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Physicist and writer Freeman Dyson to receive Rockefeller University's Lewis Thomas Prize

Mathematical physicist and critically acclaimed author Freeman Dyson will receive the 1996 Lewis Thomas Prize, which honors scientists for their artistic achievements, from The Rockefeller University.

"The Lewis Thomas Prize recognizes the scientist whose voice and vision can tell us of science's esthetic and philosophical dimensions, who give us not merely new information but cause for reflection, even revelation, as in a poem or painting," explained Torsten N. Wiesel, president of the university.

Dyson, professor emeritus of physics at the Institute for

Advanced Study in Princeton, N.J., will receive the prize from Wiesel during ceremonies at the university beginning at 5:30 P.M. Wed., May 22. Dyson also will discuss "Samuel Gompers and William Blake."

Dyson, recipient of the 1981 Wolf Prize in physics and many other honors, is the fourth person to receive the Lewis Thomas Prize, established in 1993 by the university's Board of Trustees. The late Lewis Thomas, an award-winning author and scientist who served in many positions including dean of the New York University School of Medicine and president and chancellor of the Memorial Sloan-Kettering Cancer Center, received the prize in 1993. In 1994, the university presented the prize to Nobel laureate, molecular geneticist, and author François Jacob. In 1995, Abraham Pais, professor emeritus at Rockefeller and an eminent physicist and science writer, received the prize.

"Dyson's writings are celebrated for their intellectual range and stylistic elegance," said Wiesel. Of Dyson's 1979 autobiography, *Disturbing the Universe*, *The New Yorker* wrote: "Everywhere enriched by the work of poets, it stands as the deepest and most readable account of the personal choices, influences, and interior guides of a productive scientist yet to see print." In addition to numerous articles for publications such as *The New Yorker* and *Scientific American*, Dyson wrote *Weapons and Hope*, an examination of nuclear weapons, in 1984, *Origins of Life* in 1986, *Infinite in All Directions* in 1988, and *From Eros to Gaia*, an anthology of his lectures and magazine articles, in 1992.

Born in 1923 in Crowthorne, Berkshire, England, Dyson received his bachelor of arts degree in mathematics from the University of Cambridge in 1945. He completed

See **Dyson**, page 2

Health a way of life for staff in Employee Health Office

On average, 120 people drop by each week at the Employee Health Office (EHO), a facility that provides university employees with health services, located in Hospital 118.

"We do everything from what I call simple patch-ups, like giving aspirin or decongestant, to arranging for blood work or X-rays on

campus, to facilitating an emergency response," said Mary Brust, supervisor. "Most people on campus know about us, but every now and then someone walks in and says, 'I've been here two years and never knew you were here.'"

One of the most important roles

See **Health**, page 4

RU scientist talks on neurobiology of eating disorders



Sarah Leibowitz studies the physiological effects of brain hormones on obesity, type II diabetes, and eating disorders.

Sarah F. Leibowitz, adjunct associate professor at RU, discusses "Neurobiology of Obesity and Eating Disorders" at the Friday lecture today (May 10).

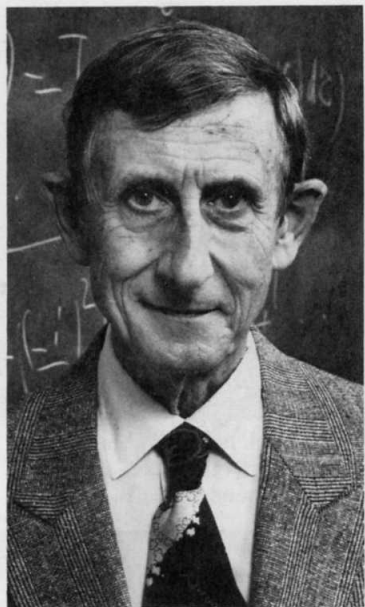
Leibowitz studies the neurobiology of nutrient balance and body weight regulation. She and her colleagues focus on peptides that stimulate appetite and weight gain. These peptides, neuropeptide Y and galanin, act in the hypothalamus, the brain's command post for energy intake and expenditure.

Using the tools of biochemistry and molecular biology, Leibowitz and her co-workers identified and characterized the actions of these peptides on eating behavior and endocrine systems. Work is now under way in her laboratory to determine the physiological role of these brain chemicals and circulating hormones in obesity, type II diabetes, and eating disorders.

"Sarah Leibowitz's work is revealing the important role that behaviors such as dietary choice have in altering the brain chemistry to favor a path of increased fat consumption and obesity," said Professor Bruce McEwen, who hosts today's lecture. "Behavior and brain neurochemicals and circulating hormones, such as leptin and insulin are all involved in body weight regulation."

See **Leibowitz**, page

Randall Hugdorn



Freeman Dyson, a member of the U. S. National Academy of Sciences since 1964, has won numerous awards for his science and his writing.

2 Immune stimulus

3 Cocaine drain

4 All the sweet stuff



Employee Health Office staff are, left to right, Mary Brust, supervisor, Kim Acquaviva, secretary, and Aurea Tuason, staff nurse.

Honorary society stimulates interest in immune system

by Jahanara Ali



Jeffrey Ravetch opened and closed his Kunkel Society lecture by connecting his work on the immune system with the work of Henry Kunkel.

The Henry G. Kunkel Society, which honors the Rockefeller immunologist who worked here for nearly four decades, held its biennial meeting at the university last week. Jeffrey Ravetch, a Rockefeller University alumnus who will rejoin the university as a full professor in the fall, gave the keynote address on "Fc Receptors: Activators and Inhibitors of Inflammation."

Prefacing the lecture with a tribute to Kunkel (1916–1983), society president Alexander Bearn said, "Kunkel singlehandedly developed the field of clinical immunology. The greatest pleasure of his life was to help young and inexperienced investigators. He was extremely modest, and rejoiced in the success of his students."

Ralph Steinman, Henry G. Kunkel Professor, introduced Ravetch, joking that "One reason for Jeff to give this lecture is that he is now acting like an antibody molecule—with one end at Sloan and one at RU as he establishes his lab." On a serious note, Steinman added, "For Kunkel, patients and clinical disease provided the incisive method. Jeff uses genetics as the incisive method."

Ravetch began his talk with one of the paradoxes of immunology as described on a slide Kunkel used in a 1971 lecture in Caspary. It read: "Definition of the etiological process of autoimmune diseases is very difficult. There are patients with high levels of autoimmune antibodies in their systems with very little disease; and there are patients with very low levels of autoantibodies, with severe disease." Ravetch described his use of

genetic methods to investigate this seeming paradox, to understand why some antibodies trigger disease and others are benign.

Ravetch said that the common thread in many inflammatory diseases is the Fc receptor (FcR). FcRs are membrane-spanning molecules present on a number of cells, such as macrophages, mast cells, and natural killer cells. When activated, they mediate the inflammatory response. Encoded by a multigene family clustered on chromosome 1 in humans, FcRs have a characteristic fold of the antibody molecule. FcRs' extracellular domain, termed the alpha chain, recognizes ligands. Different alpha chains differentiate between classes of antibody ligands, like IgE or IgG. The intracellular portion, called the gamma chain, is involved in intracellular signaling.

When IgE binds to the FcRs on mast cells, the cells undergo massive degranulation, leading to the allergic reaction, called anaphylactic response. In order to determine the role of FcRs in the allergic response, Ravetch and colleagues knocked out the gamma chain of the FcR in mice, generating mast cells with no IgE binding sites. They discovered that IgE is the single mediator of the type I anaphylactic response.

Ravetch also discussed rheumatoid arthritis and systemic lupus as paradigmatic autoimmune diseases. He explained the model for immune complex tissue injury, whereby antigen and antibody form an immune complex, which activates the complement system and causes neutrophil chemotaxis and mast cell degranulation.

Again using mice with the

gamma chain knocked out, as well as mice with a part of their complement system knocked out, he and his colleagues found that type I and type III inflammatory responses use the same pathway—the FcR pathway. They found that the cytoplasmic domain sequences, the gamma chain, were necessary and sufficient to mediate the inhibition of the antibody response. "The different responses in gamma-negative mice to IgMs and IgGs, with similar responses to IgEs and IgGs, give credence to Henry's observation that all antibodies are not equal," Ravetch concluded.

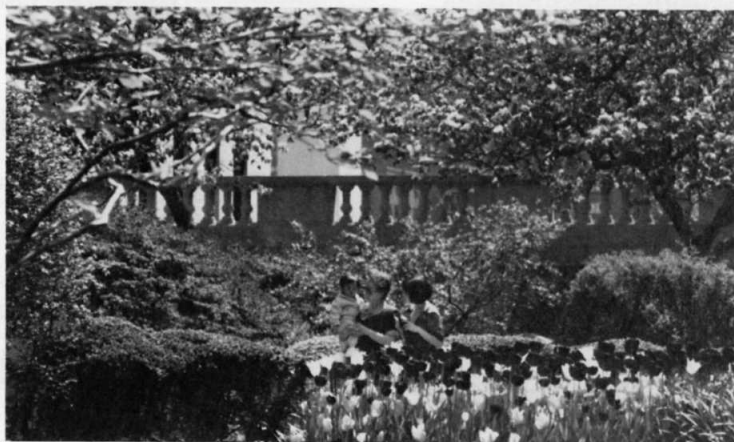
Kunkel spent his scientific career at Rockefeller, from 1945 until 1983. He emphasized clinical disease as the starting point for science, making numerous contributions to understanding autoimmune diseases, lymphoid malignan-

cies, and immune deficiency disorders. Among his internationally recognized discoveries were the elucidation of the chain structure of gamma globulin and his recognition that immunoglobulins are specialized molecules that can recognize specific antigens.

The Kunkel Society, initially formed by Kunkel's students and now with 120 members, "aims to encourage talented young physicians and scientists to become accomplished clinical investigators, particularly in immunology and related fields, as exemplified by the scientific life of Henry Kunkel," said Associate Professor John Zabriskie, a founding member who organized this year's meeting.

The society met the next day (Fri., May 3) to conduct business and hear lectures by an additional 16 immunologists.

Surrounded



At the university's annual azalea festival, held Sat., May 4 and Sun., May 5, blooming tulips and hawthorn trees engulfed visitors strolling between Flexner and Founder's halls.

Dyson

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fellowships at Cambridge's Trinity College from 1946 to 1947, at Cornell University in 1947, and at the University of Birmingham from 1949 to 1951. He returned to Cornell to become a professor of physics in 1951, leaving in 1953 to join the Institute for Advanced Study.

Dyson is a fellow of the Royal Society, a member of the U.S. National Academy of Sciences, a corresponding member of the Bavarian Academy of Sciences, an honorary fellow of Trinity College, and an Associé Etranger de l'Académie des Sciences.

Among his numerous awards and honors, Dyson received the Enrico Fermi Award from the U.S. Department of Energy, the Wright Prize from Harvey Mudd College,

the Oersted Medal from the American Association of Physics Teachers, the Matteucci Medica from the Accademia Nazionale delle Scienze dei Quaranta (Italy), the Britannica Award, the Phi Beta Kappa Award in Science for *Infinite in All Directions*, Gemant Award from the American Institute of Physics, the National Book Critics Circle Award for nonfiction, the Max Planck Medal of the German Physical Society, the Hughes Medal of the Royal Society (England), the Lorentz Medal of the Royal Netherlands Academy, and the Danny Heineman Prize of the American Institute of Physics.

The ceremony takes place in Caspary Auditorium, followed by a reception. All are welcome.

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Messing with your head

Researchers find that cocaine affects endorphin gene in the brain

by Marion E. Glick

Deep within a small region of the midbrain called the substantia nigra, neurons make the master molecule dopamine, a neurotransmitter that has a hand in nearly every job the brain oversees, from feeling complex emotions such as joy to receiving messages about basic facts like pain. Substantia nigra neurons end in another brain region, the caudate-putamen, where they release the neurotransmitter.

As part of nature's recycling program, dopamine is later transported back into the nerve endings for repacking and future use. But cocaine interferes in this dopamine feedback loop. The effects of the addictive drug result, in part, from altering the activity of a gene in the brain, according to a paper published by members of Professor Mary Jeanne Kreek's Laboratory of the Biology of Addictive Diseases in the May issue of *Molecular Brain Research*.

"Our study is the first report that any drug of abuse, in this case cocaine, alters the expression of a gene encoding an opioid receptor in the brain," said Kreek.

Modeling an engine of destruction

Based on rat studies, Kreek and her colleagues found that cocaine turns down the activity of a gene containing instructions to make the kappa opiate receptor (KOR), a molecule in the substantia nigra

that is involved in the chemistry of pain control and emotion. The resulting decrease in receptors may interfere with how the nerve cells in the region communicate.

"Fundamental research like Dr. Kreek's helps us to learn more about the addictive nature of cocaine and moves us even closer to identifying effective treatment to help the thousands of individuals affected by cocaine addiction," said Alan I. Leshner, director of the National Institute on Drug Abuse (NIDA) of the National Institutes of Health, the agency that funded the study.

In the National Household Survey on Drug Abuse, the U.S. Substance Abuse and Mental Health Services Administration determined that 1.4 million Americans, aged 12 or older, use cocaine, and of those, 640,000 were addicted and used the drug weekly.

In the current study, the scientists gave the rats injections of cocaine following a pattern that mimics human addiction without overdosing the rodents. Kreek developed this so-called "binge" model in 1988. Following the model, the rats receive 45 milligrams of the drug per kilogram of their weight daily for 14 days. The drug is given in equal doses one hour apart for three hours each day. For comparison, some rats receive injections of salt solution.

When the rats received the drug, expression of the KOR gene

"Knowing how cocaine affects the brain's chemistry may eventually be useful in developing a treatment for cocaine addiction that can block some of its endorphinlike effects without interfering with all of the body's normally occurring endorphins, such as dynorphin and its receptor, the kappa opiate receptor. We need those endorphins because they help us feel normal and cope with pain and stress and play a role in our use of energy," said Kreek.

in nerve cells in the substantia nigra decreased. However, the gene's activity remained unchanged in the nerve cells of the caudate-putamen.

In the presence of cocaine, an absence of neurotransmitter

These two brain regions are "hardwired" together by the nerves that communicate using chemicals, particularly dopamine, which is

needed for signals involving movement, and small proteins such as dynorphin, which binds to KOR. Dynorphin belongs to the endorphin family of proteins that can numb pain, create feelings of euphoria, or increase energy, which cocaine does as well.

When the drug decreases the expression of KOR genes in the substantia nigra, not enough KOR may be available to respond to the feedback signals. Dopamine production then continues for a short time and accumulates in the caudate-putamen, but the amount of dopamine eventually plateaus. When the cocaine later wears off, the addict may feel badly because not enough dopamine is available for normal cell functions.

"From our new data, we now know that cocaine's effects on dopamine also change the KOR gene activity, thus altering the intricate process of neuronal communication in the midbrain," explained Rudolph Spangler, research associate in Kreek's laboratory and first author of the paper.

Finding dependence, and independence

At the same time, as previously shown by studies in Kreek's laboratory, the drug also increases the expression of the gene that makes dynorphin in the caudate-putamen. Kreek and her colleagues are conducting further studies to determine if the increase in dynorphin gene expression is related to the decrease in the KOR gene expression.

"Knowing how cocaine affects the brain's chemistry may eventually be useful in developing a treatment for cocaine addiction that can block some of its endorphinlike effects without interfering with all of the body's normally occurring endorphins, such as dynorphin and its receptor, the kappa opiate receptor. We need those endorphins because they help us feel normal and cope with pain and stress and play a role in our use of energy," said Kreek, who also directs the Treatment of Addiction: Biological Correlates NIH-NIDA Research Center at Rockefeller, one of a few such centers in the United States established by NIDA.

Coauthors of the paper are senior research associate Ann Ho, postdoctoral fellow Yan Zhou, assistant for research Christopher E. Maggos, and research associate Vadim Yufarov.



Members of the lab of Professor Mary Jeanne Kreek (left) published findings on cocaine's disruption of neurotransmitters in the May issue of *Molecular Brain Research*. Research associate Rudolph Spangler is first author of the paper.

Potpourri

Courtesy of the artist



Pianist Andreas Haefliger will perform works by Schubert and Liszt at the Tri-Institutional Noon Recital today (May 10). The concert, to be held in Caspary Auditorium at noon, is free. All are welcome.

In memoriam

The university community mourns the passing of Lillie Mae Curry, who died of cancer Fri., Apr. 26 at age 66. Curry, who retired from Rockefeller as an assistant supervisor of Custodial Services in March, had 43 years of service with Rockefeller. Her son, Isaiah Curry, is waste handler in the Laboratory Safety Department. The funeral took place Fri., May 3.

Mother's Day sale

A bake and flower sale to benefit the Rockefeller Children's School and Infant-Toddler Center takes place today (May 10) from 8:30 A.M. to 2:30 P.M. in the Weiss Lobby.

Seminar

Suzanne M. Leal, research associate in RU's new Laboratory of Statistical Genetics (Ott lab), will discuss "Strategies for Mapping Nonsyndromic Hearing Loss Genes" today (May 10) at 11:00 A.M. in Weiss 301.

Spraying

Trees and shrubs on campus will be sprayed Sat., May 11 from 6:00 A.M. to noon. The Grounds Department advises that people on campus stay out of direct contact of the spray, close windows, turn off air conditioners, and keep pets inside. The rain date is Sun., May 12. For more information, call James Sullivan, x8801.

City food drive

On behalf of the Mother's Day-Father's Day Healthy Baby Food Drive organized by City Harvest, the Rockefeller Children's School (CS) and Infant-Toddler Center (ITC) solicits donations of infant formula, baby foods, toddler and junior food, 100 percent juice packs, pasta, rice products, and Pedialyte. Bring donations to the ITC, first floor of Sophie Frick, or the CS, ground floor of Graduate Students Residence, throughout the week beginning Mon., May 13. For more information, call Marjorie Goldsmith, x8580.

Clinical Research Seminar

Alexandre LeBeaut, of the Schering-Plough Research Institute, discusses "Interleukin-10 and Inflammatory Bowel Disease" at the Clinical Research Seminar Wed., May 15 at noon in Nurses Residence 110B.

Barbecue

The Faculty and Students Club will hold its 11th annual barbecue—rain or shine—Fri., June 7 at 5:30 P.M. on the Faculty Club Lawn. Tickets, \$12 in advance (\$14 at the door), will go on sale Mon., May 13 at the Faculty and Students Club, B floor of Abby Aldrich Rockefeller Hall, and in the Purchasing Office, Plaza A5. Contact Angie Dohnert, x8201, for more information.

Award

Joshua Lederberg, Rockefeller

University president emeritus, received the John Stearns Award for Lifetime Achievement in Medicine from the New York Academy of Medicine at the 1999 Spring Stated Meeting and Commencement of the 150th Celebration of the Academy Tues., Apr. 30. Previous RU recipients of the Stearns award include the late adjunct professor Lewis Thomas and Professor Emeritus Maclyn McCarty.

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.

Eudora for Mac and Windows:

Tues., May 14, 10:00 A.M. to noon;

Eudora for Mac and Windows:

Thurs., May 16, 10:00 A.M. to noon;

Intro to the Mac:

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

Intro to Windows:

Thurs., May 23, 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.

Health office offers referrals, lectures, and a place to lie down Leibowitz

(continued from page 1)

of the EHO is taking calls from sick employees in the mornings. "We do a lot of that. By law, we need to know who is out and why, although we keep the reasons confidential. When someone sends us a doctor's note about the illness, we are able to confirm for supervisors that we got such a note. But we never divulge its contents," said Brust. "If an illness extends into disability, or in workman's compensation cases, the EHO has records of time out," said Brust.

The EHO mission encompasses preventive care as well. They offer screening programs conducted in accord with current medical guidelines. Announced in *News&Notes*, annual screenings are for skin, prostate, and breast cancer and for diabetes and high cholesterol. Staff travel upstate to the Rockefeller Archive Center and the Field Research Center to conduct some screenings, and at the latter, testing

for Lyme disease is routine.

The office dispenses flu shots in season and administers tetanus and hepatitis B vaccinations year round. "Everyone who works with blood products should get the three hepatitis B shots," admonished staff nurse Aurea Tuason. Office staff also routinely check blood pressure for several dozen people.

Screenings, shots, patch-ups, and paperwork for disability claims are all free EHO services, as is assistance in locating doctors and specialists. If an employee's doctor wishes him or her to undergo blood work or X-rays, the EHO can arrange for these on site at a

reduced rate. "It saves the employee a trip off campus. Like much of what we do, we want people back at work in good shape as quickly as possible," said Brust.

Health awareness is another concern at the EHO. Staff help people find answers to any and all health questions. The EHO lecture series, now in its second year, covers topics that range from allergies to breast cancer to cardiovascular disease. At the next lecture, timed to precede the summer vacation season, Warren Johnson, professor of medicine and clinical public health at Cornell University Medical College, will give advice on "Staying Healthy at Home and Abroad," (Thurs., May 16, in Nurses Residence 110B at noon).

A low tech but essential bit of the EHO's armamentarium is its beds. "Sometimes, an employee needs to just lie down, to rest out a headache or a bout of nausea," said Tuason. "We're here for that, too."

In a medical emergency,
employees should dial
x1111,
24 hours a day.

(continued from page 1)

Leibowitz received her doctorate degree from New York University in 1968. She joined the university as a postdoc and guest investigator in 1968. In 1970 she became an assistant professor. She was promoted to associate professor in 1978 and became adjunct associate professor in 1984. From 1977 to 1979 she was an Alfred P. Sloan Foundation fellow.

Leibowitz is a member of the Society for Neuroscience, the New York Academy of Sciences and the American Association for the Advancement of Science. She is a fellow of the International Behavioral Neuroscience Society and the American Psychological Society and author or coauthor of more than 200 publications.

The lecture will be held at 3:00 P.M. in Caspary Auditorium and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Loun. All are welcome.