

6-3-1994

NEWS AND NOTES 1994, VOL.4, NO.30

The Rockefeller University

Follow this and additional works at: http://digitalcommons.rockefeller.edu/news_and_notes_1994

Recommended Citation

The Rockefeller University, "NEWS AND NOTES 1994, VOL.4, NO.30" (1994). *News and Notes 1994*. Book 14.
http://digitalcommons.rockefeller.edu/news_and_notes_1994/14

This Book is brought to you for free and open access by the The Rockefeller University News and Notes at Digital Commons @ RU. It has been accepted for inclusion in News and Notes 1994 by an authorized administrator of Digital Commons @ RU. For more information, please contact mcsweej@mail.rockefeller.edu.

\$5 million center for Alzheimer's research established at Rockefeller

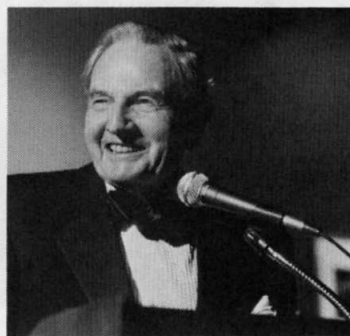
The Fisher Medical Foundation has given \$2.5 million to the university for the creation of an institute dedicated to research on Alzheimer's disease. David Rockefeller has matched the gift, creating a \$5 million base for a research and development effort to be led by Vincent Astor Professor Paul Greengard.

The establishment of the university's new Zachary and Elizabeth M. Fisher Center for Research on Alzheimer's Disease was announced on Thurs., May 26 at a press conference in Washington D.C. Speakers at the conference, which capped a three-day, international meeting on Alzheimer's held at the National Institute of Aging of the NIH and cosponsored by the Fisher foundation, included First Lady Hillary Rodham Clinton, Zachary Fisher, who heads the Fisher Medical Foundation, David Rockefeller, and

Courtesy of the Fisher Medical Foundation



Philanthropist Zachary Fisher (left) and Chairman of the Board's Executive Committee David Rockefeller have each contributed \$2.5 million for a new center on Alzheimer's research at RU.



RU President Torsten Wiesel.

Praising the new collaborative research initiative, the First Lady said, "This is an example of what we need." About four million Americans currently are afflicted with Alzheimer's, at a cost to society of \$100 billion a year, and that number is expected to rise to fourteen million by 2050 A.D. "We have an economic imperative to solve the problem of Alzheimer's disease," said Rodham Clinton.

Wiesel, speaking at the conference, said, "We are very grateful for Zachary Fisher's generosity and vision in establishing the Center with two major, interrelated components: basic research in the laboratory, and clinical research involv-

ing patients. And we thank David Rockefeller for making this new Center possible."

Mr. Fisher has funded the Center in the hope that within a decade, doctors will be able to delay the onset of Alzheimer's and slow its progress. "For a disease like this, there is never enough money," he said.

David Rockefeller, who has served on the RU Board of Trustees for half a century, noted that the new Center is in keeping with the original mission of the institute established by John D. Rockefeller, Sr. "My grandfather envisioned a biomedical research facility that would be at the forefront of scientific discovery and disease control. In this same tradition, I established a

Friday lecturer to speak on defense activation in plants

Klaus Hahlbrock, director and head of the biochemistry department at Max-Planck-Institut für Züchtungsforschung in Köln, Germany, will speak on "Signalling and Defense Reaction in Fungus-Invaded Plant Cells" at the Friday lecture today (June 3).

"Dr. Hahlbrock has made a number of fundamental contributions to our understanding of the regulation of secondary metabolite biosynthesis in plants," said Andrew W. Mellon Professor and Head of Laboratory Nam-Hai Chua, who will introduce Hahlbrock today. "His work has shed important new light onto the ways that plants fight pathogen attacks."

Plants protect themselves from pathogens by activating a multi-component response. The efficiency of this response depends on its complexity and the speed of its activation. Hahlbrock and his colleagues study the mechanisms by which pathogens are recognized, using the model system of parsley cells, or protoplasts, and fungal elicitors that bind specifically to high-affinity target sites on the plant plasma membrane.

Through the use of RNA-RNA in situ hybridization, Hahlbrock has shown that the expression of

President holds office hours

President Torsten Wiesel holds office hours every Fri., from 2:15 to 3:15 P.M.

"Everyone—faculty and staff—should feel welcome to see me in confidence with any concerns or issues they have," said Wiesel. "I have put aside this hour for us to sit down and talk."

Anyone interested in meeting with the President during office hours should call his office, x8080, for an appointment.

2 To satisfy a doctor's curiosity

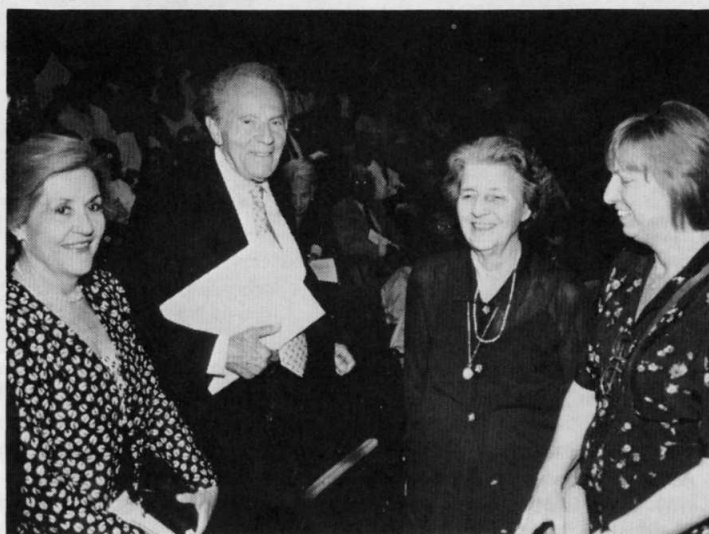
3 The cellular highway

4 Children dance and sing

See Fisher, page 2

See Friday, page 4

François Jacob receives Lewis Thomas Prize and gives lecture



Nobelist François Jacob (left) accepted the second Lewis Thomas Prize: Honoring the scientist as poet on Wed., May 25. A molecular geneticist who has written evocatively about biology, evolution, and his own life, Jacob traveled from France to receive the award from President Torsten Wiesel and Chairman of the Board of Trustees Richard Furlaud. He gave a talk on "Biology and Culture" stressing that along with the new opportunities for scientists to change society have come commensurate responsibilities. With Jacob at the prize ceremony are Genevieve Barrier (far left); the widow of Lewis Thomas, Beryl (second from right); and Judy, his daughter (right). Thomas' other daughter, Abigail, also attended.

Fisher Center

(continued from page 1)

fund for new initiatives at Rockefeller University two years ago. For these reasons, I am extremely pleased that a portion of this fund will now be devoted to Zach Fisher's effort to combat Alzheimer's disease," he said.

The Fisher center will serve as the nexus for Alzheimer's research at Rockefeller, integrating the neuroscience of the Greengard lab, the patient-oriented work at the hospital, and other campus efforts related to the lethal neurological disease. More specifically, the gift will provide facilities and advanced technologies to expand the Greengard lab's ongoing research. It will also serve to augment the clinical studies of physician-scientists.

Greengard's work on the molecular machinery of the nervous system has revealed that molecules called phosphoproteins play important roles in nerve cell response to neurotransmitters and other chemical signals. One of these phosphoproteins, APP, is fragmented into pieces that cannot be secreted from the cells. Stuck inside, they lead to the production of the protein beta-amyloid, which is a major component of the brain plaques that are a hallmark of Alzheimer's disease.

A second protein implicated in Alzheimer's is under study by Frederick Henry Leonhardt Professor and Senior Physician Jan L. Breslow. Over a decade ago, Breslow identified the gene for Apolipoprotein E, a gene that plays a key role in cholesterol metabolism. A form of Apo E has recently been identified as a risk factor for Alzheimer's. Because of the intriguing link between these harmful proteins and the onset of Alzheimer's, Greengard and Breslow are beginning a collaboration that exemplifies the Center's interdisciplinary concept. An immediate clinical objective of the Center will be to develop an accurate, early diagnostic. Another goal is formulating therapies that can slow its inexorable progress.

Zachary Fisher, a construction magnate, created the Fisher Medical Foundation for one purpose: finding a cure for Alzheimer's, which has afflicted his family. His newly established foundation will fund innovative ideas and pilot projects and will supplement NIH efforts, such as the conference that preceded the announcement of RU's new center. Fisher is one of the country's leading philanthropists, and has supported many initiatives in the Armed Forces.

Visiting clinicians pursue studies at RU Hospital

York Avenue pedestrians may pine for the tennis court, and neighbors may wish for a cool berth under a dogwood, but passing physicians yearn to know: What's it like doing research in that august RU Hospital? Two Beth Israel doctors who conducted work through the Rockefeller University Hospital's twin Clinical Scholars and Clinical Fellows Programs gave a noontime talk on May 20 to their colleagues, satisfying some of the curiosity.

Gil Cu, a nephrologist who came here a year ago as a Clinical Scholar, will continue his collaboration with Associate Professor John Zabriskie for a second year, and Konstantinos Vlachonassios, who is studying cardiology, was a Clinical Fellow mentored by Research Associate Ronald Mackintosh during his four-month stay. Physicians and physicians in training at Beth Israel Medical Center may participate in the clinical visitors programs "if there is a match between their interests and ours. We try to shape a project that will complement our own ongoing work," said Sherman M. Fairchild Professor Jules Hirsch, who is physician-in-chief at the Hospital.

While at Rockefeller, Dr. Cu isolated a rare protein that causes kidney damage in the wake of strep infections of the throat or skin. He identified it as an antigen with unique plasmin binding capacity that made it, he said, a "runaway protein," capable of breaking down basement membrane inside kidneys and sowing other destruction inside the double organ. Continuing with Zabriskie, who is studying other antigens related to streptococcus, Cu is now studying immune response to the protein in patients with acute poststreptococcal



Beth Israel doctors Konstantinos Vlachonassios (left) and Gil Cu (right) conducted research at the RU Hospital. Herbert Singer (center), of the RU Council, was instrumental in setting up the visitors program.

glomerulonephritis and further elucidating its specificity.

"We took a clinical problem and turned it into a basic research problem," said Cu. "Our goal is, if we are sure about this antigen, to eventually make a vaccine."

As a Clinical Fellow at Rockefeller, Vlachonassios designed and completed, with RU's Mackintosh and Hirsch, and Louis Aronne of New York Hospital, a statistically controlled study of the link between heart rate variability and body fat. They utilized the method of spectral analysis of Fourier transformed heart rate variability. They examined the heart rates of people across a range of stable weights (from 16% body fat to 56%) who were healthy and didn't drink, smoke, or routinely take medication. Vlachonassios and his colleagues controlled for age and respiratory frequency, which enabled them to demonstrate clearly the strong effects of these two factors on heart rate variability. These effects, they found, are greater than the effect of adiposity.

"Research such as this probes the

complex relationship of cardiac dysfunction and obesity," said Hirsch, whose lab is dedicated to the study of metabolism and obesity. "That he was able to do all this in four months was remarkable."

The Clinical Scholars and Clinical Fellows Programs with Beth Israel offers people in clinical training the chance to avail themselves of the research opportunities at Rockefeller. "And Rockefeller gets the opportunity to participate in the largest clinical facility in New York," Hirsch noted.

Herbert Singer, of the RU Council, has been crucial in solidifying the relationship between the two institutions, and the Herzog Foundation has helped revitalize the Clinical Scholars Program. "Over the years, we've had a mostly ad hoc relationship with Beth Israel, on a lab by lab basis. We'd like to strengthen the relationship now, and talks like this one make these two programs more visible," said Hirsch. And of course, they satisfy the curious.



Rockefeller University was the site of a May 20 strategy session on organizing new links within the global scientific community. Chaired by Jesse Ausubel (center back), director of the university's Program for the Human Environment, participants included Allan Bromley, science advisor to President Bush (back to camera), and Victor Rabinowitch, executive vice president of the MacArthur Foundation (to Bromley's right).

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.

Torsten Wiesel, President
Ingrid Reed,
Vice President for Public Affairs and
Corporate Secretary
Doron Weber, Director of Communications

Kay Locitzer, Editor
Joseph Bonner, Assistant Editor
Heather Leahy, Design
Robert Reichert, Photography
Media Resource Service Center, Processing

Ideas and submissions can be sent interoffice (Box 68), by electronic mail (newsno), or by fax (212-327-7876).

The Rockefeller University is an equal opportunity/affirmative action employer.

Researcher describes travels along the cellular highway system

By Susan Blum

Midway through the 1990s, neurobiologists are reveling in an excitement similar to that experienced by geneticists in the 1950s. "We now feel a great readiness to understand the workings of the brain," said Rockefeller Professor Mary Beth Hatten.

In addition to clarifying some of nature's most fundamental mysteries, a deeper insight into the brain's structure and function will provide new hope for the 20 to 30 percent of the population suffering from disorders of the nervous system—congenital abnormalities, learning and psychological disorders, or degenerative diseases such as Alzheimer's, Huntington's, and Parkinson's. Hatten described some of the discoveries emerging from her lab at a recent talk to the Committee on Trust and Estate Gift Plans, a volunteer group of estate lawyers and bank trust officers who help make Rockefeller's mission more widely known.

Hatten and her colleagues are studying the processes in embryological development by which the brain's many different types of nerve cells derive their specific identity, and its complex architecture becomes organized. Their model system is the cerebellum—the brain region that maintains balance and coordinates certain types of movement—but the general principles of how cells become patterned, connected, and nourished is similar throughout different regions of the brain, Hatten explained. Moreover, she added, "we are coming to understand that things that go wrong in development sometimes crop up as mechanisms that get unplugged in neurological diseases that develop later in life."

Structure emerges in steps

The brain emerges in a series of steps during development, Hatten said. Early on in the process, cells in a region of the embryo's most superficial layer, called the ectoderm, acquire neuronal features and form a sheet-like structure called the neural plate. This sheet of primitive neural cells then rolls up into a tube—the neural tube—from which the brain develops. As new cells are born, they leave the inside of the tube and, in waves of migration, move out through the walls of the neural tube to form the various layers of the brain.

For some time, it has been known that the migrating cells travel to their final position in the brain via cellular "highways" composed of



Professor Mary Beth Hatten spoke on how the brain's architecture becomes established at the Trust and Estate Gift Plans Dinner on May 18.

another type of brain cells, called glial cells. But until recently, the purpose of that voyage remained ill-defined.

Two possible models were posited. In one of them, dubbed "the British Plan," the destiny of cells is predetermined from the earliest period, when cells are still proliferating in the neural tube. Under the British plan, nascent neurons use the cellular highway merely as a path to reach their predestined position and fate.

In the second model, or "the American Plan," a cell's ultimate fate is determined by the neighborhoods through which it journeys along the way. Hatten explained, "In this plan, one would view the process of migration not strictly as a monorail for preset cells to ride, but rather as a mechanism by which various influences on the cells could be laid out—influences that would vary greatly depending on whether they were at 96th and Broadway or 68th and Park."

Experiments in the Hatten lab suggest that the brain employs the American Plan. The studies looked at the mutant "weaver" mouse, which, as its name implies, has defects in movement and balance. The Rockefeller researchers investigated these deficits on a cellular level, where young nerve cells fail to migrate and differentiate into granule cells, a type of cell found in abundance in the cerebellum. The scientists found that these defective cells could be "rescued"—prompted to develop and behave as normal granule cells—by placing them in a new environment replete with cells

from normal mice. These findings showed that the weaver mouse's deficit is one of cell-cell interaction. As Hatten explained, "signals within the community of cells tell them to progress to the next stage of development."

A consequence of the American Plan is that nerve cells may exhibit many different properties—and express many different genes—as they go through their journey of development. Hatten and her colleagues have collaborated with the lab of Rockefeller Professor Nat Heintz to isolate some 50 genes that mark different stages of granule cell development. "With these genes in hand, we can begin to look further into exactly how specific cell contacts might control gene expression during various stages of development," Hatten said.

A detailed knowledge of events at different stages will be a boon to understanding neurologic diseases, for, "as in building a house, the earlier the deficit, the broader the consequences," Hatten explained. If migration is defective very early on in development, "many parts of the house come down," she said. The result: catastrophic congenital defects such as anencephaly (an absence of most parts of the brain) and spina bifida (an incomplete closure of the neural tube). Migration problems occurring later in development may manifest themselves as childhood epilepsy, mental retardation, learning disabilities, or hyperactivity. Environmental factors such as alcohol, cocaine, and radiation derail migration, wreaking havoc with the establishment of brain

architecture. So, too, can many kinds of genetic defects.

Delving directly into the brain

Until recently, the impact of genetic mutations on nerve cell development could only be studied in the culture dish. But "in the past year or so, we've come to realize that the young brain itself is a wonderful vessel for putting cells back in to test exactly what we're seeing," Hatten said.

Once a gene is identified, it can either be knocked out of normal cells or restored to mutant cells that lack it. Either way, such manipulated cells can then be implanted into the brains of embryonic or early postnatal animals, to observe the effects of the genetic mutations in the context of the living, complex brain.

A number of genes discovered in collaboration with the Heintz lab are currently under study in this way. One of them is astrotactin, a gene that scientists in the Hatten lab found is needed in migration. Remarkable images of living nerve cells, generated by video technology developed by the researchers, showed that the migration of young neurons can be blocked with antibodies. This made it possible to clone the astrotactin gene.

Young neurons appear to use astrotactin to hold on to the glial fiber system, Hatten said. She added that efforts are currently underway in the lab "to knock out astrotactin in a little developing animal and see if we can actually create some of the neurological problems" caused by defects in migration, Hatten said. "Similarly, we want to know whether adding the astrotactin gene back to animals that have inherited problems will ameliorate some of their deficiencies in migration and cell patterning."

Summing up, Hatten said that the techniques of cell implantation "give us the tools to further our understanding of migration, and to begin to ask exactly how particular interactions—the neurons with each other, the neurons with glial cells, the neurons with factors at their ultimate destination—change the cell at the molecular level." She said that such insight will illuminate "exactly what genes are needed at each step," and therefore give clues to which genes might be restored in therapeutic interventions when critical functions are lost due to genetic defects, toxic assaults, injuries, or disease.

Potpourri

Courtesy of Myles Weinstein



The Jazz Mentality will perform at the Tri-Institutional Noon Recital today (June 3).

Tri-Institutional Noon Recital

The Jazz Mentality will perform at the Tri-Institutional Noon Recital today (June 3). The trio—pianist Steve Elmer, bassist Ralph Hamperian, and drummer Myles Weinstein—will be joined by trumpeter Ryan Kisor. The concert, to be held in Caspary Auditorium at noon, is free. All are welcome.

Sweat Shirt Shop sale

The RU Sweat Shirt Shop is holding a year-end sale Tues., June 7 from 10:00 A.M. to 4:00 P.M. in the lobby of Tower Building. Selected items will be reduced 10 to 50 percent, and all proceeds benefit the Children's School.

Spraying

Weather permitting, the trees and shrubs near Graduate Students Residence and Sophie Fricke and Abby Aldrich Rockefeller Halls will be sprayed Sat., June 4 from 6:00 A.M. through noon. The Grounds Department recommends that those on campus that day stay out of direct contact of the spray, close windows, turn off air conditioners, and keep pets inside. The rain date is Sat., June 11. For more information, call James Sullivan, x8001.

Barbecue

The Faculty and Students Club will hold its ninth annual barbecue Fri., June 10 at 5:30 P.M. (rain date, Fri., June 17). Tickets, \$10 in advance (\$12 at the door), are on sale now at the Faculty and Students Club, on the B floor of Abby Aldrich Rockefeller Hall, and in the Purchasing Office, Plaza A5. Contact Angie Dohnert, x8201, for more information.

Varicella Zoster Conference

The annual conference of the Varicella Zoster Virus Research Foundation will be held on July 7 and 8 in Paris. The Foundation, founded and headed by RU Council member Richard Perkin, is the world's only nonprofit group for

research and education on varicella zoster virus and the diseases it causes (chickenpox, shingles, and post-herpetic neuralgia). For more information, call the Foundation at (212) 472-7148.



Students from the university's Children's School entertained parents and friends at an arts festival last Friday. The children performed songs and dances, and displayed their artwork.

James A. Shannon (1905-1994)

James A. Shannon, former director of the National Institutes of Health and special assistant to Rockefeller University's fourth president, Frederick Seitz, died in Baltimore, Maryland on Fri., May 20.

"James Shannon was a remarkable man," said President Emeritus Seitz. "First and foremost, he headed the NIH at a critical time. His influence at our institution is felt in the links between Rockefeller and the neighboring hospitals, and is reflected in the Tri-Institutional M.D.-Ph.D. program."

Shannon graduated from the College of Holy Cross in Worcester, Massachusetts. He attended New York University, receiving a medical degree in 1929 and a Ph.D. in physiology in 1935. During World War II, his leadership in developing

Clinical research seminar

Marguerite Lederberg of the Psychiatry Service at Memorial Sloan-Kettering Cancer Center will speak on "Psycho-oncology: a historical perspective" at the Clinical Research Seminar, Wed., June 8, at noon, in Nurses Residence 110B.

Photo contest: Last chance

The deadline for entries in The Rockefeller University Children's School amateur photo contest has been extended to Fri., June 10. For more information, contact Liz De Oliveira e Silva, x7676, Leslie Aitchison, x7425, or Elle Starkman, x8991.

Cultural award

Yvonne Holland, an assistant for research in the Knight lab, received a cultural grant award from the American Scandinavian Society to

further her work in Scandinavian folk music.

Honors

News&Notes received an Award for Communications Excellence (ACE) from the New York International Association of Business Communicators in the Writing, Features category for "Viral Traffic Report" by Doron Weber, director of communications. Weber also received an ACE in the Writing, News Releases category for his press release on thalidomide research.

Call for volunteers

All those willing to help prepare for graduation or to assist in on-site activities on Convocation Day, June 16, should call Sandi Walsh, x8072, by Wed., June 8. A general meeting for volunteers will be held in the Faculty and Students Club, Thurs., June 9 at 11:30 A.M.

Friday lecture

(continued from page 1)

various plant defense-related genes is activated in a limited area at infection sites. This leads to the synthesis and accumulation of metabolites that are toxic to the pathogen or are involved in the establishment of physical barriers.

Hahlbrock attended the University of Freiburg (Ph.D., 1965), and was a research assistant in the university's department of plant biochemistry until 1967. From 1967 to 1968 he was a post-doctoral fellow at the University of California, Davis. Hahlbrock returned to the University of Freiburg as a research assistant in 1968, and became associate professor in 1973 and professor in 1974. Since 1983, he has been director and head of the department of biochemistry at Max-Planck-Institut für Züchtungsforschung in Köln. In 1984, he was named honorary professor of biochemistry in the Faculty of Natural Sciences at the University of Köln.

Hahlbrock has received a number of honors, including the Tate and Lyle Award and the Otto-Bayer Prize. He is a member of the Deutsche Akademie der Naturforscher Leopoldina and is a foreign associate of the National Academy of Sciences.

The lecture will be held in Caspary Auditorium at 3:45 P.M. and preceded by tea at 3:15 P.M.

antimalaria drugs earned him the Presidential Medal of Merit. He was director of the Squibb Institute from 1946 to 1949, then became associate director for research at the National Heart Institute. In 1952, he joined the NIH as associate director, and in 1955 he became director. After retiring in 1968, Shannon was special advisor to Seitz, who was then president of the National Academy of Sciences.

Shannon came to Rockefeller as a professor in 1970. He helped plan health-oriented research, and Rockefeller awarded him an honorary doctor of science degree in 1976. Widely recognized for contributions to research, teaching, and public service, Shannon received numerous awards, among them the National Medal of Science.