



## Anthony B. Evin joins RU board of trustees



Anthony B. Evin is a new member of the Rockefeller University's board of trustees.

Anthony B. Evin has joined the Rockefeller University Board of Trustees. His appointment was approved by the board on Wed., March 10. Evin has been a member of the Rockefeller University Council since 1987.

Evin is a general partner of Venrock Associates, a venture capital partnership which invests in early stage, technology-based companies in the life sciences and information technology areas. A Ph.D. in chemistry from the Massachusetts Institute of Technology, Evin serves as a director of Axyx Pharmaceuticals Inc., Centocor, Inc., Opta Food Ingredients, Inc., Ribozyme Pharmaceuticals Inc., and Triangle Pharmaceuticals Inc., as well as a number of other private companies.

Evin was also formerly a Director of Athena Neurosciences Inc., Genetics Institute Inc., IDEC Pharmaceuticals Corporation, IDEXX Laboratories Inc., The Liposome Company Inc., and Sepracor Inc., among others. He is a trustee of Princeton University.

### RU curious?



A large crowd turned out for last week's poster session on research at RU. Another session takes place today (March 12).

## TODAY Poster session on RU research

1 p.m. to 3:30 p.m., Weiss, 17th Floor

The Dean's Office invites the RU community to a poster session presenting the current research of graduate students, postdocs and faculty members. The session today (March 12) is part of the open house for prospective graduate students. All are welcome.

# news & notes

MARCH 12, 1999 VOLUME 9, NUMBER 19

THE ROCKEFELLER UNIVERSITY

## RU hosts a special episode of *The Charlie Rose Show* Topic is the *TIME* 100 Scientists and Thinkers



Casparry Auditorium became a television studio last week for the taping of *The Charlie Rose Show*. The air date for the program has not been scheduled yet.

**T**he *Charlie Rose Show* taped in RU's Casparry Auditorium last Wed., March 3. The topic of the program was *TIME* magazine's selection of the top 100 scientists and thinkers of the 20th century.

Guests on the program included

Daniel Dennett of Tufts University; Peter Gay of Yale University; Walter Isaacson of *TIME*; Stephen Pinker of MIT; Maxine Singer of the Carnegie Institution; Robert Gallo of the Human Virology Institute; and science-fiction author Bruce Sterling.



*TIME* magazine's managing editor Walter Isaacson (left), introduced RU President Arnold J. Levine, who addressed the audience prior to the taping of *The Charlie Rose Show*.



Before the show, Charlie Rose (right) sought out RU Professor David Ho in the audience. Ho, the scientific director of the Aaron Diamond AIDS Research Center, was *TIME*'s Man of the Year in 1996.

## President Levine meets with junior heads of lab



Last Wed., March 3, President Levine held an informal dinner at the President's House for RU's junior heads of lab. The purpose of the event, which Levine hopes to hold annually, was to recognize the important work that the junior faculty do at the university and to let them know, as Levine said in his toast, "that the president is on your side."



Friday lecture:

## RU's Roeder to discuss "molecular machines"

**R**obert Roeder, the Arnold and Mabel Beckman Professor at RU, will present the Friday lecture today (March 12) entitled "Complex Molecular Machines and the Regulation of Eukaryotic Gene Transcription."

Roeder is a biochemist whose research focuses on the molecular basis of gene activity in mammalian cells, particularly in processes such as cell growth and differentiation. The cellular and viral genes that affect these processes are controlled in large part at the level of transcription—the first step in the readout of genetic information from DNA to RNA. Roeder is particularly interested in the biochemical mechanisms involved in that process in individual genes.

Roeder's interests are severalfold: first, in the DNA tape reader (RNA polymerase) and accessory factors (general transcription machinery) that recognize start and stop signals in the DNA and are commonly used by many genes; second, in the analysis of more recently discovered cofactors that enable gene-specific regulatory factors to activate the tape-reading machinery on target genes in specific physiological processes. As he will discuss, the various accessory factors comprise surprisingly complex molecular machines.

Roeder's pioneering work in transcription began while he was still a graduate student at the University of Washington; it led to the isolation and characterization of the family of enzymes (RNA polymerases I, II and III) that copy genetic information directly from DNA—an achievement for which he won the Eli Lilly Award in Biological Chemistry in 1977. While Roeder's laboratory uses primarily biochemistry techniques, the interdisciplinary nature of RU has made for some fruitful collaborations. He notes particularly the complementary work being done by RU's new deputy for academic affairs, Professor Stephen Burley, a structural biologist who has identified the three-dimensional structure of several key components of the general transcription machinery. Similarly, a collaboration with Professor Michel Nussenzweig has allowed genetic analysis in mice of transcription factors involved in cell function. (Burley and Nussenzweig are also HHMI investigators.)

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

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**3** Telomeres

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<http://www.rockefeller.edu/rucal>

THE ROCKEFELLER UNIVERSITY — Please Post

**FRIDAY, MARCH 12**

10:30 a.m. **Genome Scan for Susceptibility Genes in Leprosy.** Ruby Siddiqui, Oxford U., U.K. Tuberculosis Club Meeting. **110B Nurses Residence.** *Coffee 10:15 a.m. Contact Claudia Manca, 327-8103.*

**MONDAY, MARCH 15**

11:00 a.m.-12:30 p.m. **Grauzone, a Gene Required for *Drosophila* Early Development, Encodes a C2H2-type Zinc-finger Protein.** Bin Chen, Dept. of Pharmacological Sciences, SUNY- Stony Brook. Seminar. HHMI Conference Room. *Contact Ulrike Gaul, 327-7621.*

4:00 p.m.-5:30 p.m. **NMR Structural Studies of Membrane Proteins.** Stanley Opella, Dept. of Chemistry, U. of Pennsylvania. NMR Works in Progress Seminar. **305 Weiss.**

4:30 p.m. **Functional Renal MR Imaging.** Vivia S. Lee, Assistant Professor of Radiology, Director of Cardiothoracic MR Imaging, N.Y.U. School of Medicine. PBMM Research Seminar. **Weill Auditorium, CUMC, 1300 York Ave.** *Contact Daniel R. Nussenzevig, 746-6282.*

**TUESDAY, MARCH 16**

4:00 p.m. **Signaling Cascades that Mediate Early Development of the Cerebral Cortex.** Pat Levitt, Professor and Chairman, Dept. of Neurobiology, U. of Pittsburgh School of Medicine. Progress in Neuroscience Seminar. **Weill Auditorium, CUMC, 1300 York Ave.** *Reception 3:45 p.m.*

4:00 p.m. **A Combinatorial Problem Related to Avoided and Under-represented Strings in Bacterial Complete Genomes.** Bai-lin Hao, Institute for Theoretical Physics Academia Sinica. Center for Studies in Physics and Biology Seminar. **B Level Conference Room, Smith Hall Annex.** *Tea 3:30 p.m. Contact Matthew Turner, 327-8184.*

**WEDNESDAY, MARCH 17**

11:00 a.m. **Mechanisms and Functions of Smad Proteins in TGFbeta Signal Transduction.** Pamela Hoodless, The Hospital for Sick Children, Toronto. Weekly Research Seminar. **305 Weiss.** *Contact Shauna Selyi, 327-8655.*

12:00 p.m. **Antigen Dependent Differentiation in Human B Cells.** Paolo Casali, Professor, Dept. of Immunology and Pathology, CUMC. Clinical Research Seminar. **110B Nurses Residence.**

**THURSDAY, MARCH 18**

11:00 a.m. **Lindbergh Perfusion Pump and Organ Culture.** Theodore Malinin, Professor of Orthopedics and Rehabilitation, and Tissue Bank Director, U. of Miami School of Medicine. **110B Nurses Residence.**

12:00 p.m. **PI 3-kinase Integrates Signal Transduction and Membrane Traffic.** Silvia Corvera, Molecular Medicine, U. of Massachusetts. Biochemistry Lecture. **E-115 CUMC, 1300 York Ave.**

3:45 p.m. **Transducing Signals.** David Baltimore, President, Caltech. Paul A. Marks Distinguished Lecture Series in Cancer Biology. **Auditorium, Rockefeller Research Laboratories, MSKCC, 430 East 67th St.** *Tea 3:15 p.m. in RRL 104.*

4:00 p.m. **The Matrix Metalloproteinases in Normal and Neoplastic Processes.** Lynn Matrisian, Professor and Interim Chair of Cell Biology, Vanderbilt U. School of Medicine. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** *Tea 3:45 p.m. Contact Rosanna Martinez, 570-3357.*

8:00 p.m. **Visualizing Antigen Recognition.** Mark Davis, Professor of Microbiology and Immunology, Investigator, HHMI, Stanford U. School of Medicine. Harvey Society Lecture. **Casparry Auditorium.**

**FRIDAY, MARCH 19**

7:30 a.m.-8:30 a.m. **Metabolic Causes of Exercise Intolerance, Myalgia and Myoglobinuria.** Salvatore DiMauro, Lucy G. Moses Professor of Neurology, Dept. of Neurology, Columbia U. HSS Distinguished Lecture. **2nd Floor Conference Room, HSS, 535 East 70th St.**

2:00 p.m. **Mechanical Unzipping of Double-stranded DNA.** François Heslot, L.P.M.C. Laboratory, École Normale Supérieure. Center for Studies in Physics and Biology Seminar. **B Level Conference Room, Smith Hall Annex.** *Tea 3:30 p.m. Contact Matthew Turner, 327-8184.*

**MONDAY, MARCH 22**

12:30 p.m.-1:30 p.m. **Dissecting the B7-CD28/CTLA-4 Costimulatory Pathway Using Gene Targeting Approaches.** Arlene Sharpe, Associate Professor of Pathology, Harvard Medical School. Immunology Lecture. **Second Floor Conference Room, HSS, 535 East 70th St.**

4:00 p.m. **Studies on the Germ Line Cells of Vertebrates.** Christopher Wylie, Harrison Chair of Development and Genetics, and Director, Developmental Biology Center, U. of Minnesota. Cell Biology and Genetics Seminar. **Weill Auditorium, C-200 CUMC, 1300 York Ave.**

**TUESDAY, MARCH 23**

11:00 a.m. **Aggresomes: a Cellular Response to Protein Misfolding.** Ron Kopito, Professor, Dept. of Biological Sciences, Stanford U. Weekly Research Seminar. **301 Weiss.** *Contact Sanford Simon, 327-8130.*

3:00 p.m. **Human Whole Genome Polymorphism Screens: Technology and Applications.** James Weber, Director, Center for Medical Genetics, The Marshfield Medical Research Foundation. Starr Center for Human Genetics Seminar. **301 Weiss.** *Contact Emily Gegeliya, 327-7387.*

4:00 p.m. **Mitochondria and the Control of Neuronal Excitotoxicity.** David Nicholls, Professor of Neurochemistry, Dept. of Pharmacology and Neuroscience, Dundee U., Scotland. Progress in Neuroscience Seminar. **Weill Auditorium, CUMC, 1300 York Ave.**

4:00 p.m. **Computing with RNA: From Ribozyme and Genetic Code Origins to Chess.** Laura Landweber, Professor, Dept. of Ecology and Evolutionary Biology, Princeton U. Center for Studies in Physics and Biology Seminar. **B Level Conference Room, Smith Hall Annex.** *Tea 3:30 p.m. Contact Matthew Turner, 327-8184.*

**WEDNESDAY, MARCH 24**

12:00 p.m. **Immune Dysfunction in SLE: Nature or Nurture.** Westley Reeves, Associate Professor of Medicine, Microbiology and Immunology, U. of North Carolina School of Medicine. Clinical Research Seminar. **110B Nurses Residence.**

**THURSDAY, MARCH 25**

12:00 p.m. **Field and Laboratory Studies of Potential Endocrine Disruptors Using a Sentinel Species, the Freshwater Turtle, *Chrysemys Picta*.** Ian Callard, Professor of Biology, Dept. of Biology, Boston U. Endocrinology and Reproductive Biology Seminar. **301 Weiss.**

2:00 p.m. **Crystallographic Studies of Proteins Involved in DNA Replication.** Gabriel Waksman, Associate Professor, Dept. of Biochemistry and Molecular Biophysics, Washington U. School of Medicine. Pels Family Center for Biochemistry and Structural Biology Seminar. **301 Weiss.** *Contact Ronnie Gulli, 327-8836.*

4:00 p.m. **T Cell Apoptosis and HIV Pathogenesis.** Eric Verdin, Professor of Medicine, Gladstone Institute of Virology and Immunology, U.C.-San Francisco. LFKRI Research Seminar. **Lower Level Conference Room, New York Blood Center, 310 East 67th St.** *Tea 3:45 p.m. Contact Rosanna Martinez, 570-3357.*

4:00 p.m. **Phytochemicals and Phyto-medicines: The Use of Herbals and Botanicals in Cancer Prevention.** Michael Wargovich, Professor, Dept. of Pathology, and Director, Division of Basic Research, South Carolina Cancer Center. CNRU Special Nutrition Lecture. **F-539 NYPH-CUMC, 1300 York Ave.**

## The Arts and Other Events

**FRIDAY, MARCH 12**

12:00 p.m. **Tri-institutional Noon Recitals.** Cavani String Quartet performing works by Boccherini and Brahms. **Casparry Auditorium.** *Free admission. Open to RU/CUMC/NYPH/MSKCC community and guests.*

## THE ROCKEFELLER UNIVERSITY Friday Lectures and Thesis Presentations

Events are held in Casparry Auditorium at 3:45 p.m. and tea is served in Abby Aldrich Rockefeller Lounge at 3:15 p.m., unless otherwise noted. All are welcome.

**FRIDAY, MARCH 12**

**Complex Molecular Machines and the Regulation of Eukaryotic Gene Transcription.** Robert Roeder, Professor, RU.

**MONDAY, MARCH 15**

**Thesis Presentation: Scaling Violation in Inclusive Jet Production.** Alexander Akopian, Graduate Fellow, RU.

**FRIDAY, MARCH 19**

**Poking and Peeking at Cell Signaling with Photons and Designed Molecules.** Roger Tsien, HHMI, Depts. of Pharmacology, Chemistry and Biochemistry, U.C.-San Diego.

**FRIDAY, MARCH 26**

**Wiring up the Brain: Genes, Growth Cones, and Synapses.** Corey Goodman, HHMI, Dept. of Molecular and Cell Biology, U.C.-Berkeley.

**FRIDAY, MARCH 19**

12:00 p.m. **Tri-institutional Noon Recitals.** Amati String Quartet performing works by Shostakovich and Beethoven. **Casparry Auditorium.** *Free admission. Open to RU/CUMC/NYPH/MSKCC community and guests.*

**TUESDAY, MARCH 23**

7:30 p.m. **Rockefeller University Film Series.** *Guantanamo.* Cuba/Spain. Spanish with English Subtitles, Color, 1994. Directed by Tomás Gutiérrez. **Casparry Auditorium.** *Free admission. Open to RU/CUMC/NYPH/MSKCC community and guests.*

**SATURDAY, MARCH 27**

5:00 p.m. **Concert.** Möbius String Quartet. RU students performing works by Janacek, Shostakovich and Brahms. **Casparry Auditorium.** *Free admission, no tickets required.*

The *Calendar of Events* is published Fridays throughout the academic year. Deadline for submitting events is 12:00 p.m. Tuesday. Events submitted by the Tuesday two weeks before the event will be announced in two consecutive calendars—space permitting.

Events may be submitted via e-mail to [rucal@rockvax.rockefeller.edu](mailto:rucal@rockvax.rockefeller.edu), through the World Wide Web (<http://www.rockefeller.edu/rucal/ru-entry.html>), or by fax (212-327-7876). Contact Kate Flynn (212-327-7900) for more information.

To reserve space for on-campus events, e-mail [roomres@rockvax.rockefeller.edu](mailto:roomres@rockvax.rockefeller.edu) or contact Julie Ranton-Francis via fax (212-327-7876) or phone (212-327-8072). Items will not be listed in the calendar without a previously confirmed room reservation.

To subscribe to the *Calendar of Events* mailing list, send e-mail to [macjorndomo@comm.rockefeller.edu](mailto:macjorndomo@comm.rockefeller.edu) with SUBSCRIBE RUCAL-L <Your Name> in the body of the message.

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Around campus:

## Malinin to discuss Lindbergh perfusion pump and recent perfusion studies

A marvel of 1930s instrumentation sits in the instruments display in the lower level of Caspary Auditorium: a perfusion pump, built by aviator Charles A. Lindbergh in the laboratory of RU researcher and Nobel laureate Alexis Carrel. With this apparatus, for the first time, whole organs could be kept alive and studied outside the body. The pump and continuing developments in organ culture that it initiated will be the subject of a lecture by Theodore I. Malinin, on Thurs., March 18 at 11 a.m. in Nurses Residence 110B.

Malinin is professor of Orthopedics and Rehabilitation and Tissue Bank director at the University of Miami School of Medicine. The author of a biography of Carrel, Malinin met Lindbergh at the Naval Medical Research Institute in the 1960s. Researchers there were attempting to duplicate Carrel's 1930s organ perfusion experiments and called on Lindbergh for help. Lindbergh later worked in Malinin's laboratory to develop a new version of the pump.

Lindbergh built the first perfusion pump after a mutual acquaintance introduced him to Carrel in 1930.



Theodore I. Malinin (far right) will discuss the Lindbergh perfusion pump on Thurs., March 18. Malinin is pictured above with Charles Lindbergh (center right) and two military officers; a working model of the perfusion pump can be seen in the background.

Carrel invited the aviator (an able engineer with an interest in biology) to work in his laboratory. Five years later, with the assistance of RU glassblower Otto Hopf, Lindbergh had designed and built an apparatus that the popular press dubbed an "artificial heart"; it

could move oxygenated fluid through an organ in pulses, like heartbeats, under sterile conditions.

Earlier efforts at organ perfusion had failed because of bacterial infection. The first organ to be successfully cultured was a cat thyroid, kept functioning for 18 days in 1935. Between 1935 and 1938, dozens of the pumps were built, and Carrel performed nearly 1,000 perfusion experiments, mainly on thyroid glands.

In 1938, Carrel and Lindbergh published a book about the work, titled *The Culture of Organs*. Although interest in the device waned after Carrel left the Rockefeller Institute in 1939, their techniques led the way to current research using organ perfusion in surgical transplants.

## Potpourri

### Save the date

Thurs., April 22, will be Take Your Child to Work day at Rockefeller University. The university will have age-appropriate activities for children ages 7 and up. *News&Notes* will provide more information in future issues.

### Lottery for cottages

Spring isn't far away, so the Housing Office is making plans to open the university's two cottages in upstate New York.

The cottages, located 53 miles from campus, are near Bear Mountain and West Point. They offer a rustic retreat on 10 wooded acres sloping toward the Hudson River. The MacInnes Cottage sleeps six in three bedrooms, and Hostage Cottage accommodates four in two bedrooms.

The deadline for entering the annual lottery for reservations is Fri., March 19, at 3 p.m. Reservation request forms are stocked in the Founder's Hall kiosk bin, just right of the main entrance.

The daily rate for the cottages is \$40, with a two-night minimum stay, for weekdays (Sun. through Thurs.); the rate is \$85 for the weekend (Fri. and Sat.). Amenities include stone fireplaces, screened porches, modern kitchens and bathrooms with showers. Blankets, utensils and phone service are provided. The living rooms contain materials on nearby hiking and other activities in the area, as well as guest books for visitors to sign.

Guests are asked to leave the cottages clean for the next people.

Complete information on the use of the cottages is posted in Founder's Hall. The Housing Office will draw requests and issue confirmations after Thurs., April 1.

### RU events hotline

Trying to find information about an upcoming event at RU? The university has a phone number with information about RU events, including the Peggy Rockefeller Concerts, Tri-institutional Noon Recitals, public lectures and symposia, along with directions to the campus. Call 327-7007.

### Music Room

The music room on the first floor of Caspary Hall is available for use. The room, equipped with a Steinway grand piano, music stands and chairs, may be reserved for time slots of one hour during the day or evening. A sign-up sheet is available on the door outside the music room.

### Above the law?

If you bring your dog to campus, please remember to abide by the city's pooper-scooper laws.

## AwardsCorner

Assistant Professor **Tom Muir** was selected to receive a 1999 Burroughs Wellcome Fund New Investigator Award in the Toxicological Sciences. Muir was also selected as an Alfred P. Sloan Research Fellow by the Alfred P. Sloan Foundation.

## Music news:

### Juilliard/RU concert

On Tues., March 30, the Juilliard/RU concert series "20th Century Retrospectives" will present a program devoted to the string quartet in the 20th century. Members of the Lark Quartet will perform works by Webern, Ravel, Gershwin and Shostakovich. The concert will be held in Caspary Auditorium at 8 p.m.; a lecture by Arnold Steinhardt will precede the concert at 6:45 p.m. Tickets are \$25 (\$15 for students). For more information, call the RU events hotline, x7007.

### Tri-institutional Noon Recitals

The Cavani String Quartet will perform at the Tri-institutional Noon Recitals today (March 12). The quartet, named after the 19th-century violin maker Vincenzo Cavani, has appeared at the Carnegie Hall Centennial Series, Alice Tully Hall, the Kennedy Center and other major concert stages. They also received a 1998 ASCAP-Chamber Music America Award for Adventurous Programming of Contemporary Music. Their recital takes place in Caspary Auditorium. Admission is free for the tri-institutional community and guests.



The Cavani String Quartet will perform at the Tri-institutional Noon Recitals today (March 12).

## RU staff members introduce "Microbes at the Movies" at the Museum of Natural History

On Sun., March 7, Rockefeller Archive Center Director Darwin Stapleton delivered the introduction to the film *The Sardinia Project*. The film is part of the American Museum of Natural History's "Microbes at the Movies" series, which accompanies the current "Epidemic!" exhibition. The 1948 film documents the Rockefeller Foundation's administration of the attempt to eradicate mosquitos from Sardinia, in order to eliminate malaria from the island. Stapleton also facilitated a discussion of the film after the screening.

Another RU employee, Public Affairs newcomer Lynn Love, delivered the introductory lecture for the AMNH microbes program on tuberculosis on Sat., March 6. Love was asked to stand in for Lisa Cartwright, humanities professor at the University of Rochester and author of the book, *Screening the Body: Tracing Medicine's Visual Culture*. Cartwright was unable to make it to New York due to severe weather in Rochester. Four films from the anti-tuberculosis campaign of 1938 to 1950 were screened as part of the program.

Love, a former student of Cartwright's, said, "It would have been a richer experience had Lisa been present, but I'm glad I could help out by delivering her prepared lecture and fielding questions after the screenings."

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

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# Rockefeller lab identifies a protein whose absence leads to cell death

BY LISA STILLMAN

In the world of cells, telomeres are a matter of life and death. These complex bits of DNA at the edge of chromosomes not only protect the chromosomes but also regulate the cell's internal clock, telling a cell when to stop dividing and when to die. Every time a cell divides, a bit of the telomere is lost, and after about 50 divisions, the cell usually dies. "What's really interesting," notes RU Professor Titia de Lange, "is that if scientists take, say, skin cells from an infant and comparable cells from an adult, the infant cells go through more divisions. This means that what researchers are observing in vitro probably corresponds to what is actually happening inside the body." Intriguing recent experiments have also shown that if scientists prevent the shortening of the telomeres, a cell can live almost indefinitely. This is an exciting time to be studying telomeres—a field that has expanded exponentially in the last decade.

In recent groundbreaking publications, de Lange's lab has found new evidence of how two human proteins, called TRF1 and TRF2 (short for TTAGGG repeat binding factors), are important in the life of telomeres.

"TRF1 and TRF2 seem to be exclusively telomeric proteins, meaning they bind here and nowhere else," explains Postdoctoral Fellow Jan Karlseder, de Lange's co-author (along with Dominique Broccoli of Fox Chase Cancer Center and Yumin Dai and Stephen Hardy of Cell Genesys) of the lab's most recent paper, published last month in *Science*.

"Because these TRF proteins are telomere-specific," Karlseder says, "we had the idea that if we messed with the proteins, something should happen to the telomere." In 1995-96 the de Lange lab began by studying TRF1, the first of the proteins to be cloned; they manipulated TRF1 in viral DNA, which they then used to infect other cell types they wanted to study. The lab had assumed that TRF1 was critical to the life of the



Professor Titia de Lange (left) and Postdoctoral Fellow Jan Karlseder are coauthors of a *Science* paper that describes the key role of a protein called TRF2 in cell death.

cell and that without it the cell would die. Instead, TRF1 turned out to be responsible for telomere length and the interaction with telomerase (the protein that specifically replicates telomeres), but TRF1 was not critical for determining whether the cell lived or died. "That was really surprising," says Karlseder.

When TRF2 was cloned by Biomedical Fellow Agata Smogorzewska and Broccoli, the lab took basically the



LEIF CARLSSON

same approach to test the function of that protein. In two separate studies, de Lange's lab found that TRF2 plays a key role in protecting the telomeres and that the loss of TRF2 can lead to one of two possible solutions: senescence or cell death.

## Professor Titia de Lange's lab has shown for the first time that telomere shortening or telomere malfunctioning can lead not only to senescence but to actual cell death.

In the first study, published last year in *Cell*, Postdoctoral Fellow Bas van Steensel, Smogorzewska and de Lange made the first observation that when TRF2 is taken off the telomeres, the chromosomes start fusing together. Then, a few days after the loss of TRF2, the cells stop dividing and show a phe-

notype that looks like senescence. "The cells without TRF2 were not dead—they continued to metabolize and become very large, but they never divide again. They are dead in a Darwinian sense, leaving no descendants, but alive thermodynamically," de Lange says.

The tumor cells the lab used in these TRF2 experiments, however, lacked a functioning p53 channel—a checkpoint that senses such problems as DNA dam-

age, stress, incomplete DNA recognition and incomplete mitosis. "The p53 protein is an extremely complex, very central protein," says de Lange, so it was important to determine what would happen in cells whose p53 channel was working.

In their new *Science* paper, the lab shows that when TRF2 is taken off the chromosome in p53-positive cells, the telomeres send a very strong DNA damage response through the p53 channel. In this case, the corrupted telomeres seem to signal to p53 that it has suffered DNA damage, and this initiates

the cell's suicide mechanism. "So this time the catastrophe really happened," Karlseder says. "It's the first time that we've shown that telomere shortening or telomere malfunctioning can lead not only to senescence but to actual cell death."

For future projects, the lab plans to test whether the response in the p53-negative cells is actually senescence, and they also plan to do a knockout of TRF1 and TRF2 in mice.

The freedom that RU provides researchers has been helpful to de Lange, who was among the earliest researchers on telomeres. ("When I was in graduate school," she notes, "I had a journal club, and in one meeting I actually discussed the whole telomere literature—all five papers.") de Lange says that Rockefeller "actually took a huge risk" by hiring her, because she wanted to work on telomeres in mammalian cells at a time when no one else was doing that. As she looked at faculty positions after her postdoctoral work with Harold Varmus at UCSF, other universities told her that it was fine to work on telomeres, but that she ought to do it in yeast because that was the standard. It turned out, though, that yeast wasn't necessarily the best model. de Lange notes, "There are interesting things going on in a mammalian system—such as senescence, apoptosis and cancer—that do not occur as such in yeast."

de Lange enjoys taking risks and being surprised in the lab—as she was with the TRF1 results. "I really enjoy being wrong, because it's only when you turn out to be wrong that you fall into a whole new understanding that is conceptually interesting. It's very boring to be right all the time."

The above research was supported by National Institutes of Health, the International Human Frontier Science Program, the Rita Allen Foundation, the Monique Weill-Caulier Trust: Irma T. Hirschl Career Scientist Award, and the Burroughs Wellcome Fund. The work of Dominique Broccoli was supported by a Merck fellowship, and the work of Jan Karlseder and Bas van Steensel was supported by the International Human Frontier Science Program fellowships.

## Purnell Choppin, president of Howard Hughes Medical Institute, is speaker at next Cohn Forum

The role for private support of biomedical research is the topic of this month's Zanol A. Cohn lecture. Purnell Choppin, president of the Howard Hughes Medical Institute, will discuss the differing roles of private and governmental support of biomedical research, historically and currently.

Choppin spent 28 years at The Rockefeller University, where he was Leon Hess Professor of Virology, vice president of academic programs and dean of graduate studies before he went to HHMI in 1985.

In addition to his research on viral structure, replication, interaction

with cell membranes and the mechanisms by which influenza, parainfluenza and measles viruses produce cell injury and disease, Choppin is a committed policy advisor and administrator.

He has been awarded the Howard Taylor Ricketts Award from the University of Chicago and the Selman A. Waksman Award for excellence in microbiology from the National Academy of Sciences. Choppin has also been awarded numerous honorary degrees and served as a member of the Advisory Council of the National Institute of Allergy and Infectious

Diseases and member of the AIDS Advisory Committee of the National Institutes of Health.

The Cohn Forum is a series of colloquia on issues in health and biomedicine. Choppin's talk on Mon., March 15 will begin at 5:30 p.m. in the Abby Dining Room, preceded by a sherry reception at 5 p.m. in the Abby Aldrich Rockefeller Lounge. Admission is free and all are welcome.

*News&Notes* will publish excerpts of Choppin's talk later this month.

The Cohn Forum's website is <http://www.rockefeller.edu/pubinfo/cohn.html>.



Purnell Choppin, president of the Howard Hughes Medical Institute, will speak at the next Cohn Forum on Mon., March 15.