

9-15-1995

## NEWS AND NOTES 1995, VOL.6, NO.1

The Rockefeller University

Follow this and additional works at: [http://digitalcommons.rockefeller.edu/news\\_and\\_notes\\_1995](http://digitalcommons.rockefeller.edu/news_and_notes_1995)

---

### Recommended Citation

The Rockefeller University, "NEWS AND NOTES 1995, VOL.6, NO.1" (1995). *News And Notes 1995*. Book 24.  
[http://digitalcommons.rockefeller.edu/news\\_and\\_notes\\_1995/24](http://digitalcommons.rockefeller.edu/news_and_notes_1995/24)

This Book is brought to you for free and open access by the The Rockefeller University News and Notes at Digital Commons @ RU. It has been accepted for inclusion in News And Notes 1995 by an authorized administrator of Digital Commons @ RU. For more information, please contact [mcsweej@mail.rockefeller.edu](mailto:mcsweej@mail.rockefeller.edu).

## Leading biophysicist to join faculty in 1996

Roderick MacKinnon, professor in the department of neurobiology at Harvard Medical School, has accepted an appointment as professor at Rockefeller and will join the faculty in fall 1996.

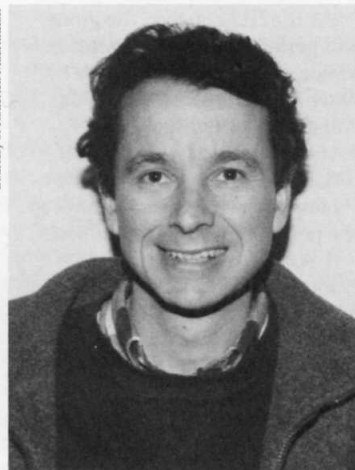
"Roderick MacKinnon is a neurobiologist working on transport of ions through cell membranes. His elegant work has added significantly to our understanding of a fundamental biological process," said President Torsten Wiesel. "We are very fortunate that he is joining our faculty."

MacKinnon studies how the structure of ion channels enables them to selectively control the flow of electrically charged atoms of

potassium, sodium, or calcium across the cell membrane. He combines electrophysiological measurements of channel function with the molecular genetic technique of site-specific mutagenesis. In his Friday lecture at Rockefeller in December 1994, MacKinnon presented some of his recent work. He found that a scorpion toxin, a peptide with a well-known molecular structure, binds extremely tightly to the extracellular entry of potassium channels. By examining this attachment, he further elucidated the structure of this critical region of the channel.

MacKinnon earned an M.D. from Tufts University School of Medicine in 1982. He served as medical house officer in internal medicine at Beth Israel Hospital, Harvard Medical School. In 1985, he began an NIH Postdoctoral Fellowship, which he completed at Brandeis University. In 1989, MacKinnon returned to Harvard Medical School as assistant professor in the department of cellular

Courtesy of Roderick MacKinnon



Roderick MacKinnon studies ion channels in cell membranes.

and molecular physiology. He transferred to the department of neurobiology in 1991, became associate professor in 1992, and professor in 1995.

MacKinnon is a member of Alpha Omega Alpha, the medical honor society. He is a Pew Scholar in the Biomedical Sciences and a recipient of the McKnight Scholars Award and the Biophysics Young Investigator Award.

## Conference at RU focuses on biomolecules

Nearly 400 scientists from around the world gathered at Rockefeller this week for a structural biology conference honoring the 100th anniversary of Louis Pasteur's death. The four-day meeting, "Stereospecificity and Molecular Recognition," included Nobel Prize winners and other experts discussing the form and function of biological molecules.

The RU conference was one of six held this year worldwide—the only one in the U. S.—to celebrate The Year of Louis Pasteur. UNESCO and the European Commission sponsored the six meetings, which also received support from 24 organizations.

Each of the six conferences addressed progress in the fields of Pasteur's major discoveries, said Maxime Schwartz, director general of the Institut Pasteur. Speaking Tues., Sept. 12 at the

See **Conference**, page 2

### Save the date:

**Drug company executive to talk on forces shaping healthcare Sept. 26**

George Poste, president of research and development at SmithKline Beecham Pharmaceuticals, will speak on "Economics, Informatics, Genetics, Ethics: The New Forces Shaping the Evolution of Healthcare" at the first Zankov A. Cohn Forum on Health Affairs of the academic year, which will take place Tues., Sept. 26 at 5:30 P.M. in the Abby Aldrich Rockefeller dining room. Look for more information in next week's *News&Notes*.

## University fund-raising reaches record high in 1994-95

Rockefeller received \$38.4 million in gifts and pledges during fiscal year 1994-95, making it the most successful fund-raising year in the history of the institution.

"Through the generosity of our trustees and friends, our Campaign for Faculty Development, which aims to raise \$82 million in private support during the next three years, has had an auspicious beginning," said President Torsten Wiesel.

"The funds we seek are essential to maintain the excellence of our current scientific programs while implementing the goals of the Academic Plan and bringing 10 to 15 new heads of laboratory to campus. We are gratified by the commitment of the extended Rockefeller community and their strong belief in our scientific mission."

The Board of Trustees set ambitious goals for the three years of the

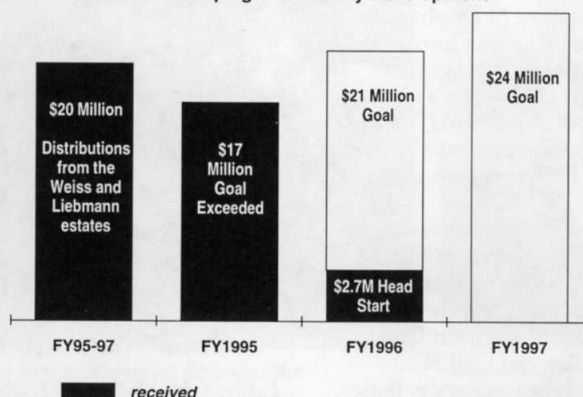
campaign: \$17 million in FY95, \$21 million in FY96, and \$24 million in FY97, for a total of \$62 million in new support. The additional \$20 million of the campaign goal comes from two generous bequests received from individuals who were longtime university friends—Benjamin Weiss and Dolores Z. Liebmann. Rockefeller received most of these estate funds in FY95.

The university raised \$19.7 million in new gifts and pledges during the 1995 fiscal year, topping the \$17 million goal set for the first year of the campaign. The additional funds have been applied toward the 1995-96 goal.

A record number of donors contributed to the banner fund-raising year. Six trustees pledged leadership gifts of \$1 million each. Members of The Rockefeller University Council were responsible for more than \$2.4 million in gifts designated for research in the neurosciences, infectious diseases, and other areas. In addition, the Council set a new record in FY95

Designed by Karen Smith

\$82 Million Campaign for Faculty Development



Note: \$2.7 million raised in FY95 has been applied toward FY96

2 Evening concert

3 Control proteins

4 Summer students

See **RU fund-raising**, page 2

## Classical quartet to sound first notes in evening concert series

The Shanghai Quartet opens the 37th season of The Rockefeller University Concerts Thurs., Sept. 28 with a program of quartets by Brahms, Hovhannes, and Mozart.

In *The New York Times* review of its most recent Lincoln Center performance, the foursome of two violins, viola, and cello earned praise for its "animated intelligence" and "sweetly glowing tone reminiscent of grand old European quartets."

Established in 1983 by one American and three Chinese musicians, the group is ensemble-in-residence at the University of Richmond, Virginia. In 1994, its debut release of works by Grieg and Mendelssohn earned critical

acclaim. A forthcoming release will feature works for strings and flute with Eugenia Zukerman.

At the RU concert, the group will perform Mozart's Quartet in F Major, K. 590, followed by Hovhannes's Quartet No. 1, Op. 8, "Jupiter." They will close the evening with Brahms's Quartet in B-flat Major, Op. 67. Associate Professor George Reeke will recap the performance in *News&Notes*.

Taking place in Caspary Auditorium, the concert begins at 8:00 P.M. A buffet supper begins at 6:00 P.M. in Abby Aldrich Rockefeller Dining Room. For information, contact Cathy Rogers, concert administrator, x8437.



The Shanghai Quartet, which has performed at Tanglewood, Lincoln Center's Mostly Mozart Festival, and venues around the world, opens the concert series Thurs., Sept. 28.

## Conference celebrates Louis Pasteur

(continued from page 1)

opening session of the RU meeting, Schwartz noted the international celebration is fitting because Pasteur was a missionary for science, working with researchers from many countries.

Nobel laureate Arthur Kornberg, of Stanford University, presented the keynote address, "Coalescence of the Biological Sciences." Excerpts will appear in *News&Notes* next week.

On Wed., Sept. 13, Professor John Kuriyan of RU and the Howard Hughes Medical Institute (HHMI) chaired a session on molecular recognition and response, and the Institut Pasteur's Henri Buc chaired a session on design of biomolecules.

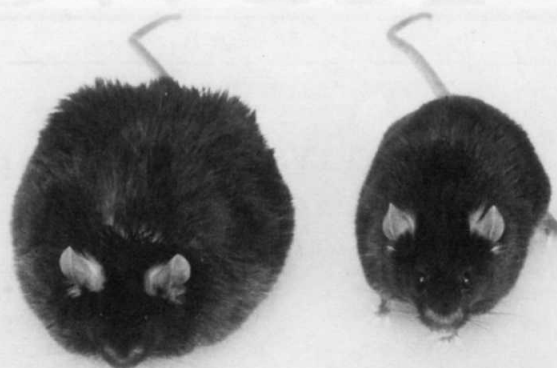
Thursday morning, Sept. 14.,

Professor Stephen Burley, of RU and HHMI, chaired a session focusing on macromolecular assemblies. After lunch, the researchers heard presentations on RNA biology in a session chaired by Dinshaw Patel of the Sloan-Kettering Institute.

The symposium's last day (today, Fri., Sept. 15) features a session called "A Chiral World," chaired by Rockefeller Professor William Agosta. Burley presents closing remarks.

Abstracts from the conference are available from the Office of Public Affairs, x8967, and on the RU home page: <http://www.rockefeller.edu/>. The Institut Pasteur, Rockefeller, and UNESCO organized the conference. Burley, Buc, Peter S. Kim of MIT and HHMI, Kuriyan, and Jean-Marie

## Of mice and media



While they're not Mickey and Minnie, this pair is recognized around the world thanks to media coverage of the July 28 report in *Science*, by Professor Jeffrey Friedman, biomedical fellow Jeff Halaas, research associate Ketan Gajiwala, Professor Stephen Burley, and others. The team documented that daily injections of the protein encoded by the obese (ob) gene, leptin, reduced the weight of mice with defective ob genes by curbing food intake and increasing energy expenditure. Of the two ob mice shown here, the one on the right was treated with leptin while the one on the left received a saline solution. After four and a half weeks of leptin therapy, the untreated mouse weighed approximately 67 grams, and the treated mouse weighed in at around 35 grams. *News* accounts aired on radio worldwide. Television and print reports appeared across North America, South America, and Europe. Burley, Friedman, and Gajiwala hold Howard Hughes Medical Institute appointments.

## RU fund-raising has banner year

(continued from page 1)

with \$900,000 in unrestricted annual gifts. The Committee on Trust and Estate Gift Plans generated \$2.2 million in private support, and a record 80 alumni contributed.

"These are ambitious goals, and we are fortunate to have the active involvement of volunteers who believe in the university to help us in realizing them," said Wiesel. "The importance of private support cannot be overestimated, especially as government support for basic research diminishes."

"Successful fund-raising is always a team effort," commented Marnie Imhoff, vice president for development. "At Rockefeller, trustees, staff, faculty, and countless volunteers and friends work together effectively and enthusiastically on behalf of the institution. The critical role that the faculty plays in our outreach efforts cannot be emphasized enough. By speaking with our guests at both informal meetings and more formal events, they help us develop new friends and make the work of the university known to a wider audience."



Maxime Schwartz, director general of the Institut Pasteur, welcomed participants to the conference Tues., Sept. 12.

Lehn of the Université Louis Pasteur arranged the scientific program.

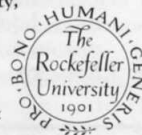
*News&Notes* is published each Friday throughout the academic year by The Rockefeller University, 1230 York Avenue, New York, NY 10021. Phone: 212-327-8967.

Torsten Wiesel, President  
Ingrid Reed,  
Vice President for Public Affairs and  
Corporate Secretary  
Marion E. Glick, Director of  
Communications

Kay Locitzer, Editor  
Joseph Bonner, Assistant Editor  
Robert Reichert, Photography  
Media Resource Service Center, Processing

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

The Rockefeller University is an equal opportunity/affirmative action employer.





# Research on homeodomains defines structure of cooperation

by Susan Blum

In the complex journey from fertilized egg to multicellular organism, homeoproteins lead the way, determining crucial decision points in body formation and cellular differentiation. The development of an animal's body regions, the formation of its limbs, the construction of its eyes—all this, and much more—is due to the action of homeoproteins, transcription factors that switch genes on or off by contacting control regions in DNA. The proteins are named for their homeodomain region, a highly conserved 60-amino acid motif that binds to DNA by means of a recognition helix.

By the late 1980s researchers knew that almost all homeodomains recognize the same four-base core sequence of DNA—TAAT. This uniformity posed a considerable challenge for scientists trying to fathom how homeoproteins work. "We had to find out what was conferring specificity," recalled Associate Professor Claude Desplan. That is, researchers had to discover why each homeoprotein activates just one particular gene, even though all recognize the same DNA motif.

Desplan tackled this problem upon his arrival at Rockefeller in 1988, fresh from a postdoc during which he had shown that homeodomains bind DNA. A year later, Jessica Treisman, then a graduate student in the Desplan lab, made a start on the answer by showing that the ninth amino acid in the recognition helix is important for specificity: change that amino acid, and the helix recognizes a different two bases directly following the TAAT motif.

But the puzzle was still not completely solved. For one thing, many homeoproteins with distinctly different biological functions possess the same amino acid at position

nine in the recognition helix. For another, extending the DNA-binding site length from four to six bases is not enough to ensure specificity because, as Desplan explains, "You can find any given six-base sequence almost anywhere in the genome."

## Cooperation is key

Clearly, additional strategies were needed to provide all the requisite specificity. For homeoproteins (as for many other transcription factors), it turns out that cooperation with other protein regions is the key. Some homeoproteins contain another, separate DNA-binding domain that teams up with the homeodomain to recognize a larger—and thus more specific—DNA target. Other homeoproteins interact with a second protein to create *dimers*—two molecules that physically join together in ways that enable their DNA-binding regions to recognize longer stretches of DNA. And some homeoproteins have the potential to use both approaches.

Such is the case with various members of the Paired class of homeoproteins, some of which contain a second conserved region, called the Paired domain. In 1991, Treisman showed that the Paired domain can bind DNA. In the years since then, other students, some recently graduated, have studied how Paired-class proteins work.

In 1993 David Wilson, who recently presented his thesis, made the surprising discovery that homeodomains from two separate Paired-class proteins can bind cooperatively to DNA. In all previously known cases of homeoprotein cooperation, the molecular interactions that brought DNA-binding sites together occurred in protein regions outside the homeodomain. "This case is the

only one we know of where all the information for the interaction is in the homeodomain itself," Wilson said.

Wilson's biochemical and genetic studies showed that the two homeodomains bind to a palindromic DNA site, one in which the two halves of the DNA sequence (in this case, two TAATs) are identical to one another when read on complementary DNA strands. He found that these sites are separated by a spacer of either two or three base pairs, depending upon the homeoprotein involved.

Having reached this point in his explorations, Wilson decided to investigate the DNA-protein interactions via x-ray crystallography, a method that reveals the 3-D position of every atom in a molecule and thereby discloses its shape. At the start of his graduate career, Wilson recalled, "I had no intention of becoming a crystallographer. But I'd worked on this problem for quite some time, and after a while I just really wanted to see what it looked like."

## Lack of structure yields structure

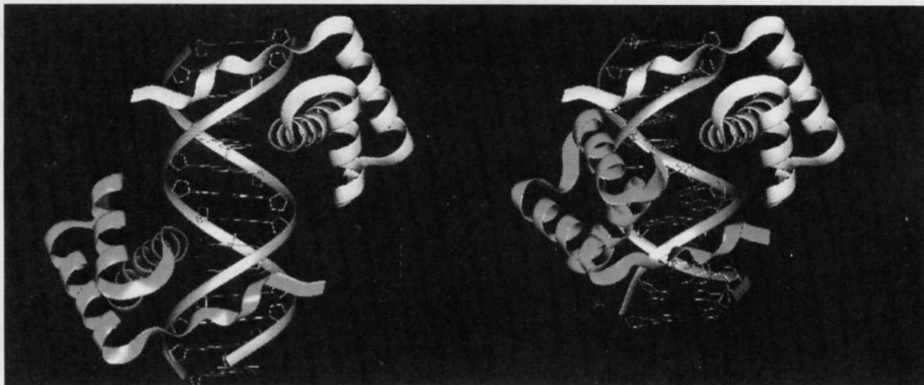
Rockefeller's unstructured organization allowed him to pursue his curiosity as far as he wanted to take it. Working in the lab of John Kuriyan, Wilson got training in crystallography and put his skills to work to solve the structure of two Paired-class homeodomains bound to a palindromic DNA site with a three base spacer. The results—the first view ever of two homeodomains bound cooperatively to DNA—appeared in *Cell* on Sept. 8, 1995.

The research reveals that for cooperative binding to happen, the DNA must be distorted about 20 degrees off its standard axis, princi-

pally at a bend at the palindrome's center. Discovering DNA distortion was not a surprise, for simple models had already predicted it. Previous crystal structures had also shown that the binding of just one homeodomain acting alone induces a kink in the DNA. But the scientists were surprised to find that even when two homeodomains are involved, all the DNA distortion occurs when the first one binds. This molecular event enables the second homeodomain to contact the first, and endows the second protein with a much-enhanced binding affinity. As Kuriyan explained, "This mechanism for binding is very different from, say, the one for a preformed dimer, where the proteins bind in solution and then together bind DNA."

Solving the crystal structure provided other insights, as well. Previous studies at Yale had shown that DNA and proteins need not form direct bonds with each other to achieve specific recognition. Rather, water molecules can mediate the connections between the two. Whether such a scenario held for DNA-homeodomain interactions had long been debated, but Wilson's high-resolution structure revealed an extensive shell of ordered water molecules collectively bound to both protein and DNA, as well as to each other.

"David's structure brought the complex into sharper focus," said Kuriyan. Indeed, the sum of Wilson's biochemical, genetic, and crystallographic work has advanced researchers' understanding of how homeodomains function. But many questions remain, and new research developments may well emerge as investigators at Rockefeller and elsewhere continue to study the proteins so essential to the development of complex creatures.



Cooperation between homeoprotein domains is the key to ensuring that specific genes are turned on. Without a kink in DNA, two homeodomains cannot bind cooperatively (left). But when the first domain binds, it distorts the DNA so that cooperation can occur (right).



David Wilson (left), who recently defended his thesis, Professor John Kuriyan (center), and Associate Professor Claude Desplan published an article on homeodomain binding in the Sept. 8 *Cell*.

# Summertime, and the learning was easy? No. Fun? Yes.

Michael Dames



Each summer, the university hosts a diverse group of students who wish to learn more about science through two separate educational efforts. The Summer Undergraduate Research Fellowship Program (SURF) offers undergraduate students an opportunity to gain scientific knowledge and research experience in Rockefeller labs, while the Science Outreach Program gives experience to high school science teachers and students. About 100 students participated in the outreach program, while 13 undergraduates were selected to join the university as SURFers. Both programs are generously supported by donations from individuals and foundations. Left: Rob deSalle, associate curator at the American Museum of Natural History, spoke on "The Science in Jurassic Park" to 200 people in Caspary Auditorium Thurs., July 13, an event sponsored by the outreach program. Right: SURFers and Rockefeller graduate fellows share pizza during a weekly journal club meeting. At each meeting, a SURF student presented a current scientific article, which was then discussed by the group.

## Potpourri

### In memoriam

The university community mourns the passing of Elizabeth (Lillian) Kellerhals, who died Sun., Sept. 3. She worked at the university for more than 20 years in the Order Service Department and in the Editorial Office of *The Journal of Experimental Medicine*.

The university also mourns Berta Scharrer, who died Sun., July 22. A volunteer at the Rockefeller Institute from 1938 to 1940, she studied secretions in brains of a cockroach species, work that presaged the field of neuroendocrinology.

### Weiss elevator repairs

Due to modernization of the Weiss Research Building elevators, elevator No. 2, the only car that goes to the basement (A level) of the building, is out of service for approximately the next three months. Anyone going to LARC from north campus should cross the Plaza and use any of the remaining elevators to go one flight down to the first floor of Weiss. To reach Weiss Café through the tunnel, climb the Weiss Building stairs. Contact Robert Francis, x8001, with any questions.

### Choral Symphony Society

The Choral Symphony Society rehearses for the fall season Tuesdays in the Caspary music room. To audition, contact David Labovitz at 864-7541.

### Museum program

The Abigail Adams Smith Museum, 421 East 61st St., presents historian Ann Douglas Sat., Sept.

16 at 2:00 P.M. Douglas will discuss her book *Terrible Honesty: Mongrel Manhattan in the 1920s*. For further information and reservations call the museum, 838-6878.

### Lecture

Maria Karayiorgou, Scottish Rite fellow and staff scientist at the Fred Hutchinson Cancer Research Center in Seattle, will discuss "Genetic Loci Contributing to Schizophrenia Susceptibility" Tues., Sept. 19 at 4:00 P.M. in Weiss 301.

### Clinical Research Seminar

Michael G. Kaplitt, postdoctoral fellow in the Pfaff lab, will discuss "Gene Therapy of the Nervous System" Wed., Sept. 20 at the Clinical Research Seminar at noon in Nurses Residence 110B.

### Medical art show deadline

Members of the university are invited to submit up to 6 slides or photographs of paintings, sculpture, photographs, or handicrafts for the Fifth Medical Complex Art Show. The show, sponsored by Cornell Medical Library and Lenox Hill Artists Forum, will be on display at the Cornell Library from November 1995 to February 1996. Send submissions to Helen-Ann Brown by Fri., Sept. 29. For more information, contact Brown at 746-6092.

### Electronics course

The Electronics Shop, a unit of Information and Computing Services, will offer a course covering analog and digital circuits entitled "Electronic Techniques." The course begins Wed., Oct. 11 at 3:00 P.M. in Caspary 1A. For further

information or to register, contact Lawrence Eisenberg, box 186 or x7896.

### Weekly Research Seminars

Dates are still available to invite speakers for the Weekly Research Seminar, which meets Wednesdays at 11:00 A.M. Submit your proposals as soon as possible to Claude Desplan, fax x8370, box 151, phone x7965, or e-mail desplan.

### Clothing collection

The Student Representative Committee's clothing collection program now has only one collection box, a red Salvation Army bin near the loading dock/receiving area east of the 64th St. gate. Donations must be placed in sealed bags before deposit. For further information, contact Peter Elias, x7842 or e-mail eliasp.

### Election

Professor Bruce McEwen has been named president-elect of the Society for Neuroscience.

### Scholars

Assistant Professor Seth Darst has been named a Pew Scholar. Associate Professor Titia de Lange was named Rita Allen Scholar.

### Award

*The Hostage Brain*, by Professor Bruce McEwen and Harold M. Schmeck, Jr., received an Award of Excellence from the Association of Medical Illustrators.

### Anniversary

*The Journal of Cardiovascular Electrophysiology* commemorated the

35th anniversary of the publication of *Electrophysiology of the Heart* by Professor Emeritus Paul Cranefield and Brian F. Hoffman in its July issue with reflections by Cranefield and Hoffman.

### Garden laurels

The university was the only institution honored by The East Side Association with their Green Thumb Award, which cited Rockefeller University's "achievements in landscaping," and made special mention of the May 1994 Azalea Festival.

### Virus alert

A new computer virus, called Winword.Concept, can infect any computer—Macintosh or PC—that uses version 6.0 or higher of Microsoft Word. If you have the virus, a message box will appear on your screen displaying the number 1. Any subsequent document saved using the File, Save or Save as... menu options will be infected with the virus. Protection against the virus available in the User's Area, Smith Hall Annex A21; in the freebies folder located on all Macs and PCs; or from the RU home page on the World Wide Web (<http://www.rockefeller.edu/>).

### Abby Dining Room

The dining room in Abby Aldrich Rockefeller Hall has reopened. Reservations are recommended. Call x8898.

### Holiday schedule

The university will close Sat., Dec. 23 for the Christmas holiday and reopen Tues., Jan. 2.