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news & notes

May 17, 1996 Volume 6, Number 29

The Rockefeller University

Markey Trust gives \$2 million for young scientists

The Lucille P. Markey Charitable Trust recently awarded a grant of \$2 million to endow the Lucille P. Markey Basic Medical Research Fund at the Rockefeller University. Income provided by the fund will help the university support promising graduate students, postdoctoral investigators, and junior faculty as they begin careers in biomedical science.

"The Markey Trust is among the university's most generous benefactors and has played an integral role in the scientific training and profes-

sional development of researchers here for many years," said President Torsten N. Wiesel. "We are honored to create this fund in Lucille Markey's name and to express our gratitude to a foundation that has done so much for so many important institutions across the country."

Since its inception in 1983, the Lucille P. Markey Charitable Trust has awarded grants totaling more than \$500 million to support and encourage basic medical research. Markey, who owned the thorough-

bred breeding and racing stable Calumet Farm and who died in 1982, established the trust in her will. As she directed, the Markey Trust will cease operations in June 1997.

In addition to Rockefeller, nine other institutions received \$2 million endowment gifts: Harvard, Johns Hopkins, Stanford, and Yale universities and the University of California at San Francisco, the University of Kentucky, the University of Michigan, the

See Markey, page 2

Rockefeller neurophysiologist to lecture on learning to move

Professor Hiroshi Asanuma discusses "Brain Mechanisms for Learning Skilled Movements" at the Friday lecture today (May 17).

Asanuma studies how the motor area of the brain regulates body movement of higher mammals. Using electrophysiological techniques to record from the inside or outside of individual neurons, Asanuma and his colleagues analyze the relationships between afferent, or incoming, signals to the motor cortex, and efferent, or output, signals from it. Work in his laboratory determined that this transfer was done at the cortical efferent zones, or cortical motor columns, which constitute the basic module of the motor cortex.

Afferent signals to the motor cortex have been known to come through the sensory cortex as well as through the thalamus. Asanuma and his co-workers found that the projection from the thalamus to the motor cortex is diffuse, but the projection from the sensory cortex to the motor cortex is specific. They recently discovered that projections from the sensory cortex to the motor cortex undergo significant changes in synaptic transmission, a phenomenon known as long-term potentiation (LTP). In subsequent studies, they found that this plasticity changes the efficiency of cortical efferent zones and constitutes the basis of motor learning in higher mammals.

Asanuma received his medical degree in 1952 from Keio University Medical School in Tokyo. In 1959, he received a doctoral degree in medical sciences from Kobe Medical College in Kobe, Japan. He joined the faculty of Osaka City University Medical School in 1959, before moving to the United States in 1965 to become an associate professor at the New York Medical

See Asanuma, page 2

Reminder: Dyson receives Thomas prize May 22

Physicist and author Freeman Dyson will receive Rockefeller University's Lewis Thomas Prize Wed., May 22 at 5:30 P.M. in Caspary Auditorium.

He will lecture on "Samuel Gompers and William Blake."

The Lewis Thomas Prize honors accomplished scientists for their artistic achievements. Dyson, now professor emeritus at the Institute for Advanced Study, has won numerous awards for his books. All are welcome to the ceremony and reception.



The university has established the labs of physician-scientists Maria Karayiorgou (left) and Markus Stoffel, both assistant professors, with help from a Markey Trust grant for molecular medicine.



RU Council hears about sensation



At the spring meeting of The Rockefeller University Council Tues., May 7, Council Chairman David Rockefeller (second from left) introduced to the council new members Donald McGlory (left) and Wendy Joseph (far right) and announced that Sydney Shuman (second from right) has been named to the council's Executive Committee. Professors Charles Gilbert and A. James Hudspeth and Assistant Professor Peter Mombaerts spoke to the group on "The Neurobiology of the Senses."

2 Computer virus

3 Brain traffic

4 Cottage vacancies

For the Friday lecture next week, see page 2.

Physical biochemist to discuss form and function of binding domains

Associate Professor David Cowburn discusses "Structural Studies in Solution of Binding Domains Involved in Intracellular Signal Transduction" at the Friday lecture next week (May 24).

Cowburn uses the tools of nuclear magnetic resonance (NMR) to provide dynamic views of molecules and their functions. NMR, a technique for observing molecules as they float in solution, employs powerful magnetic fields

and high-frequency radio waves to probe molecules and advanced computers to interpret the data. Work in Cowburn's lab focuses on the domain structure of proteins that help send messages within cells. Cowburn and his colleagues have used NMR techniques to determine the structure of Ablson kinase (Abl) Src homology (SH) domains—SH2, SH3, and SH(32)—parts of an enzyme, which if mutated, can cause a form of leukemia. Recently, Cowburn and his colleagues extended their work on the ligands for these types of molecules by developing novel probes that provide a detailed structural picture of the SH domains in signaling proteins, allowing scientists to better understand the mechanics of how domains assist the proteins in transporting messages.

Recent work also included studies of Pleckstrin homology (PH) domains in dynamin and in β -adrenergic receptor kinase. Dynamin is involved in endocytosis, in the production of vesicles. β -Adrenergic receptor kinase is a member of the G protein-coupled receptor kinases (GRKs), the serine/threonine kinases recognizing

agonist-occupied, activated G protein-coupled receptors. The role of the PH domains is still under investigation; Cowburn's lab has suggested that its PH domain may modulate the required GTPase activity of dynamin. GRKs are generally significant in many roles, including in modulating G protein-coupled receptors in olfaction, in other parts of the nervous system, and in cardiac function.

Cowburn's lecture will also include a summary of recent technical advances in NMR permitting more rapid and precise determination of structure and dynamics of proteins.

Cowburn received his doctoral degree from the Medical Research Council Biophysics Research Unit at King's College, University of

London in 1970 and a D.Sc. from the University of London in 1981. His postdoctoral work was at Columbia University College of Physicians and Surgeons after which he joined Rockefeller as an assistant professor. He was promoted to associate professor in 1978 and was named head of laboratory in 1992.

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.

Asanuma



Researchers in Professor Hiroshi Asanuma's lab study the motor cortex's incoming and outgoing signals.

(continued from page 1)

College. He was promoted to professor in 1971, then joined Rockefeller in 1972 as a professor. Asanuma belongs to the American and Japanese physiological societies.

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.

Markey

(continued from page 1)

University of Texas Southwestern Medical Center, and Washington University in St. Louis.

Over the years, the Markey Trust has contributed more than \$17 million to Rockefeller in support of junior-faculty-led laboratories, graduate fellows, and research in immunology and molecular medicine. A 1985 gift from the Markey Trust established the Henry G. Kunkel Professorship in Immunology, currently held by Ralph Steinman.

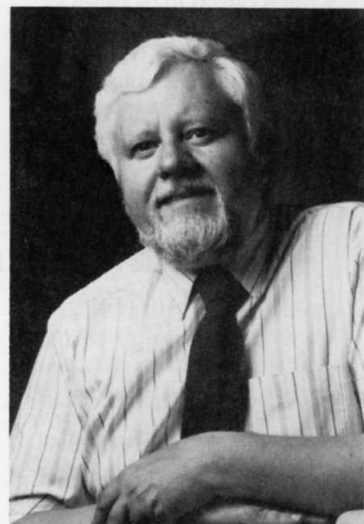
Warning:

Disguised virus can destroy PC hard drives

Computing Services would like to warn campus PC users that a virus capable of wiping out hard drives is masquerading on the Internet as the popular archiving program PKZIP.

Dubbed a "Trojan Horse" virus because it is hidden behind the name of a legitimate application, the extremely destructive program goes by four names: PKZIP300.ZIP, PKZIP300.EXE, PKZIP300B.ZIP, and PKZIP300B.EXE. To be safe, do not download any file whose name contains PKZIP300. The most recent bona fide version of PKZIP is 2.04g.

Users with questions about the virus or PKZIP may contact the Computing Services Help Desk, x8940.



Recently, Cowburn and his colleagues developed novel probes that provide a detailed structural picture of the SH domains in signaling proteins, allowing scientists to better understand the mechanics of how domains assist the proteins in transporting messages.

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"I dedicate my life to science and what thanks do I get? The fat gene! That's the thanks I get."

Neuroscientists identify gene involved in brain development

Astrotactin is a neuron's ticket to ride the glial highway

by Marion E. Glick

The migration of neurons is critical to the establishment of the cellular architecture of the brain. During fetal development, young nerve cells form a tube that will grow into the brain and spinal cord. After cells stop dividing in the developing cerebrum, they migrate through the tube's thickening wall, along a pathway of radial glial cells, to form a series of six neuronal layers. By completing this journey the neurons develop and organize the brain's structure.

The migration of young neurons in one of the simplest cortical regions of the brain, the cerebellar cortex, which controls movement and balance, continues until a child reaches the age of 2. Although a neuron's journey along the glial fiber highway is just a few millimeters, this distance is comparable to a person traveling from New York City to Chicago. The nerve cells can migrate at speeds of 20 to 50 microns per hour—about one thousandth of an inch—which is considered fast for a neuron.

One for the road

Professors Mary Beth Hatten and Nathaniel Heintz and Chen Zheng, graduate fellow in the Hatten lab, recently discovered a gene involved in directing nerve cells to their destinations as the brain grows. The gene, expressed in the neurons of mice, contains the instructions to make the astrotactin protein used by neurons to migrate along glial fibers in the developing brain.

"The gene we discovered makes a protein, astrotactin, required for young neurons to migrate along glial fibers to find their correct positions in the growing brain. This journey is important because it is the way young neurons gain their identity," said Hatten, who heads the Laboratory of Developmental Neurobiology at Rockefeller. Heintz, an investigator of the Howard Hughes Medical Institute, heads the Laboratory of Molecular Biology. With Zheng as first author, the work appeared in the April 19 *Science*.

Scientists suspect that problems with neuron migration figure in conditions such as epilepsy, and that the astrotactin findings may shed light on the development of childhood brain tumors, learning disabilities, schizophrenia, and



Researchers in the lab of Professor Mary Beth Hatten study the cellular and molecular mechanisms underlying the establishment of the cellular architecture of the vertebrate brain.

degenerative brain disorders in the elderly. Researchers already know that exposure to alcohol, cocaine, and radiation can hinder the migration of neurons during fetal development.

All the right stuff

Scientists knew that the protein astrotactin directed certain cells to their homes in the cerebellar cortex. Hatten and her colleagues identified the *Astrotactin* gene by

searching for cDNAs expressed in migrating neurons, and then testing to see which of these genes encoded proteins that stopped neurons in their tracks when faced with an antiserum. Of the 39 gene candidates so identified, one—called GC14—bore the hallmarks of the astrotactin protein.

GC14 begins with a signal peptide sequence of amino acids, implicating it is directed to the cell surface. It also contains fibronectin domains common to other well known adhesion molecules as well

as domains found in the epidermal growth factor, suggesting that the protein engages in both binding and signaling activities.

Scouting in the developing cerebellar cortex of mice, the researchers found GC14 transcripts in the depths of the external germinal layer (EGL), where cells begin differentiation. Proliferating neuron precursor cells in the upper regions of the EGL did not express *Astrotactin* mRNA or protein.

In the deeper EGL, the scientists found *Astrotactin* activity where precursor cells had completed their division and commenced their migration along the Bergmann glial fibers to reach their final destinations in the cortex.

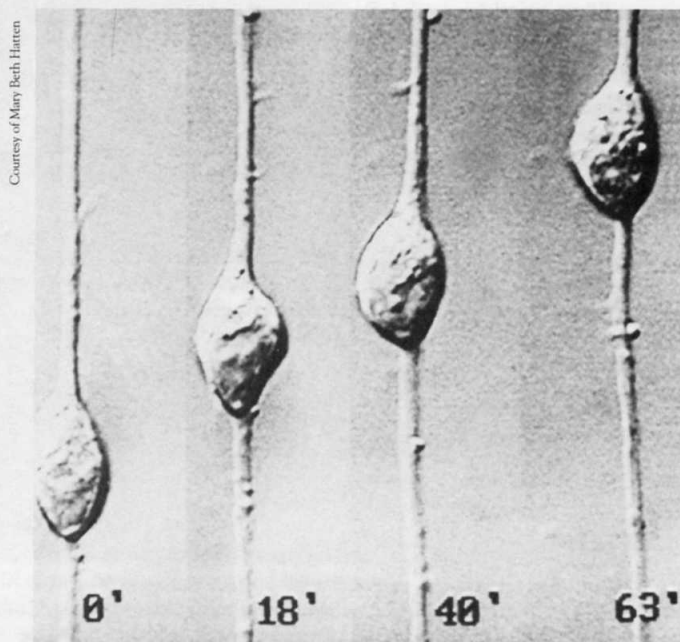
Where the genes are

The researchers found a similar pattern of expression in the developing hippocampus (the seat of memory), the cerebrum (the thought center), and the olfactory bulb (the system responsible for smelling). All four of these areas of the brain form cell layers by glia-guided migration. The team corroborated the role for astrotactin in cerebellar development with experiments in which antisera against expressed GC14 protein arrested neuronal migration, confirming the protein's role as a neuronal glue for glial binding.

Hatten and her coinvestigators also identified a second function of astrotactin. "The astrotactin protein helps glial cells to sustain their health and identity," explained Heintz. "Without a connection to astrotactin, glial cells collapse. In contrast, astrotactin is not essential to maintaining the health of neurons."

With the cloning of the *Astrotactin* gene, the research team proposes that at least three genes play a role in the migration and assembly of neurons during the development of the cortical areas of the brain in mice: the *Astrotactin* gene, the *Weaver* gene, and the *Reeler* gene. However, *Weaver* and *Reeler* occur as the result of mutations and they interfere with migration. *Weaver* prevents astrotactin production in the neuron and *Reeler* disturbs the organization of neurons at the end of their migration.

The HHMI and the National Institute of Neurological Disorders and Stroke supported the study.



This four part micrograph shows the movement of a young neuron on a glial fiber highway at 18, 40, and 63 seconds. This journey, of about one-thousandth of an inch, takes a neuron to its correct position in the growing brain.

Courtesy of Mary Beth Hatten

And they had fun, fun, fun, all those runners as they thundered away

by Sue Schneidhorst

The consensus of participants? Fun.

"Fun is what it is all about," said Robin Maloney, Rockefeller University's associate controller and assistant treasurer, as she described running the 20th annual Chase Corporate Challenge 3.5 mile race Thurs., May 9.

Maloney, who has coordinated the RU team for the race for the past eight years, said that serious runners striving to improve their fastest time and novices eager for a challenge all gave the race 110 percent.

"Our runners are doing their personal best," Maloney continued. "Even though the difference in time from the fastest runner to the person bringing it home for Rockefeller might vary by 20 minutes, everyone finishes feeling that



Robin Maloney

University participants in the Chase Corporate Challenge relaxed before the 3.5 mile race, held Thurs., May 9 in Central Park.

glow of accomplishment."

Their personal best has, for the past 10 years, earned the university a place in the international

Corporate Challenge Championship, the culminating race, which takes place in October on Park Avenue. The Corporate Challenge

is a trilogy of races, with each team competing in two. To be selected for the fourth event, the championship, a team must be in the top 10 percent of the 10,000 participating New York City corporate athletes.

Results from the May 9 race will not be published for another month, but Maloney feels confident that the Rockefeller University team will continue to earn glory for the institution.

Additional Rockefeller athletes can still sign up to compete in the second race. "New participants are always welcome," Maloney added.

Those who are serious about running or just serious about fun and would enjoy participating in the race Wed., June 26 may call Maloney, x7736. The deadline for registering is today (May 17) at 1:00 P.M.

Potpourri

In memoriam

The university community mourns Ethel M. Everly who passed away Wed., May 8 in Wood Ridge, N.J. Everly, who worked for Professor Emeritus Merrill Chase for 10 years, was the wife of the late William Everly, who cared for the animals of Professor Emeritus Maclyn McCarty.

The community also mourns the passing of Harold Mattsson, supervisor of the order service at the Rockefeller University Press, who died Sat., May 4 of throat cancer at age 68. Mattsson joined the university in 1972.

Computing Services workshops

Space is available in the following Computing Services workshops. Please leave voice mail at x7768 to register. You will be called to confirm registration.

Intro to the Mac:

Tues., May 21, 10:00 A.M. to noon;

Word for the Mac, Part I:

Tues., May 28, 10:00 A.M. to noon;

Word for Windows, Part I:

Thurs., May 30, 10:00 A.M. to noon;

Word for the Mac, Part II:

Tues., June 4, 10:00 A.M. to noon;

Word for Windows, Part II:

Thurs., June 6, 10:00 A.M. to noon.

Tri-Institutional Noon Recitals

Pianist Pedja Muzijevic and the St. Lawrence String Quartet will perform today (May 17). All are welcome. Violinist Anna Rabinova and pianist Lily Friedman will perform Fri., May 24 at noon.

The concerts, to be held in Caspary Auditorium at noon, are free. All are welcome.

Seminar

Charles Stevens, HHMI investigator and professor at the Salk Institute, will lecture on "Synaptic Plasticity" Tues., May 21 at 4:00 P.M. in Nurses Residence 110B.

Clinical Research Seminar

Associate Professor Shigeru Sassa will discuss "Molecular Genetics of the Porphyrias" Wed., May 22 at noon in Nurses Residence 110B.

Friday film

Crooklyn (USA, 1994), directed by Spike Lee, will be shown Fri., May 24 at 8:00 P.M. in Caspary Auditorium. Admission is free.

Dedication

The Rockefeller University Children's School and Infant-Toddler Center will dedicate their playground to David Lyons, who retired as vice president for business and finance in December 1995 after 26 years at RU. The ceremony takes place Wed., May 29 at 11:00 A.M. All are welcome.

Convocation volunteers

Volunteers are needed to assist with convocation activities Wed., June 12, and Thurs., June 13. The first

Want to vacation upstate? Rentals available

Weekday stays (Sunday night through Thursday night) are still available for the Rockefeller cottages during May, June, September, October, and November.

The two cottages are located less than two hours northwest of the city, near Bear Mountain. Last win-

ter, the Housing Office renovated the interiors. Housing can supply information on the cottages as well as sights and activities in their environs.

For more information or to make reservations (\$38 per night), contact Roseanne Marchesiello, x7370.



The Housing Office has upgraded Hostage (above) and MacGinnes Cottages, vacation facilities near Bear Mountain.

volunteers meeting will be Tues., June 4 at 11:30 A.M. in Caspary 1B. For more information, call Sandi Walsh x8072 or email Walsh.

Barbecue

Tickets are still available for The Faculty and Students Club's 11th annual barbecue Fri., June 7 at 5:30 P.M. to be held on the Faculty Club Lawn. Tickets are \$10 in advance (\$12 at the door) and may be purchased at the Faculty and Students Club, B floor of Abby Aldrich Rockefeller Hall, and in the Purchasing Office, Plaza A5. For more informa-

tion, contact Angie Dohnert, x8201.

Helen Keller Prize

Rockefeller University President Torsten Wiesel and his colleague David Hubel, of Harvard University, received the Helen Keller Prize for Vision Research from the Helen Keller Eye Research Foundation at a ceremony Tues., April 23.

News & Notes schedule

News & Notes will not be published on Fri., May 24 because of the Memorial Day holiday.