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The Rockefeller University

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news & notes

March 3, 1995 Volume 5, Number 19

The Rockefeller University

Rockefeller to celebrate 50 years of electron microscopy and cell biology

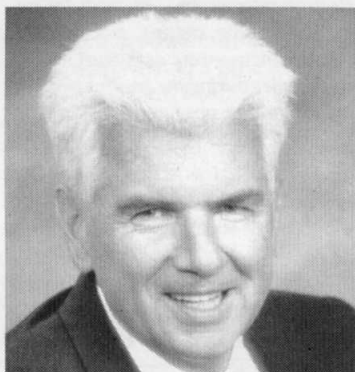
The Rockefeller University will commemorate the 50th anniversary of the use of the electron microscope in cell biology with a three-day celebration beginning Thurs., Mar. 16. "Journey Into the Cell: Celebrating 50 Years of Electron Microscopy and Modern Cell Biology" focuses on the past, present, and future of modern cell biology.

The three-day series of lectures and events marks the anniversary of the publication of the first electron micrograph of an intact cell—the work of Rockefeller scientists Albert Claude and Keith Porter in collaboration with Ernest Fullam of the Interchemical Corporation.

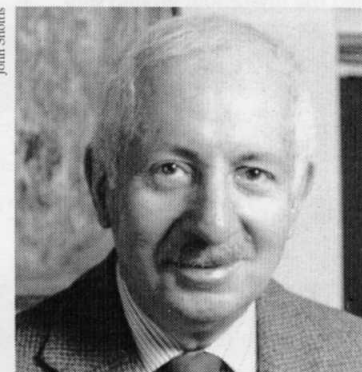
"The creativity of Rockefeller biologists in pioneering the use of

the electron microscope has shaped modern cell biology," said President Torsten Wiesel. "The celebration reminds us of the importance of technology in advancing our understanding of the fundamentals of cell structure and function. I am most grateful to Phil Siekevitz and Günter Blobel for organizing a program recognizing this critical milestone in the life of the university and life science more generally."

For the schedule of lectures and events, see page 3, which also displays a sampler of recent electron micrographs taken at Rockefeller. On page 2 is the story of the first electron micrograph and an explanation of how electron microscopy works.



Courtesy of the Lasker Foundation



John Sholtis

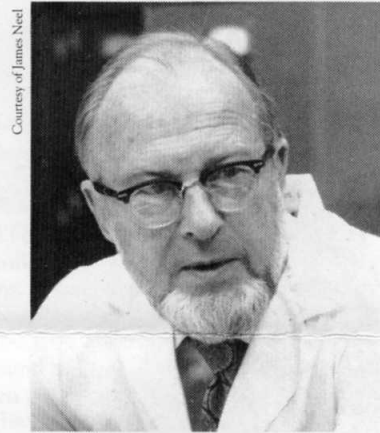
Professor Günter Blobel (left) and Professor Emeritus Philip Siekevitz organized the university's scientific celebration of electron microscopy and cell biology, which begins Thurs., Mar. 16.

Eminent geneticist to give Lederberg lecture on implications of gene research

James V. Neel, Lee R. Dice Distinguished University Professor Emeritus of Human Genetics at the University of Michigan Medical School, will give the fifth annual Joshua Lederberg Distinguished Lecture in Molecular Genetics today (Mar. 3). His topic will be "Genetic Research: The Hope of the Future?"

Neel's early training was in the genetics of *Drosophila* under Curt Stern, but an interest in human genetics led him to seek a medical degree. As a resident at Strong Memorial Hospital in Rochester, he studied the genetics of Cooley's anemia. After the Second World War, his work with the Atomic Bomb Casualty Commission in Japan resulted in comprehensive data on the effects of ionizing radiations in producing mutations in the germ cells of exposed humans. One of the first to study the genetics of diabetes, Neel has also investigated the effects of inbreeding on mortality, morbidity, and fertility in Japan and Brazil and pursued the genes for sickle cell disease in Africa. Today he will discuss the implications of genetic research.

"James Neel trained as a classical geneticist more than fifty years ago and was among the first to realize that the scientific application of genetic principles to human disease was not only a legitimate field of



Courtesy of James Neel

James V. Neel gives the fifth annual Lederberg lecture today (Mar. 3).

inquiry but one that promised medical enlightenment," said Rockefeller trustee Alexander Bearn, who will introduce Neel. "He has inspired a generation of human geneticists not only through his research but also through his enthusiasm and scientific generosity."

Neel is a graduate of the University of Rochester (Ph.D., 1939; M.D., 1944). After completing an internship and residency at Strong Memorial Hospital in 1946, he began his affiliation with the University of Michigan as an assistant geneticist. From 1956 to 1981, he was chairman of the Department of Human Genetics. In 1985, he was named Lee R. Dice Distinguished Professor Emeritus of Human Genetics and Professor Emeritus of Internal Medicine.

In addition to the Atomic Bomb Casualty Commission, Neel has been a member of numerous scientific committees, including the World Health Organization Expert Advisory Panel on Radiation and the Advisory Council of the National Institute of Aging. He is chairman of the Committee on Radiological Safety in the Marshall Islands and advisor of the Third World Academy of Sciences.

Neel is the recipient of many awards and honors, including the the Albert Lasker Basic Research Award, the National Medal of Science, and the James D. Bruce Award of the American College of

University selects Amgen for license to develop therapies based on *ob* gene

The Rockefeller University and the Amgen Corporation jointly announced Tues., Feb. 28 that the university has accepted an offer

from Amgen for the licensing of technology from the discovery last fall of the so-called obesity gene in the laboratory of Jeffrey Friedman, associate professor at Rockefeller and associate investigator of the Howard Hughes Medical Institute (H.H.M.I.).

In making the announcement, President Torsten Wiesel said, "We are confident that Amgen, the world's largest biotechnology company, will be able to quickly and effectively devise ways to treat obesity, a serious condition that predisposes people to such potentially life-threatening diseases as diabetes, heart disease, and high blood pressure."

The Friedman lab reported the isolation and cloning of the mouse

ob gene and its human homologue in the Dec. 1, 1994 issue of *Nature*. The lab spent eight years gathering evidence indicating that the gene codes for a signaling molecule produced by fat cells, which assists the brain in regulating food intake and energy expenditure. Members of the lab are now working to confirm *ob*'s role in weight regulation along with Amgen.

A university committee of trustees and senior officers recommended Amgen to the executive committee of the board under university policies adopted by the board. The committee reviewed proposals from leading pharmaceutical and biotechnology companies

2 All about electron microscopy

3 A study in contrasts

4 Historical novelist comes to lunch

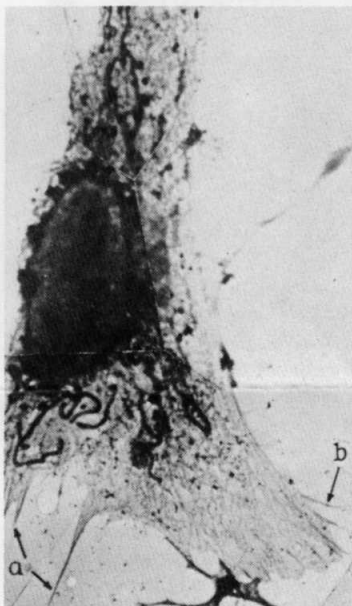
See *Amgen*, page 4

See *Neel*, page 4

When scientific explorers unearthed the complex city of the cell

by Susan Blum

Rockefeller's three-day celebration of a half century of electron microscopy and modern cell biology commemorates the 50th anniversary of the publication of



This historic first electron micrograph of an intact cell was published in *The Journal of Experimental Medicine* in March 1945.

the first electron micrograph of an intact cell—a feat accomplished by Rockefeller scientists Albert Claude and Keith Porter in collaboration with Ernest Fullam of the Interchemical Corporation.

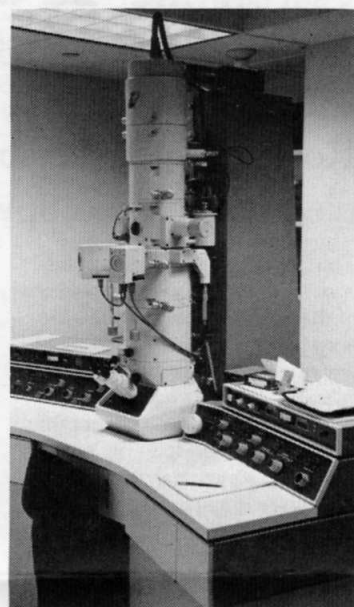
Revealed in the historic image of a cultured chick embryo fibroblast (at left) were structures that the scientists described as “filamentous mitochondria of various lengths..., scattered small elements... presumably representing Golgi bodies,” and “a delicate lacework extending throughout the cytoplasm.” In the decade or so that followed this first dramatic (but still somewhat hazy) look into the subcellular world, Claude, Porter, and other cell biologists at Rockefeller—including Christian de Duve, George Palade, and Philip Siekevitz—combined electron microscopy with biochem-

istry and cell fractionation to forge the keys to a vast cellular city. Once entered, the cell's domains could be explored—its power stations (mitochondria), recycling plants (lysosomes), protein factories (ribosomes), and protein packaging and export facilities (the lacework endoplasmic reticulum and the Golgi apparatus). For their work, Claude, Palade, and de Duve were awarded the Nobel Prize in 1974.

Today, electron microscopy remains an integral part of studies in cell biology, enabling researchers to visualize a vast array of elements within the cellular city, including its specialized neighborhoods, the infectious agents that sometimes invade it, and the macromolecules, such as DNA and proteins, that keep it alive and humming.

In his Nobel lecture in 1974, Albert Claude recalled his frustration when the secrets of the cell lay out of reach:

“I remember vividly my student days, spending hours at the light microscope, turning endlessly the micrometric screw, and gazing at the blurred boundary which concealed the mysterious ground substance where the secret mechanism of cell life might be found. At last I remembered an old saying, inherited from the Greeks—that the same causes always produce the same effects—and I realized that I should stop that futile game and try something else.”



Today, Rockefeller has two transmission electron microscopes. One magnifies a specimen up to 555,000 times its actual size; the other one up to 250,000 times. Many of the techniques and procedures essential for electron microscopy—methods for fixing, embedding, cutting, and staining the specimen—were developed here at Rockefeller during the fruitful pioneering explorations begun fifty years ago.

Speeding electrons break barrier of light microscopy

All microscopy uses some type of radiant energy to probe the structure of the specimen under study. The revelatory power of each microscopic technique is subject to the fundamental law of optics, in which the resolving power—the ability to distinguish between two neighboring objects—is directly related to the energy's wavelength. Organisms such as bacteria or organelles such as mitochondria are the smallest objects that can be envisioned with conventional light microscopes. In contrast, structures up to a hundred times smaller can be seen with electron microscopy, which uses beams of high-velocity electrons with wavelengths much shorter than visible light.

In principle, electron microscopy is similar to light microscopy. The main difference—in addition to the radiation source—is that the focus is provided by electromagnetic lenses rather than optical ones.

The source of the radiant energy is a heated filament or cathode, which emits electrons at the top of a cylindrical column about six feet high. The column is pumped to create a vacuum to prevent the electrons from being scattered by

collision with air molecules. The electrons are then accelerated from the filament by a nearby anode and pass through a tiny hole to form an electron beam that is focused by magnetic coils along the column.

In transmission electron microscopy—used for the historic micro-

graph and still commonly used today—the beam of electrons is directed through the specimen, which rests on a metal grid in the vacuum column. Usually, thin sections (about one two-hundredth the thickness of a single cell) are examined, to make possible study

of the complex and overlapping arrangement of internal cellular structures. When the sample has been stained with the salts of heavy metals, some electrons in the beam scatter more than others. The more the electrons scatter, the greater the contrast in the resultant image.

Leif Carlsson



Helen Shio (left) and Eleana Sphicas staff the electron microscopy service, located in the Shared Technology Center in the Rockefeller Research Building. The microscopists are experts in a range of techniques such as negative staining, rotary shadowing, autoradiography, cryoultramicrotomy, and immunoelectron microscopy. “If our skills and tools are amenable to the study, we’re here to collaborate,” Shio says. The collaboration can take any number of forms, from preparing and examining specimens, to teaching researchers how to use the microscopes, to suggesting fruitful analytic approaches.

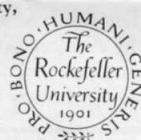
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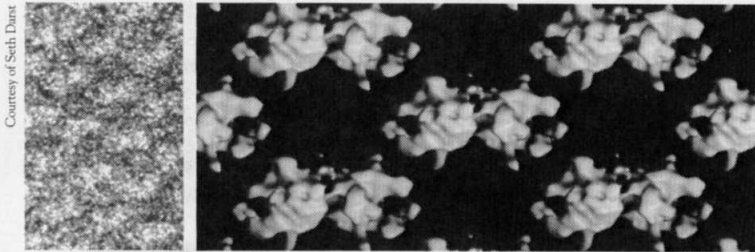
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Negative particles, positive results

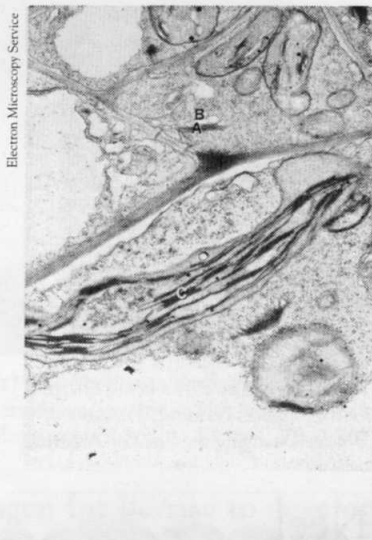
Electron microscope resolves cellular structures and biological questions

Many researchers on campus draw on electron microscopy to pursue studies on subjects such as the form and function of cells and the location of particular molecules within them. This selection of micrographs, recently produced in Rockefeller's Shared Technology Center, provides glimpses into the intracellular world disclosed by the powerful technology.

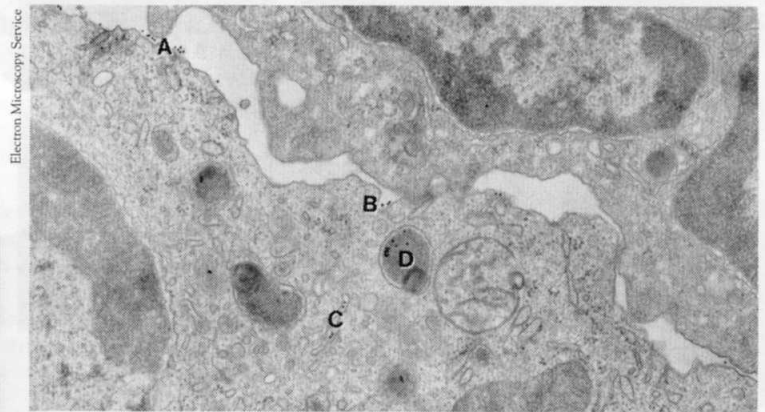


Assistant Professor Seth Darst uses a type of electron microscopy called electron crystallography to study RNA polymerase, a large protein involved in gene transcription. In this method, an electron beam of extremely high energy (and, thus, extremely short wavelength) provides maximal resolving power; it is used in low doses, to minimize destruction of the sample. Images of the molecular crystals are taken from many different angles, and a computer processes them and generates a 3-D reconstruction. On the left, above, is an electron micrograph generated from a crystal of RNA polymerase; at right, the reconstructed image.

Diane Shevell, a postdoc in the Chua lab, was studying a gene in the *Arabidopsis* plant, EMB30, which codes for a protein similar to a yeast protein called SEC7. Shevell wanted to know if plant cells with a mutant *emb30* gene had abnormal Golgi complexes, as do yeast cells with mutant *sec7* genes. Electron micrographs showed that the Golgi complexes in the mutant plant cells appeared normal. At right, a micrograph of a normal plant cell, which Shevell used as a control, shows a Golgi complex (A), transport vesicles (B), and a chloroplast, the cell's photosynthetic organelle (C).



Hui-Qan Han, assistant professor in the Greengard lab, studies synapsins, proteins implicated in the formation of synapses, the connections between neurons. Han introduced synapsin genes into fibroblast cells. Micrographs showed that these altered fibroblasts developed elongated processes characteristic of axons and dendrites. These features included the reorganization of F-actin, a cytoskeletal component, into thick cable-like bundles (straight arrows, left), as well as elongated microtubules (curved arrows), the backbones of nerve cell processes. The results suggest that synapsins may interact with actin, and possibly other elements, during neuronal development.



Postdoc Wanping Jiang and Biomedical Fellow William Swiggard, in the Nussenzweig and Steinman labs, have collaboratively identified a novel cell-surface receptor that directs antigens, or foreign proteins, from outside the cell to a specialized antigen-processing compartment within it. The electron micrograph above shows the path the receptor and antigen take through the cell. The receptors (bound to a gold-coated antibody that stands in for an antigen) can be seen at the cell surface (A). Next, they appear in a coated pit (B). Then, the receptors and antibody are seen in multivesicular endosomes (C). Finally, remnants appear in lysosomes (D), the cell's digestive organelles.

"Journey into the Cell" schedule

The university's three-day scientific celebration, "Journey Into the Cell: Celebrating 50 Years of Electron Microscopy and Modern Cell Biology," begins Thurs., Mar. 16. All lectures are in Caspary Auditorium.

Thursday, March 16:

Origins of Modern Cell Biology

2:00 - 3:00 P.M.

"The American Cradle"

George E. Palade, University of California, San Diego

3:00 - 4:00 P.M.

"The Belgian Connection"

Christian de Duve, Rockefeller

4:00 - 5:30 P.M.

Roundtable Discussion:

Christian de Duve

Rollin Hotchkiss, Rockefeller

George E. Palade

Sanford Palay, Harvard Medical School & Boston College

George Pappas, University of Illinois at Chicago

Lee Peachey, University of Pennsylvania

Philip Siekevitz, Rockefeller

Moderator: David Sabatini, NYU School of Medicine

5:30 - 6:30 P.M.

Reception (AARH Lounge)

Friday, March 17

Cell Biology Today

9:30 - 10:30 A.M.

"Mechanisms of Intracellular

Protein Transport"

James Rothman, Memorial-Sloan Kettering Cancer Center

10:30 - 11:30 A.M.

"Nucleocytoplasmic Traffic across the Nuclear Pore Complex"

Günter Blobel, Rockefeller

2:00 - 3:00 P.M.

"Megalin: An Autoimmune Antigen Located in Coated Pits"

Marilyn Farquhar, University of California, San Diego

3:00 - 3:45 P.M.

Tea (AARH Lounge)

3:45 - 4:30 P.M.

"Membrane-Bound SREBP: Sterol Sensor and Transcriptional Regulator" Part I

Michael S. Brown, University of Texas Southwestern Medical Center, Dallas

4:30 - 5:15 P.M.

"Membrane-bound SREBP: Sterol Sensor and Transcriptional Regulator" Part II

Joseph L. Goldstein, University of Texas Southwestern Medical Center, Dallas

Saturday, March 18

Public Lecture

11:00 A.M. - noon

"Inventing the Cell"

Peter Satir, Albert Einstein College of Medicine

Potpourri

Courtesy of the artists



Pomerium will perform at the noon recital today (Mar. 3).

Tri-Institutional Noon Recital
Pomerium, a 15-voice cappella ensemble, will perform the works of Guillaume Du Fay and Nicolas of Clairvaux at the Tri-Institutional Noon Recital today (Mar. 3). The concert, held at noon in Caspary Auditorium, is free. All are welcome.

Conservation society lecture
Norman Myers will give a talk entitled "Save our Biosphere!" at the Centennial Lecture Series of the Wildlife Conservation Society Tues., Mar. 7 at 6:00 P.M. in Caspary. A limited number of complimentary tickets is available to the university community. For information and reservations, contact the Office of Public Affairs, x8967.

Clinical Research Seminar
Lorraine J. Gudas, professor and chairman of the Department of Pharmacology at CUMC, will discuss "The Regulation of Cell Growth and Differentiation by Retinoids" Wed., Mar. 8 at noon in Nurses Residence 110B.

Workshops
Computing Services is offering the following workshops this month:
Introduction to DOS: Thurs., Mar. 9, 10:00 A.M. to noon;
Introduction to Macintosh: Fri., Mar. 10, 2:00 P.M. to 4:00 P.M.;
UNIX for Sequencers I & II: Mon., Mar. 13 and Mon., Mar. 20, 10:00 A.M. to noon;
Word for Macintosh I & II: Wed., Mar. 15 and Wed., Mar. 22, 2:00 P.M. to 4:00 P.M.;
Introduction to Windows: Thurs., Mar. 16, 10:00 A.M. to noon;
World Wide Web Workshop: Fri., Mar. 24, 2:00 P.M. to 4:00 P.M.
Workshops are free, but registration is required. Contact Joan Falciano, x8925, or leave voice mail at x7768.

RU Concert

Leila Josefowicz, violin, will perform at the Rockefeller University Concert Wed., Mar. 15 at 8:00 P.M. in Caspary Auditorium. For

ticket availability and information, contact Cathy Rogers, x8437.

ROCKEFOLLIES

This year's ROCKEFOLLIES will be held Tues., Mar. 21 at 7:00 P.M. in Caspary Auditorium. Tickets (\$5) can be purchased from Peggy Hempstead, x7794 or box 176. Door prizes will be awarded. To donate a door prize, contact Hempstead or Yvonne Holland, x8396.

Alumni honor

Thomas B. Tomasi, who received a Ph.D. from Rockefeller in 1965, received the George F. Koepf, M.D. Award from the Hauptman-Woodward Medical Research Institute in January for contributions to biomedical research. Tomasi is president and C.E.O. of Roswell Park Cancer Institute in Buffalo, New York.

Award

Richard D. Levere, an adjunct faculty member in the Kappas lab, received the Tinsley R. Harrison Award of the Southern Society for Clinical Investigations last month.

Amgen

(continued from page 1)

based on both scientific and financial criteria. When the licensing arrangement is finally approved by the boards of Amgen and the university, and the definitive agreement executed, it will provide a cash payment of \$20 million to the university upon signing; subsequent payments upon the achievement of defined milestones over several years that also could be significant; and royalty payments if ethical, safe, and effective drug products are developed and marketed successfully.

Under university policies, all payments to Rockefeller are shared by the university, H.H.M.I., and the inventors.

Woodstock Inn discount

The Woodstock Inn & Resort in Woodstock, Vermont is offering a discount package to university employees, now through Dec. 21. The package includes: \$95 (plus tax) per room, European plan; upgraded accommodations; reduced fees for golf, tennis, and squash; free use of fitness facilities; and no charge for children 14 and under who room with parents. If you stay at the Inn any weeknight during ski season—except Fri., Dec. 21 to Sun., Dec. 31—ski rentals and lift tickets are free for the Woodstock Resort's alpine area, Suicide Six, or Woodstock Ski Touring Center.

Send your request in writing, identifying yourself as a university employee and giving first and second choices of dates, to: Reservations, The Woodstock Inn & Resort, Fourteen the Green, Woodstock, VT 05091-1298 (fax: 802-457-6699). Reservations are accepted on the availability of space, and close-out dates apply.

Volunteers

The Recreational Therapy Department of the Hospital is looking for volunteers to escort patients to the Friday noon recitals. Contact Eva Sievert, x8474.

Toner cartridge recycling

The Purchasing Department recycles used toner cartridges. Bring empties to Plaza 104.

Diary of a young girl

Security guard Linton Hunter's daughter, Latoya Hunter, whose diary was published in 1992, was recently featured in a book entitled *Our Common Ground: Portraits of Blacks Changing the Face of America*.

Neel

(continued from page 1)

Physicians. He is a member of the National Academy of Sciences, the Academy's Institute of Medicine, and the Royal Society of Medicine.

The Joshua Lederberg Distinguished Lecture was endowed in honor of 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

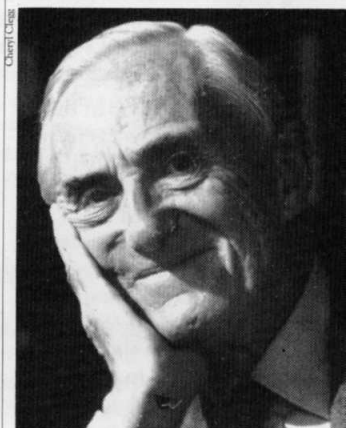
Ahrens to host luncheon for popular author

Historical novelist Patrick O'Brian will be the guest of honor at a luncheon hosted by Professor Emeritus Edward H. Ahrens, Jr., Thurs., Apr. 13.

Ahrens invites fans who wish to meet the author to attend. "Anyone who appreciates his writing is welcome," said Ahrens.

As O'Brian's readers know, his 16 (and counting) books dramatize the Napoleonic Wars by chronicling the adventures of two fictional British seamen, Captain Jack Aubrey and his naturalist friend, Surgeon Stephen Maturin. The popularity of the series is such that the publisher produces a newsletter devoted to it.

The luncheon will take place at noon in Cohn Library. Seating is limited to 15 people, so "please reserve early," Ahrens suggested. He may be reached at x8480.



Historical novelist Patrick O'Brian will be guest of honor at a luncheon at RU Thurs., Apr. 13.

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, serving as scientific counselor to world leaders and heading a number of influential committees and policy studies.

The lecture will be held at 3:45 P.M. in Caspary Auditorium and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Lounge.