



# PASTEUR PERSPECTIVES

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

Number 1  
Fall 1996

## A Message from the Director General of the Institut Pasteur

Dear Readers:

With guidance from its American Advisory Board headed by Mrs. Anastassios Fondaras, the Pasteur Foundation works to introduce the latest research developments at the Institut Pasteur to the American public and to promote exchanges between U.S. and Institut Pasteur scientists. To better accomplish these tasks, the Pasteur Foundation is pleased to introduce this newsletter, Pasteur Perspectives, which will present news from the front line of research as well as historical vignettes. In each issue, our "Cutting Edge" feature will highlight one of the most vital areas of research at the Institut Pasteur. We begin here with an overview of current cancer studies on campus.



Maxime Schwartz

Special to this issue, Dr. Howard A. Shuman, a Professor at the College of Physicians and Surgeons of Columbia University, shares his impressions about working in my laboratory as a young scientist in 1974.



The Institut Pasteur in Paris

You will read, too, about the Howard Scholarship. A devoted and generous friend of the Institut Pasteur, Mrs. Frank Howard endowed this scholarship in 1992 for the unique purpose of enabling talented young U.S. and British researchers to work at Pasteur. With

this scholarship, Mrs. Howard has ensured the perpetuation of an important tradition that has brought hundreds of U.S. scientists to our laboratories since World War II.

For more information or to learn how you can support our research, please complete the coupon on page 5 and return it to the Pasteur Foundation.

We hope you enjoy our Perspectives, and we welcome your comments.

Sincerely,

Maxime Schwartz  
Director General, Institut Pasteur

## THE CUTTING EDGE:

### FOCUS ON CANCER RESEARCH AT THE INSTITUT PASTEUR

by Hugues Fleury

At present, several Pasteur teams are conducting research on different aspects of cancer. These research efforts engage the work of approximately 100 scientists. Armed with knowledge gained from molecular and cellular biology, these men and women now seek to better comprehend the complex mechanisms of this disease and to develop new preventive, diagnostic, and therapeutic tools.

Malignancies occur when cellular multiplication and differentiation become unchecked or deregulated. The transformation to malignancy can be triggered by exposure to radiation and carcinogens, or may be due either to the occurrence of spontaneous mutations or infection by certain viruses.

#### Multiple Avenues of Research

In the domain of developmental biology, several Pasteur teams are investigating normal cellular differentiation (from the first stages of embryonic development to final differentiation giving rise, for example, to muscle and nerve cells) and the anomalies that emerge when cancerous cells appear. In a tumor, cellular proliferation continues, but differentiation generally ceases. However, there are also certain tumors, such as teratocarcinoma, in which differentiation persists; these malignancies are also the subject of advanced study at the Institut Pasteur.

The study of villin, a protein produced by normal cells of the digestive tract, is another area of ongoing cancer research. Pasteur scientists have developed a method to detect the amount of villin in the blood, which may lead to new means of detection and treatment of intestinal tumors.

In the domain of virology, several research groups are studying oncogenic viruses, those capable of transforming healthy cells into malignant ones. This transformation occurs in several stages. Study of this progressive evolution may lead to early detection and treatment of all precancerous

continued on page 2

lesions (such as dysplasias of the cervix), thereby preventing the development of cancer. Recognition of the signs of viral infection may also lead to early detection of cancerous lesions. Scientists expect that in the future these virally induced cancers may be prevented through vaccination.

Four viruses involved in the appearance of cancer are studied at the Institut Pasteur: the papilloma viruses (responsible for cervical, uterine and external genital cancers), the hepatitis B virus (a cause of liver cancer), the Epstein Barr virus (a member of the herpes family associated with lymphoma of the jaw and throat cancer), and the retroviruses of two subfamilies—HIV (responsible for AIDS and indirectly linked with lymphoma, genital cancer and Kaposi's sarcoma) and HTLV (responsible for a type of leukemia).

A genetically engineered vaccine against hepatitis B was devised at the Institut Pasteur and has been available to the public since 1989. In the case of papillomaviruses, Pasteur scientists have developed improved diagnostic tools for the early detection and ultimate prevention of cervical and uterine cancer. The search for vaccines against papillomaviruses, the Epstein Barr virus, and the HIV and HTLV retroviruses is among the priorities of the Institut Pasteur.

While the role of some viruses in cancer is established, it is important to note that they probably operate in collaboration with carcinogenic substances in our environment and our food. In addition, there may be genetic predispositions for certain cancers. Intense study of the issue of genetic predisposition is currently underway, particularly in the cases of breast and cervical cancer.

Recently, a Pasteur team developed an experimental vaccine against *Helicobacter pylori* infections. This bacterium is responsible for both stomach ulcers and cancers of the digestive tract.

A few years ago, a Pasteur group developed a test, now distributed throughout the world, that detects the cancer-causing potential of various substances.

Additional avenues of current cancer research at the Institut Pasteur include:

- the study of the genetic characteristics of B lymphocytes and their malignant transformations
- the analysis of the as yet unknown role of the protein NDPK (nucleoside diphosphokinase) in cancerous growth and metastasis

- the study of micrometastases in adenocarcinomas (glandular tumors) of the breast with the goal of diagnostic and preventive treatments
- research to pinpoint oncogenes in the epithelial cells of the intestine

In addition, a team that linked the alteration of a nuclear receptor (the retinoic acid receptor) to liver cancer and acute leukemia is intensifying its research on the causative mechanisms, while another group is working on the regulation of the melanotransferrin gene, a tumoral antigen associated with melanomas.

The hospital at the Institut Pasteur is both a participant and principal investigator in clinical trials. For example, a new clinical study is underway to compare the use of daunosome versus trichemotherapy in the treatment of Kaposi's sarcoma, a cancer associated with AIDS.

A new and highly promising area of cancer research at the Institut Pasteur involves gene therapy, a technique for reversing the cancerous process by treating the patient with genetically modified cells.

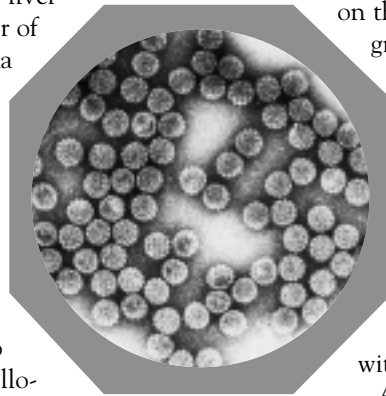
### The Epidemiologic Approach

Finally, an understanding of the epidemiology of cancer is of paramount importance. Epidemiology is the study of infectious diseases within populations rather than individuals. Not merely the mathematical analysis of data, it is a global approach uniting on-site investigations with laboratory studies.

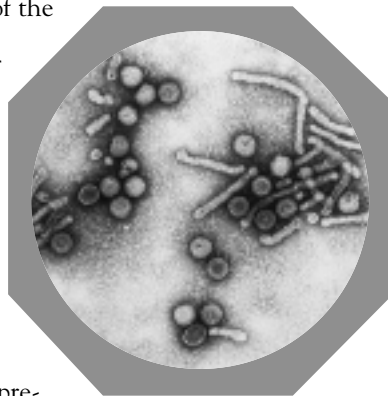
Over a century ago, Louis Pasteur and his first students in subtropical Africa and the Far East began to build an international network of the Institut Pasteur, which as of this writing has grown to include 25 institutions. This unique network greatly facilitates a global approach to the epidemiology not only of virally induced cancers, but also of all known and emerging infectious diseases.

More about the international network of the Institut Pasteur in our next issue.

*Hugues Fleury is the Editor-in-Chief of the Lettre de l'Institut Pasteur. This article was translated by Caitlin Hawke, Director of Development for the Pasteur Foundation.*



Papillomavirus



Hepatitis B virus

### ATTENTION EDUCATORS!

If you would like to borrow our film "Pasteur: A Contemporary View," to receive scholastic materials such as the Pasteur Time Line or to organize our exposition at your school, please contact us at 212.599.2050. We will be happy to accommodate your request.

## AN AMERICAN IN PARIS—1974: THE TWO CULTURES RECONCILED

By Howard A. Shuman, Ph.D.

*Editor's Note: Dr. Shuman's article is adapted from a roundtable discussion entitled "Pasteur and the 21st Century" held last spring at Columbia University. From 1974 to 1975 and again in 1981, Professor Shuman worked at the Institut Pasteur as a student and postdoctoral fellow with Maxime Schwartz. He received his Ph.D. in biological chemistry from Harvard University in 1980. Since 1982, he has been at the College of Physicians and Surgeons of Columbia University in the Department of Microbiology.*

In 1974, I was a young college graduate privileged to spend two years working at the Institut Pasteur. For me as an individual, this was a period of extraordinary growth and maturation both scientifically and culturally.

Describing the circumstances of how I came to be in contact with Pasteur allows me to credit my two most influential mentors — Jonathan Beckwith and Maxime Schwartz. Maxime, of course, has since become the Director General of the Institut Pasteur.

As a college student, I had worked part-time in the laboratory of Jon Beckwith at Harvard. Jon had been a post-doctoral fellow with François Jacob at Pasteur in the early 1960s, where he helped launch the field of molecular genetics as we know it today. At that time, he became friendly with a student in the lab of Jacques Monod: Maxime Schwartz, who was studying the mysteries of sugar metabolism and gene regulation in bacteria, making discoveries that have had far-reaching effects in almost every area of microbiology and infectious diseases.

While hanging around the Beckwith lab as a recent college graduate, I heard Jon say that his friend Maxime had visited and was looking for a postdoctoral fellow to work in his laboratory at Pasteur. When Jon asked if I was interested in pursuing that possibility though I had only just applied to Ph.D. programs, I said, "Sure. Why not?"

Upon arrival in the small office that Maxime shared with David Perrin, I experienced jet lag for the first time and promptly fell asleep as Maxime explained the intricacies of maltose metabolism in *E. coli*—our favorite object of study. Things did not improve immediately. At lunch shortly thereafter, in the Pasteur canteen, David invited me to join a table with Professor André Lwoff, who, with his students Jacob and Monod, had received the 1965 Nobel Prize for their studies on gene regulation. As opposed to the U.S., where scientists talk about science at lunch, there was a lively discussion of educational opportunities in the People's Republic of China following an article in *Le Monde*. As the discussion progressed

around the table, it eventually came to the American delegation—yours truly. In spite of being intimidated, I managed a remark intended to be completely neutral and unnoticed. The response from Monsieur Lwoff was, of course, neither neutral nor unnoticed: "That's one of the most ridiculous things I have heard in a long while!"

Work in the lab went much better. Nevertheless, it was clear that although people were quite serious about science, they were also serious about music, art, politics, and what happened in the rest of the world. To be a real person required experiences and exchanges of ideas in all of these areas. Fortunately, there are few better places than Paris for taking in culture by osmosis. This indeed turned out to be as important to me as appreciation of the Cartesian ideals of logic and clear thought. After all, the same manner of thought can apply as much to planning experiments and interpreting results as it does to analyzing the origins and effects of an impressionist painting, the organization of a symphony or the construction of a cathedral.

In the short span of two years, it was possible to see and absorb so much with

*continued on back page*

### HOW TO BECOME "AN AMERICAN AT PASTEUR"

Since World War II, more than 600 Americans have worked at the Institut Pasteur. Today, of the more than 70 nationalities represented annually in the trainee program, Americans constitute approximately 10 percent of these foreign scientists.

Highlighting the century-long traditions of American philanthropy toward the Institut Pasteur and of scientific exchanges between the Institut Pasteur and the United States, a scholarship has been established at the Pasteur Foundation to fund American and British fellows. Generously endowed by Mrs. Frank Howard in 1992, this unique fellowship is awarded by the directors of the Institut Pasteur on a merit basis to postdocs wishing to work at the institute in Paris. Depending on demand, it is granted for periods ranging from three months to a full year.

We encourage Pasteur alumni to inform their students of this fellowship. Applications for post-doctoral positions at the Institut Pasteur should be addressed to Dr. Jean-Louis Guenet, Directeur du Personnel Scientifique; Institut Pasteur; 28, rue du Docteur Roux; 75015 Paris, France. For a list of labs at the Institut Pasteur, please contact the Pasteur Foundation. Candidates should mention that they would like to be considered for the Howard Scholarship.



Nicholas Mantis, a young American recipient of the Howard Scholarship, at work in Philippe Sansonetti's laboratory at the Institut Pasteur. The laboratory studies the molecular and cellular mechanisms that permit microorganisms such as *Shigella* to cross the intestinal barrier and cause bacillary dysentery.

## A LETTER FROM THE CHAIRMAN OF THE AMERICAN ADVISORY BOARD



Fall 1996

Dear Friends of the Pasteur Foundation:

We hope you will enjoy this first issue of *Pasteur Perspectives*. With each edition, this newsletter will bring you reports of important research currently being conducted at the Institut Pasteur in Paris. In addition to news from the Institut Pasteur laboratories, the letter will include some of the rich history of this international institute, founded more than a hundred years ago by Louis Pasteur for the improvement of public health throughout the world.

There is no one alive today whose life has not been touched by the work of this remarkable man and the many scientific achievements of his institute. Last year marked the hundredth anniversary of his death, which was commemorated all over the world by scientists and laymen alike.

At present, we are preparing for the first Annual Award Dinner to be held on Wednesday, October 23, 1996, at the St. Regis Hotel in New York City. The dinner will honor Guy Wildenstein, President of the American Society of the French Legion of Honor. Governor Lowell P. Weicker, Jr., will be the keynote speaker.


More than ever, the Institut Pasteur needs financial support from the private sector to carry on the mission of its founder. In the face of new and emerging threats to public health such as the Ebola virus, mad cow disease and the hantavirus, the battles are far from over.

We hope you will consider making a tax-deductible contribution or bequest to the foundation in New York. We hope, too, that many of you will subscribe to the first Annual Award Dinner, which promises to be a memorable event. Contributions to the dinner are tax-deductible.

In the meantime, we welcome your comments on this issue of *Pasteur Perspectives* and your suggestions for future articles.

With all good wishes,

Sincerely,

  
Mrs. Anastassios Fondaras  
Chairman  
American Advisory Board

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## PASTEUR PERSPECTIVES

The Pasteur Foundation is the U.S. non-profit 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.

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### DIRECTOR OF DEVELOPMENT

Caitlin M. Hawke

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## THE YEAR OF LOUIS PASTEUR IN THE U.S.

A Word of Thanks to All Who Made It Possible

With events in more than 50 cities, the United States was second only to France in its commemoration of the 100th anniversary of Louis Pasteur's death last year. The interest we encountered in this country for the story of Pasteur's life and achievements and for the history of science in general was far greater than we dared anticipate.

The Pasteur Foundation extends particular thanks to the organizers and hosts of our exposition, lectures and films in each city. Unfortunately you are too numerous to name here, but we appreciate your great efforts in bringing the life and work of this scientist to your community.

The Pasteur Foundation gratefully acknowledges the generous underwriting of the Florence Gould Foundation, and the invaluable contributions of the Banque Transatlantique in Washington, the American Society of the French Legion of Honor in New York, the French Institute for Culture and Technology at the University of Pennsylvania, the network of Alliance Française chapters throughout the United States, *France-Amérique* and the dozens of enthusiastic hosts across the country.

We continue to lend the exposition to universities, museums and other organizations. If you would like to display the exposition or to screen the video "Pasteur: A Contemporary View," please contact us.

An article about The Year of Louis Pasteur in America will appear in our next issue.

1995 L'ANNÉE PASTEUR—LE SAVOIR EST LE PATRIMOINE DE L'HUMANITÉ

## HONORING PASTEUR: THE UNITED STATES PAYS TRIBUTE

### THE HEINZ MEMORIAL CHAPEL, PITTSBURGH

by Caitlin Hawke and Annick Perrot

Few historical figures have elicited as many homages as Louis Pasteur, not only in his native France but also throughout the world. Almost everyone is familiar with a street, square, hospital or school named for this scientist. In addition to the classic medals, stamps, banknotes and statues, Pasteur is the subject of hundreds of books and several films. His image has been memorialized in stained-glass windows and his name has been lent to a town in Quebec, an Algerian village, two transatlantic liners, a play and a rose.

In each issue, "Honoring Pasteur" will present one of the dozens of U.S. tributes to Louis Pasteur. The first is the glorious stained-glass window created in 1934 by Charles Connick for the exquisite Heinz Memorial Chapel at the University of Pittsburgh. Intended as a celebration of human achievement, the chapel depicts Pasteur in two places: in a tympanum carving as Jesus's spiritual progeny in healing and as the central figure in the "Truth" window.



Photo Credit: Herb Ferguson

"Truth" window of the Heinz Chapel

We invite readers to send suggestions and photographs of U.S. memorials dedicated to Louis Pasteur for future editions of this newsletter.

*Caitlin Hawke is the Pasteur Foundation's Director of Development, and Annick Perrot is Curator of the Musée Pasteur.*

## WE NEED YOUR SUPPORT

### WHY MAKE A GIFT TO THE PASTEUR FOUNDATION?

For over a century, discoveries made at the Institut Pasteur have saved millions of lives throughout the world.

The Institut Pasteur, a private foundation, is a unique scientific community linking 25 institutes over five continents.

In the face of new and emerging threats to public health, the battle continues.

Make everyone's well-being your business. Help perpetuate the century-old tradition of international support of the Institut Pasteur's vital work. Make a gift or a bequest to the Pasteur Foundation. For information about planned giving, please contact Caitlin Hawke, our Director of Development.

**The Pasteur Foundation is a not-for-profit organization. All gifts are fully tax-deductible. For more information, please call 212.599.2050.**

#### VISIT THE INSTITUT PASTEUR WEBSITE

For more information about the Institut Pasteur, visit our website: [www.pasteur.fr](http://www.pasteur.fr)

#### ADD YOUR NAME TO OUR MAILING LIST

If you did not receive this issue in the mail, why not join our mailing list? To receive this newsletter and/or to subscribe for a friend, please fill in the attached form and return it to us. (You may reproduce the form as needed.)

#### HELP KEEP OUR MAILING LIST CURRENT

Please send us your current address or inform us if you wish to have your name removed from our mailing list.

PASTEUR FOUNDATION 420 LEXINGTON AVENUE, SUITE 1654, NEW YORK, NEW YORK 10170

I want to help support the research conducted at the Institut Pasteur to improve worldwide public health. I am enclosing a tax-deductible gift to the Pasteur Foundation in the amount of:

\$1000    \$500    \$150    \$100    \$50  
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I would like more information on how to make a bequest in support of Pasteurian research.

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*Please make your check payable to the Pasteur Foundation.*

TELEPHONE \_\_\_\_\_

**An American in Paris** *continued from page 3*

the help of friends and colleagues. That brief period also led to my current collaborations with scientists based at Pasteur.

Part of the reason that the Institut Pasteur is such a special place, both for biology and for the world, derives from the spirit of Monsieur Pasteur himself. This spirit is still evident in the mission of the institute and its affiliates: to relieve human suffering by understanding the causes of and developing the cures for infectious diseases. No other entity serves this mission with such dedication and quality. In addition, Pasteur scientists have devel-

oped many new fields of biology not directly connected with infectious disease per se. For example, genetics of mammalian development and neurobiology are areas in which Pasteur leads the world as well.

In sum, the Institut Pasteur is an ideal center of excellence for this type of cross-cultural experience. What was true about and unique to my experience at Pasteur in 1974 remains so today, and I encourage young American scientists to consider a fellowship there and to open themselves both intellectually and culturally to the marvelous challenges that lie in wait.