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# NEWS AND NOTES 1993, VOL.3, NO.17

The Rockefeller University

# news & notes

*January 29, 1993 Volume 3, Number 17* *The Rockefeller University*


**President Torsten Wiesel *(second left)* receives a check from Ann-si and Eva Li *(right)*, daughters of the late C. H. Li, in whose memory the Hormone Research Foundation established a scholarship. Postdoctoral Fellow Yan Zhou *(left)*, from Beijing, China, is the first recipient of the scholarship.**

## *C.H. Li Scholar meets benefactors*

The first C. H. Li Scholar at The Rockefeller University, Yan Zhou, a postdoctoral fellow in endocrinology from Beijing, China, had the rare opportunity of meeting his benefactors and showing them around the lab where he works yesterday (Jan. 28).

Zhou met representatives of the Hormone Research Foundation, including the daughters of the late C. H. Li, in whose memory the scholarship was established: Ann-si Li, a veterinarian and trustee of the foundation, and Eva Li, a city planner. Also present were their families and James Fordyce, member of The Rockefeller University Council and son of the late Alice Fordyce who was a trustee of the Hormone Research Foundation and executive vice-president of the Albert and Mary Lasker Foundation.

The group met Zhou's new research team led by Associate Professor Mary Jeanne Kreek, toured the laboratory, then attended a luncheon with President Torsten Wiesel and Professor and Dean Bruce McEwen.

Zhou took a leave of absence from the Department of Physiology and Neuroscience at Beijing Medical University last November to join Kreek's laboratory which studies the biology of addictive diseases. "I think my mentor encouraged me to apply for this scholarship because I have a background in biochemistry and molecular biology," said Zhou. "With this background, I can learn things quickly in Dr. Kreek's laboratory and then bring these techniques home to China."

In Professor Ji-Sheng Han's laboratory in Beijing, Zhou studies the

*See* ***Scholar****, page 2*



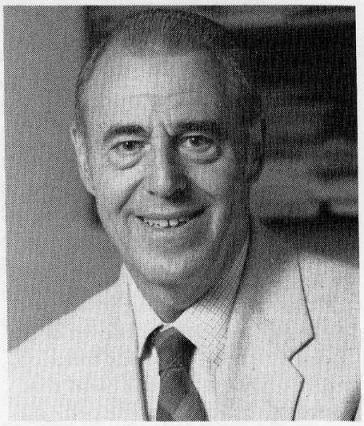
## Physics search expands RU's drive to recruit new faculty

A new search committee has been appointed at the university to look for junior and senior faculty in physics, bringing the number of active search committees to six. This week, ads are appearing in *Science*, *Nature*, and *Physics Today* announcing the physics search.

"We are looking for candidates with excellent qualifications in physics," said Professor E.G.D. Cohen, who heads the new search committee. "At the same time, we are especially interested in those whose work will be stimulating to biologists—for example, a theoretical or experimental physicist who may apply his or her work to biological problems."

President Torsten Wiesel set up the physics search committee after a visiting committee, chaired by Professor Sam Treiman of Princeton University, recommended last fall that the university would benefit from sustaining and augmenting its presence in physics and mathematics.

"The idea is to strengthen physical sciences at the university," said Wiesel. "I believe that investigators in these areas can have an enormously positive impact on the intellectual life as well as the biomedical research of this university. For this reason, I also appointed a visiting committee in chemistry which met last spring and led to an active chemistry search this fall."



John Sholtis, Media Resource Service Center

**Professor E.G.D. Cohen is chair of the new faculty search committee in physics.**

Cohen said: "We plan to work particularly closely with the chemistry search committee. There are some investigators, in structural biology in particular, who could interest both committees."

The other searches are in neurobiology; biochemistry, and structural biology; cell and developmental biology; immunology and microbiology; and medical sciences.

The faculty search committees identify and review investigators who would be suitable for positions at the university. In consultation with the Executive Committee of the Academic Council and the Scientific Affairs Committee of the Board of Trustees, the president recommends the appointments to the board for approval. In the case of a tenured position, there is also a review by an ad hoc committee composed of three members of the university faculty and a member from another institution.

Last year, the work of the committees resulted in six appointments. Kenji Adzuma, Joseph Atick, Yongwon Choi, Robert Darnell, and Seth Andrew Darst were named assistant professor and head of lab; Mary Elizabeth Hatten was named full professor and head of lab.

Anyone who would like to suggest a candidate for consideration should contact a member of the appropriate search committee:

Physics: Joseph Atick, William

*See* ***Searches****, page 2*

## New trustees visit university

**Some recently appointed trustees spent Wednesday familiarizing themselves more closely with the university. Here, *(left to right)* Trustee Alair Townsend, Assistant Professors Sanford Simon, Titia de Lange, and Thomas Sakmar, Trustee Frederick Terry, Professor James Darnell, and Trustee Evelyn Lipper meet. Trustee Edward Cooper joined the other trustees later in the day.**

# Research blooms in greenhouse

*By Jennifer Horne King*

Perched high above The Rockefeller University campus, on the roof of the 17-story Tower Building, a small greenhouse shelters hundreds of plants for Professor Nam-Hai Chua's laboratory of plant molecular biology. Built in 1986, the greenhouse is currently used to test new genetic permutations in petunia and tobacco plants.

Sander van der Krol, a postdoctoral fellow in the Chua lab from Amsterdam, Holland, uses the tranquil space to grow genetically altered petunia flowers. "We want to find out how a plant knows when and how to make its floral organs. To do this, we insert or delete genes that are known or suspected to have a specific function, then study the mutant plant that develops from the single cell. Its appearance can show very clearly whether the right genes have been successfully isolated."

Van der Krol's experiments demonstrate the importance of gene localization in organ development of the petunia: "We can move a certain gene for petal development in the genome and see dramatic effects in the appearance of these petals," he says, holding a bunch of petunia flowers. Some of these are in full bloom, with large, open petals, while others, though full-grown, have small stubs instead of petals. "We have simulated the different stages of development," he explains, "and demonstrated how the petunia grows its petals."

Van der Krol's plants can take up to five months to reach a stage at which they can be studied for gene expression. "Sometimes," he confesses, "I get impatient right at the moment when the buds have appeared. I can't wait a moment longer, run upstairs to the greenhouse, and tear open the buds to see what organs are there!" While his work may require an unusual degree of patience, van der Krol is sure that the plants are worth waiting for. "Other molecular biologists can pore over their gels and count their bands to see if the right genes are expressed," he says, "but, I can go to my plants and see the genes at work. To me, this is much more exciting. Besides, plants are easier to handle than animals: they are free of emotions and ethical controversy."

**In the greenhouse on the roof of Tower, Sander van der Krol, postdoctoral fellow in the Chua lab, checks the plants he uses to study molecular genetics.**

Surrounded by a wide assortment of petunias and a wrap-around view of the city, van der Krol checks his flowers for new developments. On one side of the greenhouse are adult petunias, most with funnel-shaped blooms, deep purple and pink. In some places, young shoots adjust to new surroundings after growing under sterile conditions in the laboratory.

On the other side of the greenhouse, Van der Krol points out a collection of tall, spindly plants with large, floppy leaves. These are tobacco plants with petunia genes inserted in them as part of the experiments of Postdoctoral Fellow Suguru Tsuchimoto, also in the Chua lab.

In a few months, van der Krol will have completed his postdoctoral studies and will return to Holland. "I realized after working here that I have been surrounded by flowers ever since I was a young boy in Holland, where flowers are such an important part of the culture. I had not planned to work with flowers for so long, but I suppose this was a natural outgrowth of my love of plants!"

# Physics added to faculty searches

*(continued from page 1)*

O. Baker, Günter Blobel, E.G.D. Cohen (chair), Mitchell Feigenbaum, Konstantin Goulianos, Nicola Khuri, John Kuriyan, Abraham Pais, and Norton Zinder.

Neurobiology: Mitchell Feigenbaum, Charles Gilbert (chair), David Gadsby, Paul Greengard, Mary Elizabeth Hatten, Nathaniel Heintz, Fernando Nottebohm, Michael Young.

Chemistry, Biochemistry, and Structural Biology: William Agosta, Brian Chait, David Cowburn, Magda Konarska, John Kuriyan, Bruce Merrifield, Peter Model (co-chair), Robert Roeder (co-chair), and Thomas Sakmar.

Cell and Developmental Biology: Günter Blobel, Nam-Hai Chua, Frederick Cross, George Cross (chair), Claude Desplan, Steve DiNardo, David Luck, Sanford Simon.

Immunology and Microbiology: Alan Aderem, Titia de Lange, Emil Gotschlich (chair), Michel Nussenzweig, Ralph Steinman, Alexander Tomasz.

Medical Sciences: Jan Breslow, Stephen Burley, D. Martin Carter, Zanvil Cohn (chair), Jeffrey Friedman, Jules Hirsch, Elaine Tuomanen.

# *Chinese scholar meets benefactors from research foundation*

*(continued from page 1)*

role of opioid neuropeptides in pain regulation during acupuncture. Neuropeptides communicate messages slowly between remote brain cells, as hormones do between remote cells in other parts of the body. Opioid neuropeptides communicate messages that modulate various factors such as stress response and body temperature.

Here, Zhou has joined Research Associates Rudy Spangler and Ellen Unterwald in studying the action of natural opioid neuropeptides in the rat brain during prolonged cocaine exposure. "We want to see if cocaine influences patterns of gene expression for these peptides in certain areas of the brain," explained Zhou. "Ultimately, we want to find out why it is that some people become addicted and others do not."

This is Zhou's first trip outside China. Already, the experience has made an impression. "I come from a developing country where science is a career that affords one the opportunity to discuss things openly," he said. "But even with this freedom, scientific experiments are greatly limited by the available funds, drugs, and technology."

"Here, things are more convenient," Zhou continued. "For example, I hardly have to wash any glassware because most of the materials are clean and disposable. In China, I spend more time cleaning glassware. It slows down the experiments." Similarly, Zhou finds that new pharmacological drugs and rapid servicing of equipment are easier to find here.

Zhou is not sure whether he will have enough time to visit other parts of the United States before he returns to China. "My only priority is to learn as much as I can and return this knowledge to Dr. Han's laboratory," said Zhou. " I want to make the most of this scholarship for my mentor, because scholarships like this one will help to accelerate development of science and technology in China."

World-renowned biochemist Choh-Hao Li contributed significantly to the progress of medicine. During his 50 years of research at the University of California at Berkeley, Li helped to isolate, characterize, and synthesize the hormones of the anterior pituitary and further elucidated the role of human growth hormone. He was awarded the Lasker Award in 1962.

Li was director of the Hormone Research Laboratory from 1950 until his death in 1987. In 1967, the Hormone Research Foundation was established, and in 1991, its trustees established an endowed fund in C.H. Li's name to bring basic scientists from Taiwan and China to The Rockefeller University.

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# Researchers track movement of molecules through membranes

*By Susan Blum*

Any chef knows that oil and water don't mix. Nature knew too, when she cooked up the recipe for intracellular organization.

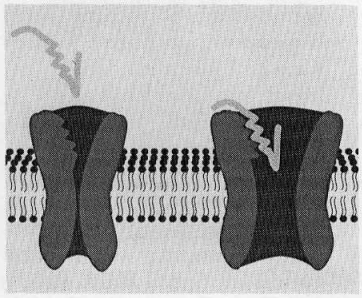
Within the cells of higher organisms are numerous compartments, or organelles, that serve specific purposes such as energy production, waste removal, and protein processing. Each of these organelles is surrounded by a membrane made of a double layer of fatty materials called lipids. The fatty membranes render each organelle impermeable to the contents of the watery cytoplasm that surrounds it. Likewise, the contents harbored within the aqueous interior of each organelle are prevented by the membrane from escaping.

This strategy promotes the cell's safety by storing potentially dangerous or reactive substances in specialized compartments where they pose no threat to the cell's normal functioning. It also fosters economy, since the substances required for any particular biochemical reaction can be sequestered together in one organelle, rather than being produced throughout the cell.

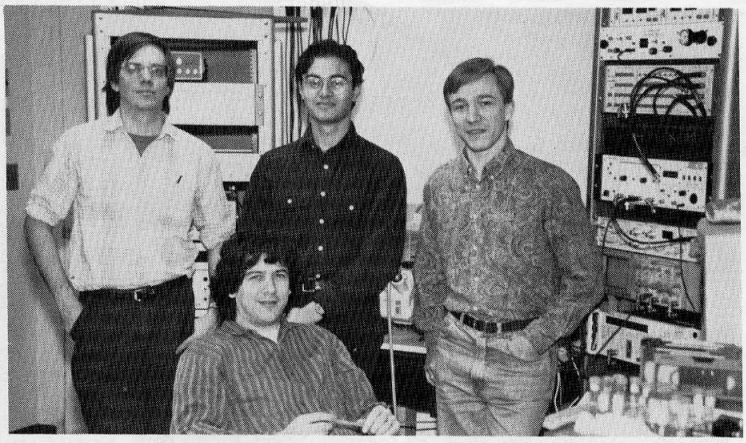
### Barriers must be breached

Useful as they may be for keeping things in that should stay in, and keeping things out that should stay out, lipid membranes present the cell with an obvious problem. How can an organelle import or export molecules when that is what the cell requires? "The cell needs a way to overcome the permeability barrier very specifically and selectively," says Rockefeller Assistant Professor Sanford Simon.

Simon began pursuing the movement of molecules through membranes soon after his arrival in 1984 as a postdoc in the lab of Rockefeller Professor Günter Blobel. He was named Assistant Professor in 1989, and was designated head of his own lab last May.



**Aqueous channels provide protein molecules with a watery passageway through the endoplasmic reticulum. "Signal sequences" bind to the channel and open it.**



**The Simon lab studies how molecules pass through various membranes. The lab includes *(back, left to right)* Assistants for Research Ed Hoff and Deborshi Roy, Postdoctoral Associate Mark Blight, and *(front)* Assistant Professor Sanford Simon.**

In the past few years, research by Simon and Blobel has provided important initial insights into how molecules move through membranes. Their investigations focused on the movement of proteins through the endoplasmic reticulum (ER). The dense network of ER membrane and the convoluted space it surrounds comprise a large organelle that serves as the first stop for all newly produced proteins that must be further processed before they take up their specialized roles.

In the 1970s, Blobel and his collaborators proposed, and then demonstrated, that nascent proteins are targeted to the proper organelle by means of a cellular "zip code" system. A key component of this system is a short stretch of amino acids, called a "signal sequence," that is found at the head of each newly produced protein and that differs according to the protein's destination. (For many but not all proteins, that destination is the ER.)

The researchers also hypothesized that, once at the proper organelle, the nascent protein moves, or "translocates," through the membrane via an aqueous channel. In this model, a protein or complex of proteins forms a channel in the membrane. The channel protects the nascent protein from contact with the membrane lipids, and creates a watery passageway through which the protein can move. Other researchers proposed an alternative strategy for translocation, whereby certain chemical characteristics of the signal sequence permits the protein simply to diffuse through the fatty membrane.

### Evidence for channels is found

In 1989 and 1991, Simon and Blobel published the first papers reporting evidence for the existence of aqueous protein-conducting channels in the ER membrane. Last year, they published another paper demonstrating that signal sequences serve as the binding molecule, or ligand, that opens protein-conducting channels in membranes of *e. coli* bacteria. These channels are similar to the ones observed in the ER.

Recently, Simon proposed a mechanism—confirmed by others—by which proteins may move through the channels. But much still remains to be learned about the channels in the ER, including the identity of the protein or proteins that form them and the molecular details of their regulation. While pursuing these questions, Simon and his colleagues are posing broader questions, too. They want to know if aqueous channels are a mechanism used by many or even all organelles to specifically and selectively move large molecules across lipid membranes. They also want to know if the molecules that travel through such channels include sugars and nucleic acids as well as proteins.

To pursue these questions, researchers in the Simon lab are studying a family of channel proteins known as ATP-binding cassette transporters, or ABC transporters for short. The proteins that make up these channels are known, and have been shown to be similar to one another. It is not yet known, however, whether they function as aqueous channels or as channels of some other sort.

The researchers are exploring the proteins' functions using two different techniques. One method draws on genetic engineering tools to mass-produce the channel protein in frog eggs. A minuscule hole is made in the egg to introduce the molecule the protein transports. The researchers can then study how the channel forms, how it is regulated, and how it functions.

The other research technique reconstitutes the proteins of interest into lipid vesicles (small, spherical membranes) and fuses them to a flat, or planar, membrane. The investigators can then use electrophysiologic measurements of ionic flow to study how the membrane channels function. It is well-established that ions flow through membrane channels, so when ionic flow is measured, it is clear that a channel of some sort exists. Though Simon cautions that the approximation is only rough, the larger the number of ions that flows across the channel in a given time, the larger the channel probably is—and, therefore, the larger is the molecule (such as a protein) that it can probably accommodate.

### Family of channels serves many roles

The ABC channel proteins Simon and his colleagues are studying come from a wide range of organisms—from *e. coli* to yeast to humans—and serve a wide range of roles. In bacteria, they import amino acids and sugars and export toxins. In yeast, an ABC protein exports a pheromone-like "mating factor." In mammals, one member of the protein family is involved in antigen presentation, while another causes resistance to many chemotherapeutic drugs when it is overproduced in cancer cells. Still another member of the family under study in the laboratory of Rockefeller Professor David Gadsby, causes cystic fibrosis when it is mutated.

The conservation of this family of proteins throughout evolution strongly suggests that they play a significant role in cellular functioning. Should the proteins turn out to function by forming aqueous channels, it will be clearer than ever that such channels are an important general mechanism for moving molecules through membranes. While shedding light on the basic biology of membrane channels, the studies of ABC transport proteins hold promise for biomedical advances, too, for a greater understanding of how these channels may malfunction in diseases and for ways to avert or compensate for the malfunction.

# Potpourri

### Tri-Institutional Noon Recital

Violist Paul Neubauer, member of the Chamber Music Society of Lincoln Center will perform at the Tri-Institutional Noon recital today (Jan. 29) with students from The Juilliard School and The Manhattan School of Music: violinist Juliette Kang, violinist Martin Riseley, violist Caroline Coade, cellist Alexis Pia Gerlach, cellist Zvi Plesser, and composer Naoyuki Takano. They will perform Takano's "Prelude for String Quartet," Luigi Boccherini's "Quintet for Strings in C Major" and Johannes Brahms's "Sextet for Strings in B-flat Major, Opus 18." The concert, to be held in Caspary Auditorium at noon, is free. All are welcome.

### Lecture

Jesse Ausubel, fellow in science and public policy at Rockefeller and director of studies for the Carnegie Commission on Science, Technology, and Government, will give a lecture entitled "The Environment of Death," as part of the Tri-Institutional Biomedical Forum in Abby Aldrich Rockefeller Lounge, Tues., Feb. 2 at 5:00 P.M.

### Dinner dance

Tickets are still available for the Holiday Dinner Dance, rescheduled to Fri., Feb. 19 at 8:00 P.M. in Abby Aldrich Rockefeller Hall. Tickets, $25 each or $40 for those who wish to help support the event, are available from the Personnel Office, the Faculty Club, the Purchasing Office, Hospital 106, Media Resource Service Center, the Cashier's Office, and the Deans' Office (for students). They may also be ordered by mail by sending a request and a check payable to "The Rockefeller University" to Angie Dohnert in the Purchasing Department, Box 258.

## *Benefits hotlines*

Hotlines are available for employees who have questions about their benefits.

- Prudential medical and dental claims: (800) 257-8230;
- Prudential Flexible Spending Account claims: (800) 678-6684;
- TIAA-CREF Participant Information Center: (800) 842-2776.

**Three members of the Rockefeller University Security Department retire this month. They are *(from left to right)* Security Guard Gregorio Rosario, Lieutenant Pedro Torres, and Security Guard Niel McKinnon.**

### Birth

Construction Manager Joseph Sanches and his wife, Marie, announce the birth of a son, Jordan Joseph, on Jan. 18.

### Award

Barbara Sutphin, health information technician in Hospital Information Systems, received the Distinguished Service Award from the Health Information Management Association of New York City on Jan. 20. The award was presented as recognition of her active membership in the organization and the New York Health Information Management Association since 1968.

### Workshop

Professor David Mauzerall contributed to the Light in Thermal Environments Workshop at Woods Hole Oceanographic Institute Jan. 10 to 12. The sources of the observed light emissions at deep sea hydro-thermal vents were discussed along with their possible use by organisms.

### Posters

Two posters from The Rockefeller University were presented at a national meeting of General Clinical Research Centers in Reston, Virginia, last month. Marie LoGuercio, director of nursing, presented "Research Nursing at The Rockefeller University Hospital, 1910-1992." Cynthia Seidman, director of Dietary Service, presented "Environmental and Genetic Considerations in Plasma Lipoprotein Levels in Identical Twins," coauthored with Rockefeller Research Associate Elizabeth De Oliveira e Silva and Robyn Arnberg, a graduate student at New York University.

### Aldus software

Computing Services now has library copies of three software packages from Aldus—Freehand, Persuasion, and PageMaker. Persuasion can be used to make slides for presentations; PageMaker can be used for page layout of publications such as newsletters; and Freehand can be used to create illustrations for commercial publication.

All three packages run on the Macintosh or the PC under Windows. The software is available on all PCs and the Mac IIci with the large monitor in the Classroom/User Area, Smith Hall A21. Because the programs are library copies, they are licensed for use by only one person at a time. Manuals are available from the consultant.

### Upgrade of anti-virus program

A new version of Gatekeeper, a free software package that protects against Macintosh viruses, is available from Computing Services. Gatekeeper 1.2.7 has fewer bugs than the previous version. It is also better able to identify the programs it is monitoring. The new version of Gatekeeper can be copied from the Freebies Folder, on all Macintosh computers in the Users Area in Smith Hall A21, or downloaded from the /mac+pc/mac software archives in the directory Public/VirusProtect on rj and rb. For further information contact the consultant, x8940.

### New Carnegie report

The Carnegie Commission on Science, Technology, and Government—co-chaired by Joshua Lederberg, professor and former president of The Rockefeller University, and William T. Golden co-chair of the American Museum of Natural History and member of The Rockefeller University Council—recently published a report, *Partnerships for Global Development—The Clearing Horizon*.

The report, based on the findings of a 12-member task force, addresses issues such as why there should be cooperation on science and technology for international development, what it should consist of, and how it should be organized. Jesse Ausubel, director of studies for the commission and Rockefeller fellow in science and public policy, guided the research and analyses for the publication. Copies of *Partnerships for Global Development* can be obtained from Ausubel, Box 234.

### Recycling film canisters

Black plastic film canisters can now be recycled through the Media Resource Service Center, located in Bronk 111. Canisters may be deposited at the service counter during regular office hours. For more information, contact Albert Sargenti, x8994.

### Arrivals

Research associate: Loucia Kochoumian, T.P. King lab.
Postdoctoral associates: Patrick Allen, Greengard lab; Susie So-Wun Cheng, Heintz lab; Ivan Hrdy Muller lab; Karen Marie Manchester; Allfrey lab; Jun Yin, Pfaff lab; Yuan-Shan Zhu, Pfaff lab
Postdoctoral fellow: Jose Luis Carrasco, Chua lab; John Dani, Hatten lab; Maria Sanchez-Vivez, Knight lab; Krzysztof Sieradzki, Tomasz lab;
Guest investigator: James Cheetham, Greengard lab; Silvia d Pater, Chua lab; Oliver Peter Ernst Sakmar lab; Michio Ishibashi, Steinman lab; Shiaoching Gong, Nussenzweig lab; Mitesh Kishor Kapadia, Gilbert lab; Johan Memelink, Chua lab; Vanya Quinones Jenab, Pfaff lab; Gail Mercurio, Sassa lab.

### Departures

Postdoctoral associate: Douglas Baird, Heintz lab; Colin Fletcher, Heintz lab; Sohail Malik, Roeder lab; Elettra Ronchi, Desplan lab;
Postdoctoral fellow: Ursala Halfte Chua lab; Gary Nolan, Baltimore lab;
Guest investigators: William R. Mann, Carter lab; Raj V.S. Venkatraj, Carter lab.