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news & notes

March 12, 1993 Volume 3, Number 23

The Rockefeller University



Research Assistant Christopher Scott (right) shows Kathy Bae and David Kwok around the Breslow lab last Friday as part of the university's third annual Minority Open House.

Minority Open House welcomes potential employees

The Rockefeller University welcomed 20 minority undergraduate students from nine colleges in the Tri-state area to the third annual Minority Open House for Life Science Majors on Friday.

"The idea behind the Minority Open House is to give undergraduate students a true flavor of Rockefeller from discussions with employees who are close to them in age and career experience," said Mary Ann George, employment supervisor in the Personnel Department, who helped organize the event. "We want to encourage minority undergraduates in pre-medical, biology, and chemistry programs to choose a career in science and, as a stepping stone to this goal, to consider a research assistant position at Rockefeller."

The Personnel Department paired the undergraduates with 10 current research assistants according to common research interests. The research assistants introduced

themselves and mingled with the students at a welcoming reception. They then took their guests on a tour of their laboratories.

Research Assistant Christopher Scott gave Kathy Bae, a senior at Lehman College, and David Kwok, a senior at Columbia University, a tour of the Breslow lab. Both had many questions: "How often do you get a chance to interact with the head of your lab? Can you attend any of the Rockefeller lectures? Do research assistants have to dress a certain way?" Scott answered their questions as he showed the students his desk area, the tissue culture room, and the Hospital where many of the lab's studies are conducted.

Lecturer to speak on protein structure

David Eisenberg, professor at the University of California, Los Angeles, will speak on "3D Profiles: Principles and Applications" at the Friday lecture today (Mar. 12).

"One of the great puzzles in molecular biology concerns the relationship between the linear amino acid sequence of a protein molecule, and its intricate, three-dimensional shape," said Associate Professor John Kuriyan. "Dr. Eisenberg will speak on the problem of predicting three-dimensional structure from amino acid sequence. He has developed new computational techniques for determining whether two or more sequences might correspond to similar, three-dimensional structures."

Eisenberg, a faculty member at

National science watch

RU scientists speak to Congress

By Doron Weber

One of several Rockefeller University scientists who maintains ties with Washington, Professor and Physician-in-Chief Jules Hirsch testified before a subcommittee of the Committee on Appropriations of the House of Representatives early this month.

"I am devoted to the concept that scientists should be making their problems known to Congress," said Hirsch, who testi-

fied on behalf of the American Society of Clinical Nutrition and the American Society for Parenteral and Enteral Nutrition during his most recent visit. He urged Congress to increase funding for nutrition programs in general and clinical research in particular.

"I find representatives are usually grateful that scientists take the time to explain their positions and special needs," he said. "Even if we don't get what we ask for immediately, it is important for scientists to participate in the process. Having our needs recognized and our language heard can make a difference in the long run."

As the source of the nation's laws and the appropriator of Federal funds, Congress exerts considerable influence over the future directions of science and technology. Hirsch is not alone at Rockefeller in believing that communicating with Congress is a worthwhile activity.

Professor Norton Zinder, who is often called on to testify, said: "I think it's essential for scientists to take every opportunity to explain their positions to government officials. After all, it's Congress who ultimately makes the decisions about funding."

Acknowledging that scientists must be able to "subtract out the politics," Zinder nonetheless believes that researchers "should be heard and heard clearly." Said Zinder, "Congress is charged with

"What I like about my work is that every day is different and I can work at my own pace, unless we're under a deadline," Scott told them. "Very quickly, you learn how much the research means to the lab head and develop a strong loyalty to the projects."

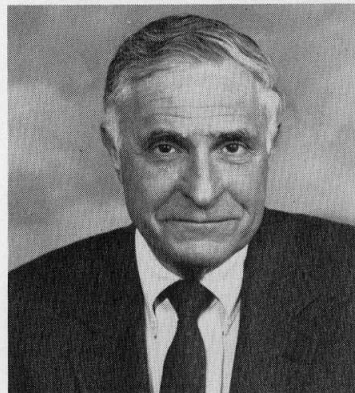
Following the lab tours, Personnel gave the students a tour of the campus and an overview of the application and hiring process.

Personnel hopes to receive many resumes following the open house. Numerous labs at Rockefeller list openings for research assistants by the end of April. Interviews are generally conducted in May for positions that begin in June and July.

the University of California, Los Angeles since 1969, is a graduate of Harvard College (B.A., 1961) and Oxford University (Ph.D., 1964). He received postdoctoral training at Princeton University and the California Institute of Technology. A member of the National Academy of Sciences and the American Academy of Arts and Sciences, Eisenberg is currently an editor of *Advances in Protein Chemistry*, a member of the Editorial Advisory Board of *Current Opinion in Biology*, and an editorial consultant for *Protein Science*.

The lecture will be held at 3:45 P.M. in Caspary Auditorium. As customary, it will be preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Hall.

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Professor and Physician-in-Chief Jules Hirsch recently testified before Congress.

2 Sabin, polio researcher, dies

3 Scientist studies rare disorder

4 Reunion helps families keep up

Albert Sabin, polio researcher who worked at RU, dies

By Mika Ono Benedyk

Albert B. Sabin, the researcher who developed the vaccine that is now the main defense against polio, died Mar. 3. Sabin spent four formative years at The Rockefeller Institute for Medical Research, now The Rockefeller University, early in his career.

Sabin came to the institute in 1935 to work in the laboratory of Peter K. Olitsky. There, Sabin learned the most up-to-date techniques of the time for culturing viruses, which involved transferring live viruses from animal to animal.

Sabin and Olitsky carried out research on the poliovirus for Simon Flexner, the first director of Rockefeller. The view then prevalent was that the virus would not grow outside the bodies of human subjects, apes, and monkeys. Sabin succeeded in cultivating the virus in isolated nerve cells.

During this time, Sabin became suspicious of the monkey-adapted

human polio strain that Simon Flexner had long used to transmit the disease to new monkeys. Indeed, the Flexner virus was flawed. While the poliovirus normally has an affinity for both nerve and intestinal tissue, the virus that Flexner used had lost most of its intestinal affinity. This had convinced researchers that people caught the virus by inhaling it. In fact, as Sabin later proved, the poliovirus normally enters humans through the digestive tract and then travels to nerve cells.

As a faculty member at the University of Cincinnati, Sabin was among the scientists who succeeded in identifying the three types of polio virus. He worked on attenuating the three types of virus to develop a live-virus vaccine for polio. He continued this work even after Jonas Salk developed a successful killed-virus polio vaccine that went on the market in 1955.

After widespread testing abroad, Sabin's vaccine was licensed in the United States in 1961. A hot

debate about the relative virtues of the two vaccines ensued, pitting the two researchers and their camps of supporters against each other.

Sabin's vaccine gradually supplanted Salk's in the United States and in most parts of the world. Whereas the Salk vaccine had to be given by injection and required booster shots to insure long-term immunity, the Sabin vaccine was swallowed in a sugar cube or syrup and provided lifetime protection against polio. Moreover, the harmless virus of the vaccine spread beyond the recipients to protect even some people who had not received the vaccine.

During his long career, Sabin also performed significant work on viruses other than polio. He was a specialist in the army during World War II, and was sent to The Rockefeller Institute's Princeton branch to work on the virus that causes dengue fever, a debilitating disease that was striking troops in the South Pacific. Sabin succeeded



Albert Sabin (1906-1993)

in developing a vaccine. Sabin's other accomplishments include developing a vaccine against Japanese encephalitis virus, isolating the virus that causes sandfly fever, and identifying a virus called echo 9 as a cause of human intestinal illness.

RU scientists believe researchers 'should be heard and heard clearly' in U.S. Congress

(continued from page 1)

obtaining the best information on a given subject. When that subject is science, then it's the scientist who knows best. I'd like to see Congress use more scientists when gathering information."

President Emeritus Frederick Seitz, whose extensive experience in Washington includes most of a decade as president of the National Academy of Sciences, believes that "this is a very critical junction" for science. Seitz points out that even

traditional friends of science such as Congressman George E. Brown, who serves as chair of the House Committee on Science, Space, and Technology, have warned that the scientific community and its advocates in government must articulate a new vision of research to meet new challenges in the post-Cold War world.

"Brown himself is very approachable but there is a general drift in the country—and in the Congress which reflects it—toward populist ideas and away from basic science.

It's important for scientists to make their voices heard."

While clearly worthwhile, testifying before Congress is not always a straightforward matter. Rockefeller Fellow Jesse Ausubel points out that Congressional hearings have different purposes, such as to gather information, to publicize an issue—or to advance the career of an individual member of Congress.

"Scientists may be put off when they first realize that the goal of a Congressional hearing is not necessarily the pursuit of the truth," said Ausubel. "There are many other agendas being followed and it is useful to understand beforehand what the motives of a particular hearing are." Nevertheless, Ausubel says there are many ways to educate Congress, including testifying at hearings, commenting on draft legislation, or simply maintaining contact with committee staff members.

Associate Professor Roger Rusack, who heads one of two projects in the Goulian lab for the Superconducting Supercollider (SSC), says that maintaining contact with Congress is especially important for multi-billion dollar programs such as the SSC or the Human Genome Project. "When so much money is involved, researchers become high profile and an open target for politicians who want them to justify why they

should spend so much money on their research. I was speaking with a Congressional aide who asked me, out of the blue, what the SSC was going to do for black people. It was an excellent question." Rusack says that the experience of explaining why it is in the public interest to fund his work has been "very educational." He said, "I accept it as a fact of life and I believe it's very important to continue to get our message across."

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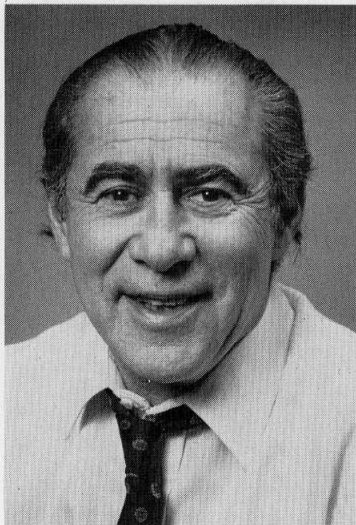
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Ingrid Grutmer



Several Rockefeller University scientists maintain ties with Washington, including Professor Norton Zinder (left) and President Emeritus Frederick Seitz.

Uncommon neurologic disorders yield uncommon insights

by Susan Blum

The patients' cases were highly unusual. All three had small-cell lung cancer, a deadly type of tumor that rapidly kills most of its victims and that almost never regresses, even with aggressive treatment. Yet—in some cases with therapy, in others without—these patients' tumors shrank or disappeared completely. This good luck, though, was not unalloyed. The cancers resolved, but the patients were plagued by an array of neurological symptoms, some so debilitating that they could no longer walk or feed themselves.

Assistant Professor Robert Darnell reported on these cases in *The Lancet* earlier this year. They are examples of the family of rare disorders, known as paraneoplastic neurological syndromes, under study in his lab. Darnell, an M.D.-Ph.D. who joined the Rockefeller faculty last fall, says his research into the syndromes allows him to pursue his two compelling interests—gene regulation and neurobiology—and his commitment to two approaches—basic research and clinical investigation.

As a graduate student in the early 1980s, Darnell was intrigued by the mechanisms that control how and when genes are transcribed (or read out) before their instructions are used to make proteins. "At that time," Darnell recalled, "studies were just starting to focus on oncogenes, genes that play central roles in signaling a cell to differentiate or multiply in response to messages from its environment." When the genes malfunction, the signaling network goes awry, and cancer can result.

But the oncogene studies were not the only ones that attracted Darnell's interest during his studies. He was equally fascinated by research in neurobiology, which was starting to elucidate the mechanisms by which neurons change in response to signaling events. "It seemed to me that both neurons and other cells in the body might use the same kinds of signaling pathways for different purposes," he said. "For instance, in most cells, these signals normally culminate in regulated cell division, and their deregulation can lead to cancer. In neurons, which do not divide, the functions of the signaling pathways are unknown, but are perhaps related to neurons' plasticity—their ability to change connections with other neurons in response to messages from their environment."



Assistant Professor Robert Darnell studies paraneoplastic neurological syndromes, rare disorders brought on by cancer.

Studies meld two interests

To pursue the interconnections between neurobiology and tumor biology, and to conduct both basic research and clinical studies, Darnell became an attending neuro-oncologist at Memorial Sloan-Kettering Cancer Center. There he worked with Jerome Posner, a pioneer in the study of paraneoplastic neurologic syndromes—disorders that melded Darnell's two main interests.

In these diseases, small numbers of tumor cells of a particular type—say, tumors of the lung or of the breast—produce a protein normally produced only by a particular type of nerve cell—say, a Purkinje cell in the cerebellum. This protein production occurs due to the expression, or activation, in the tumor cell of a gene normally turned on only in the nerve cell.

The reason for this *ectopic*, or out-of-place, gene expression is not yet understood. Perhaps it is simply the random result of the cellular deregulation that is cancer's hallmark. But Darnell is investigating another possibility: that the ectopically-expressed genes normally play important cellular signaling roles in nerve cells. Their aberrant expression in tumors would give cancer cells an advantage over normal ones, allowing them to circumvent the controls imposed by their own signaling networks. Darnell has termed such genes *onconeural* genes.

In the tumor, the proteins encoded by onconeural genes are perceived as foreign by the immune system, which mounts an effective attack against them. Darnell believes that the vigor and success of this defense supports the long-held notion that many incipient cancers are nipped in the bud without our ever becoming aware that they have occurred.

But patients with paraneoplastic disease do become aware that they have (or had) cancer—usually not because of the cancer itself, but because of the immune response it elicits. For some reason—perhaps a break in the blood-brain barrier that normally screens the brain from many substances—antibodies to the onconeural gene gain access to brain cells. The result: degenerative neurological diseases that, depending on the neurons involved, can impair balance, sight, motion, and a host of other critical functions.

Immune system difference leads to attack

Why are the onconeural proteins perceived as foreign? "The immune system probably doesn't work in the brain in exactly the same way it does in the rest of the body," Darnell speculated. Somehow, this difference prevents the immune system from "learning" that the onconeural proteins belong to the self. Thus, they provoke an immune response both in the tumor cells, where they do not occur normally, and subsequently in the nerve cells where they are usually produced.

Just as the immunologic rationale for the attack remains unknown, so does its mechanism. Do antibodies alone orchestrate the attack against onconeural proteins, or are immune cells known as cytotoxic T cells involved as well? Darnell is beginning studies at The Rockefeller University Hospital to investigate, and design ways to modulate, the immune attack in patients with paraneoplastic syndromes.

In his new lab, Darnell is also exploring the syndromes by cloning and characterizing onconeural proteins. So far, five main types of proteins have been cloned, each one representing proteins that were

hitherto completely unknown. Darnell played a collaborative or leading role in the work on three of them, and believes additional proteins may yet be found.

The characterization of many of the onconeural genes gives suggestive support to the hypothesis that they play critical roles in cellular signaling networks. For instance, one gene codes for a Purkinje neuronal protein with the "leucine zipper" motifs characteristic of many signaling proteins. Another gene, NAP, is the first identified neuron-specific adaptin—a protein that forms a bridge between clathrin, an important cell-surface protein, and the "tails" of receptors that pick up intracellular messages. A third gene, characterized since Darnell came to Rockefeller, is a nuclear protein expressed in the developing motor system, which he believes may be a novel signaling protein.

Both neuronal plasticity and neuronal death play important roles in the development and functioning of the nervous system. By investigating how onconeural genes function in signaling pathways, and exploring how immune-system responses can trigger neuronal death, Darnell's work may yield insights into some of neurobiology's most basic questions.

Research may yield therapies

His research also holds promise for therapeutic advances on a number of fronts. Insights gained through the clinical studies at The Rockefeller University Hospital may prove relevant not only to the paraneoplastic syndromes but to other autoimmune neurologic diseases such as multiple sclerosis. Moreover, the investigations into how immune system responses can trigger neuronal death may ultimately prove relevant to the treatment of degenerative diseases in which cell death is triggered by mechanisms other than direct immune attack.

Darnell's studies may also advance the fight against cancer. "The paraneoplastic syndromes identify *bona fide* tumor antigens that are targets of an effective immune response," he said. Though other cancer cells express unusual antigens, or proteins, none described to date elicits a strong enough counterattack to thwart the cancer's growth. A better understanding of how and why onconeural antigens provoke such a vigorous defensive response may lead to strategies that boost the body's ability to fend off a wider range of cancers.

Reunions help RU families in Europe stay in touch

Although they now live in several countries thousands of miles away from where they first met, many families once affiliated with The Rockefeller University get together for an annual reunion in Europe.

The families—which include those of former Rockefeller students, postdoctoral fellows, and guest investigators who were at the university between 1985 and 1992—have met for the past three years during winter or summer vacations. Seven families meet in Germany; five others in the south of France.

One family who participates in the European reunions is still at Rockefeller—Martine Moreillon, research assistant in the Tomasz lab, Philippe Moreillon, graduate fellow in the Tomasz lab, and their three children.

"Many of the people who now meet in Europe were at Rockefeller

for just a few years," explained Martine Moreillon. "We made friends easily because we all lived in Faculty House and saw each other every day with our children in the play areas. As we shared the experience of learning the language and getting lost in the city, we came to know and trust each other. Many of the children happened to be the same age, which meant that the children too, developed lasting friendships.

"In New York, the children had a lot in common," she continued. "They all felt uprooted. Now that most of them have moved back to Europe, they still have a lot in common: they can speak English together and share the experience of readjusting to European culture."

Another reunion is planned for the upcoming summer in Germany. With the children in different school systems, it is hard to find a

convenient time for everyone to meet. Fortunately, the extensive rail system in Europe makes reunions possible even when the participants do not have much time.

The German reunion includes the Langen, Schmitz, and Bahler families from Germany, the Thelen and Mirkovitch families from Switzerland, the Fromm family from Israel, and the Agger family from Denmark. The French reunion includes: the Fasano, Defoort, Courvalin, and Mege families from France, and the Van den Broecke family from Belgium.

Moreillon expects these reunions to continue for some time. "I will count on these meetings when it is our turn to leave," she said. "I will miss this place." The reunions will help her family, and others once at the university, to keep the spirit of Rockefeller alive in Europe.



Martine Moreillon of the Tomasz lab participates in an annual reunion of Rockefeller families in Europe.

Potpourri

Tri-Institutional Noon Recital
Violinist Juliette Kang will perform with pianist Robert Koenig at the Tri-Institutional Noon Recital today (Mar. 12) in Caspary Auditorium. They will play works by Schumann, Bartók, and Gershwin. Kang—who will make her official New York recital debut this month—is the winner of the Young Concert Artists International Auditions, the Yehudi Menuhin International Violin Competition, and the Concerto Competition at The Juilliard School. Today's concert is free. All are welcome.

Penny savers

Starting Mon., Mar. 15, The Rockefeller University Children's School will begin collecting pennies for Common Cents, a charity that

directs donations to programs for the poor, homeless, and unemployed. Pennies will be collected until Fri. Mar. 26 at the following locations: Tower cafeteria and 17th floor dining area, the Founder's Hall security desk, the Office of the President in Caspary 203, and Plant Operations in Boiler House 105.

Bake sale

The Ice Rink Committee is holding a bake sale in Tower lobby from 8:30 A.M. to 3:30 P.M. on Wed., Mar. 17. Proceeds will go toward the cost of the materials for building the rink. Volunteers to help with the sale should contact Martine Moreillon, x8278.

Wallyball

Two one-hour demonstrations of

the game wallyball will be held on the south squash court in GSR on Wed., Mar. 17 and Fri., Mar. 19 from 2:00 to 3:00 P.M. Wallyball, an adaptation of volleyball for squash courts, is played with two or three people on each side of the net. For more information, contact Vadim Sherman, x8829.

Metropolitan Opera concert

Five opera winners in the Eastern Regional Finals of the Metropolitan Opera National Council Auditions will perform at a benefit concert in Caspary Auditorium on Sun., Mar. 21 at 8:30 P.M. The audition program, established in 1954, is designed to discover new talent for the Metropolitan Opera. Discounted tickets to the concert and reception (formal attire required) are available to the Rockefeller community for \$20. Checks should be made out to "MONC-Eastern Region" and sent to Sandra Walsh, Box 234, by Fri., Mar. 19. Students, who may attend free of charge, must obtain tickets from the Deans' Office.

ROCKEFOLLIES 93

The annual variety show featuring home-grown talent, the ROCKEFOLLIES, will be held on Tues., Mar. 23 at 7:00 P.M. in Caspary Auditorium. This year's show has a little bit of everything, including classical guitar, karate, and a one-act comedy, directed by a member of the university and performed by three professional actors. Tickets are \$5 and may be purchased at the

door. For further information, call Yvonne Holland, x8396, David Heath, x8441, or Albert Sargenti, x8994.

Award

James M. Manning was named Distinguished Biochemistry Alumnus for the Centennial Celebration of Tufts University School of Medicine. One alumnus from each of the school's basic science and clinical departments will present a lecture on April 17. Manning will discuss the results of studies that used genetic mutagenesis to explore the mechanism of an enzyme unique to bacteria.

Employee support group

The Employee Assistance Program Consortium (EAPC) is offering a new support group for men. Issues to be discussed in the weekly sessions will include the male role in the 1990s, relationships, stress and conflicts at home and in the workplace, and family and single parenting issues. For more information, contact the EAPC, 746-5890.

Scholarship application

Orville Redenbacher of Gourmet Popping Corn is offering thirty \$1,000 scholarships to assist adults who are returning to or starting college. Applicants must be at least thirty years old and be planning to attend an undergraduate or graduate degree program, part-time or full-time, in the 1993-94 school year. Applications are available in Personnel, Founder's Hall 103.

Gerald Fetter



Children recently played a game of hockey on the ice rink. A bake sale to help support the rink will be held in the Tower lobby on Wed., Mar. 17.