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The Rockefeller University

news&notes

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Panel discusses urban health crisis

The Rockefeller University Council held its spring meeting on "Urban Health Crises: AIDS, Tuberculosis, and Drug Addiction" Wednesday. Speakers included *(from left to right)* Professor Emeritus Vincent Dole, New York City Commissioner of Health Margaret Hamburg, Associate Professor Mary Jeanne Kreek, and Professor and V.P. for Medical Affairs Zanvil Cohn. The talks will be covered in an upcoming issue of *News&Notes*.

Festival to highlight campus blossoms

In celebration of the arrival of spring, The Rockefeller University is hosting its first Azalea Festival, featuring lectures and tours of the landscaped grounds in conjunction with The New York Botanical Garden.

"We have such a wonderful campus, an oasis of greenery in the middle of New York City," said Ingrid Reed, vice president for public affairs and corporate secretary. "The university will open its gates during the azalea festival to share its botanical riches with the public. The event will also give the university community an opportunity to learn more about the campus we enjoy every day."

On Fri., May 14 , staff of The New York Botanical Garden will give a guided tour of the grounds for the university community. The tour, beginning at 1:00 P.M. on the front steps of the Hospital, will focus on the banks of azaleas that give the campus its springtime brilliance as well as on other points of

*See **Azalea**, page 2*

Lecture to feature RU clinical researcher

Gilla Kaplan, associate professor in the Laboratory of Cellular Physiology and Immunology, will speak on "The Role of Cytokines in Mycobacterial Infection" at the Friday lecture today (May 7).

In her early studies of patients with leprosy, Kaplan found that cytokines, immunological hormones, regulate the inflammatory response found in leprosy by influencing the production of a substance called Tumor Necrosis Factor α (TNFα). According to Kaplan, administration of recombinant cytokines stimulates an overproduction of TNFα in patients infected with *Mycobacterium lepry*—the organism that causes leprosy. Excessive levels of TNFα are responsible for the toxic symptoms of this and other mycobacterial diseases, namely, wasting and fever. Kaplan and her colleagues have recently shown that thalidomide, the drug of choice for treatment of the inflammatory symptoms of leprosy, selectively inhibits TNFα and TNFα-induced toxicities.

"We have reason to think that in addition to alleviating these TNFα-induced symptoms, thalidomide may prevent activation of HIV-1 (the virus that causes AIDS) from progressing from the latent phase into the more productive, free virus phase—a process also controlled by TNFα. This drug seems to have tremendous therapeutic potential."

Associate Professor Gilla Kaplan studies immunological hormones called cytokines in patients with leprosy, TB, and AIDS.

After receiving a B.S. from the Hebrew University of Jerusalem in 1971, Kaplan attended the University of Tromso, Norway, where she received a Master's degree equivalent in 1975 and a Ph.D. in 1977. Kaplan first worked at Rockefeller from 1977 to 1979 as a postdoctoral fellow in the Cohn laboratory. She then worked in the Department of Morphology at the University of Tromso, before returning to Rockefeller in 1983.

Kaplan has served on a number of international committees, including the Leprosy Panel of the U.S.-Japan Cooperative Medical Sciences Program, and her research has led to collaborations in Brazil, the Philippines, and Thailand, to name a few.

A fellow of the Norwegian Research Council for Sciences and the Humanities (1979-80), the Norwegian Cancer Society (1980-82), and the Heiser Program for Research in Leprosy (1983-85), Kaplan is a member of the Harvey Society, the New York Academy of Sciences, the British Society for Immunology, and the Nordik Society for Cellular Research.

The lecture, which is free and open to the public, will be held at 3:45 P.M. in Caspary Auditorium, preceded by tea at 3:15 P.M.

RU to close full week at year's end

The university will be closed during the entire week of Dec. 27 to 31, 1993, for the Christmas and New Year's holidays, the Personnel Office announced this week.

Traditionally, the university allots a total of four days over the course of two weeks for Christmas and New Year's, but this year these two holidays both fall on Saturdays. As a result, the senior officers of the university decided to add a day to the holiday schedule and to close the university for a complete week.

"We hope that this decision, made and announced early, will allow many in the community to plan for the extended break in ways that will be meaningful for them and their families," said Virginia Huffman, director of Personnel. "The university may also realize some modest savings in expenses."

This revised holiday schedule applies to this calendar year only. As with all holidays, the workload in some laboratories and departments may require the attendance of selected employees. Any questions pertaining to these arrangements may be directed to Personnel, x8300.

In tribute to RU scientist, Kunkel Lecture features AIDS researcher

The Kunkel Society hosted a lecture by David Ho, head of the Aaron Diamond Research Center and co-director of the AIDS unit at The New York Hospital, at The Rockefeller University last week.

"Those who knew Henry Kunkel, who was at Rockefeller for his entire career from 1945 to 1983, remember that he emphasized clinical disease as the starting point for good science," said Professor and Senior Physician Ralph Steinman in introducing the lecture. "Over and over, he would look at a disease and come up with an important piece of immunology. It was with that in mind that the Kunkel Society selected David Ho as this year's Kunkel lecturer."

Ho, educated at the California Institute of Technology and Harvard Medical School, has made many incisive contributions to research on HIV, the virus that causes AIDS, using clinical disease as the springboard for scientific investigation. Ho was at the forefront of identifying HIV in the nervous system; he was one of the first to show that the virus could be grown in monocytes; he also described the initial, acute stage of HIV infection.

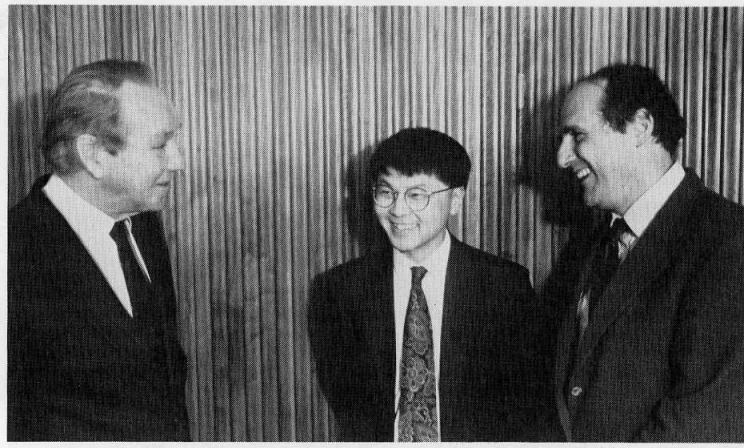
Ho devoted much of his lecture to a discussion of the acute phase of HIV infection, during which the immune system responds with relative effectiveness to reduce the amount of HIV in the blood. Studies by Ho and his colleagues have found that in the acute phase, neutralizing antibodies—proteins produced by B cells—do not appear to play a significant role in immune-system response. On the other hand, Ho implicated cytotoxic T lymphocytes, which kill infected cells directly, in this process.

Ho also described the characteristics of the virus population in newly-infected individuals. Unlike the varied viral population found in the partners who infected them, the HIV population of newly-infected persons is homogeneous. Most of the viruses have a preference for infecting a kind of immune cell called a macrophage. However, these strains of virus do not induce the formation of syncytia—large, multinucleated clusters of T cells.

Ho said the characteristics of the HIV population in early-stage disease may explain why the AIDS epidemic is not speeding up, since it is syncytia-forming viruses that hasten the dramatic depletion of T cells that is the hallmark of full-blown AIDS. He added that a greater understanding of the "profile" of viruses that prevail during early-stage disease should be helpful in designing better vaccines to prevent infection.

The Kunkel Society, which now has over 100 members, was formed in the mid-1980s by people who knew or worked with Henry Kunkel (1926-1983), senior physician and the first Abby Rockefeller Mauzé Professor at The Rockefeller University. Members meet every other year to host a prominent lecturer, listen to each others' presentations, and catch up on old friendships. The speakers at this year's meeting, organized by Associate Professor John Zabriskie, included Professor and Vice President for Medical Affairs Zanvil Cohn, Associate Professor Gilla Kaplan, and Assistant Professor Nina Bhardwaj. Professor Emeritus Edward H. Ahrens spoke at the society's dinner.

Kunkel, who was educated at Princeton University and The Johns Hopkins School of Medicine, is perhaps best known for his pioneering studies on immunoglobulins, a class of proteins that include all known antibodies. His recognition that myeloma proteins could be used a model for the study of normal immunoglobulins had a global impact on investigations of the structure, function, and inheritance of these molecules. His elucidation of the chain structure of gamma globulin and his recognition that immunoglobulins are exquisitely specialized molecules that can recognize specific antigens were internationally recognized discoveries. In addition, Kunkel's laboratory made major contributions to understanding autoimmune diseases, lymphoid malignancies, and immune deficiency disorders.



Professor and Senior Physician Ralph Steinman *(left)* and Associate Professor John Zabriskie *(right)* chat with this year's Kunkel lecturer, David Ho, head of the Aaron Diamond Research Center, before his talk last week.

The Rockefeller University Archives

Rockefeller University Professor Henry Kunkel (1926-1983) emphasized clinical disease as the starting point for good science.

Azalea Festival to include lectures and tours of colorful grounds

(continued from page 1)

botanical interest.

On Sat., May 15 and Sun., May 16, the campus will be open to the public between 1:00 and 4:00 P.M. On both days, Chris Bowler , postdoctoral fellow in the Chua lab, will lecture on "How to Make Blue Roses, Stay-Ripe Tomatoes, and Glow-in-the-Dark Daisies" at 1:15 P.M. in Caspary Auditorium. New York Botanical staff will give tours at 2:00 and 3:00 P.M. beginning at the Hospital. Visitors will be invited to stroll around campus and note the exteriors of the university's architectural treasures, which include Founder's Hall, now a National Historic Landmark, as well as several buildings, including the President's House, Abby Aldrich Rockefeller Hall, Caspary Hall, Bronk Laboratory, Sophie Fricke Hall, and Graduate Students Residence, designed by the distinguished architect Wallace K. Harrison.

In the late 1950s, when the Rockefeller Institute for Medical Research became The Rockefeller University, the eminent landscape architect Daniel Kiley designed a new plan for the campus including a range of plantings, formal gardens, and fountains. Kiley imbued the site with his characteristic blend of classic design, appreciation of nature, and sense of exuberance.

In addition to the azaleas, Kiley's plantings include a vivid array of daffodils, tulips, yews, quinces, shadbushes, ground myrtle, magnolias, cherries, dogwoods, flowering crab apples, Rose-of-Sharon, and rhododendrons. Among the trees are lindens, wisteria, weeping willows, Lebanon cedars, Japanese holly, honey locusts, and sycamores or *Plantanus orientalis*, the most famous of which—the tree "Kos"—came from a cutting from the island of Kos, where Hippocrates is believed to have taught his students 2,400 years ago.

Volunteers from the university are needed on Sat., May 15 and Sun., May 16 to help greet visitors and assist in organizing the tours. For further information, contact Patricia Sadiq, Office of Public Affairs, x8967.

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Probing how proteins and life's 'master molecule' interact

by Susan Blum

Life's master molecule, DNA, encodes all the instructions a cell requires to maintain itself, grow, and divide. But the master cannot act alone. To execute its plans, it relies on proteins, the "slaves" that (among other functions) interact with DNA to initiate and coordinate various cellular events.

Assistant Professor Kenji Adzuma is fascinated by the collaborations between DNA and proteins. His research focuses on how these interactions control recombination, the process by which DNA is shuffled within or among chromosomes to create new genetic arrangements.

Adzuma, who joined the Rockefeller faculty this year, began his career at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). There, he first turned his attention to a recombination phenomenon known as "target immunity."

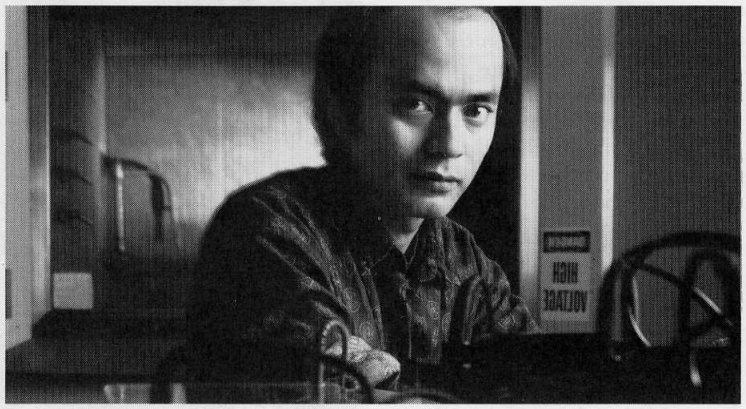
He studied phage Mu, a virus that infects bacteria. Phage Mu does its dirty work by incorporating its DNA into the DNA of its host. Once inserted into the bacterial genome, the phage hijacks the host's cellular machinery for its own selfish ends.

Phage Mu can be incorporated anywhere in its host's DNA, except near a region where another copy of the phage is already inserted. This "target immunity" prevents the second phage from inadvertently destroying the functioning of the first.

Action at a distance explored

How does the incoming phage DNA recognize the existence of another phage copy that is located some distance away? "This 'action at a distance' seemed quite mysterious," Adzuma recalled. But working with colleagues at NIDDK, he found that the action could be explained through the collaboration of two proteins, dubbed "A" and "B," produced by phage Mu. Protein B binds essentially anywhere on the bacterial DNA and promotes phage Mu's integration, while protein A binds only to specific regions of already-integrated phage Mu DNA. Proteins A and B also interact with each other in such a way that protein A bumps protein B off the DNA. Thus, a phage Mu in search of a place to roost is much more likely to integrate into a DNA region far from other phage Mus-in-residence.

Target immunity is not the only example of DNA-protein action at a distance. When the DNA code is read out into its RNA intermediate—a process known as transcription—proteins called transcription factors bind to many regulatory DNA elements spaced far apart on the gene, as well as to one another. Much remains to be learned about the baroque convolutions of transcriptional regulation, and insights gained from the much simpler phenomenon of target immunity may turn out to provide some clues.



Assistant Professor Kenji Adzuma, who joined The Rockefeller University this year, studies how DNA and protein interact to control recombination, the process by which DNA is shuffled within or among chromosomes to create new genetic assortments.

Having solved the puzzle of target immunity, Adzuma next focused on homologous recombination, the process by which similar regions of DNA on the same or different chromosomes are exchanged. Homologous recombination occurs in all cell types, from bacterial cells to human ones.

Recombination engenders genetic variety

Homologous recombination promotes variation among individuals by engendering a virtually infinite number of genetic combinations. In sexually-reproducing species, a certain degree of diversity is ensured simply by the merging of egg and sperm, since both cells contain just half of each parent's original chromosomal endowment. But even greater variety is generated by the localized chromosomal exchanges that occur during meiosis, the stage of cell division that results in eggs or sperm.

Before meiosis ends, regions of duplicated chromosomes "cross over," or swap DNA, at various points of homology, or similarity. Thus, no two chromosomes inherited from a mother or father are ever exactly the same, ensuring that no two siblings will be precisely alike unless they are identical twins who developed from one egg.

So far, homologous recombination is best understood in bacterial cells. There, it has been known for decades that an enzyme called RecA plays a central role in promoting DNA strand exchange. RecA molecules first bind to a strand of DNA that has separated from the DNA partner to which it is usually bound in a double-helical configuration. This complex of RecA protein and single-stranded DNA then captures a region of homologous double-helical DNA to form a "synaptic complex" (see illustration). Ultimately, the incoming single-stranded DNA switches places with one partner strand in the double helix.

Protein poses a paradox

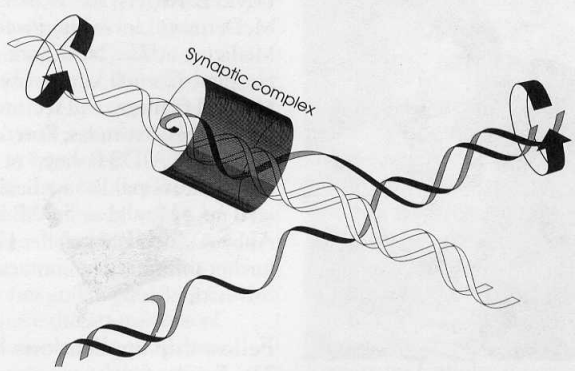
Though this much has been known for years, the details of RecA's function remain a mystery. Said Adzuma, "The paradox is that RecA must recognize specific homologies so that recombination can occur. Yet the recognition must not be limited to particular DNA sequences, since the enzyme must deal with any homologous regions it finds."

To discover how RecA recognizes homology, scientists must first resolve an even more fundamental question: when is homology recognized? One model holds that this occurs only after the double-helical DNA in the synaptic complex is teased apart into two separate strands. A second model posits that homology can be recognized when the DNA is still in its double-helical form. The mechanics of the second model require an unusual DNA intermediate known as a triple helix, while the former model leaves no room for such a structure.

The two different models are still highly debated. To help resolve the issue, Adzuma exploited his training as a biochemist to use what he terms a "wild" approach. He probed the individual hydrogen bonds linking atoms within DNA molecules in the synaptic complex. The reason? In typical double-helical DNA, each base, or subcomponent, is bound to its complementary partner by a characteristic pattern of hydrogen bonds. In triple-helical DNA, the pattern of hydrogen bonding is distinctly different.

Adzuma found that the pattern of hydrogen bonding in the synaptic complex was inconsistent with a triple-helix model—though he said he "swallows hard" and admits the possibility that the harsh chemicals used in his experiments might somehow have destroyed the triplex DNA.

To pursue the question further, Adzuma is gearing up for a new set of biochemical experiments. This time, he plans to selectively "block" either the major or minor grooves of DNA—the alternating furrows formed by the twists of the double helix's backbone. In the triple helix model, the incoming single strand must approach double-helical DNA from the major groove side. In the other model, the approach can be from either side. By blocking the grooves and observing what happens, Adzuma hopes to gain additional insights into the mechanisms of homologous recombination.



During homologous recombination in bacteria, an enzyme called RecA and three strands of DNA form a "synaptic complex." Arrows indicate the rotation of DNA that occurs as part of the recombination process.

Hospital celebrates Nurses Week

Nurses at The Rockefeller University Hospital work alongside investigators to ensure that research studies proceed smoothly and that patients are well cared for. Here, nurses Joan Goodrich, Barbara Tiddens, and Nancy Meyer *(left to right)* consult.

Nurses at The Rockefeller University Hospital will be among the thousands honored across the country during National Nurses Week, May 6 to 12.

Nurses have worked at Rockefeller alongside scientific investigators since 1910, when the Hospital was founded as the first facility in the nation exclusively devoted to clinical research. In those days, 27 nurses, who lived in Nurses Residence, worked 12-hour shifts to care for their patients, most of whom suffered from tuberculosis and pneumonia. For the first time in this country's history, nurses were employed to help carry out scientific research protocols as well as to care for patients.

Today, The Rockefeller University Hospital is a 30-bed facility. Thirteen nurses rotate through three shifts a day. While they no longer live in Nurses Residence and work 12-hour shifts, the research nurses continue to ensure that study protocols run smoothly and that patients are comfortable.

"When people think of research nursing, they think we simply collect specimens," said Barbara Tiddens, acting director of Nursing Services, who has been a research nurse for 13 years. "Actually, it involves a lot of direct bedside care. Investigators rely on nurses for their daily observations of the patients—more so than in a traditional hospital setting—and for ensuring that the patients follow their treatment to the letter in order to maintain scientific accuracy. This is not an easy task, because we don't want to seem too controlling, especially with patients who have to stay here for months on end. It's a fine balance."

The nurses at Rockefeller try to be sensitive to the special needs of their patients who suffer from chronic diseases such as psoriasis, epidermolysis bullosa, and multiple sclerosis. "The patients are willing to try out new protocols," said Tiddens. "They believe that while the studies will not necessarily help them directly, they may benefit someone else somewhere down the line."

The number and conditions of the patients at the Hospital vary tremendously throughout the year. "We have to be flexible around here—ready for anything," said Tiddens. Hospital occupancy varies depending on research protocols. Last summer the research facility was filled to capacity and an extra cot was supplied to accommodate a family member. At another time, the nurses cared for a three-day old patient and an 86-year old patient in the same week. "We whispered during rounds so as not to wake the baby," recalled Tiddens.

While the nursing regimen has changed drastically since 1910, today's research nurses display the same curiosity and dedication to science that brought nurses here so many years ago.

Marie Walsh-Kelley, who has worked as a staff nurse at Rockefeller for a year and a half, said: "Prior to coming here, I worked a long time with cardiac patients without ever knowing anything about the factors that contribute to heart disease. When I heard about the cholesterol studies at Rockefeller, I knew it could be an opportunity for me to learn more. As it turned out, I have learned about many other kinds of other diseases, too."

Delia De La Rama, a Rockefeller staff nurse who has worked at the Hospital intermittently for eight years said: "I worked with the very first methadone patients in the late 1960s. Now, methadone is used world-wide to treat heroine addiction. That is why I work here: to be on the cutting edge of the research and to enjoy the excitement of it all!"

Potpourri

Tri-Institutional Noon Recital

The Glorian Duo, featuring harpist Wendy Kerner and flutist Donna Milanovich, will play works by Saint-Saëns, Andriessen, Satie, Debussy, Tournier, Diamond, and Ibert at the Tri-Institutional Noon Recital today (May 7). A recipient of a Chamber Music America Grant and a Bronx Council on the Arts Grant, the duo won the Artists International Award and the American Harp Society's Concert Artist Program Auditions. The concert, to be held in Caspary Auditorium, is free. All are welcome.

Steve Sherman

The Glorian Duo will perform at the Tri-Institutional Noon Recital today (May 7).

Biomedical forum

David E. Rogers, the Walsh McDermott University Professor of Medicine at The New York Hospital-Cornell University Medical College, will lecture on "American Attitudes, Potent Shapers of AIDS Policy," at the Tri-Institutional Biomedical Forum on Tues., May 11 at 5:00 P.M. in Abby Aldrich Rockefeller Hall. For further information, contact Grace Silvestri, x8103.

Fellowship applications

The Faculty Committee for Fellowship Review will meet in June to review nominations for the Charles H. Revson Foundation and Norman and Rosita Winston Foundation Postdoctoral Fellowships for the 1993-94 academic year. Applications should be sent to Olivia Buckley, Development Office, Box 285, by May 15, and should include a letter of recommendation from the head of laboratory describing the applicant's research, a curriculum vitae, and any relevant information about the candidate's current funding.

Six fellowships are available to Rockefeller applicants this year. Each award provides $25,000 toward salary support and fringe benefits for a one-year term. Candidates may be in any field of research and at any stage of their postdoctoral studies. Junior faculty are also eligible for this award. Current scholars may *reapply* for a second award, but the fellowships are not automatically renewed. The term for these fellowships runs from July 1 to June 30. Each year the Revson/Winston fellows are expected to write a brief, non-technical report on their research. In addition, the fellows and faculty laboratory heads are expected to attend a dinner in the fall with trustees from the foundations.

Spraying

The spraying of the grounds, originally scheduled for Sat., May 8, has been changed to Sat., May 22, from 6:00 A.M. to noon. For more information, call James Sullivan, x8001.

Promotion

Ted Rock has been promoted to hospital administrator from assistant administrator. In his new role, he will assume responsibility for all daily operations of The Rockefeller University Hospital. Medical Director and Associate Professor Richard Galbraith will continue to be responsible for medical staff and for directing the General Clinical Research Center program.

Mother's Day special

Peter's Car and Limo Service is offering a Mother's Day special through May 9: $14 from New York City to LaGuardia Airport, $24 from New York City to JFK Airport; $25 from New York City to Newark Airport. Two hours advance notice is required. Tolls and parking are not included. Call (718) 386-6768 or fax (718) 386-5909.