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The Rockefeller University

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## Health forum to honor its founder, Zanvil Cohn Friday lecturer

### to speak on RNA splicing

A series of seminars on health research and policy issues initiated last year by the late Zanvil A. Cohn, professor and vice president for medical affairs, will reconvene this month as the Zanvil A. Cohn Forum on Health Affairs.



A biomedical forum at the university will be named after the late Zanvil Cohn.

"I am pleased that this forum on health affairs will honor our late distinguished colleague, Zanvil Cohn," said President Torsten Wiesel. "Dr. Cohn's vision was to provide a forum where important issues in health and biomedicine could be discussed in an atmosphere congenial to the exchange of ideas. The Zanvil Cohn Forum will stay true to this vision, with particular emphasis on the research and educational issues that face New York City. I hope that the forum will be of considerable interest not only to members of the university community and our neighboring institutions, but also to members of other organizations devoted to biomedical science and health care."

Trustee, Adjunct Professor and Visiting Physician Alexander Bearn, who will chair the forum's Program Committee, said: "We are very excited about the creation of the Zanvil Cohn Forum. It will provide a new opportunity to discuss contemporary issues in health and biomedicine that affect New York City, itself a microcosm of many of the world's maladies. In so doing, the forum will reflect Zan's dedica-

tion and zest for medicine, education and the human condition."

The forum, which will meet about six times each year, will consist of 30-minute presentations followed by discussion. Sessions will begin at 5:30 P.M. in the Faculty and Students Club, and will adjourn promptly at 6:30 P.M. Sherry will be served at 5:00 P.M. All are welcome.

The inaugural session on Mon., Mar. 21, will feature University Professor Joshua Lederberg, former president of the university, speaking on "The Electronic Collaboratory: New York as a Global Village." On Thurs., Apr. 14, David B. Skinner, president and chief executive officer of New York Hospital-Cornell Medical Center, will lecture. The forum will meet one more time, on Wed., May 11, before reconvening in the fall.

For further information, contact Bearn or the other members of the Program Committee: Director of the Program for the Human Environment Jesse Ausubel, Professor and Physician-in-Chief Jules Hirsch and Professor and Senior Physician Ralph Steinman.



Assistant Professor Magda Konarska will lecture today (Mar. 4).

Assistant Professor M. Magda Konarska will speak on "Relics of the RNA World: Role of the 5' Splice Site in the Spliceosome Assembly; Transcription of HDV RNA by RNA Polymerase II" at the Friday lecture today (Mar. 4).

Konarska uses the techniques of molecular biology to study the structure and function of ribonucleic acid (RNA), a substance believed to be the earliest form of genetic material. RNA plays a central role in protein synthesis by carrying out the genetic instructions stored by DNA. Before proteins can be correctly assembled, segments of RNA containing the critical instructions from DNA are cut and spliced, in much the same way that segments in a film are edited and spliced to make one contiguous end-product. The splicing of RNA is one of Konarska's major research interests.

"It wasn't until 1977 that researchers realized that the coding sections of DNA of a great many of the cells on the planet were non-contiguous and that splicing was the mechanism enabling genetic information to be joined at the mRNA level," explained Professor

## University offers free mammography screening

All female employees of The Rockefeller University who are over 35 years old are eligible for free mammography screening early next month.

"I strongly urge Rockefeller employees—especially women over 50—to take advantage of the mammography program," said Candice Scheiner, supervisor of Employee Health. "This is a wonderful service. Not only is it free to partici-

pants, it is very convenient. The screening procedure only takes about 15 minutes—registration and all—and it is offered right here on campus, in the Radiology

Department on the third floor of Founder's Hall."

Mammograms save lives by

See *RU offers*, page 2



Candice Scheiner, supervisor of Employee Health, prepares for the university's free mammography screening program, to be held in the Radiology Department in Founder's Hall.

2 Rooms offer musical hideaway

3 Tracing Avery's legacy

4 Golden age of peptide chemistry

See *RU lecturer*, page 2

## A room of one's own: RU offers musical hideaways

By Jennifer Horne King

When daily pressures mount in the lab or office, some members of the Rockefeller University community soothe their nerves by working out in the gym, strolling across campus or sipping a hot cup of tea; others more musically inclined prefer singing an aria or playing the piano in one of the university's music rooms.

"I think playing music is a wonderful way to blow off steam," said Julie Miwa, a graduate fellow in the Heintz lab. Miwa, who has played the saxophone for 10 years, practices during a Friday time slot in the Caspary music room. From time to time, she plays jazz at clubs in the city or joins other musicians from Rockefeller to perform at special university functions.

"I have to have more than one activity in my life—something other than science," she said. "Music makes the perfect complement: it provokes an immediate sense of gratification that science cannot provide. While both are intellectually satisfying, music also fulfills me spiritually and emotionally."

Michael Peng, an assistant for research in the Steinman lab, has a Thursday time slot in the music room. During this time, he practices violin or piano, two instruments he has played since age 10. "I feel fortunate to have a place to play where no one can hear me," he said. "My apartment is not very soundproof."

Peng, who occasionally meets his



Michael Peng, assistant for research in the Steinman lab, uses the university's music rooms to practice piano, and sometimes the violin.

music teacher in the Caspary music room for a lesson, plans his practice session so that he can combine serious practice with fun. This week, Peng will practice a Bach Fugue to hone his agility; later in the hour, he'll let loose on one of his favorite works, a *Fantaisie Impromptu* by Chopin and a Mozart piano concerto. "No one likes to work on technique," he said. "I try to make it enjoyable."

Three pianos, regularly tuned and reconditioned, are available for practice at Rockefeller. They are

located as follows:

- Steinway baby grand, Caspary basement, near south stairwell (this is a large room which can accommodate other instruments);
- Kawai upright, Scholar's Residence, 38th Floor (for residents of Scholars Residence and Faculty House only);
- Baldwin upright, Graduate Students Residence, ground floor (for graduate students only);

To schedule practice time or reserve a permanent time slot, contact Sandra Walsh, x8072.

## RU lecturer to speak on RNA splicing

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James Darnell, who will introduce Konarska. "Splicing is just one of several quite sophisticated functions of RNA that have led researchers to believe that RNA preceded DNA in pre-cellular evolution. Magda is making great strides in further elucidating the details of RNA splicing and replication in eukaryotic cells. I expect that her findings will provide new and important insight on cellular evolution."

In a separate line of research, Konarska is studying the replication of hepatitis delta virus (HDV) RNA by cellular enzymes called RNA polymerases that normally copy RNA from DNA. She will discuss the implications of her findings at the lecture.

A graduate of the University of Warsaw (M.Sc., 1979) and the Institute of Biochemistry and Biophysics at the Polish Academy of Sciences (Ph.D., 1983),

Konarska completed her postdoctoral studies in 1986 in the laboratory of Phillip A. Sharp at the Center for Cancer Research, Massachusetts Institute of Technology and, one year later, was appointed research associate. In 1989, she joined the faculty of The Rockefeller University to head her own laboratory.

Konarska has received numerous awards, including the Scientific Secretary Award from the Polish Academy of Sciences in 1983, the Jakub Karol Parnas Award of the Polish Biochemical Society (1985), the Jane Coffin Childs Memorial Fund Postdoctoral Fellowship (1983-86), the Lucille P. Markey Scholar Award (since 1987) and the Monique Weill-Caulier Career Scientist Award (since 1992).

The lecture will be held in Caspary Auditorium at 3:45 P.M. and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Hall. Admission is free. All are welcome to attend.

## RU offers mammography screening

(continued from page 1)

detecting breast cancer in the earliest—and most treatable—stages. The American Cancer Society estimates that breast cancer will develop in 10 percent of women over the course of their lifetimes.

The American Cancer Society currently recommends that women 35 to 40 years old should have one baseline mammogram; those between 40 and 50 should have a mammogram every two years; and those over 50 should have a mammogram every year. While there has been some controversy over the effectiveness of mammograms for women under 50—the National Cancer Institute recently raised the age it recommends women to begin mammograms from 40 to 50—statistics clearly demonstrate the health benefits of mammograms for women 50 years of age or older.

The university's screening program is conducted by "Be Smart!," a service of Memorial-Sloan Kettering Cancer Center. This service has been offered to employees annually for about four years.

The mammography program will be held on campus Mon., Apr. 4 through Thurs., Apr. 7. To register, call 1-800-8SMART8, next week (Mar. 7 to Mar. 11), from 10:00 A.M. to 5:00 P.M.

Questions should be directed to the university's Employee Health Office, x8414.



Julie Miwa, graduate fellow in the Heintz lab, plays saxophone in one of the music rooms on campus.

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# Vaccine pioneers track Avery legacy in immunochemistry

by Susan Blum

The discovery by Rockefeller investigators Oswald Avery, Colin MacLeod and Maclyn McCarty that genes are made of DNA was a landmark event in science. But this seminal work was by no means the sole contribution that Avery and his colleagues made over the course of their long and productive careers.

As Rockefeller Professor Emil Gotschlich recently reminded an audience assembled to honor Avery, "Bear in mind that when the famous paper was published in 1944, Avery was 66 years old and was in his first year of emeritus status at Rockefeller. Yet he was elected to the National Academy of Sciences in 1933, the same year he was awarded the prestigious Paul Ehrlich Gold Medal, and was elected a fellow of the Royal Society of London in 1944. These high honors were recognition not for his work on pneumococcal transformation, but for his monumental contributions to the biology and immunochemistry of the pneumococcus, and for his ability to relate these to the interaction between this organism and the human host. With these tools and insights, Avery was able to refine the treatment of pneumococcal disease and lay the groundwork for its prevention."

This aspect of Avery's work was the subject of a lecture held last month during the week-long celebration of the 1944 Avery paper. Chaired by Gotschlich, the event featured Robert Austrian and John Robbins, two scientists whose work draws on and extends upon the tradition of research in the Avery lab.

## Specific soluble substances

Austrian, professor emeritus at the University of Pennsylvania School of Medicine and a lifelong student of the pneumococcus, began the program by recounting some of the high points of Avery's career in a talk called "The Wizard of York Avenue." Upon arriving at The Rockefeller Institute in 1913, Austrian said, Avery's first assignment was to work toward developing therapeutic horse antisera for disease caused by pneumococcal types I and II. In 1917, Avery and Alphonse Dochez discovered "specific soluble substances" in the serum and urine of patients. These substances had the same serologic specificity (that is, reacted with the same antisera) as the pneumococcal strain isolated from the patient.

Work in the lab was making it apparent that the soluble substances were derived from the pneumococ-



Last month's symposium "The Legacy of Avery" featured (left to right) Robert Austrian of the University of Pennsylvania School of Medicine, Emil Gotschlich, professor at Rockefeller, and John Robbins of the National Institutes of Health.

cal capsule, and that the capsule was essential to the microorganism's ability to cause disease. In 1922, Avery began collaborating with Michael Heidelberger to better define the chemical nature of the soluble substances, and in 1923 they reported the then-astonishing news that the substances were polysaccharides, complex structures of linked sugar molecules. Before this discovery, proteins had been the only molecules thought capable of provoking an immune response.

## First vaccines developed

Austrian explained that Avery's insights into pneumococcal capsular polysaccharides eventually led to the first demonstration that these polysaccharides, when purified, could be used for an effective anti-pneumococcal vaccine. This demonstration was made in 1945 by Avery's former colleagues MacLeod (by then at NYU) and Michael Heidelberger (then at Columbia).

The first generation of vaccines fell into disuse as penicillin demonstrated its powerful ability to kill pneumococci. But studies by Austrian in the 1960s showed that the destruction of these microorganisms did not ensure the patient's survival: in fact, even with antibiotic treatment, mortality rates from pneumococcal pneumonia remained shockingly high. These studies led Austrian to spearhead an effort to refine and reintroduce pneumococcal vaccines based on capsular polysaccharides. Such vaccines, effective against many more pneumococcal strains than the original formulations, were licensed in 1977 and are now in use around the world.

Vaccines against pneumococci were not the only purified polysaccharide capsular vaccines to grow out of work done at Rockefeller under Avery's influence, if not directly in his lab. For instance,

Gotschlich reported, during the 1930s Geoffrey Rake (working in Leslie Webster's lab) reinitiated studies on the meningococcus, a microorganism that had been under intensive scrutiny by Simon Flexner in the institute's earliest days.

Rake's studies, prompted by an epidemic of meningitis, showed that the epidemic's causative strain—group A meningococci—produced a carbohydrate capsule. Drawing on these research insights, in the 1960s and 1970s, Gotschlich and his colleagues developed two purified capsular polysaccharide vaccines, one against Group A and a second against Group C meningococci (another strain that can cause epidemics). For this accomplishment, Gotschlich shared the 1978 Lasker award with Austrian and Heidelberger, two other pioneers in vaccine development.

Margaret Pittman was another Rockefeller scientist who was influenced by the work of Avery, Gotschlich reported. Working in the laboratory of Rufus Cole, in 1931 she published work characterizing the six encapsulated strains of the *Haemophilus influenzae* bacterium. She also determined that *H. influenzae* type b is responsible for most disease caused by this microorganism, including a very serious form of meningitis that can be devastating to young children. Pittman's studies ultimately led to the first generation of vaccines against *H. influenzae* type b, which were introduced in 1985.

## Work on conjugate vaccines

But vaccines based solely on purified capsular polysaccharides have limitations. Although most polysaccharides evoke the production of protective antibodies in adult humans, they prompt an insufficient antibody response in young children, and none at all in youngsters

under the age of about two. In contrast, proteins do evoke protective antibodies even in young children, and in recent years a number of scientists—Robbins a leader among them—have been working on developing "conjugate vaccines" that link purified polysaccharides to a protein carrier that boosts their immunogenic capacities.

In his talk, Robbins, chief of the Laboratory of Developmental and Molecular Immunity at the National Institute of Child Health and Human Development, described how the conceptual framework for conjugate vaccines was laid by the studies of Avery and his colleagues. These workers had initially been inspired by Rockefeller researcher Karl Landsteiner.

Landsteiner had shown that it was possible to alter the immunologic properties of small molecules, called haptens, by chemically binding them to proteins. In the decade from 1929 to 1939, Avery and his colleague Walther Goebel extended this approach to their studies of pneumococci, in order to better understand the immunochemistry of the various pneumococcal types. As a part of their program of investigation, they found that if type III pneumococcal capsular polysaccharide (or its repeating disaccharide unit) were chemically coupled to horse serum albumin, the "conjugate" stimulated the production of anti-polysaccharide antibodies in rabbits, although the animals could not mount an antibody response to polysaccharides alone.

"This work, published in 1931, is the basis for all conjugate vaccines," Robbins asserted. But the technique used by Avery and Goebel was not suited for use in humans, and the concept of conjugate vaccines languished for decades. Recently, though, research advances have led to new interest in the development of conjugate vaccines. Among the first such vaccines to be licensed were conjugate vaccines against *H. influenzae* type b, one of which was developed by Robbins and his colleagues. Since their introduction in 1990, these vaccines have virtually eliminated the incidence of invasive *H. influenzae* infections.

Conjugate vaccines are also being developed against a wide range of other pathogens, including pneumococci, meningococci, salmonellae and staphylococci. "It's a very active field, and it all has developed from the work done here at Rockefeller in the 1930s by Avery and his associates," Robbins said, paying tribute to the enduring legacy of "The Wizard of York Avenue."

# Memoirs examine golden age of peptide chemistry

The memoirs of Professor Emeritus Bruce Merrifield, *Life During a Golden Age of Peptide Chemistry*, have recently been published by the American Chemical Society as part of a series of autobiographies of 22 of the most eminent chemists alive.

Among others, Merrifield's book will interest those who would like to know more about his early studies of nucleic acid, his recent work on antagonists of the hormone glucagon and his historic conception and development of solid-phase peptide synthesis, which took place at The Rockefeller University.

"Merrifield's 1984 Nobel Prize in chemistry is special, if not unique, in modern science," writes Jeffrey I.

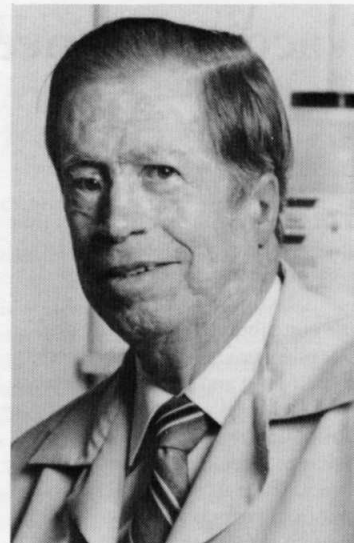
Seeman, editor of the series, in the preface to the book. "It was awarded for work conceived in his own mind and achieved by his own hand. Within 44 months.... Merrifield single-handedly revolutionized peptide chemistry with his discovery of how to synthesize peptides in a 'simpler, faster, more efficient way.'"

Despite his remarkable success, Merrifield is characteristically modest about his early efforts to develop solid-phase peptide synthesis. "When I look back at my old notebooks, I am amazed at how inefficient the early developmental work was," he writes. "I seemed always to choose the wrong reaction to do first and was not able to identify the most important parameters as

the work was progressing."

Merrifield's autobiography will also interest those curious about his early life, family and experience as an investigator at Rockefeller. Merrifield has many fond memories of the early days of The Rockefeller Institute, and describes in detail work with his mentor D. W. Woolley, his first experiences in the old faculty dining hall, and the institution's transition from an institute to a university under President Detlev Bronk. The six dozen black and white photographs scattered throughout the book add texture to Merrifield's story.

Copies of *Life During a Golden Age of Peptide Chemistry* can be obtained from the American Chemical Society, (202) 872-4200.



Professor Emeritus Bruce Merrifield recently published his memoirs.

## Potpourri

**Tri-Institutional Noon Recital**  
Guitarist Ignacio Rodas will play works for Spanish classical guitar at the Tri-Institutional Noon Recital today (Mar. 4). First-prize winner at six guitar competitions, including the Andrés Segovia competition in 1983, Rodas has made numerous international festival appearances and performed at New York's Alice Tully Hall, London's Wigmore Hall, Frankfurt's Alter Opera and the Opera Theatre of Cairo. The program will feature works by

Fernando Sor, Francisco Tárrega, Manuel de Falla, Joaquín Turina, Vicente Asencio and Enrique Granados. The concert, to be held in Caspary Auditorium at noon, is free and open to the public.

### Symposium

The Karolinska Institutet and the Rockefeller University will hold a symposium, "Eukaryotic Gene Expression and Regulating Signals" in Caspary Auditorium, Mon., Apr. 11 and Tues., Apr. 12. The symposium is free and open to all.

### Educating Congress

Associate Professor Mary Jeanne Kreek spoke to the Congressional Biomedical Research Caucus in Bethesda, Maryland on the biology of drug addiction, Feb. 28. The purpose of the caucus is to provide a forum in which Congress members and their staffs can interact directly with scientific researchers and to support the efforts of congressional committees which have invested in basic biomedical research.

### Appointments

Assistant professor/clinical scholar: Johan Hellmer, Hirsch lab.

Visiting professor: Lindley Darden, Lederberg lab.

Research associates: David Fushman, Cowburn lab; Sonoko Ogawa, Pfaff lab; Vadim Yuferov, Kreek lab.

Postdoctoral associates: George Cohen, Baltimore lab; Anne Goriely, Desplan lab; Yng-Ju Hsieh, Roeder lab; Erica Johnson and Lucy Pemberton, Blobel lab; Jiann-shiun Lai, Baltimore lab; Margherita Maffei, Friedman lab;

Konstantin Severinov, Darst lab.

### Departures

Adjunct faculty: Ronald Aronson, Crane lab; Paul U. Cameron, Steinman lab; Masami Horikoshi, Roeder lab; Thomas U. Meier, Blobel lab.

Visiting professor: Shlomo Breznitz, McEwen lab.

Research associates: Akira Akabayashi, McEwen lab; Katherine A. Sakmar, Steinman lab; Eric Schaeffer, Greengard lab.

Postdoctoral associates: Hirokazu Inoue, Hanafusa lab; Lei Rong, M. Young lab; Jolanta Vidugiriene, Cross lab.

### Discount

Nassau Printing & Copy Center, Inc., 335 East 65th St, telephone 988-9803, is offering a 10 percent discount to members of the Rockefeller community.

## Edward G. Clarke dies

Edward G. Clarke, former director of security at The Rockefeller University, died of a stroke on Monday.

Clarke came to Rockefeller in 1982 after many years of service in the New York Police Department, where he had earned 10 meritorious police service citations for his work in burglary, arson and homicide. He served as director of security at Rockefeller until his retirement in 1989. He is survived by his wife, Bernadette, and three sons.

Courtesy of the artist



Guitarist Ignacio Rodas will play works for Spanish classical guitar at the Tri-Institutional Noon Recital today (Mar. 4).



"AND IT WAS IN THIS VERY LABORATORY THAT THE THEORY OF CHAOS WAS FIRST CONCEIVED"