1-13-1995

NEWS AND NOTES 1995, VOL. 5, NO.14

The Rockefeller University

news&notes

January 13, 1995 Volume 5, Number 14 *The Rockefeller University*

David and Peggy Rockefeller dedicate concert to late trustee Albert Nickerson

The Raphael Trio will perform at the university Wed., Jan. 18 in an evening concert dedicated to the memory of Albert Nickerson, a former Rockefeller trustee and RU Council member. The concert is being underwritten through the generosity of Nickerson's longtime friends, David Rockefeller, chairman of the trustees' executive committee, and Peggy Rockefeller.

Nickerson, who was chairman and chief executive officer of the Mobil Corporation, served at Rockefeller for 36 years: as a trustee, from 1958 until 1986, and then on the council, from 1986 until 1994. Nickerson is being honored for his exemplary commitment and active involvement in all parts of the scientific program and life of the Rockefeller University.

The Raphael Trio, whose members have played together for 20 years, will give a premiere performance of "Tangos," a work they commissioned from Thomas Oboe Lee. The trio will also perform Trio No. 2 in G minor by Antonin Dvorak and Piano Trio in E-flat major by Ludwig van Beethoven.

The concert will begin at 8:00 P.M. in Caspary Auditorium. For ticket availability and prices, contact Cathy Rogers, concert administrator, x8437.

Courtesy of the artists

The Raphael Trio will perform at the university next Wed. (Jan. 18) in a concert to be dedicated to the late Albert Nickerson by Peggy and David Rockefeller, chairman of the trustees' executive committee.

Save the dates:
March 16, 17, & 18

University to commemorate 50 years of electron microscopy in cell biology

Rockefeller will commemorate the 50th anniversary of the use of the electron microscope in cell biology with a three-day celebration beginning Thurs., Mar. 16. Participants will include contributors and witnesses to the revolution resulting from this important innovation, such as Professors Emeritus Christian de Duve and Philip Siekevitz, former Rockefeller faculty member George Palade, and alumnus David Sabatini.

Among the events will be a historical roundtable discussion, a symposium organized by Professor Günter Blobel, and a program for the public on the history of the electron microscope and cell biology. Look for more information in future issues of *News&Notes*.

Clinical scholar speaks on vancomycin resistance today

Sandra Handwerger, an assistant professor and clinical scholar at Rockefeller, will speak on "Beyond the Last Resort: Mechanisms and Genetics of Vancomycin Resistance" at the Friday lecture today (Jan. 13).

Handwerger studies the resistance of gram-positive bacteria to the drug vancomycin. Vancomycin is known as the "drug of last resort" since it is often used for treatment of infections due to organisms that are resistant to other antibiotics, such as penicillin-resistant enterococci.

Although resistance to vancomycin was once considered unlikely, it was first recognized in 1988, and now accounts for more than 15% of enterococcal infections among patients in intensive care units in the U.S. Vancomycin resistance in enterococci is mediated by the *vanA* gene cluster, which encodes a peptidoglycan precursor that will not bind to vancomycin. Today Handwerger will discuss her study of the role of the *vanA* gene cluster in vancomycin resistance.

"One of the most serious problems associated with infectious diseases in American hospitals is resistance to antibiotics," said Physician-in-Chief Jules Hirsch,

See ***Handwerger****, page 2*

Hatten's Mirsky lectures trace form and function in the brain

by Susan Blum

For the past 35 years, students have come to Rockefeller over the Christmas vacation to attend the Alfred Mirsky lectures, established to ignite young students' interest in science. This year, more than 500 students listened raptly as Rockefeller Professor Mary Beth Hatten talked about what she called "the greatest mystery in our lives"—how the brain's billions of nerve cells derive their identities, and how its complex architecture becomes organized to make us who we are.

About half the mammalian genome—nearly 50,000 genes—is thought to be involved in central nervous system functioning, but scientists have so far characterized fewer than one percent of those genes. "We still have a long way to go to understand the very basics of how nerve cells are established, how their identities are set forth, and how these individual cells get organized into regions and systems," Hatten told the assembly. Her lecture series, called "Form and Function: Building the Brain," discussed some of the complex processes sculpting vertebrate brain development.

She told the group that her lab focuses on developmental events in the cerebellum, the region in the back of the brain that acts to control movement and body posture. Several factors underlie the choice of the cerebellum as a model system, she explained. Compared to

See ***High school****, page 3*

Sandra Handwerger, assistant professor and clinical scholar, lectures today (Jan. 13).

Interested in the visa lottery?

To increase the diversity of immigrants in the U.S., the Department of State is again holding its annual diversity immigrant visa program.

At Rockefeller, "there may be as many as 160 faculty members with nonimmigrant visas who are eligible," said Maria Lazzaro, assistant faculty administrator. "A few years ago one of our current faculty won a visa in this lottery."

The visa lottery, as the program is commonly known, will grant 55,000 green cards (immigrant visas) to natives from countries that have low admission rates into the U.S. The government evaluates the admission status of each country annually by tallying total immigrant admissions over the most recent five-year period. U.S. citizens, permanent residents, and naturalized citizens may apply for registration for the lottery on behalf of anyone from a qualifying country. Lazzaro stresses that the lottery is open to anyone who qualifies.

Registration for the lottery begins Tues., Jan. 31 and ends Wed., Mar. 1. Visas will be issued to winners next October. Members of the Rockefeller community can obtain information about registering to apply for the visa from the Personnel Office, Founder's Hall 103, x8300, which has a list of eligible countries and complete information about registration.

Handwerger

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who introduces Handwerger today. "An ominous development is resistance to vancomycin, the molecular basis of which Dr. Handwerger will discuss today."

Handwerger received an M.D. from the College of Physicians and Surgeons at Columbia University in 1980. After completing a residency in internal medicine at Beth Israel Medical Center in New York, she came to Rockefeller in 1983 as a postdoctoral fellow in the Tomasz lab. In 1986, Handwerger became assistant attending physician at Beth Israel Medical Center and assistant professor of medicine at Mount Sinai School of Medicine. She became assistant division chief at Beth Israel in 1989, and returned to Rockefeller in 1992 as an associate physician and assistant professor. She is also the Johanna Maria Fraenkel Clinical Scholar.

Handwerger has received the Pfizer Research Merit Award and the Glorney-Raisbeck Award from the New York Academy of Medicine. She is a diplomate in internal medicine and infectious diseases.

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. All are welcome.

Time out for art

Joseph Bonner

Cynthia Altman, art curator, installs a new exhibition of ancient American ceramics from the university's Alfred E. Mirksy collection of fine and decorative arts. The 29 antiquities, culled from the 600-piece collection, are on view on the second floor of the library in Welch Hall.

Profiles

Aquiles Sosa

Born: Santo Domingo

Number of years in the U. S.: 25

Number of years at RU: 24

Positions at RU: Rose from porter in hospital housekeeping to group leader. "I organize several floors of the Hospital, make sure there's a full supply of everything, and that showers, beds, and such are in good repair." Wears a second hat, during lunch hours, as a gym instructor, advising people on use of equipment in the campus gym.

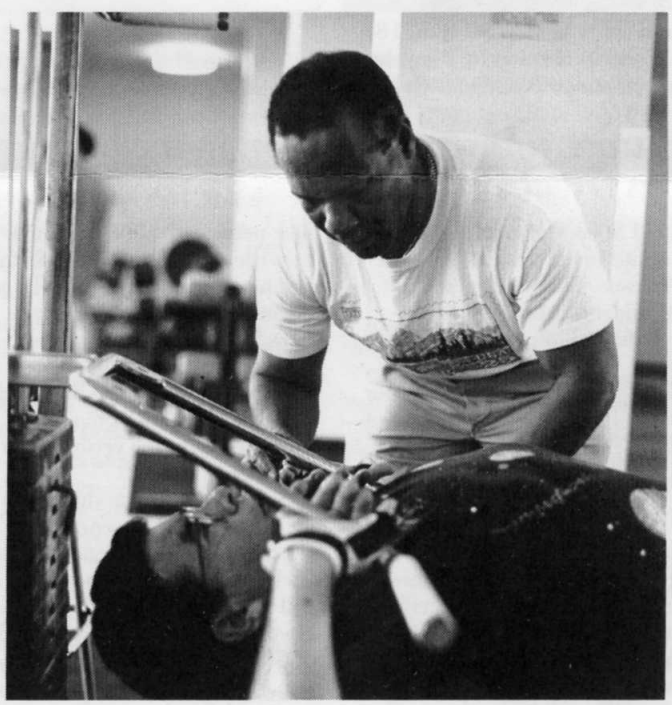
One important reason he has for staying fit: "On Memorial Day in 1987, I was mugged and shot in the stomach. My hip was paralyzed and people said I'd never walk again. But I came back, I think because I was in shape."

Contribution to gym: Offers an exercise class on Mondays, Wednesdays, and Fridays at 12:20 P.M. Ensures that equipment is working; making plans for improvements to the gym.

Contribution to gym ambience: "Every day, I try to help people to do a good workout. "

Invitation to couch potatoes: "It's my particular pleasure to help people get started exercising. You come in, I'll help you find something you'll enjoy."

One caveat for couch potatoes: "People here work out at their own risk, so you have to do what's right for you."



Aquiles Sosa assists people pursuing physical fitness at the RU gym.

Weekend activities: Rides a nonstationary bicycle; plays golf with friends and with his oldest son.

Ideal vacation: Visiting family and trying out new golf courses.

What he does when he is sitting down: Reads *Golf Digest*.

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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High school students learn about brain cells on the move

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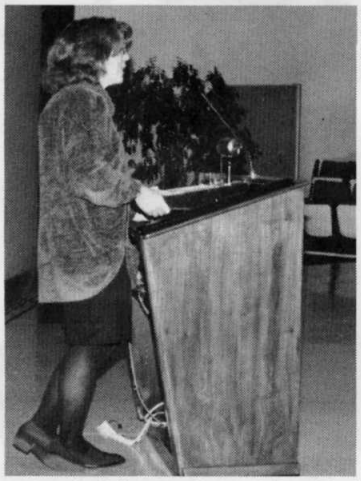
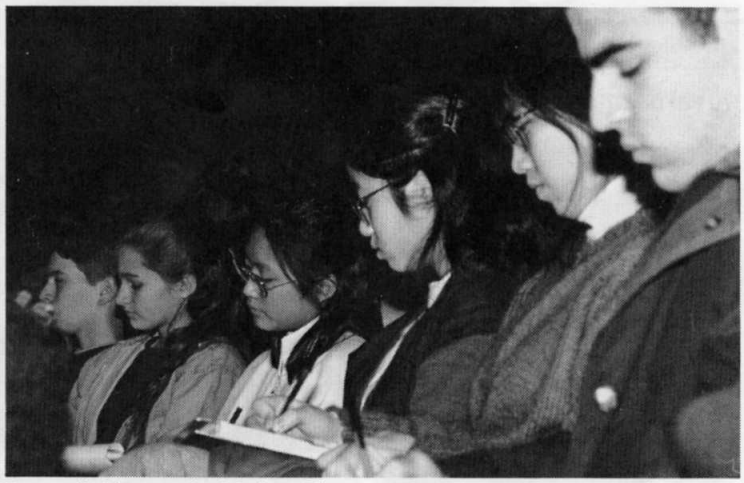
some other brain areas, it is structurally simple, with infolded regions that repeat themselves many times over. It is made up of just two principal types of nerve cells, or neurons—one of which, the granule cell, is present in such abundance that the cells can be purified and their development studied in what she termed "excruciating detail." Moreover, mutations in cerebellar neurons lead to defects in motion that are easy to spot, thus making it easier for the researchers to home in on genes that are essential for cerebellar development.



Leif Carlson



Rockefeller Professor Mary Beth Hatten (*left*) gave the Mirksy Christmas lectures on Dec. 27 and 28. More than 500 students from 54 high schools in New York and New Jersey listened raptly as she talked about brain development and scientific method.

A focus on experimentation

Throughout the two-day event, Hatten aimed not only to impart information to the students, but to give them an idea of how scientists obtain information through observation and experimentation. To begin, she told them of the work done a century ago by Santiago Ramón y Cajal, a scientist she said "who remains the greatest thinker in developmental neurobiology."

Before Ramón y Cajal, it was believed that all the cells in the brain formed one huge syncytium—a multinucleated mass of cytoplasm formed by the union of many cells. But Ramón y Cajal refined methods for staining cells in the brain, and so showed that the brain consists of billions of individual brain cells that form connections with one another through the outgrowth of cellular structures called axons. With this stunning act of observation, he "looked in the microscope, brought his imagination to bear, and brought forth the neuron doctrine," Hatten said.

Ramón y Cajal saw how, in the developing brain, undifferentiated nascent neurons first multiply in a specialized zone of proliferation. Then they sprout axons tipped by structures called growth cones, which are instrumental in helping the neurons form connections over long distances with different brain regions. Ramón y Cajal's playful spirit led him to envision each growth cone as a "soft battering ram" that somehow senses the environment, responds to it, and grows out to form proper connections with other cells. The Spanish scientist also observed that a developing neuron's shape became increasingly complex as it migrates long distances to reach its final destination, with cells that reach different destinations taking on different shapes.

Pressing questions explored

Many of the questions first raised by Ramón y Cajal's brilliant observations could be tackled in detail only a century later, with the advent of molecular biology.

As Hatten explained, among the most pressing of these questions is how the ultimate fate, or identity, of each nerve cell is specified. Does the brain follow the British Plan, in which a neuron's identity is determined by its parentage during the earliest period of cell proliferation? Or does a neuron opt for the American Plan, in which its fate is determined by the neighborhoods through which it journeys to reach its final destination?

During the first day's lecture, "Specifying the Brain's Building Blocks," Hatten described research in her lab clearly showing that the brain employs the American Plan. These studies involve the *weaver* mutant mouse. On a behavioral level, it is easy to spot mice with the *weaver* defect: They stumble and weave, bereft of the agility with which normal mice are endowed. The defect is also obvious from a look at their brain tissue. Within the region that will develop into the cerebellum, nascent granule cells are generated and proliferate, but fail to sprout axons and growth cones and to take the first steps in migration. The cells upon which the neurons migrate—the cellular highway cells known as glial cells—also look abnormal.

For many years, Hatten said, blame for the *weaver* flaw had been laid on the glia. But her research in the test tube and live animals placed the blame firmly on the granule cell. She told her young audience that unexpected results like this were an "interesting story" in how science develops. "The most exciting moments come when you realize that everything you understood up to that moment was completely wrong, and that you have to think about your subject in a completely different way," she said.

Pursuing their surprising discovery, the Rockefeller researchers found that the fault lay in a failure of cell–cell signaling among nascent granule cells. Normally, these cells send an essential signal to one another, switching on a "cassette" of genes that prompts each granule cell to go on to the next step in its developmental program. Without this community-wide signal, the development of the granule cells fails to progress. Work is now under way in the lab to clone the *weaver* gene that codes for the signal molecule, and to figure out what kind of molecule it is.

Migration along highways

It may turn out that such local signals are important not only in the early stages of brain development, but all the way through it. In her second-day session, "Organizing the Brain's Architecture," Hatten discussed how signals within the community of cells might tell them to move on to progressive stages of development during their long migration along the cellular highway of glial cells.

Such migration occurs in all the "cortical" regions of the brain, such as the cortex, the hippocampus, and the cerebellum. "It's an unbelievably tortuous process, with these cells moving along like little inchworms," Hatten said. "If you do the calculations, the cells in the cerebellum are walking about as far as from here to Chicago, and the cells in the cortex are walking as far as California."

Hatten then showed her audience remarkable movies of young neurons caught in the very act of migration. She explained that the video technology used to observe this process allowed the researchers to visualize how migration could be blocked by a particular antibody. Using the tools of molecular biology, the scientists were subsequently able to pinpoint a molecule, called *astrotactin*, which granule cells use to latch on to glial cells as they migrate. The studies showed that nascent granule cells turn on their *astrotactin* gene at a particular moment in their developmental program—the moment when they begin to leave the early proliferative stage and step on to the glial fiber.

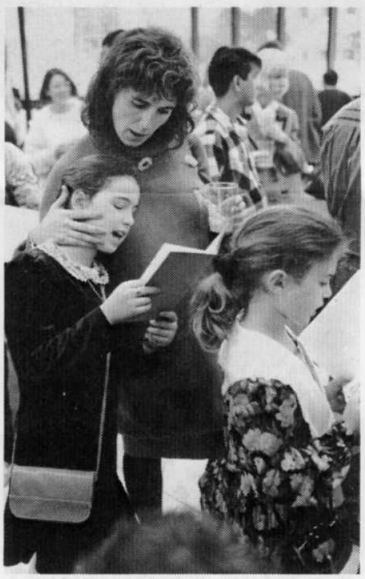
Research conducted by Hatten and Rockefeller Professor Nathaniel Heintz has shown that still other stages of granule cell migration and differentiation are marked by the expression of still other genes, or sets of genes. Hatten said, "You get the picture that as the cell migrates, there is a kind of tag relay system, where the cell goes from the expression of one set of genes to the next. This raises the expectation, which we have not yet proved, that as the cell moves along, it is signals in the environment that are tripping the control systems that turn these genes on," she said.

Should further research confirm this hypothesis, it would help explain one of the puzzling facts about brain development. "On a very basic level, one wonders why all these cells are taking this arduous journey," Hatten said. "One reason might be that migration gives neurons the opportunity to receive signals for the expression of many different sets of genes, and thus to be modified and develop into many different types of cells. And that, after all, is the business of brain development: to generate as complicated a network of cells as possible, to create the maximum capacity for complex communication."

Rockefeller feted the season with a feast of fun and festivity

Food, drink, and divertisements were offered at the university's holiday celebration, held Thurs., Dec. 22 in a spruced up Tower Café.

One performer (*left*) entertained adults; another engaged both children and parents as part of a special program for children, new this year. Mr. and Mrs. Santa Claus (played this year by Robert Katz, pharmacist, and Cecilia Cardona, secretary) once again dropped in at the party to spread holiday cheer.



Carolers gathered around a piano in Tower lobby and sang throughout the afternoon.

Below the tall Christmas tree, straw cornucopias offered an abundance of food. The gingerbread house constructed by Food Services was displayed at the party and later donated to children at New York Hospital's Pediatric Center for Special Studies.

Potpourri

Tri-Institutional Noon Recital
The DaPonte String Quartet will perform the works of Mozart and Shostakovich at the Tri-Institutional Noon recital today (Jan. 13). The concert, to be held in Caspary Auditorium at noon, is free.

Friday film
Luna (Italy, 1979), directed by Bernardo Bertolucci, will be shown today (Jan. 13) at 8:00 P.M. in Caspary. The film, which is in English and Italian with English subtitles, is free. All are welcome.

Choral Symphony Society
The Choral Symphony Society will rehearse Handel's *Theodora* every Tuesday from 7:30 P.M. to 9:30 P.M. in Caspary music room beginning Tues., Jan. 17. For further information contact David Labovitz at 864-7541.

Clinical Research Seminar
Steven Shiff, assistant professor and Fraad clinical scholar, will speak on "Nonsteroidal Antiinflammatory Drugs and Colon Cancer: Lessons in Prevention" at the Clinical Research Seminar Wed., Jan. 18 at noon in Nurses Residence 110B.

Harvey Society Lecture
Randy Sheckman, investigator of the Howard Hughes Medical Institute at the University of California, Berkeley, will speak on "Regulation of Membrane Traffic in the Secretory Pathway" at the Harvey Society Lecture Thurs., Jan. 19 at 8:00 P.M. in Caspary.

Paper play
Tickets to see the Paper Bag Players, a theater group known for entertaining children and parents in original costumes made of paper and cartons, are available at the RU Children's School. This year's production, *"Rubbish!" She Cried*, will be held Sat., Jan. 28 at 2:00 P.M. at the Kaye Playhouse at Hunter College. Tickets, $15 each, can be purchased through the Children's School, x8580. A portion of each ticket benefits the Children's School and Infant-Toddler Center.

Sweat shirt shop
The Sweat Shirt Shop is now selling *Health Guide for International Travelers* by Thomas Sakmar, Pierce Gardner, and Gene Peterson ($13) and *The Hostage Brain* by Bruce S. McEwen and Harold M. Schmeck, Jr. ($16). The shop, located in Rockefeller Research Building 133, is open every Tuesday from 11:30 A.M. to 1:30 P.M.

Cohn Forum
Alan J. Friedman, director of the New York Hall of Science, will speak on "Science Education in New York City: We Know the Problems; What are the Answers?" at the Zanvil A. Cohn Forum on Health Affairs Tues., Jan. 31 at 5:30 P.M. in the Abby Aldrich Rockefeller dining room. Sherry will be served at 5:00 P.M.

Awards
The winter 1994 issue of *Search*, the first issue of The Rockefeller University magazine in its current format, received a bronze award in the 1994 Mercury Awards International competition, which honors the highest degree of excellence in communications. Susan Blum, science writer in the Office of Public Affairs, was a finalist in the category of medical/scientific writing for her *News&Notes* article on Associate Professor Hubert Schwabl's research.