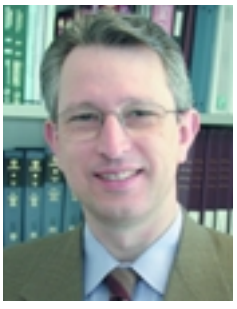
THE ROCKEFELLER UNIVERSITY 1901 CELEBRATING 100 YEARS PRO·BONO·HUMANI·GENERIS

news & notes

FRIDAY, NOVEMBER 22, 2002 THE NEWSLETTER FROM THE ROCKEFELLER UNIVERSITY'S OFFICE OF COMMUNICATIONS AND PUBLIC AFFAIRS

TODAY'S EVENTS



Massagué on TGF-beta

Joan Massagué, chairman of the Cell Biology Program at Memorial Sloan-Kettering Cancer Center, gives the Friday lecture today (Nov. 22). His talk, titled "TGF-beta Signal Transduction and Gene Regulation in Development and Cancer," begins at 3:45 p.m. in Caspary Auditorium.

Internationally recognized for his work on the control of cell growth and fate by the TGF-beta family of growth factors, Massagué and his colleagues elucidated fundamental machinery that conveys growth inhibitory signals from the cell membrane to the nucleus. Combining biochemistry and genetics, Massagué identified the TGF-beta receptors and their mechanism of activation.

He then found that a family of TGF-beta receptor kinase substrates, called Smad proteins, are transcriptional activators, thereby establishing the central concept of how this pathway operates. The end result of this process is the inhibition of cyclin-dependent protein kinases through novel inhibitors Massagué co-discovered. This contiguous set of protein-to-protein and protein-to-DNA interactions provided a direct explanation of how TGF-beta negatively controls the cell cycle. TGF-beta signaling mechanisms now are known to be crucial in embryonic development, and their disruption contributes to tumor formation and metastasis.

Massagué also is a professor at the Weill Graduate School of Medical Sciences at Cornell University and an investigator at HHMI.

Massagué received a Ph.D. in biochemistry from the University of Barcelona. He was a research fellow at Brown University until 1982, when he joined the faculty at the University of Massachusetts Medical School. He assumed his current positions in 1989. He is an elected member of the U.S. National Academy of Sciences and fellow of the American Academy of Arts and Sciences.

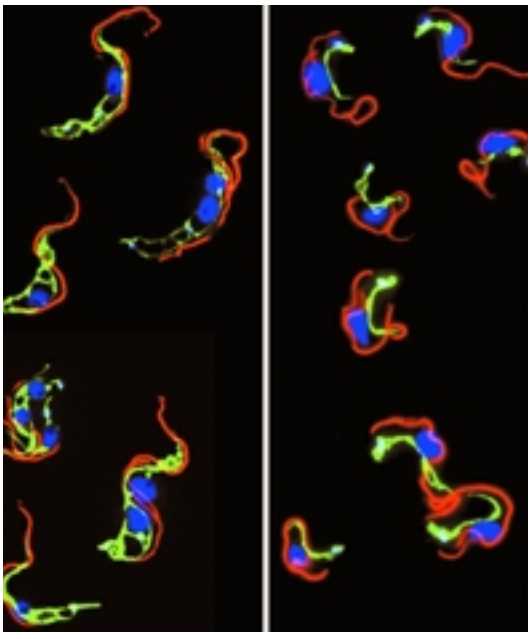
"Outlaw" organism turns informant

African trypanosome source of scientific insight

In a critical scene in the film remake of the classic 1960s TV series "The Fugitive," actor Harrison Ford sheds his coat and replaces it with another. This simple deception allows him to escape detection by the swarm of police officers trailing him.

The African trypanosome, a blood parasite that causes African sleeping sickness, is, like Ford's character in the film, a fugitive that changes its "coat" each time the human immune system is about to nab it.

Woven of 10 million copies of a single sugar-coated molecule called a glycoprotein, the trypanosome's surface changes every few days by virtue of a switch that activates a new gene.



Another basic research question trypanosomes help answer: what is the relationship between histones, a class of proteins found with DNA in chromosomes, and telomeres? *Above,* trypanosomes in various stages of the cell cycle reveal co-localization of a variant histone H3 (green) with telomeres (red).

The ability of a species to create numerous, successive surfaces as a survival tactic is known as antigenic variation. An exhausted host immune system can no longer quell infection after repeated rounds of futile antibody response.

Rockefeller's George Cross, head of the Laboratory of Molecular Parasitology, is one of a handful of pre-eminent scientists investigating the African trypanosome. In 1975 he showed that antigenic variation is based upon the amino acid arrangement of successive surface proteins of a single trypanosome lineage. Since then, he and his colleagues have identified many characteristics of the genes and proteins that are responsible for antigenic variation. Though the picture is not complete, the Cross lab has unearthed clues to the mechanisms that regulate variable-surface genes so precisely during infection.

That's why Cross, the André and Bella Meyer Professor, is betting on a molecular genetics approach to combat two diseases caused by trypanosomes: nagana, a livestock illness, and African sleeping sickness. "The parasite's antigenic variation renders vaccines unlikely to work, and older therapies such as pentamidine, suramin and melarsoprol are nearly as poisonous to humans as they are to trypanosomes."

Though other micro-organisms vary their surface antigens to counter the host's immune system, trypanosomes do so at an unrivaled rate. Also intriguing to scientists such as Cross is that the protozoan parasite is ancient, and anciently diverged, with some striking differences from multicellular beings.

Trypanosome's outlaw status sets it apart, but does not deter interest. "I've always been drawn to oddball organisms. I believe unusual adaptations can provide new insights to standard biology problems," says Shuba Gopal, a fifth-year graduate fellow in Associate Professor Terry Gaasterland's Laboratory of Computational Genomics at Rockefeller.

Seventy-five percent of trypanosomes' genes share no similarities with multicellular organisms. According to Gaasterland, the proteins made by this organism, or the ways in which they are made, are so different from ours and all other known "higher" organisms', they're provocative.

As a window to these genetic differences, Gopal studies the parasite's ability to generate messenger RNA (or mRNA) through an unusual process called "trans-splicing."

Most organisms convert their own genetic information into a usable form, called mRNA, by a process called "cis-splicing." "Cis" refers to a process of splicing together informational cassettes ("exons") that are separated by non-coding "introns" on the same piece of RNA, to make a readable transcript. This process works like a tightly safeguarded library: the cassettes' master versions always stay in the library. Copies circulate via mRNA.

Trypanosome genetic material is different in content and in form. Trypanosome genes contain no "introns" and therefore do not need to cis-splice their RNA to decode its information. "The process is closer to what we observe in bacterial transcription," says Gopal. But trypanosome genes all lack a small piece at their start, which is apparently needed for mRNA to be translated into protein, and this "mini-exon" has to be added to the RNA in a process called "trans-splicing."

When attempting to decode a DNA sequence, computers use relatively simplistic methods that cannot say, for certain, what is a real gene and what stretch of

continued on page 2

Orphaned but not abandoned

The National Institutes of Health define orphan diseases as those that afflict fewer than 200,000 people annually in the United States. The fatal sleeping sickness caused by African trypanosomes strikes between 200,000 to 300,000 people annually in equatorial Africa, the habitat of the tsetse fly, whose bite spreads trypanosomes among people and livestock.

In U.S. public health terms, African sleeping sickness is not a candidate for major research funding, nor costly drug development that would lead to cures for the disease. The AIDS and tuberculosis epidemics in developing nations eclipse the distant drama of African sleeping sickness. The trypanosomes-caused human disease is therefore an orphan. Yet, the NIH funds Cross's lab due to the intrinsic value of the organism, not to mention Cross's strong legacy of discoveries and accomplished laboratory alumni.

Championing orphan diseases is hard work. Cross travels the globe to lobby for sustained efforts to combat the diseases caused by African trypanosomes.

"If we do get new epidemics of African sleeping sickness in areas of civil strife, it's going to be very difficult to control them. We could easily begin the 21st century as we began the 20th — with significant loss of life and deep impoverishment due to the parasites."

Gaasterland would be gratified to see basic research conducted in her lab reverberate on the public health scene, too.

Orphaned and on the run, the biological outlaw known as trypanosome could someday be reformed. It is already contributing to the intellectual life of science.

—Lynn Love

calendar

NOVEMBER TWENTY-SECOND THROUGH DECEMBER ELEVENTH

WWW.ROCKEFELLER.EDU/CALENDAR.HTML

Friday Lectures and Thesis Presentations

These events are held in Caspary Auditorium at 3:45 p.m. (unless otherwise noted) and preceded by tea at 3:15 in Abby Aldrich Rockefeller Lounge. All are welcome.

FRIDAY, NOVEMBER 22

TGF-beta Signal Transduction and Gene Regulation in Development and Cancer.
Joan Massagué,
Sloan-Kettering Institute and HHMI.

MONDAY, NOVEMBER 25

Seizure-induced IL-6-type Cytokines in the CNS: Pro-inflammatory or Neuro-trophic?
Dan Rosell,
biomedical fellow,
McEwen lab, RU.

FRIDAY, DECEMBER 6

Imaging Experience-dependent Synaptic Plasticity in the Neocortex.
Karel Svoboda,
Cold Spring Harbor Laboratory.

FRIDAY, DECEMBER 13

Fairfield Osborn Memorial Lecture.
Hox Genes and Williston's Law: Developmental Genetics and the Evolution of Animal Design.
Sean Carroll,
University of Wisconsin, Madison, and HHMI.

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Suggestions for stories should be sent:
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electronic mail (newsno)
fax (212) 327-7876.

Scientific Events

FRIDAY, NOVEMBER 22

11 A.M. **Statistical Mechanics and Capacity-approaching Error-correcting Codes.**
Nicolas Sourlas,
Ecole Normale Supérieure.
B Level Conference Room,
Smith Hall Annex.

12 P.M. **Building and Demolishing a Cancer In Vivo.**
Gerard Evan,
University of California, San Francisco, Cancer Center.
Cell Biology Seminar.
116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.

MONDAY, NOVEMBER 25

11 A.M. **Understanding the Energy Landscapes Associated with Amyloid Diseases and Manipulating them to Prevent Amyloidosis.**
Jeff Kelly,
Scripps Research Institute.
Pels Family Center for Biochemistry and Structural Biology Seminar.
305 Weiss. Refreshments at 10:45.

TUESDAY, NOVEMBER 26

11 A.M. **Cell Differentiation (Notch).**
Nick Baker,
Albert Einstein College of Medicine.
Neuroscience Development Seminar.
305 Weiss.
Contact Michael Morris, 327-7144.

4 P.M. **Dengue Virus and Dendritic Cells.**
Sarah Schlisinger,
International AIDS Vaccine Initiative.
Center for the Study of Hepatitis C Seminar Series. 305 Weiss.
Refreshments at 3:45.
Contact Patricia Holst, 327-7047.
Open to RU/WMCCU/NYPH/MSKCC community and guests.

4 P.M. **Intrinsic and Extrinsic Determinants of Morphogenesis.**
Francesco Ramirez,
Mount Sinai School of Medicine.
Pharmacology Seminar.
Weill Auditorium, WMCCU,
1300 York Ave.
Coffee and cookies at 3:45.
Contact Lissett Checo, 746-6250.

4 P.M. **Tumor Necrosis Factor-alpha Gene Regulation and Genetics.**
Anne Goldfeld,
Harvard Medical School.
Center for Studies in Physics and Biology Seminar.
B Level Conference Room,
Smith Hall Annex. Coffee at 3:30.

MONDAY, DECEMBER 2

12 P.M. **The V_3 Loop: Always Changing, Always the Same.**
Susan Zolla-Pazner,
NYU School of Medicine.
CFAR Seminar.
Sixth Floor Conference Room,
ADARC, 455 First Ave.

1:30 P.M. **The Immunological Synapse: Lipid Rafts and T cell Activation.**
Paul A. Roche,
National Cancer Institute, NIH.
Immunology Seminar.
Hoffmann Auditorium, MSKCC,
1275 York Ave.

TUESDAY, DECEMBER 3

11 A.M. **Bacs and CNS Gene Expression.**
Shiaoching Gong,
Heintz laboratory, RU.
Neuroscience Development Seminar.
305 Weiss.
Contact Michael Morris, 327-7144.

4 P.M. **Hepatitis C Immunopathogenesis: From Bench to Bedside.**
David Nelson,
University of Florida.
Center for the Study of Hepatitis C Seminar Series.
305 Weiss. Refreshments at 3:45.
Contact Patricia Holst, 327-7047.
Open to RU/WMCCU/NYPH/MSKCC community and guests.

4 P.M. **Mechanisms Involved in Regulating the NF-KappaB-Pathway.**
Richard Gaynor,
University of Texas Southwestern Medical Center at Dallas.
Pharmacology Seminar.
116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.
Tea at 3:45.

WEDNESDAY, DECEMBER 4

12 P.M. **Requirement for the Hox-Cofactor PBX1 in Skeletal Patterning and Organogenesis.**
Licia Selleri,
Sloan-Kettering Institute and Cornell University.
Seminars in Clinical Research.
110B Nurses Residence.

4:30 P.M. **Multiple Mechanisms to Repair Broken Chromosomes: Connections to Cancer.**
James E. Haber,
Brandeis University.
MSKCC President's Research Seminar.
Auditorium, Rockefeller Research Laboratories, MSKCC,
430 East 67th St. Tea at 4 p.m.

6 P.M. **Cell Death Society Monthly Meeting.**
Transcriptional Down-regulation of Ataxia-Telangiectasia Mutated Protein (ATM) Radiosensitizes Human Prostate Cancer Cells.
Adriana Haimovitz-Friedman,
MSKCC.
Potential Role of Cell Membrane Microdomain in the Ionizing Radiation-induced Jurkat Cell Apoptosis.
Jianjun Zhang,
MSKCC.
UV-C Stress Reorganizes Ceramide-rich Membrane Rafts.
James Rotolo,
MSKCC.
116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.
Refreshments at 6 p.m. Contact Adriana Haimovitz-Friedman, 639-5109.

MONDAY, DECEMBER 9

12 P.M. **FGFS in Vertebrate Development.**
Gail Martin,
University of California, San Francisco.
Student- and Postdoc-sponsored Seminar Series. 301 Weiss.
Pizza luncheon at 1 p.m, 17th Floor, Weiss Research Building.
Contact Sasha Rudensky, 327-8368.

1:30 P.M. **New Structural Paradigms in Receptor Recognition and Activation.**
K. Christopher Garcia,
Stanford University.
Immunology Seminar.
Weill Auditorium, WMCCU,
1300 York Ave.

4 P.M. **Regulation of Self-renewal vs. Differentiation in *Drosophila* Stem Cells.**
Margaret T. Fuller,
Stanford University.
Molecular Biology 2002 Fall Research Seminar Series.
116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.
Tea at 3:45.

5:30 P.M. **The State of Public Health in New York City.**
Thomas R. Frieden, commissioner,
New York City Department of Health and Mental Hygiene.
Zanvil A. Cohn Forum on Health Affairs.
Abby Aldrich Rockefeller Dining Room.
Refreshments at 5 p.m.

TUESDAY, DECEMBER 10

11 A.M. **Clock Genes.**
Justin Blau,
New York University.
Neuroscience Development Seminar.
305 Weiss.
Contact Michael Morris, 327-7144.

2:30 P.M. **New York Lipid and Vascular Biology Research Club Meeting.**
Adipocytes and Adipokines: The Role of Adipocyte-derived Factors in Lipid and Carbohydrate Metabolism.
Philipp E. Scherer,
Albert Einstein College of Medicine.
The AMP-activated Protein Kinase and Regulation of Lipid Metabolism by Leptin and Adiponectin/ACRP30.
Barbara B. Kahn,
Harvard Medical School.
Defining the Lipid Storage Droplet: Unique Proteins Associated with a Dynamic Subcellular Compartment.
Dawn L. Brasaemle,
Rutgers University. 305 Weiss.
Refreshments at 5:30 in the dining room, 17th Floor, Weiss Research Building.
Contact Kie Cundey, 327-7708.
Open to RU/WMCCU/NYPH/MSKCC community and guests.

4 P.M. **Pharmacology of New Progestins Used for Contraception.**
Regina Sitruk-Ware,
Center for Biomedical Research, Population Council.
Pharmacology Seminar.
E-415 WMCCU, 1300 York Ave.
Coffee and cookies at 3:45.
Contact Lissett Checo, 746-6250.

4 P.M. **Structural Genomics.**
Chris Sander,
Sloan-Kettering Institute.
Tri-institutional Structural Biology Seminar.
Weill Auditorium, WMCCU,
1300 York Ave. Coffee at 3:45

WEDNESDAY, DECEMBER 11

12 P.M. **New Aspects of Steroid Receptor Coactivator Action.**
Bert W. O'Malley,
Baylor College of Medicine.
Endocrinology and Reproductive Biology Seminar.
305 Weiss.

12 P.M. **Resolution of Hepatitis C Virus Infection: The Role of T Lymphocytes.**
Arash Grakoui,
Rice laboratory, RU.
Seminars in Clinical Research.
110B Nurses Residence.
Contact Dale Miller, 327-8411.

4:30 P.M. **Toward Manipulating Stem Cells with Isolated Wnt Signaling Molecules.**
Roel Nusse, Stanford University School of Medicine and HHMI.
MSKCC President's Research Seminar.
Auditorium, Rockefeller Research Laboratories, MSKCC,
430 East 67th St. Tea at 4 p.m.

The Arts and Other Events

FRIDAY, NOVEMBER 22

12 P.M. **Tri-institutional Noon Recitals.** Frederic Chiu, piano.
Caspary Auditorium. Open to RU/WMCCU/NYPH/MSKCC community and guests.

MONDAY, NOVEMBER 25

8 P.M. **The Rockefeller University Film Series.**
The Match Factory Girl
(directed by Aki Kaurismaki, 1990).
Caspary Auditorium. Open to RU/WMCCU/NYPH/MSKCC community and guests.

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Battle against terror gains silicon ally

Stebbins helps bring power of "distributed computing" to bear on biowarfare

If two brains are better than one, then imagine what a network of thousands could do. That's the reasoning behind distributed computing networks, such as the non-profit organization Find-a-Drug, which has hundreds of people volunteering their idle personal computers for the mountainous task of screening billions of chemicals for new disease-fighting drugs.

That's also what inspired Assistant Professor Erec Stebbins to persuade Find-a-Drug to add bioweapons — a subject of his own research — to the organization's original list of HIV and cancer targets.

"Distributed computing networks are incredibly powerful tools," says Stebbins, head of the Laboratory of Structural Microbiology. "With the very real threat of antibiotic-resistant bioweapons upon us, it makes sense to apply this technology to the search for novel therapeutics."

Stebbins, who recently received a James D. Watson Investigator award from the New York State Office of Science, Technology and Academic Research (NYSTAR) *(see related newsbrief, page three)* for his research on the biological structures of plague, or *Yersinia pestis,* and other infectious bacteria, serves as an advisor to Find-a-Drug's new "Bioterrorism Antidotes" project.

Researchers develop new drugs in several ways, including the systematic screening of billions of synthetic compounds against specific disease-causing proteins — a massive undertaking too large for even a supercomputer to quickly process. Distributed computing networks, or "virtual supercomputers," like Find-a-Drug's chip away at this iceberg of data by harnessing the collective computing power of individual users' personal computers.

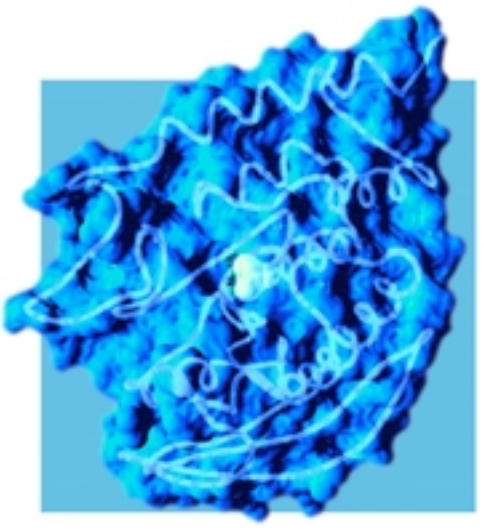
Anyone with a PC can participate simply by downloading special software from Find-a-Drug's Web site (www.findadrug.com). The software will retrieve a chunk of data over the Internet from the organization's servers; analyze it during periods when the computer is at rest; then send the results back to the servers.

The popular SETI@home virtual supercomputer, which scans outer-space data for signs of extraterrestrial life, is a testament to the power of this community-based approach: with tens of thousands of active members, it is now the fastest computer in the world. It has inspired another similar use of "distributed dynamics" technology in Folding@home, a Stanford University initiative employing idle personal computers to analyze folding pathways in increasingly complex protein fragments.

The Bioterrorism Antidotes project will apply this technology to the search for antidotes to bioweapons, beginning with the deadly plague pathogen notorious for killing over one-third of the European population during the Middle Ages.

"Plague bacterium was chosen as the first target because it was successfully weaponized in the Soviet program," says Stebbins.

Plague also was chosen because one of its primary modes of destruction, a protein called Yersinia tyrosine phosphatase (YopH), is well characterized structurally. This three-dimensional structural information allows the Find-a-Drug software, called THINK, to systematically position candidate small molecule drugs into the protein's grooves and clefts in search of a snug fit. Resulting "hits" are sent back to Find-a-Drug servers for further evaluation, and those results are made available to approved academic institutions.



The YopH protein, shown as a semitransparent molecular surface with a thin ribbon representing the polypeptide chain, is a key virulence factor belonging to *Yersinia pestis,* the biowarfare agent and cause of bubonic and pneumonic plague. The pale blue molecule at center is a bound phosphate in the enzyme's active site — the region small molecule inhibitors are expected to bind enzymes.

But, according to Stebbins, success ultimately will be measured by how many people sign up. Since Bioterrorism Antidotes launched over one month ago, 905 members have tested about 27 million compounds against YopH, resulting in over 35,000 hits.

"While this is a good start," Stebbins says, "we hope a lot more people participate. The more members we have, the more potential drug molecules we can examine, and the greater our chance of discovering new treatments."

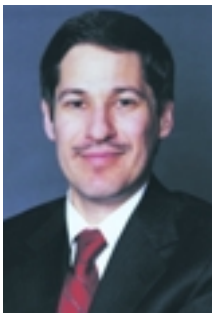
— *Whitney Clavin*

State of public health in New York: Next Cohn Forum

Thomas R. Frieden, commissioner of the New York City Department of Health and Mental Hygiene, will speak on "The State of Public Health in New York City" at the next Zanvil A. Cohn Forum on Health Affairs, 5:30 p.m., Monday, Dec. 9, in Abby Aldrich Rockefeller Dining Room.

Frieden, a world-renowned expert on tuberculosis, was instrumental in stopping New York's epidemic of that disease, which peaked in 1992; during his tenure as director of the Bureau of Tuberculosis Control, from 1992 to 1996, the city cut cases of multidrug-resistant TB by 80 percent. The program Frieden built is considered an international model for TB control.

As commissioner, Frieden believes certain public health problems require special attention. Among these are HIV/AIDS, obesity, drug abuse, alcoholism, violence, asthma, mental health care, prenatal care, cancer screening, high blood pressure and high cholesterol.



Thomas R. Frieden

Upcoming Cohn Forum speakers:

Monday, Jan. 27, 2003
Thomas R. Insel, Director, National Institute for Mental Health, NIH
Topic: "Neurosciences and Mental Health"

Monday, March 10, 2003
Greg Koski, Former Director, Office for Human Research Protections, U.S. Department of Health and Human Services
Topic: "Science and Politics of Human Subjects"

Monday, April 7, 2003
Vivian Siegel, Editor, *Cell, Developmental Cell* and *Molecular Cell*
Topic: "What's New: The View from *Cell*"

Cohn Forum is a series of colloquia on issues in health and biomedicine.
Admission is free and no registration is required.
All lectures occur at 5:30 p.m. in the Abby Dining Room.

"Outlaw" organism *continued*

sequence just coincidentally looks like a gene. If trans-splicing is required for mRNA in trypanosomes, identifying DNA signals that specify trans-splicing sites can help discriminate real genes from others that are predicted, by the computer, to be possible genes.

To this end, Gopal developed a system that classifies different kinds of splice signal data. Her goal was to learn how to predict trans-splicing signals. This has involved her in cycles of computer prediction and experimental confirmation. Each cycle improves the veracity of the predictive algorithm.

Gopal, in her bioinformatics-to-bench research, focuses on the genetic material at the "middle" of *T. brucei's* many chromosomes (11 essential, plus hundreds of mini-chromosomes).

Another trypanosome researcher at Rockefeller primarily is concerned with what occurs at the "ends" of these chromosomes.

Bibo Li, a new research assistant professor in Cross's lab, who completed a postdoctoral fellowship with Titia de Lange in her Laboratory of Cell Biology and Genetics, studies the ends of trypanosome chromosomes, called telomeres.

Telomeres in trypanosomes turn out to have the closest biochemical lettering — that is, A,C,T and G organization of nucleotides found in DNA — to our own human telomeres.

As a rich source of insight on chromosomal aging and instabilities leading to cancer, telomeres have been an important basic research topic. Rockefeller's de Lange, a leader in the telomere field, conducted her own graduate work on telomeres in *T. brucei*.

Li's tenure in the Cross lab has only begun, but the research she undertakes will illuminate more than one set of biomedical problems. By identifying proteins that act on telomeres, she will potentially contribute to further understanding of cancer onset and its possible treatments.

She can conduct endogenous gene experiments in *T. brucei* that cannot be done in humans, and reap the benefit of the parasite's rapid reproduction cycle. In addition, learning more about trypanosome telomere function could reveal a vulnerability in the parasite's system. It has been suggested that silencing *T. brucei's* telomere might reduce its capacity for antigenic variance. This knowledge could translate into a long-awaited cure for sleeping sickness.

"Li is by far the most qualified person in the world to be working on trypanosome telomeres," says Cross. "She is familiar with all the existing systems — including yeast, mouse and human — and knows how to exploit the *T. brucei* model."

The molecular genetics of trypanosomes, whether at the "middle" or the "ends," promises new insights, the dimensions of which we can only estimate.

— *Lynn Love*

"His ideas were ahead of their time"

Chromatin biology pioneer Allfrey dies at 81

Vincent G. Allfrey

Professor Emeritus Vincent G. Allfrey died Nov. 2 at Pascack Valley Hospital in Westwood, NJ, from complications of diabetes. He was 81.

Allfrey, a cell biologist, made seminal contributions to understanding how proteins in the cell nucleus, called histones, control gene activation in higher organisms.

"Vince Allfrey elegantly studied how histones affect the behavior of chromosomes," says Bruce S. McEwen, Alfred E. Mirsky Professor and a former graduate student in Allfrey's lab. "He was also a terrific mentor."

Allfrey began his career at Rockefeller in the laboratory of the late Alfred E. Mirsky, with whom he started his work on histones and protein synthesis.

"Allfrey carried the story of histone modification on his own in more recent years," says McEwen.

Allfrey's experiments provided evidence that histones are modified by enzymes that attach acetyl, phosphoryl or methyl chemical groups to them. Allfrey and others went on to show that such changes often correlate with an increased capacity for RNA synthesis. Current investigation in this field, including the work of C. David Allis, a chromatin biologist who will join Rockefeller as a head of laboratory next spring, can be traced back to Allfrey's original findings.

"I was saddened to learn of Allfrey's passing. He was a true pioneer of the field of chromatin biology," says Allis, currently a professor at the University of Virginia. "Many of the post-translational histone modifications — acetylation and methylation are two that immediately come to mind — now generating excitement were discovered by him and his colleagues.

"I am guessing many other 'Allfrey insights' soon will re-surface on our radar screens. His ideas and experiments were ahead of their time."

In addition to conducting research on nuclear proteins and gene activation, Allfrey assembled the first mass spectrometer at Rockefeller, and adapted and perfected an innovative method called non-aqueous cell fractionation to isolate the nucleus from the cell using organic solvents instead of water. Allfrey used this technique to measure enzyme activity in the nucleus, and to establish criteria for judging the quality of cell nuclei isolated from different tissues in aqueous media to carry out their normal functions, says McEwen.

Allfrey joined Rockefeller in 1941, as a laboratory helper to support his undergraduate studies at the College of the City of New York. After receiving his B.S. in chemistry — awarded by mail at the battlefront during World War II — he returned to spend another year at Rockefeller as a technician in Mirsky's lab before attending graduate school at Columbia University, where he received his Ph.D. in chemistry in 1949. After graduate school, he returned to Rockefeller as a research associate. He became associate professor in 1957 and full professor in 1963.

Allfrey was a long-term friend of Professor Emeritus and Nobel laureate Bruce Merrifield. For more than 40 years, Allfrey and Merrifield commuted together each morning from their homes in New Jersey. While Merrifield drove, Allfrey would read aloud from such books as the *Lewis and Clark Diaries* or a volume of Winston Churchill's memoirs.

"He was the best friend I had at Rockefeller," says Merrifield. "I admired him."

In addition to his scientific interests, Allfrey was an accomplished pianist. Early in his career, he was befriended by Herbert Gasser, Rockefeller's second president. Gasser invited the young researcher to play the piano at his home, where Allfrey was known to have given remarkable recitals, Merrifield recalls.

Allfrey is survived by his wife, the former Joan Brice, of Tenafly, NJ; his daughter, Barbara Claire Maldonado, of Leonia, NJ; and his son, Kevin Mark Allfrey, of Kingston, NY. In lieu of flowers, Allfrey's family requests donations in his memory to the American Diabetes Association.

— *Joseph Bonner*

Save the Date

Rockefeller's annual "Winter Wonderland" holiday party will occur at 2:30 p.m., Wednesday, Dec. 18, in the Weiss Research Building.

Jazz music and children's activities will be featured in Weiss Café, and our own Rockefeller DJ, Fazeer Ogeer, will spin dance tunes on the 17th Floor.

The holiday party is open to faculty, postdocs, students and staff of The Rockefeller University.

People in the News

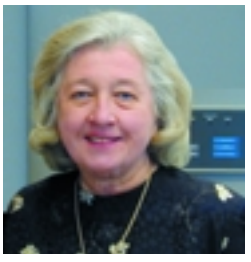
McKinney gives Capital Science Lecture

Assistant Professor John McKinney gave the inaugural talk of the Capital Science Lecture series's 13th season, sponsored by the Carnegie Institution of Washington. Streaming video of his lecture, titled "Persisting Problems in Tuberculosis," is available at http://carnegieinstitution.org/.

Kapoor named Pew Scholar

Assistant Professor Tarun Kapoor was named a 2002 Pew Scholar in the Biomedical Sciences. The awards of $240,000 over a four-year period are granted "to encourage innovation" in young investigators who show outstanding promise in the basic and clinical sciences. Kapoor's lab focuses on the design, discovery and synthesis of cell-permeable small organic molecules that rapidly perturb the function of their targets as powerful tools to dissect dynamic cellular processes.

Kreek receives NIDA grant



The National Institute on Drug Abuse (NIDA) of the National Institutes of Health (NIH) has awarded a five-year competitive renewal grant ($14.4 million) to the NIDA-NIH Research Center directed by Professor Mary Jeanne Kreek, head of the Laboratory on the Biology of Addictive Diseases. Established in 1987, the center unites bench science with clinical studies in the pursuit of the molecular and neurobiological causes of addictive diseases, including heroin addiction, cocaine dependency and alcoholism. Its ultimate mission is to translate this knowledge into new treatments.

Stebbins named Watson investigator

Assistant Professor Erec Stebbins was named a James D. Watson Investigator by the New York State Office of Science, Technology and Academic Research (NYSTAR). Stebbins will receive a $200,000 grant for structural studies of bacterial type III secretion systems. The NYSTAR program recognizes and supports outstanding scientists and engineers who, early in their careers, show potential for leadership and scientific discovery in the field of biotechnology.

Lederberg receives Rall Medal

The Institute of Medicine (IOM) of the National Academies awarded President and Professor Emeritus Joshua Lederberg the David Rall Medal during its annual meeting last month. The Rall Medal honors Lederberg for "his exemplary leadership as chair or co-chair of several IOM committees."

Chait gives first Seitz lecture

Brian Chait, Camille and Henry Dreyfus Professor, gave the first Frederick Seitz Lecture at the University of Chicago's Institute for Biophysical Dynamics last month. The lectureship, named for Rockefeller's president from 1968 to 1978, was endowed last May by Attallah Kappas, Sherman Fairchild Professor and an alumnus of Chicago's School of Medicine.

McEwen honored by APA, Columbia University

Professor Bruce McEwen has been selected to receive the American Psychological Association's 2003 Distinguished Scientific Contribution Award. The award, to be presented next August in Toronto, honors psychologists who have made distinguished theoretical or empirical contributions to basic research in psychology. McEwen also recently received the Edward J. Sachar Award from the Department of Psychiatry at Columbia University College of Physicians and Surgeons.