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The Rockefeller University

news&notes

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White House expert speaks at RU on public health

Donald Henderson speaks about the eradication of smallpox on Thursday.

Donald Ainslie Henderson, who achieved worldwide recognition in 1980 for his direction of the World Health Organization's (WHO) successful campaign to eradicate smallpox, was the guest speaker at a reception and discussion for friends of the Lederberg laboratory at The Rockefeller University last Thursday. Henderson, currently Associate Director for Life Sciences in the Office of Science and Technology Policy in the Executive Office of the President, spoke about "Public Health Challenges: A White House Perspective."

After a general welcome and introduction from President Torsten Wiesel, who remarked that the Lederberg laboratory was now "teeming with life," Joshua Lederberg, university professor and former president, introduced Henderson, a longtime colleague. Lederberg called Henderson's role in the decade-long campaign to eradicate smallpox "an unprecedented event in the history of humankind."

Henderson recounted in vivid detail the story of the international fight against smallpox which he led. In 1967, there were 10-15 million cases of smallpox and over two and a half million deaths a year in 35 countries from the dread disease. Medical efforts at the time centered on treatment rather than prevention, with only 2 percent of children in the developing world receiving vaccines. Henderson spearheaded an international program aimed at vaccinating all children, an ambitious effort demanding worldwide cooperation on a new level. Funding was very limited and his WHO staff numbered only 100. But with focused planning, skillful organization, and persistence, they managed to mobilize 200,000 national health staff and volunteers in 69 countries.

Within a decade, the immunization program was reaching 80 percent of the developing world's children by the age of 1, and WHO had in place a global mechanism for vaccinating children against 6 major diseases. On October 26, 1977, the last case of smallpox was recorded and in 1980, WHO declared that smallpox had been eradicated.

Henderson emphasized that the immunization program fostered a unique spirit of international cooperation. The Soviet Union, then at the height of its superpower rivalry with the U.S., did not initially approve of his appointment to head the smallpox program. But once they had ironed out their differences, the USSR donated over 1 billion doses of vaccine and established an excellent working relationship with Henderson.

Similarly, in 1985, when Henderson led the fight to eradicate polio in Peru, he and his WHO group were granted entry into areas controlled by the Shining Path where even the Peruvian army could not penetrate. They managed to vaccinate over a million people and, one year ago, the last case of polio in the western hemisphere was recorded. In El Salvador too, Henderson explained, all the armies would declare a truce for the three days a year when children were vaccinated. "Health can build bridges as no other sector can," he said.

In recognition of his achievements at WHO, Henderson became the first public health professional to receive the National Medal of Science in 1986.

After WHO, Henderson was Edgar Berman Professor in International Health and Epidemiology at The Johns Hopkins University and also served as Dean of the Johns Hopkins University School of Hygiene and Public Health from 1977 to 1990. The School was the first of its kind in the U.S. and is now the world's largest.

In 1990, Henderson became one of four Associate Directors in the White House Office of Science and Technology Policy(OSTP) and the first with responsibility for the Life Sciences. He said that under Alan Bromley, the president's current science advisor, the office has been expanded and strengthened because science and technology are viewed as increasingly key to the nation's economic well-being.

President Torsten Wiesel addresses Rockefeller University Council at breakfast meeting on Tuesday.

Carnegie members discuss science and the U.S. President

Beginning with its highly successful report on appointing a science advisor to the president, the four year-old bi-partisan Carnegie Commission on Science, Technology and Government has reevaluated the government's science and technology(S&T) decisionmaking structure from the Office of the President and executive agencies to the Congress and the Judiciary. An impressive series of reports recommends effective mechanisms to enable all levels of government to make the best use of scientific knowledge. Because the Commission maintains extensive liaisons with the powerful institutions it studies and because of the "star status" of its own members –a roster that includes former Presidents Gerald Ford and Jimmy Carter– the Commission's recommendations should continue shaping the national agenda over the coming years. A recent article in *Washington Technology* asserted that the Commission "is likely to be viewed over time as the single most influential force affecting technology policy development for several decades."

Joshua Lederberg, Rockefeller University Professor and former president who is co-chair of the Commission, and Rockefeller fellow Jesse Ausubel, the Commission's director of studies, have written an editorial in this week's *The Scientist* calling on the president-elect to deal with the growing importance of science and technology issues in national affairs. Doron Weber of *News&Notes* spoke with Lederberg and Ausubel about the role of science and the president.

Weber: Wasn't it your first report in 1988 that strengthened the role of the president's science advisor?
Lederberg: Yes. We view it as unfortunate that Reagan did not have a balanced commission when the questions of the strategic defense initiative (SDI) first came up. SDI, in the forum that Reagan bought it, was not achievable. It was technically out of bounds. But there was no one quite willing to tell him that.

See **Carnegie**, *page 2*

Squash at Rockefeller: drop shots and hot shots

by Jennifer Horne King

Soon the tennis net will come down, and icy patches will mar jogging trails. To stay fit during the winter or ward off holiday pounds, some may want to consider squash as a convenient, high-energy workout; it is not dictated by the weather, and two courts are right around the corner, on the lower level of the Graduate Students' Residence.

Kalyan Sundaram, senior scientist for The Population Council, says he's used the Rockefeller courts regularly for 23 years. "Because the game is so energy-concentrated, I can fit a good workout into my lunch hour and still leave time at the end of the day for my 45-minute commute," he says.

Sundaram is known for having initiated several Population Council newcomers to squash, and his mission has paid off: "Now," he says, grinning, "I can always find someone to play with on short notice." His dedication to the sport is so intense, that he continues to play despite knee surgery, and wears a $900 knee brace on the court.

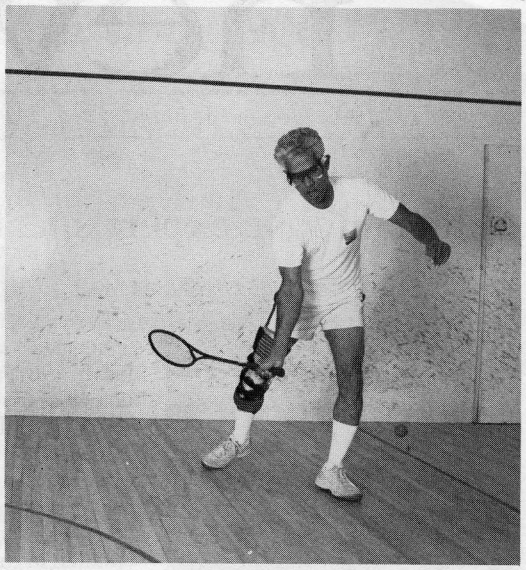
In addition to providing a good workout, squash draws out the cunning and mischief from the meekest player. Because the game involves placing the ball out of reach, winners will know how to discern, then exploit their opponents' weaknesses.

"Squash is most definitely a brains-and-body game," says Professor Emeritus Abraham Pais, who has played squash at Rockefeller since he arrived in 1963. "Even if you're not all that good," adds Pais, "you can make a good impression."

Pais especially recommends the "sly-fox approach" which he reserves exclusively for younger, cocky opponents. The Pais strategy consists of getting his opponent to expect a two-wall shot, and then, at the last minute, hitting another that uses three walls instead. "This is what makes squash so wonderful," says Pais, "you can be stupid, and still look smart."

Equipment is minimal for squash: a racquet, a ball –hard or soft– and some sneakers with good grip. Black-soled shoes are a no-no, and eye protection, such as sports goggles, is strongly recommended.

To use a Rockefeller squash court, sign up at the front desk of Founders Hall, and take along your magnetically encoded card for admittance to the athletic facilities.



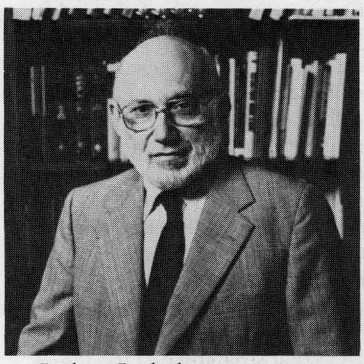
With or without the knee brace, Kalyan Sundaram hits a hard return.

Carnegie Commission

(continued from page 1)

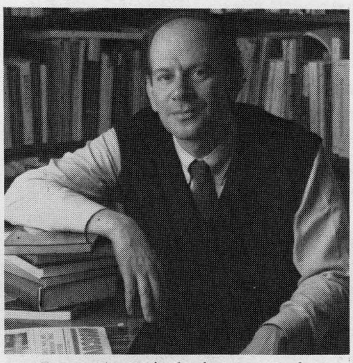
Our first report, "Science, Technology and the President", issued in 1988, recommended that the president upgrade the position of science advisor to an assistant to the president for science and technology, a cabinet level appointment. Both Democratic and Republican candidates for the presidency adopted it. To his credit, George Bush honored the pledge –although it took him over a year to do it– and appointed Yale physicist Alan Bromley to the post, giving him an office in the White House. And Bromley, in keeping with the recommendation in our report, insisted that all four OSTP associate directorships be filled for the first time.

Ingbet Gruttner



Joshua Lederberg, co-chair, Carnegie Commission

Robert Reichert



Jesse Ausubel, director of studies, Carnegie Commission

Weber: What are the scientific challenges for the next president?

Ausubel: Stopping the proliferation of high-tech weapons, rationalizing medical care systems, building a civilian technology agency, and effective widespread improvements in secondary school education in math and science. Also an informed sensitivity to the consequences of budget restrictions on investigator-initiated science.

Throughout human history an awful lot of S&T has been directed at military ends. Now, with the end of the Cold War, if we can really begin to devote more of the effort to goals of environment, health, productivity, it would be a tremendous achievement.

Weber: What should be done during the next presidential term?

Lederberg: The number one priority is early reaffirmation of Bromley's role or the appointment and confirmation of a successor. Then all the other key S&T jobs must be filled. Outstanding individuals must be recruited in a more timely way to the key posts in science, engineering, and medicine.

Ausubel: The government's technical leadership should exercise a constructive influence at the highest level on federal policies for environment, health, education, national security, and economic performance, and not only about the R&D goals in each area.

Lederberg: The president should use the President's Council of Advisors on Science and Technology (PCAST) more effectively. This group, re-established three years ago, is a remarkable resource. They can tackle the most important questions facing the next administration, such as the conversion of technical military assets in the U.S. economy to new purposes and how S&T can be better applied for economic development *and* environmental quality.

Weber: You've worked with Bush for four years. Any idea how Clinton would handle these issues?

Ausubel: We've already had requests from Little Rock for our Prune book –a description of the 60 toughest jobs in S&T.

Lederberg: I think Clinton has already committed himself to the issues we raise. If he gets elected, the urgent question is, how *quickly* will the new science advisor be appointed? It must not be allowed to drag on for a year and a half. It's very critical to make good appointments early on.

Ausubel: As Josh said, if you had to watch for one single thing, assuming Clinton is elected, look for how soon he designates his own science advisor. If he were to do that before the inauguration, it would be highly desirable. It is rumored that he has a transition team working in the area of science and that's very desirable.

The 4-year term is very short. If you don't hit the ground running, you can't accomplish much. Most of the policy creativity in any new administration comes in the first six or nine months. If you say we're going to have an initiative in the third or fourth year you're effectively writing it off altogether. So to the extent a new administration will really want to move in areas like health and the environment, you really have to watch what they do in the first six months.

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Rockefeller researchers create mouse model of atherosclerosis

by Susan Blum

Recent advances in the Breslow lab have paved the way for a dramatically new direction in heart disease research. The work, reported in the Oct. 16 issue of Cell, has resulted in the first mouse model of atherosclerosis.

Atherosclerosis is the condition in which deposits build up in the lining of the arteries and progressively limit blood flow. This arterial blockage—also known as coronary heart disease—is a major killer in industrialized nations.

Development of the condition is linked with low blood levels of the "good" cholesterol—high density lipoprotein (HDL)—and high levels of "bad" cholesterol, such as low and very low density lipoprotein (LDL and VLDL). In addition, certain "environmental" factors such as a high-fat and high-cholesterol diet, smoking, and lack of exercise often contribute to the disease.

Despite these well-documented correlations, coronary heart disease presents researchers with a medical mystery: some people do everything right—they eat well, exercise, and forswear tobacco—yet still develop coronary heart disease, while others do everything wrong, yet live to a ripe old age. For most people, though, behavioral choices can make an important difference in whether or not they get the disease.

Genes help determine susceptibility

The explanation for these differing outcomes lies in our genes. Research —much of it conducted by Breslow and his colleagues— has shown that many different genes interrelate to determine susceptibility to atherosclerosis. Naturally occurring variations in these genes lead to different degrees of susceptibility —and, in most people, these patterns allow environmental factors to have an impact.

This much is already known about atherosclerosis. But to fully elucidate the interrelationships of the genes, to tease out their subtle interactions with environmental factors, and to develop better strategies for prevention and treatment, researchers need a good animal model of the disease.

Until recently, the best animal model of atherosclerosis was the Watanabe rabbit, which spontaneously develops the disease. These animals can be used to study the progress of the condition and to test promising new drug therapies. But there are a number of drawbacks to the rabbit model. For one thing, breeding and maintaining the animals is difficult, expensive, and time-consuming. An even greater problem is that scientists who work with rabbits are restricted to the "test cases" nature spontaneously provides. There is no way to manipulate the genetic endowment of rabbits to study the complex contributions genes make to coronary heart disease.

The new mouse model overcomes these drawbacks. With a genetic endowment remarkably similar to that of humans, and a breeding cycle that produces a new generation about every two months, mice have long been a valuable source of naturally occurring genetic variations that can help elucidate gene function. Today, mouse studies are more fruitful than ever, thanks to revolutionary techniques that make it possible to tailor-make genetically altered mice.

Graduate fellow Andy Plump, the lead author of the Cell paper, employed the newest of those transgenic techniques, called gene targeting, to make a mouse deficient in both copies of the gene that codes for apolipoprotein E (Apo E). This protein plays a number of roles in cholesterol metabolism, among the most important of which is to bind to cellular receptors that remove "bad" cholesterol from the blood.

A natural ratio is inverted

By nature, the mouse is a high-HDL, low-LDL animal — one highly resistant to atherosclerosis. But Plump and his colleagues reasoned that "knocking out" the Apo E gene would invert this protective ratio and generate a mouse that is highly susceptible to atherosclerosis.

They were right. All the knockout mice developed atherosclerotic lesions by the time they were ten weeks old —an extremely early (and unexpected) age of onset. So far, Plump reports, the lesions that develop in the mice look similar in several respects to those that develop in humans. The researchers plan to follow the course of the disease in older knockout mice, and to track such factors as the extent and location of the lesions.

The Rockefeller researchers' long history of experience in studying atherosclerosis distinguishes them from a research group at the University of North Carolina at Chapel Hill that also has constructed an Apo E knockout mouse. (Their accomplishment was reported in the October 16 issue of Science.). While the North Carolina group initially approached the creation of the mouse mainly because of their interest in the techniques of genetic manipulation, the Breslow group created the mouse specifically to learn more about heart disease.

For this, the new strain of atherosclerotic mice offers a wealth of new research possibilities. For instance, says Plump, "There has been a lot of speculation about how Apo E acts in the body, but there are only two human families with members who have no measurable Apo E." Now that the researchers have a large population of mice totally deficient in the protein, they can study its function by tracking what happens when it is lacking.

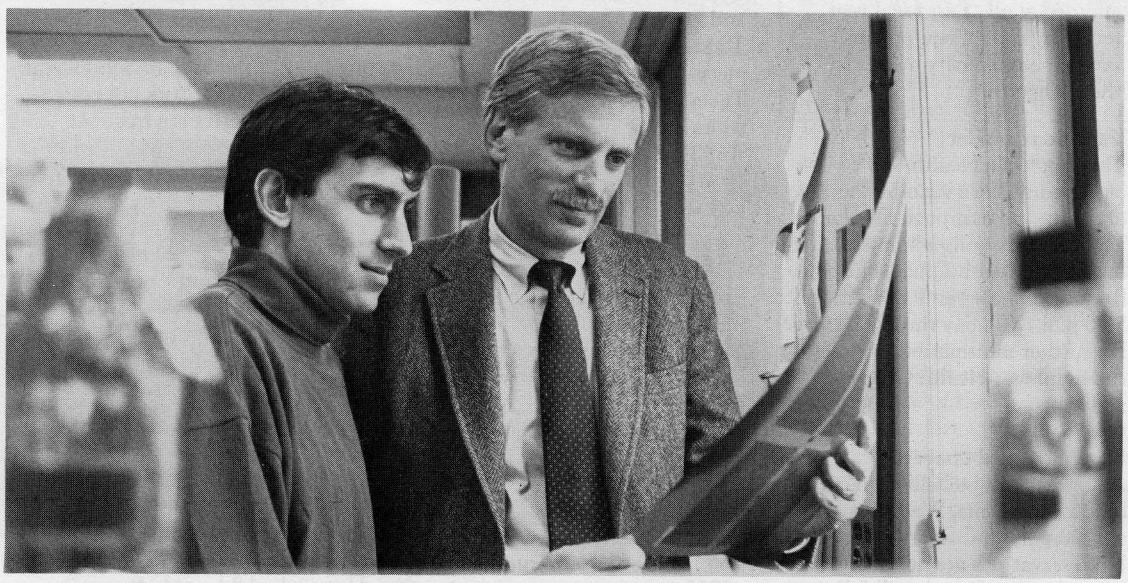
Other research possibilities offered by the mice include studies of cholesterol mobilization and absorption, and drug studies to learn how current therapies work and how new ones might work even better to halt or prevent atherosclerosis.

Diet studies are facilitated

The new strain of mice will also facilitate more sophisticated studies of diet. The knockout rodents develop atherosclerosis regardless of what they are fed, be it the standard, low-fat mouse chow or the equivalent of a high-fat Western diet. But the extent of their disease depends on the diet. "This mouse is a very diet-responsive animal," Breslow says. "The lesions are cut by 2/3 in mice that are fed the low-fat diet." Future studies should help identify subtle strategies that might optimize the role of dietary approaches to the disease.

The Apo E-deficient mouse strain is not the only transgenic mouse created in the Breslow lab. Other strains include mice with a knockout of Apo A-I (another apolipoprotein gene) as well as mice that overexpress other apolipoprotein genes involved in fat and cholesterol metabolism. Experiments that interbreed Apo E knockout mice with other transgenic strains should help untangle the complex interplay of the many genes that contribute to a susceptibility to atherosclerosis.

The experiments may also yield an animal model of atherosclerosis that is even closer to the human disease than the model provided by the Apo E knockout mice. The need for such animal models is pressing: the faster this multifactorial disease is understood, the sooner more lives can be saved by new strategies for prevention and treatment, including gene therapy. Says Breslow, "A good animal model could accelerate the pace of discoveries in this field as much as tenfold."



Research conducted by Graduate Fellow Andy Plump (left) in the laboratory of Professor Jan Breslow (right) has resulted in the first mouse model of atherosclerosis.

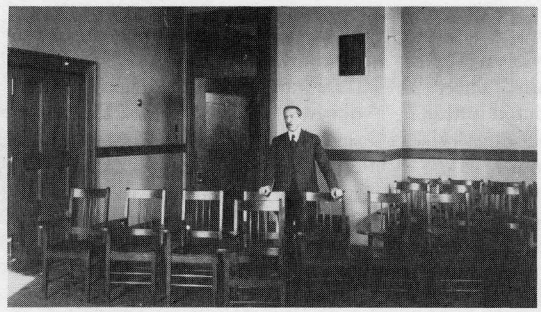
Friday lecture series at RU brings scientists together since 1906

Scientists have gathered at Rockefeller for a Friday afternoon lecture ever since 1906. The tradition started as an internal staff meeting in Founders Hall and became, under former president Detlev Bronk, a public Tri-Institutional event in Caspary Hall.

Professor Emeritus Merrill W. Chase recalls the first Friday meeting he attended as a young staff assistant, in September, 1932: "The doctors from the Hospital sat in the back and dozed if the afternoon's talk was being presented by a chemist; conversely, chemists dozed when a medical subject was being presented. By remaining awake, I learned all the basic tissue pathology that exceeded the course-work in normal histology."

Chase remembers a special arc-light projector for 35mm film. "Since it was desired to stop the forward motion and to inspect the single frames at will, the heat of the carbon-arc lamp had to be bypassed with mirrors so that the film would not burn."

Nathaniel Heintz, appointed by President Wiesel as chairman of this year's Friday Lecture Series Committee, says that lectures are selected from among many student and faculty proposals. The 15 member committee, selected by Heintz to represent the different scientific fields at the university, aims to vary the topics, and balance the number of internal and external speakers.



The Rockefeller University Archives

The Rockefeller University Archives

Photographer Edward Leaning *(left)* prepares the first Staff Meeting room in Founder's Hall for a Friday lecture, 1906. By 1959, Friday lectures had moved to Caspary Auditorium, where lecturers such as R.U. microbiologist R. J. Dubos *(right)* could address a larger, more diverse audience.

"There are three sorts of campus lecturers," says Heintz, "investigators whose work has reached a critical point and who want the Tri-Institutional community to evaluate it; investigators whose work is known, but who haven't been heard recently; and newly hired investigators who can introduce themselves and their work to the Tri-Institutional community."

Throughout the year, science lecturers from other institutions are also invited to lecture. There are five endowed slots reserved for the most prestigious among them.

Each year the lectures take on a particular focus. "One can look at the Friday Lecture Series from year to year," says Heintz, "and see how interests have changed at the university. This year, for instance, there seems to be an emphasis on structural chemistry and biochemistry, which one might have predicted in light of the newest laboratories on campus."

Heintz and the Friday Lecture Series committee receive many lecture proposals, some from students proposing their mentors, others from faculty suggesting lecturers in related fields. Heintz says that scheduling the lectures is sometimes difficult, but the end result makes it worthwhile.

Lecture proposals are still welcome for the spring and should be directed to Heintz, box 260.

Potpourri

Laboratory Equipment

Planning to get rid of some equipment? Before you do, contact David Lyons, treasurer and vice president for business and finance. He may be able to find another lab at the university that could use it.

"Everyone gains by recycling equipment," says Lyons. "One lab makes space; another gets intruments they would have had to pay for —or couldn't have afforded at all. Last fiscal year, recycling capital equipment saved the university money in the six figures."

Vaccine reminder
The Employee Health Office is offering influenza vaccination, free of charge, now through December. The vaccination is administered in Employee Health Office, Hospital Room 118, between 9:00 a.m. and 5:00 p.m., Monday through Friday. For further information, contact the Employee Health Office, x8414.

Seitz memorial concert
A concert will be held in memory of Elizabeth Seitz, Wed., Nov. 18 at 8:00 p.m. in Caspary auditorium. No reservations are necessary. All are welcome. Details will follow.

African violet, bake sales
The Children's School will benefit from the proceeds of the sale of baked goods and African violets in Tower Lobby from 8:30 a.m. to 3:30 p.m.today (Oct. 23).

Tri-Institutional Noon Recital
Argentinian classical guitarist Guillermo Fierens will play solo at the Tri-Institutional Noon Recital today (Oct. 23). A protege of Andres Segovia, Fierens has performed with the London Symphony Orchestra, Halle Orchestra, Royal Philharmonic, and English Chamber Orchestra. Today's program will include pieces by Sor, Castelnuovo-Tedesco, and Villa-Lobos. The recital, to be held in Caspary Auditorium at noon, is free and open to the Tri-Institutional community.

Laboratory PC course
The electronics laboratory is offering a course in laboratory personal computing. The first meeting, The Use of the Personal Computer in the Laboratory I, will be held Friday, Oct. 30 at 9:30 a.m. in Tower 305.

The comprehensive course, taught by Paul Rosen, is open to all university faculty, students, and staff. For further information, call x8750.

Biology workshop
The second structural biology workshop will be held at Seven Springs Center, Mount Kisco, NY, Nov.12-13. All members of the Rockefeller community who are interested in understanding biological processes in terms of biomolecular structure are invited to attend. Contact Michael Overduin at x8274 or box 6 for more information and registration.

Concert Series
Pianist Horacio Gutiérrez will perform works by Haydn, Schumann, and Liszt in Caspary auditorium on Thurs., Oct. 29 at 8:00p.m.. A graduate of the Julliard School and a favorite of New York concertgoers, Mr. Gutiérrez is a frequent soloist at Lincoln Center's "Mostly Mozart" Festival, (including a "Live from Lincoln Center" telecast), and has performed numerous times at Avery Fisher Hall. He is scheduled to play at Carnegie, Nov. 4.

There are still tickets available for the full concert series as well as series A and B. For more information, contact Cathy Rogers, X8971.

Birth
Xiaodong Wu, graduate fellow in the Kuriyan lab, and his wife, Wanping Jiang, became parents of a baby boy, Kevin J. Wu, Oct 3. He weighed 8 pounds, 9 ounces.

Appointments
Adjunct Faculty: Gary Takle, G.A.M. Cross lab.
Guest Investigator: Béla Nagy, Mauzerall lab.

Departures
Adjunct Faculty: Paul Lizardi, Luck lab; Marcus Rothschild, Kreek lab; William Scott, Cohn/Steinman lab.
Visiting Assistant Professor: Reiko Akagi, Kappas lab.
Postdoctoral Associates: Takahiro Goto, Wilson lab; Philippe Pognonec, Roeder lab.
Postdoctoral Fellows: Sibylla Geelen and Andy Hoepelman, Tuomanen lab; Maria J. Koziolkiewicz, Konarska lab.
Guest Investigator: Takeshi Kaneko, Asanuma lab.

Pianist Horacio Gutiérrez will perform on Thursday evening, Oct. 29 for The RU Concert Series.