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The Rockefeller University

news & notes

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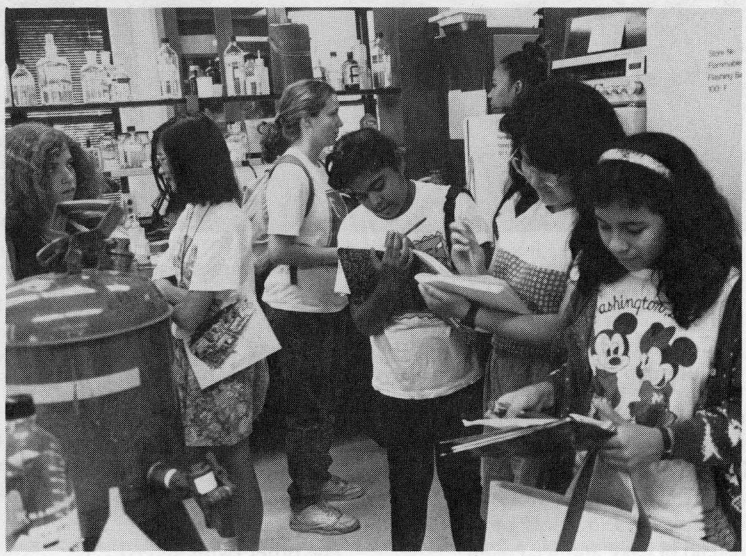


Middle school students toured some of the university's labs before attending lectures in Caspary auditorium Wednesday.

New York City students investigate science on Rockefeller campus

A group of about 50 New York City public school students visited the Rockefeller campus on Wednesday and were treated to a tour of laboratories followed by a series of talks on science. The tour was sponsored by the university's Science Outreach Program, launched in May by Dean Bruce McEwen and Bonnie Kaiser, in conjunction with the Jacob Javits Project, a three-year effort to address the needs of students gifted in mathematics and science who may not have had adequate opportunities in these fields.

"Our aim is to treat these young people, who have just finished the sixth and eighth grades, as young scientists," said Kaiser. "We want to present them with an embarrassment of scientific riches to see what really interests them." Prior to visiting Rockefeller, the students had been on the Clearwater sail and visited the New York Stock Exchange, the American Museum of Natural History, and Hunter College's Library and Geology and Geography Department. The project is based on *The Voyage of the Mimi*, a laserdisk and software package developed by the Bank Street School of Education which uses the story of a whale-watching expedition to introduce students to scientific research

At Rockefeller, the visiting students divided into six smaller groups for their lab visits. Each group was led by a volunteer student guide, one of 10 gifted minority students recruited by the Science Outreach Program to work in a university laboratory for the summer. Under Kaiser's leadership, the program has also selected five high school science teachers to gain research experience this summer.

The student guides assembled in the Treasurer's Office before the tour, where they heard about the founding and history of the university from David Lyons, vice president for business and finance and treasurer . They met the visiting sixth and eighth graders—who come from Louis Armstrong Middle School, Julia Richman, and Franklin Lane High Schools—inside the gate and led them through the campus.

After spending half an hour in selected labs—some of the students were so entranced it was hard to pull them away—the group met in Caspary Audtorium. Ingrid Reed, vice president for public affairs and corporate secretary, welcomed the students and encouraged them to consider careers in science. Professor Fernando Nottebohm spoke about bird song as a window to brain function while Assistant Professor David Thaler talked about microbiology and the generation of diversity. Molecular artist Irving Geis discussed scientific visualization and Postdoctoral Fellow Benno Ter Quile talked about oceanography and global environmental issues.

Fund-raising in fiscal year 1991-92 sets new record

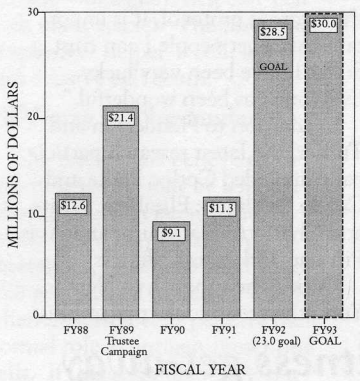
New gifts and pledges reached $28.5 million for the fiscal year that ended June 30, making 1991-92 the most successful year for fund-raising in the history of The Rockefeller University.

President Torsten Wiesel commented, "I would personally like to thank all the donors who made commitments to this institution. This high level of private support is the result of many people's confidence in the university's mission and in its future. The total is especially encouraging because it includes only a portion of the magnificent $20 million gift that David Rockefeller announced last October." Rockefeller's gift added $6 million to the year's total.

Other major contributors included: Bristol-Myers Squibb, The Carl J. Herzog Foundation, The Hormone Research Foundation, Paulo Villares, Arnold Beckman (through the Arnold and Mabel Beckman Foundation), and Jack Fishman, who was a professor at Rockefeller in the 1980s.

Marnie Imhoff, director of Development, said: "On behalf of the development staff, I want to thank President Wiesel and the university community for being so supportive of our efforts to increase private support. This year's success was a team effort that brought volunteers, trustees, faculty, and staff together in a very productive way to the benefit of RU."

The goal set by the Development Committee of the Board of Trustees for the fiscal year beginning July 1, 1992, is $30 million.



New gifts and pledges for fiscal years 1988 to 1992.

2 Seeing double? Twins come to RU

3 Findings help explain AIDS

4 Birds call to RU research assistant

Four-day fete will celebrate new building

The dedication of the new 12-story lab building—the John D. Rockefeller, Jr., and David Rockefeller Research Building—will be celebrated from Wed., Sept. 23 to Sat., Sept. 26. In addition to special exhibits in the atrium lobby and on the ninth floor of the new building, the four-day program of activities will include the dedication ceremony, an all-day scientific symposium, receptions, tours, lectures, the Anniversary and Retirement Dinner, and the Employee Recognition Ceremony.

For a schedule of the festivities, see page 2.

Individuals interested in volunteering for any of the events should contact Sandi Walsh, x8072.

Seeing double? Twins come to RU

By Mika Ono

"We think alike, we feel alike, and now that we are together all the time we even have to go to the bathroom at the same time," said Mary Henderson about herself and her identical twin Martha Turner. "Our bodies are really synchronized."

This similarity is invaluable to Elizabeth R. de Oliveira e Silva, research associate and associate physician in the Breslow lab, who recently brought Henderson and Turner—and three other sets of twins—to campus for two studies.

The first study examines the heritability of high-density lipoprotein (HDL) metabolism. HDL, commonly known as "good cholesterol," plays a role in ridding the body of the cholesterol molecules implicated in heart disease.

"We are trying to find out whether people who are lucky enough to have high HDL levels manufacture more of it or simply break it down more slowly in their bodies due to their genetic endowment," explained Silva.

After two weeks at Rockefeller eating carefully measured amounts of food prepared in the Hospital's metabolic kitchen, the twins are injected with purified HDL proteins labeled with small amounts of radioactive iodine. Blood samples are taken at set intervals after the injection. Tests measure the rate of breakdown of the labeled material in the body.

Twins are essential to this study, Silva says, because they confirm the role of genetics: "If genetics plays a key role in HDL metabolism, under the same conditions identical twins should metabolize HDL at the same rate. Fraternal twins, who have only 50 percent of the same genes, should show differences. So far this seems to be the case."

The second study examines the role of genetics in determining the responsiveness of lipid metabolism to diet. In this study, each twin is put on both high and low fat diets, and the changes in their lipid and lipoprotein levels are measured.

"We know that diet affects lipid metabolism," said Silva. "But does genetics play a role in how much lipid metabolism changes in response to a change in diet? Our preliminary data suggest that genetics is a key factor."

Recruiting dozens of identical and fraternal twins who can spend four weeks at the Hospital is no easy task. One of Silva's strategies is to attend the Twins Days Festival in Twinsburg, Ohio, which draws approximately 3,000 sets of twins every year. She also relies on advertising on the radio and in local papers, and on word of mouth.

"The protocol for these studies is very strict," Silva said. "The twins cannot eat anything that is not part of their assigned diet. Because of the rigorous protocol, it is important that I get people I can trust. So far I have been very lucky. Everyone has been wonderful."

In addition to Henderson and Turner, the latest research participants included Corlee Pralle and Carole Kuhlman; Elizabeth White and Charlotte Blackburn; and Avis Pittman and Arlis Colerick.

During their month in New York, the group took trips to Ellis Island, Times Square, a Mets game, the ballet, and a Broadway show. They also threw a birthday party for Pittman and Colerick, featuring diet Coke and sugarless gum instead of cake and ice cream because of the demands of the study.

Four sets of twins came to the univerity's campus last month to participate in a study by the Breslow lab. *Front row, from left to right:* Martha Turner, Corlee Pralle, Elizabeth White, and Arlis Colerick. *Back row, from left to right:* Mary Henderson, Carole Kuhlman, Charlotte Blackburn, and Avis Pittman.

"The Hospital staff was terrific," said Henderson, "and the food was wonderful. But the best part about coming here was spending so much time with my sister."

The other twins agreed. "I would truly recommend the experience to other twins," Pittman said.

Student, postdoc witness get-away

Two members of the Rockefeller community were recently key witnesses in the robbery of a grocery store at 64th St. and First Ave. Scott Dougan, student in the diNardo lab, and Laurent Fasano, postdoc in the Desplan lab, saw two men fleeing the scene of the crime.

"Laurent and I were waiting to cross the street at 64th and York when we saw a livery cab pull up," Dougan recalled. "One guy jumped out of the cab, dropping a gun about 10 feet from us. A second got out of the cab, picked up the gun, and ran after him. We came back 15 minutes later and the cab was surrounded by cop cars."

Dougan and Fasano approached the police and described the men in detail. One was short, had a moustache, and wore beige and white clothes. The other was tall, had a moustache and beard, and wore denim clothes and a cap.

According to Detective Walsh of the Metropolitan Police Department, the men had hijacked the livery cab in Queens, threatening the driver at gunpoint and throwing him out of the vehicle. Sometime during the robbery of the store, a witness realized that the livery cab was to be used as the getaway car and threw a bottle through one of the windows.

"They probably decided that the car was too noticeable with a broken window," said Walsh. "When they got to York Ave. they decided to escape on foot."

Fasano has a different theory about why the car was abandoned. "I think one of them tried to get away with all the loot," he said. "The way in which they ran out of the car suggested that one was chasing the other."

Schedule of dedication events

Following is a schedule of activities for the week in which the new lab building will be dedicated.

Wed., Sept. 23

- 2:00 P.M. Dedication ceremony held on the Plaza in front of the new lab building (or in Caspary auditorium in case of rain).
- 3:30 P.M. Reception (by invitation only) held on the second floor of the new building.
- 7:00 P.M. Reception and dinner (by invitation only) held on the ninth floor of the new building.

Thurs., Sept. 24

- 9:00 A.M. to 5:00 P.M. Scientific symposium. The lectures, to be given in Caspary auditorium, will focus on cell biology in the morning and neurobiology in the afternoon.
- 6:30 P.M. Anniversary and Retirement Dinner for faculty and staff celebrating their 25th, 40th, 50th, and 60th anniversaries at the university or retiring after 10 years or more of service. The event will be held on the ninth floor of the new building.

Fri., Sept. 25

- 2:00 to 7:00 P.M. A reception, tours of the new building, and special lectures for all university faculty, staff, and students. The reception will be held on the Plaza (or in the Tower lobby in case of rain). The times and locations of the lectures and tours are still to be announced.
- 5:00 P.M. Employee Recognition Ceremony honoring individuals celebrating their 10th and 20th anniversaries at the university (location to be announced).

Sat., Sept. 26

- 11:00 A.M. to 3:00 P.M. Open house, tours, and lectures for members of the community. The times and locations of the lectures and tours are still to be announced.

Further details about the festivities will be published in upcoming issues of *News&Notes*.

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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Research in Cohn-Steinman lab helps unravel mystery of AIDS

By Susan Blum

One of the major unanswered questions about AIDS has been how the disease's causative agent—the HIV virus—wreaks its havoc on the immune system. Now, new findings from the Cohn-Steinman lab, published in the July 17 issue of *Science*, point toward a solution to this long-standing enigma.

A hallmark of infection with HIV is a reduction in the function and number of helper T cells. These are the white blood cells that orchestrate a wide range of immune-system responses, including those against bacteria and viruses. The depletion of helper T cells leaves infected people susceptible to the "opportunistic" pathogens—such as pneumocystis carinii, candida, and cytomegalovirus—that healthy people can usually combat.

This much has been known for years, but a central mystery persists: Just a small fraction of helper T cells are actually infected with HIV, yet their numbers and function are severely compromised. Many theories have been advanced to explain this disparity between the number of infected helper T cells and the immune-system chaos characteristic of AIDS. One theory postulates that infection with HIV may trigger an auto-immune response that dampens the body's defenses. Another theory goes so far as to suggest that a co-factor, rather than HIV itself, is the lethal agent in AIDS.

HIV virus is lethal

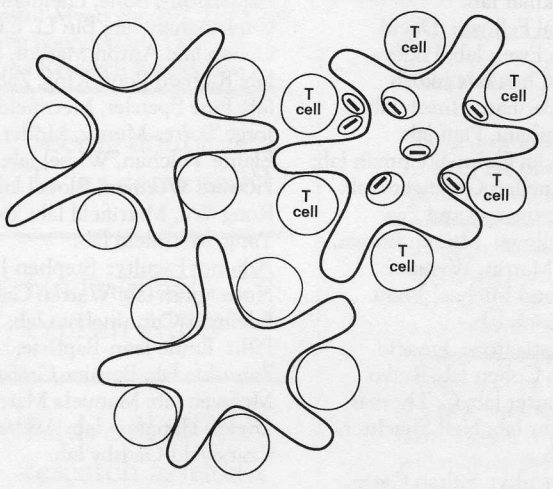
Results from the Cohn-Steinman lab point toward a different conclusion. Their work shows that the HIV virus can be lethal, indeed—even in very small quantities. "You just have to find the physiology under which the immune system is likely to be operating," says Ralph Steinman, the Rockefeller University investigator from whose research group the findings originate.

The key player in the system appears to be the dendritic cell. Dendritic cells comprise a tiny but crucial subset of white blood cells found in many different body tissues including the blood, thymus, lung, skin, gut, and tonsils.

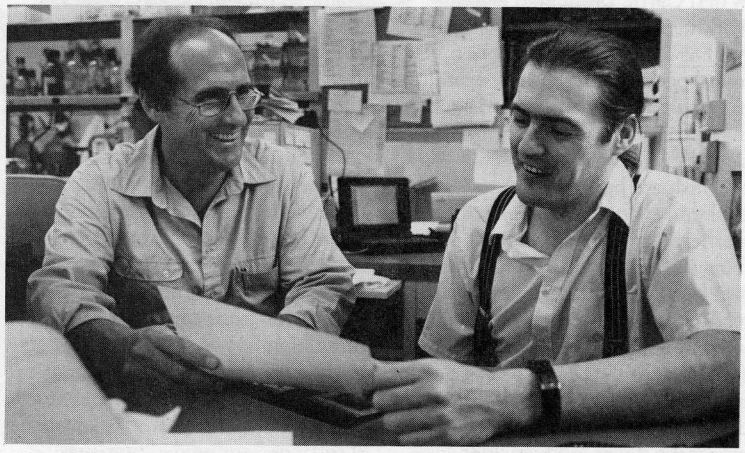
Zanvil Cohn, Steinman, and their colleagues first discovered the existence of dendritic cells in the 1970s and have been elucidating their function ever since. They have found that dendritic cells serve as sentinels that scout out "foreigners" such as invading pathogens. They present fragments of these foreigners (called antigens) to T cells, thereby stimulating them into action. In fact, dendritic cells stimulate so many kinds of T cell activity that the Rockefeller researchers call them "nature's adjuvant," in recognition of their ability to enhance immune responses.

One of the dendritic cell's most important functions is to stimulate the replication of helper T cells by presenting them with the antigens and "superantigens" to which the T cells are genetically programmed to respond. (Only a small subset of helper T cells responds to any particular antigen, whereas superantigens provoke a stronger response from a larger number of cells).

The Steinman group's *Science* paper elaborates on the role this stimulation may play in AIDS. In test-tube experiments, the research team, led by Postdoctoral Associate Paul Cameron and Graduate Fellow Peter Freudenthal, "pulsed" dendritic cells with HIV. In ways that remain unknown, the dendritic cells picked up the HIV. Helper T cells were then added to the mix, as were a type of antigen known as a transplantation antigen, or a bacterial superantigen called SEE.



The star-shaped dendritic cell carries HIV to helper T cells.



Professor Ralph Steinman *(left)*, Postdoctoral Associate Paul Cameron *(right)* and Graduate Fellow Peter Freudenthal led the group which published new findings about the HIV virus in a recent issue of *Science*.

When carrying HIV, the dendritic cells were able to present antigen and superantigen to helper T cells and prompt those cells to replicate. However, the dendritic cells also transmitted the HIV to the replicating helper T cells. Then, the T cells became a syncytium —one giant helper T cell with many nuclei. The result: an "explosive" helper T cell, infection, and massive cell death.

HIV may be "bystander"

The researchers believe these test-tube results may be a model for what happens in people with AIDS. HIV may be merely a "bystander," a cellular hitchhiker that gets carried to helper T cells when dendritic cells perform their normal role as antigen-presenting cells. If this is so, then HIV is a guilty bystander, indeed. For when it is transmitted to activated helper T cells in syncytia, a small amount of the virus can be lethal. "The interacting dendritic cells and T cells provide a microenvironment that is ominous for the rapid spread and duplication of the virus," Steinman explains. "The presence of just a small amount of virus in that milieu kills the cells that are trying to respond to antigens—such as those of the opportunistic pathogens—even though neither the dendritic cell nor the T cell is infected at the time of their initial encounter."

AIDS researchers elsewhere have proposed that dendritic cells are easily infected with HIV. The results of the Rockefeller team, who used techniques they themselves developed, are very different. In their hands, infected dendritic cells were rarely if ever found. Instead, the dendritic cells appeared simply to carry the virus and to promote infection of protective helper T cells.

Future research will determine whether all dendritic cells are immune to infection. The dendritic cells the Rockefeller team has studied so far—those found in the blood—have few CD4 receptors, the main molecular "arms" that, on helper T cells and other immune system cells, grab on to HIV and permit it to enter. Other types of dendritic cells have more CD4 receptors, and may prove more susceptible to infection. On the other hand, the researchers speculate, CD4-rich dendritic cells may also be infection-resistant, and more "vicious" as well—capable of picking up very small amounts of HIV, holding on to it for longer, and transmitting it even more efficiently.

The researchers' results have implications for therapeutic strategies against AIDS. "People have been pessimistic about antibody therapy for AIDS," says Steinman. "The feeling was that the virus is inside the cells and therefore inaccessible to antibodies. But we're saying that the thing that's killing off T cells and leading to opportunistic infections is virus that's free and picked up by the dendritic cell." In that case, appropriate antibodies may interfere with the dendritic cell's ability to carry HIV or to transmit it to helper T cells.

Much remains to be learned about the details of dendritic cell function and its interaction with helper T cells. But the new paradigm presented by the Rockefeller investigators holds out new hope for an understanding of the destruction of the immune system that occurs with AIDS, and for weapons to fight it.

Birds in the wild call to RU research assistant

When Carrie Bromleigh is not working as a research assistant in the DiNardo lab, she can often be found peering into bushes, examining nooks and crannies, and squinting at the sky. Bromleigh loves to bird-watch.

"Birds are beautiful," she said, explaining her fascination with the feathered creatures. "I find it satisfying to be in a natural setting—and I find it challenging to identify birds that I haven't seen before."

Bromleigh has identified many species right here on campus, including purple finches, robins, crows, house sparrows, starlings, mourning doves, and grackles.

"Even very common birds like pigeons can be interesting to watch," she said. "In the spring, for example, they display very distinctive mating behavior. The males follow the females around, dragging their tails on the ground, and puffing up their necks. The females usually just ignore them.

"In most species, the old birds are usually the first to find mates," she added. "They are the ones that know how to act and sing."

Now that it's summer, the greenery at Rockefeller provides a nesting site for many of the birds. Bromleigh has noticed several nests in the ivy on Founder's Hall, and one in a tree near the tennis court.

"The birds also nest in less natural settings," she said. "Starlings love to make nests on the ledges on top of the air conditioners—the gap between the air conditioner and the window is just the right size for them. And house sparrows can be found up and down York Ave., making homes in the hollow tubes in traffic lights."

Bromleigh has gone as far afield as North Carolina to bird-watch. Last month she participated in a weekend bird-watching expedition to the Palisades and otner parts of New Jersey with the Museum of Natural History.

"But you don't have to go far to see a variety of species," she said. "Central Park is a wonderful place to watch birds. In addition to being on a major migration route, it has a number of different habitats. The woodpeckers go there because of the insects in the trees. The warblers like the woods. The ducks are attracted to the ponds. There is really a lot of activity going on, right here in the middle of New York City."

Carrie Bromleigh looks for birds.

Potpourri

Green card lottery

The U.S. Department of State will accept entries in the Green Card Lottery (formally known as AA-1) through midnight on Aug. 2, 1992. The winners of the 40,000 visas will have the chance to receive permanent residency in the period from October 1992 to September 1993. For information about who is eligible and how to apply, pick up an application packet in the Personnel Office, Founder's Hall 103.

Visa applications

Faculty Administration reminds individuals traveling abroad that many U.S. consulates and embassies do not accept visa applications from third country nationals and many cannot process visa applications in one day. Individuals who will need to apply for a new visa stamp while abroad should contact Claire Mason, X8059, prior to departure for the latest information on U.S. embassy and consulate procedures.

Seminars

The Junior Faculty-Student Seminar Series offers talks at 11:00 A.M. on most Tuesdays during the year. To suggest speakers for the upcoming academic year, contact Claude Desplan, at box 151 or fax x7923 or x7965, as soon as possible.

New sequence analysis servers

Those doing genetic sequence analysis on the computer may be interested in the new services available through electronic mail. Four new servers for sequence databases are now available. The servers BLAST and BLAZE make comparisons between sequences similar to FASTA but using different algorithms. BLAST uses the BLAST algorithm and BLAZE uses the Smith and Waterman algorithm. BLAZE runs on a massively parallel computer system, producing extremely fast results. The other two new servers, GENMARK and NETGENE, analyze for protein coding regions and splice sites, respectively.

These servers are an addition to the three servers which have been available since 1989 (GenBank, EMBL, and SWISS-PROT). A vector database has just been added to the GenBank FASTA server.

All seven servers are free. More information is available in the notes file, topic.dna. Help files can be found on rockyb in /usr/public/sequence in the directories Genbank and Servers.other. For additional help, contact the consultant, x8940.

Fellowship awards

The following individuals are the recipients of the university administered fellowships for 1992-93.
Norman and Rosita Winston Foundation Fellowships: Christopher Bowler, Chua lab; Aniruddha Das, Gilbert lab; John Hanish, de Lange lab; Benno ter Kuile, Muller lab; and Yuhang Zhao, Hanafusa lab.
Charles H. Revson Foundation Fellowships: Alice Erwin, Gotschlich lab; Christine Heufler, Nussenzweig lab; Kuo-Chu Hwang, Mauzerall lab; and Yoshiaki Okuma, Roeder lab.
Merck Postdoctoral Fellowship: Boudewijn L.M. de Jonge, Tomasz lab.
Bristol-Myers Squibb Postdoctoral Fellowship in Basic Neurosciences: Jongcheol Ahn, Aderem lab.
C.H. Li Memorial Scholarship: Yan Zhou, Kreek lab.

Young Investigator Award

Pierluigi Pompei, guest investigator in the McEwen lab, was given the Young Investigator Award in recognition of distinguished research. The award was presented at the First Independent Conference of The Society for the Study of Ingestive Behavior at Princeton University in June.

Honors

L:ast month the Academy for the Humanities and Sciences, The City University of New York, voted to make Professor Emeritus Abraham Pais an honorary member in appreciation of Pais's unique contribution to the world of scholarship and his special relationship with the academy and City University. This month the Dutch ambassador in Copenhagen presented Pais with the insignia of Officier of the Order of Oranje Nassau.

Appointments

Research Associate: Dávid Pál Fenyö, Chait lab.
Postdoctoral Associates: Aniruddha Das, Gilbert lab; Kent Nastiuk, Greengard lab; Tatyana Zvyaga, Sakmar lab.
Postdoctoral Fellows: David Albeck, McEwen lab; Hideya Fukuzawa, Chua lab; Judith Goldberg-Berman, Hirsch lab; Kazuki Hagihara, Pfaff lab; Lawrence Liu, Cohn-Steinman lab; Thomas Mueller, Greengard lab.
Guest Investigators and Pew Medical Fellows: Miriam Brown, Katherine Martin, Wynne E. Morrison, and Michael Brent Turner, Hirsch lab.
Guest Investigators: Ignacio Barradas, J. Cohen lab; Reiko Nabeya, Carter lab; C. Thomas Park, Wright lab; Neil Shachter, Breslow lab.
Adjunct Faculty: Sultan Catto, Khuri lab; Samuel Gandy, Greengard lab; Nancy Greenbaum, Kappas lab; Richard Pine, Darnell lab; Anne-Marie Sapse and James Tam, Merrifield lab.

Departures

Assistant Professors: Debra Bessen, Fischetti lab; David Helfgott, Tamm lab; I-Hsiu Lee, Khuri lab, Kathryn Crossin, David Friedlander, Frederick S. Jones, Barbara Sorkin, Edelman-Cunningham lab.
Research Associate: Cong Yan, Tamm lab.
Visiting Associate Professor: Jan Sapp, Lederberg lab.
Postdoctoral Associates: Chuan Fa Liu, Merrifield lab; Jeffrey Weiser, Gotschlich lab; Mark Burgoon, Rachel Hazan, Vincent Mauro, Osamu Minowa, Edelman-Cunningham lab.
Postdoctoral Fellows: Maria Cardenas Corona, de Lange lab; Leslie Krushel, Edelman-Cunningham lab.
Guest Investigators and Pew Medical Fellows: Moritz Hansen, Christopher Kripas, Cheryl Thellman, and Steven Tucker, Hirsch lab.
Guest Investigators: Charlotte Andersson-Fisone, Edelman-Cunningham lab; Bin Li, E.G.D. Cohen lab; Anton Markos, Müller lab; Richard Poon-King, Zabriskie lab; Jane Spetzler, Merrifield lab; Jorge Torres-Munoz, Múller lab; Elaine Volchan, Wiesel lab; Howard Worman, Blobel lab; Cui Rong Wu, Merrifield lab; Yan Yang, Merrifield lab.
Adjunct Faculty: Stephen J. Clark, Nottebohm lab; Warren Gallin, Edelman-Cunningham lab; Howard Fillit, Emile Jean-Baptiste, Zabriskie lab; Bernice Grafstein, McEwen lab; Manuela Martins-Green, Hanafusa lab; Andrew Wit, Cranefield-Gadsby lab.

News&Notes schedule

The next issue of *News&Notes* will be published Fri., Aug. 28. The paper will resume a weekly schedule beginning Fri., Sept. 11.