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The Rockefeller University

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news & notes

October 30, 1992 Volume 3, Number 8

The Rockefeller University

Mellon Foundation awards RU \$2.5 million for graduate program

The university has met the terms of an Andrew W. Mellon Foundation challenge grant and will receive \$2.5 million, announced David Rockefeller at the fall meeting of the Rockefeller University Council last week. The new grant will establish a graduate research fund to be named in honor of William O. Baker, chairman emeritus of both the Mellon Foundation and The Rockefeller University Board of Trustees.

"Generations of graduate students will benefit from this most recent generosity of the Mellon Foundation," said President Torsten Wiesel. "Given the rising costs of education and basic research, the fruits of this kind of private partnership are incalculable."

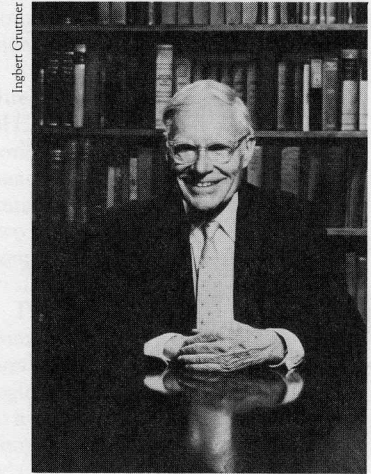
The Mellon Foundation, one of the nation's largest private foundations that supports the humanities, arts, the environment, and medical education, gave an initial \$1 million in April 1990 to support Rockefeller's graduate program. At the time, the Foundation announced that an additional \$2.5 million would be contributed if the university raised \$5 million in endowment for the program through other private sources.

The initial Mellon gift of \$1 million permanently endowed two Ph.D. fellowships in honor of Baker. Susie Jun of the Desplan lab and Andrew Millar of the Chua lab are the first two William O. Baker Graduate Fellows.

Baker, a leading international fig-

ure throughout the scientific and philanthropic communities, served first as head of research, and then as president and chairman of Bell Laboratories, from 1955 to his retirement in 1980. Under Baker's direction, research programs at Bell Laboratories created the laser, among other important scientific innovations.

Bruce McEwen, dean of graduate and postgraduate studies and RU alumnus, praised the Mellon gift and the students who will benefit from it: "This grant reaffirms the philosophy we have concerning Rockefeller's students—that they are full-fledged members of our scientific community. They are after all some of the best young minds working in their respective fields."



The Mellon graduate fund was named in honor of William O. Baker (above), chairman emeritus of the RU Board of Trustees.

New Rockefeller survey to stimulate food for thought

How satisfied are you with the overall food quality at Rockefeller? What changes would you make in the way food is served and in the seating areas? The Rockefeller Food Service wants the answers so, in early November it will give 500 members of the university the opportunity to express their opinions and recommendations in a written survey. The survey, designed by an outside company, will be the first of its kind at Rockefeller.

Surveys will be distributed by inter-office mail to a wide cross-section of the university that will include individuals who do not currently use the RU dining facilities. "Not only do we want to hear from people who use our dining facilities, but we want to make sure that



Heath Braunstein, food service director, will oversee the new survey.

we hear from people who do not dine here," says Heath Braunstein, food service director, who is overseeing the survey. "Maybe there is something that we can do to change their minds."

Because there are approximately 1,600 people on campus, the survey recipients will be determined electronically by Telecommunications to ensure a representative sampling.

In his four years at Rockefeller, Braunstein has taken people's comments and suggestions very seriously because he feels that there is always room for improvement. He placed a suggestion box at the entrance of the cafeteria to encourage feedback. However, the number of comment slips has recently dwindled. "I think this is because people don't think it makes a difference," explains Braunstein, "but

I read every suggestion, and make changes that fit in with our budget." Recently for example, the salad bar was enhanced with a wider selection of fresh items in response to a comment from the suggestion box.

Some questions in the survey use a rating scale of 1-10, with "Extremely Satisfied" at one end, "Not at all Satisfied" at the other. The ratings cover items such as availability of healthful foods, cleanliness of dining areas, and friendliness of the cashiers.

Demographic questions probe menu tendencies (grill, hot entrees, salad bar), frequency of cafeteria lunches, and frequency of in-between snacks.

A single-sheet addendum, designed specifically for Rockefeller, asks such questions as "What changes if any would you make in the way food is served and in the seating areas that would make you more likely to use the cafeteria?"

"We're after the big picture," says Braunstein. "Once the survey company tabulates the responses, and hands over the analysis, we should begin to identify the areas that need improvement." Rockefeller may be seeing some changes before the end of the year.

If Braunstein had to pick a question that matters most to him, he would choose the open-ended com-

ments sections. "I will personally review all five hundred of these if I can, because this is where one gets the most constructive feedback."

The Rockefeller Food Service tries to be competitive. This year, price hikes were smaller than they have been in the past five years. "Our competition is not on First Avenue. People won't get a better value there—greater variety maybe, but not a better price," says Braunstein. "Actually, our greatest competition comes from the brown-baggers, the people on a tight budget who bring their lunch from home."

Fifteen minutes will suffice to fill out the questionnaire, and the incentive is a free large coffee, or large fountain beverage. Completed surveys should be dropped off in a designated box by the cashiers.

2 Healthy volunteers at RU

3 SH2 structures revealed

4 Security presents new info packet

ROCKEFELLER UNIVERSITY FOOD SERVICE SURVEY

We are conducting a survey of the food service program to understand your needs and the needs of others like you. Your participation will give us a long way towards providing the kind of food service that will meet your needs. To complete the survey, simply circle the one number that corresponds to your answer for each of the items below. If a question or category of questions does not apply, please circle 0 under the "No Opinion/Not Applicable" column. Please return your completed survey to the designated area within the food service facility.

1. Overall, how would you rate your satisfaction with the food service location, using a scale where 10 means extremely satisfied and 1 means not at all satisfied?

Extremely Satisfied	Neutral	Not at all Satisfied
10	5	1
Overall food quality	10 9 8 7 6 5 4 3 2 1 0	
Availability of healthful/low-fat foods	10 9 8 7 6 5 4 3 2 1 0	
Availability of convenience foods	10 9 8 7 6 5 4 3 2 1 0	
Variety of offerings	10 9 8 7 6 5 4 3 2 1 0	
Meeting your food preferences	10 9 8 7 6 5 4 3 2 1 0	
Overall atmosphere	10 9 8 7 6 5 4 3 2 1 0	
Appearance of dining area	10 9 8 7 6 5 4 3 2 1 0	
Cleanliness of tables, silverware	10 9 8 7 6 5 4 3 2 1 0	
Cleanliness of dining area	10 9 8 7 6 5 4 3 2 1 0	
Overall quality of service	10 9 8 7 6 5 4 3 2 1 0	
Friendliness of cashiers	10 9 8 7 6 5 4 3 2 1 0	
Speed of cashiers	10 9 8 7 6 5 4 3 2 1 0	
Consistency of menu	10 9 8 7 6 5 4 3 2 1 0	
Overall picking of menu items	10 9 8 7 6 5 4 3 2 1 0	
Overall value for the money	10 9 8 7 6 5 4 3 2 1 0	

An excerpt from the new food survey to be distributed in early November.

Rockefeller researchers study healthy volunteers to understand the causes of disease

by Jennifer Horne King

Sharon Cabansag, a biology student at Kalamazoo College in Michigan, is participating in a cholesterol study for Elizabeth de Oliveira e Silva of the Breslow lab. In exchange, Cabansag gets three months of hands-on research experience in the lab, and free room and board at the RU Hospital.

"Now, I know how patients feel," says Cabansag, who is considering medical school. "I'm woken up at 6 a.m. every morning and have my blood drawn frequently... and I've been eating a very controlled diet for the past six weeks!" But Cabansag says it's a fair exchange because, while she's a patient at night, she learns how to purify high density lipoprotein (HDL), make solutions, and analyze data during the day. She says she is now learning how to do things that she only heard about in her lectures at school.

"I know I'm doing it for science," Cabansag remarks, "because sometimes I think how easy it would be to cheat on my diet. But I don't, because I'm interested to see what happens to a normal individual's plasma lipoproteins on this diet."

The study of normal function and physiologic responses in healthy persons can often lead to valuable insight about where, why, and how things go wrong in diseased individuals. Healthy volunteers are recruited by scientists through advertisements (on campus bulletin boards and in newspapers), or through educational exchange programs. Usually, there are financial or educational incen-

tives for participating. Following an interview and careful explanation of the study protocol, volunteers may agree to participate as "normal" subjects.

In elucidating the biological basis of addiction, Mary-Jeanne Kreek, associate professor and physician, uses normal volunteers to measure their neuroendocrine, gastroenterologic, and immune responses to varying levels of neuropeptides.

"I cannot just study patients with addictive diseases," says Kreek, "because I wouldn't know whether their response to the neuropeptides was due to the disease, modified by the disease, or whether it was a normal response."

Postdoctoral fellow Radmila Runic of the Phillips lab has her own reasons for using normal volunteers. She collects semen samples from male volunteers to test the contraceptive properties of compounds that are known to inhibit the transmission of the HIV virus. "I could get my samples from the RU Hospital, but those samples tend to come from infertile patients," Runic says. "How can I test a drug that impairs normal sperm motility on a sample that already has abnormal motility?"

Sometimes volunteering means putting up with an invasion of privacy, and a lot of tests. Moreover, each researcher has set rules to prevent subjects from doing things that might interfere with study results. Sometimes, these rules require a lot of self-control.

"I find that when we explain not just what we're doing, but why we're doing it, above and beyond

the consent forms, our volunteers are enthusiastic, and ultimately more compliant," says Kreek, whose studies usually involve blood drawings, urine collections and behavioral monitoring.

A long-term metabolism study from the Hirsch lab involves three-month inpatient stays at the RU Hospital on a controlled liquid formula diet. During the study, volunteers lose or gain 10% of their body weight, and at set times when body weight has stabilized, their metabolism is extensively tested.

One of these tests involves living in a "room calorimeter", a room equipped to monitor body movement, gas exchange, and collect all body wastes for 24 to 36 hours. Volunteers are flown to Phoenix, Arizona, where this specially equipped room is located.

"Someone who comes in as a volunteer doesn't leave a stranger, that's for sure," says research assistant David Markel, who helps coordinate the recruiting and scheduling for the human studies. "The people who come in have to be highly motivated. I admire them for doing this. They're doing it for the benefit of science."

Volunteer and Rockefeller employee Barbara Sutphin says that when she participated in a diet study for de Oliveira, she had to juggle coming to the Hospital each morning before 8:00 a.m. and working a full day. For this study, which also concerns HDL turnover, Sutphin had to drink a fixed amount of vodka each day while eating a high-fat diet. Sutphin is not a vodka drinker, and therefore had to find ways to make it more palatable. She finally settled on mixing it in iced-tea. Currently, she is beginning the second part of the study, which involves the identical protocol with the high-fat diet, and no alcohol.

Not only do volunteers tolerate some of the inconveniences that go along with being a study subject, but researchers say that they often come back to participate in later studies. De Oliveira says that seven sets of twins have returned for a second study concerning HDL turnover and diet in twins. "The monetary compensation we provide is negligible compared to the research data obtained," says de Oliveira, who covers travel expenses only, but offers the twins a chance to meet up over long dis-

tances and visit New York City. "I would not be sure of the subjects' commitment to science if I paid them too much. I'd like them to be as committed as I am."



Researcher Elizabeth de Oliveira sits before some photos and mementos from her volunteers.

De Oliveira has received many appreciative letters and gifts from her volunteers, including a framed needle-point of two identical-looking cherubs from one set of twins. Most of the letters express an interest in the outcome of the studies.

Researchers are grateful for the contributions of their normal human volunteers. "Volunteers are invaluable to our work, and ultimately to humankind," says Kreek. "Thanks to them, we're opening up a whole new realm of physiology."



In her home-away-from-home at the RU Hospital, study subject Sharon Cabansag inspects her special diet luncheon. The rest of her day will be spent as a research assistant in the lab.

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Rockefeller collaboration yields impressive results

by Susan Blum

Among biology's major unsolved puzzles is the intricate communication network that regulates how a cell differentiates, grows, and divides. Two papers published simultaneously by Rockefeller scientists in *Cell* and *Nature* last August moved the puzzle one step closer to solution, by describing the structures of a crucial element in the matrix of cellular communication. Appropriately enough, the work of these scientists was facilitated by the unique possibilities for communication and collaboration that exist at the University.

The papers report for the first time the three-dimensional structures of SH2 domains. These domains, or regions, are found in numerous proteins, and serve as "readers" for messages that are sent through the cell in response to a signal from a growth factor or hormone.

"To send a signal, you need something that acts as a switch, like a green light or a red light," explains John Kuriyan, who led one of the multi-lab groups involved in the research. "There are several different molecular switches, and one of the most important is whether or not a tyrosine in a particular position on a particular protein has a phosphate group attached to it. The role of the SH2 domain is to recognize the phosphorylation state by binding to phosphorylated tyrosine."

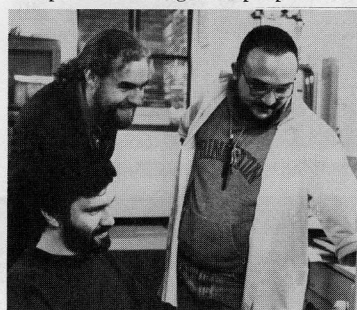
David Cowburn, the leader of the other multi-lab group, explains, "SH2 domains are vitally important in regulating normal cell differentiation, growth, and division. The uncontrolled cell growth that is a hallmark of cancer results from the breakdown of one or more of the switching mechanisms directly involved with these domains." Indeed, many oncogenes, or cancer genes, are genes whose normal function is to code for proteins containing SH2 domains. When these genes are mutated, the messages they transmit are scrambled in ways that contribute to cancer.

Before the new papers were published, only the linear amino-acid sequences of SH2 domains were known. By revealing the domains' three-dimensional structures, the Rockefeller researchers have shown how SH2 domains can recognize phosphotyrosine. Ultimately, such information may lead to a better understanding of how cancer develops, and to therapies that might halt its progress.

Scores of laboratories worldwide are studying SH2 domains. But Cowburn and Kuriyan, whose labs used completely different but complementary techniques, say that Rockefeller's unique organization and its traditional strength in oncogene research made it possible for them to be among the first researchers to report the domain's structure, and the very first to describe SH2 interactions with phosphotyrosine. (A third group, from Oxford University, reported the structure of another SH2 domain at the same time.)

In the August 21 issue of *Cell*, the team headed by Cowburn reported the structure of the SH2 domain of a protein called *abl*. The *abl* gene, which codes for this protein, is implicated in leukemias in mice and in humans, and is under study in the Baltimore lab. Bruce Mayer, a postdoctoral fellow with David Baltimore, collaborated with the Cowburn team, supplying ample quantities of the *abl* SH2 protein—a crucial step for discovering the protein's structure.

The *abl* SH2 protein was the right size for study by the nuclear magnetic resonance (NMR) techniques employed by members of the Cowburn lab. This method studies molecules as they float in solution. It exploits the magnetic properties



Collaboration facilitated the discovery of the 3-D structures of SH2 domains. *Left, clockwise from top:* Nalin Pant, Carlos Rios, and Michael Overduin are members of the Cowburn lab. *Right:* Gabriel Waksman and Dorothea Kominos are members of the Kuriyan lab.

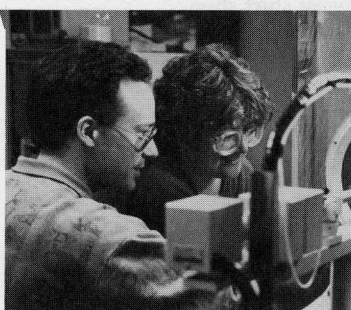
of atomic nuclei, revealing the distances between hydrogen atoms and the "cross talk" they engage in. Key players in the work of NMR measurement and interpretation were graduate fellow Michael Overduin and postdoctoral fellow Carlos Rios. Overduin derived the final three-dimensional structure of the *abl* SH2 domain.

In the August 20 issue of *Nature*, the team headed by Kuriyan reported on the structure of the SH2 domain of a protein called *src*, bound to two different tyrosine-phosphorylated peptides, or short chains of amino acids.

The *src* gene has a long tradition of study at Rockefeller, dating to Peyton Rous' discovery in 1913 that a virus can cause cancer. The viral oncogene involved was later identified as *src*. Today, the *src* gene is under study in the laboratories of Rockefeller researcher Hidesaburo Hanafusa and Memorial Sloan-Kettering investigator Marilyn Resh. Together, they provided guidance and insights that enabled postdoctoral associate Dorothea Kominos, research associate Gabriel Waksman, and research assistant Scott Robertson in the Kuriyan lab to clone *src*'s SH2 segment and overexpress it.

The Kuriyan lab used the techniques of x-ray crystallography to derive their structural information. In this technique, crystallized proteins are bombarded with X-ray beams. The beams bounce off electrons whirling around individual atoms within the crystal, and then scatter ("diffract") in all directions. Intercepted by a detector, the diffracted rays form a pattern that a computer "reads" as a map of electron density. Waksman conducted the diffraction experiments and interpreted the results.

Though the Kuriyan and Cowburn labs started their projects independently, they soon learned about one another's work.



"Rockefeller has a very high concentration of labs working on biological problems without departmental barriers. You tend to float around and talk to a lot of people," Kuriyan says.

The communication proved beneficial to both research groups. Nalin Pant, a postdoctoral associate in the Cowburn lab, had synthesized tyrosine phosphorylated peptides for studies underway in that lab. They provided these peptides to the researchers in the Kuriyan lab. When the peptides were mixed with the *src* SH2 proteins, crystals resulted that were close to ideal for the x-

ray crystallographic studies. The Cowburn group also provided the Kuriyan lab with their NMR data on the *abl* SH2 domain, which helped researchers in the Kuriyan lab interpret their electron-density maps. "It saved us a considerable amount of time," Kuriyan comments.

Reciprocally, the Kuriyan lab's three-dimensional picture of the *Src* SH2 domain provided welcome confirmation of the Cowburn lab's image of the *abl* domain. "It was immensely reassuring to see that the two structures, determined by two completely different methods, were so similar," Cowburn says.

The structures show that the SH2 domain provides a novel architectural solution for the common biological problem of binding a peptide to a protein. The region of the domain binding tyrosine-phosphorylated peptides is a "socket," while the domain as a whole has a modular structure facilitating its insertion into a wide range of proteins—a prerequisite for a domain that serves as a linker forging assemblies of proteins that pass a message along.

The description of a novel domain structure is not the only "first" to emerge from the work of the Rockefeller researchers. It also presents the first views ever of a bound tyrosine-phosphorylated peptide. Moreover, because the NMR studies visualized the SH2 domain in the absence of peptide, while the x-ray crystallography studies visualized it bound to peptide, "comparing these two structures allows us to see the SH2 domain in both its 'on' and 'off' stages," Kuriyan points out.

The structures of the *src* and *abl* SH2 domain are so similar that the Rockefeller researchers believe all SH2 domains will prove to resemble each other overall. But now a new question beckons: What structural features make each SH2-containing protein different from all the others? Though all such proteins probably bind just about all tyrosine-phosphorylated proteins, each SH2 domain has its own characteristic pattern—binding some phosphorylated proteins very strongly, and others only weakly.

Once researchers can answer these questions of specificity, they will be far closer to a fundamental understanding of how cellular messages are communicated. Those answers are not yet around the corner. But Rockefeller's unique traditions and organization hold out the promise that when they come, some of the answers will emerge from collaborations forged at the university.

Security presentation features new information packet

Joseph Nekola, director of Security, recently presented a two-page information packet and some useful off-campus safety tips at a security orientation meeting for new students.

The newly required packet, written by Nekola in response to recent changes to the Student Right-to-Know and Campus Security Act of 1990, contains facts and statistics about Rockefeller security and reported crimes on campus.

The packet recommends such things as the use of extension 1111, a 24-hour response line to report crimes or suspicious incidents (residents of Sophie Fricke and the Graduate Students' Residence must dial 327-7111). It also contains some interesting facts. For example, 36 rotating security personnel ensure a complete campus patrol every 4 hours.

Nekola, former captain of detectives for the New York City Police Department, attributed the low number of crimes on campus to excellent campus vigilance. "Seventy-five percent of intruders are caught through people reports," he said, "because people on campus know who belongs and who

doesn't." One such intruder was recently caught walking off campus with a typewriter in a bag.

To prevent such incidents, Nekola recommends engraving and



Joseph Nekola, director of Security, wrote the new packet.

securing portable equipment. "A social security number engraved in full view on any item makes it unmarketable," he noted. An engraving tool is available to the university on a sign-out basis from the Security Department.

"Overall," Nekola remarked, "the Rockefeller area is one of the safest in the city, which explains the low crime rate." Nevertheless, he warned against having a false sense of security, and advised using

68th Street when crossing over to First Avenue in the evenings. Nekola also recommended that members of the RU community be especially attentive near automatic teller machines and outside of banks in the Rockefeller vicinity, where several muggings have recently occurred.

Following Nekola's presentation, a video was shown concerning sexual assault prevention. The film focused primarily on the idea that one is not helpless in situations that involve strangers or potential attackers.

In one scenario, a woman waiting for a bus is approached by a suspicious-looking man who wants to make conversation. The woman answers his first question politely, looking at him straight in the eye, then turns away. (Here, the man either walks away, or continues to try to engage her.) When the man persists, the woman tells him firmly that she wants to be left alone. (Here again, the man may be discouraged and leave, or will act more aggressively.)

Finally, when this fails, the woman turns around and enters a shop to wait for the bus there.

The scenario stresses the use of strong signals and specific actions that can help to dissuade accosters who often test potential victims for vulnerabilities.

Students, faculty, and staff may borrow the video on sexual assault prevention from the Dean's office. In its continued effort to keep the university informed about personal and campus safety, the Security Department is planning another seminar in the spring.

Through a series of mock scenarios, the sexual assault video presents the following tips:

- trust your instincts
- use strong body language and an assertive voice to convey assurance and purpose
- make travel plans before setting out on any outing
- do not be afraid to make a scene in a public place
- physical confrontations should be a last resort
- use a buddy system whenever possible
- remember: personal safety is more important than personal possessions

Potpourri

Free literature search

A new bibliographic search program using CD plus will be available on the first floor of the Library, free of charge, 24 hours a day for one month, beginning Nov. 1. The program has the speed of an online program but provides the ease of a system designed for microcomputers. Users will be able to do their own searches and results can be printed or down-loaded to users' floppy disks. For more information contact Patricia Flowers at x8907.

Tri-Institutional Recital

Cellist Hai-Ye Ni and pianist Anne Epperson will perform works by Schumann, Poulenc, and Chopin at The Tri-Institutional Noon Recital today (Oct 30). The recital, to be held in Caspary Auditorium at noon, is free and open to the Tri-Institutional community.

New York City Marathon

News & Notes would like to hear from all RU participants in Sunday's Marathon (Nov. 1). Please call Jennifer at x8967.

Sweat shirt shop

The Sweat Shirt Shop has just received a new shipment of T-shirts and sweat shirts. The shop is open from 11:30 a.m. to 1:30 p.m. every Tuesday. Follow the yellow tracks in the tunnel by the Laundry Room.

Children's School applications

RU families should remember to submit applications for the Children's School. The places are assigned on a first-come-first-serve basis. Call Marjorie Goldsmith, x8580.

Holiday rates for guestrooms

The Housing Office is offering the Rockefeller community and their family members special holiday rates on Abby Hall guestrooms for weekends in Nov. and Dec.—two nights for the price of one. Weekends are Fri/Sat. or Sat/Sun. Reservations are subject to room availability. For reservations call x8050.

Film Series

Two masterpieces of German expressionist cinema, *The Cabinet of Dr. Caligari* (Das Cabinet des Dr. Caligari), Germany, 1920, a silent movie directed by Robert

Wiene, and *Nosferatu the Vampire* (Nosferatu-Eine Symphonie des Grauens), Germany 1922, also a silent movie directed by F. W. Murnau, will be shown free on Sun Nov. 1 at 7:30 p.m. in Caspary Auditorium. All are welcome.

Postdoctoral fellowship

Harold Brown, postdoctoral fellow in the Pfaff lab, was one of 25 to receive an award from the Ford Foundation Postdoctoral Fellowships for Minorities Program.



Putting the finishing touch on Halloween preparations at The Rockefeller Children's School.