Supérieure (hereafter called École Normale). During the following years, the Académie des Sciences in Paris, France, as well as other public contributors, funded Pasteur to establish an institute to provide rabies vaccinations, to study infectious diseases, and to disseminate this information throughout France and the rest of the world. Pasteur recruited a team of scientists from several nations with diverse scientific backgrounds to work in the laboratories of the Pasteur Institute.

The first scientists who served as directors of the first five departments at the Institute were Émile Duclaux, Charles Chamberland, Ilya Mechnikov, Jacques-Joseph Grancher, and Émile Roux. All five departments focused on research in microbiology, despite the varied scientific disciplines represented by the directors of the departments.

Émile Duclaux, who lived from 1840 to 1904, was a chemist and microbiologist, and he had studied with Pasteur at the École Normale. He had assisted Pasteur in his efforts to refute the theory of spontaneous generation, according to which living organisms could emerge from non-living matter. At the time of the founding of the Institute, Duclaux helped establish the journal *Les Annales de l'Institut Pasteur* (the *Annals of the Pasteur Institute*), which focused on the current research in microbiology and pathology. Duclaux later succeeded Pasteur as the Institute's director in 1895.

Like Duclaux, Charles Chamberland, who lived from 1851 to 1908, was also a graduate from the École Normale, where he studied physical sciences. After his graduation, Chamberland worked as curator in Pasteur's laboratory at the École Normale. Also like Duclaux, Chamberland contributed to Pasteur's refutation of the theory of spontaneous generation by noting flaws in the experimental protocols of those who wanted to invalidate Pasteur's work.

Before coming to the Pasteur Institute, Ilya Mechnikov, who lived from 1845 to 1916, was a professor of zoology and comparative anatomy at the University of Odessa, in Odessa, in what later became Ukraine. In 1886, Mechnikov administered Pasteur's rabies vaccinations in Odessa but, as he was not a medical doctor, he encountered resistance from the local community. Two years later he visited Pasteur in Paris to ask for advice on his situation in Odessa. Pasteur appointed Mechnikov as director of a department and laboratory in the Pasteur Institute. Mechnikov worked at the Institute for the rest of his life and won the Nobel Prize in Physiology or Medicine in 1908 for his work on the immune system. He helped discover phagocytes, which are immune cells that protect the body by ingesting foreign particles or microorganisms, and he developed a theory of the cellular process involving phagocytes, called phagocytosis.

Jacques-Joseph Grancher, who lived from 1843 to 1907, and Émile Roux, who lived from 1853 to 1933, were both medical doctors. Grancher had worked with Pasteur on the rabies vaccination and continued to work on a treatment for tuberculosis at the Pasteur Institute. In 1883, Roux succeeded Duclaux as director of the Pasteur Institute, and he helped develop a treatment for diphtheria, an infectious disease caused by the bacteria *Corynebacterium diphtheria* that affects the respiratory system. Roux offered one of the first courses on microbiology, called Cours de Microbie Technique (Course on Microbe Research Technique), at the Pasteur Institute in 1889. François Jacob, who lived from 1920 to 2013, a scientist who joined the Pasteur Institute in 1950, described Roux as an austere man who had a monastic devotion to Pasteur and the Institute.

The Pasteur Institute continued its research into preventative medicine into the twentieth century. During the first half of that century, scientists determined the viral and bacterial causes of many diseases, including the plague, malaria, typhus, diphtheria, tuberculosis, tetanus, yellow fever, poliomyelitis, and hepatitis B. Researchers working at the Pasteur Institute also developed treatments and vaccines to counteract the effects of those diseases on populations.

Pasteur chose particular scientists to direct the Institute's departments, which led to a tradition of recruiting a certain type of researcher. The typical Pasteurian scientist had a scientific or medical background and no affiliation with any other official academic institution. The recruits were assigned either a topic to study or a problem to solve in a particular department or laboratory. Jacob later described the Pasteur Institute as the first center of interdisciplinary research, which made use of the diversity of its workforce to focus on specific problems from a variety of angles.

The Pasteur Institute emphasized basic research and practical applications. Those aims enabled the Pasteur Institute to get support from industry, such as pharmaceutical firms, throughout most of its existence because it could provide marketable products to those firms.

The Pasteur Institute created a global network with satellite institutions in greater than thirty countries, based on the same organizing principles of the original institute in Paris. This network originally addressed medical problems in developing countries. Albert Calmette, a military doctor who lived from 1863 to 1933, was the first Pasteurian to establish an overseas branch, which he organized in 1891 in Ho Chi Minh City, then called Saigon, in Vietnam. There, Calmette worked on the development of smallpox and rabies vaccines to treat infected Vietnamese. Calmette treated about 500,000 people who had travelled to his center from across south east Asia to receive the vaccines. Calmette later worked on the development of an anti-venom serotherapy to treat bites from venomous cobras. The Pasteur Institute continued to establish satellite institutes throughout southern Asia, the Mediterranean, the Caribbean, and the African continent, enabling the organization to continue its study of tropical diseases.

After the Second World War, the Pasteur Institute focused on research in molecular biology. This endeavour began in 1951 when André Lwoff, who lived from 1902 to 1994, discovered the existence of proviruses, viral genomes that are integrated in the genetic material of host cells, such as bacteria. This discovery influenced many scientists at the Pasteur Institute to re-orient their research towards the study of bacterial cells, with a focus on the molecular basis for the functions and syntheses of those cells. This research program, triggered by André Lwoff's discovery, culminated in the achievement of the Nobel Prize in Physiology or Medicine in 1965.

The prize was awarded to François Jacob, to Jacques Monod, who lived from 1910 to 1976, and to André Lwoff, for their model of genetic regulation. Jacob and Monod proposed this model in their 1961 paper, "Genetic Regulatory Mechanisms in the Synthesis of Proteins." In this paper, they explained how regulatory proteins control cellular processes by acting as on/off switches for gene expression. Jacob and Monod expected that their model of regulation could provide a framework for understanding the process of cell differentiation during development.

The Pasteurian team of the 1950s, 60s, and 70s comprised of Lwoff, Monod, Jacob, Elie Wollman, who lived from 1917 to 2008, François Gros, born in 1925, and Jean-Pierre Changeux, born in 1936, helped establish a French tradition of molecular genetics, as some historians called it, in the second half of the twentieth century. Many Pasteurian biologists, including Lwoff, refused to adopt or dispel then current theories of heredity, a position that enabled scientists at the Pasteur Institute to pursue a variety of different research projects without regard to any specific theory. Accord-

ing to Jacob, this atmosphere within the Pasteur Institute's labs encouraged scientists to work on less studied organisms, such as lysogenic bacteria, which led to the discovery of the mechanisms involved in gene expression. Subsequently, Jacob and Monod's model of gene expression and regulation provided a conceptual basis for a research program in which molecular biologists attempted to describe the complex processes involved in embryonic development.

The Pasteur Institute faced financial difficulties between the 1930s and the 1970s because of its poorly managed commercial and industrial activities. The Pasteur Institute's financial difficulties began to change in 1971, when Monod became director of that institution. By 1974, Monod and his team had acquired public subsidies for half of its operating budget, as well as a number of private donations, to ensure the Pasteur Institute's continued existence as a private and independent research center. During this time, the Pasteur Institute built new infrastructure and new research departments.

In 1983, almost a century after its inauguration, researchers at the Pasteur Institute isolated and identified the human immunodeficiency virus (HIV), the virus that causes AIDS (acquired immune deficiency syndrome). Two decades later, researchers Luc Montagnier, born in 1932, and Françoise Barré-Sinoussi, born in 1947, from the Pasteur Institute shared the 2008 Nobel Prize in Physiology and Medicine for this discovery.

At the beginning of the twenty-first century, the Pasteur Institute had international network of research centers. From its original location, it developed ten major research centers, a teaching center to train graduate and postgraduate students, and an epidemiological reference center to identify and monitor different strains of bacterial and viral outbreaks found across the world. The Institute also includes the Musée Pasteur (Pasteur Museum) located in the institution's original 1888 building. This building houses an archive containing documents of Pasteur's life and work, as well as Pasteur's tomb.

As a non-profit private organization, the Pasteur Institute is governed by an independent board of governors, which, as of 2014, is chaired by François Ailleret, born in 1937, who oversees the institution's finances. The Institute receives funds from a variety of sources, including the French government, consulting fees, licensing royalties, contract revenues, and other private contributions. The distribution of investors enabled the Pasteur Institute to maintain its founder's original vision of an autonomous research center structured in a way that enables its scientists to pursue both basic research and practical applications in biology.

## Sources

1. Barré-Sinoussi, Françoise, Jean-Claude Chermann, Fran Rey, Marie Thérèse Nugeyre, Sophie Chamaret, Jacqueline Gruest, Charles Dauguet, and Luc Montagnier. "Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS)." *Science* (1983): 868-71.
2. Chamberland, Charles. *Rôle des microbes dans la production des maladie (Microbes' Role in Diseases' Production.)* Paris: Gauthier-Villars, 1882. <http://gallica.bnf.fr/ark:/12148/bpt6k58372790.r=Rmicrobes+dans+la+production+des+maladie.langEN> (Accessed April 7 2014).
3. Duclaux, Émile. *L'hygiène sociale (Social Hygiene)*. Paris: F. Alcan, 1902. <https://archive.org/details/lhyginesociale01duclgoog/> (Accessed 9 April 2014).
4. Gascar, Pierre. *Du côté de chez Monsieur Pasteur. (At the side of Mr. Pasteur.)* Paris: Éditions Odile Jacob, 1986.
5. Grancher, Jacques-Joseph. *Prophylaxie de la tuberculose: rapport lu au nom de la Commission de la tuberculose (Tuberculosis Prophylaxis: Report to the Committee for Tuberculosis)*. Paris: Masson, 1898.
6. Jacob, François. *The Statue Within: An Autobiography*. New York: Basic Books, 1988.
7. Jacob, François. "The Pasteur Institute." *Nobelprize.org*, 1998. [http://www.nobelprize.org/nobel\\_prizes/m/articles/jacob/](http://www.nobelprize.org/nobel_prizes/m/articles/jacob/) (Accessed February 23, 2013.)
8. Jacob, François, and Élie L. Wollman. *La sexualité des bactéries. (Sexuality of Bacteria.)* Paris: Librairies de L'Académie de Médecine, 1959.

9. Jacob, François, and Jacques Monod. "Gènes de structure et gènes de regulation dans la biosynthèse des protéines." (Genes of Structure and Genes of Regulation in the Biosynthesis of Proteins.) *Comptes rendus hebdomadaires des séances de l'Académie des sciences* (Weekly Reports of the Meetings of the Academy of Sciences) 249 (1959): 1282-4.
10. Jacob, François, and Jacques Monod. "Genetic Regulatory Mechanisms in the Synthesis of Proteins." *Journal of Molecular Biology* 3 (1961): 318-56.
11. Lwoff, André. "Lysogeny." *Bacteriology Review* 17 (1953): 269-337. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC180777/> (Accessed August 18, 2014).
12. Metchnikoff, Élie. *Immunity in Infectious Disease*. Trans. Francis G. Binnie. Cambridge: Cambridge University Press, 1907. <http://babel.hathitrust.org/cgi/pt?id=ien.35558005390543;seq=7;view=1up;num=iii> (Accessed April 9, 2014.)
13. Morange, Michel. "French Tradition and the rise of Evo-devo." *Theory in Biosciences* 126 (2007): 149-53.
14. Moulin, Anne-Marie. "Patriarchal Science: The Network of the Overseas Pasteur Institutes." *Science and Empires*, eds. Patrick Petitjean, Catherine Jami, and Anne-Marie Moulin, 307-322. Dordrecht: Kluwer Academic Publishers, 1992.
15. Pasteur, Louis. *La théorie des germes et ses applications à la médecine et à la chirurgie: Lecture faite à l'Académie de la Médecine* (A Theory on Germs and its Applications on Medicine and Surgery: Lecture at the Academy of Medicine.) Paris: G. Masson, 1878. <http://utmb.comtentdm.oclc.org/cdm/compoundobject/collection/p16721coll1/id/133> (Accessed April 9, 2014.)
16. Peyrieras, Nadine, and Michel Morange. "The study of lysogeny at the Pasteur Institute (1950-1960): an epistemologically open system." *Studies in the History and Philosophy of Biological and Biomedical Sciences* 33 (2002): 419-30.
17. Reynolds, Moira D. *How Pasteur Changed History: The Story of Louis Pasteur and the Pasteur Institute*. Bradenton, Florida: McGuinn & McGuire Pub., 1994.
18. Roux, Émile. *Étude sur les calculs de l'urèthre* (Study on Urethra Stones.) Paris: Société d'éditions scientifiques, 1894.
19. The Pasteur Foundation. "Remembrance of Things Pasteur: Pasteur Institutes USA." <http://www.pasteurfoundation.org/institutes.shtml> (Accessed February 23, 2013.)