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RU to celebrate 50 years of DNA research

Year-long series commemorates Avery lab's revolutionary discovery

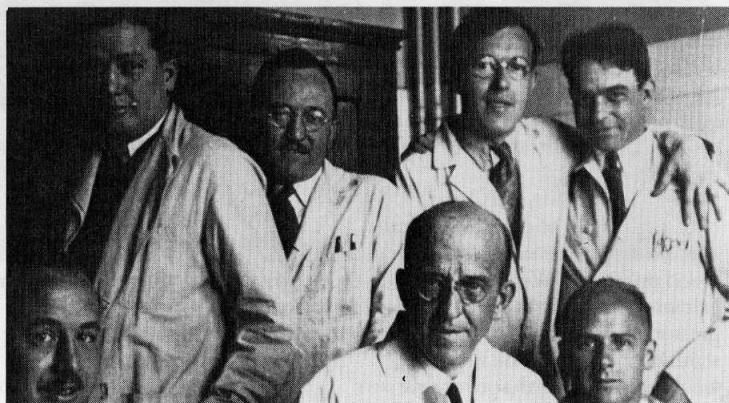
To commemorate the 50th anniversary of the discovery at The Rockefeller University that genes are made of DNA—considered by many to be the single most important scientific finding of the 20th century—the university will hold a series of special events throughout the academic year.

"The discovery of Oswald Avery, Colin MacLeod and Maclyn McCarty opened the gateway to the modern era of biology and medicine," said President Torsten Wiesel. "In celebrating this historical event, we celebrate as well The Rockefeller University's enduring mission of diagnosing and curing sickness by uncovering the inner secrets of life."

In 1944, on the sixth floor of The Rockefeller University Hospital, Avery and two colleagues, Colin MacLeod and Maclyn McCarty, discovered that genes are made of deoxyribonucleic acid—DNA. This finding, first published in *The Journal of Experimental Medicine* on Feb. 1, 1944, was totally unexpected. Before Avery, MacLeod and McCarty, no link had ever been seen between the passage of genetic information and the presence of DNA. Their paper revealed the hidden hereditary nature of the thread-like DNA fibers present in all cells. This publication laid the groundwork for the more well publicized discovery by James Watson and Francis Crick of the double-helical structure of DNA molecules.

Professor Norton Zinder, chair of the faculty committee which helped plan the celebration, added: "Avery *et al*'s finding completely

The Rockefeller University Archives



In 1944, the laboratory of Oswald Avery (center front) discovered that genes are made of DNA. (Photo circa 1932.)

altered our way of thinking about biological problems, ushering in a whole new era of science. The finding was so fundamental that much of biological research today is still building on it." Other members of the faculty committee are: Jan Breslow, Titia de Lange, Jeffrey Friedman, Emil Gotschlich and Joshua Lederberg.

The year-long series, which will be held in Caspary Auditorium, will include the following events:

- Tues., Nov. 16, 6:00 P.M. "Early Days of DNA," a public lecture by James Watson, director of

Cold Spring Harbor Laboratory;

- Wed., Dec. 29 and Thurs., Dec. 30, 10:00 A.M. The Annual Alfred E. Mirsky Christmas Lectures for New York City High School Students, "da Vinci and Darwin in the Molecules of Life," by John Kuriyan, professor, and Stephen Burley, associate professor, The Rockefeller University;

- Wed., Feb. 2, 5:00 P.M. "The Human Genome Project in its Scientific Context," a public lecture by David Botstein, professor and

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Two ceremonies to honor employees

Employees of The Rockefeller University will be recognized for their loyalty and dedication at two time-honored traditions: the Employee Recognition Reception, to be held Thurs., Oct. 28, and the Anniversary and Retirement Dinner, to be held Thurs., Nov. 4.

The Employee Recognition Reception will honor employees who have served the university for 10 or 20 years. President Torsten Wiesel will be among those honored for 10 years of service.

"Everyone on campus is invited to this event," said Virginia Huffman, director of Personnel, whose office is organizing both events with Sandi Walsh, special events coordinator. "We encourage everyone to come support their colleagues." The Employee Recognition program will be held at 3:00 P.M. on the 17th floor of Tower. A reception will follow the ceremony.

The Anniversary and Retirement Dinner will honor faculty and staff celebrating their 25th, 40th, 50th, 60th—and this year, 65th—anniversaries at the university, or retiring after 10 years or more of service. All those who have been with the university 25 or more years have been invited. A cocktail hour will commence at 6:30 P.M. on the second floor of Tower, followed by the dinner and awards program.

"Sometimes it is difficult for us to decipher service records from many years past," said Huffman. "We hope that employees who believe they are reaching a special milestone at the university but who have not yet received an invitation to either of these events will let us know. We wouldn't want anyone to be disappointed."

For more information, contact the Office of Personnel, x8300.

Leading geneticist to speak at Lederberg Lecture

Daniel Cohen, professor of genetics at the University of Paris and director of the Human Polymorphism Study Center (CEPH), will give the Joshua Lederberg Distinguished Lecture today (Oct. 22). He will speak on the "Physical Map of the Whole Human Genome."

"Daniel Cohen has emerged as one of the world's leaders in developing new technologies in human genetics as well as their application to human disease," said Associate Professor Jeffrey Friedman, who is hosting the lecture. "The application of large-scale and novel techniques in automation to the ongoing effort to build a physical map of the human genome is unprecedented and has proven to be indispensable for the tremendous progress that has been made in this field."

Cohen helped establish the CEPH as a leading institution for the study of genetics and human disease. He has helped to compile a human genetic map through the collection of 60 reference pedigrees (DNA libraries of three-generation families) which now serve as the foundation for genetic mapping efforts worldwide. Cohen and his colleagues played a critical role in identifying genes causally related to diseases including diabetes, muscular dystrophy and recessive medullary cystic kidney disease.

Cohen received his Baccalauréat (1968) and M.D. (1976) from the University of Paris. After completing his clinical training in immunology, he joined the CEPH as a founding member. In 1986, he became a professor in genetics at the University of Paris. In 1990, Cohen helped found GENE-THON, a nonprofit corporation for the identification of genes causing human disease, where studies have resulted in the piecing together of dense genetic and physical maps of the entire human genome. In 1992, Cohen became director of the CEPH.

A specialist in immunogenetic studies on AIDS for the European Economic Community and member of the European Commission on Human Genome Analysis, Cohen

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2 Calcium deficit and hypertension

3 New insights on tic disorder

4 A kiss from Mayor Dinkins

Nutrition investigator speaks at RU clinical research seminar

David McCarron, director of the National Institutes of Health's Clinical Nutrition Research Unit at the Oregon Health Sciences University, spoke about his research on Wednesday as part of The Rockefeller University Hospital's weekly seminar series.

While the role of salt in hypertension has received a great deal of publicity, McCarron's work focuses

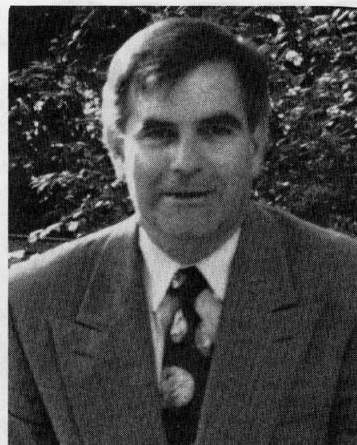
on the relation between other nutritional factors—especially calcium consumption and absorption—and hypertension. "Our research has shown that insufficient calcium intake is the single best nutritional predictor of high blood pressure," McCarron said. "In addition, as many as 40 percent of the population with high blood pressure may have problems absorbing or retaining calcium and would therefore benefit from more calcium in their diets."

Recent studies by McCarron tested the effect of giving calcium supplements to those with high blood pressure. "We found that calcium supplements lowered blood pressure by a small but clinically significant amount," he said. "I would recommend that everyone make sure they get enough calcium by eating dairy products and leafy green vegetables."

McCarron's talk was funded by a grant to The Rockefeller University from the National Dairy Council's Visiting Professorship in Nutrition Program. During his three-day stay, McCarron also spoke with investigators of The New York Hospital-Cornell University Medical School and Memorial Sloan-Kettering Cancer Center.

The Seminars in Clinical Research Series is a forum for Rockefeller's clinical investigators to discuss their own research as well as to hear about research at other institutions. Upcoming speakers in the series include:

- Oct. 27, Barbara Hempstead, Cornell University Medical Center, "Control of Cell Growth by Receptor Tyrosine Kinases";



Jennifer Horne King

David McCarron spoke about his research on the relation between high blood pressure and insufficient calcium consumption.

- Nov. 3, Thomas P. Sakmar, The Rockefeller University, "The Role of Rhodopsin Mutations in Retinitis Pigmentosa";
- Nov. 10, Margaret Bassendine, University of Newcastle, "Primary Biliary Cirrhosis: A Model of Autoimmune Disease?";
- Nov. 17, David Ron, New York University Medical Center, "Inducible Growth Arrest and Chop";
- Dec. 1, Theo Golan, Bnaizion Medical Center (Haifa, Israel), "Solar Radiation and SLE";
- Dec. 8, Josef Eisinger, Mount Sinai School of Medicine, "Historical and Biochemical Aspects of Environmental Lead Disease."

The seminars take place most Wednesdays at noon, in Nurses Residence 110B. For more information, contact Patricia Dell'Ortone, x8424. Members of the selection committee are: Robert Darnell, Naomi Fukagawa, Geoffrey Manley and Shigeru Sassa.

RU celebrates 50 years of DNA work

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chairman, Department of Genetics, Stanford University School of Medicine;

- Thurs., Feb. 3, 4:00 P.M. "Historical Roundtable," a discussion with key scientists active between the publication of the 1944 Avery, MacLeod and McCarty paper and the 1953 discovery of DNA's double-helical structure;
- Fri., Feb. 4, 3:45 P.M. Scientific symposium on the research areas pursued by the Avery laboratory—immunology, infectious disease and molecular medicine;
- Mon., April 18, 6:00 P.M. "Public Lecture on Ethics and DNA Technology," by Nancy Wexler, professor, Columbia University, and chair of the Joint National Institutes of Health/Department of Energy Human Genome Project's Committee on Ethics;
- Fri., May 6, 3:45 P.M. Scientific symposium on key areas of DNA research at Rockefeller.

An exhibit and banner marking the Avery lab discovery will be installed at the Hospital for its anniversary next week.

"The complementary relation between basic research in the natural sciences and understanding and treatment of human disease was fundamental to the Avery laboratory and remains the guiding principle of the university today," Wiesel said. "This 50th anniversary is a good opportunity for us to celebrate this relationship and to explain the mission, culture and achievements of the university to a new generation of scientists, the university's friends and supporters, and the general public."

For more information, contact the Office of Public Affairs, x8967.

Lederberg Lecture to feature leading French geneticist

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is the recipient of many awards, including the Knight of the National Order of Merit, the Rhone Rorer Prize and the Daniel Beaufour Prize of the French Academy of Sciences. He is an honorary professor at both Shanghai University II and the University of Xi'an in China.

The Joshua Lederberg Distinguished Lecture was endowed in honor of University Professor Joshua Lederberg by the Raymond and Beverly Sackler Foundation following Lederberg's retirement from the presidency of Rockefeller in 1990.

A graduate of Columbia College (B.A., 1944), and Yale University (Ph.D., 1947), Lederberg discovered a mechanism of genetic recombination in bacteria while a Ph.D. student, demonstrating that a form of sexual reproduction occurs in these microorganisms. This work earned him the Nobel Prize in Physiology or Medicine in 1958 at the age of 33.

After appointments at the University of Wisconsin and the Stanford University School of Medicine, Lederberg came to Rockefeller as its fifth president in 1978. Since retiring as president, he has returned to research as head of the Laboratory of Molecular Genetics and Informatics. Throughout his career, Lederberg has also taken important advisory roles in government.

On the lighter side of science



Leslie Aitchison

Leslie Aitchison

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New theories about tic disorder have roots in RU research

By Susan Blum

Facial and body tics can disrupt a youngster's childhood and cause problems at school and at home. Sometimes these disorders can be traced to organic brain damage, but their cause has often remained a mystery. Now, according to a recent report in the medical journal, *Pediatrics*, it appears that at least some of these hitherto-unexplained cases might be due to infection with group A streptococci.

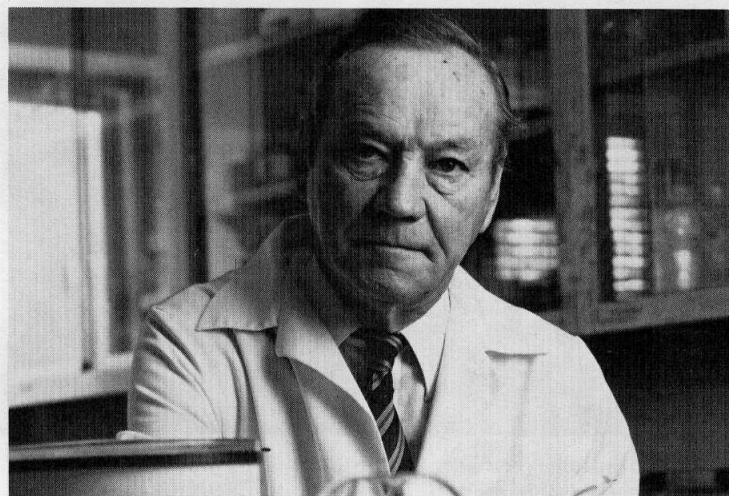
The research underlying this new hypothesis has its roots in the Rockefeller University laboratory of Associate Professor John Zabriskie, where studies focus on microbially induced autoimmune disease.

Many microbes have evolved antigens (molecular "tags") that mimic the antigens normally found on particular tissues of the host they invade. "This mimicry helps the microbes escape immune surveillance," Zabriskie explained. "If you look like the host, you may be able to hide away in your niche and avoid being destroyed." Sometimes, though, the immune system refuses to be fooled and produces antibodies against the invader's look-alike antigen. Unfortunately, these antibodies can then "cross-react" with and damage the host's tissue, too.

Zabriskie's initial studies of cross-reactive antibodies focused on those produced in rheumatic fever, a disease that can occur following infection with group A streptococci. In the mid-1960s, his pioneering research revealed that heart damage—one of rheumatic fever's major manifestations—is caused by cross-reactive antibodies that attack both the streptococcus and heart tissue.

With this discovery in mind, about a decade later Ralph Williams of the University of New Mexico, and his colleague, Gunnar Husby, consulted Zabriskie and his co-workers. Williams, who had trained under the late Rockefeller immunologist Henry Kunkel, was aware of Zabriskie's earlier studies on the heart complications of rheumatic fever, and now sought to undertake a joint study of Sydenham's chorea, another major manifestation of rheumatic fever. The chorea is a neurological condition characterized by severe facial and body tics and, sometimes, attention disorders.

Using specialized techniques they helped to develop, the Rockefeller research team discovered cross-reactive antibodies to neuronal tissue in the blood of 46 percent of the children with Sydenham's chorea whom they studied. The anti-neu-



Work in Associate Professor John Zabriskie's lab focuses on microbially induced autoimmune disease.

ronal antibodies, elicited by *Streptococcus A*, helped mediate damage to nerve cells in areas of the brain responsible for the control of movement.

Classic studies yield new insights

The Sydenham's chorea studies became classics in the medical literature, so well known that they immediately sprang to mind in the late 1980s when Louise Kiesseling, associate professor of pediatrics at Brown University and chief of pediatrics at its affiliated Memorial Hospital of Rhode Island, noticed a striking new phenomenon. She remarked that the number of children with movement disorders seen in the hospital had increased dramatically since 1989—as had the incidence of Group A streptococcal infections in the community.

The symptoms displayed by the children were generally less severe than those seen in Sydenham's chorea, but they covered a wide range of facial and body tics, and included Tourette syndrome, a disorder in which facial and body tics are accompanied by strange and offensive vocal outcries.

Kiesseling wondered whether the increase in movement disorders and the increase in strep infections might be connected, so she contacted Zabriskie and his colleagues. From them, she learned the techniques they had used in their studies of Sydenham's chorea and put them to use in her own patient population. The results of her initial investigations showed that 44 percent of the children she studied had antineuronal antibodies in their blood, and that many of these also had evidence of having had a streptococcal infection. In her article on the

research, which appeared in the July issue of *Pediatrics*, Kiesseling suggests that infection with Group A streptococcus is "strongly related" to the occurrence of movement disorders in her young patients.

Results are only preliminary

These initial results have garnered a tremendous amount of interest from the medical community and the lay public. Both Kiesseling and Zabriskie stress, however, that at this point the results are only preliminary. "It's a very interesting hypothesis, but much research remains to be done," said Zabriskie.

Indeed, he will continue to collaborate with Kiesseling in some of her future studies. For instance, she wants to pin down which particular epitopes, or subsegments, of the strep A antigen might be eliciting the antibodies that react with neuronal tissue. For this work, Zabriskie is providing samples from his ample collection of strep A antigens, and he and his colleagues will also be on hand to assist in the epitope analysis.

What might the implications for treatment be should the relationship between strep A infections and movement disorders be proved?

One treatment method might be plasmapheresis, a process that removes the offending antibodies from the blood. In 1991, Zabriskie collaborated with Alan Aron, director of the Child Neurology Section of Mount Sinai Hospital, to show that plasmapheresis could work to relieve the symptoms of Sydenham's chorea, and he believes it might also be useful for the most severe cases of other kinds of movement disorders caused by antibodies elicited by group A streptococci.

Another treatment possibility might be the use of immune-suppressive drugs. "This is not a strategy to be taken lightly," Zabriskie said, since treatments that suppress immune function can have serious side effects. But in the case of severe movement disorders, the risks of such treatment might well be worth taking.

Antibiotics might also be used. Both Zabriskie and Kiesseling stress that antibiotic treatment could not "cure" a current episode of a strep-induced movement disorder, which eventually would resolve on its own. Antibiotics are not a cure, Zabriskie explained, because by the time the tics occur, the streptococci have long since been cleared by the body. It is only the antibodies to them which remain, and which—for as yet unknown reasons—go on to attack tissues in the brain before the antibodies, too, are eventually cleared from the body.

But though antibiotic treatment cannot cure a current episode of strep-induced tics, it may be useful in preventing a movement disorder from recurring in the future. As any parent knows, one round of strep A infection does not render a child immune to subsequent infections. This is so because strep A comes in many different strains, and antibodies produced by the body against one strain do not confer immunity to others. The point, then, would be to help a tic-prone child resist future strep infections by administering potent antibiotics that may help confer a wider range of immunity. Kiesseling is currently conducting studies to see if such a preventive strategy works.

Genetic differences may be involved

Kiesseling's studies are a satisfying continuation of the studies begun by Zabriskie decades ago. In another, related, area of investigation, Zabriskie and his colleagues have identified a particular "marker" on B cells that is found in all people who develop rheumatic fever after infection with group A streptococci. They are currently seeking to characterize this marker, for they believe that it may help uncover genetic differences that make some people's immune systems more likely to produce the cross-reactive antibodies that lead to microbially-induced autoimmune disease. In the same way, Zabriskie and Kiesseling speculate, genetic differences probably help explain why some children develop tics after infection with group A streptococci, while others do not.

Mayor Dinkins presents award to RU for corporate citizenship

By Jennifer Horne King

New York City Mayor David Dinkins kissed Kate Cameron, Rockefeller University's furnishings and interiors manager, at City Hall last month. The occasion? The presentation of the Mayor's Award for Corporate Citizenship to the university in recognition of its support of a carpet installer, Fernando Mateo, and the Mateo Institute of Training at Riker's Island.

Cameron has worked with Mateo and his carpet installation company—Carpet Fashion Floor Coverings—for the past three years. "The first time we met, Fernando offered us the best bid, so he was hired," explained Cameron. "Since then, he and his men continue to offer us good bids and consistently give us excellent results. When we found out that he helps to give young delinquents a new start, we were delighted!"

As it turned out, 33-year-old Mateo had his own success story: a



Carpet installer Fernando Mateo (left), Rockefeller University Furnishings and Interiors Manager Kate Cameron and Mayor David Dinkins hold the plaque for corporate citizenship.

former first-time offender with a history of drug abuse and unemployment, he started his carpet company on credit and turned it into a booming business with a client roster that includes Bill Cosby, Walter Cronkite and

Raquel Welch. In 1991, Mateo used the profits from his lucrative trade, together with unsolicited donations and volunteer support, to found an institute that would give other first-time offenders convicted of non-violent offenses an

opportunity to make themselves more employable. The institute teaches the young Riker's Island inmates how to install carpets and provides them with a tool box when they graduate. Upon release, the youths are promised apprentice jobs at various companies.

Representatives from 13 other organizations employing Mateo—including Merrill Lynch, Chase Manhattan Bank and Con Edison—were also present to receive awards. "If only more individuals could lend a hand to help these youths the way Fernando has..." said Cameron. "We play a relatively small role in his public-private partnership. Fernando is the one who deserves most of the credit for using his profits for a good cause."

And what about the kiss? "It was a tender moment," recalled Cameron. "But I'm not sure it's going to do the mayor any good, because I haven't registered to vote!"

Potpourri

Tri-Institutional Noon Recital
Pianist Ossie Borosh, a winner of the Olga Koussevitsky Competition, will play works by Joseph Haydn, Johannes Brahms, Frédéric Chopin, Béla Bartók and Franz Liszt at the Tri-Institutional Noon Recital today (Oct. 22). The concert, to be held in Caspary Auditorium at noon, is free and open to the public.

Sunday film

Some Like It Hot (1959), directed by Billy Wilder, will be shown in Caspary Auditorium at 7:30 P.M., Sun., Oct. 24. The celebrated comedy is the story of an encounter between two musicians (played by Jack Lemmon and Tony Curtis), who pass themselves off as part of an all-female traveling band while running from the Mob, and the band's ukulele-playing vocalist, played by Marilyn Monroe. Admission is free. All are welcome.

Seminar

The Personnel Office will host a morning and afternoon seminar on TIAA/CREF Supplemental Retirement Accounts. Martin Volpe, a TIAA/CREF representative, will explain the retirement accounts and will be available to answer questions. The two sessions, to be held from 11:30 A.M. to 12:30 P.M. and from 1:00 to 2:00 P.M., will take place in Nurses Residence 110B, Tues., Oct. 26.

All are welcome. For more information, contact Personnel, x8300.

Community board meeting

Community Boards 6 and 8 will hold a joint meeting in Caspary Auditorium Tues., Oct. 26 at 7:00 P.M. On the agenda will be a review of the community district map and other issues of common concern. Meetings, which usually take place monthly, are open to the public and allot time for citizens to speak. For more information, contact the district manager for Community Board 8, Edward Benson, 427-4840, or the district manager for Community Board 6, Carol Pieper, 679-0907.

Holiday schedule

This year, the university will be closed during the entire week following Christmas—Dec. 27 to 31—for the Christmas and New Year's holidays, due to the fact that both days fall on Saturdays. The revised holiday schedule applies to this calendar year only. Questions should be directed to Personnel, x8300.

Honor

Ingrid Reed, vice president for public affairs and corporate secretary, was elected to The National Academy of Public Administration for her "distinguished record as a practitioner in public administration and management." The academy is a private, nonprofit corpora-

tion chartered by Congress to improve the effectiveness of government at all levels.

Award

Robin Nesby, assistant director of Sponsored Programs, was awarded a travel stipend by the National Council of University Research Administrators to attend one of the council's annual regional meetings. Nesby was also given council membership.

Conference chair

Meena Jhanwar-Uniyal, senior research associate in the Leibowitz lab, will chair a session on ingestive

behavior at the 23rd annual meeting of the Society for Neuroscience, to be held in Washington D.C., Sun., Nov. 7 through Fri., Nov. 12.

Free refill

At the first meeting of the Food Services Advisory Committee, the group recommended that the university reinstitute the custom of a free second cup of coffee. This recommendation was put into effect on Mon., Oct. 18 by placing carafes of coffee on the buffet in the south dining area. Those who have paid for their first cut of coffee are welcome to help themselves to a second cup.



The first evening concert of the year, held Wednesday, was a popular event. The New York Philharmonic Ensembles played to a full house and the pre-concert buffet, a new feature this year, was sold out.