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News and Notes 2001

The Rockefeller University News and Notes

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## NEWS AND NOTES 2001, FEBRUARY 16

The Rockefeller University

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# news & notes

THE NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY LECTURE

## Immunologist to discuss antibody system today

Klaus Rajewsky, a professor at the Institute of Genetics, University of Cologne, will present today's Friday lecture (Feb. 16). His topic will be "Conditional Mutagenesis as a Physiological Process and an Experimental Approach in the Antibody System."

Rajewsky's goal is to understand how lymphocytes develop and are controlled in vivo, how immunological memory is generated and maintained, and how self-aggression is avoided.

The main emphasis of his work is on B lymphocyte development from the stem cell in the bone marrow of the mouse to the memory cell, generated upon primary contact with antigen. B cell development is guided by immunoglobulin (Ig) gene re-arrangements, through expression of Ig heavy and light chains in receptor complexes on the cell surface.

The lab has identified, by gene targeting and molecular single cell analysis, "checkpoints" that the cells have to pass on the basis of receptor expression. The generation of memory B cells involves somatic hypermutation of antibody V region genes and selection of high-affinity mutants. His lab has shown that this process occurs in germinal centers, and they are now trying to understand the mechanism of hypermutation.

To understand gene function in vivo, his lab plans to further develop the approach of conditional gene targeting that they have initiated. Here the ultimate goal is to introduce mutations in genes in mice at will, in a celltype-specific and inducible manner. The mutations include gene inactivation, activation and replacement. Only in this way

*continued on page 4*

2 AROUND CAMPUS

3 IN THE LAB

4 ETCETERA

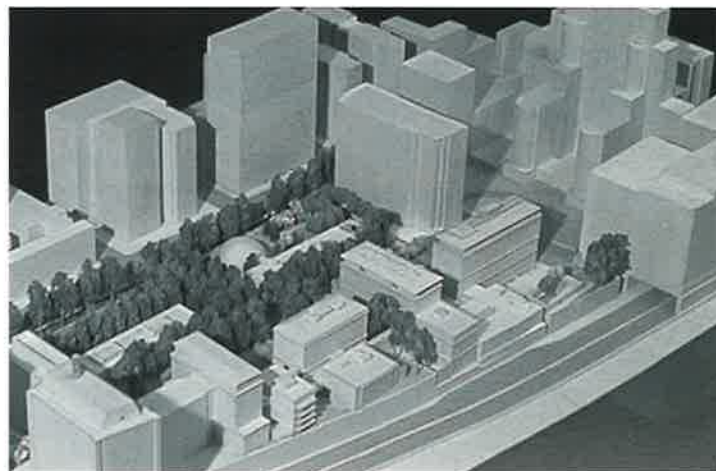
## Master space plan to support scientific expansion

As the university celebrates its 100th birthday this year, various projects—some currently under way, others planned for the near future—seek to ensure the university's physical vitality for another hundred years. This "master space plan" includes the modernization of the campus's oldest buildings and the construction of a new research tower on the north end of campus, all designed to better locate people and services to allow the best science to flourish.

In June 1999, the board of trustees approved President

Arnold J. Levine's five-year academic plan, which calls for adding new faculty in key disciplines, fostering research that crosses disciplinary boundaries, modernizing the university's research hospital and creating additional state-of-the-art laboratory space. In addition to these research imperatives, the plan addresses the changing needs of the campus community, in particular the needs of the growing ranks of younger scientists.

*continued on page 4*



A new master space plan for the university addresses the changing needs of the Rockefeller community.

## Stem cells are topic of next Cohn Forum



Steven H. Holtzman will discuss the ethical question of the "personhood" of embryos and how the current debate affects scientific research.

Steven H. Holtzman, chief business officer of Millennium Pharmaceuticals, Inc., will present the next Cohn Forum on Mon., March 12. His topic will be "Stem Cells: Persons or Therapies in Embryo?"

Human stem cells, derived from

embryos, are a unique biomedical resource with potential to help us understand complex processes of human development, as well as to treat diverse afflictions including spinal cord injury, burns and heart disease. In his Cohn Forum talk, Holtzman will explore recent NIH recommendations on stem cell research and explain why, particularly in light of the new administration's opposition to fetal tissue research, addressing the central ethical question of the personhood of embryos is crucial to continued progress.

Holtzman has been with Millennium, a pioneer and leader in the identification of the genetic basis of common human diseases, since early 1994. Under his leadership, the company has grown to over 1,500 employees and is

ranked among the top 10 companies in the biotechnology industry in market capitalization and revenues.

Before joining Millennium, Holtzman was a founder of DNX Corporation, the first commercial enterprise devoted to the development of biomedical and pharmaceutical applications of transgenic animal technology. Prior to his work with DNX, in the early 1980s, Holtzman was the founding executive director of the Ohio Edison Program, the nation's first state government program dedicated to achieving economic development through funding young technology-based ventures and collaborative university/industry research and development efforts.

Holtzman currently is serving his

second term on the National Bioethics Advisory Commission, the principal advisory body to the president and Congress on ethical issues in biomedical and life sciences. He is a member of the Biotechnology Industry Organization (BIO) Bioethics Committee, which he co-founded in 1995. He has served as a trustee of The Hastings Center for Bioethics since 1999.

The talk takes place in the Abby Aldrich Rockefeller Dining Room at 5:30 p.m. and is preceded by a reception at 5 p.m.

The Cohn Forum is a series of colloquia on issues in health and biomedicine. The Cohn Forum's Web site is [www.rockefeller.edu/pubinfo/cohn.html](http://www.rockefeller.edu/pubinfo/cohn.html).

## "Polymaths and the Piano" highlights relationship between music and science

ON FILE 00-0703 #4

The Van Cliburn Foundation and The Rockefeller University collaborated to present "Polymaths and the Piano," which showcased outstanding amateur pianists from the mathematics, scientific and medical communities. The event, on Thurs., Feb. 8, kicked off the Eleventh Van Cliburn International Piano Competition Screening Recitals.

ON FILE 00-0703 #18



After the performances, Michael Kimmelman of *The New York Times* moderated a panel discussion about the relationship between science and music.



The performers for "Polymaths and the Piano" combine their interest in music with professional careers in the fields of medicine, science and mathematics.

Seth Darst, the Jack Fishman Professor and head of a Laboratory of Molecular Biophysics, was one of the performers.



ON FILE 00-0703 #25

**Awards news**

The Gheorghe Lazar Prize of the Romanian Academy, Bucharest, was presented in December for the 1998 book *Comparisons of Stochastic Matrices, with Applications in Information Theory, Statistics, Economics, and Population Sciences*, by Joel E. Cohen, J. H. B. Kemperman and Gh. Zbaganu. It was presented to Gheorghita Zbaganu, guest investigator in the Laboratory of Populations, on behalf of the authors.

A list of faculty awards in the previous issue of *News&Notes* should have mentioned that Professor Emeritus Maclyn McCarty received an honorary doctorate from Harvard University last year.

**Papers and talks**

If you are about to publish a paper or give a scientific talk, *News&Notes* would like to know about it. Please send your information by campus mail to Box 68, by e-mail to newsno or by fax to x7876.

**Centennial Corner**

Rockefeller Professor Stephen Burley gave a scientific talk co-sponsored by The Rockefeller University and the 92nd Street Y.

**92nd Street Y lectures**

This year several Rockefeller University scientists are taking part in a lecture series co-sponsored by the 92nd Street Y, entitled "Cracking the Code of Life: Genes, DNA and You." One of the goals of these centennial lectures is to introduce Rockefeller science to a broader audience.

At the most recent of these talks, on Tues., Jan 9, Richard M. and Isabel P. Furlaud Profes-

sor Stephen Burley, an HHMI investigator, discussed "After the Genome: Tailor-made Drugs."

The next talk, on Tues., Feb. 27, will feature Professor Michael Young, who will discuss "Keeping Time with Biology." Young is the head of the university's Laboratory of Genetics.

Then on Tues., April 10, F.M. Kirby Professor A. James Hudspeth, an HHMI investigator, will discuss "Senses and Sensi-

tivity." Hudspeth is head of the university's Laboratory of Sensory Neuroscience.

The two lectures take place at 7 p.m. in Caspary Auditorium. Call 996-1100 for tickets (use discount code ROC).

**Busy man on campus:  
Alex Kogan is new director of Plant Operations**

Alex Kogan, a former consultant to The Rockefeller University, is the new director of Plant Operations. In this role, Kogan will oversee more than 100 employees in the powerhouse, custodial, grounds, maintenance, carpentry and paint shops.

Plant Operations is responsible for maintaining not only the infrastructure of the campus but also its physical appearance. "That's a challenge," Kogan says, "because our work is very visible. The campus has a beautiful landscape, beautiful buildings, a beautiful powerhouse..." A beautiful powerhouse? "Well, to us, it's beautiful," he says.

Other areas of campus, such as the steam tunnels and vaults, are not seen by most of the Rockefeller community but are vital for the functioning of the university. Kogan's team works around the clock to keep all

systems working well. Some of Kogan's challenges in the near future include ensuring that staffing levels meet the university's needs, working with utility suppliers to reduce the university's energy costs, improving public spaces and coordinating an on-line requisition program for Plant Operations work orders.

Off-campus, Kogan is nearly as busy as he is at Rockefeller. He is halfway through an MBA program at Baruch College and is the father of a six-month-old.

Kogan, who is fluent in Russian, emigrated from the Soviet Union with his parents in 1979. He received a B.S. in electrical engineering from Bucknell University in 1994 and joined what is now the Aramark Corporation. At Aramark, he served as the regional technical director for the northeast, handling

such accounts as Lincoln Center, NYU Medical Center and the American Museum of Natural History. He has been a consultant at Rockefeller since 1996, serving as both a project manager and associate director of Plant Operations.

After so many years as a consultant, what made him decide to join Rockefeller? "One thing that drew me here," he says, "is the incredible sense of community. If you ask the Plant Operations employees what their purpose is here, most will say it is to enhance scientific research. We feel very much a part of the university's mission. I think that's unique to this institution and certainly contributes to the success of our team."

Kogan finds that the university's congenial environment has practical advantages too: "People are accessible here. You can get

an answer right away. There's less red tape.

"The university community was wonderfully supportive during the transition," he says. "I couldn't be happier."



In his new role at Rockefeller, Alex Kogan will oversee the powerhouse, custodial, grounds, maintenance, carpentry and paint shops.

**Grimaud to perform at Peggy Rockefeller concert**

The next Peggy Rockefeller concert will feature celebrated pianist Hélène Grimaud.

Pianist Hélène Grimaud will perform at the next Peggy Rockefeller Concert on Wed., Feb. 28. A regular visitor to concert stages of Europe, North America and the Far East, Grimaud made her debut with the Orchestre de Paris in 1988 at the invitation of Daniel Barenboim. She has gone on to appear with

orchestras including the Berlin Philharmonic, the Boston Symphony, the New York Philharmonic, and the San Francisco Symphony. Conductors with whom she has worked include Claudio Abbado, Christopher Hogwood, Kurt Masur and Michael Tilson-Thomas.

Grimaud's 1999-2000 concert schedule included engagements with the Philadelphia Orchestra and the Atlanta Symphony Orchestra, a performance at Avery Fisher Hall with the Russian National Orchestra under Mikhail Pletnez, and recitals in San Francisco, Santa Fe and Vancouver. Her international engagements included a tour of Germany and Austria with Neeme Järvi and the Goteborg Symphony, as well as concerts

with Rome's Santa Cecilia Orchestra and the Israel Philharmonic.

Highlights of Grimaud's 2000-2001 calendar in North America include engagements with the symphony orchestras of San Francisco, Toronto, Vancouver and Indianapolis, recitals in New York, Seattle and Mexico City, and her first appearance with the Chamber Music Society of Lincoln Center. Her international engagements include performances with the Berlin Philharmonic, Orchestre de Paris and the Oslo Philharmonic. She also will give recitals in Berlin and Madrid.

Born in Aix-en-Provence, France, Grimaud began music studies at the Conservatoire there before moving to Marseilles to

work with Pierre Barbizet. At age 13 she was unanimously voted into the Conservatoire National Supérieur de Musique in Paris.

In 1985, Grimaud was awarded the first prize in Jacques Rouvier's class and participated in master classes with Gyorgy Sander, Leon Fleisher and Jorge Bolet, who said of her, "It has been a long time, a very long time, since I have met a natural talent of such quality and musical sensibility."

The concert takes place in Caspary Auditorium at 8 p.m. Please contact Jennifer Goldschlag, x8437, for more information.



**News & Notes** is published every other Friday throughout the academic year by **The Rockefeller University**, 1230 York Avenue, New York, New York 10021-6399

Phone: (212) 327-8967

[www.rockefeller.edu/pubinfo/news\\_notes.html](http://www.rockefeller.edu/pubinfo/news_notes.html)

**Arnold J. Levine**, President

**Joseph Bonner**, Director of Communications

**Lisa Stillman**, Assistant Director, Communications

**Jim Stallard**, Science Writer

Ideas and submissions can be sent interoffice (Box 68), by electronic mail (newsno) or by fax (212) 327-7876.

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# calendar

FEBRUARY SIXTEENTH THROUGH MARCH ELEVENTH

## Friday Lectures and Thesis Presentations

THESE EVENTS ARE HELD IN CASPARY AUDITORIUM AT 3:45 P.M. AND PRECEDED BY TEA AT 3:15 P.M. IN ABBY ALDRICH ROCKEFELLER LOUNGE. ALL ARE WELCOME.

FRIDAY, FEBRUARY 16

### Conditional Mutagenesis as a Physiological Process and an Experimental Approach in the Antibody System.

Klaus Rajewsky, Professor, Institute of Genetics, University of Cologne.

FRIDAY, FEBRUARY 23

### Modulating the Song of Single Synapses.

Richard Tsien, George D. Smith Professor, Stanford University Medical Center.

FRIDAY, MARCH 2

### Protein Import into the Nucleus.

Günter Blobel, Professor, RU, and Investigator, HHMI.

FRIDAY, MARCH 9

John Kuriyan, Professor, RU, and Investigator, HHMI.

FRIDAY, FEBRUARY 16

### The Use of Anti-CD11a Antibodies in the Treatment of Psoriasis vulgaris.

Mark Kagen, Research Associate and Clinical Scholar, RU. Clinical Scholar's Grand Rounds. 110B NURSES RESIDENCE. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Dystroglycan: An Extracellular Matrix Receptor and Its Role in Muscular Dystrophy.** Kevin Campbell, Howard Hughes Medical Institute, University of Iowa. Cellular Biochemistry and Biophysics Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

TUESDAY, FEBRUARY 20

### A PEST-like Sequence in Listeriolysin O Essential for Listeria monocytogenes Pathogenicity.

Amy Decatur, Department of Molecular and Cell Biology, University of California, Berkeley. Infectious Disease Seminar. 305 WEISS. CONTACT BOBBIE LARRAGA, 327-7240. OPEN TO RU COMMUNITY AND GUESTS.

12:00 P.M. **Imaging mRNA Distribution in Living Cells with Molecular Beacons.** Sanjay Tyagi, Public Health Research Institute. CFAR Seminar. SIXTH FLOOR CONFERENCE ROOM, ADARC, 455 FIRST AVE. CONTACT GARY GAILOR, 448-5163.

4:00 P.M. **Roles of DNA Duplex Destabilization in DNA Regulation.** Craig Benham, Mount Sinai School of Medicine. Seminar. B LEVEL CONFERENCE ROOM, SMITH HALL ANNEX. CONTACT ERIK VAN NIMWEGEN, 327-8184.

WEDNESDAY, FEBRUARY 21

10:30 A.M. **Biostatistics Course.** Knut Wittkowski, Biometrician and Senior Research Associate, RU Hospital. 128 HOSPITAL. CONTACT KNUT WITTKOWSKI, 327-7175. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Efflux of Cellular Lipids to High Density Lipoproteins by ATP-binding Cassette A-1 Transporter.** Alan Remaley, Clinical Pathology Department, National Institutes of Health. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

### The Large-Abrupt-Global Climate Changes of Glacial Time: What Message Do They Send Us?

Wallace S. Broecker, Columbia University. **Signaling between Nerve Cells in the Brain.** Paul Greengard, RU. **Does the Language We Speak Affect the Way We Think?** Lila Gleitman, University of Pennsylvania. **The Role of Protein Flexibility in the Function of Biomolecular Motors.** Charles S. Peskin, NYU. National Academy of Sciences Public Symposium. CASPARY AUDITORIUM.

1:00 P.M. **Structure and Dynamics of Macromolecular Assemblies Revealed by Signal-processing of Multiresolution Data.** Willy Wriggers, Department of Molecular Biology, Scripps Research Institute. Pels Family Center for Biochemistry and Structural Biology Seminar. 305 WEISS. CONTACT SETH DARST, 327-7479.

11:00 P.M. **The Mechanisms of Nuclear Import by Karyopherin  $\beta_2$ .** Yuh Min Chook, Postdoctoral Associate, RU. Cellular Biochemistry and Biophysics Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

THURSDAY, FEBRUARY 22

12:00 P.M. **Chemical Genetics and Membrane Traffic.** Tomas Kirchhausen, Professor, Department of Cell Biology, Harvard Medical School. Biochemistry Lecture. E-115 WMCCU, 1300 YORK AVE. COFFEE AT 11:45 A.M.

3:00 P.M. **Cellular Mechanisms of Higher Function.** Patrick Hof, Associate Professor, Department of Neurobiology, Mount Sinai School of Medicine. Systems Neuroscience Seminar. 305 WEISS. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Immunomodulatory Properties of DNA.** Dennis Klinman, Section of Retroviral Immunology, FDA. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

4:00 P.M. **Secondary Cancer Prevention Trial: The Women's Intervention Nutrition Study (WINS).** Barbara Winters, Leader, Translational Studies, American Health Foundation. CNRU Special Nutrition Lecture. D-417 WMCCU, 1300 YORK AVE. CONTACT LINDA COTTE, 639-8352.

MONDAY, FEBRUARY 26

### Coordination of CD8 and TCR in T Cell Molecular Recognition.

George Fu Gao, Harvard University and Children's Hospital. CFAR Seminar. SIXTH FLOOR CONFERENCE ROOM, ADARC, 455 FIRST AVE. CONTACT GARY GAILOR, 448-5163.

1:30 P.M. **Autoreactive T Cells in Lupus: Mechanisms of Tolerance Abrogation.** Joe E. Craft, Professor of Medicine and Immunology, Yale University. Immunology Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE.

2:00 P.M. **The KCNE Superfamily of Potassium Channel Subunits: Cardiac Arrhythmia, Periodic Paralysis and the MinK-related Peptides.** Geoffrey W. Abbott, Postdoctoral Fellow, Department of Molecular and Cellular Physiology and Pediatrics, Yale University. Pharmacology Seminar. E-415 WMCCU, 1300 YORK AVE. COFFEE AT 1:45 P.M. CONTACT LISSETT CHECO, 746-6250.

4:30 P.M. **Syndecan-4 Signaling during Cell-Matrix Interactions.** Paul F. Goetinck, Professor, Harvard Medical School Associate Director of Research Cutaneous Biology Research Center Massachusetts General Hospital, Cell Biology and Genetics Seminar. PAPANICOLAOU LIBRARY, A-106 WMCCU, 1300 YORK AVE. COFFEE WILL BE SERVED.

TUESDAY, FEBRUARY 27

11:00 A.M. **Positive and Negative Regulation of Sister-Chromatid Separation by the Oncoprotein Securin.** Hui Zou, Department of Cell Biology, Harvard Medical School. Cancer Biology Seminar. 301 WEISS. CONTACT BOBBIE LARRAGA, 327-7240. OPEN TO RU COMMUNITY AND GUESTS.

4:00 P.M. **Drug Discovery in the Post-genomics Era.** Timothy W. Lovenberg, Principal Scientist, R.W. Johnson Pharmaceutical Research Institute, San Diego, Calif. Pharmacology Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE. COFFEE AT 3:45 P.M. CONTACT LISSETT CHECO, 746-6250.

4:00 P.M. **Recent Studies in Organic Synthesis.** William Richard Roush, Warner Lambert/Parke-Davis Professor of Chemistry, Department of Chemistry, University of Michigan. Bio-Organic Chemistry Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 3:45 P.M.

4:00 P.M. **Traction Force Microscopy and the Mechanics of Fibroblast Migration.** Micah Dembo, Boston University. Seminar. B LEVEL CONFERENCE ROOM, SMITH HALL ANNEX. CONTACT ERIK VAN NIMWEGEN, 327-8184.

7:00 P.M. **Keeping Time with Biology.** Michael Young, Professor, RU. Genes, DNA and You: The Impact of the Human Genome Project. CASPARY AUDITORIUM. A PUBLIC LECTURE SPONSORED WITH THE 92ND STREET Y. TICKETS ARE AVAILABLE FROM THE 92ND STREET Y AT 996-1100.

WEDNESDAY, FEBRUARY 28

11:00 A.M. **Dendritic Cells: A New Tool to Regulate Immunity in the Clinic.** Madhav Dhodapkar, Assistant Professor and Clinical Scholar, RU. Medical Sciences Seminar. 301 WEISS. CONTACT BOBBIE LARRAGA, 327-7240. OPEN TO RU COMMUNITY AND GUESTS.

12:00 P.M. **Structural Interactions Regulating T-cell Responsiveness.** David Ostrov, Research Associate, Department of Biochemistry, Albert Einstein College of Medicine. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

4:30 P.M. **Dissecting the Molecular Machinery That Decodes the Genome.** Robert Tjian, Investigator, HHMI, and Professor of Molecular and Cell Biology, University of California, Berkeley. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. REFRESHMENTS AT 4:00 P.M.

7:30 P.M. **Psoriasis Support Group.** Meeting. 110B NURSES RESIDENCE. CONTACT PATRICIA GILLEAUDEAU, 327-8333.

THURSDAY, MARCH 1

11:00 A.M. **Advanced Technologies for Fast and Easy Transfections.** Jorg Dennig, QIAGEN. QIAGEN Seminar. 301 WEISS. CONTINENTAL BREAKFAST AT 10:30 A.M. CONTACT TINA BAYER, (800) 426-8157 x22316. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

continued on reverse



# calendar-2

FEBRUARY SIXTEENTH THROUGH MARCH ELEVENTH

4:00 P.M. **Modifications in Erythrocyte Structure Induced by the Malarial Parasite *Plasmodium falciparum*.** Kasturi Haldar, Professor, Departments of Pathology and Microbiology-Immunology, Northwestern University Medical School. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

4:00 P.M. **Retinol Metabolism and Gene Regulation in Normal and Neoplastically Transformed Epithelial Cells.** Lorraine Gudas, Professor and Chairman, Department of Pharmacology, WMCCU. Endocrinology and Reproductive Biology Seminar. 301 WEISS.

FRIDAY, MARCH 2

1:00 P.M.-3:30 P.M. **RU Graduate Program Open House Poster Session.** WEISS 17TH FLOOR. OPEN TO RU COMMUNITY AND GUESTS.

12:00 P.M. **Mdm2 Sumoylation—Bigger is Better.** Ze'ev Ronai, Professor, Ruttenberg Cancer Center, Mount Sinai School of Medicine. Cell Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

MONDAY, MARCH 5

1:30 P.M. **Control of Lineage Commitment in Developing T Cells.** Dietmar Kappes, Member, Institute of Cancer Research, Fox Chase Cancer Center. Immunology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

TUESDAY, MARCH 6

11:00 A.M. ***Pseudomonas aeruginosa* Signaling to Epithelial Cells: Bacterial Regulation of the Actin Cytoskeleton through Rho-family GTPases.** Barbara Kazmierczak, Division of Infectious Diseases, Department of Medicine, University of California, San Francisco. Infectious Disease/Immunology Seminar. 301 WEISS. CONTACT BOBBIE LARRAGA, 327-7240. OPEN TO RU COMMUNITY AND GUESTS.

4:00 P.M. **Selective Pressure on Stem Cell Survival Using Mutant-MGMT Gene Transfer.** Stanton L. Gerson, Chief, Division of Hematology/Oncology, Case Western Reserve University School of Medicine. Molecular Pharmacology and Therapeutics Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 3:45 P.M.

WEDNESDAY, MARCH 7

10:30 A.M. **Biostatistics Course.** Knut Wittkowski, Biometrician and Senior Research Associate, RU Hospital. 1A CASPARY. CONTACT KNUT WITTKOWSKI, 327-7175. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Development of Anti-cancer Agents That Hijack Transcription Factors.** John Essigmann, Professor of Chemistry and Toxicology, Massachusetts Institute of Technology. Student-Sponsored Seminar. 301 WEISS. PIZZA LUNCHEON AT 1:00 P.M. IN THE WEISS 17TH FLOOR. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Regulation of the Immune Response within the Central Nervous System: Relevance to Multiple Sclerosis.** Jack Antel, Professor, Department of Neurology and Neurosurgery, McGill University, Montreal. Seminars in Clinical Research. 110B NURSES RESIDENCE. CONTACT DALE MILLER, 327-8411.

4:30 P.M. **Building a Brain: Tales from Mutant Mice.** Tom Curran, Chairman, Department of Developmental Neurobiology, St. Jude Children's Research Hospital. MSKCC President's Research Seminar. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

THURSDAY, MARCH 8

4:00 P.M. **Hepatitis C Virus: In vivo Studies of Molecular Clones.** Jens Bukh, Tenure Track Scientist, Hepatitis Virus Section, National Institute of Allergy and Infectious Diseases, NIH. LFKRI Research Seminar. LOWER LEVEL CONFERENCE ROOM, NEW YORK BLOOD CENTER, 310 EAST 67TH ST. TEA AT 3:45 P.M. CONTACT ROSANNA MARTINEZ, 570-3357.

FRIDAY, MARCH 9

1:00 P.M.-3:30 P.M. **RU Graduate Program Open House Poster Session.** WEISS 17TH FLOOR. OPEN TO RU COMMUNITY AND GUESTS.

The Arts and Other Events

FRIDAY, FEBRUARY 16

12:00 P.M. **Tri-Institutional Noon Recitals.** Fitzwilliam String Quartet. Performing Purcell: *Fantazia No. 8 (Z.739)*; Borodin: *Quartet No. 2 in D major (1881)*; Purcell: *Chacony in G minor (Z.730)*; Shostakovich: *Quartet No. 4 in D major, Op. 83 (1949)*. CASPARY AUDITORIUM. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

WEDNESDAY, FEBRUARY 28

8:00 P.M. **Peggy Rockefeller Concerts.** Hélène Grimaud, piano. CASPARY AUDITORIUM. CONTACT JENNIFER GOLDSCHLAG, 327-8437.

MONDAY, MARCH 5

8:00 p.m. **Peggy Rockefeller Concerts.** Kyung-Wha Chung, violin. CASPARY AUDITORIUM. CONTACT JENNIFER GOLDSCHLAG, 327-8073.

# Opioid gene knockout mice show greater fear and anxiety

Like many other animals, rodents tend to "freeze" when they sense danger. A new paper from Professor Donald Pfaff's Laboratory of Neurobiology and Behavior, published in the *Proceedings of the National Academy of Sciences*, helps explain why.

Results of experiments on a new breed of genetically altered mice indicate that opium-like substances naturally found in the body, particularly one called enkephalin, inhibit fear and anxiety. Previous research findings had implicated these internal opioid substances in the regulation of female sexual receptivity, the ingestion of sweet solutions, and fear-related behaviors.

The Pfaff lab, along with colleagues at the Robert Wood Johnson Medical School and Queens College, reports that mice missing the gene for enkephalin had heightened reactions to three different fear- and anxiety-producing situations. The new paper strongly suggests that opioids, and particularly enkephalin gene products, act naturally to inhibit fear and anxiety. Without them, mice exhibit an exaggerated response to fearful situations.

"This mouse may comprise a new genetic model of chronic fear and anxiety," says Andre Ragnauth, a postdoctoral associate in the Pfaff lab and first author on the *PNAS* paper.

The preproenkephalin knockout (PPEKO) mice were tested in three different types of experiments: fear conditioning (which measures an animal's learned fear response), open field activity and dark-light transition. In each case, the enkephalin knockout mice showed exaggerated responses to fear- or anxiety-provoking environments, compared to their wild-type and heterozygous control groups.

## "THIS MOUSE MAY COMPRISE A NEW GENETIC MODEL OF CHRONIC FEAR AND ANXIETY."

In one test, the mice were put into an "open field" experiment, which creates an anxiety-provoking situation. A mouse that is anxious when exposed to unfamiliar situations will move around less in the new environment, and when it does move, it will tend to stay by the walls. In contrast, an animal that is not anxious will spend more time exploring the center of the open field and will travel more distance. PPEKO mice traveled significantly less distance in the center squares of the open field and spent significantly less time

in the open field than did the corresponding control groups. In a second type of experiment, the mice were placed in a test chamber that had both lighted and dark areas. This test asks two questions: If a mouse is

placed in the dark side of a standard test chamber, will it come into the light? And if so, how much time will it spend there? An animal that is afraid will tend to stay in the darkness. The lab's findings indicated that the PPEKO mice were more fearful: These animals spent significantly less time in the light side than did either the wild type or heterozygous controls. They also tended to be less active once they were on the light side of the compartment. (This result was not simply because they moved less in general; PPEKO mice on the dark side of the chamber moved as frequently as the control groups).

In a third type of experiment,

noise-conditioned stimulus ending with a mild electric shock to the foot. Then, a minute and a half later, the mouse was returned to its home cage. The next day, the mouse was placed back in the testing chamber and again exposed to identical conditions. The researchers measured animals' freezing behavior both upon hearing the auditory stimulus and upon experiencing the foot shock. All three genotypes froze in response to the auditory stimulus on the second day (as compared to the first day). Likewise, their post-shock "freezing" was significantly greater on day two than on day one. The PPEKO mice, however, froze for significantly more time on day two than did the other mice. PPEKO mice also displayed a significant increase in freezing after the shock on day two (both relative to the level on day one and to the control groups).

Thus, in each experiment, the enkephalin knockout mice appeared to show an exaggerated response to an anxiety-



Donald Pfaff is head of the Laboratory of Neurobiology and Behavior, where researchers are studying fear and anxiety response in mice.

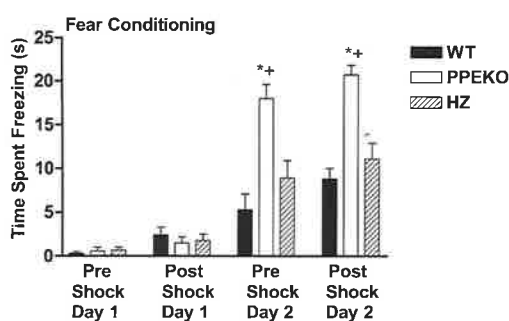
cantly different from those of the control groups. "We were surprised that the enkephalin knockout animals failed to display either substantial decreases in sucrose consumption or reductions in lordosis [sexual responsiveness] behavior," says Ragnauth. "The stable ingestive and sexual behaviors argue strongly that the increased fear and anxiety (as evidenced by reduced activity and movement in light and open areas and 'freezing' in threatening situations) were due to a selective deficit and not to some generalized and non-specific debilitation."

Future work will concentrate on the genes for opioid peptide receptors.

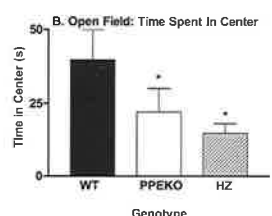
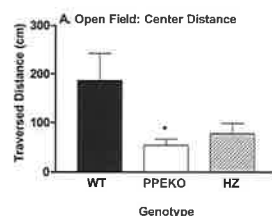
Ragnauth's and Pfaff's coauthors are Alwin Schuller of the Robert Wood Johnson Medical School, Postdoctoral Fellow Maria Morgan of the Pfaff lab, Research Assistant Johnny Chan of the Pfaff lab, Assistant Professor Sonoko Ogawa of the Pfaff lab, John Pintar of the Robert Wood Johnson Medical School and Richard Bodnar of Queens College, City University of New York.

This research was supported by the National Institutes of Health.

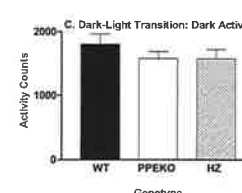
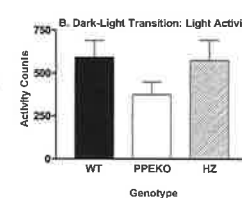
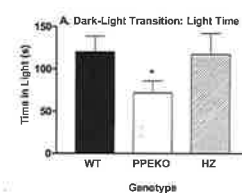
## EXPERIMENTS ON A NEW BREED OF GENETICALLY ALTERED MICE INDICATE THAT OPIUM-LIKE SUBSTANCES NATURALLY IN THE BODY, PARTICULARLY ONE CALLED ENKEPHALIN, INHIBIT FEAR AND ANXIETY.



The chart shows alterations in fear conditioning over two days in wild-type mice (WT), PPEKO mice and heterozygous mice (HZ). Researchers measured the amount of time the animals "froze" during a pre-shock auditory stimulus and to a mild shock on the foot.



In an "open field" experiment, PPEKO mice covered significantly less distance than the control groups (WT and HZ), and they spent less time in the center of the open field. The upper panel (A) represents alterations in the amount of distance traversed by the three types of mice, and the lower panel (B) represents the amount of time spent in the center.



The top figure shows the amount of time the three strains of mice spent in the "light" compartment of a light-dark experiment. The middle panel shows the level of activity while in the light. The lower panel shows activity levels while in the dark.

## ETCETERA

**Abby closed on Feb. 20**

The Abby Dining Room, Lounge and Cohn Library will be closed all day on Tues., Feb. 20, due to a privately scheduled event.

**New News&Notes schedule**

News&Notes will now be published every two weeks. The next issue will be on Fri., Feb. 23. The Calendar of Events will be published weekly as usual.

**Support group for "Improving Communications"**

The Employee Assistance Program Consortium is sponsoring a six-part psychoeducational lunchtime support group on Improving Communication Skills, starting on Mon., March 19, and running through Mon., April 23. The group will meet from noon to 1 p.m. in the Whitney Conference Room 118 at New York-Presbyterian Hospital. Feel free to bring your lunch. Call Josephine at 746-5890 to register. Group size is limited.

**Employee Assistance Program has new Web site**

The Employee Assistance Program Consortium is a free, confidential counseling service available to all employees of the five consortium members (Hospital for Special Surgery, New York-Presbyterian Hospital, Rockefeller University and Weill Medical College of Cornell University). The program now has a new Web site (eapc5.com) where you can learn more about this service.

**Recent lectures**

ON File 00-065 #29



Raymond and Beverly Sackler Foundation Scholar Joshua Lederberg, president emeritus of The Rockefeller University, gave the Raymond and Beverly Sackler Centennial Lecture on Fri., Jan. 26. His talk was entitled "Crowded at the Summit: The Future of Infectious Disease."

ON File 00-064 B



John W. Rowe, president and CEO of Aetna, Inc., presented a Zanvil Cohn Forum lecture entitled "Successful Aging," on Mon., Jan. 22.

**Space plan continued**

To fully implement the President's plan, the administration commissioned Payette Associates, a Boston-based architectural firm, to evaluate the Rockefeller University campus. Working with the President's Office and the Office of Planning and Construction, Payette produced a master space plan to determine an efficient use of space on campus to accommodate future growth. The plan was approved by the board of trustees at its meeting last November.

According to George Candler, director of Planning and Construction, "Over the last several decades, use of the campus has been weighted toward the south end, particularly in the cluster of Bronk Laboratory and the Rockefeller and Weiss research buildings. As we think about new uses of space in the future, the master space plan attempts to balance the campus and reinvigorate the north end."

The northwest corner of campus will be developed initially. The space plan calls for the construction of a 12-story research tower with three levels of underground parking on the site of the 68th Street parking lot and esplanade. The space provided in the new building will begin to satisfy the space requirements of the academic plan. An "in-fill" building is planned where the 68th Street

loading dock now stands, which will bring the area to the same level as the rest of campus and add about one acre of green space. "The goal is to provide new lab space and bring in necessary infrastructure—electrical and emergency power, a new loading dock—to the north end of campus," says Candler.

After the new construction is completed, the focus will switch to modernization of the adjacent older buildings. Candler says that personnel will be moved out of Smith Hall, which will be renovated from top to bottom. Core facilities will be brought to Smith Hall to support the research of scientists working throughout campus. Flexner Hall will also be renovated from the fourth floor down, and the ventilation, exhaust and electrical systems will be modernized.

Work is currently under way to correct structural problems on the upper levels of Founder's Hall "to make it fit for another 100 years," says Candler. The master space plan also calls for the development of an administrative hub in Founder's and Welch halls and in Nurses Residence.

"We want to move administrative offices out of spaces that are better suited for laboratory work and consolidate them in a more efficient relationship," says Candler.

Also, the gym will move to Founder's Hall from the Graduate Students Residence to accommodate expansion of the Child and Family Center.

Candler says that modernization of the 90-year-old Hospital consists of completing several "make ready" projects, which relocate people to make room for construction. The inpatient unit is being consolidated on the third floor of the Hospital. Floors four, five, and six are under construction now. To provide for distribution of modern services to all floors, two shafts have been cut through the building.

At same time, a new addition is being made: the south wing of the fifth floor will be new laboratory space, while the south wing of the sixth floor will be the central mechanical equipment room, with air handlers for the entire building.

When completed, the fourth floor will house the Breslow and Stoffel labs, the fifth floor will contain the Rice lab and the Center for the Study of Hepatitis C, and the sixth floor will provide space for incoming Physician-in-Chief Barry Coller, with room for another laboratory.

One of President Levine's goals, reflected in the master space plan, is to consolidate academic fields of interest. "Currently, it is

difficult to move labs around, space is too tight and we lack the flexibility to place labs in their most appropriate locations," says Candler.

As part of the space planning process, Payette conducted a detailed review of campus history and its growth. The new space plan will ensure that the university's future expansion is sensitive to that history, especially with respect to the landscape design of Daniel Kiley.

Payette also evaluated the deferred maintenance of each building on campus and compiled a master list of things that need to be addressed, and the offices of Planning and Construction and Plant Operations have developed a plan to address major portions of the list every year.

Overall, Candler says, the Payette plan "provides a blueprint for growth and a set of guidelines for decision making. It gives us the ability to locate people logically and allows us to plan rational distribution of space and function."

**Friday continued**

will it be possible to understand which role a given gene product plays at a given stage of development in a given cell in vivo. The main emphasis will be on developmental processes and control mechanisms in the immune system, in both health and disease.

Rajewsky has won a number of awards for his work, including the Avery Landsteiner Award; Behring-Kitasato Prize; Robert Pflieger Prize; Humboldt Research Award; Rabbi Shai Shacknai Memorial Prize, Hebrew University; Robert Koch Prize; Max-Planck-

Research Award; Dr. Albert-Wander-Memorial Prize, Bern University; UCL Prize Lecture in Clinical Science; Körber Prize for European Science and the Behring-Heidelberger Award, American Association of Immunologists.

His talk begins in Caspary

Auditorium at 3:45 p.m. and is preceded by a tea in Abby Aldrich Rockefeller Lounge at 3:15 p.m. All are welcome.

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