

9-23-1994

NEWS AND NOTES 1994, VOL.5, NO.2

The Rockefeller University

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The Rockefeller University, "NEWS AND NOTES 1994, VOL.5, NO.2" (1994). *News and Notes 1994*. Book 18.
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news & notes

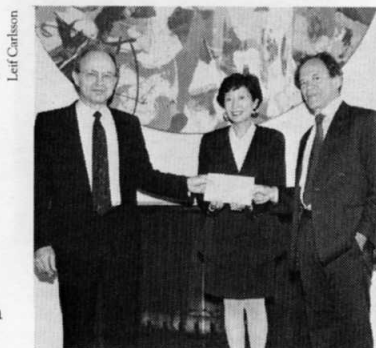
September 23, 1994 Volume 5, Number 2

The Rockefeller University

Roeder wins three-year grant from Johnson & Johnson

Professor Robert G. Roeder has been awarded a three-year, \$255,000 grant from the Johnson & Johnson Focused Giving Program. Representatives from the world's largest manufacturer of health-care products presented him with the first year's check in a ceremony Thurs., Sept 15 in Abby Aldrich Rockefeller Lounge. Following the presentation, President Torsten Wiesel thanked Johnson & Johnson and praised the company's commitment to basic research.

Roeder, the Arnold and Mabel Beckman Professor and head of the laboratory of biochemistry and molecular biology at RU, is a pioneer in the study of transcription. He and Yan Luo, a postdoctoral fellow in the lab, will use the grant to clone novel genes instrumental in immune response and to investigate their role with other DNA-binding proteins in the expression of immunoglobulin genes and related cell differentiation events. A member of the National Academy of Sciences, Roeder has received an Eli Lilly Award, a Dreyfus Foundation Teacher-Scholar Award, and an Outstanding



Left Carlsson

Professor Robert Roeder (left) received an award from Johnson & Johnson Thurs., Sept. 15. On behalf of the company, Dr. Cathy Lau (center) presented a check to Roeder and President Torsten Wiesel.

Investigator Grant from the National Institutes of Health.

Johnson & Johnson established its Focused Giving Program in 1980 to foster discoveries in biomedicine that may lead to new pharmaceuticals and health technologies; the program has awarded over \$21 million. Thirty-three scientists currently hold Focused Giving awards.

New lab safety director appointed

The university has appointed Janice Comer Bradley as director of laboratory safety. Bradley, a professional in the safety field with nearly a decade of service in medical and research environments, reviewed Rockefeller's safety and health programs in 1993 as a consultant. She replaces Edward Gershey, who resigned in August.

"I am very pleased to announce

Janice Bradley's appointment," said Fred Bohlen, executive vice president. "She was highly regarded at Brown University for her competence and leadership in supporting their biomedical programs. And having consulted here, she is already familiar with our quality program and staff."

In her new position at Rockefeller, Bradley will be responsible for laboratory safety and health programs and for ensuring compliance with all university, local, state, and federal regulations that prevent exposures and protect the environment.

"I've had the good fortune to work with several individuals here already," said Bradley. "I feel privileged to have the opportunity to work with the highly regarded professionals and scientists at Rockefeller full time now. I will try to better define the safety and

See **Bradley**, page 2

Princeton biologist to lecture today on the role of p53 in cancer

Talk is part of three-day Strang conference

Arnold Levine, professor and chair of the department of molecular biology at Princeton University, will speak on "The Role of p53 in Carcinogenesis and Cancer Susceptibility" at the Friday Lecture today (Sept. 23).

The talk is part of the First International Conference on Cancer Prevention, which is being hosted by Rockefeller and sponsored by Strang Cancer Prevention Center, The European School of Oncology, and Cornell University Medical Center. The three-day event, entitled "From the Laboratory to the Clinic: Implications of Genetic, Molecular and Preventive Research," will explore recent advances in cancer prevention, particularly in the areas of genetics, molecular biology, screening, and preventive trials. Results from the latest research will be presented to both practicing clinicians and clinical and basic researchers.

Among the nearly 30 scientists presenting talks or moderating sessions at the conference are Assistant Professor and Clinical Scholar Steven Shiff of the Hirsch-Leibel lab; Jack Fishman, a member of Rockefeller's adjunct faculty; and Michael P. Osborne, director of Strang and a visiting physician at the Rockefeller Hospital. Osborne and David M. Baldwin, president of



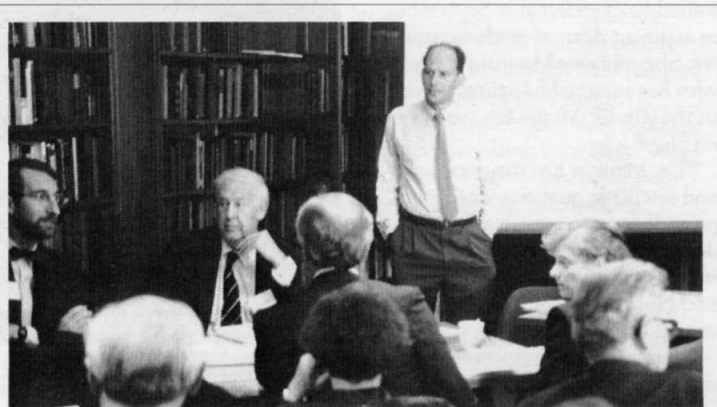
Robert P. Matthews

Princeton's Arnold Levine, who lectures today, will receive the first Strang Award for cancer research.

the David M. and Barbara Baldwin Foundation, will present the first Strang Award to Levine during today's lecture in recognition of his contributions to cancer research.

Levine will discuss his work on p53, a tumor suppressor, and its role in some forms of cancer. Mutations in p53, which impede the gene's normal function, are common in many, but not all, cancers. Levine and his colleagues are studying tumors from cancers where p53 mutations rarely occur, such as testicular cancer. In this

See **Biologist**, page 2



Jesse Ausubel, director of the Program for the Human Environment, led a day-long forum at RU on "Environment and Community Health" on Tuesday. On Ausubel's left are Dr. Alexander Bearn, RU trustee and visiting physician, and Dr. William L. Roper, president of the Prudential Center for Health Care Research and former director of the Centers for Disease Control. Others attending included Dr. Jane E. Henney of the University of New Mexico Health Sciences Center and Professor Donald F. Hornig of the Harvard School of Public Health.

2 Health office offers free screenings

3 When phage met bacteria

4 Computer talk

University health office offers free screenings for prostate cancer, cholesterol, and diabetes

As the medical community learns more about prostate cancer, coronary heart disease, and diabetes, it has been recommending early diagnosis as a key in prolonging life. Rockefeller's Employee Health Office is now sponsoring free screenings for detection of these three conditions, which are largely silent in their earliest stages.

The American Cancer Society recommends prostate cancer screening for all men age 50 and older, who are most at risk. Prostate cancer is newly diagnosed in 200,000 men and causes 38,000 deaths annually. Rockefeller's screening program has two components: Participants give a blood specimen in September to determine levels of prostate specific antigen. Chances of early detection

are improved by a physical exam of the prostate, which will be conducted at the health office on Oct. 18 by an American Cancer Society urologist, Dr. Norman Coleburn. Coleburn will also lecture in Caspary Auditorium Tues, Oct. 4 at noon on "Winning the War against Prostate Cancer."

The cholesterol screening program begins Oct. 3. According to the American Heart Association, elevated cholesterol levels in the blood (over 200 mg) is a major risk factor for heart disease, which afflicts seven million Americans and contributes to a million deaths a year. The screening at Rockefeller will be a blood test for total cholesterol and a breakdown of levels of "good" cholesterol, "bad" cholesterol, and blood fat. Parti-

cipants must fast for 12 hours prior to the exam.

The diabetes test will use blood drawn for the cholesterol test. The American Diabetes Association estimates that several million Americans may have undiagnosed diabetes.

For a prostate cancer screening, call Aurea Tuason or Candice Scheiner, x8414. Appointments for the cholesterol and diabetes blood test will be scheduled for people who fill out a form distributed on campus by the health office two weeks ago. New forms may be obtained from Scheiner or Tuason, who will schedule appointments only for those who fill them out. "Please, no phone requests for the cholesterol screening," said Scheiner.

Biologist gives lecture

(continued from page 1)

cancer, high levels of wild type, or normal, p53 are found. Levine will present evidence suggesting that a mechanism other than a mutation is responsible for the spread of these tumors.

After receiving a B.A. from Harpur College, SUNY (1951) and a Ph.D. from the University of Pennsylvania (1966), Levine worked as a postdoctoral fellow of the Public Health Service at the California Institute of Technology. He went to Princeton in 1968 as an assistant professor, and in 1976 became a full professor of biochemistry. In 1979 Levine left Princeton to chair the department of microbiology at SUNY Stony Brook School of Medicine. He returned to Princeton in 1984 as The Harry C. Wiess Professor in the Life Sciences and chair of the department of molecular biology.

In addition to the Strang Award, Levine has received a Guggenheim Fellowship and the Josef Steiner Cancer Foundation Prize. He is a member of the National Academy of Sciences, the scientific advisory boards of several cancer centers, and is the author or coauthor of more than 70 publications.

The lecture will be held in Caspary Auditorium at 3:45 P.M. and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Lounge. Admission is free. All are welcome.

The cancer prevention conference continues in Caspary until noon tomorrow (Sept. 24). For more information, contact the Office of Continuing Medical Education, New York Hospital-Cornell Medical Center, 746-2218.

Bradley

(continued from page 1)

health needs of the university and the most efficient, useful ways that lab safety can serve and support those needs. I hope to make a great program even stronger."

Bradley has a B.S. in chemistry from the University of Dayton and a master's in environmental studies from Brown University, where she worked from 1988 until now as university health and safety officer. Prior to working at Brown, Bradley worked for three years at the Veterans Administration Medical Center in Dayton, Ohio. In 1993, in addition to consulting at

Rockefeller, Bradley served on Yale University's environmental health and safety program evaluation committee, which reviewed university compliance procedures and protocols, and provided recommendations to the provost on ways to make improvements, cut costs, and reduce university losses and liabilities.

Bradley will be relocating her family to New York this year. Her husband, John Bradley, is a hospital administrator with the Veterans Administration. They have a three-year-old son, Jeffrey.



Janice Bradley, the new director of lab safety, was a consultant at RU last year.

New assistant dean of graduate studies arrives

Marguerite Mangin, a molecular biologist from Yale University, joined Rockefeller this September as assistant dean of graduate studies. She replaces Marjorie Russel, who has resumed full-time research in the Zinder-Model lab (see story on page 3).

"Dr. Mangin has the personal and scientific qualities which will provide for us a superb assistant dean. We look forward to her taking full possession of the position," said Norton Zinder, dean of graduate studies.

Mangin will be responsible for selecting students for both the Ph.D. program and the tri-institutional M.D.-Ph.D. program.

"I want to understand the university community," said Mangin. "Many of the professors I know only through their scientific reputation. It will be very helpful, in organizing the committees for student interviews and in selecting



Marguerite Mangin, a molecular biologist, is the new assistant dean of graduate studies.

students, for me to know everyone in all the labs, and I am really looking forward to meeting people."

Mangin completed her undergraduate work in biochemistry in 1979 at the University of Paris; she

continued her studies there and, in 1982, earned her Ph.D. in molecular biology with high honors. She then spent twelve years at Yale: From 1982 until 1986, Mangin was a postdoc in the department of molecular biophysics and biochemistry, studying transcription of nuclear RNA genes. In 1986, she joined the department of internal medicine in the school of medicine as an associate research scientist, working on the molecular cloning and study of a novel tumor-derived parathyroid hormonelike peptide. At Rockefeller, Mangin hopes to continue doing research, in either endocrinology or cancer.

Mangin lives in Manhattan and Old Lyme, Connecticut, with her husband Charles-Henri Mangin, president of an electronics consulting company, and their three children: Charlotte, who is 18 and attends Amherst College; Louis-David, age 15; and Maxence, age 8.

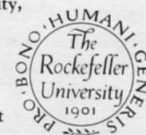
News&Notes is published each Friday throughout the academic year by The Rockefeller University, 1230 York Avenue, New York, NY 10021. Phone: 212-327-8967.

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Getting it together: Phage studies yield clues to bacterial disease

by Susan Blum

Bacteriophages, the viruses that infect bacteria, interact with their hosts in various ways. Some are moochers, setting up housekeeping inside the cell and never leaving. Others are terrorists, exploiting the cell's resources and then blowing it up. Only a rare few are considerate house guests, entering the host cell, replicating there, and then exiting while leaving the cell intact.

Though their *modus vivendi* most often makes them a bane for bacteria, phages have consistently been a boon for biologists. Fast-growing and quick to mutate, endowed with a minuscule genome, reliant on cellular proteins for some of their most basic functions, the viruses have helped scientists answer fundamental questions in molecular biology and genetics—such as what genes are made of, how they are duplicated, and how their information is read out and turned into proteins.

Now one type of bacteriophage is also providing answers to a complex question in cell biology. That question is: How do pathogenic gram-negative bacteria export their disease-causing proteins across the cells' membranes, so that the proteins can do their dirty work?

Included among the bacteria are those that cause the black plague, dysentery, salmonellosis, and gonorrhea in humans, and soft rot in plants, including vegetables. The bacteriophages in question are *filamentous phages*, the considerate viral guests that invade the host, multiply, and then exit again without doing harm. In a recent "Perspectives" article in *Science*, Associate Professor Marjorie Russel explored how the confluence of two streams of research—one on bacteria and another on phage—have resulted in a rush of new insights.

Phage studies

Much of the phage work was done here at Rockefeller, in the lab with which Russel is associated. That lab, headed by Norton Zinder and Peter Model, has a long tradition of filamentous phage research—indeed, the very existence of such viruses was discovered there in the 1960s.

In the late 1970s, right about the time that Russel arrived on campus, Model had begun work with Günter Blobel on how certain filamentous phage proteins move, or are translocated, into the cytoplasmic membrane of *E. coli*, the virus' bacterial host. Having found that bacterial



Associate Professor Marjorie Russel studies the relationship between phage assembly and the export of bacterial proteins.

proteins act on viral proteins during this process, Model collaborated with Russel, a bacterial geneticist, to find mutant bacteria that would clarify certain aspects of protein translocation.

Part of the fun of genetics, says Russel, is that "you never know exactly what you're going to get." As it turned out, the first interesting bacterial protein disclosed by her mutants in 1985 had nothing to do with protein translocation, but rather with viral assembly—the process by which the virus is constructed from its protein and DNA constituents. Besides this bacterial protein, Russel also focused on two viral proteins—p1 and p4—that are crucial for phage assembly. She's been studying phage assembly ever since.

Understanding phage assembly is important to learn not only how a phage gets it together within the host, but also how it leaves. When phages were first discovered, scientists knew that the viral genes and proteins were inside the cell, and that new viral particles were being assembled somewhere. However, those new viral particles could never be seen in the cell's cytoplasm, but only in the extracellular milieu. As Russel puts it, "There was a huge black box between the inside and the outside of the cell." In the years that followed, researchers opened that box and disclosed that there must be close links between viral assembly (occurring within the membrane surrounding the cell's cytoplasm) and the subsequent export of assembled viral particles (occurring through the cell's outer membrane). Most recently, Russel's work has suggested a model for how these coordinate processes of phage assembly and export might actually work.

Bacterial studies

As research was progressing on filamentous phage assembly and export in gram-negative bacteria, work was also advancing on how uninfected gram-negative bacteria export their own proteins to cause disease. In 1989, research at the Pasteur Institute showed that a cluster of more than ten genes was required to export pullulanase, a virulence factor produced by the plant pathogen *Klebsiella*. Remarkably, one of those genes bore a striking resemblance, or homology, to the gene coding for the filamentous phage p4 protein.

"The existence of this complicated bacterial machinery was unknown until 1989, but then everyone started discovering it in many gram-negative bacteria," Russel reports. Two different types of complex machines were found. Each had quite different protein constituents, with one exception: both sported a protein homologous to p4.

Russel and her colleagues are investigating how these p4-like proteins may be working, using p4 itself as their paradigm. Their work took a big leap forward last year, when Barbara Kazmierczak, an M.D./Ph.D. student in the lab, found that p4 proteins associate with one another in bundles of 10 or 12 molecules. Russel and Kazmierczak believe this protein bundle, or oligomer, may form a very large channel through which phage particles leave the infected bacterium, their export triggered when the assembling virus flips open a gate in the channel. P4 homologues encoded by the bacteria may form similar large channels that enable the pathogens to export their disease-causing proteins.

Russel stresses that no direct evi-

dence for such channels has yet been obtained. She and her colleagues are now working on purifying the p4 complex and, in collaboration with Assistant Professor Sanford Simon, determining whether they do indeed form channels. Should this prove true, Russel says, "It would be lovely to think that eventually agents might be found that block a channel from opening, and so keep virulence factors from being exported."

Such practical bonuses might yield therapies for disease (and fresher vegetables in the fridge!). But they won't come tomorrow. Many studies remain to be done—not only to prove or disprove the existence of channels, but also to learn what makes each p4-like molecule so picky about the one specific virus or protein it will export.

Back to the future

While making unexpected contributions to cell biology, filamentous phage are also "being reborn as a tool for molecular biology," Russel says. In the last few years, a new technique called phage display has permitted biologists to clone short segments of DNA into viral genes coding for phage coat proteins. When the virus assembles, the phage displays the short protein fragment, or peptide, on its surface, thus providing a molecular hook for various kinds of experiments.

So far, the main phage coat protein can accommodate a peptide hitchhiker no larger than between six and nine amino acids, and Russel wants to know why. "One possible explanation for the limit is the size of the p4 channel, if it is a channel," she says. In other words, a larger phage coat means a larger phage virus—one that is possibly too large to fit through the channel.

Going back to her first love, genetics, Russel hopes to find phage mutants that allow for a larger add-on peptide. Such studies will help prove or disprove her working model about the role of p4. They may also boost phage display's already-considerable power, by expanding the range of peptides available for experiments.

Thus, in only five years, research into phage p4 and its bacterial homologues has produced a wealth of results. As Russel wrote with understatement in her recent article, "The unexpected parallels [between phage assembly and bacterial virulence factor export] confirm the power of basic research in one area to fertilize another and, perhaps, to generate useful ideas."

Potpourri

In memoriam

The university community mourns the passing of William Everly, former assistant for research in the Gotschlich lab. Everly joined the Swift lab of the then Rockefeller Institute for Medical Research in 1941, and retired from the university in 1983.

Cafeteria celebration

Beginning Mon., Sept. 26, Tower cafeteria will celebrate "Back to School Week" with specials during breakfast or lunch each day. For more information, contact Amy D'Eletto, cafeteria manager, x8893.

RU concert

Pianist Garrick Ohlsson, winner of the 1994 Avery Fisher Prize, begins the university's evening concert series Tues., Sept. 27 at 8:00 P.M. in Caspary Auditorium. Ohlsson will perform the works of Beethoven, Schubert, Haydn, and Barber. For information, contact Cathy Rogers, x8437.

Clinical Research Seminar

Wade Berrettini, professor of psychiatry and pharmacology at Thomas Jefferson University, will speak on "Genetic Approaches to Behavioral Disorders" at the Clinical Research Seminar, Wed., Sept. 28, at noon in Nurses Residence 110B.

Workshops

Space is still available for the following Computing Services workshops:

- **Introduction to the Macintosh:** Wed., Oct. 5, 2:00 to 4:00 P.M.;
- **Word for Windows, Part I:** Thurs., Oct. 6, 2:00 to 4:00 P.M.;
- **Introduction to Windows:** Fri., Oct. 7, 10:00 A.M. to noon.

More workshops will be announced in future *news¬es*. To register, leave voice mail at x7768 stating your name (spelled out), extension, lab or department name, and class desired. You will be called to confirm registration. If you do not receive a call, the workshop has been filled and you will be informed when there is space in the next available workshop.

Weekly Research Seminar

Dates are still available to invite speakers for the Weekly Research Seminar (formerly the Junior

Bit by bit, computer communication expands at RU

Computing Services has introduced several new information outreach tools.

The popular e-mail program Eudora can now be used to look up campus phone numbers, via the "Ph server." To set up the "Ph" command, select "Configuration" under the "Special" menu. In the box next to "Ph server" type: ns.rockefeller.edu. Now, instead of logging on to UNIX or wrestling with a temperamental Hypercard stack, choose the "Ph" command located under the "Special" menu, type in the last name of the person you are looking for, and click the "Ph" button.

Electronic discussion groups (newsgroups) are now accessible through a threaded newsreader (*trn*) that allows you to locate one topic, or thread, within a newsgroup. Previously, news could only

be read chronologically using the program *trn*. To use *trn*, log in to rockyj, type *trn*. To move from thread to thread, hold down the shift key and >. Help is available within *trn* by typing *h* or ?.

Computing Services has created two new campus newsgroups: ru.general.news for general topics, and ru.scientific.news for scientific research conversation and collaboration. Messages can be sent to these newsgroups by using the command *Pnews*.

Campus information access has been widened by The Rockefeller University World Wide Web (WWW) server. The Web is a networked information system using hypertext—special text and graphics—that, when selected with a mouse click, transports you to the corresponding portion of the document. This can be another

page of text on the local web server, a different server in another part of the world, sounds, or graphics. Current topics available via the local WWW server include the calendar of events, RU phonebook, and Computing Services information.

To use the Web, you need a networked Macintosh, PC, or workstation (UNIX or VMS) running appropriate WWW client software, which is available (and free) from Computing Services. For those already accessing other Internet WWW servers, simply point your client to the following URL: <http://www.rockefeller.edu>.

The consultant, x8940, can provide additional information about these new services. Anyone interested in posting items on the RU WWW should contact Frank Lees, x8925.

Faculty-Student Seminar Series). Submit your proposals as soon as possible to Claude Desplan, x7965, fax x8370, or box 151.

Rehearsal space

Practice time is available in the university's music room on the first floor of Caspary. The room, which is equipped with a Steinway grand piano, music stands, and chairs, may be reserved for one hour during the day or evening. Singing rehearsals are not allowed during office hours. Contact Sandi Walsh, x8072, to sign up.

Arrivals

Visiting Professor: John Mundy,

Chua lab.

Research associate: Patrick Haslett, Hirsch lab.

Postdoctoral associates: Hitoshi Ikegami, Wilson lab; Svetlana Cupac Maric, Nussenzweig lab; Lin Wu, Breslow lab.

Postdoctoral fellows: Chenbei Chang, William Gregory Cox, and Paul Wilson, Hemmati-Briuanlou lab; Patricia Cortes, Nussenzweig lab; Simon Daefer, Zinder-Model lab; Lei Feng, Heintz lab; Xiaolu Shi, Roeder lab; Lenore Snyder, Sakmar lab; Chunyi Zhang, Pfaff lab.

Guest investigators: Sophia Arnis, Sakmar lab; Daniel G. Herrera, Alvarez-Buylla lab; Vassilliki Kozoni, Hirsch lab; Mark Ian

Liddington, Steinman lab; Pedro Persechini, Ding-E Young lab; Qun Wang, Chua lab.

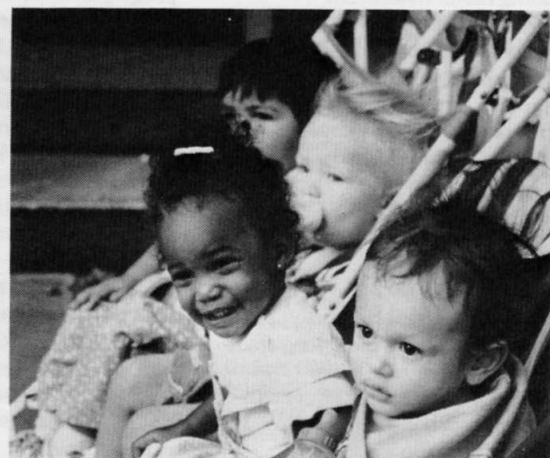
Departures

Adjunct Faculty: Douglas McBride, Hayre lab.

Research associate: Takashi Yamaguchi, Wilson lab.

Postdoctoral associates: Anat Barnea, Nottebohm lab; Hsiou-chi Liou, Baltimore lab; Nurit Porat, Gotschlich lab; Hiroko Suzuki, Hall lab; Iryna Vtiourina, Choi lab; Berrin Yanikoglu, Wilson lab.

Postdoctoral fellow: Eduardo Fajardo, Hanafusa lab; Kazuki Hagihara, Pfaff lab; William Sha, Baltimore lab.



Students of the Rockefeller University Children's School (left) meander back to class after an afternoon recess. Waiting to escape their strollers, members of the Infant-Toddler Center begin a new academic year. Both programs started this month.