

4-26-1996

NEWS AND NOTES 1996, VOL.6, NO.26

The Rockefeller University

Follow this and additional works at: http://digitalcommons.rockefeller.edu/news_and_notes_1996

Recommended Citation

The Rockefeller University, "NEWS AND NOTES 1996, VOL.6, NO.26" (1996). *News And Notes 1996*. Book 11.
http://digitalcommons.rockefeller.edu/news_and_notes_1996/11

This Book is brought to you for free and open access by the The Rockefeller University News and Notes at Digital Commons @ RU. It has been accepted for inclusion in News And Notes 1996 by an authorized administrator of Digital Commons @ RU. For more information, please contact mcsweej@mail.rockefeller.edu.

And the results are . . . Incoming class tallies up at 25

With the Mon., Apr. 15 deadline for notifying the university past, 25 students from institutions in the United States and across the world have accepted the university's invitation to join the Rockefeller graduate program this fall. A total of 50 offers were made, after screening by the admissions committee and visits of candidates to the campus.

"We are very pleased with these results, and we thank all participants in the Open House, whose enthusiasm for the recruitment process contributed immeasurably to our success," said Dean George A.M. Cross.

"We had hoped to attract about 20 students this year, so we are delighted with this strong response from such a promising group of candidates," added Marguerite Mangin, assistant dean.

Eleven of the incoming students are women and ten have done their undergraduate work at schools in other countries.

Evening symposium on campus to address emerging microbial threats

Rockefeller President Emeritus Joshua Lederberg, Assistant Professor Stephen Morse, and Professor Alexander Tomasz are among the speakers at a symposium on "Emerging Microbial Threats: Public Policy Implications" Mon., Apr. 29.

Organized by the metropolitan chapter of the Society for Risk Analysis (SRA), the event is co-sponsored by the New York Academy of Medicine, the Pan American Health Organization, Rockefeller University, and the U.S. Pharmaceuticals Group, Pfizer, Inc.

The three-hour program, which begins at 7:00 P.M., follows:

- "Welcome." Wayne Tusa, president of the metropolitan chapter of SRA, will open the symposium.
- "Explication of the Hazards and Risks." Lederberg, a Nobel laureate who is Raymond and Beverly Sackler Foundation Scholar at RU, will speak on "Newly Emerging Viruses." Tomasz, who heads the university's Laboratory of Microbiology, will discuss "Emerging Microbial Drug Resistance."
- "Waiting for the Next Out-

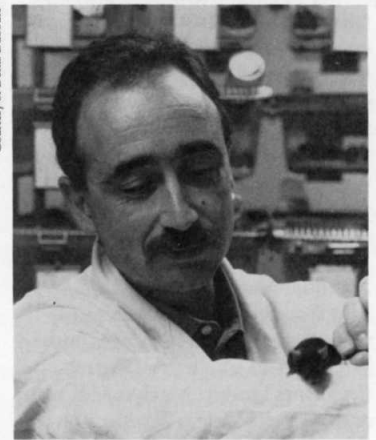
break: Will We Have a Stitch in Time?" will be the theme of a talk by Laurie Garrett, Pulitzer-Prize winning author of *The Coming Plague: Newly Emerging Diseases in a World Out of Balance* and science and health writer at *Newsday*.

- "Timely Management of the Risks: What We Need and What It Will Cost." Morse, a member of the Lederberg lab, will discuss this issue on the international level. Mitchell L. Cohen, director, Division of Bacterial and Mycotic Diseases, Centers for Disease Control and Prevention, will discuss the national level, and Marcelle C. Layton, assistant commissioner, Bureau of Communicable Diseases, New York City Department of Health, will discuss the local level.

- "Summation by the Program Chair." Miriam de Saegui, councilor of the SRA metropolitan chapter, will give concluding remarks.

All are welcome to attend the symposium, which takes place in Caspary Auditorium, though public interest in the topic may limit seating.

Science on a limb Embryologist discusses genetic control of limb formation



At the University of Geneva, members of the lab of Denis Duboule are also working to understand how fins evolved into limbs.

Denis Duboule, professor of embryology at the University of Geneva, will discuss "Genetic Control of Vertebrate Limb Development and Evolution" at the Friday lecture today (Apr. 26).

Duboule studies the genetic control of pattern formation and morphogenesis in vertebrate systems, including development of limbs and the central nervous system. He and his colleagues focus on the role of the Hox family of genes in limb development in tetrapods, or four-footed animals, and the molecular genetics and biochemistry of developmentally regulated transcription factors. Work is also under way in his laboratory to understand the evolution from fins to limbs in tetrapods.

"The clusters of Hox genes represent one of the universal patterning systems in the animal kingdom and one of the most fascinating problems in developmental biology. Denis has been the one to recognize that the colinearity between the domains of expression of the Hox genes along the antero-posterior axis of the embryo and their position in the cluster (the spatial co-linearity as defined by Ed Lewis for the UBX complex in *Drosophila*) was a conserved feature in the four vertebrate Hox clusters," said

See Duboule, page 4

Lab contracts with biotech company to stymie *S. pneumoniae*

In a collaboration to develop therapies for the prevention and treatment of *Streptococcus pneumoniae* infections involving Elaine Tuomanen, head of the Laboratory of Molecular Infectious Disease, and Robert Masure, assistant professor in the lab, the university has signed a contract with the biotechnology company MedImmune, Inc.

The lab will provide genes,

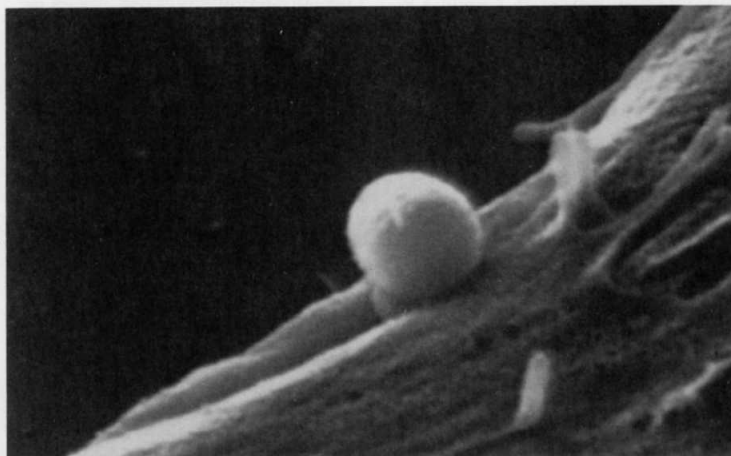
assays, and animal models to the Gaithersburg, Md., company, which will supply the lab with the *S. pneumoniae* genome sequence and will develop products.

"The availability of bacterial genome sequences is an untapped resource. No one has yet taken a

genome and used it in this type of accelerated process, in part because there hasn't been a good match between understanding a disease and knowledge of the genome of its pathogen," said Tuomanen. "This

See Tuomanen, page 2

M. Floryszak, K. McDonough, and Elaine Tuomanen



An *S. pneumoniae* bacterium besieges a human lung cell. The Tuomanen lab's collaboration with MedImmune will seek new therapies to thwart the pathogen.

2 TB conference

3 Genes, neurons,
and devastation

4 For francophiles

Hospital pays tribute to nursing Honors memory of Elizabeth Straight

Patricia Grady, director of the National Institute of Nursing Research (NINR), the newest of the National Institutes of Health, will speak on "The Integration of Bench Science and Clinical Science in Nursing Research," Wed., May 1 as part of a Rockefeller University Hospital program entitled "A Tribute to Nursing."

"Dr. Grady will discuss the contribution of her institute to the scientific basis for nursing care and to the quality of health care," said chief nursing officer Tara Cortes, who will introduce Grady. "We are pleased that she will join our tribute, which celebrates the vital role of nursing in advancing patient-oriented research at the Hospital."

The program, which anticipates National Nurses Week (Mon., May 6 to Sun., May 12), begins with presentations by Cortes and Physician-in-Chief Jules Hirsch. Professors Emeriti Maclyn McCarty and Vincent Dole will reflect on the contributions of RU nurses to

their research programs. Hospital staff will also commemorate the late Elizabeth Straight who worked at the Hospital for 30 years and served as director of nursing from 1977 to 1990.

Grady earned a master's degree in nursing and a doctoral degree in physiology from the University of Maryland. After a postdoc in neuropathology, she joined the faculty of the University of Maryland School of Medicine. She then served at the National Institute of Neurological Disorders and Stroke, where she was an extramural program administrator in the Division of Stroke and Trauma, deputy director of the institute, and, for an extended period, acting director. She was appointed director of the NINR in 1995.

Among other awards and honors, Grady received the Superior Service Award from the U.S. Public Health Service.

The program, to which all are welcome, starts in Caspary

Courtesy of Patricia Grady



The National Institute of Nursing Research, the new NIH branch, promotes science that strengthens nursing practice and improves health care. Its director, Patricia A. Grady, will lecture Wed., May 1 at the Hospital's tribute to nursing.

Auditorium at 3:00 P.M. Grady lectures at 4:00 P.M., and a reception follows in Nurses Residence 110B.

Young researchers to present findings at local meeting on tuberculosis

The first annual New York TB meeting, entitled "Recent Progress in the Study of Mycobacteria" and featuring short presentations by more than 25 junior researchers from labs throughout the metropolitan region and New Jersey, will take place at RU Sat., Apr. 27.

"Presenters will highlight the latest developments in TB research, covering the field from molecular biology to clinical studies," said Associate Professor Gilla Kaplan, who organized the meeting with Professor Issar Smith of the Public Health Research Institute. "We expect more than 90 scientists in mycobacterial research to attend. This intense research effort is the outcome of the recent concentrated focus of the NIH on expanding study of tuberculosis."

The program schedule follows:

- "Genetics and Physiology of Mycobacteria, Part I," 9:00 A.M. to 10:30 A.M.;
- "Genetics and Physiology of Mycobacteria, Part II," 11:00 A.M. to 12:30 P.M.;
- "Interactions between Pathogenic Mycobacteria and Macrophages," 1:30 P.M. to 3:15 P.M.;
- "Clinical and Diagnostic Aspects of Tuberculosis," 3:45 P.M. to 5:15 P.M.

Lectures, free and open to all, take place in Weiss 301 from 9:00 A.M. to 6:00 P.M. For more information or for lunch or cocktail and dinner reservations, contact Marguerite Nulty before 5:00 P.M. today (Apr. 26), x7763.

News&Notes is published each Friday throughout the academic year by The Rockefeller University, 1230 York Avenue, New York, NY 10021. Phone: 212-327-8967.

Torsten Wiesel, President
Ingrid Reed,

Vice President for Public Affairs and Corporate Secretary
Marion E. Glick, Director of Communications

Kay Locitzer, Editor
Joseph Bonner, Associate Editor
Robert Reichert, Photography
Media Resource Service Center, Processing

Ideas and submissions can be sent interoffice (Box 68), by electronic mail (newsno), or by fax (212-327-7876).

The Rockefeller University is an equal opportunity/affirmative action employer.

Tuomanen lab to identify gene candidates for vaccines

(continued from page 1)

collaboration will be a good demonstration of the utility of sequencing. And we're getting the chance to apply all of the recent insights in the field of microbial pathogenesis to the design of therapeutics."

Lab members will identify and give to MedImmune genes responsible for the pathogenic proteins of *S. pneumoniae* as well as the lab's patented assays and animal models for exploring them. Lab researchers led by Masure have created several libraries of mutants—including one with knockouts in individual genes—across the entire chromosome. So far, they have identified more than two dozen genes responsible for making some of the bacterium's surface proteins known to contribute to the disease.

"Obviously, we want to use the protein with the greatest effect on virulence as the antigen to stimulate an immune response," said Tuomanen. "Theoretically, you can develop a treatment with just one protein."

Finding that one will be the job of MedImmune, which will test, develop, and conduct clinical trials of vaccines. Another MedImmune collaborator, Human Genome Sciences Inc., is completing the DNA sequence of *S. pneumoniae*.

"Sequencing is time consuming and expensive. They have a warehouse of machines to do this," said

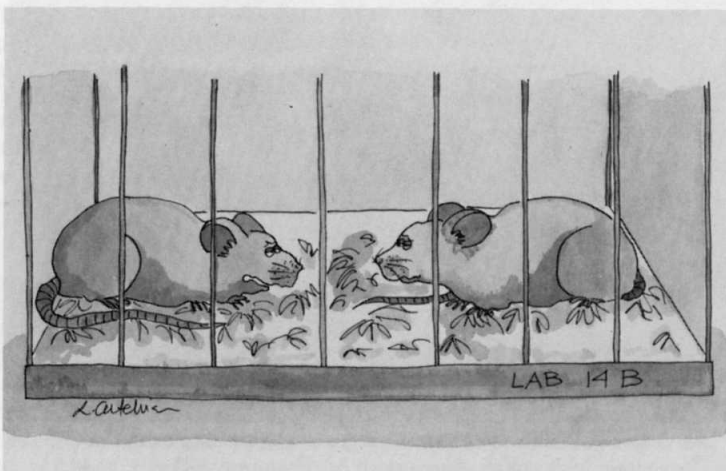
Tuomanen. "We'll use the book of *S. pneumoniae* sequences to look for and knock out the genes more effectively."

"Within the next few years, the gene sequences of many serious pathogens will be known. People will not be doing microbial pathogenesis without knowing them. That's really exciting," she added.

In the United States each year, *S. pneumoniae* causes 40,000 deaths, 3,000 cases of meningitis, 500,000 cases of pneumonia, 50,000 cases of septicemia, and 7 million middle-ear infections. Strains of the bacteria are increasingly resistant to traditional antibiotics.

The university granted MedImmune an exclusive license to commercialize products based on certain patented technologies or arising from the lab's research sponsored by MedImmune in return for license fees, milestone payments, and royalties. MedImmune focuses on products for the prevention and treatment of infectious diseases and for use in transplantation. The agreement also extends to similar work on the *Staphylococcus aureus* genome, the complete sequence of which the biotech company announced several weeks ago, and on other pathogens sequenced by Human Genome Science, Inc.

Leslie Atchison



"It's not a bad life, but it's impossible to get medical insurance."

Four researchers relate tales of genes, neurons, and disease at symposium

by Jahanara Ali

The third annual deCamp Symposium on the Neurosciences, which took place Tues., Apr. 2, featured four leaders in the field of degenerative disorders of the nervous system. The researchers highlighted the role of individual genes in complex neurological disorders with severe and varied clinical disease processes.

The first speaker, Donald Price, professor of neuroscience, neurology, and pathology at The Johns Hopkins University School of Medicine, and director of the neuropathology laboratory at The Johns Hopkins Hospital, focused on animal models for two serious neurodegenerative diseases, amyotrophic lateral sclerosis (ALS) and Alzheimer's disease.

Toxic mutations

"In both disorders, risk factors affect the same vulnerable subset of cells, the neurons," said Price. "The neurons start to dysfunction and die, which leads to clinical syndrome, including weakness and atrophy. In motor neuron disease, when the neurons die, the individual becomes paralyzed, and eventually, so many cells die that the patient dies."

Price and his colleagues have found that animals with mutations in the gene encoding the SOD-1 protein, a vital enzyme converting oxygen and hydrogen into hydrogen peroxide, provide the best model for autosomal dominant form of familial ALS. The critical mutation, replacing a glycine residue with arginine, produced mice with a motor neuron disease most similar to ALS. "These mice are normal at birth, but soon develop muscle weakness, and eventually become virtually immobile," Price said.

His lab developed transgenic mice expressing varying levels of mutant SOD-1 and found a striking correlation between the amount of the transgene product and the onset of the disease. The disease strikes earlier and with greater severity when higher amounts of protein are expressed. Furthermore, the mice producing the unmutated version of SOD-1 did not get the disease.

Price's next question is the mechanism whereby the mutant SOD renders what he calls its toxic property. "One possibility is that the mutant SOD is effective at nitration of the tyrosine residues on proteins, and one of its targets could be the neurofilaments," he hypothesized. "Alternatively, mutant SOD may act as a peroxidase, using



Speakers at the third annual deCamp Symposium on the Neurosciences were, left to right: James Gusella, Stanley Prusiner, Donald Price, and Yosef Shiloh.

hydrogen peroxide produced by the normal SOD to oxidize and damage a variety of substrates." There is evidence for both theories, concluded Price.

Expansion brings trouble

The fatal Huntington's disease (HD), which affects one in 10,000 persons, manifests its first symptoms—subtle movement disorders—in midlife. "Eventually, the individual is locked within his body," stated James Gusella, Bullard professor of neurogenetics at Harvard Medical School and director of the Molecular Neurogenetics Unit at Massachusetts General Hospital. Gusella pioneered the use of DNA polymorphisms in families to track down the chromosomal location of the human gene responsible for HD.

Studying Venezuelan families with a high incidence of HD, he and his colleagues honed in on the gene. The length of its protein product varied drastically, and they soon learned why.

"There seems to be a single defect in the coding region of the HD gene, an expansion of the three nucleotides CAG, which appears to be the source of this disease," said Gusella. In HD patients, this sequence is repeated well over 35 times, becoming longer as the gene passes from generation to generation.

Gusella and colleagues found that when a father transmits the gene, the expansion can be very large, whereas when a mother passes the gene, repeat-size changes occur infrequently. "Childhood onset is almost always correlated with paternal transmission, since age of onset is inversely proportional to repeat expansion," Gusella said.

Based on this and other evidence, Gusella concluded, "HD pathology is most likely caused by this mutat-

ed protein, which in turn produces a devastating gain in function, similar to the gain of toxic property that Price described for the ALS gene." Gusella also noted that expansion of a trinucleotide repeat has been observed for a growing number of disorders in humans, including Fragile X Syndrome and Myotonic Dystrophy.

Repair gene may do more harm than good

Yosef Shiloh, associate professor of human genetics at the Sackler School of Medicine, Tel Aviv University, studies ataxia telangiectasia (AT), a rare and usually fatal disease of the nervous system, associated with truncated limbs, premature aging, immunodeficiency, and predisposition to cancer.

Shiloh and his colleagues originally attempted to isolate the AT gene by using its phenotypic radiosensitivity. They transferred genomic DNA into AT cells and isolated cells that had lost the radiosensitivity (presumably by successfully incorporating the normal AT allele). However, as Shiloh put it, "too many genes volunteered for the same job."

The scientists decided to pursue positional cloning on chromosome 11, where they mapped the locus for AT. Eventually, they isolated a large gene encoding a 350-kD protein. One end of the gene seemed to be similar to PI-3 kinase, a signal transduction molecule. They also found that in the AT patients, this gene is one third the size of its normal counterpart.

Shiloh hypothesized that the AT gene product may resemble DNA repair enzymes and play a role in the predisposition to cancer. He suggested that "AT may be a signal transduction protein that senses

DNA damage, and its job may be to recruit DNA repair enzymes to the site of damage."

Tangled up in filaments

Stanley Prusiner, professor of neurology, biochemistry, and biophysics at the University of California, San Francisco, who recently received a Lasker award, gave a timely talk on prions, the infectious agent in a number of fatal neurodegenerative diseases, including scrapie, bovine spongiform encephalitis (mad cow disease), Creutzfeldt-Jakob disease, and Kuru.

Prions defy the traditional definition of infectious agents because they cannot replicate. Prusiner defines them as proteinaceous infectious particles that resist inactivation by procedures that modify nucleic acids.

Prusiner and his colleagues identified a small gene, consisting of a single open reading frame, that encodes a prionlike protein in cells of all individuals. The function of this protein is not known.

"The central question in this field is what is the difference between this cellular prion protein [PrP^C] and the scrapie causing prion protein [PrP^{Sc}]," Prusiner said. Insight into this question came from some spectroscopy studies, showing that the normal cellular Prp is post-translationally folded into a structure called alpha helix, whereas PrP^{Sc} is folded into beta sheets. "The beta sheet content probably allows PrP^{Sc} to polymerize under limited proteolytic conditions, and form amyloid filaments, the canonical features of scrapie," theorized Prusiner.

Discussing Prusiner's work, symposium organizer Professor Mary Beth Hatten told the audience, "I promised that today you would hear about studies of the degeneration of the nervous system that lead us to novel insights into basic cell and molecular mechanisms. Dr. Prusiner illustrates this point."

In discussing the conference after it ended, Hatten said, "The neurological diseases highlighted in the symposium are not necessarily humanity's most prevalent diseases. But what emerged from the afternoon was a hint that like mechanisms may underlie a slew of disorders, each affecting small groups of individuals. For example, the trinucleotide repeat appears to be a feature of several diseases as well as Huntington's. It's very possible that we will see a similarity in genetic mechanisms that go awry in many complex, unrelated disorders."

Potpourri

Henry Grossman



The Arcata String Quartet will perform at the Tri-Institutional Noon Recital today (Apr. 26). The concert, to be held in Caspary Auditorium at noon, is free. All are welcome.

Friday film

Vertigo (USA, 1958), directed by Alfred Hitchcock, starring James Stewart and Kim Novak, will be shown today (Apr. 26) at 8:00 P.M. in Caspary. Admission is free.

Clinical Research Seminar

Stanley E. Read, chief of the Division of Infectious Diseases, University of Toronto, and professor of pediatrics at the Hospital for Sick Children, Toronto, will discuss "Transmission of HIV from Mothers to Babies" at noon on Wed., May 1 in the Nurses Residence, 110B.

Primateology films

Films in the area of primatology will be shown Wed., May 1 and Thurs., May 2 from 11:00 A.M. to 3:00 P.M. in RRB, 110. For more information, contact Charles Weisbard, e-mail weisbac.

mation, contact Charles Weisbard, e-mail weisbac.

French food

Abby Aldrich Rockefeller Dining Room will serve French cuisine on Wed., May 1. For more information, call Alzatta Fogg, x8894.

Residents' meeting

The tenants' association of Faculty House and Scholars Residence will discuss the tenants survey and building improvements Wed., May 1 at 7:00 P.M. in Scholars Residence, 38th floor. For more information, call Jonathan Smith, x7210.

Lecture on allergies

David McConnell, clinical professor of medicine at Columbia University College of Physicians and Surgeons, will talk on "Wheezes, Sneezes, and

Springtime Breezes: Managing Your Allergies" at the Sound Mind/Sound Body lecture Thurs., May 2 at noon in Nurses Residence, 110B. All are invited to come and bring lunch.

Henry Kunkel Lecture

Jeffrey Ravetch, professor, Sloan-Kettering Institute, will lecture on "FC Receptors: Activators and Inhibitors of Inflammation" in Caspary Auditorium, Thurs., May 2 at 6:00 P.M. Ravetch will join Rockefeller as a professor in September. All are welcome.

Glycoconjugates symposium

Hunter College, CUNY, will hold its 10th Annual Symposium on "Glycoconjugates: Cellular Messengers and Mediators" Fri., May 3 from 9:00 A.M. to 5:30 P.M. at Hunter College, East 68th St. at Lexington Ave., in West Bldg., #714. Registration is not required and admission is free. For more information, call 772-5532.

Flower festival

The university's Annual Azalea Festival takes place Sat., May 4 and Sun., May 5 from noon to 4:00 P.M., presented in cooperation with the New York Botanical Garden. Tours take place at 1:00 P.M. and

Computing Services Workshops

Spaces are available in the following workshops. To register, leave voice mail at x7768. You will be called to confirm registration.

Word for the Mac, Part III:

Tues., May 7, 10:00 A.M. to noon;

Word for Windows, Part II:

Thurs., May 9, 10:00 A.M. to noon;

Eudora for Mac and Windows:

Tues., May 14, 10:00 A.M. to noon;

Eudora for Mac and Windows:

Thurs., May 16, 10:00 A.M. to noon.

In memoriam

The university community mourns the passing of Ann Quatela, former executive secretary, who died Sun., Apr. 21 after a long struggle with cancer.

Quatela joined the university in 1968 as a junior secretary. After working with Robert Leader and Atallah Kappas, in 1977 she was recruited to the President's Office, where she served four university leaders—Frederick Seitz, Joshua Lederberg, David Baltimore, and Torsten Wiesel.

"Ann was a wonderfully dedicated person and very much part of the life of the university," said Seitz. "We will all remember her sitting near the door of the President's Office, always cheerfully greeting everyone who entered. We treasure her memory, and she will be very much missed."

Quatela is survived by her mother and two brothers. The family requests those wishing to honor her memory to make donations to St. Teresa's School, 1394 Pleasantville Road, Briarcliff Manor, NY 10510.

3:15 P.M. on both days and public lectures at 2:15 P.M. David Lentz, director of the Graduate Studies Program at The New York Botanical Garden, will speak on "House Gardens of the Ancient Maya" Saturday, and Firdaus Dhabhar, RU graduate fellow, will discuss "The Good News About Stress" Sunday. To volunteer, call Gabrielle Riera, x8969. For information, call 327-8967.

RU concert

The Guarneri String Quartet will again end the Rockefeller University Concerts season with its 33rd appearance on Wed., May 8 at 8:00 P.M., performing this year in memory of Margaret Rockefeller. The concert is sold out.

Duboule

(continued from page 1)

Associate Professor Claude Desplan, who introduces Duboule today. "Furthermore, Denis has generalized this notion to other axes in the embryo (e.g., in the limbs) and has proposed a powerful model of 'temporal colinearity' to explain the clustering. This model links the timing of development to the successive opening of chromatin domains in the Hox cluster. Recently, through elegant manipulations of the mouse genome, his laboratory has brought strong support to this model."

Duboule received his doctorate from the University of Geneva in 1984. From 1984 to 1988 he was a member of Pierre Chambon's laboratory at the University of Strasbourg. In 1988 he became a group leader at the European Molecular Biology Laboratory in Heidelberg, where he worked on the molecular genetics of vertebrate development. In 1992 he joined the University of

Geneva as professor of biology. Duboule is vice president of the Biology Section of the Faculty of Sciences and director of the Laboratory of Molecular Embryology and Morphogenesis.

Duboule received the 1994 National Latsis Prize, an award given every three years by the Swiss national research foundation (analogous to the U.S. National Institutes of Health) to a Swiss biologist younger than 40. He serves on various review committees and editorial boards and is an elected member of the European Molecular Biology Organization. He is author or co-author of more than 70 publications and editor of the book *A Guidebook to Homeobox Genes*.

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. All are welcome.

Joseph Bannier



A Nicolson and Galloway work crew installs a metal lining in the fountain outside the Faculty and Students Club. Weather permitting, all six concrete pools in the Caspary Dome quadrant of the campus will receive the waterproof and weatherproof lining by June.