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news & notes

March 29, 1996 Volume 6, Number 23

The Rockefeller University

Trustees approve administrative changes Harrigan promoted, Hirsch resignation accepted, Cook endorsed

The Board of Trustees approved four administrative changes at their spring meeting Wed., Mar. 20. John Harrigan was promoted to vice president for finance and controller. Trustees also accepted, with appreciation, Professor Jules Hirsch's resignation as physician-in-chief of the RU Hospital; endorsed the appointment of Penny Cook as corporate secretary and assistant vice president for faculty and community affairs, announced several weeks

ago; and appointed Fred Bohen, executive vice president and chief operating officer, to assume the role of treasurer also.

Harrigan

Previously controller and associate treasurer, Harrigan assumes duties carried out by David Lyons, the vice president for finance and treasurer who retired in December 1995.

"John Harrigan worked closely

and effectively with David Lyons and Fred Bohen in the rigorous financial planning that has stabilized the university's operations. He was a full partner in that effort," said President Torsten Wiesel. "He has a long track record of advancing and safeguarding the university's interests in negotiations with the federal government as well as with other critical groups. We are confident that he will continue to serve the university well."

Harrigan has been responsible for accounting policies and procedures, the maintenance of systems of internal control, and internal and external financial reporting. As vice president for finance, he will work with Wiesel and Bohen in preparing and presenting the annual budget and financial plan for the university and will have increased respon-

See *Administrative*, page 4

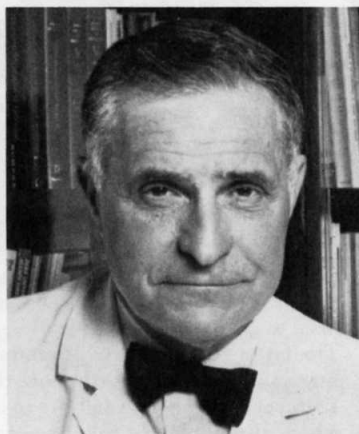
Geneticist to talk on dorsal-ventral patterning at Friday lecture



Kathryn Anderson gives the Friday lecture today (Mar. 29). See story page 4.



John Harrigan



Jules Hirsch

DeCamp symposium to focus on human genes and neurodegenerative disease

The third annual DeCamp Symposium on the Neurosciences will take place Tues., Apr. 2 in Caspary Auditorium. Entitled "Human Genetics and the Nervous System," the afternoon program comprises lectures by four leading geneticists: James Gusella of Harvard Medical School, Donald

Price of Johns Hopkins University School of Medicine, Stanley Prusiner of the University of California, San Francisco, and Yosef Shiloh of Sackler School of Medicine, Tel Aviv University.

"These scientists have immeasurably advanced genetic knowledge of neurodegenerative diseases," said Professor Mary Beth Hatten, chair of the Tri-Institutional DeCamp Symposium Committee. "But more important than their successes in locating gene markers and genes responsible for disease, their research strategies and insights have paved the way for other researchers. We hope the program will interest a wide range of neuroscientists, geneticists, and clinicians. All are welcome to attend."

Hatten opens the symposium at 2:00 P.M. Price follows at 2:05 P.M. with a lecture on "Models of Neurodegenerative Disease." Price

University community mourns Peggy Rockefeller

Margaret McGrath Rockefeller died at the age of 80 Tues., Mar. 26 of complications from heart surgery. She was the wife of David Rockefeller, honorary chairman and life trustee of the university's Board of Trustees.

"Peggy Rockefeller was a cherished member of the university community for more than 55 years. Her generosity of spirit, enormous personal warmth, and remarkable integrity will be deeply missed," said President Torsten Wiesel and Richard Fur-

laud, chairman of the board. "On behalf of the university community, we extend heartfelt sympathy to her husband and children."

Peggy Rockefeller expressed her friendship for the university in many ways—through participation in countless gatherings, support of research programs, and steadfast commitment to the Rockefeller University Concerts. The university will dedicate the Wed., May 8 performance of the Guarneri String Quartet to her memory.



At the university's 37th convocation in 1995, dedicated to David Rockefeller's 55 years of service on the Board of Trustees, he shared his thoughts with his wife of 55 years about the bust faculty commissioned in his honor.

2 Spicy story

3 Frozen goods

4 Up from D.C.

See *Four*, page 2

Visitors flock to Rockefeller's World Wide Web pages



Anthony Popowicz oversees all aspects of the university's World Wide Web pages.

As World Wide Web (WWW) fever spreads around the globe, Rockefeller home pages attract their fair share of attention: In May 1995, web surfers accessed RU web pages 45,987 times, but in February 1996, the month's tally increased more than fivefold to 254,689, according to statistics compiled by Computing Services.

"This increase is because we have much more information available. Numerous departments and labs are now on the Web, so we are getting more viewers," explained Tony Popowicz, assistant director for scientific applications.

One of the most frequently viewed postings is the 1995-1996

Scientific and Educational Programs (SEP), the guide to research on campus. The Lancefield Collection of Streptococcal Strains, posted on the Web by the Gotschlich-Fischetti lab, is also very popular.

Revealed by server addresses, RU's electronic guests hail from more than 80 countries, including such remote places as Albania, Cyprus, Estonia, Iceland, Malaysia, and Malta.

The Rockefeller WWW server tracks visitors' origins by Internet address: The 254,689 requests for information in February originated in 45,000 so-called hosts, or computers. Dividing the two numbers gives the impression that an average individual browser visits six locations within the RU site. But, Popowicz explained, "45,000 hosts does not mean 45,000 visitors. The host is the computer, and while you may be the sole operator of your computer and in your case, one host means one person, in a user services area, 4 or 40 or 400 people may access Rockefeller via a single host."

The RU server also tallies the number of times a location is accessed. The SEP listing of Nobel laureates affiliated with RU has been accessed 327 times since last May, but additional analysis would be required to determine whether one person read that list 327 times, 327 people read it, or some number in between. Similarly, one browser who peruses 20 SEP lab descrip-

tions is recorded as making 20 information requests, not one.

Last week, Computing Services moved the RU Web to a faster, more functional server that can accommodate secure interactions, such as the encrypted transmittal of confidential information. These capabilities are now under study by Computing Services for possible future offerings.

Computing Services staff are also revamping RU's Web statistics monitoring capabilities to offer people who have put information on the Web a way to easily learn how many times visitors have viewed their offerings.

Current visitor statistics, compiled monthly, may be viewed on the home page (<http://www.rockefeller.edu/Admin/stats.html>).

Spring sets saucers of saffron on campus



Every spring, hundreds of yellow, white, striped, and purple crocuses carpet the campus gardens, but a determined cook would need to gather 4,700 purple blossoms to obtain an ounce of saffron. The bitter spice gathered from the stigmas of this common New England flower was worth more than its weight in gold in the 13th century A.D., according to the *Encyclopaedia Britannica*, which also notes that folk have used it to remedy catarrh (inflammation of mucous membranes), enlarged livers, and melancholia.

Four DeCamp speakers discuss role of genes in neurodegenerative disease

(continued from page 1)

and his colleagues have used gene-targeting and transgenic methods to define the functions of the amyloid precursor protein, which plays a role in the onset of Alzheimer's disease. Using model systems, Price's group demonstrated cytoskeletal pathologies closely related to those seen in amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease) and are testing the efficacy of new therapies.

At 2:50 P.M., Gusella speaks on Huntington's disease, for which he discovered a genetic marker in 1983, validating a strategy since emulated in the study of many inherited disorders. In 1993, he and his colleagues identified the disease gene and pinpointed the gene defect causing neurofibromatosis 2. They also located genetic markers for Alzheimer's disease, ALS, and other neurological disorders.

Following a 3:30 P.M. coffee break, Shiloh discusses "Ataxia-

telangiectasia and the ATM Gene: Neuropathology Immune Deficiency and Cancer Linked through Cell Cycle Regulation." This usually fatal disease, which cripples the nervous and immune systems, has been Shiloh's primary



Professor Mary Beth Hatten organized the DeCamp symposium this year.

focus for two decades. He identified and cloned the responsible gene, and his lab is delineating the function of the gene's protein product.

Prusiner gives the final talk at 4:45 P.M. on "Neurodegeneration as Viewed from Studies of the Prion Disease." Prusiner followed his controversial discovery of the prion, a previously unknown class of pathogen, with analyses showing that it is a mutated form of a normal protein and that prion diseases can be both infectious and inherited. He and his colleagues showed how the mutated proteins can build plaques in the brain.

Hatten's remarks at 5:30 P.M. will conclude the symposium.

The Ira W. DeCamp Foundation established the DeCamp symposium in 1993 to strengthen and expand ties among neuroscientists at The Rockefeller University, New York Hospital-Cornell Medical Center, and Memorial Sloan-Kettering Cancer Center. The grant also provides funding for

seminars, lectures, and courses for students, postdocs, and faculty of the three institutions.

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Life on ice: Freezing designer mouse embryos advances science

by Joseph Bonner

Animal models provide researchers with a valuable tool to study the way genes function in living systems. By inserting foreign genes—as in transgenic mice—or inactivating specific genes—as in knockout mice—scientists can model diseases from AIDS to Parkinson's or study the development of limbs and tissues.

More than 800 transgenic lines of animals have been produced at Rockefeller since the first experiments with pronuclear microinjection in the early 1980s, estimates Annemarie Walsh, senior research associate and director of the Transgenic Service Laboratory (TSL). About 80 of these lines rest in embryonic form in sub-Arctic temperatures, preserved for future use by TSL's Cryogenic Service.

Just as frequent backups protect computer users from losing valuable data, cryopreservation—storage of embryos at low temperatures—allows researchers to “back up” their transgenic and knockout lines. “Cryopreservation of embryos is the only method that we have right now to preserve the lines,” said Walsh. “Unlike cattle and rat sperm, mouse sperm cannot be frozen without losing viability.”

“You never know what might happen to a line,” said Michael Hayre, director of the Laboratory Animal Research Center (LARC), which houses the TSL. “It could be exposed to disease, or there could be a fire or a flood. If you've stored embryos, a project may be delayed but it's not lost.”

Transgenic mice spawn need for preservation

The transgenic age began 15 years ago when Jon Gordon, then at Yale University and now at the Mount Sinai School of Medicine, successfully introduced foreign genes into the mouse genome by direct injection into the pronuclei of early embryos using a technique he called pronuclear microinjection. In 1985, Professor Jan Breslow and Walsh produced Rockefeller's first transgenic mouse using this technique, an animal designed to overexpress the gene for apolipoprotein A-1, the major protein of high density lipoprotein (HDL). As his lab created more transgenic lines and the demand for transgenic animals grew, Breslow realized the need for a core facility to serve the Rockefeller community. In 1991, with the support of the university's administration and a startup gift from the Schering-Plough Research

Institute, the TSL opened in LARC.

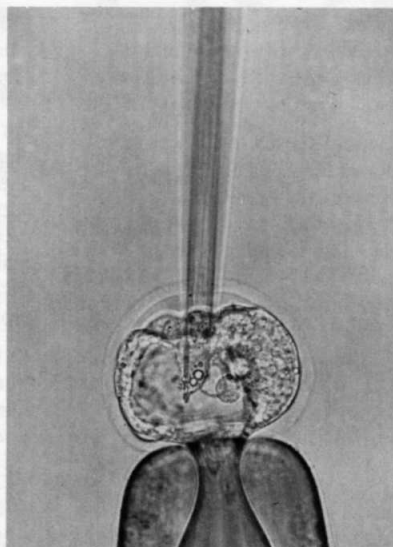
Maintaining colonies of transgenic and knockout mice requires time and money. Mice must be bred every six months, followed by a DNA analysis of the pups' tail tips. A pair or two of the tail-tipped mice must be put aside and the cycle repeated every six months. “Mice breed exponentially,” said Walsh. “Pretty soon you end up with a room full of mice.”

Cryopreservation reduces the need for—and expense of—housing and caring for large numbers of animals. “Freezing your embryos is a really good way of minimizing your lab costs,” said Hayre.

How an embryo chills out

Susan Powell, coordinator of the Cryogenic Service, freezes the embryos through an intricate process. Seven homozygous male transgenic mice mate with 3- to 4-week-old female mice. Two and a half days into the pregnancy, after the eggs have sufficiently divided—“Eight-cell embryos freeze best,” said Powell—she removes the mouse's oviducts. Syringes filled with a phosphate-buffered saline solution flush out the embryos, which are placed in vials. Dimethyl sulfoxide (DMSO), a cryopreservant, is added to prevent ice crystals from forming inside the embryos.

The embryos are then gradually chilled to a temperature just below



freezing. Powell seeds the vials with ice crystals to protect them from rupturing as the temperature decreases. After cooling the vials half a degree per minute to -80°C , the vials are plunged into liquid nitrogen, where they can remain indefinitely.

The number of embryos that need to be frozen depends on the line and the sires' genetic type. Walsh recommends 100 embryos for homozygous mice—those with two copies of the gene of interest—and 250 embryos for heterozygous mice. “Some transgenic lines are more fertile than others, and some knockouts don't breed well naturally,” said Powell. “We rely on the researchers to tell us if there are any breeding difficulties.”

To thaw embryos, Powell removes the frozen vials from the liquid nitrogen bath and lets them warm up to room temperature. When no ice crystals are visible, she adds a small portion of the buffer solution, also at room temperature, drop by drop, to dilute the DMSO. “It's crucial for the temperatures to be nearly the same, or the osmotic pressure that results can rupture the delicate membrane around the egg,” said Powell. Eighty percent of the frozen embryos survive the thawing process, she added.

Powell thaws embryos periodically and implants them into surrogate mothers

to check their viability. Progeny from the thawed embryos are mated to see if they are able to reproduce. “There was initial skepticism in the transgenic community concerning cryopreservation,” said Walsh. “People didn't think that it would work, but we've been able to red-erive every cryopreserved line.”

On the receiving end

Most of the nearly 80 lines of mice TSL has cryopreserved belong to Breslow, who makes his lines freely available to the scientific community. Cryopreservation simplifies and expedites the process of transporting mice across state lines and international borders. Most states and nearly every foreign country have laws that impose a quarantine on incoming animals. “The quarantine period often leaves the animals too old to reproduce,” said Walsh. “Because frozen embryos are virus free, they are accepted immediately.”

Walsh sends frozen embryos to researchers across the country and around the world. “We only give people embryos if there is someone on the receiving end who has been trained in the thawing and implantation techniques,” said Walsh. If the request comes from an institution close to New York, Walsh or Powell will travel to the site to train people on the correct procedures. “We've gone to companies such as Merck in New Jersey and Pfizer in Connecticut to train people,” said Walsh. “Once, a veterinarian from New Zealand came to Rockefeller and stayed for a week to learn how to thaw and implant embryos correctly.”

Iced embryos offer insurance

Stephen Duncan, assistant professor in the J. Darnell lab, freezes the transgenic mouse lines that he uses to study early liver development. “We've frozen down some lines that we used in our original analysis,” he said. “We keep them because we may want to look at them again in the future.” Duncan, who has three transgenic lines cryopreserved, may soon freeze a knockout line.

Freezing embryos offers scientists a way to standardize their data and minimize the errors that breeding may introduce. “If you publish on a line of mice and freeze embryos from that line, the embryos can be sent to another researcher who wants to reproduce the results,” said Walsh. “And the line is there if you want to go back and verify some results.”



Susan Powell, coordinator of the university's Cryogenic Service, places frozen embryos into a container of liquid nitrogen.

Leif Carlsson

Potpourri

Tri-Institutional Noon Recitals

Pianist Simone Pedroni, gold medalist at the Ninth Van Cliburn International Piano Competition, performs works by Rachmaninoff and Chopin at the Tri-Institutional Noon Recital today (Mar. 29). Violinist Kyung Sun Lee and pianist Brian Suits perform works by Mozart, Schumann, Gershwin, Suits, and Ravel next Friday (Apr. 5). The concerts, which are held in Caspary Auditorium at noon, are free. All are welcome.

Friday film

Taxi Driver (USA, 1976), directed by Martin Scorsese, will be shown today (Mar. 29) at 8:00 P.M. in Caspary. Admission is free.

Spraying

Weather permitting, the trees and shrubs on campus will be sprayed Sat., Mar. 30 from 6:00 A.M. to 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 Sun., Mar. 31. For more information, call James Sullivan, x8001.

Seminar

Daniel Michaelson, professor of neurobiology at Tel Aviv University, discusses "Cognitive Dysfunction and Neurochemical Impairments in Apolipoprotein E-deficient Mice" Tues., Apr. 2 at 10:00 A.M. in Rockefeller Research Building 110.

Italian American Day

The Abby dining room features Italian American cuisine Wed., Apr. 3. For reservations call x8894.

Clinical Research Seminars

Edward Fisher, adjunct faculty member at RU, discusses "Pancreatic Cholesteryl Ester Hydrolase—Where Is It and What Does It Do?" Wed., Apr. 3. Howard Eder, professor of medicine emeritus at Albert Einstein College of Medicine, discusses "HDL—Fact or Fiction?" Wed., Apr. 10. The seminars are held at noon in Nurses Residence 110B.

Corporate Challenge

The first race of the three-part 1996 Corporate Challenge takes place Thurs., May 9 at 7:00 P.M. in Central Park. All university employees are eligible to run the 3.5 mile course with the Rockefeller team. For applications and information, contact Robin Maloney, Founder's Hall, 2nd floor, x7736. The sign-up period for the first race ends Fri., Apr. 5 at 1:00 P.M.

Patient Oriented Research Seminar

Elizabeth de Oliveira e Silva, research associate and associate

physician in the Breslow lab, discusses "Patient Oriented Research in Lipoprotein Metabolism" Wed., Apr. 10 at 10:00 A.M. in Nurses Residence 110B.

RU concert

Soprano Susan von Reichenbach performs Wed., Apr. 10 at the Rockefeller University Concert at 8:00 P.M. in Caspary Auditorium. For ticket availability and prices, contact Cathy Rogers, x8437.

News&Notes schedule

News&Notes will not be published Fri., Apr. 5 due to the Easter and Passover holidays.

One week, two Washington women



Members of the Council on Foreign Relations and their spouses assembled in Caspary Auditorium Tues., Mar. 19 to hear first lady of the United States Hillary Rodham Clinton (far left) speak on "Women and Development." Dwayne Andreas, chief executive officer of the Archer Daniels Midland Company (at her right), moderated as Clinton fielded questions from the invitation-only audience. "Clinton's presence on campus required special security arrangements, implemented by federal Secret Service staff and members of our Security and Plant Operations staff. Sandi Walsh, coordinator of facilities use and special events, ensured that this complex event went smoothly and deserves special thanks," said Fred Bohlen, RU executive vice president. On Fri., Mar. 22, the Rockefeller University chapter of Sigma Xi hosted a lecture by U.S. Senator Barbara Boxer (far right), Calif., in the Abby dining room. After she spoke on "Investing in the 21st Century," Boxer received a certificate of recognition from the RU chapter for her conservation efforts in Congress presented by Michael Anzelone (left), chapter president and volunteer investigator in the Krueger lab, and President Torsten Wiesel.

Anderson gives Friday lecture on dorsal-ventral patterning

Kathryn Anderson, professor of genetics at the University of California, Berkeley, discusses "Drosophila Embryonic Patterning: Proteases and Signaling" at the Friday lecture today (Mar. 29).

Anderson studies how genes control early embryonic development. Her laboratory focuses on the genes controlling dorsal-ventral patterning in the early *Drosophila* embryo. Work in her lab has identified a novel signaling pathway that takes asymmetric information from outside the embryo to control the region-specific transcription of genes in the embryonic nuclei.

Using the tools of biochemistry and genetics, Anderson and her colleagues identified an extracellular ligand encoded by the *spätzle* gene as the localized component that activates the signaling pathway in the ventral part of the embryo. Her lab also showed that the signaling in the cytoplasmic

portion of the pathway is mediated by rapid degradation of a specific protein called Cactus on the ventral side of the embryo.

Anderson received her doctorate from the University of California, Los Angeles in 1980. As a postdoc in the lab of C. Nüsslein-Volhard at the Friedrich Miescher Laboratorium in Germany from 1981 to 1984, Anderson isolated and characterized mutations in 11 genes that are required for the initial specification of different cell types along the dorsal-ventral axis of the fruit fly. She joined the faculty at Berkeley in 1985 as an assistant professor and became professor of genetics in 1993.

Anderson, a fellow of the American Association for the Advancement of Science, received the U.S. National Science Foundation's (NSF) Faculty Awards for Women and was an NSF Presidential Young Investigator. Anderson serves on

the editorial boards of *Developmental Genetics*, *Trends in Genetics*, and *Developmental Biology*.

The lecture will be held at 3:45

P.M. in Caspary Auditorium and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Lounge. All are welcome.

Administrative changes approved

(continued from page 1)

sibility for establishing operating budgets for labs and departments.

Hirsch

The university administration had expected that Hirsch would serve as physician-in-chief through 1996-1997. However, he has decided to step down as leader of the Hospital this July but will continue as co-head of the Laboratory of Human Behavior and Metabolism with Associate Professor Rudolph Leibel.

"I've been involved with the Hospital for so long that it is with mixed feelings that I leave the post of physician-in-chief," said Hirsch.

"But I am looking forward to devoting more time to the studies of metabolism in my lab. There are so many promising scientific opportunities now."

Hirsch joined the Hospital in 1954 as an assistant physician, became senior physician and professor in 1967, and assumed leadership of the Hospital in 1992. The Institute of Medicine of the National Academy of Sciences elected Hirsch to membership in 1993, and among his recent honors are the Robert H. Herman Award from the American Society for Clinical Nutrition and the Joseph B. Goldberger Award in Clinical Nutrition.