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The Rockefeller University

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news & notes

March 6, 1992 Volume 2, Number 24

The Rockefeller University

Kenyans visit Rockefeller to learn about education

A five-man delegation from the Kenyan Commission for Higher Education visited The Rockefeller University on Wednesday as part of its international mission to better understand how different educational systems work. The Commission, established in 1985, has sent missions to Europe, Asia, and Africa, as well as North America, in an effort to tap the best available knowledge and create a first-class university system in Kenya.

The Kenyan team, led by Mutuku J. Mutinga, met with four Rockefeller experts in the Cohn Library over a two-hour period to discuss such issues as how to improve research and education. Rather than "reinventing the wheel," Mutinga told the Rockefeller group, his team wanted to "learn from those who have experience and have built up knowledge and success over the years."

Jerry Weisbach, Rockefeller's head of Technology Transfer and



Robert Reichert

Mutuku J. Mutinga, head of the delegation from the Kenyan Commission for Higher Education, (right) met with Bruce McEwen, professor and dean, and others from The Rockefeller University.

adjunct professor, spoke to the Kenyan team about the interface between academic science and industry. Weisbach explained how the transfer of technology fosters a more positive attitude to industry, as well as yielding financial rewards and greater support for research.

Bruce McEwen, professor and dean, spoke about the university's graduate program and its unique emphasis on "learning how to learn." McEwen explained how the university selects its limited number

See *Kenyan*, page 2

New gifts and pledges coming in at 'impressive' pace

At the Board of Trustees meeting Feb. 21, Chairman Richard M. Furlaud reported that new gifts and pledges raised during the first seven months of the current fiscal year were four times higher than the amount raised during the same period last year.

If the current trend continues, Furlaud said, "we expect more than \$30 million in new gifts and pledges this year—by far the largest amount ever raised by the university in one year, and well surpassing the year's already ambitious fund-raising goal of \$23 million. This \$30-million figure is especially impressive because it does not include the \$20-million gift from David Rockefeller announced last October."

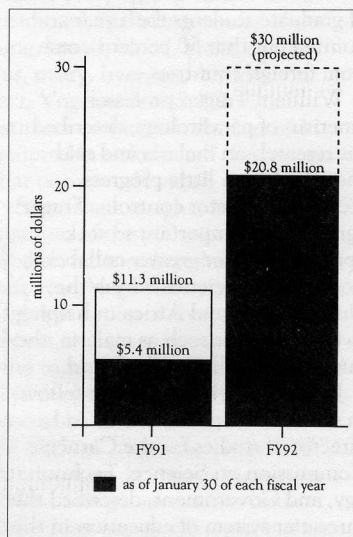
President Torsten Wiesel remarked: "This increased revenue from our friends and supporters is very heartening—as well as essential for meeting both our annual operating needs and our ambitious goals for the future. It is important to keep in mind most pledges are paid over a three- to five-year period and not all of these funds are immediately available.

"Indeed, as we begin to plan our budget for next year, we still confront an operating deficit of \$8 million and must continue to carefully limit and control our expenses. But the flow of resources for the future has been significantly enhanced, and we all must work very hard to sustain and even exceed this new level of private support. Increased pledges translate into increased cash receipts available in succeeding years."

Trustee Alexander D. Forger, who heads the university's Development Committee, noted "the university's effort to enhance the pledge pipeline is already showing some positive results this fiscal year. Cash receipts at the end of February were \$10.3 million, up 35 percent from the \$7.6 million received by the same time last year. If the current trend continues, cash

receipts may exceed \$19 million by June 30, 1992."

The university's director of development, Marnie Imhoff, commented: "Of major importance to any potential donor is the conviction that he or she is investing in excellence. The increased private support we have received is a wonderful endorsement of the outstanding science that is going on in the university's laboratories."



Total gifts and pledges for fiscal years 1991 and 1992.

Emergency mission

RU researchers fly to Canada to aid baby

Last month, in a small town in Canada, a baby was at risk for brain damage. Because little Anthony Ryan had an Rh blood group incompatible with that of his mother, he was severely jaundiced and his blood bilirubin level was very high. Ordinarily, Anthony would have been given repeated blood transfusions, but his parents were Jehovah's Witnesses opposed to clinical use of blood products on religious grounds.

On the suggestion of The Watch Tower Society, a group that keeps track of scientific developments which may help Jehovah Witnesses during medical emergencies, the pediatrician called Rockefeller University investigators Attallah Kappas and George Drummond. The Kappas-Drummond lab had developed an enzyme inhibitor for the treatment of newborn jaundice which had undergone successful trials in premature infants in Greece.

After the U.S. Food and Drug Administration and the parallel Canadian Health Ministry agency gave emergency permission for the enzyme inhibitor's use, Kappas and Drummond flew to Canada with specially prepared doses of the medication. They delivered the medication personally to ensure that the local physician was properly instructed in the use of the agent if that proved necessary and to ensure that the clinical situation for the use of the inhibitor was indeed appropriate. Officials in the Jehovah's Witness organization assisted them in this effort.

A representative of the Watch Tower Society thanked Kappas and Drummond for their kindness in helping the baby, whose condition has improved, writing that "your taking the time to travel to Sault Ste. Marie [Ontario] over the weekend was beyond our expectations." The Watch Tower Society plans to stay in touch with the Rockefeller University investigators in case other children like Anthony could benefit from the researchers' assistance.

2 'Rockefollies' show off local talent

3 Lecture chronicles cancer research

4 Rising stars to sing operatic arias at RU



Vance Zemon's *tae kwon do* troupe drew much applause at last year's 'Rockefollies.'

Luckily, organizer's wildest dreams for 'Rockefollies' didn't come true

By Olivia Gushin

Yvonne Holland and Mickey Rooney have a lot in common. Holland, like Mickey Rooney, looked around her one day, saw a lot of talent and decided to put on a show. "The Rockefollies," or the "R.U. Revue" as it was known in its inaugural year, was born.

Holland sent out letters to the entire campus, inviting one and all to take part, either on or behind the stage. That's when the recurring nightmares started. In one, 90 people showed up, all demanding their 15 minutes of fame so that the show had to run day and night for a week. In the other, absolutely no one turned up and there was no show. Neither nightmare came true.

Which is not to say the show went on worry-free. There are what Holland calls "the funnies." In 1987 someone signed up a professor to sing Australian lullabies. (He called back to say he had never heard of the genre.) Another submission came in offering to dance "The Dying Swan" from Swan Lake in sneakers.

Despite a few bogus submissions, Holland received a lot of legitimate responses which filled the program. But not everyone wanted to stand in the limelight. During the finale, one cast member kept edging further and further to the rear of the stage. He went so far back he fell into a well behind the stage and wound up in a cast.

But on the whole, most performers enjoy treading the boards. Vance Zemon, an assistant professor in the Knight lab, brought his *tae kwon do* troupe to the Rockefollies last year. As the final act on the program, Zemon and his team spent most of the show warming up in the basement of Caspary. But the highlight of his "Rockefollies"

experience was the applause the troupe received when it demonstrated how to fend off knife-wielding attackers. If you want to impress people, Zemon found, "throw them around and break boards."

Paul Rosen, research associate in the Electronics Lab, "sort of" winged his role as last year's MC. He had no role models in this capacity and "doesn't care for Billy Crystal." Nonetheless, he was a great success. Rosen says the great thing about the Rockefollies "is everybody has fun."

Holland concurs. In her 35 years at the university she hasn't been to "a more uniting event." She has met more people through the show than any other program on campus.

This year the "Rockefollies" will be April 2. Individuals interested in performing or volunteering as stage hands should contact David Heath, x8441 or Box 262.

Kenyan commission visits campus

(continued from page 1)

of graduate students each year and pointed out that 50 percent come from foreign countries.

William Trager, professor emeritus of parasitology, described his research on malaria and said there had been little progress recently on vector control. Trager agreed it was important to seek opportunities for greater collaboration between scientists from the United States and Africa in helping to fight diseases such as malaria, the number one killer in the world.

Jesse Ausubel, Rockefeller fellow in science and public policy and director of studies for the Carnegie Commission on Science, Technology, and Government, described the three-tier system of education in the United States and emphasized that an effective educational system

Foundation selects three postdocs at RU to receive new fellowships

Three postdocs at The Rockefeller University were among twenty-five winners of the new Aaron Diamond Foundation Postdoctoral Research Fellowships. The fellowships will provide James Chou of the Kreek lab, Jennifer Darnell of the Aderem lab, and Mona Freidin of the Pfaff lab with up to three years of financial support.

The Aaron Diamond Foundation Postdoctoral Research Fellowships in the Biomedical and Social Sciences were established to encourage research in AIDS or drug abuse. As a long-term goal, the fellowship program also seeks to improve the research climate in New York City by supporting outstanding junior scientists who will become independent investigators and continue their research careers in New York City. The program is supported by a \$16.6-million grant, the largest single award made to date by The Aaron Diamond Foundation, a private funder of AIDS research.

Chou's research in the Kreek lab focuses on the biological basis of narcotic addiction, cocaine dependency, and drug abuse. Diverse programs in the lab study the role of the endogenous opioid system and specific opioid receptors in addictive disease. Chou plans to learn and apply a variety of techniques aimed at increasing the understanding of the roles of various opioid peptides and receptors in the normal and abnormal physiology of the neuroendocrine, neurological, immunological, and gastrointestinal systems. A collaboration with the

Chait lab enables him to use a novel analytical technique, laser desorption mass spectrometry, to qualitatively determine the presence and integrity of opioid peptides and other related neuropeptides.

Darnell pursues research on AIDS in the Aderem lab. Most research on the development of therapeutic strategies for AIDS focuses on vaccination and on the inhibition of a necessary enzyme of the HIV virus which causes the disease. The approach taken by Darnell and Aderem is to examine how the assembly of the virus at the cell membrane—a step essential to the virus's replication—might be blocked. The first step of this assembly involves targeting one of the viral proteins, PR55gag, to the cell's outer membrane. The funded project will identify and characterize the membrane receptor to which PR55gag binds.

Freidin studies the expression of genes that code for opioid neuropeptides. The funded project will examine the regulation of the gene for proenkephalin—one of the opioid peptides that has been shown to be associated with addictive behavior in animals. By understanding the signals that stimulate or suppress proenkephalin expression under normal behavioral conditions, insight may be gained into its regulation, and possible control, in people with drug addictions.

The next application deadline for the Aaron Diamond Foundation Postdoctoral Research Fellowships is July 31, 1992. Rockefeller University's Sponsored Programs can provide application materials.

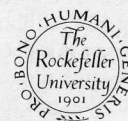
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Levine memorial lecture chronicles progress in cancer research

By Susan Blum

Understanding cancer remains one of science's most daunting challenges. The unbridled cell growth characteristic of the disease results from a breakdown in the communication systems that regulate how a cell develops, grows, and divides. These systems have not yet fully yielded their secrets. But over the past decade, enormous strides have been made in cancer research, due largely to the realization that cancer is a disease of the genes. When genes critical to cellular communication pathways are mutated or lost, cancer can develop.

Bert Vogelstein, professor of oncology at Johns Hopkins University, is a pioneer in the study of the genetic changes that can lead to cancer. Focusing primarily on colorectal cancer, he and his colleagues have shown that cancer does not result from a change in just one gene. Rather, cancer develops in a step-wise fashion due to mutations in a number of different genes.

Vogelstein discussed how cancer progresses at the Philip Levine Memorial Lecture, held recently in Caspary Auditorium. The lecture was established in 1977 by Philip Levine, a member of The Rockefeller University's scientific staff from 1925 to 1932. While at Rockefeller, Levine worked with Nobel laureate Karl Landsteiner on the discovery of the Rh factor. Much later in his career he was a visiting investigator at Sloan Kettering Institute, during which time he became interested in the relationship of human genetics to cancer.

That relationship is a complicated one, explained Vogelstein. "There are some interesting differences between 'standard' genetically-inherited diseases, such as muscular dystrophy, and cancer," he told the assembly. With muscular dystrophy, all those who have a mutation in the gene that codes for a particular protein called *dystrophin* will get the disease. With cancer, the picture is much more complex.

Because cancer is caused by mutations in a number of genes, a person who inherits one faulty gene is not fated to develop the disease, but is rather predisposed to it. Environmentally-caused mutations in other genes also have to occur. "It is the combination of inherited mutations and 'somatic' (non-inherited) mutations that eventually lead to cancer," Vogelstein said. He stressed that the ultimate source

of the mutation is not essential: "It appears that the same genes, whether inherited in mutant form or somatically mutated, can lead to cancer."

Two kinds of cancer genes

There are two types of cancer genes: oncogenes and suppressor genes. Oncogenes are genes whose normal function is to promote cell growth and division. When these genes go awry, scientists call them "oncogenes." Suppressor genes (also called "anti-oncogenes") are genes whose normal function is to put a brake on cell growth.

So far, Vogelstein said, four genes have been found to be associated with, and presumably drive, the progression of colorectal cancer. Three are suppressor genes; one is an oncogene.

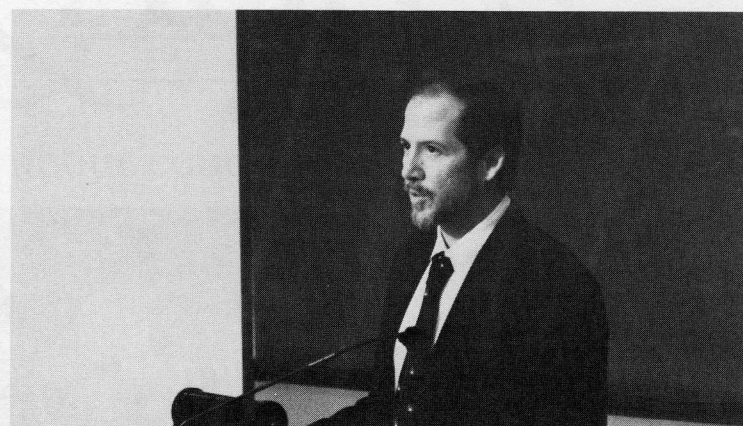
Colorectal cancer progresses in clear stages over the course of anywhere from 30 to 50 years. In that process, normal epithelial cells first develop into benign polyps, called adenomas, which gradually increase in size and cellular abnormality. Eventually, the adenomas become malignant, developing the ability to invade surrounding tissues and to travel (metastasize) to distant organs.

Vogelstein reported that in general there appears to be a particular order to the genetic mutations in colorectal cancer. "The order is not invariant, but it's certainly preferred, and appears to occur in most tumors," he said. His talk focused on the first genetic mutation, which appears to initiate the process of colorectal cancer, and the last, which appears to mediate the transition from a benign tumor to a malignant one.

The first change occurs in a suppressor gene called APC. The gene was isolated last year by two teams of researchers, one led by Vogelstein. The scientists identified APC's role in cancer initiation by studying patients with an inherited disease called familial adenomatous polyposis, or FAP. By the time they reach age 30 or 40, people with FAP have colons carpeted with polyps, a few of which have already turned into cancer. The scientists found that cells from FAP patients' benign and cancerous polyps have mutations in the APC gene. They also found mutations in the APC gene in colorectal cancer patients whose cancers are "sporadic"—that is, non-inherited.

Intriguing clues emerge

How do mutations in the APC gene initiate the multi-step process of colorectal cancer? No one yet



Bert Vogelstein, professor of oncology at Johns Hopkins University, discusses genetic changes that can lead to cancer.

knows, but some intriguing clues are emerging. Vogelstein and his team have found that the normal APC gene codes for a very large protein, and that most mutations so far analyzed cause the protein to be truncated. Moreover, he reported, they have found a region of similarity between the APC protein and a type of cell-surface receptor that controls binding to so-called "G-proteins." Because G-proteins are crucial components of cellular communication networks, disruptions of proteins that interact with them may help set the stage for cancerous changes.

Mutations in the APC gene may set the stage for colorectal cancer, but they are far from the whole story, Vogelstein stressed. In both the inherited and sporadic forms of the cancer, other mutations must also occur. The last mutation may be in a gene called p53.

p53's role in promoting cancer was first pinned down by Vogelstein in 1988, when he and his colleagues identified a mutant form of the gene in colon cancer cells. Since then, p53 mutations have been found in almost every type of cancer so far examined, including cancer of the lung, breast, blood, brain, esophagus, ovary, liver, and bladder. In fact, Vogelstein said, "One can estimate conservatively that p53 is mutated in at least half the cancers that occur worldwide."

Significant insights into the function of the p53 gene's protein product have emerged within the past year, Vogelstein reported. Multiple copies of the protein appear to join up in complexes that bind to specific DNA sequences and activate gene transcription—the process by which the codes in DNA are read out into a closely-related intermediary known as messenger RNA. The genes that are transcribed are as yet unknown, but are believed to be important for controlling cell growth. The more

faulty p53 proteins there are in a cell, the less able they are to form the complexes necessary to maintain normal cell functioning.

p53: A final checkpoint?

Vogelstein speculated that the p53 gene may be the final checkpoint in a cell's march toward cancer. "If p53 is mutated in a normal colorectal epithelial cell, or in an early tumor cell, the mechanisms for controlling cell growth are probably redundant enough that the mutation has very little effect," he said. But if the cell has already lost several other control mechanisms through mutations in other genes, p53 mutations can wreak their havoc. "p53 may function as a kind of emergency brake," Vogelstein said. "If you lose that brake once the others are gone, all hell breaks loose."

The ultimate hope, of course, is to stop cancer by halting it in its tracks. The more that is learned about genetic mutations in cancer, the better the prospects for such interventions will be. For instance, Vogelstein has already reverted cancer cells back to normal in the test tube by introducing a copy of a normal p53 gene.

But even before new cures are at hand, the new genetic insights promise to make current ones more effective. Early detection of cancer is key, so tests that flag cancer's earliest genetic mutations will make cure by surgery alone more likely. And in cases where cancer has already progressed, genetic analyses that assess the mutations will help decide which added treatments to use in the fight. According to Vogelstein, the clinical possibilities arising from the increasing knowledge of cancer genetics are "up to the imagination of the young people in the audience"—many of whom included young Rockefeller researchers just embarking on their scientific careers.

Corners

Robert Reichert



The Smith Hall rooftop offers an unusual view of the East River and beyond.

Potpourri

Promotion

Lisa C. Hudgins of the Hirsch lab was promoted from research associate and associate physician to assistant professor and associate physician.

Lunchtime Film

Pain & Healing (1988, PBS), a 60-minute video, will be shown in Tower 305, Wed., March 11, at noon. The film examines the mechanism of pain in the body and mind and investigates how much the mind can influence and even control our health and well-being.

Mac Users Group Meeting

RockMUG, The Rockefeller University Macintosh Users Group, will have its next meeting Wed., March 11, in Flexner Extension 363, 11:30 A.M. to 12:45 P.M. (note the room change). This month's meeting will feature a demonstration of the program Current Contents on Diskette, a bibliographic search package which provides access to the most current bibliographic information from thousands of science and social science journals, books, and reviews. The program allows the

user to search for title names, author names, keywords, disciplines, and specific journals. Search results are returned within two seconds.

Everyone is invited. Participants should bring their lunch; drinks will be provided. Those who would like to help plan future meetings or want to be added to the mailing list should contact Rachael Kolb or Anthony Popowicz, x8925, or send e-mail to rachael or tony.

Cottage reservations

As in past years, reservations for the MacInnes and Hostage Cottages, which are rented at the daily rate of \$27.50, will be made by random drawings. A blank reservation request form can be obtained from the Housing Office, Abby Aldrich Rockefeller Hall 318, until Fri., March 13. Forms must be returned by Mon., March 16. Confirmations will be made after April 1.

Applied Probability Day

Professor Joel E. Cohen will speak on "Random Graphs in Biology" as part of Columbia University's Applied Probability Day Fri., April 10. The conference will be held at the Kellogg Conference Center, 15th floor of the International Affairs Building (corner of Amsterdam Ave. and West 188th St.). Tickets for those registering before March 25 are \$25 (\$15 for students); tickets purchased at the conference are \$35 (\$20 for students). For more information e-mail cap@ieor.columbia.edu or write

Center for Applied Probability 322 S.W. Mudd Building, 500 West 120th St., Columbia University, New York, NY 10027-6699.

Recital

In celebration of International Women's Day, the Cassatt String Quartet, whose members are all women, will play at Tri-Institutional Noon Recital today (March 6) in Caspary Auditorium. The quartet will perform works by Mozart and Hindemith. The group has performed in halls throughout North America and abroad, including Carnegie Hall, Alice Tully Hall, the Tanglewood Music Theatre, the Kennedy Center, and the Théâtre des Champs Élysées. The concert will be co-sponsored by Cornell University Medical College's Office of Women in Medicine and Cornell's Student Chapter of the American Medical Women's Association.



The Cassatt String Quartet will perform at Tri-Institutional Noon Recital in celebration of International Women's Day.

Rising stars to sing at RU

Five highly talented and promising young opera singers—finalists in the Metropolitan Opera National Council Auditions in the eastern region—will perform at a concert in Caspary Auditorium Sun., March 8, at 8:30 P.M.

The Metropolitan Opera National Council inaugurated its Auditions Program in 1954 to extend new opportunities to young singers and to increase public awareness of their talent. Now, approximately 2,000 aspiring opera singers compete in 66 cities in the United States, Canada, Australia, and Puerto Rico.

"This program has been tremendously successful in finding new talent and helping young opera singers in launching their careers," said Jeannette S. Rohatyn, regional chairman of the National Council Eastern Region. "Fully 41 percent of the current roster at the Metropolitan Opera has participated in this auditions program."

Winners in the first-level district auditions compete in one of the 17 regional auditions. These regional winners are brought to New York each spring to compete in the national finals. This year, national winners will receive prizes of \$10,000 and will perform in the prestigious Winners Concert.

The concert on campus, which will benefit the Metropolitan Opera National Council, features Sara Seglem (age 25), Bradley Garvin (age 27), Olga Makarina (age 30), Eduardo del Campo (age 27), and Anita Johnson (age 25) singing a selection of operatic arias.

Substantially discounted tickets to the concert and black-tie reception are available to the Rockefeller community for \$15 per person. Checks should be made out to "MONC-Eastern Region" and brought to the Public Affairs Office, Nurses Residence 211, today (March 6). (Students, who may attend free of charge, must obtain tickets from the Deans' Office.)

Classified

The Rockefeller University Children's School seeks the donation of dressers—no larger than 30" x 30" x 15"—for the children's doll corner. Contact Barbara Adams, x8580.