

10-1-1993

NEWS AND NOTES 1993, VOL.4, NO.4

The Rockefeller University

Follow this and additional works at: http://digitalcommons.rockefeller.edu/news_and_notes_1993

Recommended Citation

The Rockefeller University, "NEWS AND NOTES 1993, VOL.4, NO.4" (1993). *News and Notes 1993*. Book 26.
http://digitalcommons.rockefeller.edu/news_and_notes_1993/26

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 1993 by an authorized administrator of Digital Commons @ RU. For more information, please contact mcsweej@mail.rockefeller.edu.

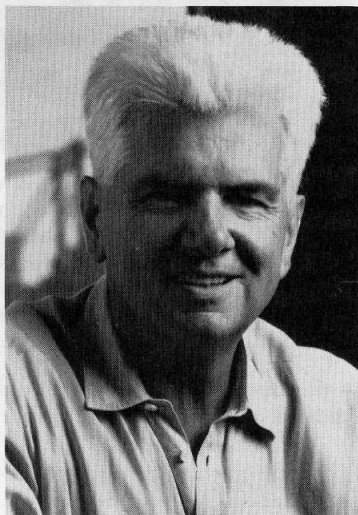
RU investigator wins Lasker Award for basic research

The prestigious Albert Lasker Basic Medical Research Award will be awarded to Rockefeller University Professor Günter Blobel today (Oct. 1) at a luncheon at the Pierre Hotel. First Lady Hillary Rodham Clinton is expected to be the keynote speaker.

"Dr. Blobel's scientific contributions represent the highest achievement attainable by an investigator: resolution of a fundamental problem in basic biology," the citation for the award says. "Specifically, his research explains how a cell can organize itself into various compartments while utilizing just one mechanism for protein production. It also demonstrates that these cellular mechanisms are highly conserved among species, and provides insights into organelle biogenesis, cellular secretion and the evolution of intracellular compartments and membranes."

The purpose of the Albert Lasker Medical Research Awards Program is to recognize and honor individuals who have made significant contributions in basic and clinical research in the diseases which are the main causes of death and disability. Since 1946, when the first Lasker Awards were presented, 50 winners of the award have gone on to win Nobel Prizes.

Blobel's work on the fundamental questions of protein transport began in the mid-60s with his interest in ribosome-membrane interaction. In 1971, together with David Sabatini in the laboratory of George Palade at The Rockefeller University, he began looking at the underlying mechanisms of these membrane-bound ribosomes in the synthesis of secretory proteins. Out of this work



Professor Günter Blobel

came the seminal proposal that information for the translocation of secretory proteins across the membrane of the endoplasmic reticulum resides in the protein's amino terminal sequence.

In 1975, this proposal was

expanded into the landmark "signal hypothesis" which holds that the signal sequence is the determinant for protein translocation and that it is recognized by a receptor that directs it to the endoplasmic reticulum membrane.

Then, in a series of experiments, he developed the first cell-free system that faithfully reproduces protein translocation. The experimental assays developed by Blobel and his group are now employed by many researchers in the field of cellular biology. Blobel's recent work includes investigations of the nuclear envelope, its lamina and its associated pore complexes.

Blobel, who received an M.D. in 1960 from the University of Tübingen and a Ph.D. in 1967 from the University of Wisconsin at Madison, is an investigator of the Howard Hughes Medical Institute. He is a member of the National Academy of Sciences and the American Philosophical Society, and an honorary member of the German Society of Cell Biology and

the Japanese Biochemical Society. He is a former president of the American Society for Cell Biology.

In addition to the Albert Lasker Basic Medical Research Award, the Albert and Mary Lasker Foundation awards the Clinical Medical Research Award and the Public Service Award. This year's winner of the clinical award is Donald Metcalf, research professor of cancer biology at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia. This year's public service award is shared by Nancy S. Wexler, professor of clinical neuropsychology at the College of Physicians and Surgeons of Columbia University and Paul G. Rogers, partner at Hogan & Hartson in Washington D.C and former member of the U.S. House of Representatives, 11th District, Florida.

Selected by a jury of scientists and physicians, Lasker Award winners receive \$25,000, a citation highlighting their achievements and a statuette.

Baltimore to give Friday lecture

Professor David Baltimore, former president of the university, will give a talk entitled "NF- κ B: An Immediate Cellular Transcriptional Response System," at the Friday lecture today (Oct. 1).

"David's work on NF- κ B is typical of his many important contributions to our understanding of the development of the immune system," said Professor Nat Heintz, chair of the Friday Lecture Series Committee. "These studies not only have identified NF- κ B as a major player in the responses of lymphocytes to a variety of stimuli, but have provided the first detailed mechanism for the activation of a cytoplasmic transcription factor and its translocation to the nucleus."

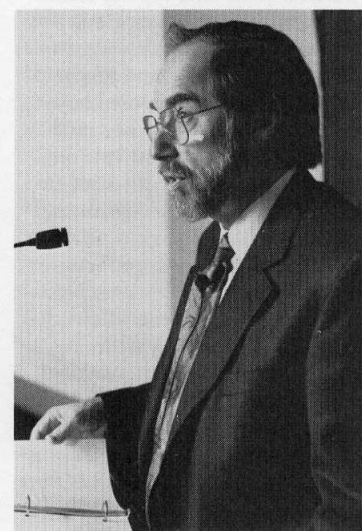
Research in the Baltimore laboratory has focused primarily on differentiation of immune system cells and cancers of these cells. The group has found that certain transcription factors, notably NF- κ B, appear to be key activators of the differentiation of B lymphocytes—the cells that make the body's antibodies.

Further investigation has shown

that NF- κ B is a factor present in the cytoplasm of most, if not all vertebrate cells. It acts as a rapid-response transcription factor allowing cells to change transcriptional patterns in response to infectious agents, inflammation or stress. Baltimore will describe results from a recent knock out of one of the genes that encodes a part of NF- κ B. He will also discuss the regulation of the factor.

A graduate of Swarthmore College (B.A., 1960) and The Rockefeller University (Ph. D., 1964), Baltimore conducted post-doctoral work at M.I.T., and at Albert Einstein College of Medicine. In 1964, Baltimore became a research associate at the Salk Institute. In 1968, he joined the faculty of M.I.T., where, by 1973, he was named American Cancer Society Research Professor. The following year, Baltimore joined the staff of the M.I.T. Center for Cancer Research. In 1982, Baltimore was named first director of the Whitehead Institute in Cambridge and in 1990, president of Rockefeller.

In 1975, at the age of 37,



Professor David Baltimore

Baltimore won the Nobel Prize in Physiology or Medicine with Howard Temin of the University of Wisconsin and Renato Dulbecco of the Salk Institute. Baltimore is also the recipient of numerous other prestigious awards and society memberships.

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

2 RU forms food advisory group

3 Seeking clues to cell cycle control

4 Expert to lecture on malaria

RU forms food advisory group

A new five-member Food Service Advisory Committee has been formed to represent community opinion on all aspects of the university's food services.

David Lyons, vice president for business and finance, and treasurer, will convene the committee. He said: "This group, which represents a cross-section of the community, will be helpful in offering us feedback and advice." Lyons explained that the university administration provides direction to Restaurant Associates about the quality of the food, the service and the cost.

"I think a lot of people don't realize that the university subsidizes food services," continued Lyons. "The subsidy had been rising. We're hoping that by offering good,

affordable food, we can bring the subsidy down to previous levels."

Committee members will initially meet monthly. All suggestions and ideas for improvement will be welcome.

Members of the Food Service Advisory Committee are: Associate Professor Alan Aderem, Graduate Fellow Elizabeth Campbell, Foreman Elbin Diaz, Professor Emeritus Bruce Merrifield and Director of Dietary Service Cynthia Seidman. In addition to Lyons, *ex officio* members are Director of Personnel Virginia Huffman, Director of Restaurant Associates Judd Newman and Corporate Secretary and Vice President for Public Affairs Ingrid Reed.

Letters to the editor:

More on the cafeteria

The Rockefeller University is an institution dedicated to the eradication of disease. Studies on campus and at other research institutes show that a low fat diet is an important component in the fight against heart disease and some cancers. It is about time that our food service reflects it.

The new cafeteria has taken us from hospital-style food to restaurant quality meals at cafeteria prices. There is a wide variety of entrees, sandwiches and prepared salads, and it is a pleasure knowing that when I order a turkey sandwich I am, in fact, getting turkey and not something with a gelatin outer surface and grizzle running through it.

As far as the prices go, I conducted some of my own research and found that, on the whole, the new cafeteria is really no more expensive than what is available around the neighborhood, which is usually lower in quality.

One last opinion, however: wake up and smell the coffee—free refills do not cost a lot to the cafeteria and they are, as they say, politically correct.

Kudos to the administration for bringing in a food service that caters to our health and our taste!

Lauren Hackett
Grants Management Specialist

Journals: whose decision?

To locate a reference for my former colleague, a dermatologist, I went last week to the Library to the *Journal of Experimental Medicine* (JEM) to find a paper by Philip D.

McMaster, who had demonstrated a second, deeper lymphatic system in the human arm. The task would be easy since there were two slender index volumes covering the entire JEM volumes with both author and subject indexes. In quarto like the early copies of the JEM, they were bound similarly and placed in the collection at the end of the runs covered.

But the shelves where these volumes had rested for years were empty! I asked where those volumes had been relocated—they had been discarded (and some said by the dumpster route). Even the index volumes were gone.

The papers bound therein delineated the beginning of medical research in this country, not only papers from the Rockefeller Institute, at a time when this was the only journal. The JEM was the pride of Simon Flexner, of John D. Rockefeller, Jr., of Peyton Rous (editor for 38 years), also of Herbert S. Gasser, of Detlev W. Bronk and doubtless of later presidents.

Their role in medical history, rarity to book sellers and value to newer institutions made such disposal serious errors in judgment. It was extant history that was often consulted: the loss disrupts the business of our university. The Library possesses what it calls a "second set," but that copy starts with Volume 91 (1950). And it lacks the index volumes.

Likewise gone are the early volumes of Jacques Loeb's *Journal of General Physiology*, one volume of which would have completed the set possessed by the present editor, Paul Cranefield.

U.S. representative visits campus



Carolyn B. Maloney (center), U.S. representative for the 14th district, met with President Wiesel and Professor Mary Elizabeth Hatten Fri., Sept. 24 to learn more about the university. Wiesel emphasized that continued support of basic research is necessary to improve the nation's health care services.

So the question of decision-making is raised. Who decided to throw out the journals, and why? Were the present editors of the JEM consulted? Or the Academic Council that represents the faculty in a broad sense? Or the trustees? I suggest that such power to act without consultation should be curtailed. Those making such ill-starred errors should hang heads in shame.

Merrill W. Chase
Professor Emeritus

Reply:

The library regrets the inconvenience experienced by Dr. Chase. However, many factors are involved in the deaccessioning of journals. Physical deterioration, broken spines, missing and torn pages usually are the determinants leading to a journal's removal, particularly those which are discarded.

What Dr. Chase experienced is unfortunate but, lacking a properly controlled physical environment and with repeated photocopying of journals, there is little that can be done to prevent the collection's physical deterioration. There was very little alternative to save the volumes of JEM Dr. Chase refers to in his letter. Only badly deteriorated volumes preceding 1950 have been deaccessioned.

The deaccessioning process is always difficult. Fortunately, the need to physically hold an item at this site has been considerably obviated by other alternatives. The entire run of JEM is maintained by The Medical Library Center of New York, the New York Academy of Medicine and 35 consortia libraries. It is available from University Microfilm, Inc. back to Volume 1, if the decision is made to replace the damaged volumes. The

Rockefeller University Press also maintains retention copies. Upon request, any article can be retrieved within a reasonable time frame.

The decision to deaccession journals has not been a unilateral one. The Faculty/Library Committee and the university's administration have been kept informed of the problems that exist in the library regarding lack of space and the deterioration of some materials due to age, use and other conditions. Deaccessioning decisions have always been made collaboratively and through consensus judgements.

Patricia E. Mac
Librarian

and Vincent Fisch
Professor and Chairperson of
Faculty/Library Committee

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
Doron Weber, Director of Communications

Mika Ono Benedyck, Editor
Jennifer Horne King, Assistant Editor
Heather Leahy, Design
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.



Studies at Rockefeller seek clues to cell cycle control

By Susan Blum

History, literature, probate court—all provide countless examples of the chaos that ensues when inheritance goes awry. The stakes are just as high on the cellular level, where disaster can result when the precious legacy of chromosomes is parceled out in error.

To ensure that such disaster is averted, there must be strict coordination and control throughout the cell cycle—the sequence of events by which a cell grows, duplicates its chromosomes and bequeaths them to the two “daughter cells” into which it divides. And, indeed, for over a century it has been known that the cell cycle is a remarkably well ordered and orchestrated event.

The two “main events” in the cell cycle—both of which must be carefully regulated—are the replication of DNA and the division of the cell into two progeny, each endowed with a complete set of chromosomes. Though the details vary among organisms, the cell cycle is generally the same for all nucleated (eukaryotic) cells.

The first phase of the cycle, called G₁, is one of cell growth, during which the cell produces and stockpiles proteins. Then, at a critical point in G₁, the cell commits to reproducing its DNA. (This point, which has various names, is called “START” in yeast cells, a favorite cell type for cell cycle studies.) Once this starting line is crossed, a slew of events occur in the next, or S, phase, including the production of many new proteins and the replication of chromosomes. Following the S phase comes another pause, G₂, during which the cell makes another commitment—this time, to divide in two. Following this critical point, the cell enters the M, or mitosis, phase. Cellular events during mitosis include the dissolution of the nuclear envelope, the formation of a microtubular spindle, the condensation of chromosomes and their subsequent distribution to the two incipient daughter cells, and the division of the original cell into two. The cell cycle is often conceptualized as having two major divisions: interphase (comprising G₁, S and G₂) and mitosis.

The major events of the cell cycle were identified long ago, but it is only within the past five or so years that scientists have begun to understand what controls them. They are learning that these control mechanisms are surprisingly similar throughout the whole cell



Assistant Professor Frederick Cross studies the cell cycle—the sequence of events by which a cell grows, duplicates its chromosomes and bequeaths them to the two “daughter” cells into which it divides.

cycle—and remarkably well-conserved for all eukaryotic cells from yeast to plants to mammals.

‘Master’ molecule triggers cell cycle events

The first insights into cell cycle control came from studies of mitosis. In 1989, two long research traditions—genetic studies of yeast cells, and biochemical studies of frog oocytes—converged to show how a particular enzyme, a type known as a kinase, serves as the “master regulator” that triggers mitosis. Kinases are enzymes that add phosphate groups to molecules, thereby changing the molecules’ functions.

The kinase that triggers mitosis is composed of two subunits. The catalytic part, called Cdc28 (or Cdc2 in some organisms) is present in constant amounts throughout the cell cycle. But the kinase can trigger mitosis only when teamed up with another, regulatory molecule, called a cyclin, whose abundance varies at various times in the cycle. A number of mitotic cyclins, members of a protein “family,” accumulate all throughout interphase. When they reach a critical level, they link up with Cdc28 molecules and activate them, thus triggering all the dramatic events of mitosis. At the end of mitosis, the mitotic cyclins are degraded, the kinase ceases to function and the cycle begins anew.

Remarkably, it turns out, Cdc28 kinase triggers not only mitosis, but START, as well. It accomplishes this very different cell cycle task by teaming up with a very different family of cyclins, known in budding yeast as the CLNs (pronounced “clins”). There are three of these cyclins—dubbed CLN 1,2

and 3. Any one of the CLN cyclins is sufficient to trigger START, but the three are not identical.

The CLNs are under study in the laboratory of Assistant Professor Fred Cross. In one line of research, scientists there are pursuing how the CLNs are regulated. As is the case with mitotic cyclins, levels of CLN cyclins are not constant throughout the cell cycle. Rather, they accumulate rapidly toward the end of G₁. Once accumulated, they link up with Cdc28 to trigger START. The Rockefeller researchers believe that a self-reinforcing feedback loop controls this accumulation, by controlling how actively the CLN genes are read out, or transcribed.

Feedback loops regulate cell cycle steps

“While studying CLN3, we got a set of results that made absolutely no sense unless the CLN genes are turning themselves on,” Cross reports. How might this feedback loop work? In one scenario, small amounts of CLN3 might link up with Cdc28, and the active kinase might then phosphorylate a protein, called a transcription factor, that dramatically boosts the transcription of CLN genes. Cross and his colleagues are working to tease out the many details that make up this loop, including the identity of the putative transcription factor.

They are also exploring the positive and negative feedback loops that control a yeast cell’s decision not to enter START but to “mate” instead. (Mating—an option sometimes available to yeast—is somewhat akin to the union of egg and sperm cells.) These feedback loops also appear to involve complex self-regulation by CLNs.

In another line of research,

Cross and his colleagues are searching for the substances, or substrates, that CLN/Cdc28 kinases phosphorylate. So far, Cross says, this field is full of “absolute blanks”—blanks that must be filled in before most of the mysteries of the cell cycle can be solved.

One molecule serves many functions

The cyclin/Cdc28 kinases are pleiotropic enzymes—that is, they trigger many different events in mitosis or in the S phase. How do they accomplish so many different tasks? Sometimes, no doubt, by phosphorylating structural proteins (the mitotic kinase, for instance, is known to act directly on certain nuclear proteins) but also, probably, by activating or deactivating other enzymes, which then go on to act further in the cell. Indeed, one widely-held theory posits that the different members within each cyclin family (three CLNs, to take just one example) serve to direct the cyclin/Cdc28 kinases to different substrates within the cell. “It would certainly be agreeable if this were true,” Cross said, but as yet few substrates have been found for mitotic cyclin/Cdc28 complexes, and none for the complexes that trigger START.

To identify some of those substrates, researchers in the lab are using novel genetic screens to isolate mutant genes in budding yeast that code for mutant substrate molecules. So far, they have isolated a number of mutations that result in cell death when CLN levels are lower than normal. Eventually, by characterizing the substrates and learning how they interact with the CLN/Cdc28 kinase, the researchers hope to fill in some of the blanks in how START is controlled.

A better grasp of all the steps in the cell cycle may ultimately lead to advances in understanding and treating cancer, which is characterized by unrestrained cell growth and division. Once the complicated networks of cell cycle control are untangled, it might be possible to intervene at specific points where that control has broken down. (Indeed, intriguing links have already been found between cell cycle control genes and the so-called “tumor suppressor” genes.) Conversely, a deeper understanding of the cellular forces that push cells to divide may help prompt the process in cases, such as wound healing, where increased cell growth and division is a boon, not a bane.

Friedheim lecturer to speak on control of malaria

Louis H. Miller, head of the Laboratory of Malaria Research at the National Institutes of Health (NIH), will give this year's Ernst A. H. Friedheim Memorial Lecture Fri., Oct. 8 at 3:45 P.M. in Caspary Auditorium. The talk is entitled "Malaria Control and Eradication: A Challenge to Modern Biology."

"There is a great deal of urgency to research on malaria," Miller said. "In Africa, cheap anti-malarial drugs such as chloroquine are rapidly becoming ineffective. There are only a few years left to develop vaccines or new drugs before mortality from malaria in Africa soars. My lecture will give examples of how basic research might lead to methods to control and eradicate malaria. This research includes studies of the parasite's receptors, attachment of receptors to red cells, and immune mechanisms in the mosquito vector that might kill the parasite or make

mosquitoes refractory to malaria."

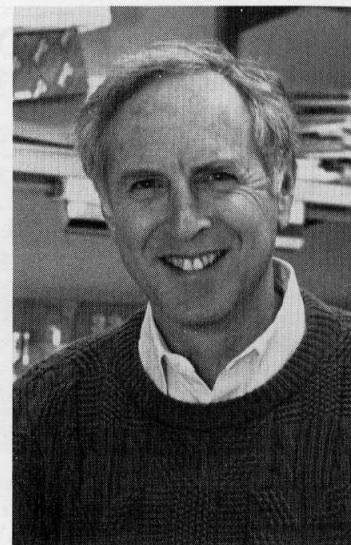
Miller is interested in all stages of the life cycle of the complex malaria parasite. He has contributed to our understanding of the receptors and ligands involved in the parasite's invasion of the red blood cell, or erythrocyte, and of the evolutionary relationships of malaria parasites. In addition, he has promoted the concept of targeted vaccination against the sexual stages of the parasite. His recent interest is the molecular genetics of the mosquito vectors of malaria.

Miller received a B.S. from Haverford College in 1956, an M.D. from Washington University in 1960 and an M.S. from Columbia University in 1964. After serving with the U.S. Army Medical Corps in Thailand from 1965 to 1967, he spent four years on the faculty of the College of Physicians and Surgeons of Columbia University as a specialist

in tropical medicine. In 1971, Dr. Miller became head the Malaria Section of the Laboratory of Parasitic Diseases at the NIH. In 1992 he became chief of the newly created Laboratory of Malaria Research there.

Miller's leadership role in malaria research has been recognized by many honors, including the NIH Director's Award (1977), the Paul Ehrlich and Ludwig Darmstaedter Prize (1985) and a Presidential Award (1992). He is also a member of the National Academy of Sciences and the Institute of Medicine.

This annual lecture series on a subject related to the therapy and prevention of parasitic diseases was endowed in honor of Ernst A. H. Friedheim in 1989. Friedheim, born in Zurich in 1899, was a distinguished scientist whose work over half a century furthered the development of new and better



Louis H. Miller, a leading expert in malaria, will lecture Fri., Oct. 8.

treatments for parasitic diseases. Friedheim was a visiting professor at Rockefeller from 1977 until his death in 1989.

Potpourri

Tri-Institutional Noon Recital

The Brentano String Quartet, a new ensemble of talented musicians, together with guest artist, violist Maria Lambros Kannen, will perform at the Tri-Institutional Noon Recital today (Oct. 1). The group will play works by Seymour Shifrin and Antonin Dvorák. The concert, to be held in Caspary Auditorium at noon, is free. All are welcome.

Sunday film

Tangos, the Exile of Gardel (1985), directed by Fernando Solanas, will be shown Sun., Oct. 3 in Caspary Auditorium. The Franco-Argentine romantic musical blends

fantasy and surrealism as it tells the story of a group of Argentinian political exiles in Paris. Admission is free. All are welcome.

Book sale

The Rockefeller University Children's School will hold a book sale on Tues., Oct. 5 in the Tower Lobby from 8:30 A.M. to 3:30 P.M. Books for children and adults as well as gift items will be sold. All items will sell for 10 percent off the retail price. All profits will benefit the Children's School.

Apple Day

The annual Apple Day, during which Apple representatives demonstrate and discuss their new products, will be held Tues., Oct. 5, from 10:00 A.M. to 3:00 P.M. in the Faculty and Students Club. Apple will donate refreshments. For more information, contact Computing Services, x8940.

Electronics course

A weekly course in electronic techniques covering analog and digital circuits will be held Wednesdays at 3:00 P.M. in Caspary 1B, beginning Wed., Oct. 6. The course will consist of one and half hour lectures and a series of five laboratory experiments (to be scheduled separately by each student). In addition, there will be two lectures on computer-based diagnostic medical instruments, computed tomography scanning and magnetic resonance imaging. For more information, contact

Lawrence Eisenberg, x7896, or leave a message, x7899.

Flu shot

The influenza vaccine will be available from 10:00 A.M. to 4:00 P.M. in the Employee Health Office, beginning Wed., Oct. 6. For more information, contact Employee Health, x8414.

German classes

Beginner-level German language classes will start Wed., Oct. 6. Classes will be held from 6:30 to 8:00 P.M. on Wednesdays in Tower 833. For further information, contact Piera Cicchetti, x8945.

Memorial

A memorial program for Alan F. McHenry, president of the Richard Lounsbery Foundation will be held Thurs., Oct. 7 at 8:00 P.M. in Caspary Auditorium.

Statistical package

Statistica, a DOS-, Windows- or Macintosh-based package, encompasses a wide array of statistical procedures in an easy-to-use program designed to work with graphics. It uses a spreadsheet model for easy database management, with import and export capability with many popular packages. There are modules for virtually all the common univariate and multivariate techniques in inferential statistical analysis, frequently with numerous options for calculation or algorithmic operations. Fully integrated is a

graphics module for very high quality output (depending on the printing device used). Rockefeller students, faculty and staff may purchase copies for any of the three parts of the program at a discount of 80 percent off list price. A set of disks costs \$200 from Computing Services. The on-line documentation is comprehensive and fully cross-indexed. According to Computing Services, Statistica's system design and calculation speed are excellent.

Catalog available

The Rockefeller University's new catalog, 1993-94 *Scientific and Educational Programs Guide*, is now available. Everyone on campus is entitled to one copy without charge. A group representative may pick up copies for his or her laboratory or department from the Office of Public Affairs, Caspary 3C. Those wishing to order multiple copies of the publication, at \$8 per copy, should contact Karen Bolger, x8967. Individuals placing bulk orders should have an account number on hand.

Free bike racks

Several used bike racks are available free from the Housing Office. Contact Joanne Greene, x8500.

News&Notes schedule

News&Notes will not be published next week due to the Columbus Day weekend. Publication will resume Fri., Oct. 15.



The Brentano String Quartet will perform at the Tri-Institutional Noon Recital today (Oct. 1).