

9-16-1994

NEWS AND NOTES 1994, VOL.5, NO.1

The Rockefeller University

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The Rockefeller University, "NEWS AND NOTES 1994, VOL.5, NO.1" (1994). *News and Notes 1994*. Book 19.
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news & notes

September 16, 1994 Volume 5, Number 1

The Rockefeller University

University awards Luce fellowships to two students

Rockefeller has awarded Clare Boothe Luce Graduate Fellowships to two students: Catherine Friedman, a third-year student in the lab of Ali Hemmati-Brivanlou, and Shasta Sabo, a new student who will be joining the lab of Paul Greengard.

The two-year fellowships are made possible by the Clare Boothe Luce Program, which was established by Luce in her will to encourage American women in science and engineering. The Henry Luce Foundation, which administers the program, awarded a \$120,000 grant to Rockefeller in the spring of 1993, after inviting the university to apply for support. The Dean's Office selected candidates who met the criteria of the grant.

"I am pleased that these fellowships are going to two such impressive and deserving women," said President Torsten Wiesel. "The selection of Catherine Friedman and Shasta Sabo was based on their academic excellence, their aptitude for independent research, and their

Courtesy of the Henry Luce Foundation, Inc.



Clare Boothe Luce (1903-1987) established a fund for women in science and engineering. Two RU students have been named Luce fellows.

potential for advancement in science."

Friedman, a 1992 graduate of the University of Michigan, was first associated with Professor Donald Pfaff's neurobiology and behavior lab and then with Professor Bruce McEwen's neuroendocrinology lab.

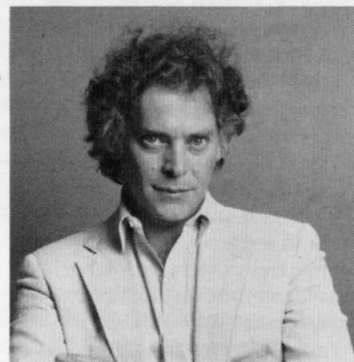
This year, she will be working with Ali Hemmati-Brivanlou on neural induction and neural patterning. Friedman was very pleased by the award: "This fellowship is designed for women in science, which is an issue I care about. So, it's nice that there's support at my level."

Sabo comes to Rockefeller from Northwestern University, where she received a B.A. in integrated sciences and biological sciences, with a concentration in neurobiology. Here, she will pursue her interest in the neurodegeneration and dementia associated with Alzheimer's disease. "I was surprised and grateful for the fellowship. Opportunities like this are great," Sabo said.

The fellowships are designated for American citizens. Although generally awarded to new Ph.D. candidates, awards may be given to continuing students who have demonstrated outstanding promise. The Clare Boothe Luce program also supports undergraduates and junior faculty.

Feigenbaum to illustrate art of mapmaking

Ingrid Grütner



Mitchell Feigenbaum lectures today at 3:45 P.M.

Mitchell J. Feigenbaum, Toyota Professor at Rockefeller, will lecture today on "World Maps and Dynamics."

The talk will focus on issues of cartography. In mapmaking, how to represent topographic curves and where to place the labels of items such as cities, rivers, and mountain ranges are major problems, in part because maps present information iconically rather than with strict spatial accuracy. These conventions and limits impose hard constraints on the design of software programs for mapmaking. In language for a general audience, Feigenbaum will give an overview of cartography and discuss ways of resolving these problems using fractals and molecular dynamics.

Feigenbaum is one of the founders of the field of chaotic dynamics. At Rockefeller, in addition to heading the laboratory of mathematical physics, he is director of the new Center for Studies in Physics and Biology, which has been established to accelerate the contributions of physics to biomedical science.

Feigenbaum has won a MacArthur Foundation Award, the Wolf Foundation Prize, and the Ernest O. Lawrence Award from the U.S. Department of Energy. He is a member of the National Academy of Sciences. He received a B.E.E. (1964) from City College of New York and a Ph.D. in theoretical physics from M.I.T. (1970).

The talk will take place in Caspary Auditorium at 3:45, preceded by tea at 3:15.

Legal scholar Ronald Dworkin to talk at Cohn forum

Ronald Dworkin, a professor at Oxford and New York Universities who has written cogently on bioethical matters, will give the first lecture in the Zanvil A. Cohn Forum on Health Affairs Tues., Sept. 20. His topic will be "Justice in the Distribution of Health Care."

"Dworkin is a scholar of international stature in the most highly charged areas of law, philosophy, and privacy. I know his philosophical and legal perspectives on health affairs will be of great interest to

the forum. It's a privilege to have him come and talk to us," said Alexander Bearn, chair of the forum's program committee.

Dworkin writes regularly for the *New York Review of Books* and has published extensively in philosophical and legal journals. His most recent book is *Life's Dominion: An Argument about Abortion and Euthanasia* (1993).

Dworkin received his B.A. from Harvard College in 1953, followed by a second B.A. from Oxford University in 1955. He returned to Harvard for a law degree, which he earned in 1957. He then clerked one year for the distinguished American judge Learned Hand. After a brief association with Sullivan & Cromwell, a New York law firm, Dworkin became a professor at Yale University Law School. In 1969, he was appointed professor of jurisprudence at Oxford, where he has remained. In 1975, he took a joint appointment at NYU. Dworkin is a Fellow of the British Academy and a member of the American Academy of Sciences. He has been a consultant on huma

Courtesy of Ronald Dworkin



Ronald Dworkin gives Cohn forum lecture Tues., Sept. 20.

rights to the Ford Foundation.

The forum on health affairs was established in 1992 by the late Zanvil A. Cohn. He envisioned a forum in which important issues in health research and policy could be informally discussed. Upcoming speakers this year are Nicholas Wade, of *The New York Times*, Oct. 25; Kathleen M. Foley, of Memorial Sloan-Kettering Cancer Center, Nov. 29; and Alan J. Friedman, director, Hall of Science, Jan. 31.

The forum begins at 5:30 P.M., in the Faculty Club. Sherry will be served at 5:00. All are welcome.

2 PETA protests at Rockefeller

3 Scientists catch some waves

4 Genes and teens

University is target of protests by activist group PETA

The work of some researchers at Rockefeller has recently been the target of protests by the activist group People for the Ethical Treatment of Animals (PETA). In its June newsletter, *Animal Times*, the group criticized the research of Alan Miller, associate professor in the Wilson lab. In August, PETA ran an ad in a local paper, *Our Town*, also attacking the work of Professor Charles Gilbert and President Torsten Wiesel. A few days later, two dozen protesters from PETA demonstrated outside the university. Two demonstrators were arrested for dumping cat excrement from a truck.

"The university is fully committed to safeguarding the well-being of laboratory animals and using them in research only when no alternatives exist," said Michael Hayre, veterinarian and director of the Laboratory Animal Research Center. "We are very scrupulous in upholding a humane program of animal care and use. Our practices conform to, and often exceed, all prevailing national standards. Rockefeller has also been at the forefront of developing alternative technologies that reduce the use of animals. But laboratory animals remain essential for much of the critical work done here and at other medical research institutions."

Essential research

Dr. Miller's research is one example of the importance of animal research. Miller uses cats to study the control of nausea and vomiting, which can be caused by

chemotherapy, radiation therapy, surgery, pregnancy, motion sickness, and diseases such as AIDS. "Almost all cancer patients who receive potent chemotherapeutic drugs suffer from nausea and vomiting. By understanding the mechanisms that trigger these conditions, we hope to design better treatments and to relieve suffering," Miller said.

Gilbert, head of the laboratory of neurobiology, uses animal models to examine the neural mechanisms of learning, memory, and visual perception. "We hope that our research will be an important step in the effort to find cures for neurological disorders that afflict millions of people," Gilbert said. Wiesel, a longtime collaborator with Dr. Gilbert, won the Nobel Prize for his research on how information is transmitted from the retina to the visual cortex of the brain and on the postnatal development of these pathways. This research, involving cats and monkeys, has led to more aggressive treatment of children born with cataracts and thus to prevention of blindness.

Lifesaving advances

Said Emil Gotschlich, Gwin-Follis Chevron Professor and head of the Animal Care and Use Committee, "Any research that involves the use of animals at Rockefeller is rigorously reviewed at several levels—by the university's veterinary staff, who oversees the humane and proper care of all animals here; and by the university's Animal Care and Use

Committee, composed of university faculty, a nonscientist, and a community member. In addition, there are reviews by the National Institutes of Health and by the American Association for the Accreditation of Laboratory Animal Care, considered the gold standard of animal care."

"It's important to bear in mind that virtually every medical advance in the past fifty years has depended on animal research in one way or another, including such advances as vaccines against polio and rubella, insulin for diabetics, coronary bypass surgery, medication for high blood pressure, phototherapy for infant jaundice, cataract surgery, kidney dialysis, hip replacements, and leukemia chemotherapy," noted Gotschlich.

An "extremist" group

Since the PETA campaign began, the university has consulted with Mary Brennan, executive vice president of the Foundation for Biomedical Research, a nonprofit group representing the scientific and medical community on the humane and responsible use of laboratory animals. "PETA is not so much concerned with protecting animal welfare, as most of us are, but with *abolishing all* animal research," cautioned Brennan. "They are extremists who cloak their radical agenda under the guise of compassion."

To ensure that its essential animal research continues unimpeded, the university has tightened security,

Martin Reschenhal

A little night music



Pianist Garrick Ohlsson performs at Rockefeller Tues., Sept. 27.

Garrick Ohlsson, winner of the 1994 Avery Fisher Prize, begins the university's evening concert series with a piano performance on Tues., Sept. 27, at 8:00 P.M. in Caspary. He will perform works by Beethoven, Schubert, Haydn, and Barber. Eight performances are scheduled for the series. For information, call Cathy Rogers, x8437.

ty, set up a special phone number to receive and monitor complaints, and answered letters and queries from the public. Anyone with questions about the university's policy on animals should contact Hayre at x8535 or Gotschlich at x8157. Copies of the policy are available from Hayre or Public Affairs, x8967. Press inquiries should be directed to Doron Weber, director of communications, at x8968.

New director at RU Press

Michael J. Held assumed directorship of The Rockefeller University Press on July 5th. He comes to the position after seven years with *The Journal of Clinical Investigation*, a monthly published by the press.

In announcing the appointment, Ingrid W. Reed, vice president for public affairs, said, "We are pleased that Michael has agreed to direct the press. His leadership in making the JCI successful and profitable, his experience with computers in publishing, and his knowledge of the peer review process and biomedical research will be very useful in shaping the future of the press."

Held is responsible for all aspects of the press—editorial, production, fulfillment, advertising, and promotion. The press currently publishes *The Journal of Cell Biology*, *The Journal of Clinical Investigation*, *The Journal of Experimental Medicine*, and *The Journal of General Physiology*. The JCI is owned by the



Michael Held is the new director of the RU Press.

American Society for Clinical Investigation, while the other journals are owned by the university. The press also has a limited book program; this fall, it will publish *The Hostage Brain* by Professor Bruce McEwen and Harold M. Schmeck, Jr., a former *New York Times* medical writer.

Held said, "I'll be introducing

electronic publishing technologies so that we can do prepublication work in house. That should reduce the lag between manuscript acceptance and publication, which is a major concern of scientists today. I also hope to expand the number of journals we publish."

Held has worked in biomedical publishing for over a decade. He has a B.A. in English, German, and linguistics from Juniata College (1975) and two M.A. degrees in linguistics from the Pennsylvania State University (1979 and 1981).

"I would be happy to exchange ideas with anyone in the university community, especially now, when I'm trying to define how the press can best contribute to the university's future," said Held (x8571, box 291, or e-mail held).

Raymond T. Fastiggi, who served as interim director of the press, has been named associate director of finance by Held.

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.

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Catching some rays: Scientists seek enlightenment from cell receptors

by Susan Blum

Multicolored leaves, twinkling stars, soaring birds—the wonders of the visual world seem infinitely varied. Yet they all boil down to one basic, biophysical constant: Photons—packets of light energy—activate receptors on the surface of cells in the retina, setting off cascades of intracellular events that result in vision by day and by night.

Researchers in the lab of Associate Professor Tom Sakmar are illuminating some of the events that occur when light activates a receptor called *rhodopsin* in rod cells, the retinal cells responsible for vision in dim light. In so doing, the scientists hope to shed light on a broader subject, as well: the general mechanisms whereby messages are sent, or *transduced*, by all of rhodopsin's molecular cousins, collectively known as the superfamily of "G-protein-linked cell surface receptors."

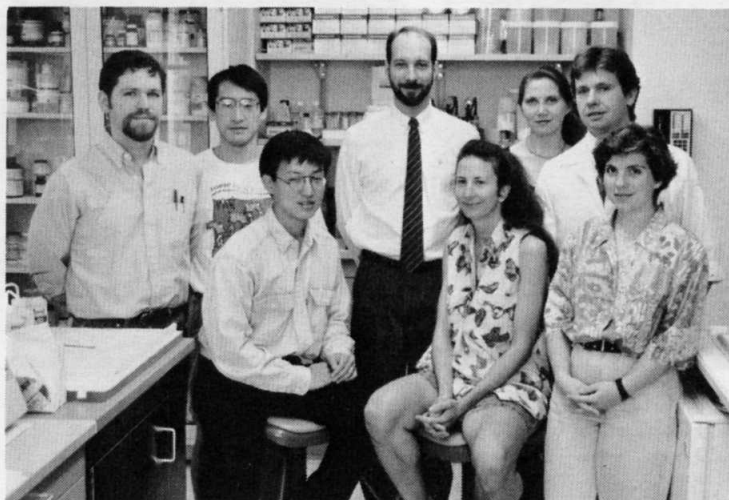
Family resemblances

G-protein-linked receptors are the largest family of cell surface receptors, the sentinel proteins that enable cells to receive information from one another and from the outside environment. So far, more than 200 different G-protein-linked cell surface receptors have been identified. Each is specialized for its own particular function, but all share certain characteristics.

For instance, every G-protein-linked cell surface receptor threads through the cell's fatty surface membrane seven times. When activated by its own specific messenger—be it a hormone, neurotransmitter, or growth factor, a smell, taste, or photon—the receptor in turn activates its own particular "G protein"—a molecular switch that flips between an on and off state. Switched on, the G protein then activates a specific "effector" molecule, which sends the incoming message further along.

Rhodopsin, the rod cell receptor, is a two-part molecule. One component, opsin, weaves through the cell's surface membrane. Retinal, the other component, is chemically linked to opsin. When light of the proper wavelength hits the rod cell, retinal changes its conformation and rhodopsin is activated. The activated rhodopsin then switches on its G protein, *transducin*, which in turn activates an effector molecule called a phosphodiesterase.

Sakmar and his associates have used an unusually wide range of techniques to study the molecular



Associate Professor Thomas Sakmar (center) studies the vertebrate visual protein rhodopsin with colleagues (left to right) Stephen Gravina, Stephen Lin, Christopher Min, Lenore Snyder, Tatyana Zvyaga, Cliff Sonnenbrot, and Sophia Arnis.

interactions set in motion when a photon tickles rhodopsin. Biophysical, biochemical, and molecular biological methods have all been enlisted to obtain information about how the molecules' structures relate to their functions. Such a multidisciplinary approach is made possible both by rhodopsin's special characteristics—because it is a pigment, it is amenable to spectroscopic analysis—and by Sakmar's undergraduate and postgraduate training in chemistry.

On the whole, Sakmar says, "we take a pretty chemical approach to the study of biological problems." For example, the researchers have exploited spectroscopy to pinpoint exactly which chemical groups in opsin and retinal shift protons around as they undergo their characteristic conformational change upon activation. But the researchers routinely employ the techniques of molecular biology and biochemistry, too, in order to engineer, express, and analyze mutant proteins. In this way, for example, they located regions in rhodopsin that appear to play key roles in activating transducin. They are also using such techniques to study the interaction of transducin with the pathway's effector molecule.

Relating research to disease

The approach the lab takes to study signal transduction is about as basic as basic research can get, Sakmar says. Nonetheless, as a trained physician as well as a chemist, he is clearly compelled by the accumulating body of research that directly links defects in signal transduction to disease.

The more scientists learn about

how incoming signals prompt fundamental cellular activities such as growth, differentiation, division, and even death, the more it becomes evident how messages gone amok might wreak cellular disaster. In recent years, a number of diseases (including some cancers) have been traced to misfunctions in G protein signal transduction pathways. Some of the afflictions have been traced to misbehaving G proteins, while others are linked to malfunctions in the cell surface receptors. For instance, receptors apparently are to blame for one form of hyperthyroidism and for a type of precocious puberty. In both cases, the receptors in question are mutated in such a way as to be constantly, or *constitutively*, active, even in the absence of an incoming signal. Moreover, at least one visual disorder—congenital stationary night blindness—has been traced to constitutive activity of the rhodopsin receptor.

Retinitis pigmentosa

Mutations in rhodopsin are also involved in retinitis pigmentosa (RP), the most common form of inherited blindness. Among these mutations are those that occur in rhodopsin's cytoplasmic surface—the region that peeks into the cell after the molecule completes its seven passes through the cell membrane. The Rockefeller team found that some of these mutations leave intact rhodopsin's ability to be activated by light, but impair its ability to bind or activate the G protein, transducin.

These findings suggest that some cases of RP may result from disruptions in signal transduction. But a

full understanding of the complex disease is still far off. More than 60 different mutations in rhodopsin can cause RP, and many of them occur nowhere near the protein's cytoplasmic face. Might some of the mutations affect signal transduction, while others affect the cell's metabolism, and still others its structural integrity? Currently, researchers can only speculate how the various rhodopsin mutations might contribute to the disease's varied manifestations. And to make matters yet more complicated, mutations in a number of proteins besides rhodopsin are also known to cause the disease.

Taking new paths

Clearly, many questions remain about rhodopsin and other proteins in the rod cell's signaling pathway. But as Sakmar and his co-workers plan their next wave of investigations into this system, they are branching out in some new directions, as well.

"We've learned enough about rhodopsin that it's now time to see if what we've learned applies to other physiologically important receptors," Sakmar says. "We're interested in directly testing the hypothesis that structural features of rhodopsin affecting its activity are in fact present and important in other receptors."

They have chosen two receptors to study. One, the D4 dopamine receptor, plays a key role in central nervous system signaling; malfunctions in this system may be tied to schizophrenia. The other, the glucagon receptor, is a vital player in the cellular signaling systems that maintain the body's blood sugar level; diabetes results when these systems go awry.

Studies on the glucagon receptor are being conducted in collaboration with members of the Merrifield lab, which has long had an interest in the subject. The collaboration already has one paper in press, which pinpoints a single amino acid in the receptor that plays a key role in binding its messenger molecule.

Sakmar calls the paper a real turning point for the researchers, who have always viewed their studies on vision as a way to see deeper into general mechanisms of signal transduction via G-protein-linked cell surface receptors. He says, "In many ways, the glucagon receptor is quite different from rhodopsin. Yet we've been able to apply much of what we've learned about rhodopsin to this other receptor. So far, it's working out quite well."

A summer of microbiology at RU: Teens learn about genes and gels

Thanks to a unique initiative forged by Associate Professor Elaine Tuomanen with an all-girl's school, the Science Outreach Program, and a biotech company, important scientific discoveries were made this summer at Rockefeller—by teenagers.

Tuomanen had mentored students from the Convent of the Sacred Heart in the past. One girl who had worked in her lab ended up at M.I.T. Two others had found significant receptors for pneumococci on human cells. Impressed with these results, Tuomanen invited students at the school to join her lab for a summer of microbiology.

Seven students jumped at the opportunity. To support them all, Tuomanen procured assistance from Alkermes, a blood-brain barrier company in Boston. Tuomanen then turned to Rockefeller's outreach program. Coordinator Bonnie Kaiser helped arrange for the participation of a Sacred Heart science teacher, Sheila Gilligan, who collaborated with Tuomanen in developing the summer project.

Gilligan was one of six new teachers chosen to spend two summers gaining research experience at Rockefeller. Kaiser said that the outreach program, which introduces research to high school students and science teachers, hosted 70 students and a dozen teachers in 33 Rockefeller labs this summer. Professor Bruce McEwen, director of the program, said, "The enthusiasm of the visiting students and teachers, and their ability to get rapidly into real science, is a tribute to them and to the reciprocal enthusiasm of the Rockefeller community. The outreach program has



Sheila Gilligan, a science teacher from Convent of the Sacred Heart, works with Kimberly Zick, one of seven high-school students who worked in Associate Professor Elaine Tuomanen's lab this summer through Rockefeller's Science Outreach Program.

made rapid progress under Bonnie's imaginative supervision."

This year, Kaiser asked outreach teachers to meet weekly with small groups of students to talk shop. "They get the students to focus on essential questions," said Kaiser. "It's a very sophisticated teaching they get to practice."

But, Gilligan asserted, it requires a "certain quality of student. These girls carry on without you poking them in the back." The seven recruits were: Maria Bradley-Moore, Nok Chhun, Jenny Min of the Bronx High School of Science, Jessica Nowilla, Lylette Pizarro, Judy Shen, Josephine Taverna, Kerry Tynan of Our Lady of Mercy Academy, and Kimberly Zick.

Gilligan and Tuomanen decided to choose a project with potential medical applications. With Assistant Professor Rob Masure, they first put the girls through basic training. "We filled in from high school science to the level of

understanding it takes to do molecular biology," said Tuomanen. In just ten days, the students learned sterile technique, gel electrophoresis, and other basic lab techniques. Each summer intern then got one gene to characterize. Tuomanen had rounded up the usual suspects—in this case, genetic accomplices in cell death, the kind of cell being pneumococcus and the death resulting from antibiotics. The "binding triggers a suicidal enzyme in the bacteria," Tuomanen explained. "We use the verb trigger because we don't understand how it happens. It's a black box. We asked the kids to look for genes in the black box."

Tuomanen got what she requested: Of the seven genes the girls characterized, one turned out to be a sensor—a gene on the surface of the bacteria that monitors the environment, checking on matters such as whether antibiotics are storming the cell's walls.

"The best gift was that they suc-

ceeded scientifically. It was the high point of the summer, when they put that DNA sequence into the data bank," remembered Tuomanen. "Everyone was piled over the edge of the computer waiting to see what it was. And it came back as a sensor. We suspected there had to be a sensor. Now we know we are on the right path."

But the discovery was more than a new datum, she said. "They ran up and down the corridors, shouting, 'we did it.' They knew it was a real discovery, it has to do with real medicine, it's going to impact real people. Events like these can define which direction you take in life."

Gilligan concurred that the summer's main lesson was not about science per se but rather about the scientific journey. "Here there's no right answer at the end of the experiment. If you repeat the experiment and get the same results, you know it's the right answer. You learn to do good science."

Kaiser said the group submitted "elegant research reports. Clearly they had mastered the science driving the lab work."

Said Gilligan: "I've been surprised that these girls of sixteen have the maturity to explore the possibilities that might help them decide what to do with their lives." But Gilligan also vouched for the girls as girls. Outside the lab, she asserted, they gab. "We talk regular teenage talk. We laugh a lot," Gilligan said.

Tuomanen usually celebrates the identification of a gene with a party and a cake. At the weekly meeting just before summer's end, the girls were wondering, now that they had their genes, would they get to eat their cake, too?

Potpourri

In Memoriam

The university community mourns the passing of Richard B. Salomon, RU Council member and father of university trustee Richard E. Salomon. A memorial service will be held today (Sept 16) at Brown University, where he was an alumnus and benefactor.

Birth

Karen Smith, senior major gifts officer in the Development Office, and Aron Buksan have a new addition to their family: Catherine Rose, born on July 14. Catherine weighed 7 pounds, 4 ounces at birth.

Beer

The Faculty and Students Club inaugurates a new beer, Fullers ESB, today. All are invited to welcome real beer to Rockefeller. Address queries to club president David Gadsby, x8680, or club manager Pat Griffin, x8078.

Medical Complex Art Show

Members of the university community are invited to submit up to 6 slides or photographs of paintings, sculpture, photographs, or handicrafts for the Fourth Medical Complex Art Show. The show, sponsored by Cornell Medical Library and Lenox Hill Artists Forum, will be at the Library, from Nov. 1994 to Jan. 1995. Send submissions to Helen-Ann Brown until Sept. 30. For more information,

contact Brown, 746-6092.

Weekly Research Seminar

Dates are still available to invite speakers for the Weekly Research Seminar (formerly the Junior Faculty-Student Seminar Series). Submit proposals to Claude Desplan, fax x8370, box 151, or phone x7965.

Volunteers

The hospital is seeking volunteers with an interest in arts and crafts to help patients enjoy leisure time. If interested, call Eva Sievert, x8474.

RU Calendar

Items for The Rockefeller University Calendar of Events should be submitted to Joseph Bonner via e-mail, bonnerj, fax, x7876, or interoffice mail, box 68.

Abby Dining Room Reopens

The Abby Aldrich Rockefeller dining room is open again for luncheon service.

To celebrate, Food Service is offering a reduced price next week (Mon., Sept. 19 to Fri., Sept. 23): the buffet will be \$7.50 plus tax per person. Next Friday (Sept. 23), a drawing will be held to win a voucher for five free lunches. To enter, stop by the dining room next week and fill out an entry.

Once again, frequent diners may earn a free lunch after paying for nine; and groups of four or more celebrating birthdays or anniversaries may request, a day in advance, a free cake (resuming Oct. 3).

For reservations, call x8894.