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News and Notes 2000

The Rockefeller University News and Notes

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## **NEWS AND NOTES 2000, VOL.12, NO.10**

The Rockefeller University

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# news & notes

THE NEWSLETTER OF THE ROCKEFELLER UNIVERSITY

FRIDAY LECTURE

## Lundblad to discuss telomeres

Victoria Lundblad, an associate professor in the Department of Molecular and Human Genetics at Baylor College of Medicine, will present today's Friday lecture (Dec. 1). Her topic will be "Recruitment of End Protection and Replication Complexes to the Telomere."

Genomic integrity depends on a number of different processes affecting chromosome replication and stability. Research in Lundblad's laboratory is focused on telomeres, the specialized structures found at the ends of linear chromosomes that are required for proper chromosome function. The primary mechanism for replicating the ends of the chromosome is a telomere-specific DNA polymerase called telomerase. In the last few years, there has been increasing interest in telomere length regulation, due to a series of observations associating telomere length and telomerase activity with tumorigenesis and aging. However, a detailed picture of the structure of telomerase and how it interacts with the end of the chromosome in vivo has been lacking, in part due to a lack of molecular tools for dissecting this problem.

Lundblad's lab has approached this problem by using the budding yeast *Saccharomyces cerevisiae* as an experimental system for studying telomere function.

*continued on page 2*



Victoria Lundblad studies telomeres, the specialized structures found at the ends of linear chromosomes that are required for proper chromosome function.

## Rockefeller scientists garner awards

This has been another outstanding year for scientists at the university, both in terms of accomplishments in the lab and in the number of honors bestowed upon Rockefeller researchers. Three of the scientists recently honored are included below.

### Arnold J. Levine

President Levine has been awarded the Keio Medical Science Prize for his "work in tumor virology and molecular oncology leading to the discovery of *p53* and its recognition as a tumor suppressor gene." The prize, bestowed by the Keio University Medical Science Fund, is awarded annually to both a Japanese scientist and a non-Japanese scholar. Levine's co-recipient this year is Yusuke Nakamura of the Institute of Medical Science of the University of Tokyo.

### Robert Roeder

Arnold and Mabel Beckman Professor Robert Roeder has been awarded a Gairdner Foundation International Award. The purpose of these awards is the recognition of individuals whose work or contribution constitutes tangible achievement in the field of medical science.

Roeder is honored "for his pioneering contributions to the field of transcription of genetic information, a theme of central importance in the biology of eukaryotic (nucleated) cells. He is recognized especially for his description of the complex array of protein factors involved in transcription, notably his analysis of three RNA polymerases and the development of assays for their activities. He has continued to make significant contributions to the identification and cloning of eukaryotic transcription fac-

tors and to pursue the detailed characterization of the transcription apparatus and its regulation, work which has important applications in medical science."

### Günter Blobel

John D. Rockefeller Jr. Professor Günter Blobel, an HHMI investigator, has been elected to the Institute of Medicine. Current active members elect new members from among candidates chosen for their major contributions to health and medicine or to related fields.

Election to the Institute is both an honor and an obligation to work on behalf of the organization in its governance and studies. With their election, members make a commitment to devote a significant amount of time as volunteers on committees engaged in a broad range of studies on health policy issues.

Only these three sent AS prints - ALL others in this issue sent AS Electronic Files.



Top to bottom: Rockefeller University President Arnold J. Levine, Professor Robert Roeder and Professor Günter Blobel all recently received honors for their scientific achievements.

## Campus is invited to participate in "pedigree" exhibit

Last month a new exhibit was installed for the university Centennial in the lobby of the Rockefeller Research Building. Titled "Mentors and Students: An Intellectual Pedigree of The Rockefeller University," it shows selected lineages of Rockefeller scientists that span the 20th century.

The pedigree chart is silk-screened on a blackboard, and within hours of chalk being placed in the tray, some Rockefeller community members added missing names to the family tree: Max Bergmann, for

example, a chemist who was a student of Emil Fisher (also on the pedigree), and Bergmann's protégés William Stein and Stanford Moore.

Drawing family trees is a way of understanding history that everyone is familiar with. By looking at the university's scientific pedigree, it is easy to see at a glance how disciplines such as cell biology took shape at Rockefeller.

Because the pedigree shows only the lineages that are continuous

*continued on page 2*



The pedigree chart is silk-screened on a blackboard, so as to be interactive. Members of the Rockefeller community are invited to pick up a piece of chalk and add names to the tree. In addition, the exhibit includes a book with pages for every laboratory at the university today to draw or paste in its pedigree.

## Peggy Rockefeller concert features clarinet, piano

Distinguished American clarinetist Jon Manasse will perform in a joint recital with pianist Peter Orth at the next Peggy Rockefeller concert on Wed., Dec. 13.

Manasse's recent solo appearances include performances at Lincoln Center and other international concert halls. He has given acclaimed concerto performances with Gerard Schwarz and the Mostly Mozart Festival Orchestra, both at Lincoln Center's Avery Fisher Hall and in Tokyo.

An avid chamber musician, he has been featured in New York City programs with the Chamber Music Society of Lincoln Center and at Carnegie Hall's Weill Recital Hall, Alice Tully Hall and the Walter Reade Theatre (on Lincoln Center's "Great Performers" series).

He is principal clarinetist of both the New York Chamber Symphony and the American Ballet Theatre Orchestra. He has also served as guest principal clarinetist of the New York Pops

Orchestra and a guest clarinetist with the New York Philharmonic.

In 1979, Orth won first prize in the Naumburg International Piano Competition, an award that catapulted him into the American Music mainstream. He has been a guest soloist with virtually every major orchestra in North America and has collaborated with a host of today's most distinguished conductors. His solo career includes recitals at Alice Tully Hall, the John F.

Kennedy Center for the Performing Arts and other major concert halls. An active and esteemed chamber musician, Orth has collaborated with the Manhattan and Muir String Quartets and Germany's Auryn Quartet.

The concert begins in Caspary Auditorium at 8 p.m. For information about the Peggy Rockefeller concerts, contact Jennifer Goldschlag, x8437.

2 AROUND CAMPUS

3 IN THE LAB

4 CALENDAR

Infectious disease  
symposium

#00-051



The university hosted a Centennial Symposium on Antibiotic Resistance and Infectious Disease on Nov. 9. During a break, participants gathered outside Caspary Auditorium for a photograph.

CFC applications are  
available now

Applications are now available for the 2001-2002 academic year at the Child and Family Center. The center serves children from infancy to age five. For an application, please contact Marjorie Goldsmith, x8580.

Sweatshirt Shop  
holiday hours

The university's Sweatshirt Shop (located on the first floor Bronk) is open Fridays from noon to 2 p.m. and will be open Mon., Dec. 18, to Fri., Dec. 22, from noon to 2 p.m. All proceeds benefit the Rockefeller University Child and Family Center.

## 2000 Toys for Tots Campaign

You can help a child enjoy the holidays this year. The Media Resource Center has sponsored the Toys for Tots campaign on campus for the last eight years. Last year was the most successful year with over 100 toys donated by Rockefeller University employees. Look for the "Toys for Tots Train" in the Weiss Lobby. It will be there from Mon., Dec. 4, to Mon., Dec. 18. If you have any questions, please contact John Sholtis, x8949.



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Ideas and submissions can be sent interoffice (Box 68), by electronic mail ([newsno](mailto:newsno)) or by fax (212.327.7876). Copyright, 2000, The Rockefeller University

## Pedigree continued

from the university's founding to the present day, many important areas of research are missing from it. Physics, mathematics, biophysics, and neuroscience, for example, came to Rockefeller in the 1950s and 1960s, and so they do not have a long heritage here. Portions of the history of these disciplines will be addressed in later Centennial exhibits and publications.

As the university celebrates its 100th birthday, different aspects of its history have been explored—during The Rockefeller University Centennial History Conference, held Nov. 13 and 14, and in the exhibits in Founder's Hall, the Abby Aldrich Rockefeller Lounge and on the Centennial Web site. But the pedigree, situated in a lobby through which nearly everyone at the university passes, is uniquely accessible and interactive.

The chart also makes plain how short 100 years is. Several of the university's current faculty are living links to the founding members of the scientific staff. Abigail O'Sullivan, a participant in the history conference from Oxford University, noted that these ties make history a more closely held part of Rockefeller's culture than is the case at other institutions. Nobody, she pointed out, remembers first-hand the early years of Oxford, a university that is 800 years old.

"The Mentors and Students exhibit builds on an interest in pedigrees that already existed at Rockefeller," says Betsy Hanson, of the Public Affairs office. "I had talked to Professor Tom Sakmar and Professor Emeritus Bruce Merrifield and knew that they had traced the genealogies of Rockefeller chemists." The two faculty members talked about these scientific lineages during

the symposium last Oct. 20, when the American Chemical Society dedicated the campus as a National Historic Chemical Landmark. Merrifield created a wall chart that is displayed outside his laboratory on the fourth floor of Flexner Hall.

In addition, Professor Emeritus Norton Zinder has sketched pedigrees based on his own knowledge and information in the book by George Corner entitled *A History of The Rockefeller Institute, 1901-1953*.

"That book contains an exhaustive list of the scientific staff at Rockefeller up until 1953," says Hanson, "but no such lists exists for the second half of the century." Because the university tripled in size during the 1960s and has expanded more since then, many more scientists have worked here since 1953 than before that date.

The book that accompanies the "Mentors and Students" exhibit is a first attempt to compile this information. It contains pages on which each present-day laboratory can draw or paste in a tree or list of graduate students, postdoctoral fellows, and other research scientists who work in the lab now and who were there in the past.

When the exhibit is taken down at the end of the Centennial celebrations, the university will have a record, in the book, of who was here during this landmark year. And by organizing the information as a pedigree, the book will also make visible networks of collaboration and the spread of Rockefeller-trained scientists to institutions around the world.

## Friday continued

Using several large-scale mutant screens, she and her colleagues have recovered a number of yeast genes, called EST genes (for "ever shorter telomeres"), that are required for telomere replication and long-term viability in yeast.

This led to the identification of the long-sought-after catalytic component of telomerase, encoded by the EST2 gene; as part of a collaboration with Thomas Cech's laboratory, her lab has shown that the Est2 protein has structural and enzymatic similarities to conventional reverse transcriptases.

In addition to providing insight into the mechanism of telomerase catalysis, this result has striking evolutionary implications, by demonstrating that reverse transcriptases are not employed solely for the replication of parasitic genetic elements

but also are necessary for normal cellular growth.

In parallel with EST2, they identified several additional EST genes that are required for telomerase function in vivo but which are dispensable for in vitro enzymatic activity. This suggests that these additional genes encode critical positive regulators of telomerase, and one research focus in Lundblad's laboratory is directed at determining the specific roles of these Est proteins, using both biochemical and genetic approaches. Their genetic screens also had an unexpected additional benefit, in that the lab also uncovered genes that are required for protection of chromosome termini.

They have shown that one of these genes, CDC13, encodes a protein that binds to telomeric DNA in vitro and thus is likely to be present at chromosome

termini in vivo. They have proposed that the Cdc13 protein serves a dual function while bound to the end of the chromosome: it protects telomeres from degradation, and it also regulates telomerase by mediating access of the enzyme to chromosomal termini.

Lundblad's lab is currently testing several aspects of this model, by asking whether this proposed regulatory role is due to a direct interaction between the Cdc13 protein and telomerase or is a more indirect consequence of modification of telomeric chromatin by Cdc13p.

Finally, her lab has recently discovered that a set of proteins previously implicated for their role in repair of double-strand breaks also provide essential functions at the end of the chromosome. This challenges a long-standing idea that telomeres and

double-strand breaks are functionally distinct.

The lab's current efforts in this area are directed at determining what distinguishes the function(s) of these proteins at telomeres as opposed to their action at DNA strand breaks.

Lundblad received her Ph.D. in biochemistry and molecular biology from Harvard University in 1983, working with Nancy Kleckner. She was a postdoctoral fellow in the laboratories of Jack W. Szostak at Harvard Medical School and Elizabeth Blackburn at the University of California, Berkeley. She joined Baylor College of Medicine in 1991.

Lundblad's talk begins at 3:45 p.m. in Caspary Auditorium and is preceded by a tea in Abby Aldrich Rockefeller Lounge at 3:15 p.m. All are welcome.

University  
holiday party:  
save the date!

The university's annual holiday party will take place in Weiss Cafe and Weiss 17 on Thurs., Dec. 14 from 2:30 p.m. to 4:30 p.m. The event will feature a variety of music, food and children's events.



## Rockefeller laboratories identify molecule that senses osmotic pressure in vertebrates

Researchers at the Howard Hughes Medical Institute and Rockefeller University have identified a molecule in vertebrates that senses osmotic pressure—the measure of saltiness essential for living cells—and may provide an inroad into understanding inner ear function and the sense of touch.

The molecule, called VR-OAC (Vanilloid Receptor-related Osmotically Activated Channel), is an ion channel that responds to changes in osmotic pressure of extracellular fluid. Osmotic pressure is the pressure exerted by salts and proteins dissolved in bodily fluids. When osmotic pressure outside a cell decreases, this leads to an increased tension in a cell's membrane, like the tension in a balloon as it is inflated, a physical stimulus which in turn opens up the channel, allowing ions, among them calcium ions, to pass through, which elicits a cascade of intracellular events.

In the case of sensory cells and nerve cells, this is converted into electrical signals to the central nervous system. The scientists cloned VR-OAC from rat, mouse, chicken and human gene libraries. The ion channel was detected in cells from the inner ear, the osmoregulator centers of the brain in the hypothalamus and from cells surrounding whiskers, a rodent's snout hair known to be very sensitive to touch. The presence of VR-OAC in the latter cells suggests that this receptor may also be involved in the sense of touch.

The research was led by Wolfgang Liedtke, a research associate in the Laboratory of Molecular Genetics headed by Jeffrey M. Friedman, an investigator at the Howard Hughes Medical Institute, and Stefan Heller, a former postdoctoral researcher in the Laboratory of Sensory Neuroscience at Rockefeller headed by A. James Hud-

speth, also an investigator at the Howard Hughes Medical Institute. Heller is now an assistant professor at Harvard Medical School. Liedtke discovered VR-OAC while looking in a region of the brain called the hypothalamus for genes operative in the regulation of body temperature. The hypothalamus monitors and regulates a score of vital parameters in the body, including osmotic pressure, energy balance and temperature.

### A MOLECULE CALLED VR-OAC MAY BE KEY IN HELPING TO REGULATE THE SALT AND WATER HOUSEHOLD OF CERTAIN CELLS.

Of those, systemic osmotic pressure is the most aggressively defended setpoint value in vertebrate animals, including humans. An increase in osmotic pressure leads to the sense of thirst and drinking behavior, and osmoreceptors in the hypothalamus send signals to nerve cells that manufacture antidiuretic hormone (ADH), the primary regulator of body water.

Liedtke found VR-OAC expressed in neurons in brain structures called the circumventricular organs. Most of the brain is protected by the blood-brain barrier, a gateway that allows only certain substances to pass into the brain. The circumventricular organs are located inside the brain, but outside the blood-brain barrier. Circumventricular organs are recognized as important sites for communication of the central nervous system with the remainder of the organism through the blood/serum.

Liedtke collaborated with Heller and colleagues in the Laboratory

of Sensory Neuroscience who had cloned VR-OAC from a chicken inner ear gene library. Liedtke thought that VR-OAC could be an ion channel that responds to osmotic pressure. They showed that VR-OAC was also present in hair cells of the inner ear, which Hudspeth's lab has studied and functionally characterized. These cells are the principal mechanotransductive cells essential for the perception of sound and the sensing of

acceleration in the inner ear's sense of equilibrium. VR-OAC may be key in helping to regulate the salt and water household of these cells.

"As an alternative model and a more general concept, VR-OAC could be part of sensory cells' mechanosensitive molecular apparatus, an exciting possibility," says Liedtke. "We are very eager to examine this in follow-up studies."

Working with hamster cells driven to express VR-OAC, the researchers showed that VR-OAC is exquisitely sensitive to subtle changes in osmotic pressure. VR-OAC does not respond to changes in temperature, but it is "fine-tuned" by temperature, with maximum sensitivity at body temperature in mammals (37°C/98.6°F) and in birds (40°C/104°F).

"Our laboratories then began to characterize the properties of what we now know to be an osmotically gated channel," says Friedman. "These studies showed that, indeed, the channel

opens in response to decreased salt concentration, or osmolarity. This opening admits a small amount of calcium, which in turn triggers the release of a burst of calcium from storage depots inside the cell. When this happens in key nerve cells in the brain's osmotic regulatory region, we suspect that these receptors would fire and produce a host of responses that affect thirst, salt intake and perhaps even salt excretion."

VR-OAC is a member of the new family of vanilloid receptor-related genes, which have several exciting functions, namely sensitivity to osmotic pressure, and possibly to mechanical stimuli, painful heat and to capsaicin, the pungent ingredient of hot peppers.

Liedtke's, Heller's, Hudspeth's and Friedman's co-authors are graduate student Yong Choe, Andrea M. Bell and Charlotte S. Denis in the Laboratory of Sensory Neuroscience; and postdoctoral associate Marc A. Martí-Renom, Ph.D., and Associate Professor Andrej Šali, Ph.D., head of a Laboratory of Molecular Biophysics, all at Rockefeller.

*This research was supported in part by the National Institute of General Medical Sciences, the National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institute on Deafness and Other Communication Disorders, all part of the U.S. National Institutes of Health. Choe was supported in part by a graduate fellowship from the National Science Foundation. Šali is a fellow of the Alfred P. Sloan Foundation.*



Micrograph depicting the lamina terminalis adjacent to the anterior hypothalamus of a mouse. The area labeled "III" is the frontal portion of the 3rd ventricle, part of the cavity system of the brain that is filled with cerebrospinal fluid. "VOLT" denotes organum vasculosum lamina terminalis. This part of the lamina terminalis lacks a functional blood-brain barrier. The nerve cells labeled in blue (dark spots in micrograph) express VR-OAC and can sense the osmotic pressure in the serum, a physiological setpoint held tightly at 295 mmol/kg. These neurons are regarded as primary sensory cells for the "milieu interne" and have been shown to have relevant functional connections to the neurons producing antidiuretic hormone, the principal hormonal regulator of bodily water.



Chinese hamster ovary cells expressing the vanilloid receptor-related osmotically activated channel (VR-OAC) after stimulation with hypotonic buffer solution. Increased intracellular calcium concentration was visualized as green fluorescence emitted by the calcium sensitive dye fluo-4 (light areas of micrograph).

Images courtesy of Wolfgang Liedtke

## In memoriam: John D. Gregory

John D. Gregory, an associate professor emeritus and former head of the Laboratory of Biochemistry of Connective Tissues, died Mon, Nov. 20, at his home in Monkton, Maryland. He was 77 years old.

Gregory became a research associate at the Rockefeller Institute for Medical Research in 1947, working with Lyman Craig on

the purification and chemistry of polypeptide antibiotics and the development of methods and apparatus for countercurrent distribution.

In 1949, he went to Massachusetts General Hospital, where he worked with Fritz Lipmann on the chemistry of coenzyme A, enzyme chemistry and purification, and sulfate

metabolism. He returned to Rockefeller in 1957 as an associate professor, again working with Fritz Lipmann, who had moved to Rockefeller that year.

He became a head of laboratory in 1967 and retired in 1991 as an emeritus associate professor. For nearly 40 years, Gregory studied the body's connective tissues, specifically the fibrous collagen

proteins and carbohydrate-protein compounds called proteoglycans that comprise connective tissues. In their early research, Gregory and his colleagues developed new techniques for extracting proteoglycans from cartilage tissue and for determining their chemical composition. They later isolated and characterized the four types of proteogly-

cans present in the corneas of rabbits. He and his colleagues also studied how proteoglycan changes in human skin contribute to changes during the processes of wound healing and aging, and in various skin diseases.



# calendar

D E C E M B E R 1 T H R O U G H D E C E M B E R 1 5

E V E N T S

## 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, DECEMBER 1

**Recruitment of End Protection and Replication Complexes to the Telomere.** Victoria Lundblad, Associate Professor, Depts. of Molecular and Human Genetics and Biochemistry, Baylor College of Medicine.

WEDNESDAY, DECEMBER 6

**Thesis Presentation. Cis Regulation of the Recombination Activating Genes and Their Expression in Peripheral B Cells.** Wong Yu, Biomedical Fellow, Nussenzweig lab, RU.

FRIDAY, DECEMBER 8

**Targeting Olfaction.** Peter Mombaerts, Assistant Professor, RU.

FRIDAY, DECEMBER 1

12:00 P.M. **Mechanisms That Help Maintain Genome Integrity.** Jesper Svejstrup, Imperial Cancer Research Fund, UK. Molecular Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

MONDAY, DECEMBER 4

12:00 P.M. **Selective Packaging of Primer tRNALys3 during HIV-1 Assembly.** Lawrence Kleiman, McGill U. AIDS Center. CFAR Seminar. SIXTH FLOOR CONFERENCE ROOM, ADARC, 455 FIRST AVE. CONTACT GARY GAILOR, 448-5163.

1:30 P.M. **The Signaling Adaptor Molecules and Lymphocyte Development, Activation and Autoimmunity.** Hau Gu, Head, Lymphocyte Development Unit, Laboratory of Immunology, NIAID, NIH. Immunology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

4:30 P.M. **Bves, A Novel Cell Adhesion Molecule That Regulates Coronary Vasculogenesis.** David M. Bader, Professor of Medicine and Cell Biology, Vanderbilt U. School of Medicine. Cell Biology and Genetics Seminar. PAPANICOLAOU LIBRARY, A-106 WMCCU, 1300 YORK AVE. COFFEE WILL BE SERVED.

4:30 P.M. **How Does the Sodium Pump Pump? Structural Insights from Cysteine-scanning Mutagenesis.** Jean-Daniel Horisberger, Institut de Pharmacologie et de Toxicologie, Université de Lausanne. PBMM Research Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE. COFFEE AT 4:15 P.M.

TUESDAY, DECEMBER 5

11:00 A.M. **Applied Precision's CCD Scanner to Analyze Microarray Data.** Mark Rand, Application Manager, Applied Precision. Meeting. 110B NURSES RESIDENCE. REFRESHMENTS AT 10:55 A.M. CONTACT GREGORY KHITROV, 327-7064.

11:00 A.M. **Identification of Xkid, a Chromokinesin That Binds Chromosomes in Metaphase and Is Degraded in Anaphase.** Hironori Funabiki, Dept. of Molecular and Cellular Biology, Harvard U. Chromosome Biology/Gene Expression Seminar. 305 WEISS.

11:00 A.M. **Regulation of Programmed Cell Death in the Nematode *C. elegans*.** Shai Shaham, UCSF Molecular Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. REFRESHMENTS AT 10:45 A.M. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

11:00 A.M. **Structural Determinants of HIV-1 Genome Recognition and Assembly.** Michael Summers, Professor, U. of Maryland. Pels Family Center for Biochemistry and Structural Biology Seminar. 301 WEISS. CONTACT ROSER BUSQUETS, 327-7050. COFFEE AND COOKIES AT 10:45 A.M.

4:00 P.M. **Design of Nitric Oxide Synthase Inhibitors.** Owen Griffith, Professor and Chairman, Dept. of Biochemistry, Medical College of Wisc. Pharmacology Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE. COFFEE AT 3:45 P.M. CONTACT LISSETT CHECO, 746-6250.

4:00 P.M. **Inhibition of COX-2 Gene Expression by PPAR $\gamma$  Ligands.** Andrew Dannenberg, Professor of Medicine, WMCCU, Director of Clinical Programs and Head, Molecular Carcinogenesis Laboratory, Strang Cancer Prevention Center. CNRU Research Lecture.

117 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. CONTACT LINDA COTTE, 639-8352.

4:00 P.M. **Receptor-mediated Signaling in Bacterial Chemotaxis: Does *E. coli* Have a Brain?** Jeff Stock, Princeton U. Center for Studies in Physics and Biology Seminar. B LEVEL CONFERENCE ROOM, SMITH HALL ANNEX. TEA AT 3:30 P.M. CONTACT ERIK VAN NIMWEGEN, 327-8184.

WEDNESDAY, DECEMBER 6

10:00 A.M. **Neural Codes, State Dependency and Computational Rules of Reinforcement Vocal Learning in Songbirds.** Daniel Margoliash, U. of Chicago. Neural Plasticity and Learning Seminar. 305 WEISS. CONTACT CONSTANCE SCHARFF, 327-8381. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

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

11:00 A.M. **Brain Systems Involved with Memory Formation and Maintenance.** Allison Doupe, U. of Chicago. Neural Plasticity and Learning Seminar. 305 WEISS. CONTACT CONSTANCE SCHARFF, 327-8381. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

12:00 P.M. **Exploring RNA and Protein Sequence Space with Directed Evolution.** Jack Szostak, Professor of Genetics, Harvard Medical School, Investigator, HHMI, and Alex Rich Distinguished Investigator, Mass. General Hospital. 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.

2:00 P.M. **Inward Rectifying K Channels: From Molecular Mechanisms to Human Disease.** Colin G. Nichols, Professor of Cell Biology and Physiology, Washington U. School of Medicine. PBMM Research Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE. COFFEE AT 1:45 P.M.

4:30 P.M. **The Genetics of Morphological Change in *Drosophila*.** Eric Wieschaus, Professor, Princeton U. MSKCC President's Research. Auditorium, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

THURSDAY, DECEMBER 7

12:00 P.M. **Maintaining Male Reproductive Function: Testosterone Biosynthesis under the Onslaught of Stress and Environmental Toxicants.** Matthew P. Hardy, Senior Scientist, Center for Biomedical Research, Population Council. ENDOCRINOLOGY AND REPRODUCTIVE BIOLOGY SEMINAR. 301 WEISS.

3:00 P.M. **Neural Networks for Attentional Control of Sensory Processing.** Ron Mangun, Professor, Center for Cognitive Neuroscience, Duke U. Systems Neuroscience Seminar. 305 WEISS. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Malaria, Here Today and Probably Tomorrow, Too: One View of the Escape and Invasion Tactics of Malaria Parasites.** John W. Barnwell, Senior Biomedical Research Scientist, Division of Parasitic Diseases, Centers for Disease Control, National Center for Infectious Diseases, Atlanta, Georgia. 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. **Mechanisms of Carcinogenesis and Aging: Role of Nutrition.** John Richie, Leader, Cancer Susceptibility Program, American Health Foundation, Valhalla, N.Y. CNRU Special Nutrition Lecture. D-417 WMCCU, 1300 YORK AVE. CONTACT LINDA COTTE, 639-8352.

FRIDAY, DECEMBER 8

10:00 A.M. **The CD1 System and the Immune Response to Mycobacterial Lipid and Glycolipid Antigens.** Timo Ulrichs, Albert Einstein College of Medicine, Dept. of Microbiology and Immunology, TB Club Seminar. 110B NURSES RESIDENCE. REFRESHMENTS AT 10:15 A.M. CONTACT CLAUDIA MANCA, 327-8103.

12:00 P.M. **Upstream and Downstream of p53 and Its Relatives.** Carol Prives, Dept. of Biological Sciences, Columbia U. Cell Biology Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

10:00 P.M. **Efficient Structure Solution and Refinement with MAD Phasing.** Axel Brunger, Stanford U. Lecture. 110 ROCKEFELLER RESEARCH BUILDING. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

MONDAY, DECEMBER 11

10:00 A.M. **Optimizing Score Functions for the Detection of Remote Homologs.** Richard Goldstein, Associate Professor, Dept. of Chemistry, and Associate Research Scientist, Biophysics Research Division, U. of Michigan. Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST.

1:30 P.M. **How the TCR/CD28, PKC- $\theta$  and the Cytoskeleton Tickle Each Other.** Amnon Altman, Head, Division of Cell Biology, La Jolla Institute of Allergy and Immunology. Immunology Seminar. SECOND FLOOR CONFERENCE ROOM, HSS, 535 EAST 70TH ST.

3:30 P.M. **Biology and Functional Genomics.** John Quackenbush, Associate Investigator, The Institute of Genomic Research. Seminar. 103 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 E. 67TH ST.

4:30 P.M. **The Ryanodine Receptor/Calcium Release Channel as a Macromolecular Complex.** Andrew R. Marks, Professor of Medicine and Pharmacology, Columbia U. College of Physicians and Surgeons. PBMM Research Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE. COFFEE AT 4:15 P.M.

TUESDAY, DECEMBER 12

11:00 A.M. **Compartmentalized Biochemical Signaling in Dendritic Spines.** Bernardo Sabatini, Cold Spring Harbor Laboratory. Neuroscience Seminar. 301 WEISS. CONTACT BOBBIE LARRAGA, 327-7240. OPEN TO RU COMMUNITY AND GUESTS.

12:00 P.M. **Expression Linkage Approaches for Mapping Type 2 Diabetes Genes.** Susan Sell, Assistant Professor of Genetics and Co-Director, Genetics Core, Clinical Nutrition Research Center, U. of Ala. at Birmingham, and Adjunct Faculty, Ariz. State U. Starr Center for Human Genetics Seminar. 110B NURSES RESIDENCE. CONTACT EMILY HUFFMAN, 327-7387.  
2:00 P.M. **Insulin Resistance: Insights from Targeted Mouse Mutants.** Domenico Accilli, Head, Diabetes Research Unit, Columbia U. **Hypothalamic Regulation of Insulin Action.** Luciano Rossetti, Albert Einstein College of Medicine. **Dyslipidemia Associated**

**with Insulin Resistance.** Henry Ginsberg, Columbia U. NY Lipid and Vascular Biology Research Club Meeting. 301 WEISS. REFRESHMENTS AT 4:00 P.M. CONTACT KIE CUNDEY, 327-7708. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

4:00 P.M. **Metastasis-related Genes as Potential Biomarkers/Therapeutic Targets for Metastatic Prostate Cancer.** Timothy Thompson, Professor of Urology and Molecular and Cellular Biology and Radiology, Baylor College of Medicine. Molecular Pharmacology and Therapeutics Seminar. 116 ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 3:45 P.M.

WEDNESDAY, DECEMBER 13

10:00 A.M. **The Dynamics of Neuronal Replacement in Birds.** Linda Wilbrecht, Graduate Fellow, RU. Neural Plasticity and Learning Seminar. 305 WEISS. CONTACT CONSTANCE SCHARFF, 327-8381. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

11:00 A.M. **New Approaches to Brain Repair.** Hynek Wichterle, RU. Neural Plasticity and Learning Seminar. 305 WEISS. CONTACT CONSTANCE SCHARFF, 327-8381. OPEN TO RU/WMCCU/NYPH/MSKCC COMMUNITY AND GUESTS.

2:00 P.M. **Neural and Molecular Mechanisms of Memory.** John H. Byrne, Professor and Chair of Neurobiology and Anatomy, U. of Texas, Houston, Medical School. PBMM Research Seminar. WEILL AUDITORIUM, WMCCU, 1300 YORK AVE. COFFEE AT 1:45 P.M.

4:30 P.M. **Implications of the Human Genome Project for Medicine and Society.** Francis Collins, Director, National Human Genome Research Institute, NIH. MSKCC President's Research Seminar—Charles B. Smith Lecture. AUDITORIUM, ROCKEFELLER RESEARCH LABORATORIES, MSKCC, 430 EAST 67TH ST. TEA AT 4:00 P.M.

## The Arts and Other Events

SUNDAY, DECEMBER 10

3:00 P.M. **The Chamber Orchestra of Science and Medicine.** John McCauley, Conductor. Debut concert of a chamber orchestra of soloists performing Handel: *Concerto Grosso in B Minor, Op. 6, No. 12*; Dvorak: *Allegro Guisto/Menuett from Czech Suite, Op. 39*; Haydn, *Symphony No. 82 in C Major*. Chamber Music Concert. CASPARY AUDITORIUM. REFRESHMENTS WILL BE SERVED. CONTACT ROBERT DARNELL, 327-7460.

WEDNESDAY, DECEMBER 13

8:00 P.M. **Peggy Rockefeller Concerts.** Jon Manasse, Clarinet, with Peter Orth, Piano. CASPARY AUDITORIUM. CONTACT JENNIFER GOLDSCHLAG, 327-8437.

THURSDAY, DECEMBER 14

2:30 p.m.–4:30 p.m. **Annual Holiday Festivity.** WEISS BUILDING (CAFÉ AND 17TH FLOOR). OPEN TO RU COMMUNITY AND GUESTS.

FRIDAY, DECEMBER 15

9:00 A.M. **Child And Family Center Winter Sing-Along.** WEISS 17TH FLOOR. REFRESHMENTS AT 8:30 A.M. IN THE WEISS 17TH FLOOR NORTHEAST AND SOUTHEAST DINING ROOMS. CONTACT KATHY BURKE, 327-8580.

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