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The Rockefeller University

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June-July 1986
Volume 17, Number 5

News and Notes

Front row, from left, Bruce McEwen, David Rockefeller, Norman Ramsey, Rodney Cool, Joshua Lederberg, William O. Baker, Anthony Cerami, Mary Rifkin. On the steps, Ph.D. recipients and their presenters.

Ph.D. Awarded to 19; Norman Ramsey Receives Honorary Degree

President Lederberg presented the Ph.D. degree to 19 graduates on June 17 at the University's 28th commencement ceremonies and conferred an honorary doctor of science degree on Harvard physicist Norman F. Ramsey, a Rockefeller trustee since 1977.

In keeping with the University's custom, the afternoon's program was limited to talks by faculty presenters who explained the significance of the work of the degree recipients to an audience of families and friends assembled in Caspary Auditorium. Dr. Ramsey was presented by Professor Rodney L. Cool, co-leader of the University's laboratory of experimental high-energy physics.

Professor Anthony Cerami, dean of graduate and postgraduate studies, opened the ceremonies at which Associate Deans Bruce S. McEwen and Mary R. Rifkin served as marshals, placing the University's blue-and-gold-trimmed hoods on the graduates' shoulders. Also participating were Dr. William O. Baker, chairman of the board of trustees, and David Rockefeller, chairman of the board's executive committee.

Norman Ramsey's work in physics has ranged from molecular beams to particle physics, and he has conducted precise measurements of electric and magnetic properties of nucleons, nuclei, atoms, and molecules. He received A.B. and Ph.D. degrees from Columbia University, B.A., M.A., and Sc.D. degrees from Cambridge University, and M.A. and D.Sc. degrees from Oxford University.

He has been at Harvard University since

(continued on page 2)

Professor Emeritus Fritz Lipmann, 1953 Nobel Prize-winning biochemist and a member of the Rockefeller faculty since 1957, died on July 24 as *News and Notes* was going to press. An article about him will appear in the next issue.

Honors and Awards

Professor **James E. Darnell, Jr.**, Molecular Cell Biology, was one of 10 recipients of the 1986 Gairdner Foundation international awards, which honor outstanding contributions in the field of medical science. Dr. Darnell shared his award with Dr. Philip Sharp of M.I.T. for work concerned with messenger RNA formation in eukaryotic cells.

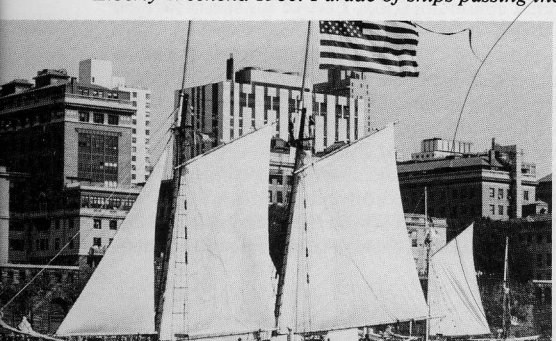
Professor **Christian de Duve**, Biochemical Cytology, was awarded an honorary doctor of medicine degree by the Karolinska Institute at a ceremony in Stockholm, May 29.

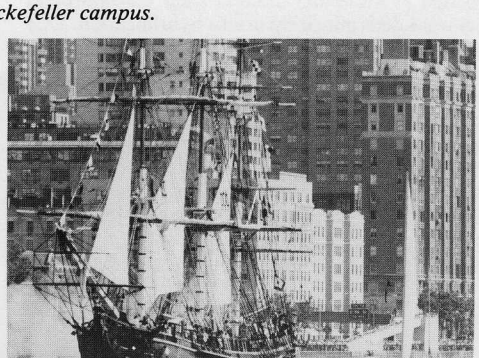
Professor Emeritus **Rollin D. Hotchkiss** was elected a foreign member of the Royal Danish Academy of Sciences in April.

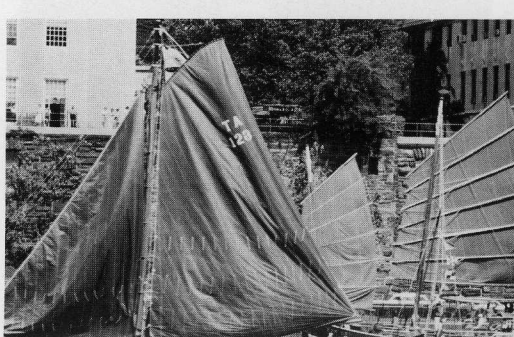
Professor **Bruce Merrifield**, Biochemistry, was awarded an honorary doctor of science degree by Bowling Green State University and delivered a plenary lecture at the 18th Central Regional Meeting of the American Chemical Society held at the university, June 4-5. Dr. Merrifield also received an honorary doctor of science degree from his alma mater, the University of California at Los Angeles, at its commencement ceremony, June 22.

Professor **William Trager**, Parasitology, was presented the Manson Medal by the Royal Society of Tropical Medicine and Hygiene at its annual meeting in London, June 19. The Manson Medal is the Society's most distinguished award and has been given every three years since 1923, a year after the death of Sir Patrick Manson. The previous American recipient was the late Theobald Smith in 1932, when he was director emeritus of The Rockefeller's laboratory of animal plant pathology.

Liberty Weekend 1986: Parade of ships passing the Rockefeller campus.







Ph.D. Awarded to 19

(continued from page 1)

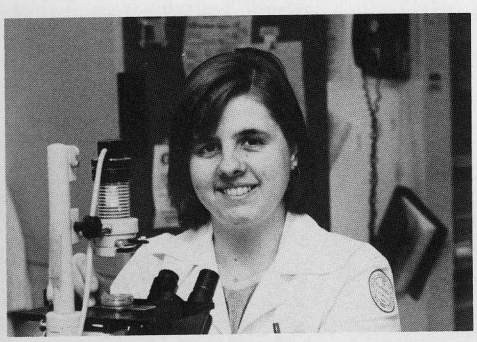
1947, where he and his associates discovered the deuteron electric quadrupole moment, proposed the first successful theory of the chemical shift for the magnetic shielding of nuclei in nuclear magnetic resonance (NMR), and developed high-precision methods of molecular beam spectroscopy, including the atomic hydrogen maser.

Condensations of the presenters' remarks follow. The degree recipient's name appears first.

DONNA T. ANTHONY

Lee Rubin

Neurons interact with their target cells by liberating small molecules, called neurotransmitters, which diffuse to the target cells and cause appropriate electrical changes. Thereby, information is propagated from one cell to the next. The neuromuscular junction is the prototypic synapse. Motor neurons, which innervate muscles involved in voluntary movement, respond to stimulation by releasing the neurotransmitter acetylcholine (ACh). ACh binds to muscle membrane proteins called ACh receptors (AChRs). These receptors have five subunits, which, in response to the binding of ACh, unmask a channel or small pore in the membrane. Sodium ions enter the channel and cause a change in the voltage across the muscle membrane, and this voltage change indirectly produces muscle contraction. The nerve-muscle system is set up to ensure that each nerve stimulus results in one muscle contraction. This is accomplished in several ways. One is that the muscle cell packs enormously high concentrations of the AChR specifically in the part of the cell beneath the nerve. There are very few AChRs elsewhere. Also, AChRs have particular physiological properties that limit their response to ACh. One of these is their ability to turn off or "desensitize" following prolonged activation by ACh. In part, this allows the muscle to return to a relaxed state. Although these properties of the AChR are well recognized, they are not understood in any detail. For her thesis, Donna Anthony actually studied both properties. Donna examined them in muscle cells growing in cell culture and treated somewhat artificially so that they formed numerous clusters of AChRs. This made them easier to study and manipulate. She also took advantage of an important observation she made—that cells infected with a virus, Rous sarcoma virus, cannot cluster their AChRs at all. She then identified a protein, a tropomyosin in fact, present inside normal muscle cells and forming part of their cytoskeleton, or backbone, which was totally absent from the virally infected cells. She produced a monoclonal antibody specific for this tropomyosin and used it to prove that it was a molecule whose identity had been unknown previously. With this reagent, we may soon be able to show directly that the presence of this tropomyosin confers upon muscle cells the ability to aggregate their AChRs appropriately. As if this were not enough, in collaboration with Pam Middleton and Steve Schuetze at Columbia University, and Kathryn Miles and Rick Huganir at Rockefeller, Donna investigated AChR desensitization. She showed that a particular discrete change in the AChR, a cyclic AMP-mediated phosphorylation of two of its subunits, rendered the AChR much more likely to be desensitized. This provided another striking example of the way in which crucial physiological properties of nervous system molecules can be modified by intracellular events. Donna is now returning to Cornell University Medical College. She is interested in a combined clinical and research career in psychopharmacology.



Donna T. Anthony

Adriane M. Antler

ADRIANE M. ANTLER

Hidesaburo Hanafusa

From studies in the past decade, it became evident that the alteration of certain cellular genes can cause cancer in humans. The altered genes responsible are called oncogenes, and their prototypes in normal cells are known as proto-oncogenes. One of the important goals of cancer research is to identify the function of these proto-oncogenes and to understand the nature of alterations that lead to cancer. At least some proto-oncogenes are highly conserved in evolution and related genes can be found in DNA of *Drosophila melanogaster*, indicating that the common precursor genes had already evolved about a billion years ago. The *Drosophila* system is also well suited for the genetic analysis of the function of a gene. Adriane Antler has focused her research on identification of *Drosophila* genes homologous to proto-oncogenes in mammalian and avian ells. Her initial attempts to detect DNA fragments homologous to known oncogenes of the tyrosine-kinase family led to the identification of two fragments, both of which she isolated as molecular clones. Their chromosomal loci were determined by in situ hybridization. One of them, localized to 58A on chromosome 2R, appeared to be newly identified. The sequence analysis of this gene revealed its extensive homology to the kinase domain of the oncogene called erbB, which appears to be a homologue of the human epidermal growth factor receptor gene. Expression of RNA in developmentally staged flies suggests a role for this gene in growth and development. A protein similar to the human epidermal growth factor receptor in molecular weight and in immunological cross-reactivity was also found in the fly. Her analysis thus revealed the strong conservation of the erbB proto-oncogene in evolution and provided the groundwork for elucidation of the function of src-related oncogenes in *Drosophilia*. Adriane wishes to use her talent in a liaison between business and science. She has accepted a position in the biotechnology patent division of a law firm and will receive further education at Fordham University School of Law.

EVAN S. BALABAN

Peter R. Marler

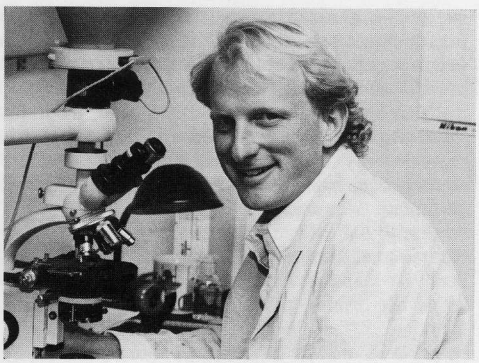
Evan Balaban came to The Rockefeller with an ambition to find a new approach to the biology of culture in animals. The search eventually brought him to a thesis on learned local dialects in birdsong. After diversions into the developmental neurobiology of hybrid crickets, and the possibility of direct manipulation of *Drosophila* courtship song by recombinant DNA techniques, he focused in on a remarkable analysis of geographical variation in birdsong dialects, their genetic correlates, and their meanings to the birds themselves. By elegant use of computer-synthesized songs for playback experiments, both in the field and in the laboratory, he established the role of different song features, especially syntax in song recognition. The result is a major contribution to our understanding of cultural phenomena in animals and their genetic implications. He will stay on at Rockefeller as a postdoctoral fellow, with a plan to collaborate with Professor Nichole DeDouarin at the College de France in Paris, working on the behavior of neural chimeras, between quail and chickens. A bird that as a result of embryological tissue transplants has a brain that is part chicken and part quail offers novel insights into the ways in which neural mechanisms control behavior. If the technique can be extended to songbirds with learned dialects, studies on the neurogenetics of culturally transmitted behavior may indeed become feasible.

Evan S. Balaban

RICHARD A. CANADY

Fernando Nottebohm

Rick Canady came to RU in 1980 with an interest in animal communication. Part of his thesis focused on a species, the canary, that learns its song under the influence of testosterone. This same hormone induces changes in the anatomy of a cell type that is part of the forebrain song control system. Brain cells have long processes, called dendrites, which they use for gathering information. Other brain cells form special contacts on these dendrites. These contacts, used for conveying information, are called synapses. Rick used light- and electron-microscopic methods to show that the number of den-



Richard A. Canady

drites and synapses of testosterone-sensitive cells in forebrain nucleus RNA increases with testosterone, so that more information now reaches those cells. Rick identified the other two cell types, elsewhere in the forebrain, that provide this information and showed that the relative position of the synapses they form on the hormone-sensitive cells, defined by distance from the soma and placement on dendritic spines or trunk, is not noticeably altered by testosterone. That is, each hormone-sensitive cell may now be privy to an expanded version of "more of the same." Rick and others, no doubt, will refine this interpretation and test its generality so that we better understand how gonadal hormones regulate the acquisition and expression of behavior. Rick was fortunate to have the assistance in his work of Drs. Timothy DeVoogd (Cornell University) and Gail Burd (University of Arizona). Rick will spend an extra year at RU testing some of the implications of his findings.

SANDRA L. COTTINGHAM

Susan Schwartz-Giblin

Much of the most detailed neurophysiology studying the control of movement in higher animals has been done to explain movements of the limbs. Yet many important behaviors, including those with high emotional content, begin with postural adjustments of the trunk, using, for example, the deep back muscles. Sandy Cottingham has discovered that two major neuronal systems descending from the brainstem to the spinal cord cooperate to control deep back muscles in the rat, and that these systems in turn are influenced hierarchically by midbrain and hypothalamic neurons that are implicated in emotional behaviors. The effects of stimulating one major descending system, the lateral vestibulospinal tract, on electrical activity of the deep back muscles were facilitated greatly by concurrent stimulation of the other descending system, the medullary reticulospinal tract. These two influences can converge directly at the motoneurons responsible for these muscles, but also probably use interneurons in the lumbar spinal cord. In turn, stimulation of the midbrain central gray potentiated the electromyographic effects of either the lateral vestibulospinal tract or the medullary reticulospinal tract. In all of these cases, the potentiating stimulus would cause a shorter latency response in the muscles and more muscle units to react. When hypothalamic nerve cells were destroyed, deep back muscle responses to reticulospinal stimulation were reduced over a time course similar to behavioral changes. Thus, Sandy's results link the physiology of hypothalamic neurons, responsible for a variety of emotional behaviors and endocrine controls, to the physiology of motor control systems that actually express the behaviors in question. As an M.D.–Ph.D. student, she will complete her medical training and then start her postdoctoral research on topics that combine experimental and clinical aspects of neurobiology.

EMILY A. EVANS

Günter Blobel

Emily Evans came to Rockefeller with two undergraduate degrees, an A.B. in biology from Barnard College and a B.S. in chemical engineering from Columbia University School of Engineering and Applied Science. She was therefore well prepared to face the challenge of her thesis project, namely, to purify and to characterize eukaryotic signal peptidase. This endoproteolytic enzyme is an integral protein of the endoplasmic reticulum (ER) of all eukaryotic cells and specifically removes the signal sequence from secretory, lysosmal, and numerous membrane proteins. Unexpectedly, the purified enzyme turned out to be a complex of at least five polypeptide chains present in apparently stoichiometric amounts. As the enzyme is presumably near or at the site where secretory, lysosomal, and numerous membrane proteins are conducted across the ER membrane ("translocation" site) and as the enzyme itself is likely to be represented by only one polypeptide, there is the exciting possibility that the other polypeptide chains are components of these long-sought-after "translocation" sites in the ER. To explore this important idea, Emily has decided to begin her postdoctoral work here.

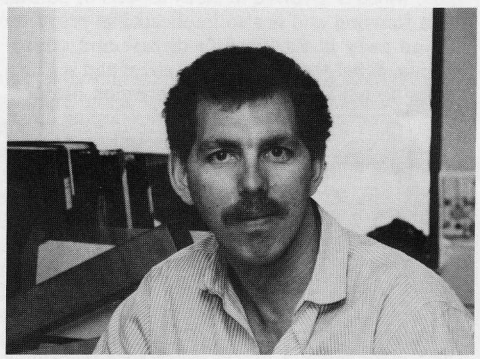
Emily A. Evans

WENDY J. FANTL

James M. Manning

Carbon dioxide is considered a metabolic end product carried by the blood and exhaled through the lungs. Wendy Fantl's thesis work was concerned with the process by which hemoglobin in the blood helps carry out that function. She refined a reaction in protein chemistry and applied it to a very specific site on hemoglobin, which was considered a likely place to carry CO_2. The hemoglobin derivative that Wendy studied was very closely related to the CO_2 adduct, but it was much more stable and thus easier to study. Using this derivative, she succeeded in resolving some very thorny and intricate questions about the functions of hemoglobin, especially the controversial Bohr effect. The compound that she prepared also forms the basis of a new line of investigation in the lab. It turns out that this derivative has some properties that are desirable for a blood substitute. Another ramification of Wendy's thesis work is that we will now be in a position to study other aspects of the possible physiological role of carbon dioxide as a regulator of various proteins in the body. Wendy will continue her studies on the elements of blood at the University of California in San Francisco, where she will be studying one of the new growth factors derived from blood platelets.

Wendy J. Fantl



Jeffrey M. Friedman

JEFFREY M. FRIEDMAN

James E. Darnell, Jr.

Sometimes our curiosity gets the better of us—that cliche might apply to Jeff Friedman. Certainly his curiosity has at least changed his life. Jeff had finished his residency at Albany Medical College and passed the boards in internal medicine when he came to see me in 1981. He had decided that the practice of medicine, at which I have reason to know he is quite expert, didn't seem to offer him sufficient fulfillment and he had decided he wanted to become a graduate student. Somewhat skeptically I listened and advised him to settle for a postdoctoral fellowship and go into academic medicine. A second visit a few months later, at which Jeff described a series of quite reasonable experiments, convinced me that he was serious and could well be suited for basic experimental work. He applied and was admitted to our Ph.D. program. After six months or so of learning to isolate RNA and DNA, still all in one piece, Jeff began experiments on liver regeneration, a phenomenon that allows mammals to maintain the correct amount of liver tissue after injury. The experiments showed with up-to-date nucleic acid techniques the several levels of gene regulation that are required to repair the loss of liver tissue. From that point Jeff moved, and by his efforts helped move the entire lab in the direction of studying the details of specific gene function in the liver, pursuing the question of what DNA sequence elements are necessary and how they are recognized in the manufacture of the major serum protein, albumin. This work helped open a new chapter in the investigation of tissue-specific gene function, a central problem in developmental biology. Jeff has now moved into a position as a Howard Hughes Associate Investigator and assistant professor here on our faculty. He will study a fascinating peptide called cholecystokinin, which is formed in both the brain and the GI tract, and which he hopes will be a model for understanding some phases of endocrine function in the brain.

WILMA J. FRIEDMAN

Bruce S. McEwen

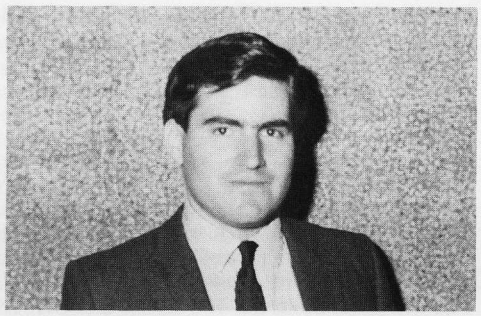
When and how do nerve cells develop their specialized abilities to produce chemical signals like transmitters and hormones? To ask these questions in the developing brain, Wilma Friedman utilized sensitive binding assays to measure receptors and equally sensitive chemical assays to detect transmitters and their enzymes. With her outstanding knack for lab work, Wilma also employed the important technique of tissue culture, in which cells can be grown outside of the body in order to more closely monitor and manipulate their development. She studied a neurotransmitter known as dopamine, which is involved in many aspects of normal brain function and is also implicated in processes that go awry in Parkinson's disease and schizophrenia. What she found is that stress and sex hormones do not crucially affect expression of dopamine. However, the excitation of developing dopamine neurons by another neurotransmitter does increase dopamine development. Wilma's elegant and clear-cut results thus point towards the local environment of developing dopamine neurons as having a particularly important role in their neurotransmitter differentiation. In much of this work, Wilma was fortunate to have the additional guidance of Dr. Ira Black and Dr. Cheryl Dreyfus from our neighbor, Cornell University Medical College. Their input made a crucial difference in helping Wilma determine the path which her research and future career will follow. Wilma is a native New Yorker who went to Oberlin College in Ohio and became a psychobiology major and a collegiate fencer. Her return to New York has enabled her to hone her intellect in developmental neurobiology and to redirect those fencing reflexes toward the precise dissection of embryonic brain tissue. Her next step is to go further east to Uppsala, Sweden, where she will begin to investigate actions of nerve growth factor.

Wilma J. Friedman

WILDER FULFORD

Peter Model

Wilder Fulford has contributed significantly to our understanding of the filamentous phage life cycle. His principal effort has been to define and clarify the nature of the control loop which allows the phage, on entering the cell, to very rapidly expand its pool of DNA and phage components, and then rather abruptly move into a steady state mode, in which it limits the rate of synthesis of its components so that the host can continue to grow, divide, and make more phage. Important in this control loop are elements of translational control mediated by specific inhibition of the initiation of



Wilder Fulford

translation of certain genes, and a mechanism by which a naturally occurring fragment of an enzyme seems to counteract the action of its parent protein. He has left us with a description, in molecular terms, of the nature of the elements controlling the growth dynamics which probably exceeds what is known for any other organism, and he has done this with a series of very clever experiments which, I'm sure, will serve as an example for future related work. Wilder is a man of boundless energy and curiosity, and one of the most effective experimentalists I have ever met. His interests are not bounded by science; he is a familiar at many of the more avant garde art galleries in New York, knows more about the New York disco scene than the rest of us put together, and bakes an outstanding apple pie. He has also read and subjected to relentless scrutiny and editing practically every paper that has come out of the lab for the last few years. In consequence of his wide interests, Wilder has run into the economic limitations of being a scientist earlier than others. He has also been concerned about the prospects for stable research funding and permanent job opportunities. Consequently he is seeking a place in the business world. This saddens me, since I think he has great natural aptitude for creative research. In a year in which one of New York's leading law firms has given a cost of living increase to their new fledgling lawyers which is about equivalent to the whole of a postdoctoral stipend, I can hardly blame him. I wish him success, but not too much success, since it is my great hope that he will return to the fold.

SHELLEY HALPAIN

Bruce McEwen

Shelley Halpain arrived at Rockefeller University with undergraduate research experience at UC Irvine in studying an important brain structure known as the hippocampus. Her fascination with this structure and its role in memory, and with a neurotransmitter called glutamic acid, led her into a series of rigorous studies on the regulation of the receptors for glutamate. Shelley found that one type of glutamate receptor is different from all others and is regulated by chloride ions. In fact, she suspects that it may not be a traditional receptor but rather a binding site related to transport of glutamate into the cell. Another form of the receptor is regulated by calcium ions, and adrenal stress steroids also have an influence on the number of glutamate receptors in hippocampus. Shelley's work also helped to further develop the important technique of autoradiography as a means of quantitatively mapping receptors in the brain. The clarity of her results, gathered in spite of formidable technical difficulties, is a tribute to her skill and perseverance. Shelley is a Californian and a worldly one. She had the good sense to come East for her graduate education, and, in fact, I recall that her first visit to New York, before becoming a graduate student, was on her way to Italy for spring vacation. However, Shelley has not permanently lost her native ways—or at least her California time sense—for it seems that she often appears in the lab at 11 A.M. and then doesn't leave again until well after midnight. Shelley plans to join the laboratory of Professor Paul Greengard for postdoctoral work.

Shelley Halpain

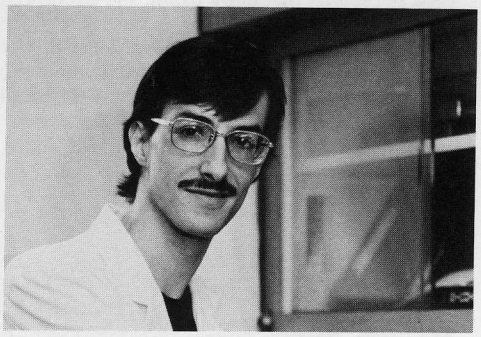
Linda Hanley-Bowdoin

LINDA HANLEY-BOWDOIN

Nam-Hai Chua

The world's most abundant protein is a chloroplast enzyme called ribulose 1,5-bisphosphate carboxylase. This enzyme is composed of eight copies each of a large and a small subunit. The large subunit (rbcL) is encoded on the chloroplast genome and is synthesized within the organelle. Linda used cloned plastid DNA templates and chloroplast extracts to analyze maize rbcL mRNA synthesis in vitro. Several significant findings emerged from her work. Three maize rbcL RNAs, which have different 5′ ends, have been observed in vivo. Linda demonstrated that the rbcL gene has a single transcription start site and that the longest RNA species is the primary transcript. Using homologous and heterologous chloroplast extracts, she showed that the longest RNA is processed to the shorter rbcL RNAs. Subsequently, Linda located the promoter of the maize rbcL gene to a 49 base pair region flanking the 5′ terminus of the longest RNA. The DNA sequence immediately upstream of the transcription start site shares homology with bacterial promoter sequences. She examined this homology at a functional level by comparing the transcription of mutant rbcL promoter templates in vitro using chloroplast and *E. coli* RNA polymerases. These studies established that although there are many similarities between plastid and bacterial promoters, chloroplast and *E. coli* RNA polymerases have distinct promoter recognition properties. Analysis

of the mutant templates also revealed that chloroplast promoters interact with each other. Transcription of an adjacent gene is altered by mutations in the rbcL promoter region. Linda's research has provided important insights into chloroplast gene expression at the molecular level. Some of the mechanisms her work characterized are procaryote-like in nature, while others may prove to be unique to chloroplasts. In the fall, Linda will apply her knowledge of plant molecular biology to the study of plant-pathogen interactions in the laboratory of Dr. Olen Yoder at Cornell University.



William Heath

WILLIAM HEATH

Bruce Merrifield

William Heath came to Rockefeller from the University of Indiana where, as an undergraduate, he had obtained a good laboratory training in protein chemistry. He joined our laboratory to learn about the chemical synthesis of peptides and proteins and decided to focus on some of the newly discovered mitogenic growth factors, including epidermal growth factor. Since this 53-residue peptide contains three tightly folded disulfide loops that are critical for activity, it was clear that certain side reactions of cysteine had to be overcome before a good synthesis could be expected. Bill completed a detailed study of the removal of protecting groups from cysteine by HF as a function of acidity and scavenger and made important improvements in the technique. His mechanistic studies in collaboration with Dr. James Tam have led to a generalized understanding of strong acid deprotection. The assembly of epidermal growth factor could then be accomplished in high yield, and the purified, folded, disulfide-containing product was homogeneous by several criteria. Bill found it to be as active as the native peptide in receptor binding and thymidine uptake assays. This opened the way to the synthesis of several analogues for an investigation of the role of composition and conformation in the functioning of this class of peptides and for the identification of structures that will separate receptor binding from cell growth and division. Bill will continue his training as a postdoctoral fellow at the Harvard Medical School, where he will move into some of the more biological aspects of his field.

Peter J. Hotez

PETER J. HOTEZ

Anthony Cerami

At the turn of this century, John D. Rockefeller Sr. established the United States Sanitary Commission in order to eradicate hookworms from the southern United States. Scientific advances and public health measures enabled the commission to be so successful in this eradication program that when it became The Rockefeller Foundation, new objectives were selected. Unfortunately, this success story has not been repeated in many places in the world. Today nearly one billion people continue to be infected with hookworms. Yet, in spite of its widespread nature, very few scientific investigations have gone on since the original flurry prompted by the Sanitary Commission. For example, the budget world wide for research on hookworm disease is approximately $100,000. It is into this scientific void that Biomedical Fellow Peter J. Hotez chose to enter. I am not sure when Peter first decided to work on hookworms, but I do know that from the first day he arrived from Yale that is all he talked about. Hookworms are his love. This may seem hard to fathom since they look like monsters from a horror movie. They gain entrance to the body by boring through the skin in the feet. Then moving by a tortuous route, which involves climbing up the trachea in order to be swallowed, they finally come to roost in the intestine. They attach with several sharp teeth to the intestinal wall and suck blood like a small vampire. Relentlessly, they remove this vital material until the host is unable to replenish the supply fast enough. This leaves the host unable to carry out normal physical functions. To give an idea of the magnitude of the problem, hookworms in aggregate cause a loss of blood equal to the complete exsanguination each day of the population of Houston. That is a lot of blood. What did Peter plan to do? He reasoned that like all good blood-sucking creatures, hookworms had to have a mechanism to prevent the blood from clotting while they ate. He further surmised that if one could interfere with this eating by inhibition with antibodies, it might constitute a vaccine against hookworms. Peter was able, with Nguyen Le Trang, to isolate and characterize a protein from the saliva of hookworms which was the proposed anticoagulant. It is not practical to isolate enough saliva from hookworms to use it as a vaccine, however. In order to circumvent this problem, Peter had to team up with George Newport and Nina Agabian of Berkeley to use DNA technology to clone and express this protein in bacteria. This approach has allowed the preparation of enough material to begin a clinical trial in dogs which is now underway to test its efficacy as a vaccine. Peter has returned to Cornell, where he is finishing his medical degree. We hope that he finishes soon so that he can resume his role in hookworm research and The Rockefeller Foundation can finish the task in the rest of the world that the Sanitary Commission began.

SATORI IWAMOTO

James E. Darnell, Jr.

In biology, the understanding of a complete metabolic cycle is often required before we can learn how the cycle is regulated. This axiom is true for transcription, the act of copying RNA from DNA. While it is true that most current experimental emphasis in the transcription field is focused on how to correctly start copying an RNA, it is also very important to understand how the enzyme RNA polymerase knows that it has copied enough and the time is

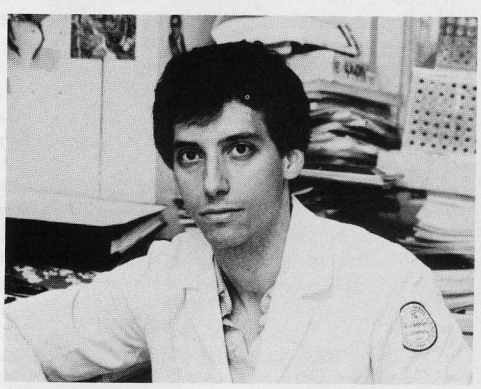
Satori Iwamoto

ripe to terminate. Satori Iwamoto focused the major part of his thesis work on how human RNA polymerase II stops transcription in the proper place. He devised a very sensitive means of measuring this delicate event in the nucleus of human cells so that he could be sure he was catching the most newly completed molecules that could be studied. This was important because the ends of newly completed molecules are quickly destroyed and hard to measure. With his new technique, Satori convincingly demonstrated the first case of regulated termination in human cells, i.e., a case where the polymerase stopped at a early station in one case and at a later station in another case. Without this important first step, we would be hard pressed to pursue the molecular basis of transcriptional termination, much less its regulation. In addition to his work on transcriptional termination, Satori had another fascination as a student: the definitive proof that the DNA double helix is wound in a right-hand fashion, as Watson and Crick originally suggested. In association with Professor Ming-Ta Hsu, he proved this fact with an elegant electron-microscopic demonstration that made the right-hand winding visible. Satori decided near the end of his graduate studies that he wanted to apply his molecular skills to medicine and is now at Harvard Medical School.

RICHARD I. LAPPIN

Lee Rubin

Rich Lappin came to my lab a few years ago interested in working on "cells, not molecules." We had noticed previously that neural activity exerted very important influences on muscle development. This observation seemed important because neural activity is suspected to be a prime regulator of complex aspects of nervous system function. Memory,



Richard I. Lappin

for instance, is an event which depends on activity in particular sets of brain cells. Rich chose to study the manner in which activity controls the appearance of the muscle enzyme acetylcholinesterase. This enzyme is present in very high concentrations beneath the nerve on muscle cells. Its activity is truly essential in coordinating the muscle's response to nerve stimulation. Hence, it is a favorite target for both insecticides and for nerve gasses used in chemical warfare. Rich found that muscle contraction itself was the main regulator of acetylcholinesterase synthesis. Muscle contraction, he determined, was involved in regulating the synthesis of a peculiar form of the enzyme in which the active subunit is linked to a collagen-like tail subunit which anchors it in place in the synaptic region. He also found that what was important about muscle contraction was the increase in levels of Ca^{2+} which occur in the muscle cell during contraction. His results also made it seem likely that these increases Ca^{2+} were involved in turning on expression of the gene for the tail subunit itself. To understand these regulatory events in greater detail, Rich unfortunately found himself working with molecules. He produced monoclonal antibodies which recognized each subunit of the enzyme, thereby succeeding in something which had been found difficult by most investigators. He then used antibodies to carry out what is called "expression cloning—a technique whose goal is the identification of the genes responsible for producing the enzyme subunits. He was able to pick up potential probes for the genes of each subunit. Thus, we are now left with valuable reagents which should enable us to begin to understand how electrical activity regulates gene expression in the nervous system. Rich is now returning to Cornell University Medical College to complete the joint M.D.-Ph.D. degree.

HONORARY DEGREE

NORMAN RAMSEY

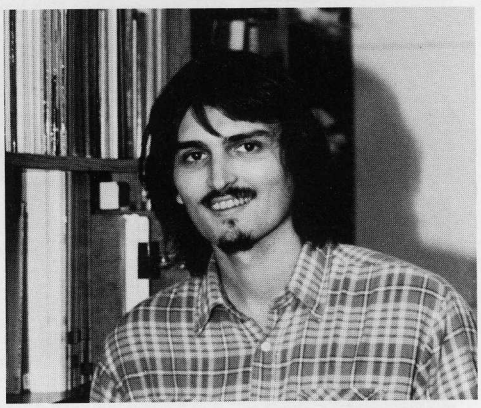
Rodney L. Cool

The range in the scientific activities of Norman Ramsey, Higgins Professor of Physics of Harvard University, is so broad and so varied that I can select only a few vignettes from the complete picture of his career. I do hope that I may convey to you the tremendous vigor and dedication that are so characteristic of his scientific personality. He holds Ph.D. degrees from Columbia University and from Cambridge University in England. At Columbia, he was a student of Professor I. I. Rabi, who was awarded an honorary degree on this platform in 1979. Upon graduation, he became involved in the scientific activities of the World War II era, heading groups at the MIT Radiation Laboratory that developed the first 3-centimeter-wavelength magnetrons and related radar systems. Subsequently, he worked on the Manhattan Project as a group leader and later a chief scientific officer. He returned to Columbia University in 1945, where he studied the properties of molecules and nuclei using molecular beam resonance techniques. During this period, he became executive secretary of a group formed to found a laboratory to provide eastern universities with a center with access to scientific instruments too large or too expensive for individual universities. He and his late wife are widely credited with a decisive role in locating that laboratory at Camp Upton, Long Island, naming it the Brookhaven National Laboratory. This laboratory has developed into a major scientific center. He also served as the first chairman of its physics department before joining the Harvard faculty in 1947. Dr. Ramsey's diverse research interests have led to key contributions to the magnetic moments of nuclei, the shape of nuclei, and the nature of nuclear forces. He invented the method of using separated oscillatory fields to excited resonances, which provides extremely high resolution in atomic and molecular spectroscopy and forms the practical basis for the most precise atomic clocks. In collaboration with his students, he invented the atomic-hydrogen maser, which allows still greater spectroscopic resolution and serves as the basis for the most precise measurements of time. These precise measurements of time have had an enormous impact on astronomy and tests of the theory of relativity. His program to measure the elusive electric dipole moment of the neutron is legendary. A measurement of this extremely small quantity would provide a decisive test of theories of the origin of the violation of parity and time reversal invariance in weak interactions. Several decades of increasingly sensitive and ingenious experiments have reduced the upper limit on this value and eliminated many prospective theories. These experiments continue to be a focus of his research activities today. Professor Ramsey is a dedicated educator. When he received the Karl Taylor Compton Award of the American Institute of Physics in 1985, he was praised for his "spirited teaching and impeccable taste in physics problems worthy of attack." He has supervised the theses of approximately 85 Ph.D. students during 40 years at Harvard—a monumental number, and quite possibly a record in experimental physics. Professor Ramsey is widely recognized and admired as a statesman of science. In addition to his role in the founding of the Brookhaven National Laboratory during World War II, he was a consultant to the Secretary of NATO. From 1960 to 1972, he was a member of the General Advisory Committee of the United States Atomic Energy Commission. In 1963, he chaired the High-Energy Physics Panel of the President's Scientific Advisory Committee. From 1966 to 1981, he was President of University Research Associates, a consortium of 55 American universities of which this University is a member. URA operates the FERMI National Accelerator Laboratory in Illinois. In 1978, he was President of the American Physical Society. He has been a member of the board of trustees of The Rockefeller University since 1977. Dr. Ramsey's contributions to science have been recognized by many awards: the Presidential Order of Merit, the E. O. Lawrence Award, the IEEE Award of Honor, the Rabi Prize, and the Karl Taylor Compton Award. He holds the degree of Honorary Doctor of Science from Case-Western Reserve University, Middlebury College, and Oxford University in England. Mr. President and members of the Board of Trustees, it is an honor and a great personal pleasure to present Professor Norman Foster Ramsey, distinguished physicist, dedicated educator, and statesman of science as a candidate for the degree of Doctor of Philosophy, *honoris causa*.

PETAR D. SIMIĆ

M. A. B. Bég

Legend has it that the phenomenon of solitary waves was discovered, in the nineteenth century, by an amateur English scientist. He was watching, so the story goes, a barge being pulled along a narrow canal by a pair of horses. When the barge was suddenly stopped by an obstacle, he saw a single crest roar ahead along the surface of the water. He had the presence of mind to mount his horse and give chase. Evidently, the shape of the undulation did not change as it sped along. Whether this was a credible sighting is no longer relevant. We now know that nonlinear wave equations can indeed yield solitary-wave or soliton-like solutions. Their importance is being increasingly recognized in physics as well as other sciences. The work of Petar Simić has to do with the role of solitons in the theory of elementary particles. In the first part of his thesis, he presents a formalism for the description of the physical phenomena that occur in the presence of monopoles of a specific genus, the ones that arise as soliton-like solutions of the field equations in theories that unify strong and electroweak interactions. One interesting effect here is the breakdown of time reversal invariance in both strong and electromagnetic interactions. That such an effect should occur in the presence of electrically



Petar D. Simić

charged magnetic monopoles, albeit of a different genus, was first noted by Dr. Norman Ramsey, distinguished member of our board of trustees. In a sense, the incisive analysis of Simić extends and completes work initiated by Ramsey some twenty-five years ago. In the second part of his scholarly thesis, Simić proposes an interesting way of extracting low-energy hadrodynamics—well described by models of the type first constructed by Murray Gell-Mann and Maurice Lévy—from what is now regarded as the more fundamental theory of strong interactions: quantum chromodynamics or QCD. The elementary particles here are quarks and gluons; the observed strongly interacting fermions, such as protons and neutrons, may be identified either as bound states of confined quarks or as solitons. The contribution of Simić sheds light on the complementarity of these descriptions. Simić will continue his work at the University of California at Los Angeles, where he has accepted a three-year appointment beginning September 1 of this year.

HAZEL L. SIVE

(Degree granted in absentia)

The topic of Hazel Sive's thesis was "The Regulation of Human Histone Gene Expression: An Analysis In Vivo and In Vitro." Her research advisor was Robert G. Roeder.

NANCY E. THOMAS

(Degree granted in absentia)

The topic of Nancy Thomas's thesis was "Substrate Conformation and Hydrogen Bonding in the Active Sites of Protein Kinases." Her advisor was Emil T. Kaiser.

MacArthur Award to Shapley

Professor Robert Shapley is one of 25 MacArthur Foundation Fellowship recipients for 1986. The Foundation cited Dr. Shapley's contributions to understanding how the eye and brain analyze and recognize visual images, research conducted in the biophysics laboratory of Professor Floyd Ratliff.

Dr. Shapley received his Ph.D. at The Rockefeller in 1970. He became an assistant professor in 1972 and an associate professor in 1976.

The MacArthur Fellows Program provides unrestricted five-year fellowships ranging from $164,000 to $300,000, depending on the age of the recipient.

Lab Report: Washing Away Whooping Cough

As a result of adverse side effects of the DTP (diphtheria, tetanus, and pertussis) vaccine, parents are becoming wary about having their children innoculated. Consequently, death tolls due to pertussis (whooping cough) have climbed in England and Japan, and the number of cases in the United States is increasing.

While there is no cure for this highly contagious disease, Rockefeller researcher Elaine Tuomanen, a member of the microbiology laboratory, is developing an aerosol inhalant designed to wash the bacteria from its attached site in the windpipe.

Unlike bacteria that invade the body via the bloodstream, whooping cough bacteria remain on the surface of the windpipe. They are protected from the bloodstream defenses, but are accessible to the air we breathe. To keep from being blown away, they anchor themselves to cells in the bronchial passageway on projections called cilia, which resemble the fibers of a carpet. When the cells are healthy, the undulating cilia prevent foreign matter from entering the lungs and help maintain the throat's protective mucous lining. Attached pertussis bacteria, however, release toxins that, among other harmful effects, destroy the cilia, which in turn permits the build-up of mucus and impairs breathing.

Dr. Tuomanen is experimenting with a form of sugar molecule that chemically resembles the ciliary anchoring sites for the pertussis bacteria. Administered via an aerosol mist, the sugar molecules attract and bind to the bacteria, causing them to detach from the cilia. Bound to the sugar, the bacteria are carried up the windpipe and harmlessly swallowed and digested.

For cases in which a patient has been exposed but has not yet contracted the disease, Dr. Tuomanen has developed monoclonal antibodies that occupy the pertussis anchoring sites on the cilia. With the sites blocked, the bacteria have nowhere to roost and are rendered ineffective.

Dr. Tuomanen has found both treatments to work effectively against the disease in culture. They are currently being tested on laboratory animals.

Children's School Reunion

Calling all long-lost alumni! The Rockefeller University Children's School is having its 20th anniversary celebration on November 9, from 3 to 5 P.M., on the 17th floor of the Tower, and all alumni are invited. If you know the whereabouts of any alumni who have moved, please contact Barbara Adams, the school's director, at extension 8580 or box 50.

Conjugation and Transduction

Two seminal events in the history of genetics happened 40 and 35 years ago, respectively, as a result of the work of President Lederberg and Professor Norton D. Zinder, head of the University's laboratory of genetics.

Dr. Lederberg and Dr. Zinder spoke at a retrospective symposium, "A Celebration of Forty Years of Bacterial Conjugation and Thirty-Five Years of Bacterial Transduction," held in Caspary Auditorium on May 16. Other speakers were Barbara J. Bachman and Edward A. Adelberg of the Department of Human Genetics, Yale University.

Hotchkiss Honored

Professor Emeritus Rollin D. Hotchkiss, who has been associated with the University since 1947, was an invited speaker at the inaugural convocation symposia of the State University of New York's School of Public Health Services in Albany on March 21.

Dr. Hotchkiss, who holds an appointment as research professor at SUNY, Albany, was awarded an honorary doctor of science degree by the new school for his half century of contributions to molecular biology, which include the first isolation, in pure form, of an antibiotic, and the validation by direct chemical analysis of the postulated DNA nature of the bacterial transforming agents and the quantitation of the transformation process.

The School of Public Health, only the second of its kind in New York State, is a combination of the resources of the State University of New York and the State Health Department laboratories. Dr. Hotchkiss spoke on "Cycles in Genetics and the Academic Metabolism."

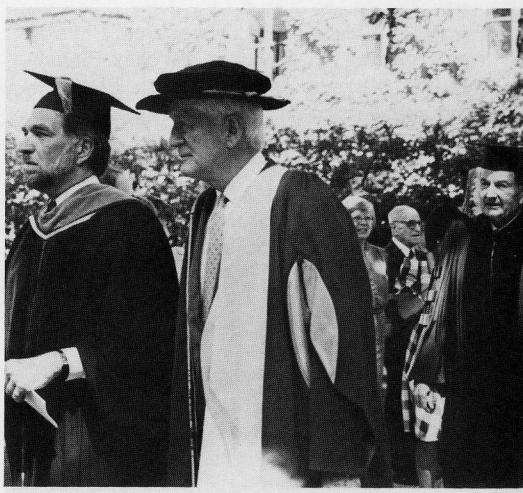
In addition to presenting a retrospective of 40 years of molecular biology, he offered a satire of education in the second part of his talk, which was formulated, he explained, by an extraterrestrial named Brakal who had transmitted into his computer a report on a 50-year study of the "Effects of High Metabolic Rate and Impatience on Cycles of Support for Science on Developing Planets." According to Brakal, educational institutions on Earth do not always put academic matters first and he noted that he will watch with considerable interest and optimism what will happen at the new school.

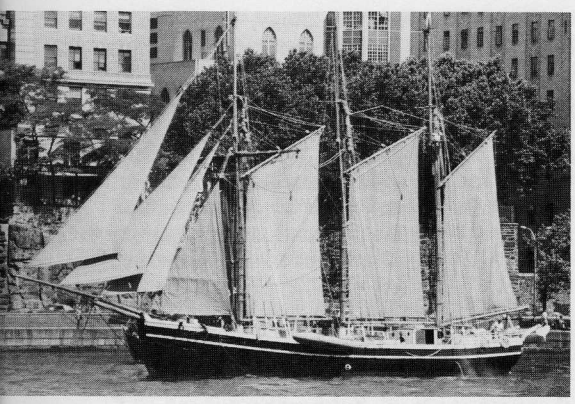
Auerbach Addresses High School Students

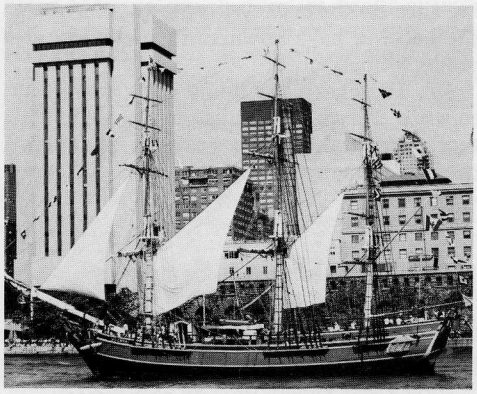
Professor Arleen Auerbach, a member of the laboratory of investigative dermatology, was the keynote speaker at the March of Dimes Tenth Annual Tina Russo Convocation for High School Students at Wagner College on Staten Island on March 27. The convocation is named in honor of Tina Russo, a Staten Island March of Dimes board member for almost 40 years.

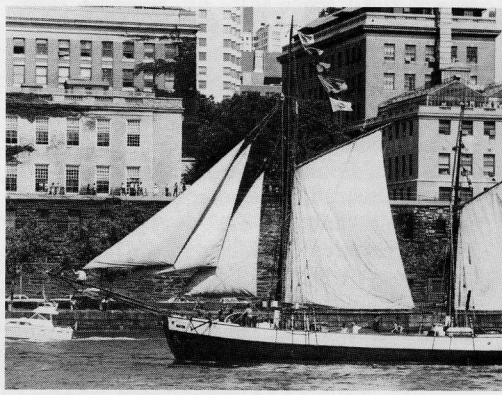
Dr. Auerbach opened the convocation, which is organized to encourage students to pursue careers in the life sciences, with a discussion of her studies of Fanconi anemia, a genetic syndrome of varied physical malformations, bone marrow failure, and often leukemia. Dr. Auerbach has established an international registry for patients with the disorder, in collaboration with Dr. Traute Schroeder of the University of Heidelberg. Data from the registry will help to better define the disease and to assess the effectiveness of different therapies.

In April, Dr. Auerbach was a guest speaker at a meeting of the South Shore Rotary Club of Staten Island. This organization held a very successful fundraising benefit on behalf of Fanconi anemia, the proceeds of which were donated to Dr. Auerbach's laboratory, for research on this disease.









Briefs

Professor **Michael Brownlee**, Medical Biochemistry, addressed the 46th annual scientific meeting of the American Diabetes Association, in Anaheim, California, June 22–24. He reported on his research involving the ability of the compound aminoguanidine to prevent diabetic vascular disease in laboratory animals.

Professor **D. Martin Carter**, Investigative Dermatology, addressed a hearing of the U.S. House of Representatives Select Committee on Aging on May 21 on "Skin Cancer: Older Americans at Risk." As he reported, the half-million cases of skin cancer reported annually in this country represent 30 to 40 percent of all cancers diagnosed. One of the major concerns in Dr. Carter's laboratory is the biology of aging and its effects on the skin.

Professor **Anthony Cerami**, Medical Biochemistry, delivered a lecture to the 68th annual meeting of The Endocrine Society on June 27th in Anaheim, California. The topic of his talk was "Cachectin—A Macrophage Protein That Induces a Catabolic State."

Professor **Nicola Khuri**, Theoretical Physics, was a visiting professor at the Max-Planck-Institüt, Munich, for the month of April, conducting research and lecturing on problems in mathematical physics.

Senior Fellow **William Lowrance**, Director of the Life Sciences and Public Policy Program, has been elected to the board of trustees of The Keystone Center, a national environmental policy negotiation organization with headquarters in Keystone, Colorado.

Professors **Peter R. Marler**, Animal Behavior, and **Torsten Wiesel**, Neurobiology, spoke at the Sixth Annual Conference of The Institute for Child Development Research, entitled "Brain Beyond Genes: Epigenetic Regulation of Synaptic Circuits and Their Function," held in New York, June 2-4.

Professor **Neal E. Miller**, Physiological Psychology, was a guest of the Dashisha University in Kyoto, Japan, June 6-15, and delivered the Neesima endowment lectures. He spoke on "Experimental Studies of Fear (Anxiety) and Their Clinical Implications" and "Effects of Psychological Stress and Coping on the Health of the Body."

Trustee **P. Roy Vagelos**, president and chief executive officer of Merck & Co., Inc., has been elected chairman of its board of directors.

Professor **Jonathan Winson**, Neurophysiology, presented a lecture, "The Biology of the Unconscious," at a conference, "Resighting, Reciting, Resiting the Future," at Montana State University, Bozeman, held in conjunction with the Smithsonian Institution exhibit, "Yesterday's Tomorrows: Past Visions of the American Future," at the Museum of the Rockies.

Trustee **James D. Wolfensohn**, president of James D. Wolfensohn, Inc., an advisory and investment firm, has been elected chairman of the board of trustees of the Institute for Advanced Study, in Princeton, New Jersey.

Children's School Store

The Rockefeller University Children's School is opening a store that will feature sweatshirts and other items usually available at the sales held during the year in the Tower lobby. It will be in Room 107 of Gasser Hall beginning in mid-September and will be open one day every week. All proceeds will benefit the Children's School. Future sales will be held in the Tower lobby on December 4 and March 4.

Personals

Born June 22 to **Ellen G. Fuss**, a nutritionist in the Hospital, and her husband, Dr. Richard Fuss, a son, Jonathan Scott.

Graduate fellow **Ruth Montgomery**, Cellular Immunology, was married on June 14 to John Platoff, a professor of music at Trinity College, Hartford, Connecticut.

Pamela Lee Elliot Dies

Pamela Lee Elliot, a member of the University's administrative staff from 1961 to 1974, died on July 5, in Armonk, New York. She was 61 years old.

As an assistant to two presidents, Detlev Bronk and Frederick Seitz, Mrs. Elliot had major responsibility for grant and faculty administration. She is survived by her husband, Roger C. Elliot, who at the time of his retirement in 1974 was the director of administrative services for the University.

Deaths

Catherine Gallaway, 68, who retired in 1983 after 20 years as assistant to the division director of the Center for Biomedical Research of the Population Council, on June 17.

News and Notes is published five times a year from October through July. This is Volume 17, Number 5. Suggestions for articles are welcome and may be sent to *News and Notes*, Box 194, phone extension 8968 or 8970. Commencement photographs, Lloyd Edwards and George Byron; Ships, John H. Sholtis.