

PASTEUR PERSPECTIVES

THE NEWSLETTER OF THE PASTEUR FOUNDATION DEVOTED TO THE WORLD OF THE INSTITUT PASTEUR

THE CUTTING EDGE

by Hugues Fleury

CROSS-DEPARTMENTAL COLLABORATION: PASTEUR'S NEW TRANSVERSAL RESEARCH PROGRAMS

When he took the helm of the Institut Pasteur in January 2000, Philippe Kourilsky announced his vision: the continuation of excellence in biological research for the benefit of humankind. To ensure the institute's ongoing preeminence, Dr. Kourilsky introduced a number of strategies intended to bring renewed vigor to research programs by optimizing the efficiency and competitiveness of Pasteurian research. A key innovation is the introduction of Transversal Research Programs (TRPs).

Effectively decompartmentalizing research, these programs encourage the dynamic interfacing of varied yet complementary laboratories in order to apply diverse abilities and points of view to narrowly defined subjects. A key characteristic is that each project has realistic, achievable, short- and medium-term goals often involving great potential for public



A cyanobacterium, the subject of a Transversal Research Program

health applications. Initially, each TRP will be operational for two years, with the possibility of an extension to a third year. The programs are cross-departmental and preferably will not be directed by senior laboratory heads; instead, junior researchers will be involved and post-doctoral scientists will be recruited specifically for the TRPs. Strategic cross-departmental collaboration will lead to greater freedom in scientific exchange, resulting in new and fruitful industrial and public health applications. The goal of the programs is to nurture collaborations and groupings of abilities that would not otherwise take place, leading to the reinforcement of existing themes and the exploration of new possibilities. Therefore, each TRP must involve at least three units, services or research groups.

The TRPs are coordinated by Marie-Aline

continued on page 2

THE PASTEUR FOUNDATION CELEBRATES ITS 15TH YEAR

by Marie-Hélène Marchand

This year marks the 15th anniversary of the establishment of the Pasteur Foundation in New York.

Its precursor, the Rapkine French Scientist Fund, was incorporated in 1951 in memory of the work of a remarkable Pasteur scientist and humanist, Louis Rapkine (1904-1948). In August 1940, after France fell to the Nazis, Rapkine devised a rescue plan in collaboration with the Rockefeller Foundation in New York to save an elite corps of French scientists from wartime persecution. Thanks to his efforts, some 30 scientists and their families successfully emigrated. Louis Rapkine was an exceptional and noble figure to whom the field of biochemistry owes a great deal.

Following the war, while France was rebuilding, French researchers found themselves in great need of materials. In 1951, three years after Rapkine's death and as a tribute to him, the Rapkine Fund was established in New York for the purpose of purchasing scientific materials for use in France. The Institut Pasteur was one of the fund's primary beneficiaries.

A charitable organization in New York overseen by Bethsabée de Rothschild, the Rapkine Fund played an important role in establishing an enduring tradition of American philanthropic giving to the Institut Pasteur.

The Pasteur Foundation

In 1985, when it became apparent that an American purchasing agent was no longer required, the name of the fund was changed to the Pasteur Foundation to underscore its most important affiliation. Since then, with the invaluable and generous assistance of its American Advisory Board led by Mrs. Anastassios Fondaras, the Pasteur Foundation, a 501(c)(3) corporation, has striven to raise awareness of Pasteurian research. Over the years, the Pasteur Foundation has also benefited from the guidance and help of the French Embassy and the New York French Consulate General. Through grants, gifts and bequests, and the organization of annual special events such as the U.S. premiere of the film *Tous les matins du monde* and an evening

continued on page 3



Bloch, a graduate of the École Polytechnique and the University of Paris VII, where she received her Ph.D. in microbiology. Dr. Bloch brings to this position significant industrial experience, particularly in her role as a former secretary general of research and development at Pasteur Mérieux Connaught.

One request for proposals will be launched each year. Late this spring, Dr. Bloch and her colleagues conducted the first selective review of proposals submitted by many Pasteur research groups; the proposals were based on themes suggested by both Institut Pasteur directors and group members. The themes include:

- diseases and cellular biology
- cancers associated with infectious diseases
- geriatric illnesses, infections and quality of life
- environment, air and water
- allergy and asthma
- development of new antibiotics and antivirals

In July, 17 TRPs were announced. Each group will unite researchers, engineers and technicians and link at least three labs, fostering a true synergy of abilities. Three of the programs selected will involve Pasteur's International Network.

TRPs: Two Examples

STATE-OF-THE-ART DIAGNOSTIC TESTS FOR PLAGUE AND CHOLERA

Both plague and cholera are serious bacterial diseases; plague affects the populations of 20 countries, while over 80 countries report cholera. International health regulations require that cases of these diseases be reported for epidemiological surveillance purposes.

Plague is zoonotic, which means it can be transmitted from animals to humans (in this case from rodents via infected fleas). The most common form is bubonic plague



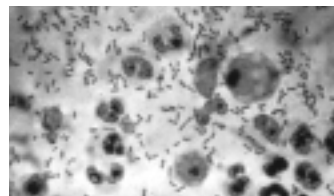
Vibrio cholerae

(see *Pasteur Perspectives* No. 6, Spring 1999). Untreated, it can lead to a highly contagious pulmonary form that results in many epidemics.

Cholera also persists; today the world is experiencing the seventh cholera pandemic, caused by a particular serogroup of *Vibrio cholerae* that began to spread in 1961. Between 1997 and 1998, the number of cases doubled; in 1998, 300,000 cases—resulting in 10,000 fatalities—were reported to the World Health Organization (WHO). By 1999 the pandemic had spread even further, for the first time resulting in epidemics on the island of Madagascar. It is likely that an eighth pandemic is underway, involving a new serogroup of the bacterium.

A simple but indispensable tool is needed to stem the spread of these diseases: a test to diagnose the first cases of an outbreak and to help in surveillance to curtail the rise of epidemics. Currently, all so-called rapid methods of detection are prohibitively expensive and difficult to conduct in developing countries.

Dr. Farida Nato, a research engineer in the Antibody Engineering Lab directed by Jean-Luc Guesdon, will head the plague and cholera TRP. This lab will be linked with the Cholera and Vibriion Lab and the Molecular and Medical Bacteriology Lab, which also serves as a WHO Collaborating Center for plague. Suzanne Chanteau



Yersinia pestis, the cause of plague

and her group from the Institut Pasteur of Madagascar will also participate in the field. The primary goal of their efforts is the development of two simple-to-use tests that will yield rapid diagnostic results.

Rapidity is essential to treatment, to the administration of prophylaxis and to the mobilization of an effective public health response.

As a first step, two trial tests are under development. Their efficacy will be evaluated on clinical samples and ultimately in the field under epidemic conditions. The tests will be based on immunochromatography, a technology that uses antigen-antibody reactions that can be read in 10 minutes. They will be less expensive than the currently available tests. Eventually, immunochromatography will be used to diagnose other infectious diseases, always in the context of public health in economically disadvantaged countries.

DETECTING NEUROTOXINS OF CYANOBACTERIA IN WATER

Formerly called blue algae, cyanobacteria are a key to atmospheric oxygenation. Those present in water produce neurotoxins. For humans, the potential risk of these particular cyanobacteria resides in drinking-water sources as well as recreational resources like pools. In the summer, these cyanobacteria can grow quickly, resulting in dense populations that produce pockets of gas; the pockets bubble to the water's surface, where the neurotoxins are ingested by animals who drink the water.

These bacteria are used as study models because they possess diverse adaptive properties that enable them to integrate structural and functional morphological changes in response to fluctuations of light or nutritional conditions in the environment. The Institut Pasteur has a unique collection of over 700 pure strains of cyanobacteria obtained from a vast range of ecosystems. One goal of the TRP working with cyanobacteria is to identify the neurotoxin-producing strains in the collection. The group will use mammalian cell lines (in collaboration with the Expression of Eucaryotic Genes Lab) and nicotinic receptors found in the nervous systems of fish (with the Molecular Neurobiology Lab) as research models. The project is also linked with the Macromolecular Structural Chemistry Lab. Once a method is developed to detect neurotoxins in water, it can be applied by environmental agencies that monitor water quality to benefit the environment and public health.

Michael Herdman, a researcher in the Microbial Physiology Lab directed by Nicole Tandeau de Marsac, will head this TRP.

FIVE-YEAR GROUPS: ENCOURAGING YOUNG SCIENTISTS

The Institut Pasteur has initiated an ambitious new program: the formation of five-year groups, open to young candidates selected from a pool of brilliant researchers both within and outside the institute. Intended to draw upon the energy, flexibility and potential of junior researchers by assigning them greater responsibilities, 50 such groups will be formed over the next few years. In addition to their limited duration, the five-year groups are restricted in size: each group will be comprised of a head scientist, two to three researchers and, in most cases, a post-doc, a technician and/or an engineer. Promising young American scientists and those of other nationalities who are interested may apply by contacting the deputy director general for research, teaching and public health, Alain Gouyette (gouyette@pasteur.fr). An international call for proposals was issued in October.

THE PASTEUR FOUNDATION TURNS 15

continued from page 1

featuring the Broadway hit *Contact*, the Pasteur Foundation has fostered the tradition of American giving, garnering more than \$9 million over the last 15 years.

As a prime example, the Florence Gould Foundation of New York has been a faithful supporter for many years,



The newest Pasteur laboratory, financed by the Gould Foundation

providing grants for basic research on leprosy, for scientific exchanges and for sophisticated laboratory equipment. Most recently, the Gould Foundation funded the construction of a state-of-the-art high-security laboratory inaugurated in October.

The Howard Scholarship is a testament to American individual philanthropy. Endowed in 1992 by a cherished donor, the late Mrs. Frank Howard, this scholarship brings young American and British scientists to work at the Institut Pasteur (*see the inset above right*). American bequests, the most famous of which was that of Wallis Warfield Simpson, Duchess of Windsor, have also significantly enhanced the activity of the Institut Pasteur.

Beyond its mission to raise funds for scientific research conducted at the institute, the Pasteur Foundation brings to its American supporters news of the rich history of the institute as well as recent research developments. Events to commemorate the centennial of Louis Pasteur's death were held in over 50 U.S. cities throughout 1995, "The Year of Louis Pasteur." *Pasteur Perspectives*, published twice yearly, highlights current developments on the Pasteur campus. The Pasteur

THE HOWARD SCHOLARS

Established by the late Mrs. Frank Howard to bring U.S. and British scientists to work at the Institut Pasteur

YEAR	RECIPIENT	LABORATORY
1992	John Collins	Gene Molecular Biology
1993	Douglas Feinstein	Antigen Biochemistry
1994	Nicholas Mantis	Molecular Microbial Pathogenics
1994	Louis Miller	Cellular Immunophysiology
1996	Steffan Anderson	Venoms
1997	Jonathan Weitzman	Oncogenic Viruses
1997	Dana Philpott	Molecular Microbial Pathogenics
1997	Michelle Rathman	Molecular Microbial Pathogenics
1998	Tracy Letain	Cellular Physiology
1999	Francis Ennis	Arboviruses and Hemorrhagic Fever Viruses
1999	Karsten Tedin	Intracellular Bacteria Genetics
1999	Stuart Edelstein	Molecular Neurobiology
1999	Lucia Barker	Mycobacterial Genetics
2000	Karen Wright	Organic Chemistry

Foundation also provides resources to American science and French teachers.

From the first American contributions given directly to Louis Pasteur for the creation of his institute over 100 years ago to the many more recent gifts and bequests, the rich history of American philanthropy has literally changed the face of the Institut Pasteur and greatly enhanced the course of its research by financing the construction of new buildings, providing equipment and sponsoring young American scientists.

We gratefully acknowledge all those who have played a role in these first 15 years, from our treasured donors to our friends who have made provisions in their estate plans on behalf of the Pasteur Foundation. We thank you all, because each gift has made a difference.

Marie-Hélène Marchand is Executive Vice-President at the Institut Pasteur.

With so much more to accomplish as the Institut Pasteur faces increasing research costs and demands, this fall the Pasteur Foundation is establishing two new societies to meet the challenges of the new millennium. Details will appear in the next issue.

- Donors who have named the Pasteur Foundation in their wills or who have made a planned gift will gain membership to the Osiris Society.
- The Corporate Society of Pasteur Friends recognizes those corporations committed to making an annual gift of \$2,500 or more for three years.

For more information, please contact Caitlin Hawke at the Pasteur Foundation, 212.599.2050, or return the coupon on page 4.

**MORE TO THE POINT:
BRIEF NEWS FROM PASTEUR**

GENOMICS: At "Genomes 2000," an international colloquium held this spring at the Institut Pasteur, two important announcements were made:

- **Sequencing of a Listeria Genome:** *Listeria monocytogenes* causes serious cases – and some epidemics – of food poisoning. Listeriosis is a threat to both public health (20%-30% of cases are fatal) and to the food industry, due to the enormous cost of product recalls. A European consortium coordinated by the Institut Pasteur has completed the sequencing of this genome, which will lead to new tools to curtail and treat infection.
- **Sequencing of the Leprosy Genome:** The Institut Pasteur and the UK's Sanger Centre announced the complete sequencing of *Mycobacterium leprae*, which causes this chronic infectious disease characterized by ulcers of the skin and internal organs, deformity and paralysis. Essential for research and control of leprosy, the decoded genome can now be compared to that of the mycobacterium that causes tuberculosis with the goal of producing new therapies. The sequencing was financed in part by the Heiser Program for Research in Leprosy and Tuberculosis of the New York Community Trust.

GENE THERAPY: A Pasteur group has demonstrated the efficacy of a new gene transfer system derived from genetically altered human immunodeficiency virus (HIV). Extensive research on the molecular behavior of the AIDS virus has yielded an understanding of the cell-penetration mechanism employed by its viral DNA, opening the possibility of promising innovative use of an otherwise harmful virus. The therapy uses non-virulent HIV as a beneficial Trojan horse to deliver healthy genes to individuals suffering from genetic disorders. It may also prove useful in gene therapy for AIDS and various cancers.

CANCER PAPILOMAVIRUSES: A second gene, one that causes susceptibility to potentially cancerous papillomaviruses, has been identified by Pasteur scientists. (See *Pasteur Perspectives* No. 7, Fall 1999.) Analysis of a series of such genes should lead to a better understanding of why certain individuals are more susceptible than others to viruses and other infectious agents.

PASTEUR PERSPECTIVES

A 501(c)(3) organization, the Pasteur Foundation is the U.S. nonprofit affiliate of the Institut Pasteur. Located in New York City, the foundation works to introduce the research conducted at the Institut Pasteur to the American public, to develop exchanges between Pasteurian and U.S. scientists, and to raise funds for Pasteurian research. For more information, please contact the Pasteur Foundation.

A copy of the latest annual report may be obtained, upon written request, from the Office of the Attorney General, Charities Bureau, 120 Broadway, New York, New York 10271.

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THREE PASTEUR SCIENTISTS RECEIVE AWARDS FROM THE HOWARD HUGHES MEDICAL INSTITUTE

In July 2000, the world-renowned Howard Hughes Medical Institute in Maryland announced the names of the 45 recipients of a new, innovative \$15 million grant program for non-U.S. researchers. There are three Pasteur scientists among the distinguished beneficiaries: Pascale Cossart, Robert Menard and Philippe Sansonetti.

The specific intent of this grant program is to help find new ways to combat malaria, tuberculosis, Lassa fever and similar parasitic illnesses. Explaining the philosophy of the program, HHMI President Thomas R. Cech said, "These diseases cause great suffering around the world, particularly in developing countries, yet they receive inadequate scientific attention. There is great opportunity to apply the new tools of molecular biology and related fields to learn exactly how these diseases cause so much harm and to develop fundamentally new approaches to controlling or even curing them. We've identified a group of outstanding scientists who can push this research forward." The five-year awards range from \$225,000 to \$450,000.

Pascale Cossart and her team in Pasteur's Bacteria-Cell Interactions Lab study the molecular and cellular basis of the pathogenic power of *Listeria monocytogenes*, discussed in the spring 1999 issue of *Pasteur Perspectives* (No. 6). *Listeria* is a food-borne bacterium that causes serious illness and now serves as a study model for intracellular parasitism. Dr. Cossart has received numerous awards for her work in this field, including the Helena Rubinstein-UNESCO prize, the French-American Richard Lounsberry Award, and the Nestlé prize.

Robert Menard and his team investigate the pathophysiology of malaria infection. They have developed genetic tools to identify key parasitic and cellular molecules that enable the parasite to enter the hepatocytes and their intracellular transformation. A former assistant professor at New York University School of Medicine, Dr. Menard directs Pasteur's Malarial Biology and Genetics Lab.

Philippe Sansonetti and his team at Pasteur's Enterobacteria Laboratory study the molecular, cellular and tissue-related aspects of the shigella bacterium's invasion and destruction of the intestinal wall, which causes a deadly diarrheal disease that kills one million people each year, mostly children. In their quest for a vaccine, these scientists also examine the body's defense mechanisms against this infection. Dr. Sansonetti has received many distinctions, including the Grand Prize of the French Academy of Medicine, the Robert Koch Award and the prestigious Louis Jeantet Prize for Medicine.

EXTERNAL SCIENTIFIC AND STRATEGIC ORIENTATION COMMITTEE

by Caitlin Hawke

Headed by Nobel Laureate Harold E. Varmus, this international committee will help evaluate scientific and strategic trends at the Institut Pasteur. The committee is part of Philippe Kourilsky's policy of openness and excellence at the institute. The new steering committee will make recommendations and help to identify the best possible avenues with which to link Pasteur's programs to other international research.

Dr. Varmus, former director of the National Institutes of Health and new director of Memorial Sloan-



Dr. Harold E. Varmus

Kettering Cancer Center, will come to the Pasteur campus in January to preside over the first committee meeting. Winner of the 1989 Nobel Prize in Medicine with J. Michael Bishop for their discovery of the cellular origin of retroviral oncogenes, Dr. Varmus is one of the world's leading figures in science today. He is joined on the committee by seven other distinguished scientists, including Gustav Nossal of Australia, Anthony S. Fauci (the director of the U.S. National Institute of Allergy and Infectious Diseases at the NIH in Bethesda, Maryland), and Piet Borst, Pierre Chambon, Fotis Kafatos, Gottfried Schatz and Pierre Vassalli from Europe.

INVEST IN A HEALTHY FUTURE

One of the world's premier centers of fundamental research, the Institut Pasteur is entirely dedicated to life sciences and human health. We need your help to continue this work.

Please consider making a year-end, tax-deductible contribution or a bequest to the Pasteur Foundation, a 501(c)(3) corporation. Planned wisely with your attorney, a specific, percentage, contingent or residual bequest to the Pasteur Foundation could save your estate (and thereby your heirs) substantial tax payments while benefiting scientific research and enabling you to leave your personal impression on the Institut Pasteur. Many of our friends have found this the simplest way to support the Institut Pasteur. Please consult your estate advisor and/or attorney for advice on how best to achieve your goals.

For further information, contact Caitlin Hawke at the Pasteur Foundation, 212.599.2050.



A TOOL FOR FRENCH TEACHERS Bring Science to the French Classroom

“À la découverte de l’Institut Pasteur,” a set of 40+ flashcards, is the perfect way to bring scientific concepts and vocabulary into the advanced French-language classroom. Covering the history, discoveries and scientific contributions of the institute, these cards provide timely, relevant departure points for conversation. In recognition of a contribution of \$25 or more, the Pasteur Foundation will send you the flashcards as our gift.



SAVE THE DATE
MONDAY, NOVEMBER 20, AT 6:15 P.M.
A LECTURE IN FRENCH AT THE U.N.

Genèse de la découverte: la vie et l’oeuvre de Louis Pasteur

Dr. Paul Brey, Conférencier

A wine reception will follow the lecture.

Dr. Brey of the Paris Institut Pasteur will lecture in French at the United Nations’ Dag Hammarskjöld Auditorium as part of the Franche-Comté Festival on Monday, November 20th, at 6:15 P.M.

Franche-Comté’s most famous son, Louis Pasteur, was born in Dole in 1822 and raised in Arbois. It was in this region of France that he conducted one of his experiments on spontaneous generation, leading to a definitive refutation of this theory in 1864. After he established the role of microbes in fermentation, Pasteur quickly made the leap to studying infectious diseases. This led to his work on a rabies vaccine, perhaps his most famous discovery, notwithstanding what has come to be known as the process of pasteurization. Dr. Brey’s lecture will explore the legacy of this scientific pioneer.

This lecture is free and open to the public but requires advance registration for security purposes. To register, please call 212.599.2050 or send e-mail to: PasteurUS@aol.com by 6 P.M. Thursday, November 16th. For this event, please enter the U.N. on First Avenue at the northeast corner of 42nd Street by way of the gate near the bus stop.

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Please note: Gifts to the Pasteur Foundation are tax-deductible to the extent provided by law.