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The Rockefeller University

news & notes

November 19, 1993 Volume 4, Number 10 *The Rockefeller University*

Marcelo Magnasco *(left)* has been promoted to assistant professor and head of lab; Frederick Cross has been promoted to associate professor.

Trustees promote two faculty

At a meeting of the Board of Trustees Wednesday, physicist Marcelo Magnasco was promoted from postdoctoral fellow to assistant professor and head of lab, and Frederick Cross, a molecular geneticist, was promoted from assistant to associate professor.

"I am pleased that Marcelo Magnasco, a brilliant young physicist who is interested in biological problems, will head a lab at the university," said President Torsten Wiesel. "I would also like to congratulate Fred Cross, an outstanding young Rockefeller alumnus, on his promotion to associate professor."

Magnasco has recently adapted a model originally designed to explain chemical reaction rates to biological processes involving molecular motors, such as muscle contraction and mechanisms which transport chemicals in eukaryotic cells. This work suggests that there may be an optimum temperature for the operation of these processes. Magnasco is also working on theoretical aspects of froths and bubbles.

Magnasco is a graduate of the University of La Plata, Argentina (Licenciado en Fisica, 1987) and The University of Chicago (Ph.D., 1992). He has been both a postdoctoral fellow at The Rockefeller University and visiting scientist at the NEC Research Institute at Princeton since 1992. His awards include the William Rainey Harper Dissertation Fellowship (1991) and the Sydney Bloomenthal Dissertation Fellowship.

Cross and his colleagues are studying the control of the cell cycle in yeast, which acts as an experimental model for research in fundamental genetics. Specifically, his laboratory is looking at the beginning of the cell cycle, called START, a critical step toward the replication of DNA and eventual division of the cell.

Cross, a graduate of Swarthmore College (B.A., 1978), completed graduate studies in the Hanafusa lab at Rockefeller (Ph.D., 1984). After

*See **RU Faculty**, page 2*

Board names new trustees, hears faculty presentations

The Board of Trustees elected two new members Wednesday: Joseph Goldstein, Nobel laureate affiliated with the University of Texas Southwestern Medical Center, and Donald Pels, chairman and president of Pelsco Inc. In its meeting, the board also heard presentations from faculty groups on academic planning and new programs currently being initiated.

"I am delighted that two such distinguished individuals are joining our Board of Trustees," said President Torsten Wiesel. "They will each bring unique talents and insights to the board and will help this university flourish for many years to come."

Goldstein won the Nobel Prize in Physiology or Medicine with Michael S. Brown in 1985 for their discovery of the basic mechanisms controlling cholesterol metabolism. The finding led to a new pharmacologic approach to the treatment of cardiovascular disease.

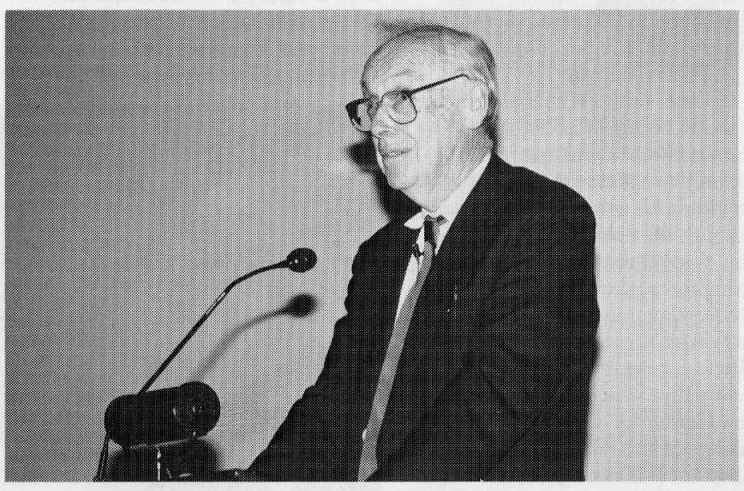
A graduate of Washington and Lee University (B.S., 1962) and University of Texas Southwestern Medical Center (M.D., 1966), Goldstein has been affiliated with the University of Texas since 1972. He currently holds a number of titles at the university's Southwestern Medical Center: chairman of the Department of Molecular Genetics, Paul J. Thomas Professor of Medicine and Genetics, Regental Professor, and recipient of the Distinguished Chair in Biomedical Science. In addition, Goldstein is professor of internal medicine at the university's medical school, senior attending physician at Parkland Memorial Hospital and non-resident fellow at The Salk Institute. He is on several editorial boards and is a consultant to a number of pharmaceutical and biotechnology companies. In addition to the Nobel Prize, Goldstein received the Albert D. Lasker Award in Basic Medical Research (1985) and the National Medal of Science (1988).

Pels, a graduate of the Wharton School (B.S., 1948) and New York University (J.D., 1953), began his career at Filene's in Boston, Arthur Young & Company and the American Broadcasting Corporation. In 1959 he became executive vice president and board member of Capital Cities Communications. In 1969, he became chairman, president and chief executive officer of LIN Broadcasting Corporation. He assumed his current position, chairman and president of Pelsco Inc., in 1991.

Pels is active on a number of boards, including those of American Public Radio, Barnard College, Capital Group (L.A.) ICA (advisory committee), New York

*See **Board**, page 2*

Lecture inaugurates RU celebration



Leif Carlson

A lecture by James Watson, co-discoverer of the double-helical structure of DNA, drew a standing-room-only crowd Tuesday. The event inaugurated the university's celebration of the 50th anniversary of Oswald Avery, Colin MacLeod and Maclyn McCarty's discovery that genes are made of DNA.

Long-time employees celebrate special milestones at Rockefeller

By Jennifer Horne King

65 years: *M. Pedersen*

Sixty-five years ago, Margery Pedersen came to The Rockefeller University to take on her first job as clerk in the accounting department. "My mother wanted me to be a teacher like most girls in those days," recalled Pedersen. "But I soon realized, much to her chagrin, that I am more of a numbers person than a teacher. So, I rebelled in my own way: I came to Rockefeller. Little did I know I would have such a wonderful time and stay here so many years!"

During her time as an accountant, Pedersen climbed to the rank of manager of accounting services. Among her souvenirs, Pedersen has fond memories of a bridge club made up of Rockefeller colleagues. Four of them met each day for half an hour during lunch for 22 years.

In 1975, Pedersen retired. A short time after, she received a call from Edward H. Ahrens, now professor emeritus, for some assistance with his accounts. Her expertise in accounting was sorely missed, and before long, she was assisting the Hirsch, Wiesel and Breslow labs with their grants and budgets.

" I don't have a single complaint about my time here," said Pedersen. "And not many people can say that about their work, can they?

60 years: *W. Trager*

Professor Emeritus William Trager, a pioneer in the field of malaria research, has reached his 60th year at The Rockefeller University. Only a handful of people can claim such a distinction.

"It doesn't feel like 60 years," said Trager, who started as a postdoc in the department of animal pathology at Rockefeller's Princeton Laboratories in 1933. "But there are fewer and fewer people who can say they started work here at the time that Simon Flexner retired; or gave a seminar before an audience that included Theobald Smith; or shared a corridor with the likes of Eugene Opie and Peyton Rous!"

Trager first came to the Manhattan campus in 1950, when the Princeton Laboratories closed. As captain in the Army's Sanitary Corps during the Second World War, he and his colleagues made significant contributions to the earliest anti-malarial research, testing different drugs and calculating optimum dosages in New Guinea and Australia. In 1964, Trager was appointed professor. He became professor emeritus in 1980.

"When I first entered the field, parasitology was not considered very important," Trager recalled. "People thought it had more to do with taxonomy and clinical work. Now, with the availability of improved culture methods, and advances in biochemical and molecular biological techniques, the field has expanded and attitudes have changed. The adaptations seen in parasites and their interaction with the immune system have contributed new insight to the fields of genetics, molecular biology and immunology." Trager, who is still active in his laboratory, has few regrets: "I had every reason to remain here for this long. How could one not stay at a place that has continued to foster the exchange of innovative ideas, so vital to the advancement of science? For me, being emeritus does not mean sitting around and sharing words of wisdom. Rather, it means getting on with my work, which is what I love to do."

The Anniversary and Retirement Dinner Nov. 4 celebrated special anniversaries of long-time employees of the university. Professor Emeritus William Trager and Consultant Margery Pedersen, shown here with President Torsten Wiesel *(center)*, each have the rare distinction of serving over six decades.

Board names two new members, hears presentations

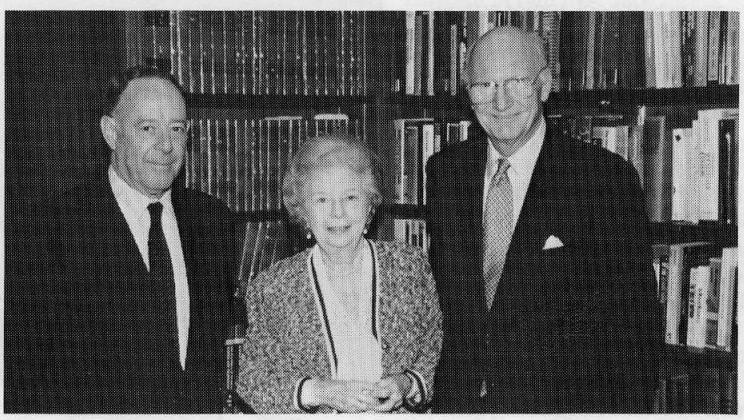
(continued from page 1)

Philharmonic and WNYC Foundation. He has also served on the boards of Lafayette Radio, Mariner Funds, Mutual of America (chairman of the investment committee), Oppenheimer Funds, Pinelands and U.S. Trust Company.

In other business at the meeting of the Board of Trustees, two of the university's academic planning committees made presentations, providing an overview of research issues in the field, describing current work at the university and outlining future directions. The Physics Committee co-chairs, Professors Nicola Khuri and Mitchell Feigenbaum, reviewed their plans, which included the new Center for Theoretical Studies in physics and biology. In addition, Assistant Professors Joseph Atick and Marcelo Magnasco discussed their research and interaction with the biologists on campus. The work of the Microbiology and Immunology Committee was presented by its co-chairs, Professors Emil Gotschlich and Ralph Steinman; they were joined by Professor Alexander Tomasz.

The trustees also named Theresa Lang trustee emerita at the meeting. Lang joined the board at the end of 1986, after two years as a member of The Rockefeller University Council. She was chair of the board's Hospital Committee. The committee's new chair is Eugene Grisanti.

In addition, they reelected Gustavo Cisneros, Pehr Gyllenhammar, Anne de la Renta, Frederick P. Rose, Richard S. Salomon, Stephen Stamas and P. Roy Vagelos to the board.



Attending The Rockefeller University Board of Trustees meeting Wednesday were *(left to right)* Donald Pels, who was elected to the board, Theresa Lang, who was named trustee emerita, and Richard Furlaud, chairman of the board.

Two RU faculty promoted

(continued from page 1)

completing postdoctoral work at Hutchinson Cancer Center in Seattle (1985-1989), he returned to Rockefeller as an assistant professor. His awards include an National Science Foundation Predoctoral Fellowship (1978-81), a Helen Hay Whitney Fellowship (1985-88) and a Lucille P. Markey Scholarship (1988-present).

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Fly eye studies yield new view of development and cancer

By Susan Blum

Looking out through their multifaceted eyes, fruit flies merely see what is essential for their short, simple lives. But peering into those eyes, biologists see phenomena far more subtle and complex. Within the crystalline lattice of the *Drosophila* eye, scientists are beginning to glimpse the pathways underlying the cellular processes that characterize an organism's normal development from fertilized egg to adult and to learn how disturbances in these pathways can lead to cancer.

"Many aspects of development in general are reflected in the development of the *Drosophila* eye," said Ulrike Gaul, a developmental biologist who joined Rockefeller University's faculty this fall. For instance, studies of the fruit fly eye are yielding clues into how cells make the many choices that determine their ultimate fates.

In the beginning, the incipient fruit fly eye is nothing more than a sheet of undifferentiated epithelial cells. Yet by the time the process of eye development is completed, this sheet has been transformed into a well-organized structure replete with highly specialized cells. The mature eye consists of a repeated array of about 800 units called ommatidia, each of which contains 20 cells—eight photoreceptor cells (R1 to R8), four lens-secreting cone cells and eight accessory cells.

Neighboring cells send signals

How does this complicated structure emerge? "The ommatidia are assembled by gradual recruitment of undifferentiated cells into growing clusters," Gaul explained. In all ommatidia, the sequence of events is exactly the same. The R8 cell differentiates first, after which comes the recruitment of the other photoreceptors in the following order: R2 and R5, then R3 and R4, R1 and R6 next, and finally R7. Subsequently, the cone cells and other accessory cells are recruited. In each case, the signals for these recruitment events are communicated as cells "talk" to their immediate neighbors, sending messages that start at the cell surface and travel down to the nucleus, where they regulate the activity of particular genes.

Gaul has been studying these developmental events since she was a postdoc in the University of California, Berkeley, lab of Gerald Rubin, a pioneer in the study of fly eye formation. There, using ingenious "enhancer trap" screens, Gaul discovered a number of hitherto-

Assistant Professor Ulrike Gaul studies the development of the fruit fly eye, finding clues to how cells make the many choices that determine their ultimate fates.

unknown genes that act at specific times in eye development. In her new lab at Rockefeller, she plans to explore several of these genes, including one that may set the whole process of eye development in motion by triggering the differentiation of the R8 cell.

Initially, though, much of the work in Gaul's lab will focus on one particular gene she first cloned and characterized in 1992. This gene, called *Gap1*, is a player in one of the best-studied photoreceptor recruitment pathways—the one that leads to R7 cell differentiation.

The importance of *Gap1* can only be understood by taking a sojourn down the convoluted cellular signaling route known as the "Ras pathway." Ras proteins are central molecular switches that, when turned on, pass along many signals controlling cell growth and differentiation. The Ras switch is "on" when the protein binds a small nucleotide called GTP, and "off" when Ras uses its own catalytic activity to hydrolyze GTP into a related molecule called GDP. When the Ras signaling pathway is over-activated, cell growth and differentiation become deregulated, and cancer can result. Indeed, about one third of all human cancers involve mutations in the *Ras* gene.

Ras pathway is very common

Researchers have found the Ras signaling pathway in an astonishing number of creatures, from yeast to worms to flies to mammals. Thanks to work in a number of labs, including Rubin's, many of the pathway's components have been specified for the message that results in R7 cell differentiation. For instance, the pathway involves a cell-surface receptor called "sevenless"; a ligand molecule, called "boss," which binds to the sevenless receptor; a guanine nucleotide exchange factor called "SOS" and its adapter, called "Drk;" and—Gaul's contribution—Gap1.

Gaul's initial studies of Gap1 were important for a number of reasons, aside from the obvious one of providing still more evidence of the similarities among all Ras pathways. For one thing, her investigations helped to resolve a debate then-ongoing about the role of GAP proteins. Some researchers believed that they serve only as negative regulators, by tremendously enhancing Ras proteins' ability to hydrolyze GTP and thus switch to their "off" state. But others believed that GAP proteins also serve as "effectors" of Ras—that is, as molecules that help pass Ras's message along. Gaul's research, which showed no evidence for an effector role for Gap1, helped build the now-general consensus that GAP molecules serve only as negative regulators. Her studies also indicated that the fly likely has a number of GAP-like molecules in addition to Gap1.

Here at Rockefeller, Gaul is continuing to pursue the R7 differentiation pathway both "upstream" of Gap1—that is, before Gap1 comes into play—and "downstream" of Gap1, as Ras1 effectors swing into action.

For these studies, she employs a particularly sensitive genetic screen that uses minimally active *Gap1* mutants to highlight the function of other molecules involved in the signaling pathway. Gaul strongly believes such highly sensitive screens are essential to tease out the numerous genes that probably still lie hidden along the Ras pathway.

"Much has been learned about the Ras pathway recently, but the picture is still over-generalized," Gaul asserted. Indeed, she reported, "the number of genes that we're pulling out with our screens is greater than the number suggested by studies that use other methods."

How does one pathway send many signals?

Figuring out the full complement of genes involved in the Ras signaling pathway is just part of the puzzle biologists must eventually solve. Equally important is to understand how this one pathway type can send so many specific regulatory messages to specific cells at specific times.

Clearly, the specificity of the message is partly determined at the head of the pathway, in the relationship of an incoming ligand molecule and a cell-surface receptor destined to recognize it. It is also influenced at the message's nuclear destination, where a cell's particular developmental history helps determine which genes can be activated at any given time.

But, Gaul asserts, specificity is also likely to be ensured through variations in the central components of the Ras signaling pathway. "Some of the core components of the Ras-pathway 'cassette' might always be identical, but I think we will find that other components may vary in ways that help confer specificity," Gaul predicted.

As just one example, she points out that the various GAP molecules characterized so far are very similar in their catalytic domains (the regions that enhance Ras's ability to hydrolyze GTP) but quite different in other regions. Along with her genetic studies, Gaul is currently comparing a number of fly GAP proteins, to discern how the variable portions of their structures might contribute to specificity.

"The full complexity of the Ras signaling pathway has yet to be addressed," Gaul summed up. As she continues to look into the fruit fly's eye as a model system, more aspects of that complexity may well come into view.

Lecture to feature neuroscientist

Urs Rutishauser, professor at Case Western Reserve University School of Medicine, will speak on the "Regulation of Cell-Cell Interactions During Neural Development" at the Friday lecture today (Nov. 19).

Rutishauser and his colleagues have proposed a new mechanism for the regulation of cell-cell interactions in the development of the nervous system that involves a large cell surface carbohydrate called polysialic acid.

"It's a deceptively simple compound, but we have been able to show that by attenuating cell-cell adhesion it helps to form appropriate connections between cells of the nervous system and to remodel old ones," he explained. "This has led us to think that it may be a key player in contributing to both the assembly and plasticity of the nervous system. We're testing this hypothesis on many levels."

After receiving a B.S. (*magna cum laude*) from Brown University in 1967, Rutishauser obtained a Ph.D. in 1973 from The Rockefeller University, where he continued his work, first as assistant professor (1974-79), then as associate professor (1979-83). He then joined the faculty of Case Western Reserve University as professor of genetics and neuroscience.

Rutishauser has received many awards, including a Merit Award from the National Institutes of Health (1993).

The lecture will be held at 3:45 P.M. in Caspary Auditorium, preceded by tea at 3:15 P.M.

Walther Goebel (1899-1993)

Walther F. Goebel, professor emeritus at The Rockefeller University, died Nov. 1 of natural causes. Goebel was a world-honored biochemist who for more than half a century directed his research efforts toward an understanding of the body's chemical defense against infection by microorganisms.

Goebel's career at Rockefeller began in 1924 in Oswald Avery's lab, which later made the historic discovery that genes are made of DNA. Throughout his career, Goebel studied the role of bacterial carbohydrates in infection and resistance and related their chemical structure to their ability to evoke immunity to disease.

Among Goebel's early achievements was the synthesis of an artificial antigen which was practically identical to those formed by living pneumococci. When injected into rabbits, the artificial antigen protected them against infection by highly virulent microorganisms. This was the climactic proof of the concept, developed by Rockefeller investigators, that the antigenic specificity of the pneumococcus resides in the chemical configuration of the polysaccharides which constitute the bacterial capsule.

Goebel also studied the chemical nature of endotoxins, particularly those elaborated by dysentery bacilli, and devoted some years to the elucidation of the nature of the receptors on the cell surface of enteric microorganisms that are sensitive to certain strains of bacteriophage (viruses that infect bacteria). Later research was devoted to the chemical nature of colicines, potent antibacterial agents produced by many strains of enteric microorganisms.

Another of Goebel's contributions, which is still marketed today, is a preparation of ferrous gluconate, used for treating iron deficiency.

Goebel was born in Palo Alto, California on Dec. 24, 1899. He earned a B.A. (1920), M.A. (1921) and Ph.D. (1923) degrees from the University of Illinois and served there as a scholar in chemistry from 1920 to 1921 and a fellow from 1921 to 1923. He continued his graduate work at the University of Munich, Germany, from 1923 to 1924 when he joined Rockefeller as an assistant in chemical immunology. He was named an associate in 1927, associate member in 1934, and member in 1944, a title that changed to professor when the institute became a graduate university in 1954. After his retirement in 1970, Goebel worked as a volunteer doing chemical immunology research at the Walker Laboratory, Sloan-Kettering Institute for Cancer Research.

A member of the National Academy of Sciences, Goebel received honorary degrees from Rockefeller (1978) and Middlebury College (1959). He was the first recipient, in 1973, of the European Society of Immunologists's Avery-Landsteiner Prize, an award named after Oswald Avery and Karl Landsteiner, two Rockefeller scientists who played major roles in laying the foundations of modern chemical immunology.

Goebel is survived by two daughters, Cornelia Goebel Branson and Anne Goebel Barkman, six grandchildren and three great-grandchildren.

Potpourri

Tri-Institutional Noon Recital

The Artaria Quartet of Boston will perform works by Ludwig van Beethoven and Hugo Wolf at the Tri-Institutional Noon Recital today (Nov. 19). The quartet has performed throughout North America and Europe, and has given nationwide radio broadcasts. The concert, to be held in Caspary Auditorium, is free.

Sunday film

Tilai (Burkina Faso, 1990), will be shown at 7:30 P.M. in Caspary Auditorium, Sun., Nov. 21. Winner of the 1990 Special Jury Prize at Cannes, the film is the story of a man who returns to his fiancée after two years to find that she has been married off to his father. Admission is free.

Rockefeller University concert

Spanish pianist Alicia de Larrocha will perform works by Surinach, Mompou, Turina, Granados and Albéniz as part of the Rockefeller University Concerts, Wed., Nov. 24 at 8:00 P.M., in Caspary Auditorium. She has won four Grammy Awards, the Dutch Edison Prize and the Spanish Medallo d'Oro for artistic merit. Admission is $17 per person; $7 for students and postdocs of the Tri-Institutions. For more information or reservations, contact Cathy Rogers, x8971.

Magic show

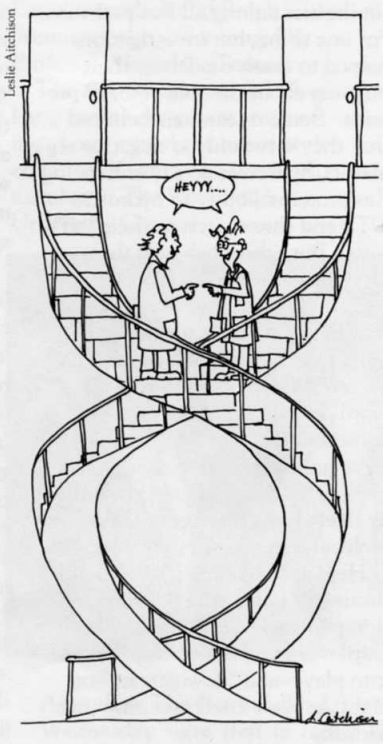
Singer-magician "Magical David" will perform, Sat., Nov. 20 at 2:00 P.M. in Caspary Auditorium. Admission is $4. Proceeds will benefit the Children's School.

Sweat Shirt Shop hours

The Sweat Shirt Shop will open from 8:00-9:30 A.M. during Thanksgiving week (Nov. 22, 23 and 24). In addition, the shop will open during its regular hours, Tues., Nov. 23, from 11:30 A.M. to 1:30 P.M. Teddy bears and umbrellas are now available. Proceeds benefit the Children's School.

Holiday stress management

The Employee Assistance Program will sponsor a "Holiday Stress Seminar," led by Diane Dobbs, a clinical social worker at Beth Israel Hospital, on Thurs., Dec. 2, from noon to 1:00 P.M. in Nurses Residence 110B.



WATSON AND CRICK DISCOVER THE DOUBLE HELIX

Grant or fellowship deadlines

The Office of Sponsored Programs advises all faculty members with a grant or fellowship deadline between Fri., Dec. 24 and Mon., Jan. 3 that all applications should be into the office by Thurs., Dec. 23 at 3:00 P.M. for review and signature. The university will be closed for the holiday vacation the next week. Contact Penny Cook, x8054, with questions.

Faculty and Students Club

At the annual meeting of the Board of Directors of the Faculty and Students Club, Professor David Gadsby was elected president of the board; Professor Nathaniel Heintz and Associate Professor Marjorie Russel were elected directors; and Director of Purchase and Supply Sonia Reynes was appointed secretary-treasurer. The other directors are: Vice President for Business and Finance and Treasurer David Lyons, Professor Emeritus E.G.D. Cohen, and Professor John Kuriyan. Secretary Angie Dohnert is assistant-secretary. Professor Nam-Hai Chua retired from the board.

Rockefeller University Today

The fall 1993 issue of *The Rockefeller University Today* has been published. Copies are available during business hours from the Public Affairs Office, Caspary 3C.

News&Notes schedule

News&Notes will not be published next week due to Thanksgiving.