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News and Notes 2000

The Rockefeller University News and Notes

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The Rockefeller University

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Expanding role of physics and math in biology to be highlighted at Tues., Jan. 11 symposium

The interfaces between biology, physics and mathematics will be explored Tues., Jan. 11, at an afternoon symposium in Caspary Auditorium entitled "Modeling Life Processes." Sponsored by Rockefeller University and the Institute for Advanced Study in Princeton, the symposium will feature talks by seven leading scientists in fields ranging from virology to evolutionary biology to physics.

"This symposium will highlight some of the exciting applications of physics and mathematics to solving biological problems," says President Arnold J. Levine, who helped organize the meeting. "We will discuss how mathematics can be used to model diseases and probe the evolution of signal transduction networks in cells and how physics can help us study questions regarding neurobiology and perception."

Following introductory remarks by Levine and Phillip A. Griffiths, director of the Institute for Advanced Study, the talks will begin at 1 p.m., with RU Professor Joel Cohen discussing "Models of Chagas Disease." Chagas disease is an insect-transmitted parasitic disease common in South and Central America, similar to African sleeping sickness. Cohen has undertaken a field study in rural northwest Argentina to collect data for the development of a mathematical model of the transmission risk to humans.

From 1:30 to 3 p.m., a trio of talks will focus on the study of gene expression patterns to reconstruct signal transduction networks in cells. George Church, professor of genetics and director of the Lipper Center for Computational Genetics at Harvard Medical School, will discuss "Measuring and Modeling Regulatory DNA Motifs and Networks." Peter D. Karp, director of the Bioinformatics Research Group at SRI International, will speak on "Qualitative Modeling from Genomes to Pathways." And Walter Fontana, research professor at the Santa Fe Institute and a member of the Institute for Advanced Study, will discuss "RNA as a Model System for the Study of Evolution."

Following a break from 3 to 3:30 p.m., RU Professor Mitchell Feigenbaum, director of RU's Center for Studies in Physics and Biology, will discuss "Metrics in Vision and the Low Moon."

At 4 p.m., a pair of talks will explore the mathematical modeling of HIV infection. RU Professor David D. Ho, scientific director of the Aaron Diamond AIDS Research Center, will talk about "HIV Replication Dynamics and Implications for Vaccine Development," followed by Alan S. Perelson, group leader of Theoretical Biology and Biophysics at Los Alamos National Laboratory, discussing "Mathematical Models of HIV-1 Dynamics in Plasma and Lymphoid Tissue." All are welcome.

Hospital honored for top marks by JCAHO

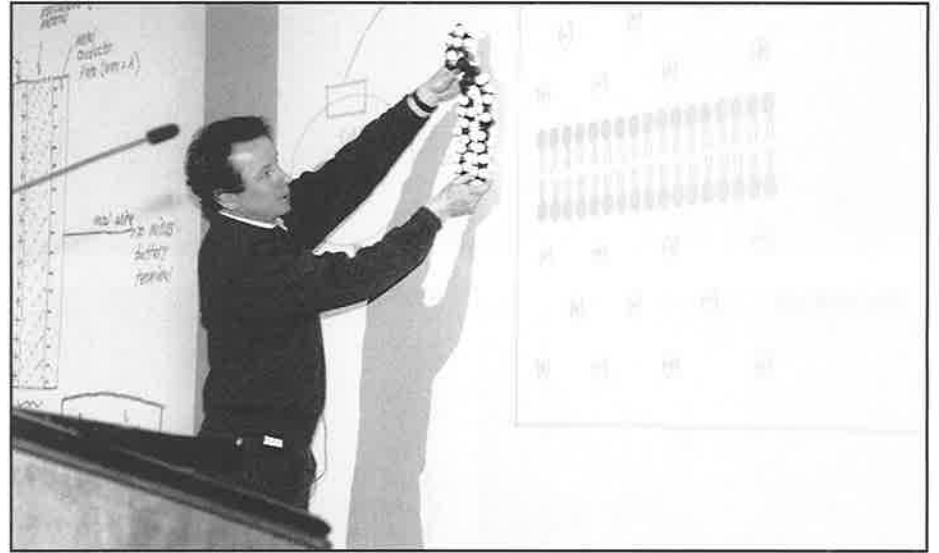


The staff of the Rockefeller University Hospital gathered on the Hospital steps in recognition of the high marks the institution received on its most recent review by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). The JCAHO surveys hospitals and nursing homes every three years, evaluating the quality of patient care and safety, appropriate hospital policies, operating procedures, physical plant and documentation. Hospital staff members were honored with a reception at the President's House on Wed., Dec. 22. "Our patients have always received the most up-to-date medical care," Vice President for Medical Sciences Emil Gotschlich said. "It's a credit to everyone here that this institution continually operates at the highest standards."

Photo by Paul Schneck.

Students are "enlightened" by Mirsky lecture

99-043B (8)



Nearly 400 high school students attended the 40th Annual Alfred E. Mirsky Christmas Lecture Series on Science at RU on Tues., Dec. 28. Professor and HHMI Investigator Roderick MacKinnon presented this year's talk, in which he discussed the role electricity plays in biology and the mechanisms nature has designed to regulate electric signals that allow us to think, see, move and eat. The all-day lecture consisted of two talks, between which students had the chance to break for a pizza lunch, ask questions of the scientist and observe electric fish in a 500-gallon fish tank. The Mirsky lectures are



Photos by Paul Schneck.

99-043B (27)

designed to expose high school students to a level of scientific mentoring usually reserved for the best graduate students in the country.

RU employees show their spirit over holiday break

While most of campus was quiet over the holiday break, some departments, such as Custodial, Plant Operations, Engineering, Computing Services and Security were bustling as usual during the week-long vacation.

In the spirit that exemplifies Rockefeller University, the 27 members of the Security Department worked to make sure that campus safety and security were maintained over the holiday break. Fewer people on campus called for tighter security measures, such as increased patrols of the campus. "The teamwork and dedication of this department is immeasurable. Some employees rescheduled their vacations to ensure campus safety," says Michael John, Security Operations manager.

This year, in addition to the usual holiday preparations, extra precautionary steps were taken for New Year's Eve. Two tours consisting of 14 guards worked extended hours to secure the campus into the New Year. The first tour worked from 3 p.m. to 2 a.m.; the second from 10 p.m. to 7 a.m. In addition to monitoring the campus, the guards patrolled its perimeters, including York Ave. and the area around the pedestrian bridge. Other safety measures included tight control of the campus gates and careful checking of all IDs and packages. Thanks to the dedication and team spirit of the Security

Department, the New Year passed without incident, and the transition of the computerized security system to the Y2K was flawless. Joseph Nekola, director of security, was very pleased with the hard work and cooperation of the staff.

Prior to the actual turning of the clock, the guards gathered in Nurses Residence to celebrate the arrival of the new millennium. "While those of us on duty were unable to celebrate the new year with friends and family, we did get to celebrate with our second family—members of campus security," says John. Sergeant Anthony Drummond, who has worked at RU for 12 years, says he had no reservations about working New Year's Eve: "I knew the university would be a safe place to be at the turn of the century."

The efforts of other employees who worked during break were also vital to the smooth operations of the university. The commitment and teamwork demonstrated by these employees contribute to the success of the institution.

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RU community celebrates at the Holiday Festivity



Holiday Festivity photos by Ken Levinson.

Campus generosity helps make holidays brighter



The 1999 holiday Toys for Tots drive was a success. The two-week toy drive collected two large cartons for disadvantaged children. John Sholtis, associate director of Media Services (the department that hosts the annual drive) says, "This year's response was the best we've had yet. We are very thankful to all who participated." In recognition of the RU community's generosity and participation in this year's toy drive, the Marines Corps presented RU with the Commanders Award.

The goodwill of the RU community was also evidenced by the success of the winter Pennies for the Pantry collection. The collection baskets, which were placed in Weiss Café, helped raise over \$700 for the Yorkville Common pantry, a local nonprofit pantry that provides food for New Yorkers in need.

Photo courtesy of Akinola Famuyiwa.

SciFinder Scholar

SciFinder Scholar, a tool designed to search chemical literature, will be available to RU researchers and students on a trial basis during January. With more than 22 million listings including 12 million organic substances, the database is the largest database, CAS registry of its kind available today.

With the program users can search for chemical substances by chemical name, chemical structure, formulas or CAS registry number, and find literature relevant to a topic of interest, by a specific author and by CA abstract number or patent number.

A demonstration of the database will be given Wed., Jan. 12 from 12:30 to 2 p.m. in 302 Weiss. All RU researchers and students are welcome.

1999 FSA Participants

If you participate in the Flexible Spending Account benefit, please be aware that all claims for medical expenses you incurred in 1999 must be made before April 15, 2000. Claim forms are available in Human Resources. If you have questions regarding your flexible spending account, call Human Resources, x 8300.

Back to the Future

Manju Hingorani, a postdoctoral fellow in the O'Donnell lab, was one of the twelve winners in *Science* magazine's recent essay contest that invited readers to imagine the life of a scientist in the year 2050. Hingorani's fictional vision of the future, entitled "S(t)imulating Science," is featured in the Fri., Dec. 24, 1999 issue.

BookCorner

Outsmarting Managed Care, a new book published by Times Books and written by Bruce A. Barron, is a guide to help consumers get the most from their managed care plan. Barron is a former RU faculty member and former senior medical director at Empire Blue Cross/Blue Shield. He now serves as an associate professor of clinical OB/GYN at Columbia-Presbyterian Medical Center.

Courtesy of media negs on file

99-044 #2

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Picking bones: RU research team finds molecule that controls the balance of bone creation and destruction

by Lisa Stillman

Researchers at RU and the Howard Hughes Medical Institute (HHMI) have identified a novel molecular mechanism by which a molecule called TRANCE controls the balance between bone formation and bone destruction. The research, published in the Dec. 22 issue of the journal *Molecular Cell*, provides long-sought-after answers to questions about bone metabolism and has important implications in the treatment of bone diseases such as osteoporosis and rheumatoid arthritis.

"We finally have begun to make headway in understanding the molecular mechanisms that regulate bone physiology. Our data will help propel the development of novel therapies to treat diseases of bone which afflict hundreds of millions of people worldwide," says Yongwon Choi, associate professor and head of the Laboratory of Immunology, who is the senior author on the paper. Choi is also an associate investigator at HHMI.

The creation and destruction of bone are closely intertwined processes. The skeleton is continuously remodeled through the coordinated action of osteoblasts (which form bone) and osteoclasts (which break down bone in a process called resorption). Together, these cells are critical for the development, renewal and repair of the skeleton. The two systems work in harmony in a healthy person, but when the balance is disrupted, severe diseases such as arthritis and osteoporosis can result. In addition, bone loss can begin at a very early age; it is exacerbated in post-menopausal women and can eventually lead to osteoporosis and an increased risk of life-threatening fractures. Biomedical fellow Brian Wong, in Choi's laboratory, identified a factor called TRANCE in 1997 and showed, in collaboration with other laboratories around the world, that it is the critical factor that controls breakdown of bone by osteoclasts.

The knowledge of how TRANCE works could provide specific ways to block or enhance the function of osteoclasts, depending on the disease. Therefore, Choi and Wong, in the Laboratory of Immunology, along with Daniel Besser, a postdoctoral fellow in the Laboratory of Molecular Oncology, set out to explore the signaling events regulated by TRANCE in osteoclasts.

"The known signaling events turned on by the TRANCE receptor could not account for the dramatic morphologic and cytoskeletal alterations caused by TRANCE in osteoclasts. We were looking for some-

thing completely novel," recalls Wong. This provided the first evidence that c-Src might be regulated by TRANCE and its receptor (TRANCE-R). Research on c-Src was first pioneered at Rockefeller by

know how. We were excited when Brian suggested a collaboration attempting to link TRANCE to c-Src," recalls Besser.

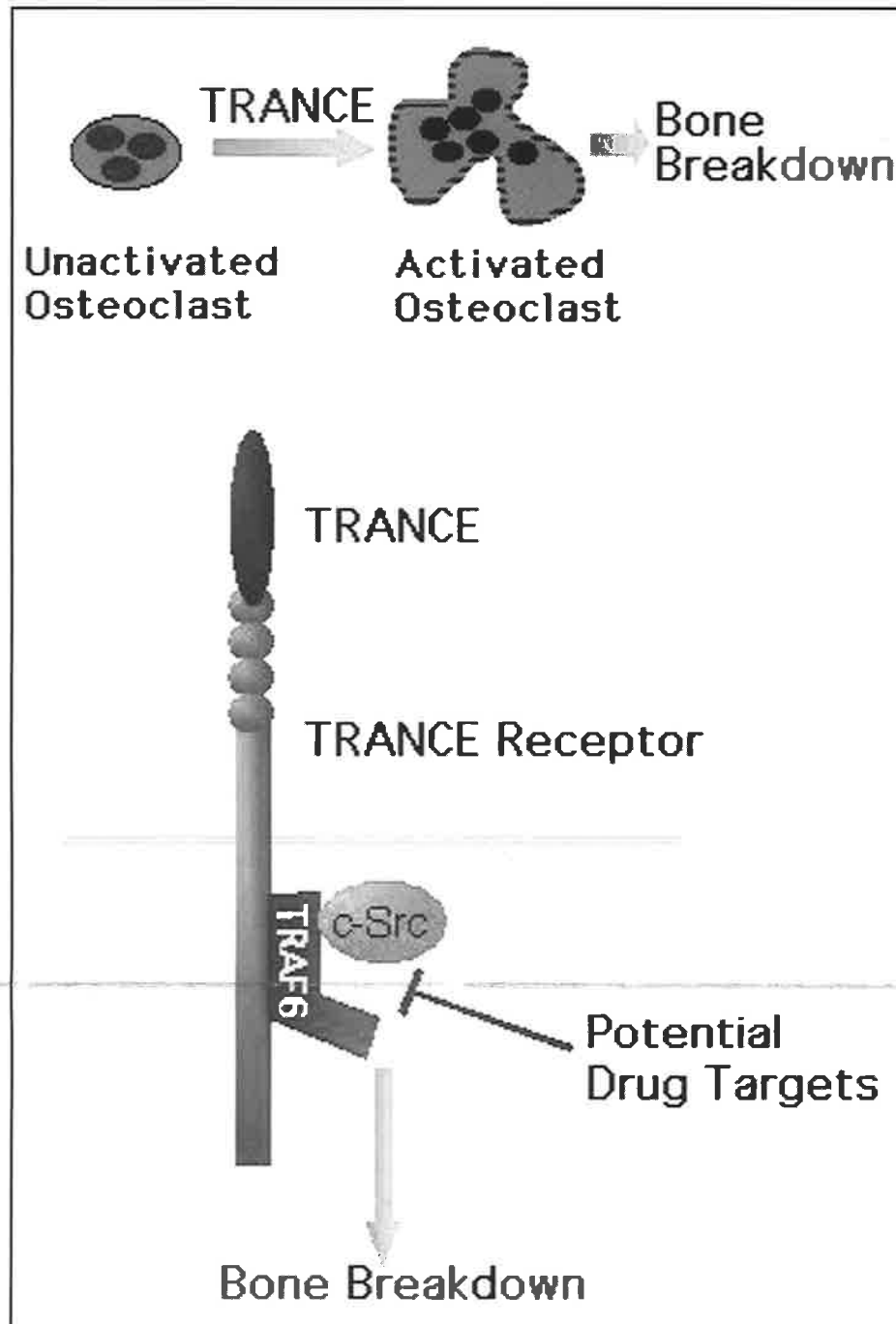
In the *Molecular Cell* paper, the Rockefeller team demonstrates that TRANCE directly regulates c-Src, and it does so through an adapter protein called TRAF6, which acts as a bridge to physically link c-Src to the receptor. Since TRAF6 and c-Src have very selective functions in osteoclasts, pharmacologically inhibiting these molecules may allow for the treatment of bone diseases without the side effects caused by some currently used drugs. "The manner in which TRANCE activates c-Src is unique. The kind of molecular detail we have provided may allow the identification of novel drug targets specific to diseases involving osteoclasts," says Wong. Their molecular model was corroborated by data from a recent study showing that mice engineered to lack TRAF6 exhibited the same defects in osteoclasts as the c-Src knockout mice.

Their results have even broader implications. The same molecules involved in mediating the effects of TRANCE are also involved in controlling the effects of other aspects of the immune system.

The authors hope that, in addition to answering important questions about basic bone biology, this new finding can offer a drug target to alleviate the bone destruction caused by arthritis and osteoporosis. Wong, who recently completed his Ph.D. at Rockefeller, says that this type of research is exciting since it is a clear indication of how basic research can directly translate into potential therapies. "If you know the nuts and bolts of a disease, the chances of finding a cure are infinitely increased," he says.

Other authors on the paper include biomedical fellow Joseph Arron and postdoctoral fellow Nacksung Kim, of the Laboratory of Immunology; and assistant for research Masha Vologodskaja, of both the Laboratory of Immunology and HHMI. Hanafusa is now at the Osaka Bioscience Institute in Japan.

This work was supported by the National Institute of Allergy and Infectious Diseases and the National Cancer Institute, both part of the National Institutes of Health. Wong and Arron were supported by NIH Health Medical Scientist Training Program grants. Besser was supported by a fellowship from the Norman and Rosita Winston Foundation.



The Rockefeller researchers showed that a molecule called TRANCE directly regulates c-Src, and it does so through an adapter protein called TRAF6, which acts as a bridge. This discovery has implications for the treatment of bone diseases such as osteoporosis and rheumatoid arthritis. Diagram courtesy of the Choi lab.

thing completely novel," recalls Wong. Seeking clues from gene "knockout" experiments, the researchers noted that when a gene called c-Src was removed, mice exhibited defects in their osteoclasts

Professor Emeritus Hidesaburo Hanafusa, former head of the Laboratory of Molecular Oncology and a co-author of the paper. "We knew that c-Src was involved in bone biology, but we didn't

Five Nobel laureates grace RU campus



Following the most recent awarding of the Nobel Prize to an RU scientist, five Nobel laureates gathered in Welch Library. Standing from left to right are Torsten Wiesel, R. Bruce Merrifield and Joshua Lederberg; seated are Günter Blobel (left) and Christian de Duve. In all, Rockefeller has been home to 20 Nobel Prize winners since its founding as the Rockefeller Institute for Medical Research in 1901. Photo by Robert Reichert.

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THE ROCKEFELLER UNIVERSITY—Please post

TUESDAY, JANUARY 11

12:55 p.m.–5:00 p.m. **Modeling Life Processes.** Joel E. Cohen, Professor, RU; George Church, Professor of Genetics, and Director, Lipper Center for Computational Genetics, Harvard Medical School; Peter D. Karp, Director, Bioinformatics Research Group, SRI International; Walter Fontana, Research Professor, Santa Fe Institute, and Member, Institute for Advanced Study; Mitchell Feigenbaum, Professor and Director, Center for Studies in Physics and Biology, RU; David D. Ho, Professor and Scientific Director, Aaron Diamond AIDS Research Center, RU; Alan S. Perelson, Group Leader, Theoretical Biology and Biophysics, Los Alamos National Laboratory. Institute for Advanced Study-RU Symposium. **Casparly Auditorium.** Refreshments will be served. Contact Jill Benz, 327-8092. Break at 3 p.m. in Abby Aldrich Rockefeller Lounge. All are welcome.

WEDNESDAY, JANUARY 12

10:30 a.m. **Biostatistics Course.** Biostatistics Course. **128 Hospital.** Contact Knut Witkowski, 327-7175. Open to RU/WMCCU/NYPH/MSKCC community and guests only.

12:00 p.m. **New Insights into p53 and Its Relatives.** Carol Prives, Professor, Columbia U. Seminars in Cancer Biology. **Casparly Auditorium.** Contact Jill Benz, 327-8092. All are welcome.

12:00 p.m. **The Roles of CD4+ T Cells and Nonclassical Effectors in Antitumor Immunity: Implications for Vaccine Development.** Suzanne Topalian, Senior Investigator, Surgery Branch, NCI, NIH. Seminars in Clinical Research. **110B Nurses Residence.**

12:30 p.m. **SciFinder Scholar Database.** Wentsai Wang, Senior Account Consultant, Chemical Abstract Services. Demonstration. **302 Weiss.** Contact Pat Mackey, 327-8909. Open to RU community and guests only.

THURSDAY, JANUARY 13

4:00 p.m. **Subunit Assembly and Macromolecular Organization of Ion Channels.** Min Li, Associate Professor, Johns Hopkins U. School of Medicine. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** Tea at 3:45 p.m.

FRIDAY, JANUARY 14

12:00 p.m. **Pack Your Chromosomes, We're Going to the Poles.** Douglas Koshland, Staff Member, Carnegie Institution of Washington; Associate Investigator, HHMI. Molecular Biology Seminar. **116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** Refreshments at 11:45 a.m.

MONDAY, JANUARY 17

12:00 p.m. **Development of a Peptide Fusion Inhibitor Drug.** Dana Bolognesi, Trimeris Incorporated. CFAR Seminar. **Sixth Floor Conference Room, ADARC, 455 First Ave.**

TUESDAY, JANUARY 18

7:30 a.m.–5:00 p.m. **VZV and the Immunocompromised Patient.** Conference chairs: Anne A. Gershon, Professor of Pediatrics, and Director, Division of Pediatric Infectious Diseases, Columbia U. College of Physicians and Surgeons; Kathleen M. Foley, Attending Neurologist, Pain and Palliative Care Service, MSKCC; and Richard Payne, Chief, Pain and Palliative Care Service, MSKCC. A Scientific Conference on the Impact and Treatment of Infections Caused by the Varicella-Zoster Virus on Immunocompromised Patients due to HIV/AIDS Infection, Cancer, Transplantation and Age. **New York Academy of Medicine, 1216 Fifth Ave. (at 103rd St.).** Presented by the VZV Research Foundation in Partnership with Columbia U. College of Physicians and Surgeons. Registration fee is \$75, which includes conference, breakfast, lunch and mid-morning coffee break. For further information please contact the VZV Foundation at 472-3181 or e-mail gbertot@vzvfoundation.org.

WEDNESDAY, JANUARY 19

12:00 p.m. **The Role of Forkhead Transcription Factors in Insulin Action and Diabetes.** Domenico Accili, Professor of Medicine, and Director, Diabetes Research Unit, Division of Endocrinology, Dept. of Medicine, Columbia U. Seminars in Clinical Research. **110B Nurses Residence.**

3:00 p.m. **Use of Single Nucleotide Polymorphism (SNP) Maps in Complex Disease Mapping, Pharmacogenetics and Toxicogenetics.** Eric Lai, Head, Department of Molecular Genetics, GlaxoWellcome, Inc. Starr Center for Human Genetics Seminar. **301 Weiss.** Contact Emily Gegeliya, 327-7387.

3:45 p.m. **Transfer of Genes into Hematopoietic Progenitors: Progress and Promise.** Joseph R. Bertino, Member and Chairman, Molecular Pharmacology and Therapeutics Program, Attending Physician, Lymphoma Service, Dept. of Medicine, MSKCC; and Malcolm A.S. Moore, Member, Cell Biology Program, Attending Biologist, Division of Hematologic Oncology Service, Dept. of Medicine, MSKCC. Cancer Lecture. **116 Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** Tea at 3:15 p.m.

4:30 p.m. **Neuroscience Group Meeting.** Radha Rangarajan, Graduate Fellow, RU; and Hynek Wichterle, Graduate Fellow, RU. Neuroscience Group Meeting. **302 Weiss.** Sandwiches, fruit, cookies and beer at 4:15 p.m. in 302 Weiss. Contact Shawn Boggs, 327-7144. Open to RU community and guests only.

7:15 p.m.–8:45 p.m. **New York Structural Biology Group.** Please note: talks may not necessarily be in this order: **How Proton Translocation Drives Rotation in the ATP Synthase.** Mark Girvin, Albert Einstein College of Medicine; **A Kinetic and Structural Framework for Helicase Activity by DexH/D Proteins.** Anna Marie Pyle, Columbia U.; **Structure and Mechanism of the mRNA Capping Apparatus.** Stewart Shuman, SKI. New York Structural Biology Group Meeting. **Casparly Auditorium.** Contact Anne Roche, 327-8836. Reception, 8:45 p.m., in the Faculty and Students Club, where sandwiches will be served. All are welcome.

THURSDAY, JANUARY 20

3:00 p.m. **Development of the Prefrontal Cortex Cognitive Abilities.** Adele Diamond, Shriver Center. Systems Neuroscience Seminar. **305 Weiss.** Open to RU/WMCCU/NYPH/MSKCC community and guests only.

4:00 p.m. **Cancer Chemoprevention by Organoselenium Compounds.** Karam E. El-Bayoumy, Chief, Cancer Etiology and Prevention, American Health Foundation, Valhalla, N.Y. CNRU Special Nutrition Lecture. **D-417 WMCCU, 1300 York Ave.** Contact Linda Cotte, 639-8352.

4:00 p.m. **Does the Immune System REALLY Distinguish Between Self and Non-Self?** Polly Matzinger, Laboratory of Cellular and Molecular Immunology, NIAID, NIH. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** Tea at 3:45 p.m.

The Arts and Other Events**FRIDAY, JANUARY 7**

12:00 p.m. **Tri-Institutional Noon Recitals.** Mark Kosower, cello, and Jee-Won Oh, piano. Performing works of Schumann, Beethoven and Kodály. **Casparly Auditorium.** Contact John Gerlach, 327-7776. Open to RU/WMCCU/NYPH/MSKCC community and guests only.

THURSDAY, JANUARY 13

8:00 p.m. **Rockefeller University Film Series.** Kasper Hauser (1974). Directed by Werner Herzog. **Casparly Auditorium.** Open to RU/WMCCU/NYPH/MSKCC community and guests only.

FRIDAY, JANUARY 14

12:00 p.m. **Tri-Institutional Noon Recitals.** Ondar and The Eagles of Tuva, with Tom Rütishauser. Performing the centuries-old Tuvan art of throat-singing, in which a soloist can sing several notes simultaneously. They also play drums and traditional Tuvan instruments—the bowed igil and the doshpuluur. **Casparly Auditorium.** Contact John Gerlach, 327-7776. Open to RU/WMCCU/NYPH/MSKCC community and guests only.

**THE ROCKEFELLER UNIVERSITY
Friday Lectures**

These events are held in Casparly Auditorium at 3:45 p.m. Tea is served in Abby Aldrich Rockefeller Lounge at 3:15 p.m. All are welcome.

FRIDAY, JANUARY 14

Molecular Dynamics and Biological Impact of DNA Damage Repair. Jan Hoeijmakers, Professor in Medical Genetics, Erasmus Universiteit, and Dept. of Cell Biology and Genetics, Medical Genetic Center Rotterdam, The Netherlands.

FRIDAY, JANUARY 21

Molecular Analysis of Neural Crest Development. Marianne Bronner-Fraser, Professor, Division of Biology, Caltech.

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