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The Rockefeller University

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RU receives \$2.5 million for study of molecular medicine

The Lucille P. Markey Charitable Trust recently awarded a grant of \$2.5 million to The Rockefeller University. The grant, pledged over five years, will fund research in molecular medicine, a field which applies discoveries in molecular biology to the study, prevention, and treatment of human disease. The grant will support four new positions in molecular medicine at the university—two junior heads of laboratories and two post-doctoral fellows.

"This gift will enable us to attract highly qualified investigators and will help the university expand and strengthen its faculty," said President Torsten Wiesel. "I would like to thank the Markey Trust and Louis Hector, Markey's chairman and a Rockefeller trustee emeritus, for their generous support."

The Markey Trust has been increasingly concerned about the gap between basic research and the practice of medicine. "There is broad general concern today that the extraordinary discoveries of modern molecular biology are not being utilized with sufficient speed in the study of human disease, diagnosis, and treatment—the so-called 'bed-bench' gap," said Hector. "We hope our General Organizational grants will serve as models for training of future medical scientists who will help bridge this gap."

Last week, the trust announced General Organizational grants totaling \$11.5 million to support universities and medical schools involved in the training of basic

scientists and clinicians. In addition to Rockefeller, the institutions were Columbia University, Stanford University, the University of Chicago, the University of Virginia, and Yale University.

The Markey Trust was established in 1983 exclusively for the support and encouragement of basic biomedical research. Since then, the trust has made grants totaling more than \$15 million to The Rockefeller University. The trust has supported junior faculty, graduate fellows, and the establishment of the Henry G. Kunkel Professorship in Immunology, currently held by Professor Zanvil A. Cohn, vice president for medical affairs.

Newsletter fields voice-mail inquiries

When Ruth Moses, voice mail administrator, designed the Voice Mail Newsletter that began publication in January, she was thinking primarily of confused voice mail users and frustrated callers.

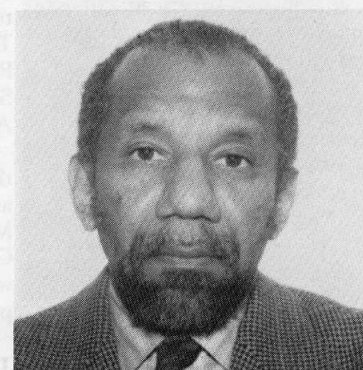
"It is clear that many people still have questions about the new system even though some attended our training sessions and have instructions," said Moses. "I wanted to create a newsletter that could field some of these questions and help users make the most of the AUDIX voice mail system."

The first issue of the newsletter explains how to disable AUDIX's Forwarding (FWD) and Send All Calls (SAC) functions so that calls are not routed to voice mail after

Lecturer to speak on roots of violence

Felton Earls, a Harvard University professor and child psychiatrist who is conducting a 10-year multi-city study on the causes of antisocial behavior, will speak on "Understanding and Preventing Violence: A New Challenge in Public Health," today (Feb. 5). The talk, which begins at 3:45 P.M. in Caspary Auditorium, is part of the weekly Friday lecture series.

Earls is a psychiatric epidemiologist interested in the factors leading to violent behavior. As director of the Program on Human Development and Criminal Behavior at Harvard, he is conducting a comprehensive longitudinal study, which will follow more than 10,000 children, adolescents, and young adults, from prenatal months through age 32. Earls and



Psychiatrist Felton Earls

his colleagues hope to isolate the characteristics that predispose or lead children to crime and to identify key social, psychological, and biological roots of delinquency, antisocial behavior, and crime. His lecture will discuss the goals, methods, and wide-ranging implications of the study.

Among the many influences that will be explored will be the roles of families, schools, and peer groups. Community and environmental factors such as drugs, alcohol, and exposure to lead paint will be included. The study will entail extensive use of interviews, health, psychological, and educational testing and the review of hundreds of thousands of school, medical, and criminal justice records.

Earls holds the dual posts of professor of human behavior and development at the Harvard University School of Public Health and professor of child psychiatry at the Harvard Medical School. Before going to Harvard, Earls was professor and director of the Division of Child Psychiatry at Washington University School of Medicine in St. Louis. His extensive publication record includes studies of behavioral problems in preschool children, mental health of children of alcoholic parents, risk factors for violence, HIV infection in adolescents and young adults, and international aspects of child and adolescent mental health.

Earls has served on many national committees, including the Advisory Council of the National Institute of Mental Health. Most recently, he chaired a panel of the Office of Technology Assessment that prepared a report on adolescent health for the U.S. Congress.

2 Talk on multi-cultural education

3 T cells yield secrets

4 Biomedical forum features RU fellow



Ruth Moses, voice mail administrator, is the editor of the Voice Mail Newsletter which debuted last month.

Furlaud named chair of American Express Company

Richard Furlaud, chairman of The Rockefeller University Board of Trustees, was elected non-executive chairman of American Express Company by the firm's board of directors on Monday. He will replace James D. Robinson III, who announced last week that he has resigned from his responsibilities at American Express effective Feb. 22.

"I am honored by the decision of American Express's Board," Furlaud said. "However, I want to emphasize that my new appointment will in no way diminish my commitment to The Rockefeller University, which remains a top priority for me."

Furlaud, who has been on The Rockefeller University Board of Trustees since 1976 and was elected chairman in 1990, was president of Bristol-Myers Squibb Company from 1989 to 1992 and chief executive officer of Squibb Corporation from 1968 to 1989.

He currently serves as chairman of the American Express Board's Compensation, Benefits, and Nominating Committee and as a director of Shearson Lehman Brothers, where he is a member of the Board's Finance Committee. In addition, Furlaud is a director of Bristol-Myers Squibb, Olin Corporation, and International Flavors & Fragrances, Inc.; trustee of the John M. Olin Foundation; and member of the Chase Manhattan Bank International Advisory Committee, Council on Foreign Relations, and Board of Overseers of Memorial Sloan-Kettering Cancer Center.



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Speaker to address issues in multicultural education

Leslie R. Williams, professor of early childhood education and chair of the Department of Curriculum and Teaching at Teachers College, Columbia University, will speak at The Rockefeller University on multicultural education, Wed., Feb. 10. The lecture is co-sponsored by The Rockefeller University Children's School and the Office of Public Affairs.

"Leslie Williams is an expert in the field of multicultural education and curriculum development," said Marjorie Goldsmith, director of the Children's School. "Her insights will undoubtedly interest many parents at the university. At the

Children's School, we have a very diverse group of children, many of whom have lived in more than one country and speak more than one language."

After completing her degree in education at Teachers College, Williams began a career in curriculum design in Alaska, where she participated in the creation of one of the first full-day Head Start programs. She traveled through several states as Head Start demonstration teacher, staff developer, and parent involvement specialist. Williams returned to Teachers College for advanced studies in early childhood education and then joined the faculty there.

As co-founder of the National All-Day Kindergarten Network, Williams is consulted by public and private schools throughout the Tri-state area and across the country. She is co-author of several books, including *ALERTA: A Multicultural, Bilingual Approach to Teaching Young Children*.

The lecture, to be held at 7:30 P.M. in Tower 301, is free and open to the Rockefeller community. Baby-sitting will be provided at the Children's School for children over the age of three, from 7:15 P.M. to 9:00 P.M. at a cost of \$3 per child. Call the Children's School, x8580, ahead of time to reserve a spot for baby-sitting.

Leibel named head of laboratory at RU Hospital

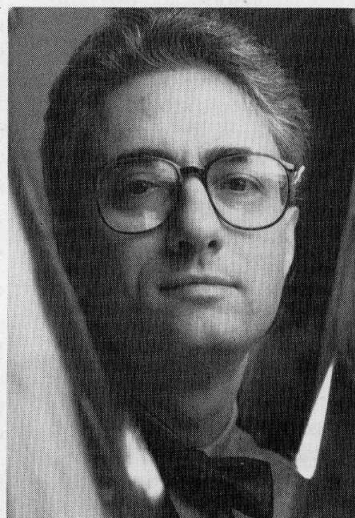
Associate Professor Rudolph Leibel has been named head of laboratory. He will work with Professor and Physician-in-Chief Jules Hirsch in the Hirsch-Leibel lab.

Leibel studies the relationship between food intake, energy expenditure, and adipose tissue in people and animals. Excess energy storage, or obesity, has been linked to a variety of disorders, including high blood pressure, heart disease, and diabetes. Leibel has been working with Associate Professor Jeffrey Friedman on the isolation and characterization of two mouse genes, *ob* (for obesity) and *db* (for diabetes) that are important in the signal system that regulates body weight. His work has recently extended to the identification of homologues of these genes in human families in which obesity is prominent. Leibel is also working on the identification of genes which predispose obese animals and humans to the development of diabetes.

At The Rockefeller University Hospital, Leibel and Hirsch are

conducting a large study of the effects of experimental weight change on energy metabolism in obese and normal-weight subjects. These studies are designed to identify the mechanisms by which body weight is regulated in humans. Leibel is also investigating the links between where people store fat (in the stomach area or on the hips, thighs, and buttocks) and their risk for disease.

A graduate of Colgate University (1963) and Albert Einstein College of Medicine (1967), Leibel taught pediatrics at Harvard University Medical School (1972-78), and has held hospital appointments at the Children's Hospital Medical Center (1972-78), Massachusetts General Hospital (1972-78), and Cambridge Hospital (1972-78). In addition to his appointments at The Rockefeller University, Leibel is associate professor of clinical pediatrics at Cornell University Medical College and associate attending pediatrician at The New York Hospital.



Rudolph Leibel, associate professor and head of lab.

Newsletter answers voice mail questions

(continued from page 1)

will be published every other month. Some of these issues may address other telecommunications topics as well. "New labs will undoubtedly have questions about the system, as will new voice mail subscribers and experienced users who want to try new AUDIX applications," she said. "I also want to use this newsletter to inform the campus of AT&T updates to The Rockefeller University system."

As voice mail administrator,

Moses ensures that people make the most of a sophisticated system. "Voice mail users will always have questions," she said. "They can call me any time. Now they can also turn to this newsletter for hints, short-cuts, and tips on trouble-shooting."

"I think that deep down people want to talk to a human voice," she continued. "Automated voices make people uncomfortable and intimidated."

For a copy of the telecommunications newsletter or information pertaining to voice mail, call

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T cell studies yield clues to development and disease

by Susan Blum

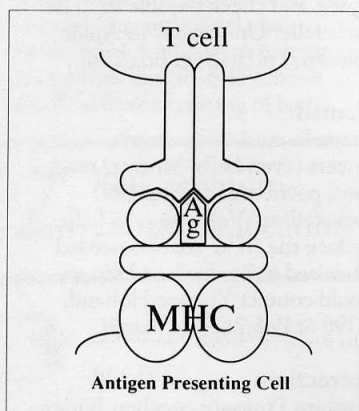
As the catastrophe of AIDS attests, humans cannot survive without properly-functioning T cells—the immune system cells that orchestrate the destruction of pathogenic invaders. But the critical importance of these cells is much better understood than the mechanisms by which they obtain—and maintain—their defensive capabilities.

It has been known for some time that in developing animals immature T cells undergo a process of selection. Cells able to mobilize attacks against the self are destroyed or inactivated, while those with the potential to defend against foreign pathogens are permitted to proliferate. Key molecular players in this selection process are the receptors that stud the T cell's surface, and the major histocompatibility (MHC) molecules, present on other cells, that present fragments of proteins, or antigens, to the T cell receptor.

When T cells are maturing during development, the only antigens available for presentation to T cell receptors are "self-antigens," fragments of proteins belonging to the body's own tissues. T cells that "see" no self-antigens, or that bind the ones they see too avidly, are destroyed or inactivated, thus ensuring that mature T cells will not mount an attack on the self. Only those T cells with receptors that bind self with the "proper" affinity are allowed to survive. Later in life, once the animal is born, the surviving T cells are able to respond to foreign antigens presented by the MHC molecules.

T cell development poses a contradiction

Though this much is understood



Left: T cells bind regular antigens (Ag) by means of a lock-and-key fit involving the antigen, the MHC molecule, and two components of the T cell receptor. **Right:** Superantigens are bound in a much less specific fashion, and so activate a much wider range of T cells.

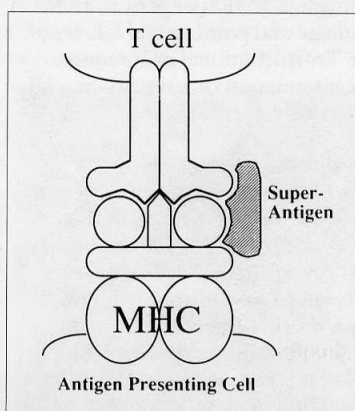
about T cell selection, its underlying mechanisms remain unknown. "Some developing T cells see self-antigen and live, while others see self-antigen and die. It's a very intriguing contradiction," says Rockefeller Assistant Professor Yongwon Choi. Choi, also an assistant investigator of Howard Hughes Medical Institute, is pursuing the cellular signaling events at the heart of this contradiction.

Complicating his search is the absence of good test-tube models for events taking place in developing animals. One way Choi circumvents this problem is to study other immune system phenomena that may shed light on T cell development. Ultimately, these studies may also result in a better understanding of diseases, such as cancer and AIDS, that involve the death or abnormal functioning of T cells.

As one part of his studies, Choi is investigating how helper T cells (a particular subset of T cells) interact with a class of antigens known as "superantigens." Rather than rousing one in 10,000 or 100,000 helper T cells, a superantigen goads 25 or 30 percent of them into action. Oddly enough, once the superantigen-stimulated T cells have proliferated, they sometimes subsequently become inactive or self-destruct through a cell death program known as apoptosis.

Superantigens bind in an unusual way

The first superantigens to be studied were the enterotoxins produced by *Staphylococcus aureus*. Among the pioneering researchers investigating these antigens were the researchers in whose lab Choi was a postdoc—Philippa Marrack and John Kappler of the National



Jewish Center for Immunology and Respiratory Medicine in Denver. In 1989, researchers in the lab, including Choi, found that superantigens are able to stimulate a large percentage of the T cell population by exploiting an unusual binding mechanism that requires far less specificity than the normal "lock-and-key" fit (see illustrations).

In other research in 1987, Kappler and Marrack had found that a certain strain of mice had a considerable "hole" in their T cell repertoire. These mice lacked a particular subset of T cells possessing a particular type of receptor. The scientists had postulated that such clonal deletion might be explained by the presentation of a self-superantigen to immature T cells during development. Choi, who had studied the Mouse Mammary Tumor Virus (MMTV) as a graduate student, conducted research in their lab showing that a MMTV gene did, in fact, encode a superantigen that could cause the clonal deletion.

MMTV is a retrovirus—a virus whose DNA copy can be incorporated into an animal's chromosomes and passed along to the next generation. As such, it is known as an "endogenous virus." Thus, in a developing animal, endogenous MMTV can cause clonal deletion if one of its genes codes for a protein that acts as a self-superantigen. But if an MMTV infects a mouse after it is born, as an "exogenous" virus, the superantigen encoded by one of its genes can cause the massive T cell proliferation characteristic of other superantigens. Like those superantigens, MMTV can also cause subsequent T cell inactivation or death.

The fact that MMTV is a retrovirus has led Choi to examine other retroviruses to see if they, too, encode superantigens. (Evolutionary considerations suggest this might be likely, for the initial T cell proliferation provoked by superantigens gives the retrovirus many additional T cells to infect.) One such retrovirus under study in his lab is HTLV-I, which infects helper T cells and causes leukemia. Another is HIV, the causative agent of AIDS. HIV's major targets are helper T cells, and one of the disease's characteristic late-stage symptoms is a massive depletion of this type of immune-system cell.

Does HIV encode a superantigen?

According to Choi, the evidence



Assistant Professor
Yongwon Choi studies T cells.

that HIV encodes a superantigen is suggestive, but mixed. Far more research is required to settle the question. But should it turn out that HIV does not itself encode a superantigen, these immune-system super-stimulators may still be involved in AIDS. "Many of the viruses already present in the body may have 'silent' superantigens that are only produced when HIV is also present," says Choi. These activated superantigens could contribute to the T cell depletion seen in AIDS.

Whatever the ultimate role of superantigens may turn out to be, Choi is hopeful that his fundamental interest in T cell development and his studies of AIDS will prove mutually reinforcing. For instance, his overlapping interests may help solve a puzzle that challenges many AIDS researchers. Though the issue is currently being debated, many researchers (Choi among them) believe that only a small proportion of helper T cells are infected with HIV. Why, then, do so many helper T cells ultimately die?

Choi points out, "If you present antigen to helper T cells from people who are HIV negative, the cells that are primed to recognize the antigen proliferate. But if you do the same thing with the uninfected T cells of people who are HIV positive, the cells primed to recognize the antigen die, rather than proliferate." This paradox recalls the question that intrigues Choi about T cell maturation during development: Why do some T cells see self-antigen and live, while others see self-antigen and die? The phenomena look to Choi like two sides of the same coin. The challenge is to figure out how the coin is minted.

Biomedical forum features RU fellow

How and why have the major causes of death in the United States changed since the beginning of the century? This was the question that Jesse Ausubel, fellow in science and public policy at The Rockefeller University and director of studies for the Carnegie Commission on Science, Technology, and Government, addressed at the Tri-Institutional Biomedical Forum Tuesday.

Ausubel's lecture was the fifth in the new series of lectures on biomedical topics, The Tri-Institutional Biomedical Forum, organized by Zanzil Cohn, professor and vice president for medical affairs.

"I started the Tri-Institutional Biomedical Forum last fall to provide opportunities for Rockefeller University researchers to meet and share their interests in medical and clinical research with their New York City colleagues," Cohn said. "The forum begins with informal discussions and sherry, and concludes with a 30-minute lecture."

In his lecture Tuesday, Ausubel used his analysis of statistics from the U.S. government to argue that the human environment has had a major impact on mortality rates since 1900.

The growth of modern sanitation

and better ventilated buildings have cut down the incidence of infectious diseases, Ausubel said. At the turn of the century, waterborne diseases such as typhoid and cholera were major killers. By 1940, the combination of water filtration, chlorination, and sewage treatment had almost eliminated them.

Similarly, air-borne infectious diseases such as tuberculosis and influenza were leading causes of death in 1900. By 1910, they had begun to decline. In the next 30 years, they receded as a cause of death by an order of magnitude. Ausubel attributed the decline primarily to improvements in the built environment—such as the replacement of tenements and sweatshops with more spacious and better ventilated homes and workplaces. Public health measures, new medical treatments, and reduced exposure also contributed.

While individuals were less likely to die from infectious disease as the century progressed, they were more likely to die from cardiovascular disease. "If infections were the killers of reckless urbanization, cardiovascular diseases are the killers of modernization," Ausubel said. "While getting out of the subway and into your Ford may



Jesse Ausubel (right), fellow in science and public policy, speaks with Zanzil Cohn, professor and vice president for medical affairs, before Ausubel's talk, entitled "Death and the Human Environment: America in the 20th Century," on Tuesday.

have reduced the chance of influenza, it increased the risk of heart disease."

Cardiovascular disease, which has been the leading killer since about 1920, is gradually being challenged for first place by cancer. Ausubel predicted that, if current trends continue, cancer will surpass cardiovascular disease as the leading cause of death by 2010. "The major causes of current forms of cancer, particularly tobacco smoke and dietary imbalances, can be vastly reduced," he said. "But if cancer is a degenerative disease of aging, one form of cancer will succeed another, assuring it a long stay at the top of the most wanted list."

A discussion of the impact of scientific discoveries, topics for further research, and statistical analysis followed the lecture. Copies of the lecture are available from Ausubel, x7917.

The Tri-Institutional Biomedical Forum is usually held at 5:00 P.M. on the first Tuesday of every month in Abby Aldrich Rockefeller Hall. Upcoming speakers in the series include Edward Ahrens, professor emeritus; Alexander Bearn, trustee, adjunct professor, and visiting physician; and David Rogers, Walsh McDermott university professor of medicine at The New York Hospital-Cornell Medical Center.

Potpourri

Tri-Institutional Noon Recital
Award-winning pianist Jean-Efflam Bavouzet will play works by Haydn, Bartok and Liszt at the Tri-Institutional Noon Recital today (Feb. 5) in Caspary Auditorium. Admission is free. All are welcome.

African violet, bake sales
The Children's School is holding a

Valentine Bake Sale and African Violet Sale in Tower Lobby from 8:30 A.M. to 3:30 P.M. today.

Sunday film

The Night of The Hunter, starring Robert Mitchum, Shelley Winters, and Lillian Gish, tells the story of a psychopathic preacher searching for hidden money. The film will be shown in Caspary Auditorium, on Sun., Feb. 7, at 7:30 P.M.

Benefit

The Children's Orchestra Society will hold an event in honor of its Artistic Board of Directors—Emanuel Ax, Isidore Cohen, Yo-Yo Ma, and Michael Tree, as well as a new member of the board, Janet Fisher—on Tues., Feb. 9, at 7:00 P.M. on the 17th floor of Tower. It will include a musical presentation by select chamber groups from the society. Tickets are \$75 each. Proceeds will benefit the society's scholarship fund and The Rockefeller University Children's School. Call Gigi Ferrante, (516) 674-3046, for more information.

Rockefeller University concert
The Lafayette String Quartet will

perform works by Haydn, Bartok, and Beethoven at 8:00 P.M. on Wed., Feb. 10, in Caspary Auditorium. The four women of the Lafayette String Quartet are Artists-in-Residence at the Canadian University of Victoria School of Music. They will use matched Amati instruments on loan from the University of Saskatchewan at Saskatoon. Admission is \$17 per person, \$7 for graduate and postdoctoral fellows of the Tri-Institutional community. For information or reservations, call Cathy Rogers, x8971.

Computer course

The Electronics Lab is offering a 10-week course, "Computers in the Laboratory, Part 2, Instrumentation and Applications." It will focus on computer-based instrumentation, experimental control, data acquisition, and analysis. An organizational meeting will be held Fri., Feb. 12, from 10:30 to 11:30 A.M. in Caspary 1B. For further information, contact Gordon Silverman, x8611 or Box 297.

Dinner dance

Tickets are available for the univer-

sity's Mid-Winter Dinner Dance, Fri., Feb. 19 at 8:00 P.M. in Abby Aldrich Rockefeller Hall. Tickets, \$25 each or \$40 for those who wish to help support the event, are available at locations around campus, including the Faculty Club, Media Resources, the Personnel Office, the Cashier's Office, and the Deans' Office (for students). Tickets can also be ordered by mail by sending a request and check payable to "The Rockefeller University" to Angie Dohnert, Purchasing, Box 258.

Wanted

Wanted: musicians, singers, dancers (even belly-dancers), magicians, poets, etc., for the 1993 Rockefellerlies. Volunteers to help produce the show are also needed. Interested individuals and groups should contact Yvonne Holland, x8396 or Box 262, for details.

Correction

Assistant Professor Stephen Burley was omitted from the list of members of the Physics Search Committee in last week's issue of *News&Notes*. Associate Professor John Kuriyan was incorrectly included in the same list.



The Lafayette String Quartet is featured in the evening concert on Wed., Feb. 10.