

PASTEUR PERSPECTIVES

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

MEET THE FELLOWS: SHAWN M. GOMEZ

Dr. Gomez, one of our Pasteur Foundation Fellows and Florence Gould Scholars, is a bioinformatician who has been awarded a Pasteur Foundation Post-Doctoral Fellowship to work in the Insect Biochemistry and Molecular Biology Laboratory at the Institut Pasteur. Dr. Gomez moved to Paris with his wife Andreyra and their two-year-old son Xavier in June of 2002. His article describes his unique approach to research and how he applies it to a mosquito-borne disease that causes a staggering million deaths each year.

NETWORKING: A WAY TO DECIPHER DISEASE

By Shawn M. Gomez

Imagine that you are an alien from some distant planet who has been charged by your superiors with the unenviable task of discovering how human societies work. One approach may be to observe the activities of a large number of individuals, perhaps in a populous city like New York. Here you will observe people going about their daily lives—eating, sleeping, busy at work (or perhaps not), going to a movie, having a conversation, and so on. While the study of individuals is helpful and often fascinating, interactions among people and how their relationships provide a framework for human society is of equal and perhaps even greater interest to you. What are the roles of various groups? How do they function? What are the characteristics of individuals who play key roles in their groups? Which groups are sufficiently important to exert influence over others? With information on individuals and groups and the interactions among them, you are likely to come away with a comprehensive understanding of how human societies function.

Our alien visitor's task is essentially the same as that faced by biologists today. The discipline known as "systems biology" strives to understand not only the function of individual components (genes, proteins, etc.) within the organism but also the relationships among them. A more formal definition of systems biology reads as follows: "the synergistic application of experiment, theory and modeling toward the understanding of biological processes as whole systems instead of isolated parts." For example, consider a single protein, which in some circumstances can act as a switch,

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GYPSY GALA SETS A RECORD

By Elizabeth Fondaras and Agnès Hibon

Our friends turned out in unprecedented numbers on April 14, 2003, for our most successful gala to date: an avant-première performance of the Broadway hit *Gypsy*, starring Bernadette Peters. Under the patronage of the Ambassador of France and Mrs. Jean-David Levitte and the Consul General of France in New York and Mrs. Richard Duqué, the evening grossed nearly \$400,000 in a season best known for its tense moments in French-American diplomacy, the war in Iraq, a Broadway musicians' strike and SARS. Even with the deck stacked so heavily against it, the gala was as sweet a success as any we have ever had—all thanks to our donors. Most of the proceeds will fund the Pasteur Foundation Post-Doctoral Fellowship Program for U.S. researchers to work in Institut Pasteur labs.



Gala Co-Chairman Agnès Hibon with underwriter David Williams of Aventis Pasteur and his wife Mary.

We thank each and every donor for making the gala an extraordinary event. Very special thanks to underwriters Aventis Pasteur and The Honorable Anne Cox Chambers; and to benefactors Dr. Judith P. Sulzberger, CDC IXIS North America CEO Luc de Clapiers, and Merck & Company.

Additional major support came from Yvonne and Barry Cohen, Michel David-Weill, Kristina and Guy Wildenstein, Cathie and Callum Barton, Antonia and Spiros Milonas, and Mr. and Mrs. Arthur Ross. Additional major corporate supporters included The Procter & Gamble Company, Cadwalader Wickersham & Taft LLP, Novartis, Bloomberg LP, JP Morgan Chase, Sankyo Pharma, Davis & Gilbert, Greenberg Traurig, Fortis Financial Services LLC, BNP Paribas, L'Oréal, and Wilke Farr & Gallagher LLP.

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turning on and off another neighboring protein by binding to it and altering its shape or some other physical characteristic. Not only do such molecules form simple pairs; they can also create multiple links, forming a “chain,” or pathway, responsible for transmitting a signal to different regions within the cell or even between cells. Such signaling pathways can “tell” a cell to reproduce itself by dividing into two identical copies. Errors in just a single link in this pathway may prevent the cell from being able to stop division, which may in turn lead to the beginnings of cancer. Perhaps even more important is the fact that, like the individual genes and proteins that constitute them, the pathways themselves are not isolated: they are free to communicate and influence each other’s behavior. The result is a vast and extremely complex network of interactions that in part generates our biological diversity.

The focus of my work at Pasteur is the creation of novel methods, mathematical models and computer algorithms, that will lead to a better understanding of these networks by helping to predict what they look like and how they behave; for example, which specific molecules interact with each other to form pathways, and at what point(s) in the network do two or more pathways interact? Currently I am attempting to answer these questions in my study of *Anopheles gambiae*, a species of mosquito responsible for transmitting malaria to humans. Malaria is a devastating disease that infects approximately 500 million people and kills between one and three million each year. Over 40% of the world’s population is at risk of contracting the disease, caused by a parasite composed of just a single cell. The deadliest of these parasites, *Plasmodium falciparum*, is transmitted from person to person by the female *Anopheles gambiae* mosquito.

NEXT CALL FOR APPLICATIONS ANNOUNCED

The next deadline to apply for a Pasteur Foundation Post-Doctoral Fellowship is **Friday, February 6, 2004.**

For application guidelines, please visit our website at: www.pasteurfoundation.org or contact our New York office.

With the recent sequencing of the genomes of all three organisms (*Anopheles*, *Plasmodium* and, of course, humans), it is now possible to address a number of questions more rigorously, among them the following: What genes are involved in helping mosquitoes become resistant to insecticides? Why are some species of mosquitoes incapable of carrying and transmitting malaria? What interactions take place between the malaria parasite and its human and mosquito hosts? Questions such as these can often be answered only within the context of networks. At the Institut Pasteur, we hope to glean clues from the structure of these networks that will provide information on the function of many individual genes; at present, the purpose of 50% of *Anopheles* genes remains

unknown. We are also attempting to isolate the genes involved in insecticide resistance and how these genes are regulated. One extremely important and challenging area of research has involved the attempt to understand which molecules and pathways in *Anopheles*, *Plasmodium* and humans interact with each other at the place and time at which a person is injected with *Plasmodium* by an infected mosquito.

While many important questions remain unanswered, ongoing studies and continuing progress should help to bring about substantial advances in our ability to understand and combat malaria. Furthermore, it is likely that the knowledge gained and approaches developed will also prove critical in the prevention and cure of other human illnesses.

THE FACTS

NAME: Shawn M. Gomez

DATE OF BIRTH:

August 7, 1968

PLACE OF BIRTH:

Nogales, Arizona

B.S. (1990), M.S. (1993):

Aerospace Engineering Sciences
(University of Colorado, Boulder)

D.ENG.SC. (2000):

Biomedical Engineering
(Columbia University, New York City)

LAST POSITION: post-doctoral fellow at the

Columbia Genome Center

LAST ADDRESS: Riverside Drive, New York City

MENTORS: Marvin Luttges, Andrey Rzhetsky

MOST PERSONALLY MEANINGFUL DISCOVERY:

my wife



THE LIGHTER SIDE:

HOME ARRONDISEMENT: 14th

FAVORITE METRO STATION: Arts et Métiers

FAVORITE GUILTY PARISIAN PLEASURE:

an occasional *pain au chocolat*
on the way to work in the morning

FAVORITE PARISIAN/FRENCH TOURIST SITE:

Picasso Museum

FAVORITE RECENTLY LEARNED FRENCH WORD

OR EXPRESSION: “Bof!”

FAVORITE FRENCH FILM: *Wages of Fear* (1953)

FAVORITE FRENCH WINE:

no decision yet, but definitely red

FAVORITE PIECE OF LAB EQUIPMENT:

coffee maker or computer

WHAT YOU MISS MOST ABOUT THE U.S.:

friends and family

WHAT YOU’LL MISS MOST ABOUT FRANCE:

friends and baguettes

Do you own an apartment in Paris?

If you own a Parisian apartment that you would like to rent, please contact us. We are organizing an informal network of U.S.-based apartment owners to help our American post-doctoral fellows in their quest for medium-term housing. The advantage to you? You can arrange to collect your rent in dollars and be secure in the knowledge that your renters are dependable, gifted American scientists working at the Institut Pasteur. Contact Caitlin Hawke for more information: 212.599.2050 or email: PasteurUS@aol.com

A NEW INTERNSHIP PROGRAM FOR UNDERGRADUATES

The Pasteur Foundation announces the creation of its **Paul W. Zuccaire Internship Program**, scheduled to launch in 2004 and financed through 2006. The goal of the program is to promote and support French-American exchange in the basic sciences, primarily at the undergraduate level, and to encourage American students to consider international scientific careers by bringing them to the Institut Pasteur and its laboratories in Paris.

A native of France who emigrated to New York and became an entrepreneur with the foundation of his own insurance agency, Paul Zuccaire left a distinguished legacy. We are grateful to his daughter Alice Zuccaire and the board of the Zuccaire Foundation for their generous support of this program.

If you are a college student or a university professor with students interested in applying for this program, please contact the Pasteur Foundation for further details.

MORE TO THE POINT: NEWS IN BRIEF FROM PASTEUR

AIDS 20 YEARS LATER: In July, exactly 20 years after the discovery of HIV by the Institut Pasteur team of Françoise Barré-Sinoussi, Jean-Claude Chermann and Luc Montagnier, Paris hosted the largest international conference ever held on HIV/AIDS. Within the context of this event, the Fondation Mondiale SIDA/World AIDS Foundation conducted a symposium. This foundation was created in 1988 by the Institut Pasteur and the U.S. Department of Health to finance AIDS research and activities designed to help developing countries address the pandemic at a local level. In 15 years, it has implemented 300 programs in 70 countries. The overall goal of the Parisian meetings was to establish a guide, based on the conclusions of the past two decades of research, to the formation of future approaches to AIDS in the Third World, which is home to a staggering 95% of all infected individuals.

DRUGS FOR NEGLECTED DISEASES INITIATIVE: The Institut Pasteur has joined a group of prominent health and research organizations in France as well as Brazil, India, Kenya and Malaysia that, working with Doctors Without Borders, launched this important initiative in July. The new nonprofit organization, known as DNDi, is devoted to the fight against diseases overlooked by the pharmaceutical industry's drug development process because of the lack of profitability in their markets, found among the world's poorest populations. DNDi will invest \$250 million over 12 years to create six or seven new medications for diseases such as sleeping sickness, leishmaniasis and Chagas disease, three deadly afflictions that affect over 350 million people annually. DNDi will work closely with the United Nations, the World Bank and the World Health Organization (WHO).

SARS AND INTERNATIONAL COOPERATION: Last fall, an alarming new pneumonia-like illness of viral origin appeared in Asia and quickly spread. Cases were soon identified in the U.S., Canada and Europe. The Institut Pasteur was one of 11 international

research organizations mobilized by the WHO to study and contain the disease. The response to the outbreak was, in short, an example of international scientific cooperation on an unprecedented level that helped not only to contain the epidemic, but also led to the swift sequencing of the virus. With 8,000 cases and 800 deaths to date, SARS serves as a vivid reminder of how epidemics are exacerbated by modern travel and how vulnerable the world is in the face of new infectious agents.

TUBERCULOSIS: The WHO predicts that, if left unchecked, tuberculosis will cause over 45 million deaths by 2020. Through its genomic study of the TB mycobacterium, the Institut Pasteur is developing a vaccine that more efficiently incorporates the non-virulent aspect of the currently available BCG vaccine. Published last fall, this work, directed by Stewart Cole, head of Pasteur's Bacterial Molecular Genetics Unit, is based on comparative studies of the genomes of bacilli that code for virulence.

HOPE—AND DIPSTICKS—IN THE TIME OF CHOLERA AND PLAGUE: The use of dipsticks for rapid diagnosis of both bubonic and pneumonic plague has been developed and evaluated at the Institut Pasteur in Madagascar and Paris. Plague can now be detected in 15 minutes at a patient's bedside. This represents considerable progress in combating this re-emerging disease that is often fatal without early treatment. Pasteur researchers have also developed cholera dipsticks, which have just been tested successfully in the field.

CLINICAL TRIALS TO BENEFIT CHILDREN: Shigellosis, a virulent dysentery that kills between 600,000 and a million children annually, may be preventable through vaccination. The Institut Pasteur will collaborate with a Belgian biotechnology firm in clinical trials to test a vaccine. The first phase, conducted in Bangladesh by the Walter Reed Army Institute and the WHO, showed the vaccine to be harmless in adults and children.



GIVING: TWO RECENT EXAMPLES



The French Connection

We salute and thank the students of Archbishop Spalding High School's Société Honoraire de Français in Severn, Maryland, for their faithful generosity. These academically distinguished juniors and seniors, under the guidance of their moderator Kim Riley, have selected the Pasteur Foundation for the past three years as a French-American cause worthy of their support. To Archbishop Spalding and its Société Honoraire de Français: *Nous vous en sommes très reconnaissants!*



An Extraordinary Bequest from Irma A. Howard

Born almost 100 years ago, she was a New Yorker and a Parisian. According to her nephew Edward Jones, she was also a ballet dancer, a race-car driver, a swimmer and a skier. Upon her death in 2000, Irma Howard named the Institut Pasteur as a co-beneficiary of her estate, bequeathing almost \$6.5 million to the institute. In 1992, she created the Institut Pasteur's Mrs. Frank Howard Scholarship for U.S. and British researchers to work in its Paris laboratories. Her nephew explained: "She was interested in research, and that is what really fascinated her about Pasteur. The creation of the scholarship was among her best charitable acts; she really enjoyed that tremendously." With her magnificent final gesture to science, her legacy continues at the Institut Pasteur. With fond remembrance, we pay tribute to Irma Howard.



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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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I would like to help support the research conducted at the Institut Pasteur to improve worldwide public health by making a tax-deductible gift to the *Pasteur Foundation* in the amount of:

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I have enclosed a contribution of \$25 or more and would like to receive your thank-you gift: the 30-minute DVD *Pasteur: A Contemporary View*.*

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*The Pasteur Foundation is a 501(c)(3) organization. *NB: If you choose to receive the DVD, it will limit the deductibility of your donation.*

GYPSY GALA SETS A RECORD *continued from page 1*



Arthur Sulzberger and his sister Judy Sulzberger with their spouses Budd Levinson and Allison Cowles



Mary and John Young of the Florence Gould Foundation with Philippe Kourilsky, Director General of the Institut Pasteur



Jean-David Levitte with gala Co-Chairman Elizabeth Fondaras and Tony Randall

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Cari and Richard Duqué with gala Corporate Chairman Luc de Clapiers



Barbara and Joseph Pieroni

We sincerely regret that space constraints do not permit a full listing of all our donors. This unavoidable omission does not diminish our gratitude to each and every participant.

THIS FILM IS NOW ON DVD; SEE DETAILS ON BACK.

Pasteur: A Contemporary View

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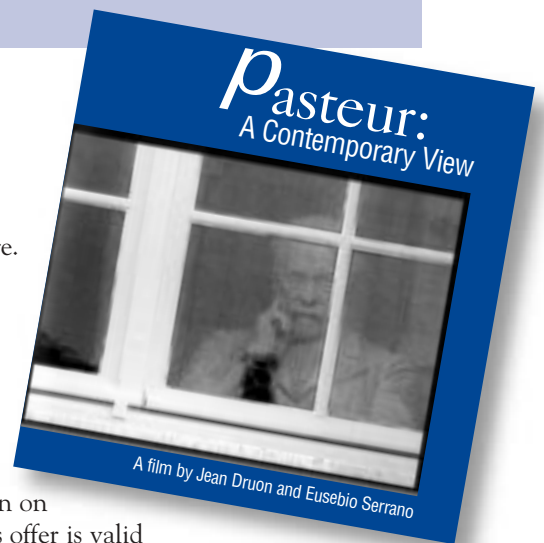
Pasteur: A Contemporary View

ATTENTION SCIENCE EDUCATORS: A DVD ON LOUIS PASTEUR FOR YOUR CLASSROOM

We are pleased to announce that, due to popular demand, *Pasteur: A Contemporary View* is to be reissued on DVD. It will be available before the end of the year in recognition of contributions of \$25 or more.

This 30-minute film was produced in 1995 in honor of the centennial of Louis Pasteur's death. It demonstrates simply and beautifully the brilliance of Pasteur's insight and experiments in microbiology while describing the scientific legacy that endures today. *Pasteur: A Contemporary View* takes the audience where the fruits of this legacy are particularly alive: to the heart of the Institut Pasteur where, for over a century, Pasteur's heirs have continued to apply their knowledge for the progress of humanity.

If you would like to own this film, please check the DVD box on the coupon on page 4 and return it with your contribution of \$25 or more. Please note that this offer is valid only while supplies last. The DVD is intended for use on U.S. players, and the Pasteur Foundation is not responsible for compatibility issues. Supply may be limited—send in your gift today!



French teachers: If you are interested in a similar reissue of the French version on DVD, let us hear from you!